HB

277

file 1

STATE OF ALASKA
THE LEGISLATURE

POUCH Y - STATE CAPITOL
JUNEAU, ALASKA 99811
907-465-3800

LEGISLATIVE AFFAIRS AGENCY

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May, 1988

Copies of minutes listed below were originally included in this file. The minutes are available on the STA 3 database CMPR. In order to save space copies of minutes have not been left in the files.

Mary Van Nimwegen

House Hess:

February 11, 1988

March 10, 1988

April 21, 1988

My Name is Ellen Ramlett
Member of Alaska Dissatisfied Parents Together
& a health
I'm A parent, A
concious person. I think
House Bill 277 should be
passed.
I challenge you to vote
based on fact, not fear.
By fear I mean that some
groups fear that ALASKANS
WON'T VACCINATE their children,
given A choice. You have
heard testimony that
many children HAVE been harmed
by VACCINATIONS, Parents know their
able to make an informed choice for their children
children best & should be
The CONCLUSION that AK
immunization program has
prevented disease is
false.

I think the MAIN REASON
I feel so STRONGLY About
Choice in ANY mandatory
giving of medicine is that
I'm 32 years old &
I myself was drugged
most of my childhood.
In the last 10 years I've
learned A lot About myself
AND gained A lot of my health
back thru NATURAL methods.
I'm sure I was VACCINATED
fully. My mother told me. I had
measles AS AN INFANT. I had
ASTHMA age 2 thru 12, IN
retrospect I think I would have
been better off without the
VACCINATIONS given that my
CONSTITUTION was ready to begin
living. Had my parents been
informed they may have chosen NOT to VACCINATE

Giving A child A VACCination does NOT make sure they won't get that disease. I got measles after being VACCINATED for them. I have heard of other children who got mumps after being VACCINATED for them while their UNVACCINATED sibling remained well.

ONE MAN kept saying why take A chance? Parents need TO know that they are taking A chance when they choose TO VACCINATE. And in my opinion A child's immune system can better able to resist disease W/O VACCINATIONS.

If all Dr.s were held accountable for the effects of VACCINATIONS ON their patients there would be

If you believe the immunizations work why are you afraid of my child not being immunized?

I believe it is my right and responsibility as a parent to ~~learn~~ be educated on the effects of immunizations. It is on the ~~education~~ basis of learning that I can make the decision for my child.

I might also state that I have 2 sons. My older son was immunized for mumps. He had them twice once on each side

My youngest son was exposed to the mumps and ~~has~~ did not come down with the mumps.

Connie Conaway
Anchorage

ATTACHMENT II



REFUSAL OF IMMUNIZATION

As the parent/guardian of _____

Name Age Birthdate

_____

School Grade

I do not wish to have my child receive the following immunizations:

(Check Disease)

Rubeola (Measles) . . . . . ☐

Rubella (German Measles). . . . . ☐

Mumps . . . . . ☐

Poliomyelitis . . . . . ☐

Diphtheria. . . . . ☐

Tetanus (Lockjaw) . . . . . ☐

Pertussis (Whooping Cough). . . . . ☐

Comments . . . . . .

. . . . . .

_____

Signature of Parent/Guardian Date

Nebraska

LEGISLATIVE BILL 59

Approved by the Governor April 20, 1979

Introduced by Koch, 12

AN ACT to amend Sections 79-404 and 79-440.01, Reissue Revised Statutes of Nebraska, 1943, relating to schools; to require examination and immunization of certain students as prescribed; to provide exceptions; to provide procedures; and to repeal the original sections.

Be it enacted by the people of the State of Nebraska,

Section 1. That section 79-404, Reissue Revised Statutes of Nebraska, 1943, be amended to read as follows:

79-404. (1) The district board or the board of education, in all classes of school districts, shall not admit any child to the first grade of any school of such district unless such child has reached the age of six years or will reach such age on or before October 15 of the current year; Provided, that in the event any child has successfully completed the kindergarten or beginner grade such child may enter the first grade of any such school regardless of age.

(2) The board in all classes of school districts shall not admit any child into the kindergarten or beginner grade of any school of such school district unless (a) such child has reached the age of five years or will reach such age on or before October 15 of the current year or (b) such child has demonstrated through recognized testing procedures approved by the State Board of Education that he is capable of carrying the work of those grades.

(3) The school board or board of education may require a birth certificate prior to entrance of a child into the beginner grade and shall require evidence of a physical examination by a qualified physician and ~~such immunization as required by the board~~ within six months prior to the entrance of a child into the beginner grade and the seventh grade, or in the case of a transfer from out-of-state to any other grade of the local school; Provided, no such physical examination or ~~immunization~~ shall be required of any child whose parent or guardian shall object thereto in writing, ~~on the grounds that such physical examination or immunization is contrary to the religious tenets of an established church of which he is a member or adherent~~. The cost of such physical

examination shall be borne by the parent or guardian of each child who is examined.

This section shall not be construed to prohibit any district board or board of education in its discretion, from establishing and supporting financially, programs to which attendance shall be voluntary which they deem beneficial to the education of prekindergarten children, nor shall this section be construed to allow any school district to fail to meet its responsibilities under Chapter 43, article 6.

Sec. 2. That section 79-444.01, Reissue Revised Statutes of Nebraska, 1943, be amended to read as follows:

79-444.01. Each board of education and the governing authority of each private school in this state shall require each child--under--twelve--years--of--age student to be protected against measles, mumps, rubella, poliomyelitis, diphtheria, pertussis, and tetanus by immunization before-being-permitted-to-attend-any--school under-its-jurisdiction, prior to November 1 of each school year for original enrollees or, in the case of a student transferring from another school, within sixty days after the enrollment date, unless a parent or guardian of such child student presents a written statement that he or she does not wish to have such child student so immunized. In-the-case-of-any-child--enrolled in-school-on-September-2,-1973,-the-immunization-required by-sections-79-444.04-and-79-444.02-shall-be-effected--no later-than-September-1,--1973. Such written statement shall be kept in the student's file. Any student who does not comply with this section shall not be permitted to continue in school until he or she shall so comply.

The cost of such immunization shall be borne by the parent or guardian of each child student who is immunized; Provided, that such cost shall be borne by the Department of Health for those children students whose parents or guardian are financially unable to meet such cost, for such service, to-the--extent--that--funds--are specifically-available-for-such-purposes.

Sec. 3. The Department of Health shall adopt and promulgate rules and regulations relating to the required levels of protection, the evidence necessary to prove that the required examination or immunization has been received, and the reporting of each student's immunization status. The Department of Health shall furnish local school authorities with copies of such rules and regulations and any other material which will assist in the carrying out of this act.

Sec. 4. At the time the parent or guardian of any child is notified that such child must have a physical examination pursuant to section 79-444, or immunizations pursuant to section 79-444.01, he or she shall also be notified in writing of his or her right to submit a written statement refusing a physical examination or immunization for his or her child.

Sec. 5. Any person violating the provisions of this act shall be guilty of a Class V misdemeanor.

Sec. 6. That original sections 79-444 and 79-444.01, Reissue Revised Statutes of Nebraska, 1943, are repealed.

DPT MODEL STATE VACCINE REFORM LEGISLATION
(November 1984)

I. Introduction

In May 1984, Maryland became the first state in the Nation to enact vaccine reform legislation, which had been supported by Dissatisfied Parents Together (DPT). The attached article from the October 1984 edition of State Legislatures Magazine, entitled "Maryland Controls Vaccine", describes the background and provisions of the new Maryland law.

Briefly stated, the primary goals of the Maryland law were:

(1) Parent Information: to mandate that parents be given written information on the risks, as well as the benefits, of vaccines before children are vaccinated (including identification of possible severe reactions, contraindications to the vaccines, reasons for delaying vaccination, etc.);

(2) Record Keeping and Reporting: to require doctors and clinics to record and report serious vaccine reactions to health authorities, and to keep records on vaccine manufacturer and lot number for each shot given;

(3) Follow-Up: to require state health departments to compile information on serious reactions, to send that information to the federal Health and Human Services Department and to the State legislature, and to follow-up on the long term effects to children who suffer vaccine reactions;

(4) Greater Doctor Discretion: to make clear the general vaccine contraindications, i.e. the circumstances under which vaccine should not be given to a child, or should be delayed, and to give doctors discretion to decide on a case-by-case basis when the vaccine should not be given to a specific child; and

(5) Making School Entry Requirements Consistent with These Changes: to assure that children with medical exemptions cannot be excluded from school or punished in any other way.

Since enactment of the new Maryland law, Dissatisfied Parents Together (DPT) has received numerous inquiries and letters about the new law. State chapters of DPT, State legislators, and other interested persons have contacted DPT and asked, "How can we get the vaccine laws in our state changed?"

In order to respond to this question, Dissatisfied Parents Together (DPT) has put together this paper on Model State Vaccine Reform Legislation.

DPT recognizes that the laws and politics of each state are different. Thus, the model bill presented here is intended only as a guide; the model will have to be adapted to the particular form of the laws in each state and to the particular conditions existing in each state. Nonetheless, it is hoped that the model bill language will be a useful starting point for parents and State legislators who are considering State vaccine-reform legislation.

This paper begins by setting forth the exact language of the new Maryland vaccine reform law in Part II. (The numbers along the left side of the law are included to enable the reader to see where the Maryland law's approach might be amended to deal with other concerns and issues. See Parts III and IV of this paper for further discussion of these other issues and concerns.

The Maryland law deals primarily with the pertussis (whooping cough) or "P" part of the DPT vaccine. Part III of this paper identifies how the model presented by the Maryland law could be changed to apply to all man dated vaccines.

The Maryland law gives physicians greater discretion to make case-by-case judgments as to which children should not receive the vaccine. It did not address the question of whether (and under what circumstances) parents should be permitted by law to object to their children's vaccination. As of December 1983, twenty-two states permitted parents to object to mandated vaccines on the basis of "personal conviction or philosophic objection." Part IV of this paper identifies how the model presented by the Maryland law could be changed to assure a parent's right to object to vaccination on personal, philosophic, or other grounds.

Dissatisfied Parents Together (DPT), as a national organization, neither recommends, nor opposes the language contained in Parts III and IV of this paper. Whether any of these changes or additions should be made is a matter for state-by-state determination. The language that is provided is offered simply as an option that state chapters of DPT and state legislators may consider. In deciding whether to pursue any of these options state chapters of DPT should take into account the pre-existing law in each state, the political feasibility of various changes in each state, the administrative requirements in each state, and the status of infectious disease control in the state.

Finally, Part V of this paper is a copy of the testimony given by DPT President, Jeff Schwartz, in support of the Maryland legislation. This testimony is presented not only to explain the bases for DPT's support of the bill, it is also presented as a possible model for other parents to present their testimony in their states, talking about their particular experiences and difficulties.

Finally, if any state legislator or DPT state chapter wishes to get further information or advice, please call DPT National Headquarters at (703) 938-DPT3 and we will respond as soon as we are able.

II. The Maryland Law: A Base Model

The following legislation was enacted by the General Assembly of the State of Maryland and signed into law by the Governor on May 29, 1984:

AN ACT concerning

State Mandated Immunizations - Pertussis

FOR the purpose of defining certain terms; providing for the development and dissemination of information concerning pertussis and the pertussis vaccine; requiring parents to be informed about State mandated immunizations including the risk of pertussis and pertussis vaccines; requiring record keeping and reporting by health care providers and the collection of data by the Department of Health and Mental Hygiene with respect to pertussis and major adverse reactions to pertussis vaccines; requiring the Department to issue certain guidelines; establishing criteria under which pertussis vaccines should not be administered; and generally relating to pertussis and the administration of pertussis vaccines.

BY adding to

Article - Health - General
Section 4-204(c); and 18-328 to be under the new part 19 "Part V. Pertussis"
Annotated Code of Maryland
(1982 Volume and 1983 Supplement)

BY adding to

Article - Education
Section 7-402(a)(3)
Annotated Code of Maryland
(1978 Volume and 1983 Supplement)

SECTION 1. BE IT ENACTED BY THE GENERAL ASSEMBLY OF MARYLAND, That the Laws of Maryland read as follows:

Article - Health - General

4-204

(c) Whenever a resident birth occurs, the Secretary shall promptly provide parents of the newborn child with information on immunizations mandated by this state or required for admission to a public school in this state.

PART V. PERTUSSIS

18-328

(A) in Part V. of this Subtitle, the following words have the meanings indicated.

(B) "Health Care Provider" means any licensed health care professional, organization, or institution, whether public or private, under whose authority pertussis vaccine is administered.

(C) "Pertussis Vaccine" means any vaccine that contains materials intended to prevent the occurrence of pertussis, whether or not the materials are administered separately or in conjunction with other materials intended to prevent the occurrence of other diseases.

(D) "Major Adverse Reaction: means:

(1) Any serious illness, disability, or impairment of mental, emotional, behavioral, or physical functioning or development, the first manifestation of which appears within 7 days after the date of administration of pertussis vaccine and for which there is reasonable scientific or medical evidence that pertussis vaccine causes, or significantly contributes to, such effect; and

(2) Any other reaction, which the Department, after consultation with the medical and Chirurgical faculty of Maryland, determines by guideline is a basis for not continuing with pertussis vaccine administration.

18-329

(A)(1) Prior to the administration of pertussis vaccine, the health care provider shall provide to the individual's parent or guardian written information satisfying the requirement of this subsection, and appropriate inquiries attempt to elicit the information necessary to make the determinations required by § 18-332(B) of this subtitle.

(2) the information required under § 4-204(C) of this article, as to pertussis vaccine, and under paragraph (1) of this subsection shall include:

(I) the frequency, severity, and potential long-term effects of pertussis;

(II) possible adverse reactions to pertussis vaccine which, if they occur, should be brought to the immediate attention of the health care provider;

(III) a form listing symptoms to be monitored and containing places where information can be recorded to assist in reporting to the health care provider, local health officer, and the Department;

(IV) measures parents should take to reduce the risk of, or to respond to, any major adverse reaction;

(V) early warning signs or symptoms to which parents should be alert as possible precursors to a major adverse reaction;

(VI) when and to whom parents should report any major adverse reaction;

(VII) a summary of the immunization requirements adopted under § 7-402(A) of the Education Article -- including those related to pertussis vaccine; and

(VIII) the information required under Section 18-322(A)(1) through (3) of this subtitle.

(B) The Department by guideline and consistent with § 18-331(B) of this subtitle shall prescribe the form and content of the information provided to parents in accordance with this section.

18-330

(A) At the time of administration of pertussis vaccine to an individual, the health care provider shall record in a permanent record to which the patient or the patient's guardian shall have access on request:

(1) the date of each vaccination;

(2) the manufacturer and lot number of the vaccine used for each;

(3) any other identifying information on the vaccine used; and

(4) the name and title of the health care provider.

(B) Within 24 hours any health care provider who has administered pertussis vaccine to an individual and has reason to believe that the individual has had a major adverse reaction of the vaccine shall:

(1) record all relevant information in the individual's permanent medical record; and

(2) report the information, including the manufacturer's name and lot number to the local health officer who shall immediately forward the information to the Department. On receipt of the information, the Department shall immediately notify the vaccine manufacturer.

18-331

(A) By guideline, the Department shall establish a system, sufficient for the purposes of subsections (B) and (C) of this section, to collect data from the local health officers, from public and private health care providers, and from parents on the incidence of pertussis and major adverse reactions to pertussis vaccine.

(B) On the basis of information collected under this subsection and of other information available, the Department shall periodically revise and update the information required by § 18-329 and the guidelines adopted under § 18-332 of this subtitle.

(C) (1) The Department shall report to the United States Centers for Disease Control all information collected under § 18-331(A), including that received under § 18-330(B) of this subtitle.

(2) Subject to § 2-1312 of the State Government Article, the Department shall report annually to the General Assembly the incidence of pertussis and of major adverse reactions to pertussis vaccine.

18-332.

(A) The Department shall adopt guidelines, after notice and public hearing in accordance with the Administrative Procedures Act, setting forth:

(1) The circumstances under which pertussis vaccine should not be administered;

(2) The circumstances under which administration of the vaccine should be delayed;

(3) Any categories of potential recipients who are significantly more vulnerable to major adverse reactions than is the general population; and

(4) Procedures to notify all physicians of the content of the final guidelines and all updates issued thereafter.

(B) The administration of pertussis vaccine to an individual may not be required by any provision of law if, in the physician's medical judgment:

(1) The circumstances specified under subsection (A)(1) or (2) of this Section are present; or

(2) Taking into account the information specified under Subsection (A)(3) of this Section as well as all other relevant information, and the risk to the potential recipient outweighs the benefits both to the potential recipient and to the public in administering the vaccine.

(C) Nothing in this Section shall be construed to affect any emergency authority of the Secretary under any other provision of law to protect the public health.

Article - Education

7-402

(a)(3) Any requirement for the administration of pertussis vaccine shall be consistent with § 18-332(B) of the Health - General Article.

SECTION 2. AND BE IT FURTHER ENACTED, That this Act shall take effect January 1, 1985, and that all guidelines authorized or required to be promulgated under Sections 18-328 through 18-332 of the Health - General Article, as enacted by this Act, shall be promulgated no later than January 1, 1985.

Notes on the Maryland Law

Two particularly unique aspects of Maryland law need to be noted.

RE[illegible]T: SERIOUS ADVERSE REACTION FOLLOWING RECEIPT OF PERTUSSIS VACCINE.

Patient's Name and _____ Sex _____ Age _____

Address _____ Phone _____

Describe Reaction. (Include date vaccine was administered and type of vaccine)

_____

_____

_____

Hospitalized?_____ Name of hospital _____

CUT ALONG THIS LINE

If your child has a serious reaction following pertussis vaccine, this information must be reported to the health authorities. Normally, this will be done by your doctor or clinic once they have knowledge of the event. You also may file a report, by completing the form above and submitting it to your respective local health department listed below.

NAMES, ADDRESSES AND PHONE NUMBERS OF MARYLAND'S LOCAL HEALTH DEPARTMENTS

Allegany, Box 1745, Willowbrook Road, Cumberland, 21502	777-5600
Anne Arundel, Health Services Bldg., J Harry S. Truman Pkwy., Annap., 21401	224-7095
Baltimore, New Courts Bldg., 401 Bosley Ave., Towson, 21204	494-2724
Calvert, P.O. Box 980, Prince Frederick, 20678	535-5400
Caroline, Box 10, 411 Franklin St., Denton, 21629	479-0556
Carroll, Box 845, 540 Washington Rd., Westminster, 21157	857-5000
Cecil, Court House Annex, 2nd Floor, Elkton, 21921	398-5100
Charles, Box 640, LaPlata, 20646	934-9577
Dor[illegible], Rt. 50 & Woods Rd., Box 319, Cambridge, 21613	228-3223
Frederick, 12 E. Church St., Frederick, 21701	694-1700
Garrett, Garrett Co. Medical Center, Oakland, 21550	334-8111
Harford, 119 Hays St., Box 191, Bel Air, 21014-0191	838-3047
Howard, 3450 Court House Dr., Box 476, Ellicott City, 21043	992-2333
Kent, College Ave., Ext., Box 359, Chestertown, 21620	778-1150
Montgomery, 100 Maryland Ave., Rockville, 20850	681-5000
Prince George's, Hospital Rd., Cheverly, 20785	386-[illegible]300
Queen Anne's, 206 N. Commerce St., Centreville, 21617	758-0720
St. Mary's, Tudor Hall Dr., P.O. Box 316, Leonardtown, 20650	475-8921
Somerset, Box 129, Dr. Robert Johnson Health Center, Westover, 21871	651-0822
Talbot, 100 S. Hanson St., Box 480, Easton, 21601	822-2292
Washington, 1302 Pennsylvania Ave., P.O. Box 2067, Hagerstown, 21740	791-3200
Wicomico, 300 W. Carroll St., Salisbury, 21801	749-1244
Worcester, P.O. Box 249, Snow Hill, 21863	632-1100
Baltimore City, 111 N. Calvert St., Baltimore, 21202	396-4387
State Health Dept., 201 W. Preston St., Baltimore, 21201	225-0677

Turn page for more →

IMPORTANT INFORMATION AVAILABLE TO YOU

Each time your child is given a DTP shot, the following information is recorded in a permanent record and is available to you from your doctor or clinic upon request:

- the date and time of day the vaccine was given,
- the DTP dose number,
- the name and title of the person who gave the shot,
- the vaccine manufacturer name, and
- the vaccine lot number.

You should keep information concerning the dates of any vaccine given to your child in a permanent immunization record plus the details of any reactions that may occur until your child enters school. The Maryland Department of Health and Mental Hygiene, Division of Immunization, 201 W. Preston Street, Baltimore, MD 21201, provides a personal Maryland Immunization Record for this purpose.

IMMUNIZATION REQUIREMENTS FOR ENTRY TO SCHOOL

There is a law in Maryland that requires children to have certain immunizations in order to enroll in a public or private school. Before a child is allowed to attend school, proof of immunization must be shown. Proof of immunization consists of a written record showing the month, day and year of each immunization, along with the signature of the person or clinic which administered each dose.

The following immunizations are currently required in Maryland:

- DTP — 4 doses for pupils less than 7 years of age,
- DT/Td — 3 doses for pupils 7 years of age and older,
- Polio — 3 doses for pupils less than 18 years of age,
- Measles — 1 dose of live virus vaccine on or after the first birthday, or a blood titer of at least 1:4, and
- Rubella — 1 dose of live virus vaccine on or after the first birthday, or a blood titer of at least 1:8.

As with pertussis, there are medical reasons that could exempt some children from mandated immunizations, the law allows a religious exemption, also.

SUMMARY

You have the right to receive and understand the information contained in this booklet. If you don't understand any part of it, ask to discuss it before your child receives pertussis vaccine.

Maryland law requires that most children receive, among other vaccines, pertussis vaccine in order to attend school. However, your child could be exempted temporarily or permanently from this mandate if he or she meets the appropriate conditions for such exemptions that are outlined in this booklet.

Under Maryland law, if your doctor decides that your child should not get the vaccine, his judgment is final. It cannot be reversed by the State or Local Health Department or by school officials. Except in an emergency, your child cannot be kept out of school because of the doctor's decision not to give your child the vaccine.

DHMH PRAMP
[illegible]

IMPORTANT INFORMATION ABOUT PERTUSSIS AND PERTUSSIS VACCINE

Prepared for you by:

The Maryland Department of Health and Mental Hygiene
The Medical and Chirurgical Faculty of the State of Maryland
The Maryland Chapter of the American Academy of Pediatrics

INTRODUCTION

This booklet is intended to answer some of the questions you may have about pertussis (whooping cough) and pertussis vaccine. You should read this information before your child receives the DTP vaccine.

Pertussis or whooping cough can be a serious disease. In some persons, especially very young children, it can cause permanent brain damage or even death. In order to protect persons from whooping cough, Maryland law requires most children to get four DTP shots before they go to school.

However, not all children have to get pertussis vaccine. In some cases, the "P" part of the DTP vaccine can cause serious reactions, including permanent brain damage or even death. So some children should not get the "P" part of the DTP vaccine at all. Also, for some children the series of pertussis vaccine should be delayed.

So it is very important to read and to understand this information about the disease and the pertussis vaccine to protect your child's health. If there is something in this booklet you don't understand, ask the person who gave you the booklet to explain it.

WHAT IS PERTUSSIS (WHOOPING COUGH)?

Pertussis, also known as whooping cough, is a highly contagious disease caused by the bacteria, *Bordetella pertussis*, and is spread through the air to others. The disease starts with cold symptoms and progresses to repeated, violent coughing spells which can interfere with eating, drinking and breathing. The coughing spells may be accompanied at the end by a "whooping" sound while the victim struggles to inhale. The disease will normally last for one-to-two months.

WHAT ARE THE RISKS OF GETTING WHOOPING COUGH?

According to the Centers for Disease Control (CDC), in the past ten years an average of 1,800 cases of pertussis have been reported each year in the U.S. Since many cases go unrecognized or unreported, the real numbers could be much higher.

Over half of the reported cases occur in children under 1 year of age. Most reported cases of whooping cough involve children under 5 years of age. This is why vaccination in early life is so important. Older children and adults, even those who have been vaccinated, can also contract the disease and are believed in many cases to be the source of infection in the younger children.

Although there is some disagreement about how effective the vaccine is, most children who receive the series of pertussis vaccine are protected from whooping cough. The disease is often milder in vaccinated children who do become ill with the disease.

WHAT ARE THE POSSIBLE DANGERS OF WHOOPING COUGH?

In the U.S. over the last ten years, an annual average of 8 deaths has occurred following the disease. While fatality is low, almost all deaths are among children under 1 year of age, most in those under 6 months.

While there is no specific treatment for pertussis, prompt medical attention and supportive care can be successful in reducing the severity and complications of the disease.

WHAT ARE THE POSSIBLE DANGERS OF THE PERTUSSIS PART OF DTP VACCINE?

Most U S doctors and public health officials believe that the benefits of pertussis vaccine outweigh the risk of reactions to the vaccine for most children. Most children have only a low fever, some crying and/or soreness after a DTP shot. Some have no reaction at all.

Some children, however, have serious reactions to the "P" part of the DTP vaccine. These reactions may include convulsions, seizures, shock-collapse (turning blue or pale, limp, non-responsive), a fever of 105 degrees F. or more, high-pitched unusual cries, unusually long sleeping with great difficulty waking the child, or crying which lasts more than 3 hours and cannot be stopped. Any of these signs should be reported to your doctor or clinic at once.

In some cases serious reactions to the vaccine can involve long-term uncontrolled seizure disorders, brain damage, and even death.

There is a great deal of disagreement over how often these serious reactions happen. The pertussis vaccine is known to cause serious reactions more often than other vaccines. An effective test to screen the pertussis vaccine for its potential to cause reactions is not available. It is not known how many children die or get long lasting disabilities after the DTP shot is given, yet clearly children who get DTP shots are at somewhat greater risk of serious reactions than those who get DT shots, without the "P".

This is why parents, doctors, and clinics need to give careful consideration before giving this vaccine and need to be alert to possible serious reactions which may occur.

DOES THE LAW REQUIRE ME TO GET PERTUSSIS VACCINE FOR MY CHILD?

Maryland law requires most children to receive several different immunizations before they can enter school – pertussis vaccine is one of them. In order to enter school, a minimum of 4 doses of DTP is required, 5 are recommended.

Not all children are required to get DTP shots. Maryland law allows some children not to have the "P" part of these shots if:

- the child has any condition listed in the following section ("Which Children Should Not Receive Pertussis Vaccine?").
- the parents object due to their good faith religious beliefs and practices (in which case the objections must be universal and not for pertussis vaccine alone), or
- the doctor decides that because of your child's particular situation, the risks of the vaccine outweigh the benefits to the child and the public. For instance, if a parent, brother, or sister of the child to be given the vaccine has epilepsy, seizures, or other diseases of the central nervous system, or has had a severe reaction to a DTP shot, the doctor may choose not to give the vaccine.

WHEN SHOULD A CHILD'S DTP SHOTS BE DELAYED?

A child's DTP shots should be delayed if he or she:

- has a fever or ear or chest infection or is sick at the proposed time for vaccination, or has not completely recovered from a past illness;
- has had a previous convulsion, seizure, or nervous system illness, until it can be determined that no more seizures are happening and the condition is stable and under control, or
- is receiving chemotherapy or radiation treatments which may reduce the immune response of the child to vaccines.

A child's shots can be continued after he or she is well.

WHICH CHILDREN SHOULD NOT RECEIVE PERTUSSIS VACCINE?

It is generally agreed that some children should not get the "P" part of the DTP vaccine. The pertussis vaccine should not be given to your child if:

- he or she has an underlying neurologic or seizure disorder which is getting worse or is uncontrolled;
- he or she is seven years of age or older; or
- he or she has already had an earlier DTP shot and had any of the following reactions after the shot:
  - a measured fever of 105 degrees F. or greater (some manufacturers believe a temperature of 103 degrees F. or greater is a contraindication, therefore, this also should be reported to your doctor),
  - a severe allergic reaction,
  - collapse or shock-like state,
  - persisting, inconsolable crying lasting 3 hours or more, or an unusual high-pitched cry;
  - convulsion(s) with or without fever occurring within 7 days, or
  - other severe problems of the brain occurring within 7 days, this includes prolonged sleeping and inability to wake child, unusual twitching of the body or unusual staring.

Some vaccine manufacturers state that a family history of central nervous system disorders is an absolute reason not to get whooping cough vaccine (the P part of the DTP vaccine). However, the Centers for Disease Control and the American Academy of Pediatrics disagree with the manufacturers on this issue. Therefore, any family history of central nervous system problems should be considered carefully with your doctor before vaccination.

Your child should not need further pertussis shots if he or she has had laboratory confirmed whooping cough. This also should be considered with your doctor.

If a child should not receive pertussis vaccine, he or she can still be protected against diphtheria and tetanus by receiving DT vaccine rather than DTP.

ARE CERTAIN CHILDREN MORE LIKELY TO HAVE A SERIOUS REACTION TO DTP VACCINE THAN OTHERS?

The medical experts do not agree on the reasons why reactions following vaccination happen, nor can they predict in which children serious reactions will occur. But there are some factors which may make children more likely to have serious reactions.

A child may be at higher risk of a serious reaction to the "P " part of the DTP vaccine if he or she:

- has had a serious reaction to a previous DTP shot;
- has a neurologic illness, including seizures or convulsions, the severity of which is changing or uncontrolled, or
- has a fever or infection or is sick when the shot is given.

HOW TO REDUCE THE RISK OF A SERIOUS REACTION TO PERTUSSIS VACCINE

It is important that a child's medical history be provided to the doctor or clinic before he or she receives the pertussis vaccine. Such a history should include, but not necessarily be limited to, the following information:

- major birth problems;
- your child's and family's history of convulsion (seizure) or neurological illness;
- any allergy;

- recent or present illness;
- medicines or treatment currently taking; and
- your child's and family's history of previous vaccine reactions.

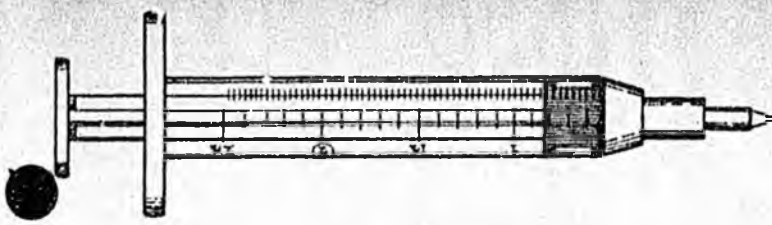
Besides providing your doctor with your child's medical history, there are other things which can be done to reduce the risk of a serious vaccine reaction. One thing you can do is take your child's temperature before he or she is vaccinated to make sure he or she has no fever. Another is to make sure your child has no obvious signs of infection at the time vaccine is given. If your child's throat is red or the child has been pulling his or her ears, this may be a sign of infection and should be discussed with your doctor.

WHAT SIGNS TO LOOK FOR IN A SERIOUS REACTION TO VACCINE

It is important to observe your child carefully at periodic intervals after vaccination, particularly during the first 72 hours. If your child has any of the following symptoms after a DTP shot, write down the details on this form to help you report the correct information to your doctor or clinic:

SYMPTOM	DATE	TIME	DURATION	DESCRIPTION
Measured fever nearing 105 degrees F				
High-pitched, unusual crying				
Persistent, inconsolable crying (3 or more hours)				
Inability to wake child, unusually prolonged sleeping				
Shock or collapse; loss of muscle control, turning white, blue or gray; limpness				
Convulsion, seizure, unusual repeated twitching, jerking, startling, or staring spells				
Loss of sensory or muscle control, paralysis, limping, loss of speech, hearing or sight				
Difficulty or stoppage of breathing				
Severe local reaction, large red, blue or purple coloring with extended swelling near where the shot was given				

If any of these events happen after your child gets a DTP shot, call your doctor or clinic at once. Tell them about the shot, when it was given, and about your child's reaction. *Arrange for a prompt examination at the doctor's office, clinic, or emergency room.* When things settle down, write down in detail exactly what happened.



Dissatisfied Parents Together (DPT)
128 Branch Road, Vienna, VA 22180
(703) 938-DPT3

May 22, 1987

Mrs. Shannon Kohler
President, Alaska DPT
Box 1746
Soldotna, AK 99669

Dear Shannon,

Enclosed are the new regulations issued by the Maryland State Health Department in regards to the vaccine safety legislation that was passed in Maryland.

As you can see by the Mar 1987 date, this information is just now reaching the health care providers in Maryland. This law was not implemented at the date it was given. Since health care providers are only now receiving this information on giving information to parents, recording manufacturer, date, batch number and recording and reporting adverse reactions to the state, it would be difficult for anyone in the state health department to analyze data collected by this new law that has not previously been available. The data will only now be available to analyze because prior to Mar 1987, the data does not exist.

Sincerely,

Kathi Williams

Kathi Williams, Director
Dissatisfied Parents Together (DPT)

Title 10
DEPARTMENT OF HEALTH AND MENTAL HYGIENE

Subtitle 52 PREVENTIVE MEDICINE

10.52.05 Pertussis and Pertussis Vaccine

Authority: Health-General Article, §4-204(c)
Annotated Code of Maryland

Notice of Final Action

On April 17, 1986, new Regulations .01 — .05 under a new chapter COMAR 10.52.05 Pertussis and Pertussis Vaccine, were adopted by the Secretary of Health and Mental Hygiene. These new regulations, which were proposed for adoption in 12:26 Md. R. 2558 — 2560 (December 20, 1985), have been adopted as proposed.

Effective Date: May 19, 1986.

ADELE WILZACK
Secretary of Health and Mental Hygiene

[Md. R. Doc. No. 85-R-473-F. Filed at Div. of St. Doc. April 23, 1986.]

.01 Definitions.

A. "Department" means the Maryland Department of Health and Mental Hygiene.

B. "Health care provider" means any licensed health care professional, organization, or institution, whether public or private, under whose authority pertussis vaccine is administered.

C. "Major adverse reaction" means any:

(1) Serious illness, disability, or impairment of mental, emotional, behavioral, or physical functioning or development, the first manifestation of which appears within 7 days after the date of administration of pertussis vaccine and for which there is reasonable scientific or medical evidence that pertussis vaccine causes, or significantly contributes to, the effect; and

(2) Other reaction, which the Department, after consultation with the Medical and Chirurgical Faculty of Maryland, determines is a basis for not continuing with pertussis vaccine administration.

D. "Patient" means the individual to whom pertussis vaccine is being administered.

E. "Pertussis vaccine" means any vaccine that contains materials intended to prevent the occurrence of pertussis, whether the materials are administered separately or in conjunction with other materials intended to prevent the occurrence of other diseases.

.02 Requirements for Health Care Providers.

A. Before the administration of pertussis vaccine, the health care provider shall provide to the patient's parent or guardian written information addressing:

(1) The frequency, severity, and potential long-term effects of pertussis;

(2) Possible adverse reactions to pertussis vaccine, which, if they occur, should be brought to the immediate attention of the health care provider;

(3) A form that lists symptoms of possible pertussis vaccine adverse reactions to be monitored and which contains places where information can be recorded to assist in reporting to the health care provider, local health officer, and the Department;

(4) Measures parents should take to reduce the risk of, or to respond to, any major adverse reaction to pertussis vaccine;

(5) Early warning signs or symptoms to which parents should be alert as possible precursors to a major adverse reaction to pertussis vaccine;

(6) When and to whom parents should report any major adverse reactions to pertussis vaccine;

(7) A summary of the immunization requirements adopted under Education Article, §7-402(a), Annotated Code of Maryland, including those related to pertussis vaccine;

(8) The circumstances under which pertussis vaccine may not be administered;

(9) The circumstances under which administration of pertussis vaccine shall be delayed; and

(10) Categories of potential recipients who are significantly more vulnerable to major adverse reactions to pertussis vaccine than is the general population.

B. Before the administration of pertussis vaccine, the health care provider shall, by appropriate inquiries, attempt to elicit the information necessary to determine, based on a physician's medical judgement, whether:

(1) Pertussis vaccine should not be administered to the patient;

(2) Administration of pertussis vaccine should be delayed; or

(3) The risk to the potential recipient of the vaccine outweighs the benefits both to the potential recipient and to the public in administering the vaccine.

C. The circumstances under which the administration of pertussis vaccine shall be delayed or may not occur are established by the Immunization Practices Advisory Committee (ACIP) to the Public Health Service. The Department will notify all health care providers of these circumstances.

D. A physician who determines, pursuant to §B, that the administration of the pertussis vaccine to a patient shall be delayed or may not occur shall submit to the local health officer the name, address, date of birth, and the basis for the determination for each patient.

E. Pertussis vaccine should not be given if in the physician's medical judgement, taking into account any categories of potential recipients who are significantly more vulnerable to major adverse reactions than is the general population, as well as all other relevant information, the risk to the potential recipient outweighs the benefits both to the potential recipient and the public in administering the vaccine.

F. At the time of administration of pertussis vaccine to a patient, the health care provider shall record, in a permanent record to which the patient's parent or guardian shall have access upon request:

(1) The date each dose of pertussis vaccine is administered;

(2) The manufacturer and lot number of the vaccine used for each;

(3) Other identifying information on the vaccine used; and

(4) The name and title of the health care provider who authorized the vaccine to be administered and the one who administered it.

G. A health care provider who has administered the pertussis vaccine to a patient and who has been informed by the parent or guardian of the patient, or has reason to believe that the patient has had a major adverse reaction to pertussis vaccine, shall within 24 hours of receipt of that knowledge:

(1) Record to the extent of his knowledge all relevant information in the patient's permanent medical record; and

(2) Report information, including the manufacturer's name, date of administration, type and lot number of the vaccine, a brief description of the reaction, and other specified information on a morbidity report card, to the local health officer. These reports can also be made by telephone.

.03 Requirements of Local Health Officers.

A. Upon receipt of notification of a major adverse reaction to a pertussis vaccine, the local health officer shall:

(1) Notify and forward the morbidity report card to the Department within 24 hours; and

(2) Assure that the necessary information to fill out a "Report of Adverse Event Following Immunization" is obtained.

B. At the time of completion, the Report shall be submitted to the Department.

.04 Requirements of the Department.

A. Whenever a resident birth occurs, the Department shall promptly provide parents of the newborn child with information included in Regulation .02A(1)—(10) of this chapter.

B. The Department shall prescribe the form and content of the information about immunizations provided to parents at times of birth and of administration of pertussis vaccine, according to Regulation .02A(1)—(10) of this chapter.

C. Upon receipt of information regarding a major adverse reaction to a pertussis vaccine, the Department shall immediately notify the vaccine manufacturer of the following:

(1) Date of immunization;

(2) Lot number of vaccine; and

(3) Type of reaction.

D. The Department shall establish a system to collect data from local health officers, from public and private health care providers, and from parents, on the incidence of pertussis and major adverse reactions to pertussis vaccine. This system shall be organized so that periodic revisions and updates of information and guidelines may be made. In addition, the information collected shall be sufficient for any reports required by the Department on pertussis and major adverse reactions to pertussis vaccine.

E. On the basis of the data collected and of any other information available, the Department shall periodically revise and update:

(1) The information provided to parents at the times of birth and of administration of pertussis vaccine;

(2) The information provided to health care providers regarding pertussis immunization deferral or exemption, and all other information otherwise regarding risks and benefits to the patient and to the public; and

(3) Other pertinent information on pertussis and pertussis vaccine.

F. The Department shall report to the centers for disease control (CDC) the incidence of pertussis and major adverse reactions to pertussis vaccine.

G. The Department shall report annually to the General Assembly on the incidence of pertussis and of major adverse reactions to pertussis vaccine.

H. The Department shall notify by mail or other means, or both, all health care providers of their responsibilities relevant to these regulations as well as other appropriate materials (for example, ACIP recommendations, parent information pamphlets, and morbidity report cards). Revisions of these and new materials shall also be distributed in the same manner.

.05 General.

Nothing in these regulations shall be construed to affect any emergency authority of the Secretary of Health and Mental Hygiene under any other provision of law to protect the public health.

State of Maryland

PREVENTIVE MEDICINE ADMINISTRATION

Address Replies to P.O. Box 13528
Baltimore, Maryland 21203

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

201 WEST PRESTON STREET • BALTIMORE, MARYLAND 21201 • (301) 225-6677

ADELE WILZACK, R.N., M.S., SECRETARY

ERIC M. FINE, M.D., M.P.H., DIRECTOR

March, 1987

Dear Doctor:

Enclosed are the materials you requested concerning the new Pertussis and Pertussis Vaccine regulation (COMAR 10.52.05) that became effective in Maryland on May 19, 1986. These materials will assist you in complying with the regulation; they are:

- o Pertussis Regulation
- o July 12, 1985 ACIP Recommendations for DTP Vaccine
- o Guidelines for Implementing the Pertussis Regulation
- o Reporting Card for Adverse Reactions to Pertussis Vaccine
- o Pertussis Patient Information

It is important that you review all the enclosed material. Section .02, Items A through G, in the regulation outlines your particular responsibilities. The Guidelines further delineate those responsibilities. Within the ACIP Recommendations for DTP, you will find detailed information on vaccine use, precautions and contraindications, side effects and adverse reactions, and other vital information on Pertussis and Pertussis Vaccine.

As specified in Section .02, G (2) of the regulation, you are <u>required</u> to report any "major" (as defined in Section .01, C) adverse reaction associated with the administration of pertussis vaccine to your respective local health department. This can be accomplished by mailing a standard morbidity report card to the local health department or by telephoning the information to them. After they receive your initial report, someone from the health department will contact you to get more details about the reaction.

Section .02, A of the regulation, describes in detail the type of information that must be given to the parent or guardian of a patient before pertussis vaccine is administered. To assist you in complying with this provision of the regulation, the Department, in conjunction with the Medical and Chirurgical Faculty of Maryland and the State chapter of the American Academy of Pediatrics, has prepared the pamphlet, "Important Information About Pertussis and Pertussis Vaccine." Feel free to reproduce the number of copies you will need for your practice.

If there is any way we may assist you further in carrying out your part of this regulation, please contact either of us.

Sincerely,

Feng-Ying C. Lin, M.D., M.P.H., Chief
Center for Clinical Epidemiology

Robert E. Longenecker, Chief
Division of Immunization

FYCL/REL/mw
Enclosures

The New Epidemiology of Measles & Rubella by James D. Cherry University of California, Los Angeles. Dr. Cherry is a Professor of Pediatrics at the Univ. of Calif., L. A. School of Medicine and an attending physician at UCLA Hospital and Clinics. 1980 ARTICLE, Hospital Practice, July 80 Pp 49-57

This is the lead in to article

"Both diseases have been effectively controlled in the pediatric population that, in the prevaccine era, harbored them. However, with the shift in prevalence to adolescents and young adults, it is possible the diseases may be "time bombs"."

The Prevaccine era: Clinical studies showed: 95% of Americans had had measles by age 15. Serologic studies of young adults entering military service show 99% had measles/rubella antibodies. Highest incidence in the prevaccine era was in children 5 to 9, next highest under 5, only 10 % occured in children over 10 and 3% in persons over 15.

possible because "real" immunity was established?

A.W. Hedrich in 1933 published a landmark study on epidemiologic patterns of measles in Baltimore from 1900 to 1931. He reported that when 68% of the children less than 15 years of age were immune to measles epidemics did not develop.

1976 & 1977 Los Angeles County 67 children were studied for measles hemagglutination inhibiting antibody (HIA) titers after "booster" shots.

Direct Quote

The results: "In short, the data suggested that a booster dose might not have any lasting effect on waning immunity."

Spring 1977 - outbreak UCLA campus. 34 cases [18 thought they were immune (11 by vaccination, 6 by natural disease, one by both)]
506 students underwent serologic screening, 9% had HIA titers of less than 5 and thus, presumably , were susceptible to measles: *in other words, the outbreak had developed in a population that appeared to be 91% immune.* Some were reimmunized with same result as above (i.e. the

Direct Quote

booster did not foster increased immunity): "In short, there was extremely poor correlation between histories of immunization and either susceptibility to or protection against measles. Antibody responses in vaccinees cast doubt once again on the efficacy of revaccination (but not, it should be emphasized, on the efficacy of belated *primary* vaccination)"

Of 212 students and campus employees who were vaccinated during the study and who could be followed, 58 complained of vaccine associated reactions.

Rubella Since 1969 Rubella activity has declined about 70% (aprox administration of 83 million doses). But as with measles there has been a shift in age groups susceptible to rubella. Before rubella immunization less than 25% of reported rubella involved patients 15 or older. BY 1975

62% was in the 15 or older. By 1976 & 1977 70 % in 15 and older (Highest in the 15-19 yr group)

"The decline in congenital rubella is curious because the number of infections in women of child bearing age has remained the same. Anyway, it is clear that the apparent stability in the control of congenital rubella is precarious."

Atypical Measles - Usually occurs in recipients of killed vaccine. Atypical measles was first noted in 1965. It is a serious illness with fever, headache, abdominal pain, myalgia, yellowish red, maculopapular, frequently vesicular and petechial skin rash, and pneumonia. It lasts one to three weeks, recent reports suggest increasing duration and severity.

"Since "only" about 1.8 million doses of killed vaccine were distributed between 1963 and 1967 and since "only" an estimated 600,000 to 900,000 children received two or three doses of killed vaccine in those years, it was expected in the early 1970's that the problem would disappear quickly."
"It is a disease of significant morbidity in young adults and adolescents: It also presents a diagnostic challenge for primary care physicians unfamiliar with exanthematous diseases, particularly those illnesses normally confined to the pediatric population.

CLINICAL STRATEGY

The 'New' Epidemiology of Measles and Rubella

JAMES D. CHERRY *University of California, Los Angeles*

Both diseases have been effectively controlled in the pediatric population that, in the prevaccine era, harbored them. However, with the shift in prevalence to adolescents and young adults, it is possible the diseases may be "time bombs."

This is the first of five articles on the current concepts and problems of immunoprophylaxis. The second, "The Problems of Poliovirus Immunization" by Vincent A. Fulginiti, will appear in the August issue. "Live, Attenuated Varicella Vaccine—Where Do We Go From Here?" by Philip Brunell and "Pertussis Immunization: Prospects, Problems, and Perspectives" by Edward A. Mortimer Jr. will follow in September and October, respectively. The series will conclude in November with a discussion of "Rabies Prophylaxis in the 1980s" by Stanley A. Plotkin.

Dr. Cherry is Professor of Pediatrics at the University of California, Los Angeles, School of Medicine and Attending Physician at the UCLA Hospital and Clinics.

After more than 16 years of routine measles immunization and more than 10 years of routine rubella immunization in the United States, it is clear that we have done well in controlling both diseases; it is also clear, I think, that we can and should do better. In both instances, the need for improvement centers on a better understanding of herd immunity; in measles, however, there is also a continuing need for us to redress past mistakes whose consequences are still with us. Consequently, a major focus of this article will be the view that greater control of measles and rubella demands that we make an effort to identify and immunize susceptible adolescents and young adults.

Let us begin with measles. In the early 1960s, about 400,000 cases of measles were reported in the United States each year, with about 400 deaths annually. Measles vaccines were introduced in 1963, and by the years 1974–76, the incidence of the disease had dropped to about 30,000 cases per year, with about 30 deaths annually. Thus, the efficacy of measles immunization in the nation is impressive. Equally impressive is the safety of the vaccines used during the past 10 years. Severe reactions to the vaccines occur at a rate of approximately one per million children immunized, and severe illness or death is over a thousand times more likely to occur in a person who acquires the disease naturally than in one who becomes ill as a result of vaccination.

In 1978, the federal government announced that its aim was to eradicate indigenous measles from the country by 1982. What are the prospects for attaining this goal, given our current measles immunization strategy—namely, immunization of 90% or more of the U.S. population between the ages of one and four years?

To a great extent, the answer can be found by considering the history of measles epidemiology in the United States before and after vaccine introduction. Prior to immunization programs, clinical surveys showed that at least 95% of Americans had had measles by age 15; serologic studies of young adults entering military service showed that 99% had previously had measles. The highest incidence in the prevaccine era was in children of five to nine years, the next highest in those under five; only 10% of cases occurred in children over age 10, and only 3% in persons over age 15.

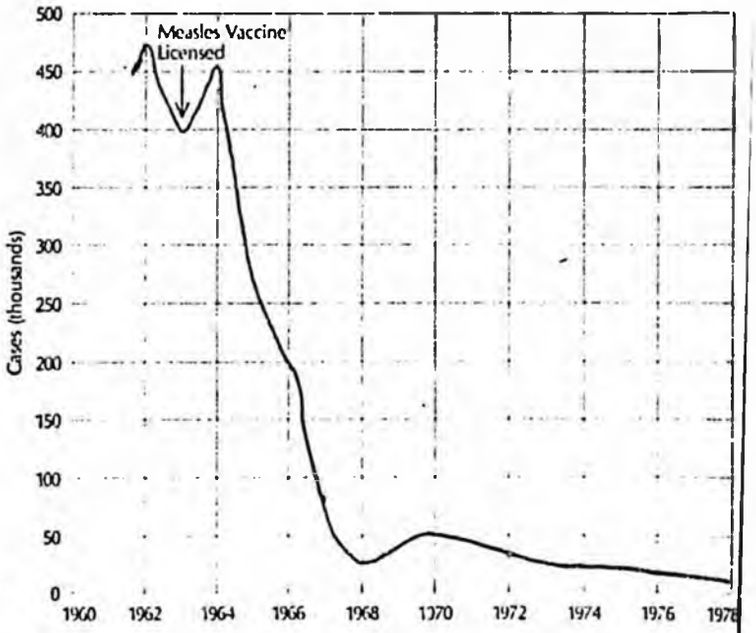
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The prevaccine era, of course, was also a time when we began to formulate concepts of herd immunity. In 1933 A. W. Hedrich published a landmark study on epidemiologic patterns of measles in Baltimore from 1900 to 1931. He reported that when 68% of the children less than 15 years of age were immune to measles, epidemics did not develop. Today we would regard that proportion of immunes to susceptibles as too low, but we still retain the basic concept—that there exists a threshold of herd immunity that will prevent epidemics.

As for the postvaccine era, 1963 saw the licensure of two types of measles vaccine for use in the United States: the Edmonston B strain vaccine (using live, attenuated virus) and a formalin-inactivated killed-virus vaccine. Difficulties were associated with both. The Edmonston B vaccine frequently produced high fevers, and to prevent this, gamma globulin was often administered concomitantly. Febrile reactions were not seen with the killed vaccine, but its major problem (which was quickly realized) was that it did not produce lasting protection by itself. Accordingly, as a sort of compromise solution, a common practice in early measles immunization programs was to give multiple doses of the killed vaccine followed by a single dose of the live vaccine. Another common practice at the outset was to begin immunization in infants by nine months of age, often as early as six months.

By 1964, it was clear that nine months of age (or younger) was too early to begin immunization. By 1965, another live vaccine (Schwarz strain), further attenuated to prevent febrile reactions, was licensed, but many physicians continued concomitant administration of gamma globulin. In 1968, the vaccine currently in use in the United States (the more attenuated Enders' line) was licensed.

The immediate impact of immunization on the incidence of measles was



Since the introduction of measles vaccines in 1963, the overall prevalence of the disease in the United States has dropped by more than 90%, from about 400,000 cases per year in the early 1960s to about 30,000 in recent years (left). At the same time, however

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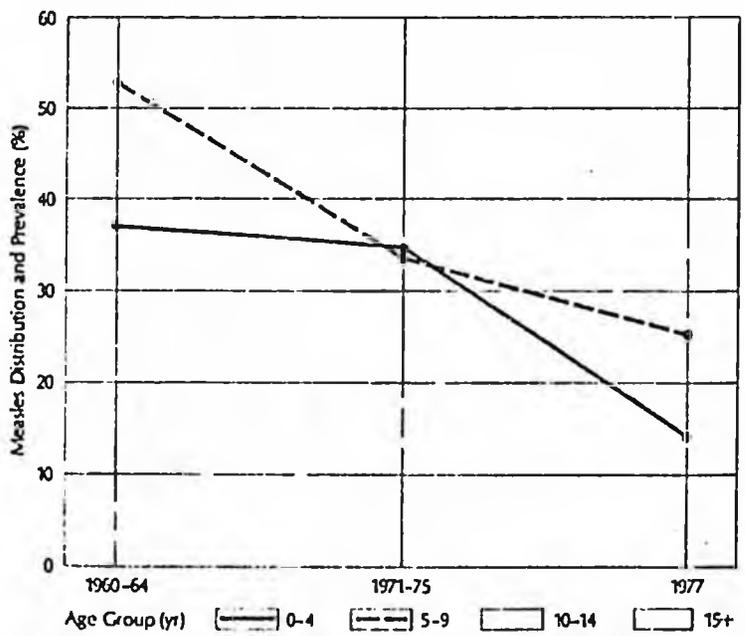
he overall prevalence of the disease fro ut 400,000 cases per year (left). At the same time, however,

less than dramatic, mainly because vaccine distribution did not reach all segments of the pediatric population. Beginning in 1966, however, federal assistance for vaccine purchases by state public health departments was made available. From that point until about 1970, the incidence of measles in the United States fell dramatically. In 1964, for example, there were 458,083 cases of measles reported; in 1968, there were only 22,231. Interestingly, the United States Immunization Survey for 1968 estimated that about 59% of children between one and four years of age and 50% of those between five and nine years of age had received measles vaccine.

In 1969, rubella vaccine was licensed, and at the same time we experienced the beginning of a short-lived period of complacency about measles. From then until 1971, federal funds for measles control were restricted, the number of doses administered was allowed to lag below the birthrate, and there were instances in which the measles vaccine that was used was carelessly stored (too much heat or light), overdiluted, or otherwise improperly handled. Predictably, measles case reports increased sharply in 1970 and 1971. After 1971, however, federal funding for measles control was resumed, adherence to proper storage and handling procedures was emphasized, and immunization after one year of age was widely performed.

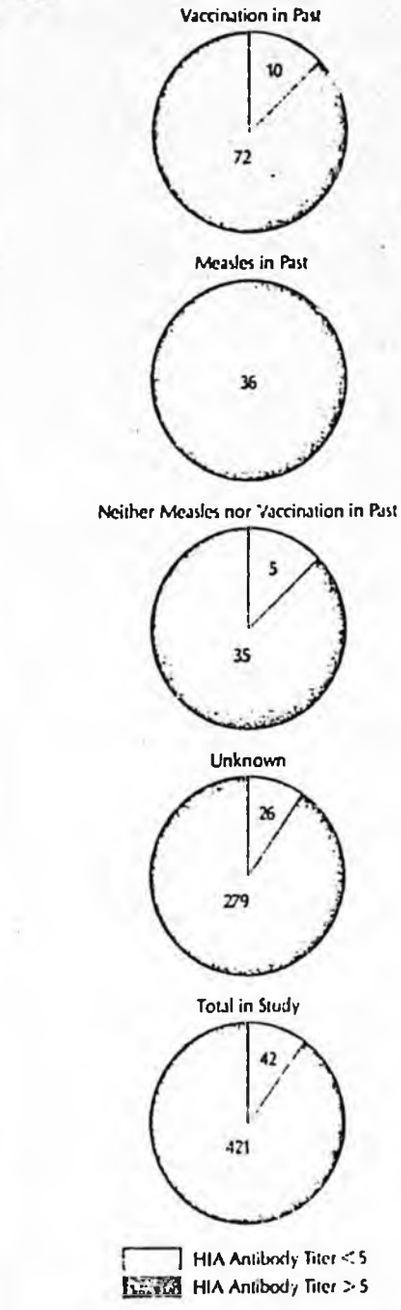
The next few years were relatively quiet on the measles front, but in 1976 and 1977, another surge in case reports occurred. What was unusual about this upswing was that as many as 60% of the cases (in which age was known) occurred in individuals over age 10 and 26% in those over age 15. In other words, the epidemiology of measles had changed dramatically, shifting from the younger to the older age groups.

Why? One factor was the large number of susceptibles who had never been vaccinated against or infected by measles. For example, the United States Immunization Survey noted that only about 67% of children who



there has been a dramatic shift in age-specific attack rates, with relative measles prevalence in older age groups rising; in the early 1960s, less than 10% of cases involved patients aged 10 or older, compared with over 60% in 1977 (right).

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When antibody data were correlated with history in 463 UCLA students, 12% of those reporting prior measles vaccination and 8.5% of those who did not know their immune status had HIA titers below 5, conversely only 12.5% of those reporting an acquired immunity had the same evidence of apparent susceptibility

were 10 to 13 years old between 1973 and 1976 were immunized against the disease. Also contributing were the same mistakes that were made in early immunization programs. The incidence of true primary vaccine failure—that is, lack of antibody response in patients given the right vaccine under the right conditions—was probably negligible, occurring in no more than an estimated 5% of vaccinees.

What about the possibility of waning immunity in those who *had been* vaccinated? In the 1970-71 epidemic, studies in the St. Louis area indicated that about one half of 10,000 cases of measles occurred in vaccinees, and about half of these vaccinees had been less than one year old at the time of immunization. Some of the affected children in St. Louis had mild, apparently modified, disease. About one third of the vaccine failures showed only secondary specific antibody (IgG) response, that is, evidence of prior immunologic stimulation to measles without subsequent protection. Similar data for Cincinnati were reported by C. C. Linnemann Jr. et al and for New Haven by A. Schluederberg et al, both of whom noted a large number of "vaccine failures" in patients whose IgG was responsive but whose IgM was not. The attack rate in St. Louis was significantly higher in those vaccinated four years or more before the epidemic than in those vaccinated within the subsequent three years. This finding was recently echoed by J. S. Marks et al in their study of a 1976 outbreak in the Newark, Ohio, area; there the attack rate was significantly greater in patients vaccinated 10 years or more before the outbreak than in those vaccinated within the subsequent nine years. In short, since these studies indicated that vaccine failure rates increase with time, one could make a case for evidence of waning immunity; however, the influence of improper immunization in these "failures" could not be discounted.

One practical question raised by these findings was whether booster doses might correct the problem of waning immunity—if, that is, waning immunity existed and was in fact a problem. Unexpectedly, some answers were provided during 1976 and 1977 in a Los Angeles County program designed to provide primary immunization to children who had slipped through previous immunization programs.

The data were clearest in 67 of the children studied. All of them had initial measles hemagglutination-inhibiting antibody (HIA) titers of less than 5. It turned out that 27 of these children responded to immunization with a primary IgM response indicative of primary immunization. But there were 26 other patients whose response to vaccination consisted solely of a rise in IgG measles antibody. We postulated that most of the latter group probably had been vaccinated previously; later we were able to confirm that. Indeed, half of them had. The contrast in antibody response between these children (given booster doses) and those vaccinated for the first time was dramatic. In the primary vaccinees, the initial mean postimmunization titer was 73, and a year later it was 30. In the booster vaccinees, there was only a modest initial rise in titer, and after a year the level was almost back to where it had been before the booster. In addition, we noted a lack of "take" in 14 other children, most of whom probably had been immunologically stimulated previously. In short, the data suggested that a booster dose might not have any lasting effect on waning immunity.

In the spring of 1977, an outbreak of measles on the campus of UCLA provided an opportunity to study the epidemiologic and serologic characteristics of the disease in young adults of the vaccine era. A number of interesting points emerged. First, a total of 34 cases of measles were documented, the most important finding being that 18 involved patients thought they were immune (11 by reported vaccination, six by reported

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One further note: Of 212 students and campus employees who were vaccinated during the study and who could be followed, 58% complained of vaccine-associated reactions. During a three-week reporting period, fever (16%), eye pain (15%), bed confinement (17%), and skin rash (7%) were the most notable complaints; three vaccine recipients experienced especially severe reactions, including high fever, persistent eye pain, and prolonged bed confinement (only one of the three reported having been vaccinated previously). Thus, the impression was that measles vaccine may be more reactogenic in adults than in children; however, because serologic screening had not been done prior to immunization, the nature of the reactions (aberrant immunologic vs vaccine viral infection in the susceptible host) could not be determined. Recently, two studies, one at a military base and the other on a college campus, have revealed no severe reactions in more than 600 vaccinees; these findings are encouraging. but why the other reactions at UCLA?

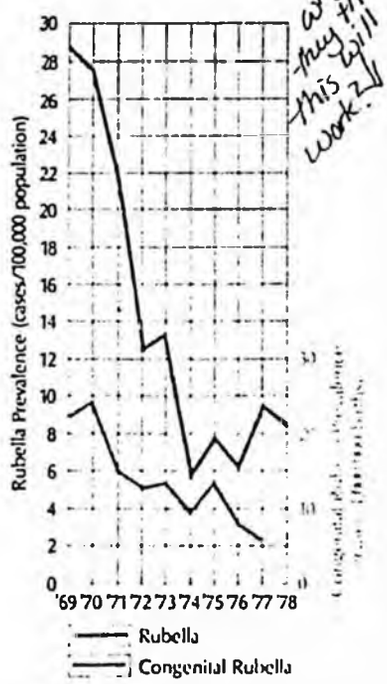
Before turning to my recommendations, there is one other point to be addressed: atypical measles. This syndrome was first noted in 1965 but did not receive much attention until 1967, when V. A. Fulginiti et al reported a number of cases. It is characterized at first by acute onset of fever, headache, abdominal pain, and myalgia; two to three days later, a yellowish red, maculopapular, and frequently vesicular and petechial skin rash appears, beginning distally and then spreading centrally. In many patients, the extremities are edematous, and pneumonia occurs in almost all (but may not be detected by x-ray). The illness has been described as lasting one to three weeks, but recent reports suggest increasing duration and severity: in 1979, for example, D. B. Martin et al reported persistent residual nodular densities in chest x-rays of patients up to six months after the acute episode of atypical measles.

Although atypical measles has been reported very rarely in patients inoculated with live vaccine only, it usually occurs in recipients of killed vaccine. Since "only" about 1.8 million doses of killed vaccine were distributed between 1963 and 1967, and since "only" an estimated 600,000 to 900,000 children received two or three doses of killed vaccine in those years, it was expected in the early 1970s that the problem would disappear quickly. Eventually (if its pathogenesis involves killed vaccine) it will, but in the meantime, atypical measles is still very much with us. It is a disease of significant morbidity in young adults and some adolescents; it also presents a diagnostic challenge for primary care physicians unfamiliar

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with exanthematous diseases, particularly those illnesses normally confined to the pediatric population. Moreover, the possibility of misdiagnosis is heightened when the syndrome is incompletely expressed and the patient's vaccination history is fragmentary, unelicited, or not considered. In the years to come, still more cases undoubtedly will occur, and in many the etiology will go unrecognized.

Where, as we try to make our way toward elimination of indigenous measles by 1982, does all of this lead us? The most clear-cut finding is the shift in the incidence of measles from younger to older age groups. Unfortunately, many of the other points we have reviewed, in an attempt to explain and come to terms with this shift, are clouded by uncertainties. For example, waning immunity in vaccinees does appear to exist, but its occurrence in properly immunized individuals has not been determined, and its epidemiologic significance is unknown. There is also, I think, good evidence indicating that booster doses to counteract waning immunity will be ineffective, with present vaccines at least. It is clear, too, that we cannot reasonably expect to identify susceptible adolescents or adults simply on the basis of history. On the other hand, it appears that if we elect to immunize *everybody* in the older age groups, a high percentage (perhaps as much as 80% to 90%) of such vaccinations will be unnecessary because of previously acquired immunity. In addition, the prospect of multiple doses of live vaccine entailed by such a shotgun approach raises the possibility of abnormal sensitization to the virus and consequent vaccine reactions. Then again, in the epidemics of 1970–71 and, especially, of 1976–77, we are faced with evidence that measles can spread despite high levels of herd immunity; in particular, the UCLA outbreak, in the face of 91% immunity, does not bode well for a national policy whose goal is 90% immunity. Finally, there is the persisting problem of atypical measles, the prevention of which would seem to call for reimmunization with live vaccine; here, too, there exists a risk of untoward reactions (in one study of 75 former recipients of killed vaccine, 13% had severe local reactions to live vaccine), but generally, the reactions of revaccination are considerably less severe than the alternative: atypical measles at some unspecified future date.



Since vaccine licensure in 1969, rubella cases in the United States have dropped 70%, the prevalence of congenital cases has dropped more modestly. Data for recent years may be incomplete.

The conclusion, I think, is that if we are truly going to eliminate measles in the United States, we must make a greater effort to track down and immunize susceptible adolescents and young adults; to do so requires serologic screening—in colleges, the military, industry, various institutions (including hospitals), and physicians' offices. If we settle for 90% immunity in children and ignore older age groups, we will continue, for the most part, to block major epidemics, but we will also continue to develop an expanding cohort of adolescents and adults in whom there are many susceptibles. As long as they stay in this country, these susceptibles will be relatively safe—probably increasingly so as more and more children are immunized. But once susceptibles travel to the many parts of the world where the virus is more prevalent or endemic, they will run the risk of getting measles and exposing others upon their return; thus, if such disease is not prevalent at the outset, it could become so on occasion.

Admittedly, screening programs in adolescents and adults would be expensive, but so, too, would be a program of mass, unscreened immunization or programs of emergency immunization in developing outbreaks. We must also acknowledge that questions remain about measles serology—for example, what titer shall we agree upon as the cutoff indicator of immunity? The risk of morbidity in older patients either vaccinated for the first time or revaccinated (i.e., killed-vaccine recipients) must also be

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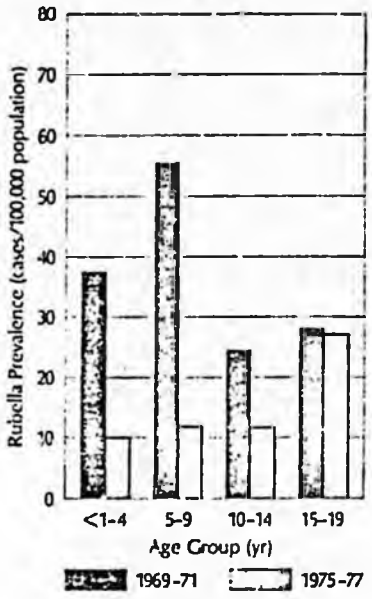
considered, but immunization based on serologic screening would appear at least to have the virtue of reducing or eliminating unnecessary vaccinations.

Another "selling point" for this ambitious undertaking is that measles screening could be combined with rubella screening for the same age groups. Why also rubella? With the distribution of over 83 million doses of rubella vaccine since 1969, rubella activity in the United States has dropped about 70%, despite periodic upswings in incidence. But as with measles, this drop has been accompanied by a shift in the age groups susceptible to rubella. Essentially, we have controlled the disease in persons 14 years of age or younger but have given it a free hand in those 15 or older. Before the advent of rubella immunization, less than 25% of reported rubella cases in this country involved patients 15 or older. By 1975, however, 62% of rubella cases in patients of known age occurred in the 15-or-older group; in 1976 and again in 1977, the figure was slightly more than 70%, and the attack rate has been highest in those between 15 and 19 years of age.

Of course, the point of rubella immunization is not prevention of rubella but prevention of the congenital rubella syndrome. Since 1969 and 1970, when the CDC's National Congenital Rubella Registry listed 78 and 90 cases, respectively, the number of reported cases has declined and *apparently* has remained relatively stable at about 30 to 40 per year (data for the last three years or so must be regarded as incomplete because of a common lag in recognition of the syndrome). This decline in congenital rubella is curious because the number of infections in women of childbearing age has remained the same. It is perhaps artifactual and explained by the fall in the fertility rate in the United States and also the more frequent use of therapeutic abortion. Anyway, it is clear that the apparent stability in the control of congenital rubella is precarious.

First, whatever herd immunity goal may have been envisioned at the outset, the level reached in the pediatric population has been no greater than 70% (some of the reasons for this will be discussed later). Second, prior to vaccine licensure, approximately 15% to 20% of women of childbearing age were susceptible to rubella; recent serologic surveys indicate that a similar percentage of women of that age group are still susceptible. Third, in the last couple of years, outbreaks of rubella have occurred in junior and senior high schools, colleges, military bases, and such noteworthy places of employment as hospitals.

As is well known, rubella control to date has been attempted by two different strategies: the so-called U.S. approach (immunizing one-year-olds, other preschoolers, and children between five and nine years) and the so-called U.K. approach (immunizing 11- to 14-year-old girls). Unfortunately, data on the efficacy of the British approach are generally lacking, but at a 1976 meeting on the subject it was stated that in the face of a 72% vaccination rate in the target population, the incidences of rubella and congenital rubella remained unchanged. However, in a recent serologic survey 93% to 96% of women born after 1956 (who would have been offered rubella vaccine in school) were found to have antibody. On the other hand, it is clear that the U.S. approach, whatever its own shortcomings, has not only dramatically reduced the incidence of rubella but also has significantly impeded the epidemic potential of the disease: since 1969, there have been no epidemics in U.S. children. A major concern with the U.S. approach was whether immunity would wane over the years; thus far, rubella vaccine apparently has remained effective, although the possibility that natural challenge has boosted immunity in vaccinees cannot be ruled out.



Data from Massachusetts, New York City, and Illinois indicate that rubella vaccination has controlled the disease in patients aged 14 and younger but not in those in the 15-to-19 age group.

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In the United States, one potential problem that militated against immunizing girls 11 to 14 years or older was the possibility that pregnant or soon-to-be-pregnant subjects (and their fetuses) might be inadvertently exposed to the virus. Concern about this was (and probably still is) so great that many physicians were discouraged from vaccinating older susceptible female patients; too often, the prudent recommendation that serologic testing be performed before vaccination of any female adolescent or adult became, rather than a tool to promote appropriate rubella immunization, a deterrent to any immunization at all—whether serologic testing was available or not.

In this regard, it has turned out that more than 300 pregnant women *were vaccinated* inadvertently in the United States during the past 10 years or so. In most cases, pertinent serologic data are absent, but we do know of about 70 infants born to previously seronegative women who had been immunized during or shortly before pregnancy. No infant had any obvious congenital malformations, but there were two with evidence of subclinical in utero infection (elevated rubella-specific IgM in one and elevated IgG at age 24 months in the other). Moreover (echoing studies performed prior to widespread rubella immunization), rubella virus has also been found in the products of some aborted pregnancies in previously susceptible women vaccinated during pregnancy. Thus far, the overall observed risk of malformation has been zero, but the actual risk is probably greater; it has been estimated at no more than 5.4%, which contrasts with a risk of at least 30% from natural infection.

In considering the reasons for rubella susceptibility in older U.S. age groups, another point that needs to be recalled is that four different rubella vaccines have been used in this country. At present, the only one currently licensed is the RA27/3 (available since January 1979), which is derived from human tissue culture—a reason for initial reluctance to use it. Field trials and four- to seven-year follow-ups of this vaccine have indicated a failure rate of about 3%. Of the other vaccines, the HPV77 DK12 strain (used from 1969 to about 1973) and the Cendehill strain (used from about 1970 to 1976) have had similar or perhaps slightly higher failure rates. But neither of these vaccines was very widely used in this country. Through 1978, most U.S. vaccinees received the HPV77 DE5 strain, and for this vaccine the failure rate was similar to the other vaccines. Of the four vaccines, geometric mean antibody titers have been the highest with the currently licensed (RA27/3) vaccine.

Does low or undetectable rubella antibody after vaccination mean susceptibility to reinfection? First of all, reinfection has been noted in patients with vaccine-induced or natural antibody, and the lower the titer, in general, the greater the likelihood of reinfection. But no study to date has documented illness or viremia in reinfected patients, nor is there evidence that an asymptomatically and aviremically infected mother can transmit infection to her fetus, although the possibility remains that such a patient might transmit infection, through pharyngeal excretion of virus, to another susceptible individual and thereby jeopardize herd immunity. IgM and IgG characterization of antibody response in vaccinees with low or absent titers might indicate whether they have partial immunity to natural disease, but in this regard H. H. Balfour Jr. and D. P. Amren have reported that RA27/3 revaccination in a small group of former HPV77 DE5 recipients resulted in boosterlike rises in rubella HIA titers from low or undetectable levels and that high titers were maintained for at least 10 weeks thereafter.

What about adverse reactions to rubella vaccine? In children, skin rash and lymphadenopathy occasionally occur, and transient pain in peripheral

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small joints has been common in some studies. Joint symptoms (arthralgia and transient arthritis) appear to be more frequent and more severe in susceptible female adults than in children, but they are generally short-lived (beginning two to 10 weeks after immunization and lasting one to three days) and rarely recur. Aside from pregnancy, the major contraindications to rubella vaccination (which are similar to those for measles immunization) include immune-deficiency diseases or suppressed immune response occurring in leukemia, lymphoma, and generalized malignancy or when steroids, alkylating agents, antimetabolites, or radiation are being used; patients with febrile illnesses should not be vaccinated until they have recovered.

Where does all of this lead us? The first point is that we should continue to improve rubella immunization rates in children, extending protection to well over 90% of that population and as close to 100% as possible. The second point is simply that the same goal should apply to susceptibles in older age groups.

Since more than two thirds of reported rubella cases in the United States involve patients in their mid-teens or older, since almost one third of the pediatric population was never covered by rubella immunization programs, since a history of rubella immunization (without documentation) is likely to be an unreliable index of immunity in older persons, and since many older individuals are already immune to rubella, comprehensive serologic screening programs to identify susceptibles would seem to be in order—all the more so as time passes and the "herd" of adolescent and adult susceptibles grows. It may be argued that screening for older female susceptibles should be emphasized (as a mandatory part of school entrance requirements and in premarital screening programs, prenatal clinics, or family planning centers, for example); older male susceptibles should not be ignored, however, and will probably require equal attention in schools and colleges, the military, and places of employment if the epidemic potential of the disease in older age groups is to be blocked. Perhaps nowhere is the need for identifying susceptibles more pronounced than in hospitals (staff and patients), but the risk of rubella (and, ultimately, congenital rubella syndrome) exists wherever older seronegative individuals congregate.

If recent U.S. experience with rubella (and measles) has taught us anything about immunoprophylaxis and herd immunity, it is that our national population is not one herd, monolithic and static, but several herds, each responsive to its own epidemiologic dynamics. Levels of immunity achieved in one herd—no matter how high—may not be protective for another herd; rather, they may simply reveal how unprotected some herds are (adolescents and young adults), as compared with others (preschoolers and most prepubertal children). Clearly, herd immunity in the United States today is not strictly comparable to that in Baltimore during the first 30 years of this century.

A conservative, watch-and-wait approach to recent shifts in the age-specific incidences of rubella and measles may arguably be advocated, especially when one considers that surveillance programs for each disease are poor and need to be improved in order to provide better data, identify developing outbreaks, and facilitate their management. Certainly, the dollar commitment that would be necessary to control these diseases more fully is awesome—and so, too, the logistics of implementation and enforcement. On the other hand, the available evidence suggests that these diseases may be time bombs. And the costs of an explosion could far exceed those of defusing them now. □

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Rubella Susceptibility in Sixth Graders: Effectiveness of Current Immunization Practice

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ABSTRACT. Rubella hemagglutination inhibition antibody titer was determined for 702 sixth grade students from nine randomly chosen schools in a community served well medically. Rubella immunization had been given by private physicians, the health department, hospital clinics, and through a mass immunization effort in 1970. The overall susceptibility rate, as defined by a rubella hemagglutination inhibition titer of less than 1:8, was 15%. Susceptibility did not differ significantly in regard to sex, race, or source of vaccine. Of 469 children with a documented rubella immunization, 13.2% were susceptible or vaccine failures. Menarche was reported by 30% of the girls. To increase the level of protection against rubella during the childbearing years, continued emphasis on early childhood immunization combined with consideration of a booster rubella immunization for preadolescents is recommended. *Pediatrics* 65:1086–1089, 1980; *rubella, rubella vaccine, immunization policy, vaccine failure, serologic survey.*

The major clinical sequelae of rubella are the fetal wastage and anomalies of the congenital rubella syndrome that occur with rubella infection in early pregnancy. Thus, prevention of infection in the fetus is the principal goal of the rubella immunization effort.[1] As a means of ensuring this protection, Krugman[2] suggested that the feasibility of administering rubella vaccine to all girls entering the sixth grade be considered.

In previous serologic surveys of rubella vaccinees, protective antibody response has been reported in more than 95% of susceptible children who are immunized after 12 months of age.[3] In these studies, vaccine was administered to the recipients by the investigators under well-controlled circumstances. Less well studied is the effectiveness of the vaccine when administered by a variety of providers under variable conditions.

Knowledge of the level of rubella susceptibility among sixth grade students is necessary to determine the feasibility of recommending rubella vaccine for all girls at the sixth grade level. It also serves as a measure of the effectiveness of immunization practice in a community when carried out by a variety of health providers. To provide this data, a serologic survey of public school sixth grade children was done.

METHODS

In Winston-Salem, NC, an urban community of 140,000 population that is well served medically, children have received rubella vaccine since 1969 from several providers: various private physicians, health department clinics, and a mass rubella immunization effort in 1970. Serologic screening by rubella hemagglutination inhibition (HI) antibody titer was offered to all sixth grade students in nine schools selected randomly from the 18 schools with sixth grades. Parents who granted permission for their child's participation in the study reported by questionnaire the age, sex, and race of their child, history of clinical rubella, type of immunization received, date and source of the immunization, and for girls, history of menarche.

School immunization records of participants and nonparticipants were reviewed for documentation of rubella immunization. Participation of the student in the school free lunch program was used as an identifier of lower income families. In the Win-

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A team consisting of two or more physicians, school health nurse, and school health assistant visited each of the nine schools for blood collection. A specimen of 10 ml of whole blood was collected, spun down, and the separated serum was frozen. Rubella HI titer was determined by the Virology Laboratory of the North Carolina Division of Health Services. This laboratory regularly participates in Communicable Disease Center proficiency testing and performs 50,000 HI antibody titers annually. An HI antibody titer of less than 1:8 was considered indicative of susceptibility to rubella.[15] Parents and physicians of susceptible children were informed of the test results. Parents of susceptible children were urged to contact their child's physician or clinic for advice about rubella immunization. Statistical analysis was done by χ^2 test.

RESULTS

Of 1,400 sixth grade students in the nine schools, 702 (50%) received parental permission for participation. In only two of the nine schools was participation less than 50%. Analysis of the data from the schools with less participation did not differ significantly from the schools with higher participation. Therefore, the results were combined. Of the participants, 47.4% were boys and 52.6% girls; 69.5% were white and 30.5% nonwhite; 24.6% were from low-income families as defined by enrollment in the free lunch program. The demographic characteristics of participants compared to the entire sixth grade of 2,990 students are shown in Table 1. Participants did not differ significantly from the entire sixth grade population in regard to sex or race. The study population had significantly fewer low-income students ($P < .01$), than did the entire sixth grade. The mean age of participants was 11.4 years. A history of menarche was given by 30% of the girls in the study.

Overall susceptibility rate to rubella was 15%. As shown in Table 2, male students, white students, and higher income students showed a greater serologic susceptibility to rubella than did the female,

TABLE 1. Demographic Characteristics of Participants Compared to Entire Sixth Grade

	Participants	Total 6th Grade
No.	702	2,990
Boys	47.4%	51.5%
Girls	52.6%	48.5%
White	69.5%	66.5%
Nonwhite	30.5%	33.5%
Free lunch (low income)*	24.6%	30.0%

* $P < .01$ by χ^2.

TABLE 2. Susceptibility Rate by Sex, Race, and Income

	Susceptible (%)
Boys	16.5
Girls	13.6
White	16.0
Nonwhite	12.6
Free lunch (low income)*	10.2
Nonfree lunch	16.5
Overall susceptibility	15.0

* $P < .05$ by χ^2.

TABLE 3. Susceptibility Rate by Source of Vaccine

Source	Susceptible (%)
Private physician	12.5
Health department	12.1
Mass immunization	16.6
Unspecified clinic	16.7

nonwhite, and low-income students. By χ^2 analysis, there was no significant difference in susceptibility rate by sex or race. The difference between free lunch and non-free-lunch participants was statistically significant ($P < .05$).

It was possible to identify the source of rubella vaccine for 58.0% of the participants. The susceptibility rate did not differ significantly among the various sources of the vaccine as shown in Table 3. A history of rubella immunization was given by 78.5% of participants. The susceptibility rate was significantly lower (13.4%) in those with a history of immunization, whether it was documented or not, than in those without a history of immunization (20.5%).

Rubella immunization was documented by home or school record in 469 (66.8%) of the participants. Of these, 62 were susceptible, giving a vaccine failure rate of 13.2%. These 62 students made up 59.0% of the total number of susceptible students. For students in whom rubella immunization could not be documented, the susceptibility rate was 18.5%. The 85% of students with protective titers consisted of 7.1% with an HI titer of 1:8, 21.4% with 1:16, and 56.5% with 1:32 or greater.

DISCUSSION

Prior to rubella vaccine, rubella occurred with a pattern of epidemic spikes every six to nine years with peaks of 100 to 500 cases per 100,000 population.[4] Since the introduction in 1969 of rubella vaccine, the number of reported rubella cases in the United States has declined dramatically to less than ten cases per 100,000 population annually. There has been a parallel decrease in the reported cases of congenital rubella syndrome.[5]

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In the United States, immunization policy has been to routinely immunize children 1 to 12 years of age and to selectively immunize susceptible women of childbearing age who are not pregnant and who will avoid pregnancy for a three-month period following immunization.[4] The vaccine has been used primarily for preschool children and early elementary school children. Since the adoption of this immunization policy, the incidence of reported rubella in adolescents and young adults has not decreased significantly. In contrast to the prevaccine era when 60% of rubella cases occurred in children below 9 years of age, since 1976, more than 70% of reported cases have been in individuals 15 years of age and older.[5]

The present study found that 15% of sixth grade students are susceptible to rubella. Conversely, 85% show serologic evidence of protection as defined by an HI titer of 1:8 or greater. This finding from an urban community that is well-served medically may be a higher rate of protection than actually exists in areas not served as well. By comparison, a prevaccine survey of Cincinnati school children in 1968 reported a 26% susceptibility rate in sixth grade students and an identical rate for grades 7 through 12.[6] In other studies of the prevaccine era, a range of 10% to 25% susceptibility rate to rubella was observed in adolescents and young adults.[6] The success of the current immunization program in decreasing the occurrence of rubella in very young children may be a factor in allowing unimmunized children to reach adolescence without the immunity of exposure to natural rubella virus.

Of the 469 students who had a documented rubella vaccination, 13.2% had a HI antibody titer of less than 1:8. These students, defined as vaccine failures, accounted for 59% of those susceptible to rubella. Schiff et al,[9] reported a 13.3% vaccine failure rate in a 1972 survey of first grade children. It cannot be determined from the present study whether this represents a failure of initial seroconversion or a loss of antibody over time. When vaccine is administered by a variety of providers the opportunities may be greater for use of an ineffective lot of vaccine, improper storage of vaccine, or improper timing of the vaccine. Horstmann[3] reported that among initial seroconverters, there is a group of responders with low antibody titers of 1:16 or less. From this group she found a 26% loss of detectable serologic evidence of immunity within five years after immunization.

A limitation of any serologic survey is the definition of protection or susceptibility by quantitative antibody response. Vaccine efficacy is really only borne out by response in vivo to exposure to natural virus and may not perfectly correlate with serologic susceptibility. For individuals who have seroconverted, whether from vaccination or natural rubella, but whose titer has declined to less than 1:8, there is evidence to suggest that upon re-infection with rubella, viremia is an unlikely event.[5] Unfortunately, the subgroup of serologically susceptible individuals who so respond to re-infection is not identifiable by practical means, nor is the actual risk of viremia known.

In the previously mentioned survey of first grade children, Schiff et al[9] found a susceptibility rate of 35% in the low socioeconomic group compared to 14.2% and 14.9% in the middle and high income groups, respectively. This is in contrast to our findings. Acknowledging the limitation of free lunch participation as a rather crude socioeconomic indicator, the lower income students in our survey were less susceptible than upper income students, 10.2% vs 16.5%, respectively. This difference may represent an increased opportunity for natural immunity among lower income children, or possibly improved access to health services. It may also represent a study bias in that lower income children are slightly under-represented among participants. Those lower income participants whose parents gave permission may be those most likely to have received immunizations. School records of nonparticipants were reviewed for rubella immunization, but were not complete enough to allow valid comparison.

The finding of a 13.2% susceptibility rate in students with a documented immunization compared to 18.5% in students without documentation emphasizes the importance for physicians, health departments, and schools to insist on adequate documentation of rubella vaccine. State immunization laws need to require documentation of immunizations for students in all grades, not just at school entrance.

Duration of vaccine-induced immunity is a critical factor in determining rubella immunization strategy. In a 7½ year follow-up of rubella vaccinees, Schiff et al[10] reported a downward trend in titers and loss of detectable antibody in a few students who received either HPV-77, DK-12, or Cedenhill vaccine. While current immunization policy has been successful in protecting many children against rubella, a level of protection has not been achieved, particularly in older children and adolescents, that will prevent future outbreaks of rubella. It has been demonstrated that even protection rates as high as 86% will not prevent introduction and spread of rubella virus,[11] making it unlikely that the circulation of wild virus can be prevented by present immunization strategy.

The effect of current immunization practice to shift to adolescence the majority of rubella cases at a time when vaccine-induced immunity may be dwindling causes concern that the potential risk of congenital rubella may actually be increased, although this has not been observed in terms of

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reported cases. As a strategy for further reducing the susceptibility rate during the childbearing years, a recommendation for routine primary or booster rubella immunization of preadolescent girls should be considered in addition to the current emphasis on early childhood immunization. Because of their role in recent outbreaks,[12] consideration should be given to immunizing preadolescent boys as well.

In a benefit-cost analysis of rubella immunization policy, Schoenbaum et al[13] projected both economic advantage and greater reduction in congenital rubella through vaccination of girls at age 12 years in comparison to vaccination of children at age 2 years, assuming 80% acceptance of vaccine by the target groups. The strategy of vaccination of children at age 2 years combined with vaccination of girls at age 12 years gave the greatest potential reduction in congenital rubella, but was less advantageous economically than vaccination only at age 12 years.[13] The assumptions and estimates on which this analysis was based may not be accepted by everyone.

The finding of 30% of sixth grade girls having reached menarche is a major obstacle to a recommendation for routine rubella immunization at this grade level. Serologic testing of 30% of girls at this age is impractical and costly, yet immunization of postmenarchal girls raises concern about inadvertant vaccination of possibly pregnant students. Although evidence from a small number of cases suggests that the risk to the fetus of congenital malformation is very small, if any, when rubella vaccine is given during pregnancy,[14] it is not possible at present to dismiss concern about this risk. As an alternative, giving the vaccine at the fourth or fifth grade level would reduce the likelihood of pregnancy being present in a vaccine recipient. The development of arthralgia following rubella immunization has occurred primarily in postpubertal girls and should be an infrequent adverse effect in this age group.

The recent licensing in the United States of RA 27/3 strain of rubella vaccine is another factor in consideration of a change in immunization policy. It has better immunogenicity than previous rubella vaccines,[15] and thus may improve the immune status of future adolescents who receive it in early childhood. Monitoring of the long-range effect of this vaccine on susceptibility during childbearing years as well as study of the actual, as opposed to theoretical, effect of a second rubella immunization in preadolescents are needed to guide decision-making about immunization strategy.

SUMMARY

The finding in the present study of 15% of sixth grade students susceptible to rubella, a rate similar to that of the prevaccine era, indicates the need for additional measures to reduce the risk of congenital rubella syndrome. Adoption of a policy of routine primary or booster rubella immunization of preadolescents should be considered in an effort to enhance protection during the crucial childbearing years. The questions that remain unanswered as to long-term duration of rubella antibodies, the meaning of declining titers, and the risk to the fetus of maternal re-infection with rubella indicate a need for continued serologic monitoring to determine the effectiveness of rubella vaccine and of immunization practice.

ACKNOWLEDGMENTS

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The authors are grateful for the contributions of Pansy Whicker, School Health Coordinator, the school health assistants of Winston-Salem/Forsyth County Schools, the school health nurses of Forsyth County Health Department, and the Virology Laboratory of the North Carolina Division of Health Services.

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#21

THE JOURNAL OF PEDIATRICS

JANUARY 1971 Volume 78 Number 1

Interesting — hints at many of the specifics of immunologic reactions

MEDICAL PROGRESS

Present status of measles and rubella immunization in the United States: A medical progress report

Saul Krugman, M.D.

NEW YORK, N. Y.

EXTRAORDINARY progress as well as anticipated and unanticipated problems have occurred in the wake of the development and licensure of measles and rubella vaccines. This medical progress report will review the present status of the safety and efficacy of these vaccines for the control of measles and rubella.

From the Department of Pediatrics, New York University School of Medicine.

The Willowbrook studies on measles described in this report were conducted in collaboration with Dr. Joan P. Giles.

The measles vaccine studies were supported by the Health Research Council of the City of New York under Contract No. U-105c.

Presented in part at the Annual Meeting of the American Academy of Pediatrics, San Francisco, Calif., October 19, 1970, and at the Pan American Health Organization, World Health Organization International Conference on the Application of Vaccines Against Viral, Rickettsial, and Bacterial Diseases of Man, Washington, D. C., Dec. 14-18, 1970.

Reprint address: 550 First Ave., New York, N. Y. 10016.

MEASLES

The isolation of measles virus by Enders and Peebles,[1] its adaptation to the chick embryo by Milovanović and associates,[2] and its subsequent attenuation by Katz and associates[3] were followed by the development and licensure of 2 measles vaccines in the United States in 1963: live attenuated measles-virus vaccine (Edmonston B type) and formalin-inactivated alum-precipitated vaccine.[4] At the time of licensure it was obvious that febrile reactions caused by live Edmonston B vaccine occurred too often and were too severe to justify routine use of the vaccine as an immunizing agent. Consequently, many physicians preferred to administer the vaccine with a simultaneous inoculation of measles immune globulin. Other physicians chose to use either killed measles vaccine or a combined killed-live measles vaccine regimen. However, by 1967 it was apparent that the immunogenic and

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protective effects of inactivated measles vaccine were transient. Moreover, atypical measles with manifestations which were suggestive of delayed hypersensitivity occurred in recipients of killed vaccine when they were exposed to live measles virus months or years later.[5-7] The clinical manifestations of these reactions included high fever, an atypical rash, edema of the extremities, pneumonitis, and occasionally pleural effusion and abdominal pain.

Inactivated measles vaccine is no longer available for use in the United States. Two live further attenuated vaccines* are used extensively in this country. These vaccines, derived from the Edmonston strain, were produced by additional chick cell passages at a lowered temperature. The Schwarz strain vaccine was developed in 1961 and licensed for use in February, 1965. The "Moraten" vaccine was licensed in 1968. These further attenuated vaccines are less reactive and more acceptable than the original Edmonston B vaccine. However, the antibodies which they induce decline more rapidly and persist at a lower level than those observed after natural measles infection or immunization with Edmonston B vaccine.

Six months after the further attenuated vaccine, Schwarz strain, was licensed for use in the United States, an editorial in the *New England Journal of Medicine* expressed concern about the potential long-term efficacy of this preparation.[8] It stated, in part, "In contrast to the antibody plateau resulting from natural measles or Enders' Edmonston B vaccine, a prolonged decline in antihemagglutinating antibody follows Schwarz further attenuated vaccine. . . . The progressive decline in antibody observed during the first 2 years after vaccination with further attenuated vaccine suggests that a qualitative difference in immunogenicity between these vaccines may exist and raises the possibility that if this decline continues at the same rate, resistance to infection will eventually be lost."

This editorial caused unnecessary confusion and uncertainty about the efficacy of further attenuated measles vaccine. Shortly after its publication additional data became available indicating that measles antibodies had persisted for at least 3 years after vaccination with the further attenuated vaccine (Schwarz strain). A subsequent editorial in the same journal stated, "In the light of these more recent findings, physicians and public health officers can be reassured that the currently available licensed measles vaccines, Edmonston B type and further attenuated type, appear to be effective for the prevention of measles."[9]

How does one reconcile this favorable prediction in 1965 with reports in 1969 describing the occurrence of measles in previously immunized children?[10-12] Before commenting on these reports it is important to record the present status of our studies on immunity to measles, which have been in progress since 1960.[13, 14] Our observations have been made in 2 groups: (1) institutionalized children at the Willowbrook State School and (2) home-dwelling children of the East Nassau Health Insurance Plan group. The routine use of measles vaccine for all susceptible children at Willowbrook eradicated the disease in this institution by 1963; no cases have occurred since that time. Consequently, immunized children in this institution have not been exposed to measles during the past 7 years. In contrast, at least 37 per cent of the Health Insurance Plan home-dwelling children have had repeated exposures to measles during the 8 to 8½ year postvaccination period of observation.

Persistence of measles antibody in institutionalized children following natural infection and immunization. Serial samples of serum were obtained from 68 children who had natural measles between 1960 and 1962: 46 children who received live attenuated measles vaccine, Edmonston type, during the period February, 1960, to March, 1962; 40 children who received the Edmonston-type vaccine plus immune serum globulin from

*Commercially available as Liruqen, Pitman-Moore Co., Indianapolis, Ind., and Moraten, Merck Sharp & Dohme, West Point, Pa.

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October, 1960, to October, 1961; and 115 children who received further attenuated measles vaccine, Schwarz strain, from November, 1961, to March, 1963. All serum specimens were tested for measles antibody by the highly sensitive hemagglutination-inhibition test described by Norrby.[15]

The results of the 8 to 10 year follow-up are illustrated in Fig. 1. The pattern and persistence of the antibody responses were similar for all 4 groups. The simultaneous administration of gamma globulin and Edmonston-type vaccine was associated with a decrease in the geometric mean antibody levels. The use of Schwarz strain vaccine was also associated with antibody levels which were lower than those observed after natural infection or after Edmonston B vaccine. All children who participated in this study had detectable measles antibody during the 8 to 10 year follow-up period of observation. Only one of 115 children who received Schwarz strain vaccine had no detectable antibody 7 years after vaccination (Fig. 2).

Persistence of measles antibody in home-dwelling children following immunization with live further attenuated measles virus vaccine (Schwarz strain). During an 8½ year follow-up of 210 children, more than 37 per cent of this group were exposed to measles without developing clinical evidence of the disease. All 56 children who were tested at 8½ years had detectable measles hemagglutination-inhibition antibody; the geometric mean titer was 1:60 (Fig. 3).

A comparison of geometric mean antibody titers in the home-dwelling children who had repeated exposures to measles with titers in institutionalized children who were not exposed is shown in Fig. 4. The significantly higher titer at 8 years in home-dwelling children, 1:60, as compared with the lower

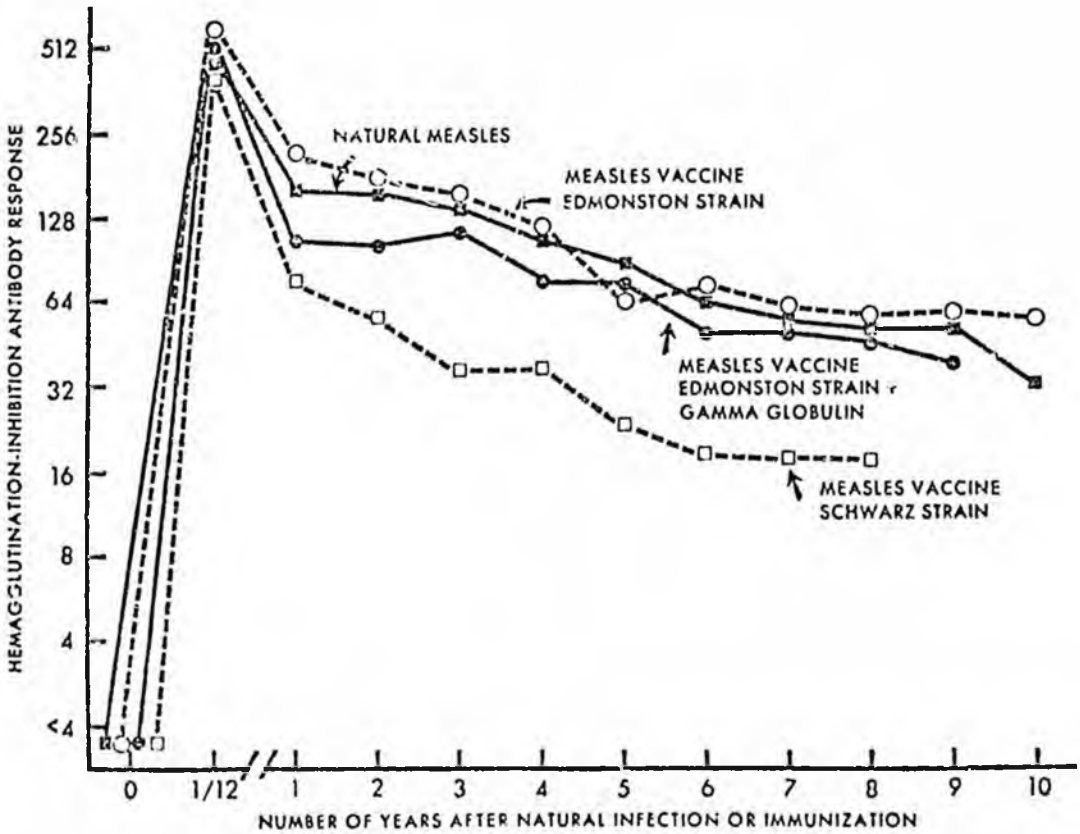


Fig. 1. Geometric mean hemagglutination-inhibition antibody titers following natural measles infection and vaccination with live attenuated measles virus vaccines, (a) Edmonston strain, (b) Edmonston strain plus gamma globulin, and (c) Schwarz strain.

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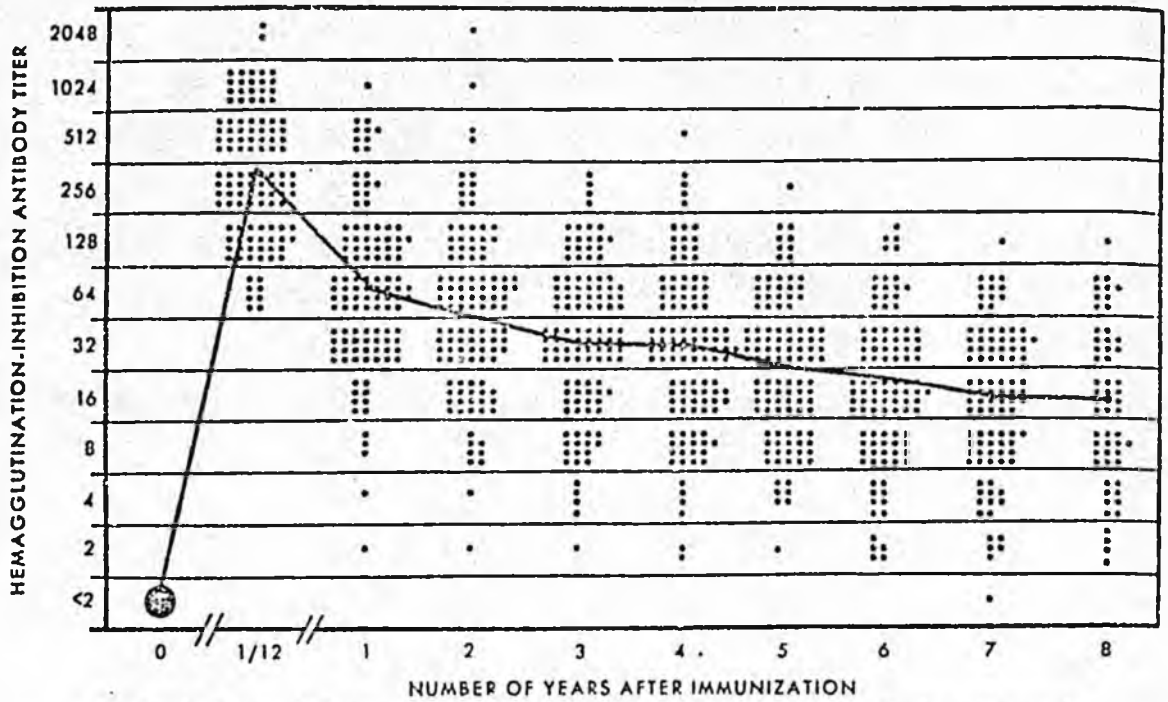


Fig. 2. An 8 year follow-up of institutionalized children who received live further attenuated measles virus vaccine, Schwarz strain. The black dots represent the individual hemagglutination inhibition antibody titers and the solid line represents the geometric mean antibody titer.

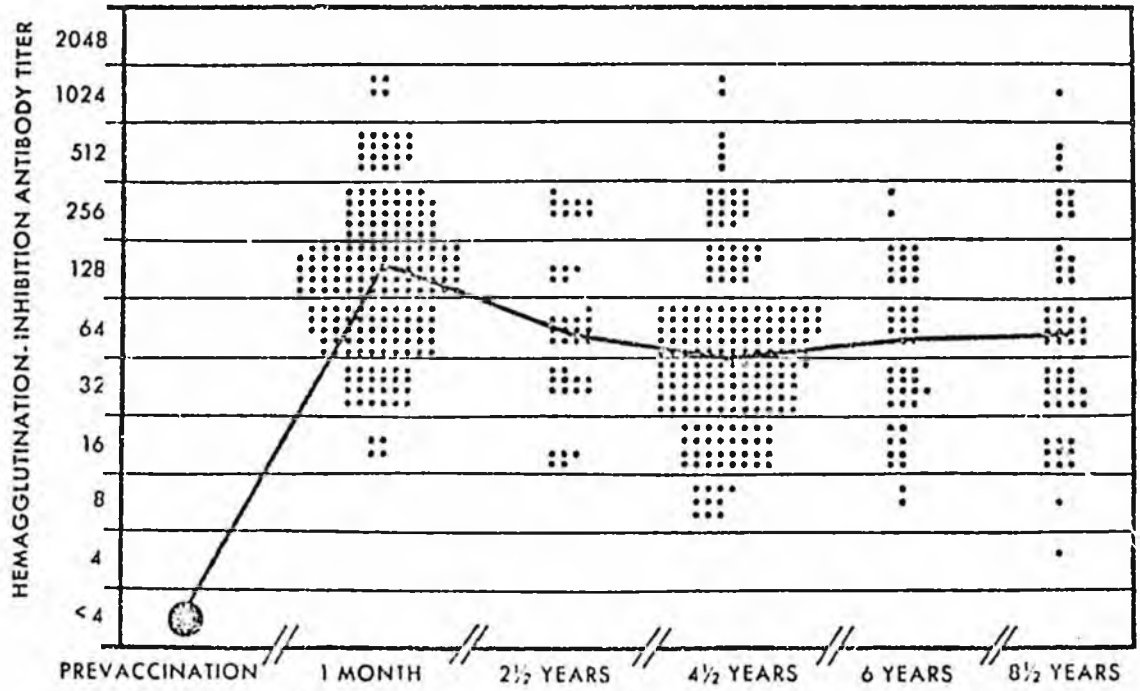


Fig. 3. An 8½ year follow-up of home-dwelling children who received live attenuated measles vaccine, Schwarz strain, and 0.2 ml. of gamma globulin. These children had repeated exposures to measles, unlike the institutionalized children (Fig. 2) who had no exposure.

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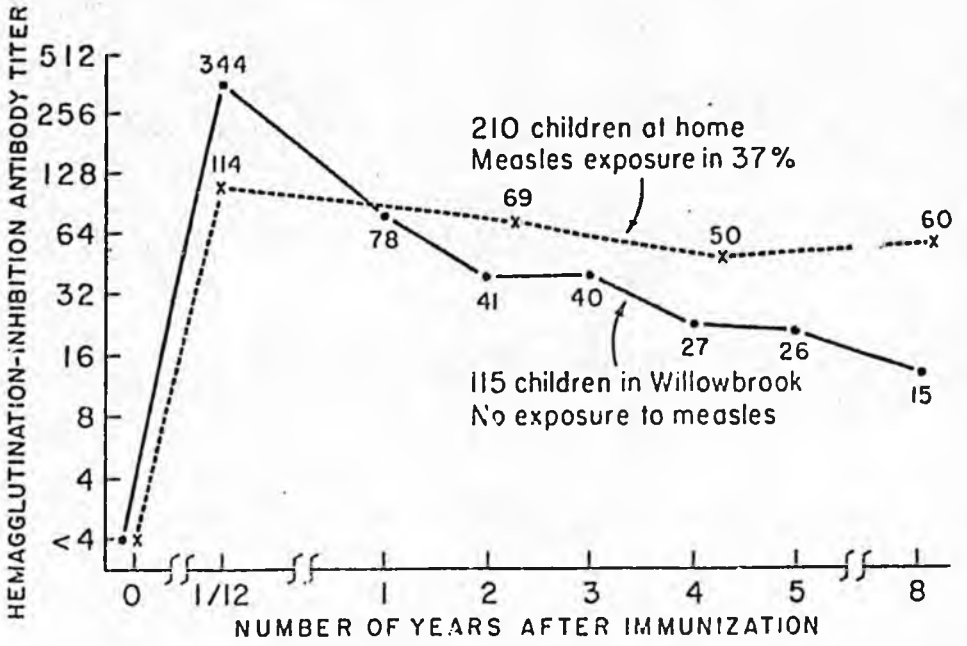


Fig. 4. Comparative geometric mean antibody titers of the institutionalized and home-dwelling children depicted in Figs. 2 and 3.

titer of 1:15 in the institutionalized children probably reflects a booster response associated with reinfection following exposure to wild measles virus. In spite of repeated exposures to measles, the Health Insurance Plan children were solidly protected against the clinical disease.

The typical antibody response following primary infection of 10 children with live attenuated measles virus is shown in Fig. 5. Hemagglutination-inhibition antibody was first detectable on the tenth day, and peak levels were observed by the twenty-seventh day. In contrast, reinfection of 25 previously immunized children was characterized by an initial rise of hemagglutination-inhibition antibody on the first day; peak levels were observed as early as the twelfth day. The phenomenon of reinfection with booster response has been seen typically in children with low hemagglutination-inhibition antibody titers (less than 1:64); it has not usually been observed in the presence of relatively high antibody titers (exceeding 1:128).

The available evidence indicates that following the priming that occurs with the initial measles virus infection, any subsequent reinfection will be characterized by a booster type of antibody response. Panum, in his classic description of the epidemic of measles in the Faroe Islands in 1846, observed that all old people who had measles in the previous epidemic in 1781 were protected against the disease in spite of lack of exposure during the intervening period of 65 years. This experience demonstrated that repeated exposure was not an essential prerequisite for permanent immunity to measles.

Our longitudinal studies on immunity to measles have provided evidence to support the prediction that live vaccine-induced immunity will be just as protective against clinical measles as naturally acquired immunity. We have never seen a case of measles in a child who was shown to have an antibody response following immunization with live measles vaccine.

Measles in previously immunized children. The reported cases of "measles in previously immunized children" probably represent failure to achieve a primary live vaccine-virus infection because of one or more of the following factors: (1) Administration of vac-

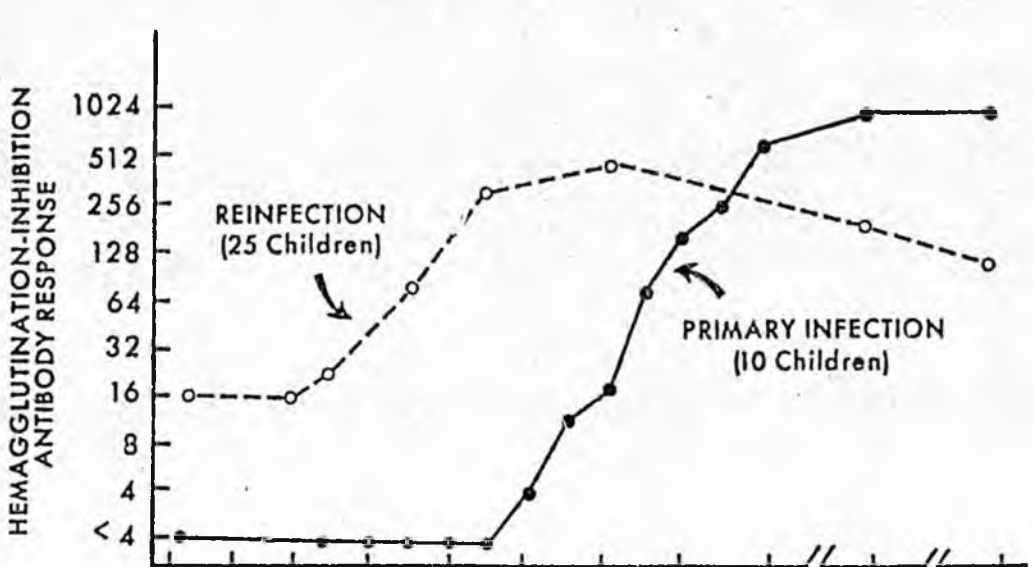


Fig. 5. Pattern of hemagglutination-inhibition antibody response following primary infection and reinfection with live attenuated measles vaccine. The hemagglutination-inhibition antibody titers represent mean levels of 10 children with primary infection and 25 with reinfection. Note booster response associated with reinfection.

cine before 12 months of age when maternal measles antibody may have been present. Suppression of the antibody response is most apt to occur when measles immune globulin is given with the vaccine to an infant with residual transplacentally acquired antibody. (2) Administration of vaccine virus which may have been inactivated by inadequate refrigeration, by excessive exposure to light, by use of the wrong diluent containing a potentially virucidal preservative, or by unknown factors. Currently licensed live measles vaccines have been characterized by a seroconversion rate of approximately 98 per cent. Consequently, it is reasonable to anticipate a 2 per cent attack rate in children who were inoculated but not immunized with measles vaccine.

The effect of age on the antibody response of children to live attenuated measles vaccine (Edmonston B with immune serum globulin) is shown in Table I. Among infants 9 to 11 months of age, 86 per cent had a hemagglutination-inhibition antibody response. In contrast, the seroconversion rate in children who received vaccine after 12 months of age was 97 per cent. This study highlights the importance of following the current recommendations of the American Academy of Pediatrics Committee on Infectious Diseases: "In general live measles vaccine should be administered at about 12 months of age or shortly thereafter." In certain developing countries and in certain epidemic situations it may be wise to immunize infants between 6 and 12 months of age. However, under such circumstances a second inoculation of vaccine should be given after 12 months of age to protect infants who failed to respond to the first inoculation.

Table I. Measles hemagglutination-inhibition antibody response in infants and children who received live attenuated measles virus vaccine, Edmonston Type, plus gamma globulin

Age group (months)	*No. of children vaccinated*	*Hemagglutination-inhibition antibody response*	
		No.	*Per cent*
9-11	123	106	86
12 or more	899	872	97

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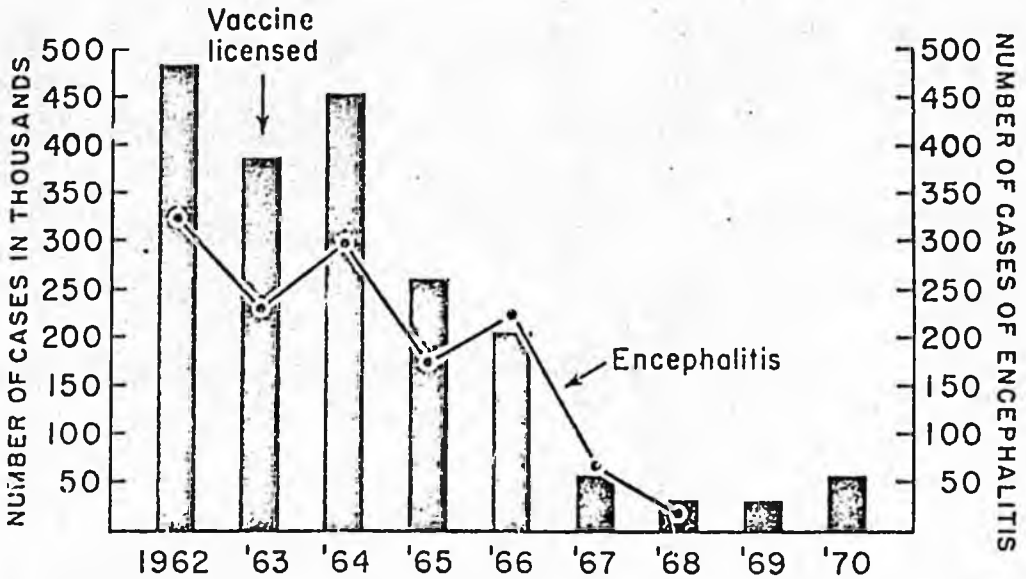


Fig. 6. Reported cases of measles and measles encephalitis in the United States from 1962 to 1970.

The causes of vaccine failure have varied during the reported outbreaks.[10-12] The Governor's Island report[10] identified 73 cases of measles of which 11 (15 per cent) were in previously immunized children and 62 (85 per cent) in those who were unimmunized. However, the attack rate was 2.4 per cent in previously immunized children and 33.5 per cent in unimmunized children; over-all vaccine efficacy was 92.7 per cent. The report from Florida[11] highlighted the occurrence of measles in 18 children who received live measles vaccine and immune serum globulin before they were 12 months of age. The Ohio report[12] involved 14 previously immunized children and 46 who were not vaccinated. The attack rate in the unimmunized group was 52.4 per cent, whereas that of children immunized by the local health department was 1.2 per cent; vaccine efficacy was 99 per cent. However, 17.9 per cent of the children previously inoculated by one private physician in the same city developed measles, a vaccine efficacy of only [illegible] per cent. The measles vaccine in this physician's office was exposed to temperatures which may have caused a decrease in vaccine potency.

Present status of live measles vaccine. Prior to licensure of live attenuated measles vaccine in March, 1963, approximately 500,000 cases of measles and 300 to 400 cases of encephalitis were reported in the United States each year. The extensive use of vaccine has been followed by a dramatic decline in the incidence of measles and encephalitis (Fig. 6). An all time low was reached in 1968 and 1969 when approximately 25,000 cases were reported, a decreased incidence of 95 per cent. The rising incidence of measles in 1970 has not been related to vaccine efficacy but rather to a failure of delivery of health care to infants and children from various poverty areas. The occurrence of measles in previously immunized children is not a result of waning immunity.

The dramatic decline in the incidence of measles encephalitis has been very reassuring. It is obvious that the risk of encephalitis following natural measles infection, approximately one per 1,000 cases, is significantly greater than the risk of vaccine-associated encephalitis, estimated to be about one per one million vaccinees. The incidence of encephalitis of unknown etiology in the United States in 1968 was 1.2 cases per one million children, one to 9 years of age.[10] It seems clear that postvaccination encephalitis has not been an important problem.

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The association of subacute sclerosing panencephalitis with natural measles has been well documented.[17] This late neurologic sequela of measles is very rare. It will be difficult to assess the risk of subacute sclerosing panencephalitis without knowledge of the immune status of a child prior to vaccination. During the course of our studies we detected serologic evidence of immunity to measles in approximately 15 per cent of children, 3 to 8 years of age, in spite of the fact that their parents denied a prior history of measles.[18] The extensive use of live measles vaccine during the past 7 years has not been associated with an apparent increased incidence of subacute sclerosing panencephalitis.

Conclusion. At the present time 2 safe, potent, and highly effective live measles vaccines are licensed for use in the United States.* The control of measles will depend on the appropriate use of these vaccines. It will be essential to include the oncoming as well as the present generation of susceptible infants and children in routine immunization programs.

A single dose of vaccine should provide long-term immunity against measles for approximately 98 per cent of inoculated children. The available evidence indicates that reinfection of persons with low levels of antibody has no clinical significance. The booster response induced by reinfection has not been associated with clinical manifestations of the disease.

Measles will continue to occur among the small group of children (approximately 2 per cent) who may be at risk because of failure to respond to an inoculation of vaccine. The solution to this problem is complex. It would be difficult to condone the routine use of a second dose of vaccine because 98 per cent of children are likely to be protected by one inoculation. Many millions of dollars would be wasted each year for the unnecessary vaccination of immune children. It would be more appropriate to use these funds for the solution of other critical health problems.

*Lingen and Moraten. Lingen is the trade name for live further attenuated Schwarz strain vaccine, a product of the Pitman-Moore Co., Zionsville, Ind. Moraten is the trade name of more attenuated Enders' Edmonston virus, a product of Merck Sharp & Dohme, West Point, Pa.

RUBELLA

The extensive epidemic of rubella in the United States in 1964 and its serious consequences have been well documented.[19] The epidemic was responsible for the death and disability of many thousands of infants and for the anguish and despair of their parents. The cost in terms of hospitalization, medical care, rehabilitation, and special education for the multihandicapped survivors has been estimated to exceed 2 billion dollars. This devastating experience highlighted the need for an effective vaccine as the most logical solution of the rubella problem. The extraordinary progress toward this goal was revealed at the International Conference on Rubella Immunization which was held February 18 to 20, 1969.[20]

The development of live attenuated rubella virus vaccine has been remarkably similar to the experience with live measles vaccine. However, the time interval between isolation of virus,[21-22] subsequent attenuation,[23] and licensure in 1969 was 7 years for rubella as compared with a 9 year period for measles. The use of the vaccine has also been accelerated; more than 19 million doses of rubella vaccine as compared with 3.5 million doses of measles vaccine had been given within approximately one year after licensure.

The proceedings of the International Conference on Rubella Immunization provided a comprehensive report of various phases of rubella immunization.[20] The data presented provided the basis for a prelicensing statement on rubella vaccine prepared by the Advisory Committee on Immunization Practices of the Public Health Service and the Committee on Infectious Diseases of the American Academy of Pediatrics.[24] The 2 committees recommended the use of the vaccine for girls and boys between one and 12 years of age, emphasizing that young school children deserve the highest priority because

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they are the major source of virus dissemination in the community. The vaccine was not recommended for pregnant or potentially pregnant women because of the possible risk of fetal infection with the vaccine virus. The committees stated that women of childbearing age should be considered for vaccination on an "individual" basis, if the possibility of pregnancy in the following 2 months could be avoided. Ideally, the immune status of a woman should be determined by performing a rubella hemagglutination-inhibition test. Susceptible women on an effective contraceptive regimen would be good candidates for rubella immunization. The immediate postpartum period would be an excellent time to vaccinate susceptible women.

The goal of the current large-scale immunization program for children is to prevent congenital rubella by providing indirect protection for mothers of rubella-susceptible children and providing girls with immunity to rubella which, hopefully like the natural disease, may be long lasting.

The first goal is the immediate protection of susceptible women if an epidemic of rubella occurs in 1971 or 1972. Rubella epidemics in the United States generally recur at 6 to 9 year cycles; the last one occurred in 1964. The most likely sources of infection of susceptible pregnant women are their own rubella-infected children. Consequently, the immunization of all children in a household should provide indirect protection for their susceptible mothers of childbearing age. In addition, immunization of school children should protect their susceptible teachers. The extensive use of rubella vaccine in 1970 should have a significant effect on the incidence of rubella in communities which have participated in the program. It will be interesting to compare the results of well-immunized and poorly immunized communities.

The second goal of the rubella immunization program in the United States is based on the premise that a primary infection with attenuated rubella vaccine virus will have the same immunologic consequences as a primary infection with wild rubella virus. As indicated in the section on measles, the question of duration of immunity following the use of live further attenuated Schwarz strain vaccine, which was a cause for concern in 1965, is no longer considered a problem. The questions about rubella will be answered by the accumulation of data from studies designed to evalaute the significance of reinfection and the related potential problems of communicability and duration of immunity. The results of these studies on rubella vaccine-induced and natural immunity may or may not reveal quantitative differences which do not apparently exist with measles.

It is well known that the phenomenon of reinfection is a characteristic of rubella as it is of measles.[13, 25-29] Consequently, 2 crucial questions must be answered: (1) Is a reinfected, previously vaccinated, or naturally immune individual contagious? (2) Is there a risk of viremia in a reinfected individual? Answers to these questions will be derived from knowledge of the immunity following naturally acquired infection, vaccination, and rubella reinfection.

Primary rubella infection—naturally acquired. Studies on the natural history of rubella have elucidated the virologic and serologic events of the primary infection.[30] → tonsil area?
Rubella virus is present in the pharynx and blood approximately one week before onset of rash; it may persist for 2 weeks and in rare instances as late as 3 weeks after onset of rash. Viremia, which occurs about one week before onset of rash, is no longer detectable by the second or third day of the exanthem. Antibodies are first detectable shortly after onset of rash, reaching a peak approximately one month later. Recent studies have shown that the pattern and persistence of antibody following natural rubella were similar to those following measles.[31] A 5 year follow-up of 223 women who had rubella during the 1964 epidemic indicated that the rubella hemagglutination-inhibition antibody titers ranged between a low of 1:8 and a high of 1:2,048 or greater. As indicated in Table I, 5 years after natural

→ presence of virus in blood of host

→ symptomatic eruption of sores during course of disease

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measles the antibody titers ranged between a low of 1:8 and a high of 1:1,024.

Studies by Davis and associates[28] have provided the quantitative data needed to clarify the problem of communicability. Significantly larger amounts of virus are present in the pharynx and blood of patients during the prerash period of natural rubella. The amount of virus decreases 100-fold to 1,000-fold by the third to fifth day after onset of rash. This finding supports the epidemiologic observation that patients with rubella are most contagious before onset of rash and are rarely contagious after the third day of rash. These virologic and serologic events are essentially the same in subclinical rubella infection (rubella without rash).

An extraordinary study of an epidemic of measles in Greenland in 1962 may contribute to a better understanding of the communicability of rubella. A correlation between time of exposure and communicability was observed during this epidemic.[32] It was obvious that the available health facilities would be inadequate to cope with the problems associated with a major outbreak. Accordingly, it was decided that a "guided epidemic" would be the best solution for a potentially critical situation. The area was divided into 3 quarantinable units: the 800 inhabitants of the town of Umanak, the 500 inhabitants of the 4 most remote settlements, and the 700 inhabitants of the 5 nearest settlements. The plan involved the deliberate exposure of large groups of susceptible individuals to a person or persons with measles; half of the adults and half of the children in each household were asked to volunteer for "artificial infection."

The results of this unique plan were very interesting. Approximately 400 persons visited a patient named Josef on the *first* day of his measles rash. Josef coughed twice in the face of each person! In spite of this exposure, the large number of contacts did not develop measles. Consequently, 3½ weeks later the procedure was repeated but this time patients in the catarrhal, prerash stage of measles were chosen as the source of infection. Under these circumstances the disease was successfully transmitted to the susceptible contacts.

It is well known that measles virus is present in the nasopharynx during the first day of rash, as well as during the catarrhal period of the disease. The failure to transmit the infection on that day was probably a reflection of the minimal quantity of virus present at that time. Although a culture of the throat may have been positive, the amount of virus may not have been adequate to initiate infection. The larger quantities of virus present during the catarrhal period were undoubtedly responsible for the communicability of the disease.

An evaluation of the various epidemiologic and experimental studies on rubella as well as measles suggests that a positive throat culture is not necessarily an indication of communicability. The dose or quantity of virus delivered appears to be the major factor.

Primary rubella infection—vaccine induced. The natural history of primary infection following inoculation of live attenuated rubella virus was well documented in various reports published in the proceedings of the International Conference on Rubella Immunization[20] and in a more recent report by Davis and associates.[28] Similarities and differences have been observed in vaccine-induced infections as compared with natural rubella infections in regard to clinical reactions, virus shedding, antibody response, and communicability.

Clinical reactions. The typical lymphadenopathy and 3 day rash of natural rubella are rarely seen following vaccination; fever is even less common. On the other hand, transient arthritis and arthralgia may occur as frequently after vaccination as it does after natural rubella. It is difficult to compare the relative frequencies of vaccine-associated and rubella-associated joint manifestations because the extensive prospective observations during vaccine trials provided data which could not be obtained under the conditions of epidemic or endemic rubella in the community.

Prior to the licensure of rubella vaccine

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it was obvious that transient joint manifestations occurred in 25 to 40 per cent of women and in 1 to 2 per cent of children[33, 34] and that arthritis and arthralgia were milder in susceptible women who received the Cendehill strain as compared with those who received the HPV-77 strain in dog kidney. The extensive experience since licensure of the HPV-77 strain has revealed an increased incidence of joint manifestations in children who received the HPV-77 strain in dog kidney cell culture (Rubella Virus Vaccine, Philips Roxane Laboratories, Inc., Columbus Ohio) as compared with those who received HPV-77 in duck embryo cell culture (Meruvax, Merck Sharp & Dohme, West Point, Pa.). As yet, comparative data are not available following extensive use of the Cendehill strain in rabbit kidney cell culture (Cendevax, Smith, Kline and French Laboratories, Philadelphia, Pa.), because this vaccine was licensed later.

Under the conditions of normal pediatric or general practice a 1 to 2 per cent incidence of transient arthritis and arthralgia would be a relatively unimportant event. On the other hand, the administration of 100,000 doses of vaccine to children in the same community at about the same time could be associated with a pseudoepidemic of 1,000 to 2,000 cases of painful joints. The problem could be compounded because the incidence of joint manifestations in children receiving dog kidney vaccine is approximately 5 per cent or more. In addition, in spite of adequate briefing in package inserts, newsletters, articles in medical journals, and a special letter to all physicians from the Public Health Service, many practitioners were not aware of the well-known phenomenon of benign, transient rubella arthritis. Consequently, many children were admitted to hospitals for study to rule out a diagnosis of rheumatic fever or rheumatoid arthritis, an exercise which caused unnecessary anxiety and expense.

Virus shedding. The appearance of vaccine virus in the pharynx is a phenomenon associated with all of the licensed vaccines. It is clear that attenuated virus is shed for a briefer period of time and in much smaller amounts than wild rubella virus. Meyer and associates[35] have reported that virus-positive throat swabs from vaccinated children contain 100 times less virus than similar swabs from children with natural rubella. Moreover, the attenuated virus has lost much of its capacity to induce an infection by the respiratory route.

Viremia, which is so easily detectable during natural rubella, has been difficult to detect in vaccine-induced infection. Viremia, if present, must be a transient phenomenon characterized by minimal quantities of virus.

Antibody response. Antibody levels following vaccination are significantly lower than those associated with natural rubella. Moreover, there is a delay in the appearance of antibody with increasing attenuation of rubella virus.[20] We consistently detected hemagglutination-inhibition antibody 14 to 17 days after primary infection with wild rubella virus. In contrast, hemagglutination-inhibition antibody following vaccination was usually detected a week or more later, reaching peak levels 6 to 8 weeks after vaccination. In general, antibody levels following vaccination were fourfold to eightfold lower than those observed after natural rubella. This finding was similar to our experience with further attenuated Schwarz strain measles vaccine and natural measles (Fig. 5). It is clear that a definitive answer to the question of persistence of antibody and duration of immunity following rubella vaccination must await the results of surveillance studies.

Communicability. In spite of rare isolated reports which suggest the possibility of communicability,[25, 36] the overwhelming evidence indicates that vaccinated virus-shedding individuals are not contagious. In our experience the attenuated rubella vaccine was not communicable under the same conditions in which we observed a 90 per cent attack rate in susceptible children who were exposed to wild rubella virus.[37] A recent report by Scott and Byrne[38] demonstrated the lack of communicability of the vaccine virus when susceptible pregnant women were ex-

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posed to their vaccinated children. Examination of serum specimens obtained before and after exposure revealed no serologic evidence of infection. The available evidence indicates that the potential risk of communicability is negligible. Consequently, there is no contraindication for the use of vaccine in community programs involving children whose mothers are pregnant.

Reinfection rubella. The available evidence indicates that reinfection may occur in persons who have had natural rubella or rubella vaccine. Recent reports by Horstmann and associates[27] and Davis and associates[28] indicated that reinfection was more common in previously vaccinated individuals than in those who had had natural rubella. Evidence of a booster response following exposure to rubella was observed in 80 per cent of previously vaccinated individuals as compared with less than 10 per cent of those who had had natural rubella.[27] Similar observations were reported earlier by Wilkins and associates[25] and Schiff and associates,[26] when they challenged previously vaccinated persons with a relatively unattenuated strain of rubella virus. In most studies there has been a significant correlation between the level of rubella hemagglutination-inhibition antibody and the probability of reinfection. Persons with low levels of antibody were more likely to be reinfected.

Reinfection has been characterized by a fourfold or greater rise in hemagglutination-inhibition antibody and, occasionally, by the presence of small amounts of virus in the pharynx for a brief period of time as compared with primary rubella infection. Viremia has not been detected during the course of reinfection. It is logical, therefore, to assume that the potential risk of fetal infection during reinfection may be negligible or nonexistent. The final answer to this crucial question will come from data accumulated from studies similar to those described by Boue and associates.[29] They are observing 3 women who were immune prior to their exposure to rubella during the early weeks of pregnancy. Sucrose density gradient studies revealed that the specific rise of rubella hemagglutination-inhibition antibody in the 3 pregnant women was IgG, a response characteristic of reinfection rather than primary infection. Even if none of the 3 infants have clinical, virologic, or serologic evidence of congenital rubella at birth, it will be essential to have additional evidence before a final judgment is made, since not all infants are infected as a result of maternal primary rubella infection during the first trimester of pregnancy.

During the early course of our studies on the natural history of rubella,[30] we had an opportunity to obtain serial samples of blood from patients with primary rubella infection and from others who were reinfected with wild rubella virus. The results of serial hemagglutination-inhibition antibody studies in 8 children with primary infection and 5 children with reinfection are shown in Table II. Antibody following primary rubella infection was detectable by the fourteenth to seventeenth day after exposure. Evidence of a booster response following reinfection was observed one week earlier, by the seventh to eleventh day after exposure. The initial response to the primary infection was specific rubella IgM, followed several days later by IgG. In contrast, the booster response consisted of IgG antibody exclusively. Viremia and pharyngeal rubella virus, which were detected during primary infection, were not detected during reinfection.

Rubella reinfection could prove to be a blessing rather than a problem. A primary infection with wild or attenuated rubella virus, like wild or attenuated measles virus, may "sensitize" or prime a person for life. Subsequent exposure to the virus at a time when humoral antibody may be low or nondetectable may be followed by minimal local multiplication of virus which in turn may provoke a prompt boost of antibody, thereby preventing the occurrence of viremia. These immunologic events may inhibit virus multiplication, thereby eliminating the potential problem of communicability.

Conclusion. The potential problems associated with the rubella vaccination program

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Table II. Serial hemagglutination-inhibition antibody titers following primary natural rubella infection and reinfection

	No. of days after exposure to rubella virus														
Titer	*0*	*3*	*4*	*5*	*7*	*8*	*10*	*11*	*12*	*13*	*14*	*15*	*17*	*21*	*28*
Primary infection															
Coo	< 8	< 8	—	< 8	< 8	—	< 8	< 8	< 8	—	64	—	128	128	512
Sul	< 8	< 8	—	< 8	< 8	—	< 8	< 8	< 8	—	< 8	—	32	1,024	—
McO	< 8	< 8	—	< 8	< 8	—	< 8	< 8	< 8	—	< 8	—	64	128	128
Vas	< 8	—	—	< 8	< 8	—	< 8	< 8	< 8	—	256	—	1,024	4,096	4,096
Ren	< 8	< 8	—	< 8	[illegible]	—	< 8	< 8	< 8	—	< 8	—	32	4,096	—
Dan	< 8	< 8	< 8	—	< 8	—	< 8	—	< 8	—	< 8	—	32	—	64
Mil	< 8	< 8	< 8	—	< 8	—	< 8	—	< 8	—	< 8	—	16	32	256
Spe	< 8	< 8	< 8	—	< 8	—	< 8	—	< 8	—	8	—	128	--	4,096
Reinfection															
Ber	64	—	—	—	—	256	—	512	—	128	—	128	—	—	—
Lan	256	—	—	—	—	256		1,024	—	—	—	1,024	—	—	512
Pan	128	128	128	—	128	—	2,048		1,024	—	—	256	—	—	256
Her	128	256	—	—	4,096	—	4,096	—	512	—	512	—	—	—	512
Bax	512	512	—	—	512	—	4,096	4,096	—	—	—	512	—	—	1,024

Underlined numbers indicate first evidence of detectable antibody following primary infection and first evidence of booster response after reinfection. Results are recorded as the reciprocal of the rubella hemagglutination-inhibition antibody titer.

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in the United States were carefully reviewed in an excellent editorial by Dr. John F. Enders.[40] He presented a fair and objective evaluation of the possible significance of reinfection, potential communicability of the vaccine virus, and duration of immunity. In the concluding paragraph of his editorial he stated, "Accumulating doubts such as these of the long-range effectiveness of the rubella vaccination program should not be allowed for the present to interfere with its continuation." It was regrettable, however, that Dr. Enders' comments were reported out of context by several newspapers. The most blatant distortion of the editorial appeared in a bold headline of the highly respected *New York Times* on August 4, 1970, stating, "Virologist suspects harm in rubella vaccine but would continue its use." During the first week of August, 1970, the combined efforts of all the communications media--newspapers, radio, television, and later, magazines--created a new rubella problem which caused unnecessary anxiety and confusion for physicians and parents who were participating actively in the rubella immunization program. The distorted reports were also transmitted to many other countries.

At the present time 3 safe, immunogenic, well-tolerated, attenuated rubella vaccines are licensed for use in the United States, the HPV-77 strain in duck embryo cell culture, the HPV-77 strain in dog kidney cell culture, and the Cendehill strain in rabbit kidney cell culture. In the wake of extensive large-scale studies, it became apparent that the HPV-77 strain in dog kidney cell culture was not acceptable for routine use in large-scale public health programs involving children; it caused joint manifestations which were significantly more frequent, more severe, and more prolonged than those observed with the other 2 vaccines. The RA 27/3 strain of attenuated rubella vaccine, developed by Plotkin and associates[41] and described at the International Conference on Rubella Immunization, has not been discussed because it has not yet been licensed for use in the United States.

In my opinion the current recommendations for the use of live attenuated rubella vaccine in the United States represent the most logical and most feasible approach for the solution of the rubella problem in this country. Additional experience gained from current and future studies should provide advisory committees with data which may be used as a basis for modifications of the present vaccination program. The recommendations for the use of measles vaccine have been modified on several occasions during the past 7 years. New information which will become available will dictate the need for continuation or modification of current recommendations for the use of rubella vaccine in the United States.

The aim of the present rubella immunization program in Great Britain is to concentrate their efforts on 2 groups: all girls between the ages of 10 and 14 years and susceptible women of childbearing age who have no detectable rubella hemagglutination-inhibition antibody. They realize that this program is not likely to have much effect if an epidemic were to occur within the next few years. On the other hand, they believe that their program may have theoretical advantages for long-term protection against congenital rubella.

In contrast, the immediate aim of the rubella program in the United States is twofold: to routinely immunize girls and boys, one to 12 years of age, the major disseminators of wild rubella virus, and to immunize *susceptible* women of childbearing age on an individual and selective basis. If the immunity does not prove to be durable, it may be appropriate to recommend a second inoculation of vaccine for all girls, who were vaccinated in infancy or early childhood, when they reach the age of 12 years.

The problems associated with the vaccination of women of childbearing age have been aggravated by the failure of many physicians to abide by the following recommendations of the Public Health Service and American Academy of Pediatrics Committees: (1) test for susceptibility by performing a rubella hemagglutination-inhibition test, (2) if immune, do not vaccinate, and

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(3) if susceptible, vaccinate only if pregnancy can be avoided during the subsequent 2 month period. During the past year many hundreds of women had therapeutic abortions because they became pregnant after receiving rubella vaccine without a previous test for susceptibility. It is likely that a hemagglutination-inhibition test would have revealed evidence of immunity in 85 to 90 per cent of them. The incredible toll in terms of unnecessary anxiety and cost could have been prevented by the performance of this simple, highly specific, relatively inexpensive test.

During the 1964 rubella epidemic physicians were helpless in their efforts to protect susceptible pregnant women. The use of many thousands of doses of gamma globulin had little effect on the incidence of congenital rubella. The development and recent licensure of live attenuated rubella vaccines represents an historic event in the field of preventive medicine. The appropriate use of these vaccines should have a major impact on the control of the rubella problem.

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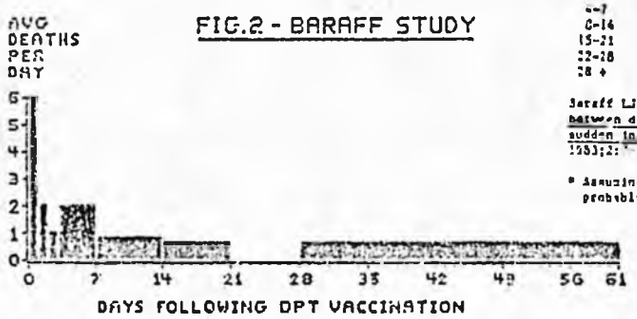
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As it turns out, a number of surveys exactly like this have actually been performed, and the results are graphed in Figures #2-#6. Figures #2 through #5 obviously show a very large number of deaths occurring in the first few days following DPT. These are not "bumps" in the graphs; they are mountains.

FIG.2 - BARAFF STUDY



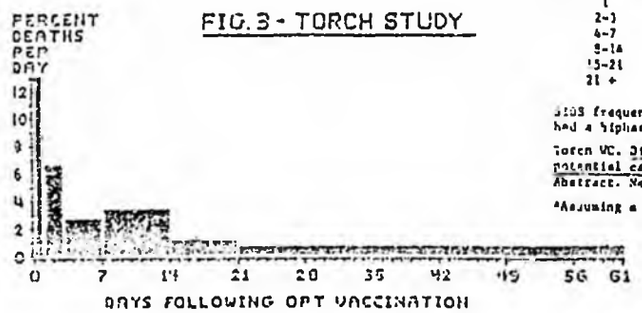
53 of 145 SIDS victims had received DPT:

Days from DPT to Death	Number Deaths	Avg.Num per Day
1	6	6
2	2	2
3	1	1
4-7	8	2
8-14	6	0.86
15-21	4	0.57
22-28	0	0
28 +	26	0.78*

Baraff LJ, Ablon WJ, Weiss RC. Possible temporal association between diphtheria-tetanus toxoid-pertussis vaccination and sudden infant death syndrome. Pediatric Infectious Disease 1983;2: 11.

* Assuming a maximum number of 61 days between DPT and SIDS; probably a conservative assumption.

FIG.3 - TORCH STUDY



2/3 of 70 SIDS cases had received DPT:

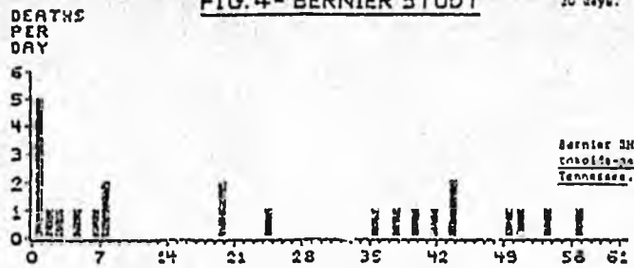
Days from DPT to Death	% of Cases	% per Day
1	13	13
2-3	13	6.5
4-7	11	2.75
8-14	24	3.43
15-21	9	1.29
21 +	30	0.75*

SIDS frequencies peaked at age 2 months in the non-DPT group and had a biphasic peak occurrence at 2 and 4 months in the DPT group.

Torch WC. Diphtheria-pertussis-tetanus (DPT) immunization: a potential cause of the Sudden Infant Death Syndrome (SIDS). Abstract. Neurology 1982;32:A149.

*Assuming a maximum number of 61 days between DPT and SIDS.

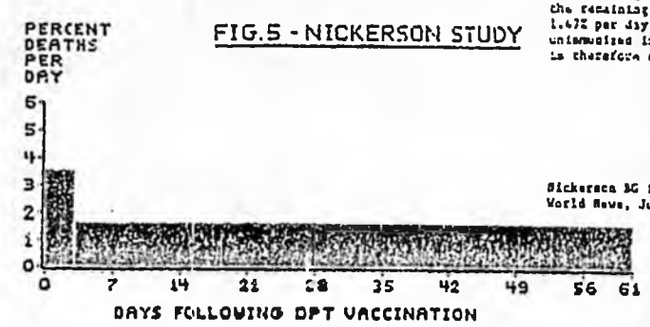
FIG.4- BERNIER STUDY



33 of 35 SIDS victims had received DPT; the number of deaths as shown were recorded on a per day basis. An additional 9 deaths occurred between 61 and 140 days, or on the average 1 every 10 days.

Bernier RH, Frank JA JR, Bondurant TJ Jr et al. Diphtheria-tetanus toxoids-pertussis vaccination and sudden infant deaths in Tennessee. Journal of Pediatrics 1982 101:419-421.

FIG.5 - NICKERSON STUDY



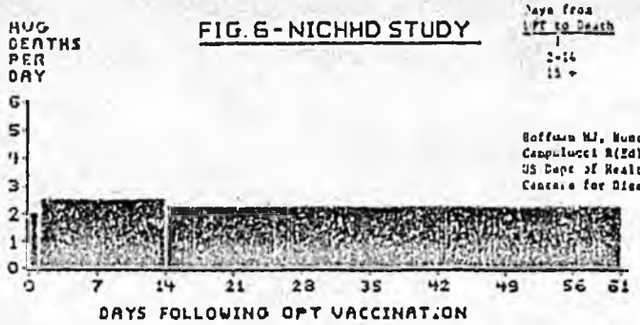
Of 601 SIDS victims 10.4% died within 72 hours of immunization, or an average of 3.47% per day. Assuming a baseline of 61 days the remaining 89.6% of deaths would occur at an average rate of 1.47% per day. NOTE: This group includes both immunized and unimmunized infants; the clustering effect in the first 3 days is therefore assumedly "diluted".

Dickerson BG Jr: SIDS-Immunization Link Questioned. Medical World News, June 10, 1985.

Could these "mountains" have occurred just by chance? The answer is yes, but the likelihood of their occurrence by chance is extremely small. Dr. Baraff, for example, calculated the chances of finding 6 of 53 deaths occurring on the day of the shot to be less than 1 in 2000. Dr. Daniel Shannon of the NEIDSF calculated a very similar probability with regard to the data of the Bernier study. That is a very small probability, and the probability of obtaining virtually the same results by chance alone in 4 independent surveys is smaller still---ridiculously small. The obvious explanation of course is that DPT is causing some deaths that are rightly or wrongly called SIDS. If DPT did not cause these "mountains", what did?

But what about Figure #6, the NICHHD study? Here is a large-scale study, conducted by a whole panel of SIDS experts, which demonstrates no apparent connection between DPT and SIDS. The number of deaths per day is almost perfectly uniform. How can this discrepancy be explained? Is this study right and the others wrong, or vice versa? Or was a different method used in the NICHHD study which might help to explain how such an opposite conclusion could be reached?

FIG. 6 - NICHHD STUDY



163 of 380 SIDS victims had received DPT. Cases screened from study included infants on whom no autopsy was performed and infants whose autopsies exhibited "major deviations from standardized autopsy protocol".

Days from DPT to Death	Number Deaths	Avg. Num per Day
1	2	2
2-14	33	2.54
15 +	130	2.34

Hoffman HJ, Hunter JC, Hasselmeyer EG. SIDS and DPT. In: Campbell-Reid R(Ed). 17th Immunization Conference Proceedings. US Dept of Health & Human Services, Public Health Service, Centers for Disease Control, Atlanta, Ga. 79-88.

The answer here is that the NICHHD study did in fact employ a different method than the other 4 surveys, and the difference lies in the method of selecting SIDS cases for study. Whereas Baraff, Torch, Bernier, and Nickerson counted any and all infants in the time period and area under examination who were reputed to have died of SIDS, i.e. whose death certificates read "SIDS" or "crib death", the NICHHD panel screened out certain cases beforehand. Some excluded from study were infants on whom no autopsy had been performed, and infants whose autopsies contained findings that varied from a "standardized" SIDS autopsy as defined by the panel. It is extremely common for autopsies of "suspicious DPT-SIDS" victims to contain deviations from the classic SIDS autopsy; a few examples of such non-SIDS findings (of the many we are personally aware of) are encephalopathy of the brain and cerebral hemorrhage. The question is: which types of cases did the NICHHD panel exclude and which did they include in their prescreening process? Unfortunately, despite repeated attempts to have this question answered, no reply has been forthcoming. Did the NICHHD, perhaps unwittingly, "load the dice" by excluding from study those cases they needed most to include? And where does this leave the parents of babies whose deaths have been ruled SIDS by the local coroner, and are now ruled not SIDS by the NICHHD? It is important to underscore: If the NICHHD did inadvertantly exclude DPT deaths (ruled SIDS) by excluding atypical autopsies, when Baraff, Torch, Nickerson, etc. included these atypical autopsies, this would explain the apparent contradictions in findings, and lead us to suspect that: indeed DPT does not appear to cause real SIDS deaths, but some DPT deaths are being misdiagnosed as SIDS. And a footnote on the apnea babies (used to be called "near-SIDS-miss") with regard to all of this: current research is only finding a 5% overlap between apnea-suffering babies and SIDS victims. This overlap is so small that we would not expect any of the studies we've discussed to clearly demonstrate DPT risk for apnea-prone babies. Until more studies on the effect of DPT on such babies are done, we are left with Dr. Shannon's frightening experience where about 20% of such babies required resuscitation within 24 hour of DPT.

The jury is still out on the question of whether or not DPT causes some real SIDS deaths. There are many, including Dr. Loring Dales, head of immunization for the state of California, for whom the NICHHD does not settle this issue: "...enough other evidence exists to cause continued concern that the vaccine may rarely cause SIDS, so that need is felt for continued investigation of the matter...". (Source: Dales, L. 1984. Pertussis Vaccine and SIDS. Cal. State Dept. Health Services: SIDS Newsletter, Summer, 1984.)

A final note on the studies: the experts have engaged in a lot of debate over the merits of the various studies. Baraff and Torch, for example, have been criticized for not using a "case-control" method, like that used by the NICHHD. And yet Alvan Feinstein, Professor of Medicine at Yale, and a widely respected authority on medical statistics, said about the "case-control" method: "hidden bias can substantially distort the results." This is a particular danger when a group is treated as being homogenous when it is really comprised of many different entities. Everyone agrees that SIDS is a catch-all term for many different causes of death, i.e. SIDS victims are not a homogenous group.

The debate over study design can go on (and will) indefinitely, and is beyond the scope of this brochure. Meanwhile, babies are dying. It is true that Baraff and Torch had no control groups, but it is equally true that no plausible explanation for their findings, outside of DPT's responsibility, has ever been advanced. "It's all a coincidence" is hardly a plausible explanation. The treasure of our babies' lives deserve a better explanation than that, and immediate intensive research.

A final note: The poor quality of SIDS autopsies and the misclassification of DPT deaths as SIDS is hindering progress on the prevention of many types of infant deaths. If we could exclude DPT (and other non-SIDS) deaths from SIDS studies, true SIDS risk factors would be more likely to become clear. The DPT (and other non-SIDS) victims could be "cloudying the water," and postponing the discoveries that will save babies' lives.

1986 UPDATE

The "abstract" of the Nickerson study has been published (Nickerson BG, Robinson BK: How many Sudden Infant Death Syndrome victims were recently immunized? Abstract, A261, J Soc Ped Res).

Nickerson concludes that "a relationship between SIDS and immunization accounts for less than 6.3% of total SIDS deaths." If we apply his finding of an approximate 6% excess of deaths beyond those expected by chance within 3 days of DPT, to the 8,000-10,000 estimated deaths ruled SIDS (correctly or not) each year, we find 480-600 babies in the U.S. each year whose deaths are "vaccine-related".

This study raises serious questions about the DPT benefit/risk ratio, as CDC has estimated 450 deaths from whooping cough per year in the absence of pertussis vaccine. (Hinman A et al. 1984. Journal of the AMA 251(23): 3109-13.)

Case	Pregnancy	Birth	Health from birth to 1st DPT	Age & health at time of 1st DPT	Reactions	Interval DPT to death	Coroner ruling	Family History: Allergy	Family History: Severe DPT Reaction	Family History: Epilepsy	Family History: Other
Baby Girl 1	uneventful	normal	excellent	2 months; healthy	leg twitching; strange screaming; did not eat	10 hours	SIDS	asthma, excema, allergies	yes	yes	
Baby Girl 2	uneventful	normal	problems with formulas; otherwise excellent	2 months; had a cold; otherwise healthy	extreme paleness; unresponsive; oversomnolence; unconcolable screaming	6½ days	SIDS	allergies incl. cow milk			migraine
Baby Boy 3	uneventful	normal	excellent	2 months; had a cold; otherwise healthy	unconsolable screaming	12 hrs	SIDS	cow milk allergy			
Baby Boy 4	uneventful	normal	excellent	2 months; healthy	high pitched screaming; limpness; diarrhea; cold extremities	33 hrs	irreversible shock due to probable DPT reaction	milk intolerance	yes	yes	migraine
Baby Boy 5	uneventful	normal C Sec (labor failed to progress)	excellent	2 months; healthy	repeated bouts of high pitched screaming	15 hrs	SIDS				diabetes
Baby Boy 6	uneventful	routine repeat C Sec; TTN; O_2 support 6 hrs; Apgar 9,9	resolving breast jaundice; otherwise excellent	1½ mo; trace of jaundice; end of ear infection; otherwise excellent	unconsolable crying; jerking of extremities with high pitched vocalizing, staring, diarrhea, limpness	5 days	SIDS	cow milk & other allergies	yes, & severe reaction to other vaccines		migraine convulsions
Baby Boy 7	uneventful	vaginal; breathing support req. briefly; discharged 48 hrs after birth	Hosp 3 days w/ virus at age 2 mos; otherwise healthy	3 months; healthy	excessive sleeping; eyes bloodshot & swollen; congestion; episodes of eye-crossing; terrible cough	10 days	SIDS	asthma; excema; food allergies	yes		convulsions
Baby Girl 8	uneventful	normal	excellent	3 months; end of cold/ runny nose; otherwise healthy	terrible screaming; limpness	4 hours	SIDS	asthma; excema; allergy incl. cow milk	yes	yes	
Baby Girl 9	uneventful	normal	excellent	2 months; at end of cold; otherwise healthy	back arched scream at time of shot; eyes rolled up; high pitched unconsolable scream	3 hours	SIDS				migraine

Neurology 1982

SESSION ON CHILD NEUROLOGY I

Morning Meeting

Friday, April 30 9:30 AM—11:45 AM (Alexandria)

Chairman: Robert Vannucci, Hershey, PA
Secretary: Jay Pettegrew, Dallas, TX

8:00 AM	Poster Presentations III	(Washington Ballroom)
8:30 AM	Exhibits	(Hall B)
9:00 AM	S. Weir Mitchell Award Essay	(Sheraton Ballroom)

Duration of Therapy for Neonates with Seizures

9:30 AM 1

LAURA R. MENT and SAMUEL L. BRIDGERS, New Haven, CT

Neonatal seizures constitute a significant problem in the Neonatal Intensive Care Unit (NICU) population, occurring in approximately 3% of neonates admitted to our NICU. Varying recommendations have been made on the duration of anticonvulsant therapy following neonatal seizures. Concerns over adverse effects of phenobarbital on developing infants must be balanced against the likelihood that seizures will recur without medication. Infants treated in our NICU for neonatal seizures were tapered off phenobarbital if they had normal neurologic examination and normal EEG at corrected age 3 months, and no history of seizures since discharge. In the 23 infants fulfilling these criteria, with mean birthweight of 2810 grams (range, 630 to 4120 gm) and mean gestational age at birth of 37 weeks (range, 25 to 43 weeks), seizure etiologies included asphyxia (9), intracranial hemorrhage (4), familial neonatal seizures (2), metabolic abnormalities (2), sepsis (1), infarct (1), narcotic withdrawal (1), and undetermined (3). With a mean follow-up to age 13 months (range, 6 to 29 months) in 22 infants, none has suffered recurrent seizures. A normal 3-month evaluation allows safe withdrawal of anticonvulsants in infants with a history of neonatal seizures, regardless of etiology.

Generalized Neonatal Seizures in Primates: Focal Inhibition of Protein Synthesis in Vulnerable Regions

9:45 AM 2

C.G. WASTERLAIN and B. DWYER, Los Angeles, CA

A new method for quantitative autoradiographic measurement of brain protein synthesis with I-[^{14}C]-valine was used to study twin pairs of newborn marmoset monkeys (4 to 7 days old) and rats (4 days old) during generalized bicuculline seizures (5 mg per kilogram IP 30 minutes). In controls, the rate of [^{14}C]-valine incorporation into proteins was high in hippocampal cell bodies and in some layers of the lateral geniculate nuclei; slightly lower in cortex, moderately lower in caudate and thalamus, and considerably lower in white matter. In marmosets, seizures resulted in a profound inhibition of protein synthesis in hippocampus and cortex, while some layers of the lateral geniculate nuclei remained extremely active in protein synthesis and other regions showed intermediate changes. These regional variations were much less striking in rats.

The remarkable focality of the inhibition of brain protein synthesis in generalized bicuculline seizures in primates may bear a relationship to the selective vulnerability of some neuronal populations to epileptic damage.

Diphtheria-Pertussis-Tetanus (DPT) Immunization: A Potential Cause of the Sudden Infant Death Syndrome (SIDS)

10:00 AM 3

WILLIAM C. TORCH, Reno, NV

A recent report of eight DPT-associated cot deaths in Tennessee, and knowledge of four sudden deaths within 3½ to 19 hours of inoculation in Nevada (in three infants and one 3-year-old child) stimulated a study on the relationship of SIDS to DPT immunization in over 200 randomly reported SIDS cases. Preliminary data on the first 70 cases studied shows that ⅔ had been immunized prior to death. DPT #1, 2, and 3 were administered on the average at age 2, 4, and 6 months, respectively. In the DPT SIDS group, 6.5% died within 12 hours of inoculation; 13% within 24 hours, 26% within 3 days, and 37%, 61%, and 70% within 1, 2, and 3 weeks, respectively. Significant SIDS clustering occurred within the first 2 to 3 weeks of DPT #1, 2, 3, or 4. The age range of the DPT group was 59 days to 3 years (mean age, 3 months); for the non-DPT group, 17 to 172 days (mean age, 2 months). SIDS frequencies peaked at age 2 months in the non-DPT group, and had a biphasic peak occurrence at 2 and 4 months in the DPT group. DPT #1 and 2 were associated with more SIDS than #3 or 4 (ratio 30:11:4:1). Males and females were equally affected. Cot death occurred maximally in the fall winter season in the non-DPT group, but was nonseasonal in the DPT group. Death occurred most often in sleep in healthy allergy-free infants following brief periods of irritability, crying, lethargy, upper respiratory tract symptoms, and sleep disturbance. Autopsy findings in both groups were typical of SIDS, (e.g. petechiae of lung, pleura, pericardium, and thymus; vascular congestion;

pulmonary edema; pneumonitis; and brain edema). In conclusion, these data show that DPT vaccination may be a generally unrecognized major cause of sudden infant and early childhood death, and that the risks of immunization may outweigh its potential benefits. A need for reevaluation and possible modification of current vaccination procedures is indicated by this study.

Local Cerebral Glucose Utilization in the Beagle Pup Model of Intraventricular Hemorrhage

10:15 AM 4

LAURA R. MENT, CHARLES C. DUNCAN, RICHARD LAMBRECHT, and WILLIAM B. STEWART, New Haven, CT, and Upton, NY

Intraventricular hemorrhage (IVH) is a major neurologic problem of preterm infants and is thought to be a manifestation of alteration in blood flow to the germinal matrix. Neonates with IVH often have long-lasting hypoglycorrhachia, which may imply profound alterations in cerebral metabolism. Such metabolic alterations could have significant neurodevelopmental consequences. Therefore, we have utilized the ^{14}C-2-deoxyglucose (2DG) method to study local cerebral glucose utilization (LCGU) in the beagle pup model of IVH. Six pups (12 to 48 hours, 300 to 425 gm weight) were anesthetized, tracheotomized, paralyzed, and ventilated. Arterial blood gases and blood pressure were obtained through a femoral artery cannula. IVH was induced (and later documented by neuropathology) by removal of 20 to 25% of their total blood volume via a femoral venous catheter, followed by rapid venous reinfusion 5 minutes later. Five additional pups served as controls. In the hemorrhage pups, MABP was 80 mm Hg prior to the withdrawal of the blood, 65 mm Hg during the hypotensive phase, and 93 mm Hg following reperfusion. Control pups had MABP 82 mm Hg throughout. Fifty minutes following the induction of IVH, LCGU was measured. ^{14}C-2DG concentrations were 23, 12, 20, and 18 μCi for the cortex, white matter, caudate nucleus, and germinal matrix, respectively, of the controls. For the experimental group, 2DG concentrations included cortex, 19; white matter, 17; caudate nucleus, 19; and germinal matrix, 17 μCi. In the presence of IVH, LCGU throughout the brain becomes homogeneous, and although cerebral blood flow changes may be localized to specific regions of hemorrhage in this model of IVH, there may be an uncoupling of blood flow and metabolism throughout the brain.

The Cerebrophysiologic Response of Neonatal Dogs to Graded Hypertension

10:30 AM 5

RICHARD S. K. YOUNG, SUSAN K. YAGEL, and RUDOLFO AZZIZ-BAUMGARTER, Hershey, PA

We have previously determined regional cerebral blood flow (CBF) in the newborn dog during normotension and hypotension. We have now measured the cerebral physiologic responses of newborn dogs to graded hypertension, using an autoradiographic method with ^{14}C-iodoantipyrine as indicator. Newborn mongrel dogs (1 to 10 days of age) were given an intravenous infusion of metaraminol (0.041 to 0.082 mg per kilogram per minute) to raise mean arterial blood pressure (MABP) from 61 ± 5 to 91 ± 3 or 105 ± 6 mm Hg ($p < 0.001$). These elevations in MABP led to widespread increases in CBF, particularly in diencephalon (thalamus: from 22 ± 10 to 56 ± 13 ml/100 gm/min, $p < 0.001$), brainstem (medulla: from 28 ± 10 to 74 ± 22 ml/100 gm/min, $p < 0.001$), and cerebral white matter (from 6 ± 2 to 12 ± 3 ml/100 gm/min, $p < 0.001$). In addition, all animals developed marked subarachnoid or intraventricular hemorrhage.

In the newborn dog, CBF is held constant or "autoregulated" at MABP of 30 to 80 mm Hg. Although hypotension leads to reductions of CBF only in periventricular and occipital white matter, hypertension produces widespread increases in CBF. These findings suggest that periventricular leukomalacia is related to cerebral ischemia, while cerebral hemorrhage results from acute increases in CBF.

The Effect of Glucose Supplementation on Neonatal Hypoxic-Ischemic Brain Damage

10:45 AM 6

THERESA VOORHIES, DONALD G. RAWLINSON, and ROBERT C. VANNUCCI, New York, NY

The observation that glucose treatment increases the survival of hypoxic perinatal animals provides the rationale for the administration of glucose to asphyxiated newborn infants. However, studies in adult animals suggest that glucose supplementation accentuates hypoxic-ischemic brain damage. To resolve the apparent paradox, 7-day postnatal rats underwent right common [illegible]. Histologic analysis revealed alterations only in those rats subjected to both carotid artery ligation and hypoxia. Infarction ipsilateral to the arterial occlusion occurred in 50% of both glucose-treated animals (four of eight) and saline controls (three of six). In all the glucose-treated animals, infarction involved the entire territory of the right middle cerebral artery, whereas in only one

Surgeon General's Report on

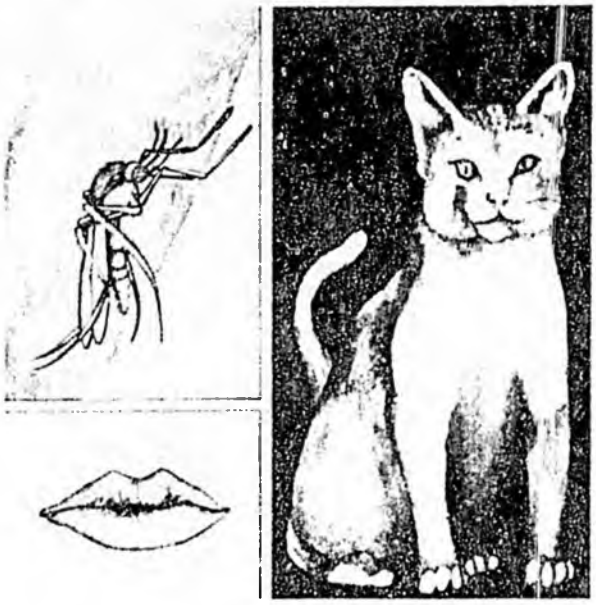
ACQUIRED IMMUNE DEFICIENCY SYNDROME



cuts to the blood or other body fluids of the infected child a highly unlikely occurrence. Even then routine safety procedures for handling blood or other body fluids (which should be standard for all children in the school or day care setting) would be effective in preventing transmission from children with AIDS to other children in school.

Children with AIDS are highly susceptible to infections, such as chicken pox, from other children. Each child with AIDS should be examined by a doctor before attending school or before returning to school, day care or foster care settings after an illness. No blanket rules can be made for all school boards to cover all possible cases of children with AIDS and each case should be considered separately and individualized to the child and the setting, as would be done with any child with a special problem, such as cerebral palsy or asthma. A good team to make such decisions with the school board would be the child's parents, physician and a public health official.

Casual social contact between children and persons infected with the AIDS virus is not dangerous.



Insects

There are no known cases of AIDS transmission by insects, such as mosquitoes.

Pets

Dogs, cats and domestic animals are not a source of infection from AIDS virus.

Tears and Saliva

Although the AIDS virus has been found in tears and saliva, no instance of transmission from these body fluids has been reported.

AIDS comes from sexual contacts with infected persons and from the sharing of syringes and needles. There is no danger of infection with AIDS virus by casual social contact.

Testing of Military Personnel

You may wonder why the Department of Defense is currently testing its uniformed services personnel for presence of the AIDS virus antibody. The military feel this procedure is necessary because the uniformed services act as their own blood bank in a time of national emergency. They also need to protect new recruits (who unknowingly may be AIDS virus carriers) from receiving live virus vaccines. These vaccines could activate disease and be potentially life-threatening to the recruits.

opinion will be a much more phenomenon in American life than the person who the opinion himself, Bruce

is no question that Franklin pular and effective teacher. He as one student put it, the only at Stanford who both advo- d lived according to Marxist d thus exposed students to principles in a fashion that no ully committed was capable of. was perhaps inevitable that who had the habit of signing his letters "death to all Fascist pigs" and frequently identified the university as part of an educational-industrial complex that he held responsible for the Vietnam war, should clash with the Stanford administration, who correctly identified Franklin's long-range goal as stopping the "normal" activities of the university.

Dershowitz and other civil libertarians have pointed out that the quasi-legal nature of campus hearings—which exclude, for example, the right to challenge prospective jurors—provides fewer guarantees of due process than exist in criminal law. Thus the dismissal of persons such as Franklin for "just cause," as interpreted by most faculty members in U.S. colleges and universities, may nonetheless result in the weakening of academic freedom. Disagreeing with this view, however, advisory board chairman Kennedy told *Science* that, his dissent on Franklin's dismissal notwithstanding, he believes existing procedures do protect academic freedom. The result at Stanford, in any event, has been to leave the university a quieter, but possibly less interesting, place.—ALLEN L. HAMMOND

Division of Biologics Standards: The Boat That Never Rocked

can be few graver opportu- r man-made disaster than the munization campaigns that are line in many countries. Should cine preparations become con- d with an undetected agent in the host cells, such as a using virus, a whole genera- vaccinees could be put in jeop- his, of course, is no science writer's horror story—it has al- appened once; millions of peo- e been injected with a monkey own as SV40, which was found to be contaminating polio and rus vaccines. The virus causes in hamsters; no one yet knows may do in man.

of forswearing all vaccines and the return of epidemic dis- he necessary safeguard against ccidents is vigilant surveillance earch. The government institu- trusted with this duty is the n of Biologics Standards (DBS), an agency set on the campus National Institutes of Health, in a, Maryland. The DBS has re- been the focus of unfavorable . A Civil Service grievance ee recommended censure of the 's management for allowing a research scientist, J. Anthony to be harassed by his super- (*Science*, 25 February), and and his attorney, James S. have accused the DBS of scientific mismanagement in a document made public by Senator Abraham Ribicoff (D–Conn.) (*Science*, 3 March). The significance of the specific charges raised by Morris and Turner has yet to be determined, but their indictment prompts a number of general questions about the role of the DBS in vaccine regulation. How well has the DBS research program been managed? What are the important decisions that have faced the DBS and how has it approached them? What kind of a track record does the division have in fulfilling its regulatory responsibilities?

These questions are hard to answer from the outside, in part because of the clublike, partly closed nature of the vaccine community. Federal responsibility for vaccines does not rest solely on the DBS, but is diffused over a handful of committees with interlocking memberships. Thus, if the mass annual inoculations against influenza were indeed the "forcing on the public [of] a bogus situation. . . . The vaccine we were promoting was not having any beneficial effects,"* it is not too clear whether responsibility would lie with the DBS for certifying an inefficacious vaccine or with a second body, the Center for Disease Control's Advisory Committee on Immunization Practices (ACIP), whose function is to decide who should be vaccinated against what. Again, when the typhus vaccine shot into every U.S. Army recruit since World War II turned out in 1969 to be producing insufficient antibody even though it had regularly passed the DBS tests, it was unclear whether the DBS or the Armed Forces Epidemiological Board (AFEB) should claim fatherhood of the fiasco. Federal responsibility for the development of new vaccines is notably imprecise. Both the DBS and another segment of the NIH, the Infectious Diseases Branch of the National Institute of Allergy and Infectious Diseases, are permitted to develop new vaccines, but neither has specific responsibility for doing so.

Besides the haziness of responsibility, the picture is also blurred by a reluctance among vaccine workers to discuss problems openly when they arise. This is because of the understandable fear that public confidence in vaccines—and vaccine authorities—will be eroded. As one participant—in fact, the chairman of the NIH committee that studied the Morris-Turner charges—said at a recent conference on vaccines: "From our debates on what is best or what is wrong, we are conditioning the public to reject measures that sometimes, in some situations, are very important."† The importance attached to presenting an unruffled surface to the public is exemplified by the SV40 incident of 1961; even when the contaminating virus was found to be oncogenic in hamsters, the DBS and its expert ad-

* A. D. Langmuir, *International Conference on the Application of Vaccines* (Pan American Health Organization, Washington, D.C., December 1970), p. 614. Langmuir, now at the Harvard University Medical School, was formerly head of the epidemiology branch of the Center for Disease Control at Atlanta, Georgia.

† A. S. Benenson, *International Conference on the Application of Vaccines* (Pan American Health Organization, Washington, D.C., December 1970), p. 612.

visory committee decided to leave existing stocks on the market rather than risk eroding public confidence by a recall. Even after the polio accidents of 1955, the scandal that led to the creation of the DBS from the former Laboratory of Biologics Control, continuity was stressed as much as change; the assistant chief of the laboratory, Roderick Murray, became the director of the DBS, and the chief of the laboratory became a lab chief in the DBS.

None of this implies that faults have been covered up or that the public has been conspired against in any way; but there are dangers that problems will be underemphasized in any system that discourages the fullest possible discussion, as some believe the DBS does. For instance, a recent article on the reactions associated with viral vaccines concludes: "There has been a tendency on the part of certain higher government circles to play down any open discussion of problem- ated with vaccines. . . . Perhap. as has been overdone. Scientists now find themselves in the position of balancing the benefits of a vaccine against the risks, yet are in no position to judge what the long-term risks are."‡

Evaluating the risks of vaccines is one of the tasks of the DBS, which is charged with ensuring the safety and quality of biological products. Of the six laboratories of the DBS, one deals exclusively with blood products, one with inspection and control activities, and the remaining four with vaccines. For fiscal 1972 the DBS has a budget of just over $9 million, of which roughly $2 million is devoted to an extramural contract research program. The in-house budget of the DBS is split roughly equally between research and control activities (no exact figure is available).

Without doubt the DBS has capably fulfilled its minimum function, that of ensuring the immediate safety of vaccines. What is at question is whether the DBS has adequately carried out such broader responsibilities as improving the quality of vaccines and assessing the longer term risks and benefits associated with vaccine use. To carry out such responsibilities, the DBS might be expected to support an aggressive, centrally directed research program, closely coordinated with regulatory decisions.

In fact, the DBS research program is neither evidently aggressive, nor strongly directed, nor ranked in equal importance with regulatory activities. The attitude of the present management toward research is more one of toleration than active encouragement. Over the last decade, DBS Director Roderick Murray has not been notably successful in increasing the DBS's research competence. Although Murray has been director since 1955, when the DBS was created, the division in its early years was closely supervised from the NIH front office by James A. Shannon, then director of the NIH, and associate director Joseph E. Smadel. Smadel eventually transferred to the DBS as a laboratory chief, from which position he, in effect, directed the division until his death in 1963. During this period, the DBS staff grew from 54 to 249 positions; between 1963 and the present, the DBS has enjoyed a net increase of 11 persons, although its responsibilities have grown in far greater proportion. The only major growth in DBS research activities since 1963 was the establishment of the contract research program in 1966. But the program originated from elsewhere on the NIH campus and was assigned to the DBS by the NIH front office.

Headless Research Program

What many consider to be a major structural weakness in the present DBS research program is the absence of a scientific director. Although this function might be expected to be performed by the director of the DBS, Murray has left the planning of research to the initiative—some say the whims—of the laboratory chiefs. The only attempt at central coordination of research was in 1966, when the NIH front office assigned Leon Jacobs, a toxoplasma expert, to direct the new contracts program. Jacobs also took the title of scientific director, but left the DBS within 2 years, apparently because Murray allowed him no authority over the in-house research program. The NIH front office (where Jacobs is now assistant director for collaborative research) has made no attempt to install a second scientific director of the DBS, presumably because of the experience of the first.

Despite the absence of central direction, some DBS scientists believe the various lab chiefs have coordinated their activities to cover all the essential areas of research, at least in relation [illegible] their staff. Others complain that the DBS has not been allowed to develop. Says [illegible] scientist Kendall O. Smith, [illegible] fessor of microbiology at the [illegible] of Texas Medical School, S[illegible]: "There are inexcusable gaps [illegible] research program, specifically [illegible] to the safety of the viral substrates to grow vaccines. It's one [illegible] ultraconservatism that makes [illegible] less obvious than they are." [illegible] former DBS scientist, B[illegible] now chairman of the microbiology [illegible] partment at the University of [illegible] criticizes the scanty efforts to [illegible] ticipate research problems. "[illegible] time the DBS got upset with [illegible] before something came up [illegible] ing," Young told *Science*.

Specific research areas [illegible] the DBS coverage is most [illegible] faulted are the improvement of [illegible] vaccines, particularly influenza [illegible] tussis, the hypersensitivity [illegible] associated with certain kinds [illegible] and the study of the various [illegible] and other viruses that are [illegible] taminants of vaccines.

Besides lacking scientific [illegible] the DBS research program [illegible] ably also suffered, or failed [illegible] from the use made of the [illegible] of scientific counselors. As [illegible] inally constituted to look [illegible] search program of the [illegible] board has, according to M[illegible] only one real suggestion [illegible] and even that was not [illegible] Since membership is drawn [illegible] ranks of the most distinguished [illegible] tists in the vaccine field [illegible] would not seem to have [illegible] the best possible advantage [illegible] present members complain [illegible] have been used only as a [illegible] board," and clearly the [illegible] DBS research program [illegible] very different if the board [illegible] existed.

Research Findings Un[illegible]

Potentially more serious [illegible] organizational weakness [illegible] sources is the attitude [illegible] agement toward research [illegible] have implications for re[illegible] sions. There is no proof [illegible] management has deliberately [illegible] suppressed scientific da[illegible] seems to have been a cu[illegible] seeking out or pursuing [illegible] with implications for a[illegible] cision. Present and former [illegible] tists repeatedly use the

toward research that might lead
regulatory change or decision.
ding to C. W. Hiatt, formerly
chemist at the DBS and now at
niversity of Texas Medical School,
ntonio, "The intellectual attitude
DBS management was not hos-
long as your research didn't rock
at. We only got ourselves tangled
en we got involved in any way
ontrol responsibilities. The oc-
s when actual findings were ig-
were very, very few. But there
ncipient instances of that, when
rganization would prefer you
get into a given area."
a scientist who is still with the
The DBS is negative toward re-
The main concern of the man-
it is to fulfill their regulatory
n, and there is a certain air of
e toward basic research. . . .
is something about Murray that
comes back to the same theme,
rock the boat.'"
Young, a former DBS scientist
is endorsed the Morris-Turner
ns of the DBS management, de-
the DBS attitude toward re-
as being one of "suppression,
ent, and censorship of individ-
stigators such as Morris, Eddy,
nd Hiatt. I finally came to rea-
you had either to compromise
or leave. Morris and Eddy are
heroes in that place because
yed and fought. The others
ith their feet and left."
s has stated that he was re-
rom influenza control duties
he raised questions about the
of the vaccine. Eddy was de-
fter demonstrating in 1961 that
us causes tumors in hamsters.
liatt, and Young left the DBS
ng reasons, but each had dif-
ongly with the DBS manage-
er particular research issues
felt should prompt a regula-
sion. Hiatt, as senior chemist
S, believed that manufacturers
e required to institute a stan-
strial check test to ensure that
servatives had not been added
es. "Most chemists with any
industrial background would
in not insisting that this kind
ing be followed," Hiatt told
"but the management felt I
erating its importance."
ecific issue that concerned
the procedure for screening
y cells used in growing vac-
detect all the possible con-
taminating viruses, you need to hold the cells for much longer than the 2 weeks specified in the DBS regulations. One of the chief ways I became obnoxious to the DBS management was in continuing to press for a longer incubation time. I think it is unforgivable that the DBS did not change their regulations" Smith told *Science*.

What alarmed Young was the discovery by a DBS research contractor of herpes virus in the dog kidney cells in which it was proposed to produce rubella vaccine. Yet, Young says, he could not get the DBS authorities to investigate the matter further; "The DBS puts almost total trust in the manufacturers to do all the most important testing work. The DBS simply reads the manufacturers' protocols."

Part of the dissatisfaction felt by these scientists could be due to the apparent uncommunicativeness of the DBS management in explaining its actions. Murray, who in fact has delegated little if any of the decision-makng power in the DBS, is not by nature expansive. "Even those who work with him rarely know his opinion on a matter," says a colleague. Another factor in the distrust felt for the management's attitude toward research may be one related to the nature of scientists. "Scientists are particularly hard to direct unless they feel a certain amount of respect for the personality directing them," says one vaccine specialist. "Murray has done reliable, consistent work on hepatitis, but is not much known scientifically."

But the personnel problems of the DBS seem to go deeper than just the handling of scientists. The Morris grievance hearing last year resulted in a committee recommendation that the DBS management be censured for allowing Morris to be harassed. The NIH front office does not accept this verdict. Says Robert W. Berliner, NIH deputy director for science, "If the DBS deserves censure, it is because they tolerated Morris for as long as they did. Morris was disruptive, insubordinate, and failed to take adequate action to straighten out the problems of the flu vaccine potency." (Morris's position is that he did try to improve flu potency tests, even though DBS managers ignored the results of existing tests.) Morris, however, is not alone in finding the DBS management hard to live with; besides the scientists who have left, some 20 or so members of the present staff of the DBS are involved in personnel disputes of various degrees of severity.

How has the management of research contributed to the DBS decision-making process? Significantly, maybe, many of the most important decisions made by the DBS have been reached with the aid of large, often international, conferences. Murray says the licensing of live polio vaccine in 1961 was the hardest choice he has faced because there were three different virus strains from which to select, but he emphasizes that the decision was made on a collective basis, not by him alone.

Decisions on Rubella and WI-38

Another important decision was the licensing of rubella vaccine in 1969, when again there was a choice of virus strains—one developed by three scientists in the DBS (Harry M. Meyer, Paul D. Parkman, and Hope E. Hopps) and another by Stanley Plotkin of the Wistar Institute. There is no reason to suppose that individual DBS scientists acted other than entirely honorably, but the DBS as an institution was put in a classic conflict of interest position in having to decide upon a vaccine it had itself developed. The position was made the more invidious when a particular manufacturer, Merck Sharp and Dohme, abandoned its own strain of rubella virus in favor of that developed by the DBS. Even if Murray was scientifically justified in awarding the vaccine license to Merck Sharp and Dohme with the DBS virus strain, he failed to do so in a manner that was obviously fair to observers inside or outside the DBS. Says former DBS scientist Smith of the rubella decision: "The situation was not handled in a manner that could clearly be seen to be just. Murray must have seen it coming step by step. He could have stopped it but didn't." According to Paul S. Moorhead of the University of Pennsylvania and a member of the board of scientific counselors, "The handling of the rubella vaccine was an obvious conflict of interest and the DBS made no obvious attempt to head it off."

Perhaps the single most important decision to have faced the DBS—although Murray says he does not regard it as important—is that of whether to make vaccines in primary cells or in continuously passaged cells. In brief, the advantage of continuously passaged cells is that they can be exhaustively tested for normality, the absence of contaminating viruses, and so forth. By contrast, primary cells, which are taken directly from animal tissues such as

monkey kidney or duck eggs, may carry the viral flora unique to their host, yet for economic reasons can only be screened in a comparatively cursory manner. §

In 1962, a continuously passaged cell line derived from a human fetus was established by Leonard Hayflick, then at the Wistar Institute. Hayflick's cells, known as WI-38 cells, have been used for vaccines in other countries and, since 1965, by the U.S. Armed Forces. Yet the first WI-38 vaccine for U.S. civilian use was licensed by the DBS only last month.

Why did the DBS take a decade to make up its mind on WI-38 cells? Hayflick, now at the Stanford University School of Medicine, gave *Science* the following account of his efforts to persuade Murray to come to a decision on the cells. By 1963–1964, it had become clear, Hayflick says, that the DBS was highly resistant to licensing vaccines produced in WI-38 cells, though the reasons for this opposition were never stated. It was also clear that in most major vaccine developments embraced by the DBS, the primary risk-taking happened to have been borne outside the United States. (For example, live polio vaccine was licensed by the DBS after the Soviet Union had injected more than 15 million people. Live measles vaccine was first tested out, not on U.S. citizens, but on the inhabitants of the Upper Volta.)

Since it seemed that U.S. citizens would not get the benefit of WI-38 cells until foreign countries had taken the risk, Hayflick told *Science*, he organized an international committee called the Cell Culture Committee, to promote the use of WI-38 cells abroad. In 1967, Yugoslavia became the first country to license WI-38–grown polio vaccine. The U.S.S.R. adopted the cells in 1970, and England and France followed suit in 1971.

There is a respectable reason for being wary of WI-38 cells—the theoretical possibility that they might contain a human cancer agent somehow more insidious than those known to exist in animal cells. The DBS could be respected if it had taken this position, but, surprisingly, Murray has never taken any position at all on WI-38 cells, on the grounds that no manufacturer has applied to produce a WI-38 vaccine. To Hayflick, this is simply a stratagem for refusing to discuss the issue because, he says, no manufacturer would risk investing in a new type of vaccine before getting "an informal reading in face-to-face confrontation that Murray will be amenable." A nonscientific reason in persuading Murray to reverse his position may have been pressure from manufacturers who, according to *Drug Research Reports* (21 July 1971), said they would quit making polio vaccine unless allowed to do so in WI-38 cells.

Asked what new scientific facts had come to light to justify reversal of the DBS position, Murray told *Science* only that the "DBS acted promptly to move towards the problems of licensing such a product when it received a license application." Says a senior scientist in the DBS: "To this day I don't know what Murray thinks about WI-38 cells and I don't know why he has decided to license them now. It's another breakdown in communication. By refusing to discuss controversial issues, Murray has many times made the controversy worse."

Since many of the accidents with vaccines have occurred when new processes were introduced, it is probably sound policy not to make changes unless there are clear benefits in sight. Murray is widely praised, for example, for his refusal to allow mineral oil adjuvants to be put into vaccines, despite heavy pressure from manufacturers and parts of the academic community. (Oil adjuvants were recently tried in England with adverse results, an experience that has validated Murray's position.) No one disputes the fact that Murray practiced a conservative policy as director of the DBS, but some see his conservatism in a positive, others in a negative light. Vernon Knight, chairman of the microbiology department at the Baylor University College of Medicine, Houston, says of Murray: "He has a record of absolute honesty and total devotion to protecting the public. If there is any criticism, it is that he has been overdeliberate. But frankly, that is the way to stay alive in this business." Another view is that of Paul S. Moorhead: "If Murray does nothing, he doesn't get much criticism; but if he makes an innovation, then he is really under pressure." According to former DBS scientist Kendall O. Smith, "About 90 percent of the problems in this field will work themselves out if left alone. If you don't change much, you don't risk much. I feel that people have admired as Murray's servatism is only his inability to leadership in a growing field." one scientist acquainted with the "Murray doesn't really make decis So people don't realize from the ou that things don't really happen u there is a broad consensus both i and outside the DBS."

Problems with Potency

Failure to make certain impo scientific decisions openly and fr position of evident strength is pro one consequence of a weakly ma in-house research program. Anot the sometimes weak-kneed stanc DBS has taken in persuading man turers to improve the quality of vaccines. In ensuring vaccine safet DBS has a record blemished onl errors that sprang from the sta knowledge at the time. (These ar SV40 incident of 1961, the hyper tivity caused by the killed measles cine used in the early 1960's, an the opinion of some, the licensi a rubella vaccine which was grov dog kidney cells and which cause expectedly severe side effects.) Bu DBS is also required to ensur quality of vaccines and, in som stances, has been less than zealo doing so. For 10 years, the DB well as higher government off failed to realize that the division sessed the legal authority to ensu efficacy of vaccines (*Science*, 10 M The confusion that has reigned ov potency of influenza vaccine sin least 1957 is now officially ascrib the DBS to the failure by ma turers to calibrate the colorimeters in assessing the vaccines potenc have taken more than a decade quire that manufacturers stand their measuring instruments is an outstanding record for a regu agency.

Another potency problem oc with typhus vaccine, developed early 1940's and used essentiall changed to immunize all army r at an annual cost of hundreds of ands of dollars. In 1969, the Forces Epidemiological Board that some vaccine lots were not good antibody responses, even they had passed the DBS's potenc It is not known for how many before 1969 the army had been useless vaccine, but the incide some doubt on the general alert the DBS's quality control proc

§ For example, the DBS requires the monkey kidney cells used in growing live polio vaccine to be held for only 28 days in order to ensure that they contain no SV40 virus. According to A. Girardi of the Wistar Institute, SV40 may remain latent for up to 35 days. Nor does the DBS require monkey kidney cells to be screened for chromosomal abnormalities—a possible indicator of cancerous tendencies—a test they would probably fail in large numbers.

logical tests are imprecise, and should not be faulted for having to solve problems that were the prevailing state of the art. Of the DBS's problems with potency tests seem to have much from lack of manage- lack of science.

rview, the various blemishes on escutcheon that have come to recent months are less signifi- the 17-year safety record the behind it. The division was set event recurrence of the 1955 cident and, under Murray's hip none has occurred. Murray isted and outperformed half a mmissioners of the Food and Administration, and many would the belief of the NIH front of- Murray has an excellent record rnment official responsible for a y agency. The chief imperfec- the DBS arise from the nature fice, not its holder. Despite the ss of the federal system for ng vaccines, the major responsi- volves on the DBS, whose director has too much power, too much pressure, and too little protection. There is no limit to the director's term of office and yet no effective mechanism for subjecting his scientific decisions to peer review and peer support. There are conflicting pressures from manufacturers, the scientific community, and, more recently, from the consumer movement. Says one vaccine specialist, "The DBS is the most thankless job in the world—you have to be some kind of a Jesus Christ to do a perfect job. You have to give Murray points for staying power—he hasn't cut and run."

Where Murray has strayed from perfection is probably in taking the narrowmost conception of the division's responsibilities. Safety has been assured, but the improvement of vaccines has been pursued less aggressively. The characteristic posture of the DBS has been one of stand-pat conservatism rather than innovative leadership. A common theme underlying the complaints of critics inside and outside the DBS is Murray's unwillingness to make decisions and even—if the harsher critics are correct—to pursue lines of enquiry that might render necessary a regulatory decision.

Such an attitude is probably inevitable, however, granted the DBS's stretched resources and the belief, presumably endorsed by Murray's superiors, that the DBS should be primarily a rule-making operation with a subordinate and undirected research program. Given these ground rules, it is hard to be sure that anyone else could have bettered Murray's long record in protecting the public from hazardous vaccines.

For the future (Murray is due to retire in 2 years' time), possible changes suggested to *Science* by Turner, Morris, and scientists inside and outside the DBS, include the following proposals. The whole mechanism of biologics control should be reviewed in the light of consumer protection—the DBS should probably assume from the manufacturers the prime responsibility for conducting the more crucial tests of vaccine safety. Preparation should also be made to cope with the surge of new biological products that may be devel-

Briefing

liance for Hearts

n't very long ago at all that Edward M. Kennedy, of Massa- and Representative Paul G. of Florida, were carrying the for opposite sides in the long times bitter tussle ov r who was ge the federal government's against cancer. Apparently the no permanent scars though, the two Democrats say they're orces to back another billion- medical onslaught—this time heart, lung, and circulatory

ews conference held late last a chandeliered room of the uilding, precisely halfway be- e House and Senate wings, nd Kennedy sat shoulder-to- to announce their simultaneous ion of the National Heart, ssel, Lung and Blood Act of bill they both acclaimed as the most important piece of gislation to come before Con- s session.

ill proposes to spend $1.29 billion over the next 3 years on cardiovascular and lung disease, in contrast to current annual funding of $232 million. Under the heading of control programs, $90 million of the new money would go to establish 15 community "screening and education" centers. (The bill doesn't say how these would relate to the Regional Medical Program for heart, cancer, and stroke services run by the Department of Health, Education, and Welfare.) The remaining $1.2 billion would be funneled through the National Heart and Lung Institute to support 15 new clinical R & D centers for cardiovascular disease and 15 new centers for pulmonary disease.

Joint support of the bill by Rogers and Kennedy is especially significant since the two Democrats head the respective House and Senate subcommittees that will handle it. Staff aides for Kennedy and Rogers say the bill's chances of passage are further enhanced by the absence of administrative provisos of the kind that led to last year's contest over the cancer bill.

Approval by Congress, however, may be the least of the heart and lung bill's problems. Even if the appropriation committees grant all the money that the bill authorizes, which is by no means assured, there is no guarantee that the White House will spend it. The Nixon Administration, like its Democratic predecessor, is not in the habit of spending all or even very much of the money Congress generously appropriates for crusades of its own, particularly when those crusades seem designed—if only in part—to overshadow the administration's.

In the present case, the White House seems to be under the impression that the $22 million increase it proposed with some fanfare earlier this year for heart, lung, and blood diseases is generous enough. Congressional Democrats —or at least those on Kennedy's and Roger's subcommittees—disagree. And while their motives may be pure, there is room for suspicion that, by upping the ante nearly an order of magnitude, the Democrats may hope to sink their claws into at least one substantial health issue in an election year when issues of any kind are notably scarce. After all, who's to say that the 790,000 Americans who die from cardiovascular and lung diseases each year are less deserving than the 340,000 who succumb to cancer?—R.G.

oped o[illegible] the next decade. The director of the L[illegible] should have responsibility for organizing the research program as well as the regulatory activities of the division.

In addition, federal responsibility for vaccine development should be clarified, in a way that ensures the DBS does not develop vaccines in-house. There should be some court of appeal against the director's decisions. Since the DBS acts, in effect, for the academic community on behalf of the public, there should be a stronger connection with the academic world than occasional ad hoc conferences and a rubber-stamp board of scientific counselors. Standing committees of scientists might be established—one to oversee research and another for regulations—so as to buttress the director's posture toward manufacturers. Problems with vaccines should be more openly discussed, and herd immunity should be sought by means other than treating the public as one. Most importantly, the boat in which the DBS director sits should be strong and flexible enough to withstand the occasional rocking.—NICHOLAS WADE

APPOINTMENTS



W. G. Bowen



M. H. Bernstein

William G. Bowen, provost, Princeton University, to president of the university. . . . **Marver H. Bernstein**, professor of politics and public affairs, Princeton University, to president, Brandeis University. . . . **David R. Derge**, dean for administration, Indiana University, to president, Southern Illinois Univer[illegible]ty, Carbondale. . . . **Timothy W. Costello**, professor of psychology and management, New York University. . . . **N. Ferbee Taylor**, vice president for administration, Univ[illegible] North Carolina system, to ch[illegible] University of North Carolina, [illegible] Hill. . . . **Ivan L. Frick**, presiden[illegible] Colle[illegible]ge, to president, Elmhurst [illegible] . . . **Harold P. Hanson**, dean, [illegible] School, University of Florida, [illegible] president for academic affairs [illegible] university. . . . **Archie R. Dyk[illegible]** cellor, University of Tennessee, [illegible] to chancellor, University of Te[illegible] Knoxville. . . . **Victor Jones**, [illegible] of engineering and applied physi[illegible] vard University, to dean, [illegible] School at the university. . . . [illegible] G. Cook, assistant professor o[illegible] tion, University of Wisconsin, [illegible] School of Education, Ferris St[illegible] lege. . . . **William Happ**, opera[illegible] search analyst, U.S. Army C[illegible] Engineers, to dean, School of E[illegible] ing, Sacramento State College [illegible] **Leonard E. Goodall**, vice cha[illegible] University of Illinois, Chicago [illegible] to chancellor, University of M[illegible] Dearborn. . . . **Conrad T. Burr**[illegible] fessor of chemical engineering, [illegible] tan College, to dean, School of [illegible] ing at the college.

RESEARCH NEWS

Cancer Radiation Therapy: Potential for High Energy Parti[illegible]

Although the causes of cancer are still unknown, treatment with radiation therapy alone or in combination with chemotherapy and surgery helps to save hundreds of thousands of lives a year. Large doses of radiation, however, damage healthy tissues in addition to destroying tumors and thus may cause severe side effects. The use of high energy particles instead of the conventional x-rays or gamma rays may make possible significant improvements in radiation therapy, according to a growing number of physicists and radiotherapists, and the preliminary results of several laboratory and clinical trials seem to support this belief.

Both the physical and radiobiological properties of energetic particles indicate that they may be able to alleviate some of the problems of conventional radiotherapy, although clinical trials are needed to ascertain that new and untoward effects do not occur. The potential uses of particle radiation may be restricted to localized cancers—a category of diseases that does not include some of the most common, such as lung and breast cancer. Nonetheless, the use of particle radiation, if its potential advantages turn out to be clinically significant, may be able to help the large number of patients who now die from localized cancers despite treatment with conventional radiotherapy.

Practical applications of particle radiation in cancer therapy may be slow in coming. Except on a small scale, the necessary clinical trials are not now being conducted in this country, and there appears to be little likelihood of systematic trials with many types of particles in the near future. Despite the large increases in funding for cancer research, relatively little support is available for radiotherapy research, including particle radiation. National Cancer Institute support for investigations of particle radiation totaled [illegible] $1 million in fiscal year 1971; [illegible] that NCI officials estimate may [illegible] $2.5 million by fiscal 1973. One [illegible] according to NCI, for the relati[illegible] level of funding is a shortage [illegible] fied radiotherapists who are in[illegible] in particle radiation. Research p[illegible] have been rejected by the peer [illegible] system for lack of scientific [illegible] a consequence, according to o[illegible] official, of the naiveté in radiobi[illegible] matters on the part of the p[illegible] who proposed them.

Whatever the reason, several [illegible] laboratories that have an int[illegible] using their particle accelerators [illegible] cer research may find it impos[illegible] do so, and in one case the lack [illegible] sources of funding may result [illegible] closing of the laboratory.

The current interest in medi[illegible] for particle radiation contrasts [illegible] with the attitudes that have p[illegible]

Survey of Childhood Malignancies

ALICE STEWART, M.D., and RENATE BARBER, D.Phil.

IN ITS original form the survey of childhood malignancies conducted by Oxford University included children under 10 years of age who died of cancers or leukemia during the years 1953–55, but it has recently been decided to extend the survey to include deaths since 1955 (table 1). In the final study population there will be children born in 18 consecutive years, 1943–60, whose deaths were spread over 8 calendar years (1953–60). Data collected during the second part of the survey (1956–60 deaths) will differ in several respects from the data on 1953–55 deaths, but the general plan remains the same, and both investigations fall into the broad category of retrospective surveys. All varieties of malignant disease are included and approximately half the deaths are due either to leukemias or to lymphosarcomas. Most of the children will be under 10 years of age at death, but some older deaths may eventually be included in the new population.

The survey of 1953–55 deaths began in October 1956 and was the work of 2 General Register Offices (notifying centers), over 200 local health authority departments (collecting centers), and 1 university department (coordinating center). The same team will be responsible for the survey of 1956–60 deaths, which began in April 1961. In each survey group the original study population included all children in England, Scotland, and Wales who died before their 10th birthday during the survey years.

The authors are with the department of social medicine, Oxford University, Oxford, England. Dr. Stewart is reader in social medicine and Dr. Barber is the holder of the Henry Goodger scholarship for research into blood diseases. *The fieldwork in the study was carried out by county and county borough health departments. The study was aided by grant No. C.5392 from the U.S. Public Health Service. This paper was also published in the Medical Officer, London, January 5, 1962.*

Survey of 1953–55 Deaths

A detailed study of official statistics of mortality preceded the survey of 1953–55 deaths. According to these statistics the risk of dying from a malignant disease after the age of 40 has barely altered in recent years, but the risk of children and young adults dying from these diseases has appreciably increased. In particular, children between 2 and 4 years of age have been more affected by the unfavorable trend of leukemia mortality than any other age group under 70 years (*1*).

These findings suggested that, provided a sufficiently large number of childhood deaths from cancers and leukemias (cases) could be identified and compared, point by point, with suitable controls, there might be a reasonable chance of identifying some of the factors influencing the prevalence of these diseases.

Original aims. Hewitt's critical analysis showed that the recent increase in leukemia deaths happened sooner in technically advanced countries than in other parts of the world and appeared to be more closely related to medical services than to wealth. In Britain the adverse effect of this increase began to be felt at the beginning of the century and received a "postwar fillip"; during the years 1945 to 1953 a striking feature of British and United States statistics was an increase in leukemia deaths in children between 2 and 4 years of age. This was the main reason for deciding to interview mothers of both cases and controls and obtain

firsthand accounts of the children's medical histories and social background. It was also decided that pro formas should include questions about (*a*) illnesses of the mothers and children and X-rays before and after birth; (*b*) treatments with modern drugs; (*c*) living conditions; and (*d*) relatives.

Shortage of cases. Though Britain has a population of 50 million, less than 700 children die of malignant diseases each year. It was necessary, therefore, to plan the survey on a nationwide basis, and to seek the cooperation of public health departments. All county and county borough health departments agreed to take part and to assume responsibility for the fieldwork. Consequently, there were no regional gaps among the 1,640 traced cases, which were originally obtained from 1,973 death certificates supplied by General Register Offices in London and Edinburgh (table 2).

On receipt of the names and addresses of the dead children, the coordinating center sent to each collecting center a list of local cases and the pro formas for recording case and control data. In the larger centers more than one "survey doctor" was appointed, but it was agreed in advance that whoever interviewed the mother of a case should also interview the mother of the corresponding control, also that controls should be obtained from birth registers and not from other sources. To insure uniformity one doctor from the coordinating center briefed all the other doctors and provided them with a written set of instructions.

Selection of controls. The instructions stated that each dead child, or case, was to be paired off with a live child, or control, matched for sex, age, and district, but otherwise picked at random from a local birth register.

The control selection list shows how the control was chosen for a boy (John Smith) who was born in 1952, lived in Sheffield, and died of leukemia in 1958. The names and addresses are imaginary, but other items are genuine.

The names and addresses of five possible controls were obtained from a register of births in the district which included the home address of the dead child. The list indicated the order of priority of selection and included boys born on the same day as the dead child, the next day, and so on. On this occasion the first family selected had moved to an unknown address, but the second was still living at the same address and the mother was willing to be interviewed. She was eventually seen by the doctor who had already interviewed Mrs. Smith.

Table 1. Calendar years of births and deaths of children dying of malignancies, 1953–60, survey of childhood malignancies, Oxford, England

Cohorts		Age at death		Followup period (0–10 consecutive years)	
Births	Deaths	Years	Months	1953–60	1953–55
1943	1953	9–10	108–119	1	1
1944	1953–54	8–10	96–119	2	2
1945	1953–55	7–10	84–119	3	3
1946	1953–56	6–10	72–119	4	3
1947	1953–57	5–10	60–119	5	3
1948	1953–58	4–10	48–119	6	3
1949	1953–59	3–10	36–119	7	3
1950	1953–60	2–10	24–119	8	3
1951	1953–60	1–9	12–119	8	3
1952	1953–60	0–8	0–107	9	3
1953	1953–60	0–7	0– 95	8	3
1954	1954–60	0–6	0– 83	7	2
1955	1955–60	0–5	0– 71	6	1
1956	1956–60	0–4	0– 59	5	0
1957	1957–60	0–3	0– 47	4	0
1958	1958–60	0–2	0– 35	3	0
1959	1959–60	0–1	0– 23	2	0
1960	1960	0	0– 11	1	0

NOTE: In each set of figures, 1 year is incomplete. For example, among the 1960 births children born in January and dying the following December would be only 11 months old.

Table 2. Regional distribution of deaths from malignant diseases in children 0–10 years of age, 1953–55 and 1956–60, survey of childhood malignancies, Oxford, England

Authority	1953–55		1956–60 (original cases)
	Original cases	Traced cases	
Counties:			
Northern England	69	62	118
Midlands	344	290	619
Southern England	711	568	1,191
Scotland [1]	118	89	100
Wales	67	58	125
County boroughs and burghs:			
Northern England	77	70	106
Midlands	307	261	488
Southern England	107	92	192
Scotland [1]	152	134	131
Wales	21	16	27
All local authorities:			
England	1,615	1,343	2,714
Scotland [1]	270	223	231
Wales	88	74	152
All regions	1,973	1,640	3,097

[1] 1956 deaths included with deaths for 1953–55.

The definition of a district varied according to the density of the population and in rural areas often included several villages. If necessary, more than one list of possible controls was compiled, but in the survey of 1953–55 deaths two-thirds of the controls were first choice, and over 90 percent were obtained from a list of five names. Far and away the commonest reason for not obtaining a first choice control was the one shown in the selection control list, namely, that the family had left the district.

In the survey of 1953–55 deaths, if the parents of a dead child had moved to a new local authority area, the rule that a case/control pair should be seen by the same doctor was broken. In the survey of 1956–60 deaths each control will be obtained from the district in which the parents of the corresponding dead child are now residing. In the new survey, therefore, there should be no exceptions to the rule that the same doctor sees each member of a case/control pair. If, however, the proportion of "transfers" is the same as in the original survey, approximately 2 percent of case/control pairs will not be exactly matched for district.

Survey of 1956–60 Deaths

In the interval between the two surveys some facts have been discovered for the first time and others have acquired a new significance:

1. Three independent, retrospective surveys, using different types of controls, have shown a raised incidence of prenatal X-rays among children who subsequently died from malignant diseases (*2–4*).

2. One prospective survey (followup) of children irradiated in utero has shown a raised incidence of harmless somatic mutations (*5*):

Serial No. 1222

CONTROL SELECTION LIST

For John SMITH Sex M Born on 6.9.52 in Sheffield 3

Priority	Name and address			Selected control (X) [1]
1st	8.9.52	JONES	56 School Lane	D MOVED AWAY
2d	9.9.52	STANLEY	40 Stockport Road	H X
3d	10.9.52	WILLIAMS	5 East Street	H
4th	11.9.52	PETERS	20 Clarke Street	H
5th	11.9.52	HIGGINS	2 Woodside Drive	D

[1] State reasons for not selecting the control of choice (first name on list) or other alternative.

Note: D, domiciliary delivery; H, hospital delivery.

another, concerned only with leukemia deaths, has so far produced negative results (*6*).

3. In 1959 it was discovered that mongolism is due to a chromosomal abnormality which is probably caused by nondisjunction or faulty mitosis during the last reduction division of the gamete (*7*). As a result of this unequal division, mongols carry an extra autosome (No. 21) in all their cells.

4. Though pneumonia is still a common cause of infant deaths among mongols, there have been fewer deaths in recent years (*8*). There are also indications of a substantial increase in the number of mongols dying of leukemia since 1954 (*9*).

5. About 20 percent of mongols have atypical leucocytes (*10, 11*).

6. Hewitt's analysis of leukemia mortality (*1*) covered the period 1930–53. It has since been shown that, in Britain, the peak of leukemia mortality (2–4 years) appeared for the first time in the late 1920's and reached its present height in the mid-1950's (*12*); also, that the pneumonia death rate for children under 5 years began to decline in the late 1920's and reached its present low level in the mid-1950's (*13*).

7. There is a relationship between a child's position in his sibship and his risk of infection, and an exactly opposite relationship between this position and his risk of developing leukemia. Since older children bring infections into their houses, the infection risk is lowest for first-born children and progressively increases as the number of older children increases. Per contra, the leukemia risk is highest for first-born children and progressively decreases as the number of older children increases. Other malignant diseases in childhood do not show this relationship (*14*).

8. Compared with other cancerous children and with healthy controls, the leukemic children in the survey of 1953–55 deaths had a raised incidence of pneumonia and other serious pyogenic infections. The excess was largely due to children who had not been X-rayed in utero and who died before the age of 5 years. These illnesses were exceptionally common among the 19 mongols who died of leukemia, none of whom had been X-rayed before birth.

9. If prenatal irradiation, which usually takes place 7 to 9 months after conception, is a direct cause of leukemia, deaths caused in this way should be directly related, in time, to these exposures. The actual age distribution of such deaths will depend on the incubation period for leukemia, which is not at present known. But unless all childhood leukemias are initiated in the third trimester—an unlikely proposition—it should eventually be possible to demonstrate a difference between the age distribution, at death, of irradiated and nonirradiated cases. A recent study of first-born children in the survey of 1953–55 deaths suggests that leukemias due to prenatal irradiation have a characteristic age distribution, and that these cases die, on the average, 8 months later than nonirradiated cases (*15*). This, in turn, suggests that the vast majority of childhood leukemias are the direct result of events which tend to occur at or near conception.

10. There are several indications that retinoblastomas occur in two forms, one genetically transmitted and one not (*16, 17*).

11. Expectations of cancer in twins are complicated by the fact that twins are more likely than other children to be X-rayed in utero, but in no large series of childhood cancers has there been any indication of an excess of identical cancers among identical twins (*12, 14*). Unpublished results from the survey of 1953–55 deaths suggest that there may in fact be a deficiency of monozygotic twins among cancerous children. In the control group two-thirds of the twins had a twin sib of the same sex. This is the expected proportion, and there were no differences as between the twins who were X-rayed before birth and the other twins. In the case group (children who died of leukemias and cancers) there were 36 twins, 24 of whom had been X-rayed in utero. In this group of 24 X-rayed cases, the expected and observed members of twin sibs of like sex were the same (16). Among the remaining 12 cases not X-rayed before birth, there were only 2 twin sibs of like sex, though the expected number was 8.

The ways in which these and other findings have influenced the design of the 1956–60 survey require some explanation.

Working hypothesis. The natural history of cancers in man might suggest that malignant cells arise de novo and are due to specific, localized changes in the nuclei of somatic cells. But

it is becoming increasingly evident that this is only part of the story.

The Rous theory of co-carcinogenesis (*18*), which is now supported by numerous experiments in animals (*19*), postulates different stages in the formation of a malignant tumor. Normal cells are first converted into "latent cancer cells" by the action of carcinogens or "initiating agents," which produce "hereditable cellular changes" in exposed tissues. This action is irreversible and is followed by a long or short "latent period." Eventually, under the influence of a "promoting agent," the latent cancer cells begin to multiply and form a tumor. According to Berenblum (*20*), promoting agents have the dual action of increasing mitotic frequency and delaying maturation, and the type of cell which can lead to a cancer after being acted upon by an initiator is the comparatively rare kind which normally replenishes tissues; that is, stem cells.

This raises the possibility that cancers in man are due to initiation and subsequent promotion of stem cells. This would include pluripotential cells—ova, spermatozoa, and zygotes—in the category of cells which can develop premalignant properties; so it is necessary to ask why familial cancers and multiple cancers in the same individual are not more common, and why one rarely finds identical cancers in identical twins.

At first sight the absence of twin affinities suggests that there are no genetically transmitted cancers in man other than the obvious ones; namely, retinoblastomas, neurofibromas (Von Recklinghausen's disease) and cancers associated with intestinal polyposis. But the early stages of Von Recklinghausen's disease and intestinal polyposis show that tissues derived from premalignant cells may be at a disadvantage compared with tissues derived from normal cells. It is therefore possible that matching cancers in identical twins are rare, not because germ cells cannot develop premalignant properties, but because a fetus, particularly a twin fetus, derived from a premalignant zygote has a very poor chance of surviving.

If, as a result of initiation, a somatic cell produced a line of cells which were inferior to other cells, the inferior cell line might be eradicated before promotion occurred, thus removing all risk of a cancer developing at the site of initiation. But if, as a result of initiation of a germ cell, a zygote produces a line of inferior premalignant cells, it would usually be impossible for all the cells to be destroyed without causing death. Hence, initiation of a twin zygote might more often produce an abortion than twin cancers.

The few exceptions to the rule that there are no familial cancers are important for two reasons. They show that it is possible for a human zygote to survive a premalignant change, and they suggest that this change is due to a single gene substitution or point mutation. If a premalignant state merely reflected a general change in the cytoplasm, or a change which affected the nucleus as a whole, one would expect a premalignant change in a pluripotential cell to produce multiple cancers more often than not. In practice, familial cancers tend to be confined to certain cell types and to organs which are less likely to cause death, if wholly composed of inferior cells, than to other parts of the body.

Nevertheless, a point mutation in a somatic cell or germ cell might be preceded by changes in the cytoplasm and accompanied by other changes in other genes. For instance, a change in the cytoplasm might cause faulty mitosis the next time the cell divided: on one occasion faulty division of the nucleus might involve only one gene, on another occasion, several genes on the same chromosome, and on yet another occasion, several genes in several chromosomes. The risk of immediate death of the cell would be proportional to the number of genes involved, and it is unlikely that any cell would survive an accident which involved more than one chromosome. If, however, the cell survived faulty division of one chromosome, all that would matter, from the point of view of the subsequent development of a cancer, would be whether or not a gene controlling the nature of specific daughter cells had undergone a premalignant change.

If a mitotic aberration happened during formation of a somatic cell and the cell survived, the remote effects of a change in several genes on the same chromosome—deletion, duplication, translocation, or inversion—might be the same as a change in only one gene. But if the

faulty mitosis happened during formation of a germ cell or zygote, that is, a pluripotential cell, all the genes involved in the accident would influence the end result. A fetus possessing only one inferior, premalignant cell system might survive to produce a child who appeared to be normal at birth and subsequently developed malignant changes in the defective tissues: but a fetus possessing several abnormal cell systems would probably die in utero. Even if the pregnancy terminated in a live birth, the child would have several congenital defects and would be unlikely to survive long enough to develop a cancer.

So far as we know, the only congenital disease due to involvement of an autosome in a mitotic aberration which is both common and compatible with several years of life is mongolism. Mongolism, or trisomy of chromosome No. 21, is also the only congenital disease which is consistently associated with one type of malignant disease, namely leukemia: and this association was not discovered until the life expectancy of mongols increased from less than 2 years to over 14 years. Before the discovery of antibiotics, mongols usually died of pneumonia during infancy, and there is no doubt that a low resistance to bacterial infections is part of the mongoloid syndrome. Hence it is reasonable to suggest that one of the genes controlling leukopoiesis is situated on chromosome No. 21, which is also one of the smallest autosomes.

The size of a chromosome sets a limit to the number of genes which can be damaged during mitosis. There should therefore be a correlation between the size of a chromosome and the number of times that faulty division of the said chromosome causes death of the cell. In this way the position of an important leukopoietic gene might influence the prevalence of childhood leukemias. But before developing this theme it is necessary to consider what effects a "preleukemic change" in a germ cell might have and how these would compare with the effects of a similar change in a somatic stem cell (leukocyte precursor).

According to the theory outlined above, a preleukemic change in a germ cell would probably involve several genes on the same chromosome and would in any case impair the efficiency of all circulating leukocytes. Consequently, if the fetus survived, the risk of an infection death during infancy would be exceptionally high, and only children who escaped these early deaths would die of leukemia. Moreover, any reduction in infant mortality, due either to prevention or cure of infections, would adversely affect the leukemia death rate (*1* and chart).

Premalignant conditioning of a leukocyte precursor in an adult, that is, a somatic cell, would also impair the efficiency of daughter cells, but in such cases the existence of healthy leukocytes derived from normal stem cells would provide some protection against infections. Consequently the risk of an intercurrent death should be comparatively small, and to produce an adverse effect on the leukemia death rate there might have to be a substantial decrease in the infection death rate.

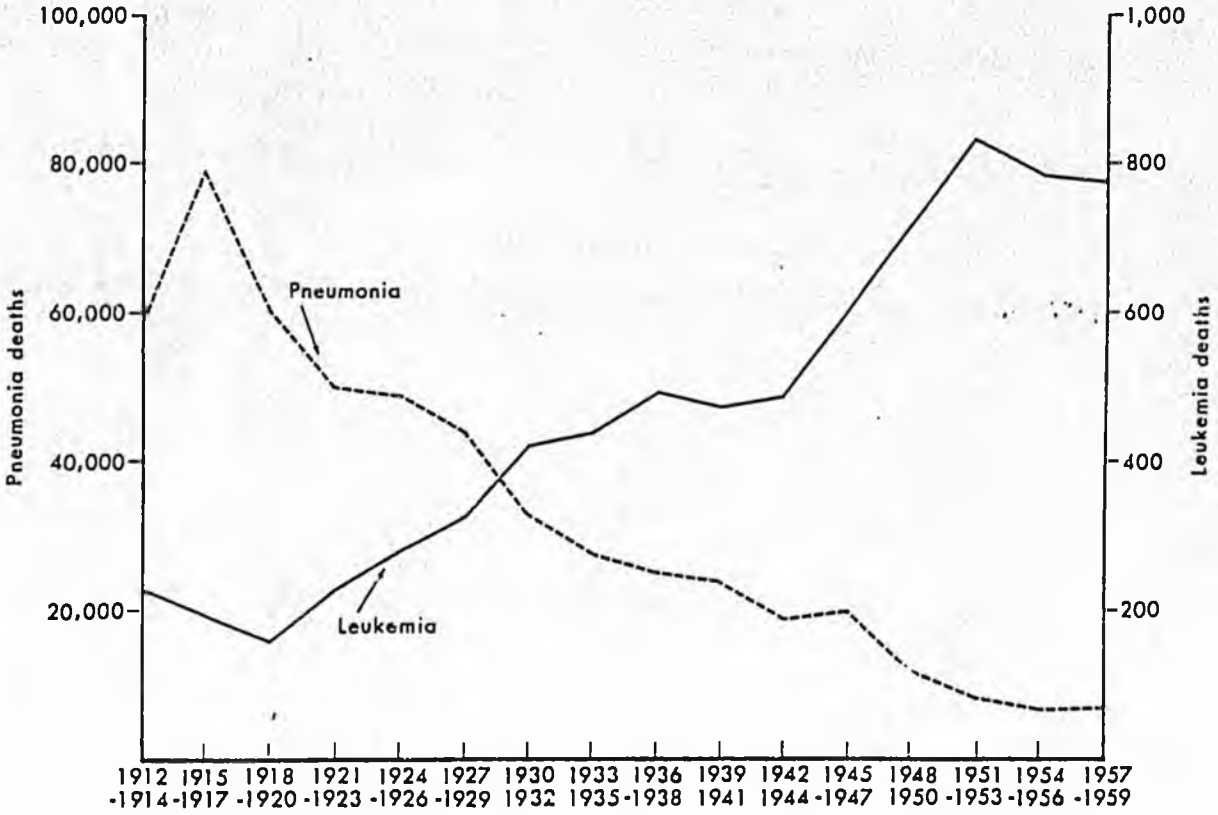
Finally, if it is possible for faulty mitosis during the formation of a germ cell to impair the efficiency of leukocytes, and to pave the way for subsequent malignant changes in leukocyte precursors, one would nowadays expect a retrospective survey to reveal a raised incidence of potentially lethal infections among children who subsequently developed leukemia, provided that antibiotics were easily accessible.

In the 1958 report of the survey of 1953–55 deaths from cancer and leukemia (*2*), a raised incidence of pneumonia among the children who subsequently died of leukemia was mentioned. But the possibility that this finding was important and related to the high incidence of mongolism was not considered until 1959, when the origins of mongolism were explained for the first time. Once it was realized that mongolism was due to a chromosomal abnormality which had been present since conception and which predisposed not only to infections but also to malignant changes in the cells which protect the body against infections, the possibility that other cases of leukemia and cancer in childhood were due to lesions which predated or coincided with conception had to be considered.

Reexamination of the data on 1953–55 deaths from cancer and leukemia (*9*) showed that pneumonia was the commonest, but not the only potentially lethal, infection which was



Deaths from leukemia and pneumonia in children 0–10 years of age, England and Wales, 1912–59, by 3-year periods



recorded more often in the medical histories of children who subsequently died of leukemia than in the histories of children who subsequently died of other cancers. Since a raised incidence of these serious infections was a striking feature of mongols and other children who died of leukemia before the age of 5 years and were not X-rayed in utero, it was suggested that there might be two distinct varieties of leukemia in childhood: one initiated at or before conception and associated with a low resistance to infection (common form) and the other initiated in utero or after birth and associated with a normal resistance to infection (rare form).

The family histories of the survey children were scrutinized for evidence of a raised incidence of nonmalignant blood diseases in the relations of leukemic children. The data proved inadequate for this purpose but they did succeed in showing that, despite their rarity, "cancer fraternities," that is, the same malignant disease affecting more than one member of a sibship, were more common than would be expected if they were merely chance phenomena.

There were other indications in the original data that genetically transmitted cancers were not confined to retinoblastomas, but it was not possible to be certain that this was so. Hence the decision to extend the survey and redesign the pro formas so that there would be some possibility of testing the theory that faulty mitosis during or before zygote formation is a common cause of malignant disease in childhood, though these diseases may also be due to mitotic aberrations involving somatic cells. It was also hoped that the new data would help to settle the controversy about prenatal X-rays being a cause of malignant disease in childhood.

This controversy exists because it is impossible to be certain that, in the retrospective surveys mentioned above, the normal incidence of prenatal X-rays was correctly estimated. It is therefore important to obtain evidence which is independent of control data. If all children born in a given period who subsequently died

of malignant disease could be traced, it would be a relatively simple matter to decide whether "irradiated" and "nonirradiated" cases had different age distributions. The survey of 1956–60 deaths will not provide all the facts required, but if it is successful, the data will include an 8-year followup of children born between 1950 and 1953 and may be sufficient for the purpose (table 1).

Other theoretical considerations. The suggested working hypothesis would only be acceptable if it offered a rational explanation of the following facts. First, infants apart, the risk of developing a malignant disease decreases with age before puberty and increases with age after puberty. The age distribution of children with cancers, that is, the age at death, varies with cell type. Cancers of nervous tissues are commonest in the first and second years, renal cancers and retinoblastomas in the third year, leukemias in the fourth year, and lymphosarcomas in the fifth year. Second, compared with other cancers, leukemias have always been relatively common in childhood and are nowadays the commonest variety of malignant disease in childhood. In adults less than 10 percent of malignant diseases are leukemias.

Age distribution. So far nothing has been said about the nature of "promoters" except that there is reason to think that in normal circumstances they do no harm, and merely encourage mitosis. Since it is only in the presence of premalignant cells that a promoter ever produces a cancer, it is possible that "natural promoters" include growth factors (general promoters) and also repair mechanisms and defense mechanisms (local promoters). Assuming that this is so, and that there is a sizable population of premalignant genes in newly formed zygotes, one would expect the risk of promotion during childhood to decrease with age (general promoters) and the risk during adult life to increase with age (local promoters). One would also expect a temporary increase in risk during puberty, but this would be difficult to detect in national statistics because these only show deaths in 5-year age groups. Lee (*21*), who obtained deaths for individual years, has shown that there is a temporary increase in the leukemia death rate during adolescence. Since malignant cells are incapable of maturing much beyond the stage which they have already reached, one would also expect to find that, when promotion occurred within a few weeks of conception, the resulting tumor contained less well differentiated cells than when promotion occurred later. One purpose of the survey is to discover whether there is any correlation between age at the onset of the fatal disease and the maturation phase of the cancer cells.

Preponderance of leukemias. It has already been suggested that the small size of chromosome No. 21 may be related to the fact that leukemia is a relatively common variety of cancer in childhood. According to this theory a gene controlling leukopoiesis should be situated on chromosome No. 21, and leukemia might be the result of this chromosome being involved in a mitotic aberration.

Provided a preleukemic state was the result of faulty mitosis in a leukocyte precursor, that is, in a somatic cell, there might be no obvious side effects due to involvement of other genes on the same chromosome. But if the change affected a germ cell there would be important side effects if neighboring genes were damaged. There are fewer genes at risk in chromosome No. 21 than in other autosomes, and in view of what is now known about mongolism, these genes may be less essential for vital processes than genes on other chromosomes.

The statistical association between mongolism and leukemia was one reason for postulating a leukopoietic gene on chromosome No. 21. Another reason is the so-called Philadelphia chromosome. This is the name which has been given to an abnormality which has been found in the leukocytes of some, but not all, cases of myeloid leukemia in adults (*22*). The chromosome involved is either No. 21 or No. 22, which are difficult to distinguish, and its appearance suggests that during division of a leukocyte stem cell part of the chromosome was lost.

According to the theory outlined above, there would be nothing paradoxical about finding a partial deletion of a chromosome in some cases of leukemia, and a duplication (trisomy) of the same chromosome in other cases. Nor would it be surprising to discover that when the chromosomal abnormality is found in all cells, the leukemia occurs early and is accompanied by

other congenital defects, and when it is found only in leukocytes, the leukemia occurs late, and there are no congenital defects.

Another feature which has probably influenced the prevalence of leukemias in childhood has already been mentioned: namely, the lowering of the infant mortality rate. Thirty years ago cancers of nervous tissues, that is, neuroblastomas and cerebral tumors, more often caused death in childhood than leukemias, and it is only since the discovery of sulfonamides that leukemias have taken first place.

Progress. With these ideas in mind the second part of the survey was launched in April 1961. Once again county and county borough health departments have assumed responsibility for the fieldwork and already arrangements have been made to trace more than three-quarters of the children who died between 1956 and 1960 (table 2). As in the survey of 1953–55 deaths, each dead child will be paired off with a live child of the same age and sex, and doctors will interview mothers. The mothers' descriptions of their children's illnesses, X-ray exposures, and family histories will be recorded on specially printed schedules and the more important items will be checked with hospital records.

Pedigree data. In the survey of 1953–55 deaths some information about the mother's relatives was obtained, but comparatively little attention was paid to the father and his side of the family. Mothers were asked if they knew of any relatives who had died of cancer or leukemia, but their answers showed that they knew, offhand, less about their husbands' relatives than about their own. In the survey of 1956–60 deaths more extensive family histories will be recorded and a new method of collecting pedigree data has been devised.

Each mother will be visited first by a health visitor assigned to her parish. The health visitor's instructions are: (*a*) to obtain the cooperation of the mother; (*b*) to ascertain the date of birth of the dead child (this is needed to obtain the control); (*c*) to explain what is required; and (*d*) if necessary to help the parents to complete schedule X, Enumeration of Relatives.

In general, schedule X will be given to the mother about a week before the doctor calls, together with a covering letter which asks her to record, under printed headings, all that she and her husband know about "the four grandparents of the survey child and all their direct descendants, including stillbirths and miscarriages." The printed headings include position in sibship, illnesses and X-ray experiences (parents), all causes of death and other specified illnesses (other relatives), dates of birth and present state of health or cause of death (sibs), miscarriages and stillbirths (mothers and grandmothers).

Control selection lists. Schedule X is an example of an innovation made in the light of earlier experiences. Another example is the entry alongside each name on the Control Selection List of the letter D (domiciliary delivery) or H (hospital or nursing home delivery). Knowing as we now do that the cases in the survey of 1953–55 deaths had a higher incidence of prenatal X-rays than the controls (*2*), it is clearly important to know whether first choice controls are representative of the population at large in respect of birthplace: also whether failure to obtain 100 percent of first choices has biased the control group in this respect.

Other sources of bias. Retrospective data collected by several doctors direct from mothers of living and dead children are subject both to recording bias (doctors) and to reporting bias (mothers). By insisting from the beginning that the records from each case/control pair be compiled by one doctor, the first type of bias should have affected case and control data equally, and should not have been an important source of error in the earlier reports (*2*, *9*). It is less certain that the second source of error has not affected these reports, and the suspicion still remains that the findings in respect of prenatal X-rays were due to "memory bias" (*23*).

A knowledge of the ways in which the original case and control groups differed from one another should make it possible to collect more convincing data in the new survey. On this occasion answers to questions which are expected to reveal differences between cases and controls will be systematically checked. In addition, several new questions will be asked for the express purpose of discovering whether events which could not possibly have affected

the children, for example, X-rays of the parents after birth of the child, are reported with equal frequency by parents of both cases and controls. In the original survey only positive statements about abdominal X-rays during pregnancy were confirmed by asking X-ray departments to produce the original records. In the survey of 1956–60 deaths addresses of antenatal clinics and X-ray departments will be automatically recorded, and the intention is to check negative statements about X-rays on a sample basis, and positive statements on a comprehensive basis.

Checking records. As soon as the completed pro formas are returned to Oxford they are examined to see if they are internally consistent and to decide what type of postal followup is required. The object of this is to obtain hospital records of the fatal illness and confirmatory evidence about the following statements:

- X-rays and illnesses of the mother during the pregnancy of the survey child, including anemias and threatened abortions.
- Relatives with anemia or other blood diseases, including leukemias.
- Relatives with "matching" cancers: that is, the same type of cancer as the "index" case.
- Relatives said to have died at an early age from an obscure cause.

In addition, approximately 25 percent of negative statements about X-rays and other antenatal events will be checked by asking antenatal clinics to make an abstract of the original notes on a specially printed form (schedule G). If necessary, more information will be obtained from the mothers, and some parents will be asked if they are willing to have sibs of the survey child examined. Twins will be included in this group; also children who have lost more than one sib, or have two or more relatives with blood diseases: for example, leukemia, pernicious anemia, purpura, acholuric jaundice, and aplastic anemia.

Present status. At the time of writing (September 1961), 220 case/control pairs have been completed and 85 "lost" cases have been returned to Oxford. The proportion of lost cases is high, but this is not surprising since it takes longer to complete the records for a case/control than to discover that a family has moved to an unknown address (49 cases), or that the mother is either not willing to cooperate (30 cases), or not in a fit state to be interviewed (6 cases). Already a considerable amount of information about the lost cases has been obtained from other sources, such as hospitals, welfare clinics and schools, and in two cases this was sufficient to justify finding a "matched" control.

The results of the postal followup suggest that the numbers of X-ray records which are still available are larger than the numbers which have been destroyed and may be sufficient to test the accuracy of the mothers' statements. There has been no difficulty in obtaining from hospitals either the original records of the fatal illnesses or abstracts of the original notes on specially printed forms (schedule A). So far none of the mothers who have been interviewed has resented a followup letter and most of them have been able to complete schedule X. We feel confident that, provided they are given sufficient time, the parents of our survey children will be able both to enumerate their relatives and to tell us where to look for hospital records and death certificates. It is too soon to say how many of the children who died between 1956 and 1960 will eventually be traced, but the prospects are at least as promising as they were at the same stage of the survey of 1953–55 deaths.

Summary

The survey of childhood malignancies originally included only children who died between 1953 and 1955 but has recently been extended to include later deaths. In the final study population there will be children who were born in the 18 consecutive years 1943–60 and whose deaths were spread over the 8 calendar years 1953–60.

The method of collecting data and selecting controls for the 1953–60 deaths remains the same, but the pro formas have been revised and there will be more systematic checking of mothers' statements against hospital records.

It is hoped to settle the controversy about the effects of prenatal X-rays by comparing the ages of irradiated and nonirradiated children, and thus obviate the need to place reliance on control data.

It is suggested that the first stage in cancer promotion is a mitotic aberration and that the

commonest cause of childhood cancers is faulty mitosis during division of a germ cell. Following such an accident the risk of death before a tumor has time to develop is much higher than the corresponding risk following faulty mitosis in a somatic stem cell. Consequently there are no "twin affinities" and there is a low incidence of familial cancers.

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Radiation Symposium

A symposium on the technological needs for reduction of patient exposure from diagnostic radiology will be held March 5–6, 1962, in the main auditorium of the Health, Education, and Welfare Building, Washington, D.C. The symposium, sponsored by the Public Health Service, will evaluate present knowledge and discuss future investigation in four main categories: human and phantom dosimeters; radiographic equipment; fluoroscopic and intensifier equipment; and radiographic grids, screens, and films.

For further information and tickets, contact Dr. M. L. Janower, Division of Radiological Health, Public Health Service, Washington 25, D.C.

of such controls in experiments concerned with the role of oncogenic transformation *in vitro* by known agents.

With the recognition of the S antigen the question arose concerning its relationship to the SV40 tumor-homotransplantation antigen of Habel and Eddy (1963) because of its orientation at the cell surface where, presumably, the Habel antigen is also located. The materials provided by the present series of experiments appear to offer means of investigating this problem experimentally by comparing the oncogenic titer of cells from S-positive, T-negative lines with the titer of homologous oncogenic nonexposed lines in SV40-immunized hamsters according to Habel's technique (1962). Experiments of this kind are in progress.

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Differential Bacteriophage DNA Replication after Induction of a Strain of *Escherichia coli* Doubly Lysogenic for φ80 and φ80dlac

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A double lysogen of *Escherichia coli* containing prophages φ80 and φ80dlac (with a temperature-sensitive repressor for phage induction) has been investigated for yields of the two bacteriophages under different conditions of growth and lysis. The yield of φ80dlac is strongly dependent on the growth medium used. In growth medium A approximately equal amounts of φ80 and φ80dlac are obtained. In growth medium B a reasonable yield of φ80 is produced but very little φ80dlac is produced. This is due to the fact that very little φ80dlac DNA is produced in an induced culture in medium B. A minor modification of Campbell's model for prophage excision is suggested in which homologous parts of the two prophages interact to form one intact phage chromosome. If this mechanism of excision prevailed in medium B it could account for the low yield of transducing phage.

INTRODUCTION

The factors controlling the induction of temperate bacteriophages are the subject of much current investigation. In order for induction to occur, a cytoplasmic repressor encoded by the prophage must be destroyed. According to recent studies (Weisberg and Gallant, 1968) protein synthesis is necessary in order for the detachment of the prophage λ to occur after the repressor is destroyed. The work of Signer and Beckwith (1966) suggests that in the related virus φ80 this may involve the synthesis of enzymes which specifically promote recombination in the phage attachment site region and therefore may be responsible for phage detachment.

This paper is concerned with a doubly lysogenic strain of *E. coli* containing φ80 and φ80dlac as prophages. The φ80dlac was derived from the φ80 particle in the manner described by Signer and Beckwith (1966). According to the Campbell (1962) model for the formation of a transducing phage, both prophages should contain similar attachment sites for the bacterial chromosome. The two phages should in fact be isogenic except for the region containing the transducing fragment. Because of this, one would expect induction and replication of both prophages in the double lysogen should be subject to the same control factors. In the course of attempting to optimize phage yield it has been observed, contrary to expectation, that the *relative* amounts of the two prophages are subject to large variations dependent on growth conditions. A description of our most striking findings is contained herein.

MATERIALS AND METHODS

Media

Medium A: LB broth, per 1 liter distilled water; bactotryptone (Difco), 10g; yeast extract, 5 g; NaCl, 10 g; 20% glucose, 5 ml; and 1 *M* $CaCl_2$, 2.5 ml added after autoclaving.

Medium B: per 1 liter distilled water: KH_2PO_4 (anhydrous), 5.6 g; K_2HPO_4 (anhydrous) 28.9 g; yeast extract, 10 g; thiamine, 10–15 mg; and 25% glucose 40 ml added after autoclaving.

L-broth: per 1 liter distilled water: bactotryptone (Difco), 10 g; yeast extract, 5 g; NaCl, 5 g; 5 ml 20% glucose, 5 ml; and

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Development of S and T Antigens and Oncogenicity in Hamster Embryonic Cell Lines Exposed to SV40[1]

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Cultures of 7 nononcogenic lines of Syrian hamster cells originating from the same pool of embryonic tissues were exposed to SV40. Four months later tests for "Surface" (S) and "Tumor" (T) antigens and for oncogenicity were performed on cells deriving from these cultures and on cells from homologous unexposed cultures which were maintained under the same conditions. Cells from 4 of the virus-exposed lines exhibited S antigen, and 2 of these also exhibited T antigen. Neither antigen was detected in cells from unexposed cultures. Among cells from exposed cultures only those exhibiting one or both of the antigens were found to induce tumors in hamsters. Among those from unexposed cultures, 2 had clearly become oncogenic. The latter were homologous with the virus-exposed cultures which exhibited S antigen only. Results of tests for S and T antigens on the cells of tumors resulting from implantation of exposed and unexposed cells revealed an exact qualitative correlation between the distribution of these antigens in the tumor cells and in the homologous cells prior to implantation. The proportion, however, of T-positive cells which was low in the cultures before implantation was found to approach 100% in the homologous tumor cells.

In general the results provide evidence that the synthesis of S antigen is specifically determined by the SV40 genome and may take place independently of the synthesis of T antigen. Because of concurrent "spontaneous" oncogenic transformation in homologous cultures not exposed to SV40, no association between the capacity to synthesize S antigen and the development of oncogenic potential was established.

INTRODUCTION

Oncogenic transformation not associated with the development of "tumor" (T) antigen in hamster[3] lung and liver cells exposed to simian virus 40 (SV40) has been described by Diamandopoulos and Enders (1965). In another series of experiments van der Noordaa and Enders (1966) failed to detect T antigen in primary cultures of newborn hamster lung cells during a period of 8 weeks after exposure to SV40. Because of lack of direct evidence it was impossible at that time to decide whether transformation was associated with persistence of the viral genome or represented spontaneous acquisition of oncogenicity. Recognition of "surface" (S) antigen by Tevethia and his coworkers (Tevethia and Rapp, 1965; Tevethia *et al.*, 1965) in SV40-transformed cells ap-

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[3] Throughout "hamster" refers to golden Syrian hamster.

peared to offer means whereby this problem might be further investigated. Accordingly, tests for S antigen were done and found to be positive in 3 of the 6 lung cell lines and 1 of the 5 liver cell lines to which we have just referred. S antigen, although not consistently associated with oncogenic potential in the liver lines was clearly detected only in lung lines that were oncogenic (unpublished observations). These findings suggested that in the lines synthesizing S antigen the SV40 genome might be present but possibly in a more repressed or incomplete state, since synthesis of T antigen was not observed.

To obtain further relevant data, the experiments described here were undertaken in which established lines of "normal" hamster embryonic cells were employed. These lines were selected because they permitted the simultaneous study of uninoculated control cultures, which were comparable in all other known respects to those exposed to the virus. The procedure adopted was basically analogous to that employed in experiments with the lung and liver systems (Diamandopoulos and Enders, 1965), i.e. the virus was added and the cultures were allowed to remain without cell transfer for a period of 3 months when cell passages were resumed.

MATERIALS AND METHODS

Virus. SV40, strain VA 45-54, was grown in monolayer cultures of line AH-1 Grivet monkey kidney cells (Günalp, 1965). $TCID_{50}$ 0.1 ml as determined in this system was log 6.2.

Cells. (a) Hamster embryo cell lines. Seven uncloned lines, all of which originated from the same pool of hamster embryonic tissues (Diamandopoulos and Enders, 1966) were employed. Cells were grown in Puck's medium with addition of 10% inactivated horse serum and 10% fetal calf serum. When tested for oncogenicity (Diamandopoulos and Enders, 1966) at the 15th and 30th passages (10 and 15 months, respectively, after initiation), none of these lines produced tumors after subepithelial implantation of 10^6 cells into the Syrian hamster cheek pouch. As routine, passages were carried out at weekly intervals. At the 30th passage level aliquots of cells of each line were frozen and stored. After 6 months the cells were quickly thawed at 37°C and propagated according to procedures previously described (Diamandopoulos and Enders, 1966). (b) Monkey cells. Cultures of the AH-1 line of grivet monkey kidney cells (Günalp, 1965) were grown in monolayers employing Puck's medium containing 10% inactivated horse serum and 10% fetal calf serum.

Tests of oncogenicity. Cell suspensions were prepared, enumerated, and implanted subepithelially in aliquots of 0.5 ml containing 10^6 cells, into both cheek pouches of weanling male Syrian hamsters, according to procedures already described (Diamandopoulos and Enders, 1966). As routine, 6 animals were used for each cell suspension tested.

Immunofluorescence techniques. (a) Tests for T antigen were performed by the indirect fluorescence antibody technique as previously described (Diamandopoulos and Enders, 1965). (b) Tests for S antigen were carried out by the indirect immunofluorescence antibody technique originally described by Möller (1961). Briefly, the cells growing in tissue culture as monolayers were brought into suspension with 0.3% trypsin, washed once with Eagle's medium containing 10% fetal calf serum and 3 times with Tris-buffered saline (TBS), pH 7.4. After the final wash, 10^6 cells were allowed to react with 4 drops of serum from SV40-vaccinated hamsters that had resisted transplantation of 100,000 hamster cells transformed by SV40. After incubation for 1 hour at 37°, the cells were washed 3 times with TBS and were allowed to react with antihamster γ-globulin horse γ-globulin conjugated with fluorescein isothiocyanate. After incubation for 30 minutes at 37° in the dark, the cells were washed 3 times, drained, suspended in buffered glycerol (pH 7.0), and examined in a Zeiss fluorescence microscope. Only the cells showing a bright green fluorescence in the form of a ring around the cell were counted as positive. A cell line was called positive for S antigen only if more than 50% of the cells showed specific membrane fluorescence. Controls included either the normal hamster serum or serum from adenovirus type 12 tumor-bearing hamsters allowed to react with the cells under test. Cells known to contain SV40 specific S antigens were also included in each test. The preparation of S antibody and the numerous tests carried out to demonstrate the specificity of the reaction are described elsewhere (Trevethia *et al.*, 1965, 1967).

TABLE 1

TESTS FOR ONCOGENICITY AND THE DEVELOPMENT OF S AND T ANTIGENS IN 7 LINES OF HAMSTER EMBRYONIC CELLS EXPOSED AND NONEXPOSED TO SV40

Lines	Oncogenicity	"S" Antigen[a]		"T" Antigen[a]		Oncogenicity[a]		Tumor Cell "S"		Tumor Cell "T"		Serum "Anti-T"	
	10 and 15 Months	4 months		4 months		4 months		3 months		3 months		3 months	
	Non-SV40 Exposed	SV40 Exp.	Non-Exp.	SV40 Exp.	Non-Exp.	SV40 Exp.	Non-Exp.	SV40 Exp.	Non-Exp.	SV40 Exp.	Non-Exp.	SV40 Exp.	Non-Exp.
E	–	+	–	–	–	+	+	+	–	–	–	–	–
P	–	+	–	–	–	+	+	+	–	–	–	–	–
M	–	+	–	1-3% +	–	+	–	+		100% +		+	
2Ps	–	+	–	0-1% +	–	+	–	+		100% +		+	
Ks	–	–	–	–	–	–	–						
Ps	–	–	–	–	–	–	–						
I	–	–	–	–	–	–	±						

[a] Lines were frozen for six months, then thawed for experiment. S = surface, and T = tumor, antigens.

RESULTS

Two monolayer cultures of each of the 7 nononcogenic hamster embryonic cells lines in the 32nd passage were prepared in test tubes (16 × 150 mm). At the same time and employing the same cell suspensions, 4 cultures of each line were prepared on coverslips carried in Leighton tubes. On day 3 after the cultures were established, 0.1 ml of undiluted stock SV40 was added to one of each of the 2 test tube cultures and to 2 of each of the 4 Leighton tube cultures of each cell line. In addition, 0.1 ml of stock virus was added to each of 2 coverslip cultures of the AH-1 line of grivet monkey kidney cells in Leighton tubes. Comparable uninoculated cultures of monkey kidney cells were included as controls. All cultures were then incubated at 37°. At 24 and 48 hours after addition of SV40, cover glasses were removed from inoculated and uninoculated Leighton tube cultures and the cells were examined for presence of T antigen by the indirect immunofluorescence technique. A majority of the SV40 exposed grivet monkey cells showed after 24 hours typical intranuclear fluorescent staining and the numbers of such cells had increased by 48 hours. Specific fluorescence was not seen in uninoculated monkey cell preparations, nor in any of the SV40-exposed or unexposed hamster cell cultures.

The remaining 7 SV40-exposed hamster cell test tube cultures with their 7 unexposed homologous cultures were subsequently maintained for 3 months with twice weekly changes of growth medium but without subculture. Frequent microscopic examination gave the impression that the cell populations in the virus-exposed cultures increased slightly as compared with those in the unexposed group. At the end of the 3 month period, 4 successive passages at weekly intervals of the cells from each of the 14 cultures were made, dividing the cells by one half at each passage. Cultures of the 4th passage were tested for presence of S and T antigens, for plating efficiency, and for oncogenic potential. The results of the tests for these antigens and for oncogenicity are summarized in Table 1. Plating efficiencies, since they failed to show any significant differences between SV40-exposed and un-

of such controls in experiments concerned with the role of oncogenic transformation *in vitro* by known agents.

With the recognition of the S antigen the question arose concerning its relationship to the SV40 tumor homotransplantation antigen of Habel and Eddy (1963) because of its orientation at the cell surface where, presumably, the Habel antigen is also located. The materials provided by the present series of experiments appear to offer means of investigating this problem experimentally by comparing the oncogenic titer of cells from S-positive, T-negative lines with the titer of homologous oncogenic nonexposed lines in SV40-immunized hamsters according to Habel's technique (1962). Experiments of this kind are in progress.

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MATERIALS AND METHODS

Media

Medium A: LB broth, per 1 liter distilled water; bactotryptone (Difco), 10g; yeast extract, 5 g; NaCl, 10 g; 20% glucose, 5 ml; and 1 *M* $CaCl_2$, 2.5 ml added after autoclaving.

Medium B: per 1 liter distilled water: KH_2PO_4 (anhydrous), 5.6 g; K_2HPO_4 (anhydrous) 28.9 g; yeast extract, 10 g; thiamine, 10–15 mg; and 25% glucose 40 ml added after autoclaving.

L-broth: per 1 liter distilled water: bactotryptone (Difco), 10 g; yeast extract, 5 g; NaCl, 5 g; 5 ml 20% glucose, 5 ml; and

exposed cells, are not presented. From Table 1 it is apparent that in all the uninoculated cultures neither S nor T antigen was demonstrated. Cells from 3 of the SV40-exposed cultures also failed to synthesize these antigens (Ks,Ps,I). Cells of the 4 remaining cultures that were exposed initially to SV40 developed S antigen (E, P, M, 2Ps), and in 2 of these (M, 2Ps), cells synthesizing T antigen were also found. It is of interest that in these two lines the proportion of T antigen-positive cells was low. That this low ratio of T positive to T negative cells was maintained *in vitro* was shown by examination of cultures of the same lines which were subjected to 2 additional passages.

Tests for oncogenicity demonstrated that cells of 2 of the uninoculated lines (E and P) acquired this property during the course of the experiment since progressively growing tumors developed in both cheek pouches of all hamsters into which they were implanted. Uninoculated line I probably became weakly oncogenic, since a single small tumor (3 mm) developed in one of the 6 hamsters, each of which received 10^6 cells. Among the SV40-exposed lines, 4 became oncogenic (E, P, M, 2Ps) as indicated by rapid and vigorous growth of the tumor masses in all animals tested. The pathogenesis and morphologic manifestations of these tumors as compared with those induced by cells of uninoculated lines will be described elsewhere.

To determine whether the cells of tumors induced by cell lines remained unchanged in respect to the synthesis of S and T antigens, tumor tissues were trypsinized and cell suspensions thus obtained were grown as monolayers and examined in the first passage by the immunofluorescence technique. These results are also summarized in Table 1. It is evident that correlation was complete between the presence or absence of S and T antigens in all the strongly oncogenic lines before and after passage *in vivo*. It is noteworthy, however, that in the case of the lines that originally exhibited small numbers of T-positive cells (lines M and 2Ps), all or nearly all of the homologous tumor cells were capable of synthesizing this antigen.

Immunofluorescence tests for the presence of anti-T antibody in the sera of animals bearing large tumors induced by intramuscular implantation of the 6 strongly oncogenic lines are also recorded in the table. As expected, this antibody was detected only in sera from animals bearing tumors in which T antigen was demonstrable.

DISCUSSION

Although the possibility still remains that the emergence of neoantigens following exposure to SV40 depends upon derepression of cellular antigens, much evidence is now at hand favoring the view that T antigen in non-virus-producing SV40-exposed cells depends upon the persistence of viral genetic material. Our findings, that S antigen appeared in cells of hamster embryo lines previously exposed to SV40 but not in cells of the unexposed homologous lines maintained under the same conditions, provides additional data suggesting that this antigen may also depend upon persistence of the SV40 genome.

If it be assumed that information for the synthesis of both antigens is provided by the viral genome, the results reported here suggest that the genome may be expressed in one of two ways, i.e., in coding for the synthesis of both S and T antigens or in coding for that of S antigen only. This reasoning is based on the demonstration that in the descendants of 2 of the lines of cells exposed to SV40, S and T antigens were synthesized, whereas in 2 other lines similarly treated S antigen alone was reproduced. Relevent to the foregoing concept are the recent results of Kluchareva and co-workers (1967) indicating that the synthesis of S antigen precedes the synthesis of T antigen. Parenthetically, we may add here that in addition to those postulated, the viral genome may assume still another state which would code for T antigen only. The present experiments, however, afford no indication of whether this may or may not occur.

We have no knowledge of the nature of the factors which determined whether only S antigen or both S and T antigens will be synthesized. One may speculate, however, that these factors are, in part at least, cell-dependent, since in lines of SV40-exposed hamster lung cells (unpublished observations) only S antigen has been demonstrated, whereas in hamster heart cells maintained under comparable conditions both antigens were found (unpublished observations). Uncloned cell lines originating from the mixed tissues of whole embryos were used in the experiments reported here. The observed variation, therefore, in the reproduction of the two antigens among these various lines might reasonably be attributed to differences in composition of cell population, which may have taken place during the long period of independent cultivation *in vitro*. On this assumption one may further conjecture that in certain of the embryonic lines the populations came to consist entirely of cells which were either completely resistant to infection, or, if infection did indeed occur, coding for these antigens by the viral genome was entirely repressed. In other lines we may suppose that only cells permitting the expression of that portion of the genome specifying the synthesis of S antigen were present, while in those lines in which both antigens were found cells allowing complete expression of the genetic factors for each antigen were represented. That population differences existed in two of the lines at least, is given some support by the observation that in the SV40-exposed lines which exhibited cells with S and T antigens, the proportion of T-positive cells was small when first observed and remained constant on further subculture.

In presenting the foregoing ideas it was assumed that the viral genome remains intact, at least in respect to its capacity to provide information for the synthesis of the two antigens. Alternatively, however, one can visualize structural losses in portions of the viral genome specifying one or both of these antigens which might be brought about by factors present in cells of different origin. If a way can be found to recover infective virions from cells of the lines synthesizing only S antigen, evidence might be obtained in support of one or the other of the mechanisms just proposed. Thus, should structural loss of a portion of the genome be responsible, cells which are potentially capable of synthesizing both antigens should be found to synthesize *only* S antigens when exposed to infective virus recovered from S-positive, T-negative lines. With this possibility in mind, experiments will be undertaken to determine whether by the cell fusion technique which Gerber (1966) has recently applied to induction of SV40 in non-virus-producing lines, the replication of infective virions in S-positive, T-negative lines can be induced.

In hamster cells previously exposed *in vitro* to SV40 a correlation between the presence of T antigen and the capacity to induce tumor formation has been demonstrated (Diamandopoulos and Enders, 1966). In the present experiments the attempt was made to determine whether in S-positive, T-negative cells a similar correlation could be established. As stated at the beginning, in tests for S antigen in several SV40-exposed, T-negative hamster lung cell lines, S antigen was detected in 3 which were shown to be oncogenic, while this antigen was not found in 3 remaining lines which failed to induce tumor formation. Although these findings suggested a correlation between the presence of S antigen and oncogenicity, this could not be affirmed, since comparable SV40-non-exposed lines were not available as controls. Consequently the possibility remained that spontaneous oncogenic transformation might have occurred independently of the capacity to reproduce S antigen. In the present experiments with hamster embryo cell lines such controls were included. The results, nevertheless, again failed to answer the question conclusively, since not only the two S-positive, T-negative SV40-exposed cultures became oncogenic, but during the same period of observation the two homologous unexposed cultures also acquired this property. However, tumors induced by the 2 S-positive lines (M, and 2Ps) that exhibited a small proportion of T-positive cells, consisted preponderantly of T-positive cells. Therefore, the S-positive, T-negative cells originally present in these lines may not have been oncogenic. Further experiments employing cloned lines from these sources that consist of cells with only S antigen may serve to clarify this point.

The demonstration of the acquisition of oncogenicity by cells in cultures, comparable as far as was known in all respects except for exposure to virus should be noted. It reemphasizes the necessity for the inclusion

Near disaster with the Salk vaccine

THE scientific community is breathing easier over an event that, at the time, seemed to be one of the most horrifying medical mistakes in history.

It is now almost certain that a recently-discovered virus, unwittingly put into hundreds of thousands, if not millions, of doses of early Salk vaccine, will not cause cancer in human beings. But for a while the evidence pointed in the other direction.

The virus, which has been the subject of much secret medical concern, is known as simian virus 40 (SV40). When discovered in the kidney tissues of Rhesus monkeys, SV40 was considered a stray organism, one of many latent viruses that lurk about man and animal without doing any damage.

In 1961, came the frightening report that SV40 could cause cancer when injected in newborn hamsters. Alarm gripped every public health man in the country. Hundreds of thousands of children had been infected with this virus since the Salk vaccine was introduced in 1955.

Considerable comfort, however, was taken in the fact that SV40 was dangerous only in newborn hamsters. Furthermore, the dosage needed to infect hamsters was much greater than the children were likely to have gotten.

But the report touched off a flurry of research activity on SV40 and produced more disturbing findings. The tumor-producing property of SV40 was not limited to the hamster, it was discovered. A rat species also came down with tumors.

In August, 1962, a leading investigator found the hamster could be infected as late in life as 22 days, a period that corresponds more closely to the age of younger children who received most of the vaccine. There also was some evidence the SV virus could produce slight, non-cancerous infection in man, and when put in human tissue culture could cause some cell changes suggestive of tumor growth.

This meant a definite study had to be made of the statistics in the Salk-treated children themselves. The National Institutes of Health undertook that analysis.

Fortunately, a tidy, built-in experimental model existed because the early use of Salk vaccine was controlled. In 1954, Salk vaccine was field tested among 400,000 first-, second- and third-grade children in 44 states. In 1955, it was licensed as a commercial product and administered to first and second graders in all states under a free vaccination program by the National Foundation. By July, 1955, six million children had been inoculated.

The stored specimens of the vaccine lots were available in Washington. They were analyzed for simian virus content and matched against the death rates in the various states.

The results, published in *The Journal of the American Medical Association*, were gratifying. They showed the mortality rates in cancer have been no greater in the four years since 1955 than in the four before.

There is a slight increase in leukemia, but the same increase is shown in states receiving no SV40 in the vaccine.

"There is no reason to suspect the slight increase in leukemia mortality rates is related to SV40," said the experts, Dr. Joseph F. Fraumeni, Jr., medical officer, and Dr. Robert W. Miller, chief of the epidemiology branch of the National Cancer Institute.

The comparisons were made only to 1959 because complete vital statistics are only available to that point.

Since the incubative period of a potential cancer virus may be longer than four years, continued surveillance will be necessary.

It would be premature to conclude that SV40 is harmless, Dr. Fraumeni says, but the lack of effect thus far is highly encouraging.

SV40 also has been involved in the early Sabin vaccine. It may be included in further study. Since its discovery, however, SV40 has been rigidly excluded from both Sabin and Salk vaccines.

Comfort can also be drawn from an event in the 1930's when several million people were vaccinated against yellow fever virus.

This virus was propagated on chick embryos. Years later it turned out that chickens harbor one or more viruses that produce cancer in chickens.

These presumably went into the vaccine that treated millions of people, but there is no evidence of an increase in cancer incidence in this group.

—*Arthur J. Snider*

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Edited by **DOUGLAS M. CONSIDINE**

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ETTING EFFECT. The falling-off in brightness toward the gin of an illuminated field, due to the mutilation of the more ique bundles of light by the combined effects of diaphragm and s aperture. This is a source of trouble in photographic objectives en they are used at large apertures, or close to the limit of their ly-illuminated fields.

NCENT'S ANGINA. Ulcer.

NEGAR EEL (*Nematoda*). A minute roundworm, *Anguillula rbatrix*) *aceti*, found in the "mother" of vinegar. It reaches a gth of 2 millimeters. The worms have been found in other situa-s, including the human bladder.

NYL CHLORIDE. Chlorine Organics.

NYON FIBERS. Fibers.

PER FISHES (*Osteichthyes*). Of the order *Isospondyli*, family *adiodontidae*, viper fishes have an unattractive, snake-like appear-e, which is dramatized by their large fanglike teeth. The three cies all inhabit deep ocean waters, ranging from very cold to pical. The longest of these species attains a length of about 10 hes. In catching its prey, the fish swims with its mouth wide open l upper fangs extended so as to spear the victim. Studies have wn that these fishes engage in vertical migrations, moving upward ne 1,500 feet at night, but not known to surface.

PER (*Reptilia, Sauria*). A poisonous snake with a pair of long ular fangs near the front of the upper jaw. Most species of vipers also characterized by the relatively short and thick body and the ad triangular head. The group includes the typical vipers of the l World and the pit vipers of North and South America.

The Old World vipers include a number of Asiatic, European, and ican species bearing the name viper and in addition the two cies known as the asp and eja. The Egyptian horned viper is metimes known as the cerastes from the name of the genus to ch it belongs. The African puff-adder is a viper, named from its of inflating the body when disturbed. This name has unfor-ately been borrowed for an entirely harmless snake of the eastern ited States, related to the hog-nosed snake. It is variously known he puffing or spreading adder or blowing viper. When disturbed it tens its body and makes an impressive bluff, but it is quite nless.

Many of the Old World vipers are dangerous. Their poison is ilar in nature to that of the pit vipers.

RAL PNEUMONIA. Respiratory System.

REO. Warbler.

RGA. Hydrometeors and Precipitation.

RGO. One of the earliest named constellations; the sixth sign of Zodiac. References to Virgo are found in every known literature are always connected in some manner with a maiden and the est. Among the Egyptians, Virgo was associated with Isis, who said to have formed the Milky Way by dropping innumerable at heads in the sky.

stronomically, the constellation is famous for the large cluster of xies found in it. Sir William Herschel found no less than 323 xies in this part of the sky, and more recent observations have ed the number to more than 500. It also contains a large number ariable stars and the well-known bright star, Spica. (See map mpanying entry on Constellations.)

RGO CLUSTER. A cluster of galaxies totaling more than 300 ers and occupying an area approximately 12° in diameter. of the galaxies are spirals, a fact which may be due to the close ximity of this cluster. The distance to the Virgo cluster is approxi-ely seven million light-years. See also Galaxies.

RTUAL OBJECT (Optics). Object (Real).

VIRTUAL TEMPERATURE OF AIR. Atmosphere (Earth).

VIRTUAL WORK. Work (Virtual).

VIRUS. Viruses are considered to be the smallest infectious agents capable of replicating themselves in living cells. The majority of these extremely small infectious particles fall within a size range of about 0.02–0.25 micrometer and can only be visualized directly with the aid of an electron microscope. The precise mechanism of how a virus transfers its nucleic acid to the host cell, and how the normal function of the cell is directed toward the production of progeny, remains obscure. Although extensive research continues, viruses pose some of the most fundamental problems encountered in molecular biology. Until about the early 1960s, viruses were named for the diseases which they caused—thus mumps virus, measles virus, influenza virus, yellow fever virus, smallpox virus, etc. It is only within relatively recent years that large quantities of several of the viruses can be obtained *in vitro* in cell cultures. Better methods of virus purification have enabled investigators to carry out chemical tests which were hitherto impossible. Many of the biological tests for viruses, such as complement fixation, hemagglutination, or cytopathic changes in cell cultures and serum-virus neutralization tests in cell cultures or animals, are extremely sensitive, and these methods are used routinely for viral identification. There are a few viruses, however, whose identification depends upon biochemical tests, and still others for which biochemical tests in conjunction with biological tests are useful aids for identification. Progress has been made in the classification of viruses beyond simply associating them with the names of the diseases which they cause.

Viruses studied in detail have a core of nucleic acid surrounded by a protein coat or coats. The viral nucleic acids are of two types, ribose (RNA) or deoxyribose (DNA). They represent the genetic material necessary for the replication of intact virus progeny. Nucleic acid extracted from purified virus using phenol or dodecyl sulfate is easily destroyed by the homologous nucleases which are present in normal sera or tissues. DNA is destroyed by the enzyme deoxyribonuclease and RNA by ribonuclease, and this is one means of identifying the type of nucleic acid. The intact virus is not affected by these enzymes.

Without a protein coat, the nucleic acid is ordinarily incapable of entering a cell. Entry can be accomplished by washing the cells to remove any serum and by pretreating the warmed cells with hypertonic salt solution. On entry into the cell, the viral nucleic acid induces the synthesis of a new protein coat from the host material. Some viral nucleic acids are capable of replicating at least one virus cycle in hosts which do not permit replication by the whole virus. Poliovirus nucleic acid has been known to give rise to whole virus in embryonic chick cells, a host which is not susceptible to infection with poliovirus; polyoma virus nucleic acid has produced whole virus in *B. subtilis*, a bacterium. In general, the DNA viruses multiply in the nucleus of the host cell and RNA viruses in the cytoplasm. Some of the RNA viruses appear to emerge as buds from the cell membrane as seen in the electron microscope.

The nucleic acids and the proteins which they control exist in an orderly fashion. In the RNA viruses, the nucleic acid may be in either a cubical or a helical form; the DNA viral nucleic acids occur only in a cubical form. The cubical nucleic acids are enclosed in a container or capsid made up of similar protein subunits or capsomers in crystalline array, usually as an icosahedron. Certain groups of viruses are consistent in that they are the same size, and the number and arrangement of the capsomers are the same. In some of the RNA viruses the nucleic acid is arranged as a double- or single-helical structure surrounded by protein subunits. The combination of nucleic acid and protein may constitute the whole virus, or there may be additional outer membranes which contain lipids. Viruses which have lipid membranes can usually be inactivated by ether, chloroform or bile salts.

The two groups of viruses RNA and DNA are further divided according to size, morphology, and biological and chemical properties. Thus the cubical RNA viruses which are ether stable are divided into the picornaviruses and the reoviruses. The name picornavirus comes from "pico" meaning "very small" and "rna" indicating the type of nucleic acid. Included in the group are the enteroviruses: polio, Coxsackie, and foot-and-mouth, etc. The reoviruses cause inapparent infection in humans and other animals, and their relation-

as in producing vaccine-induced en

to spontaneous disease is uncertain. They are morphologically ilar to the wound-tumour virus of clover, and a small cross ctivity with this virus by means of complement fixation has been eported.

The arboviruses are those which undergo a biological cycle in both rthropods and vertebrate hosts. Not all of these viruses have been tudied for fundamental chemical characteristics. Those which have en studied were found to be cubical RNA viruses, sensitive to the ction of ether and relatively unstable.

The myxoviruses and rabies are examples of RNA helical viruses, hich contain an outer, etherlabile, lipid-containing membrane. The yxoviruses include the influenza, parainfluenza, mumps, newcastle, man SV5 and SV11, and possibly also measles, rinderpest and dog stemper viruses. Most of the myxoviruses have an affinity for ucins. They adhere to the surface of erthyrocytes causing them to gglutinate, and the substance responsible for the adhesion is neuraic acid. Adsorption to the cell surface is inhibited by mucoroteins which are present in sera and other biological fluids. *Vibrio olera* produces an enzyme known as receptor destroying enzyme DE), which when added to erythrocytes prior to adding virus, hibits cell attachment and prevents hemagglutination. Less is own about the biochemical aspects of measles, dog distemper, derpest or rabies viruses.

Information is lacking concerning the symmetry of a large number RNA ether-sensitive oncogenic viruses. The fowl leucosis, murine ukemia and mouse mammary carcinoma viruses make up this up.

ll of the known DNA viruses have cubical symmetry. Two groups ich are ether stable are the papovaviruses and the adenoviruses. ere are also two groups of DNA viruses which are generally ether nsitive: the herpes viruses and the pox viruses. All of the herpes uses are ether labile, but ether stability varies within the pox virus up. See also **Recombinant DNA.**

The chemical nature of many viruses, which either do not grow l or do not lend themselves to purification, is unknown. The Riley dehydrogenase virus is a nonpathogenic virus which is gnized only by an increase in lactic dehydrogenase in the blood nfected mice. A lipovirus described by Chang causes marked radation of infected cells and releases a lypogenic toxin dissoe from infectivity, which is capable of inducing fatty degenera- in other uninfected cells. A marked increase in the maglobulin fraction of blood serum of mink infected with Aleumink disease is an indication of infection with a virus which es a color change in the fur and often sickness and death.

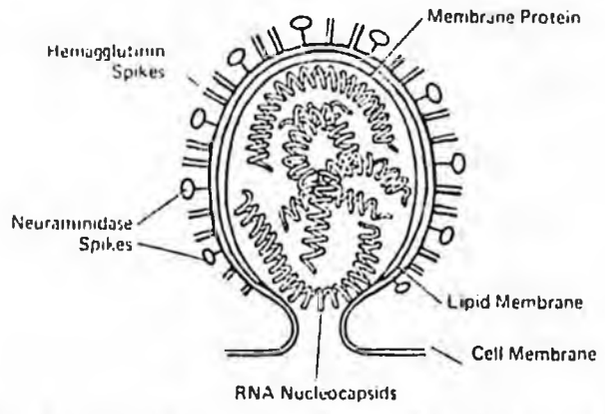
he chemical characteristics of viruses are not only an aid in their dication and identification but are also useful in understanding ature of known viral or viral-induced host antigens and possibly e control of disease. The adenoviruses, for example, contain at three protein moieties, and certain types are capable of inducing or more new host antigens—the chemistry of which is unknown resent. The viral proteins can be separated by gel diffusion and ated with complement fixation. One moiety is the toxic protein h causes the host cell to degenerate; another corresponds to the p antigen common to all the 31 types of adenoviruses; the third type specific protein.

number of viruses induce the host cell to elaborate a substance n as interferon which will inhibit the growth of many viruses in of the same species but not in cells from other animal species. ferons produced by an influenza virus and also a herpes virus both active against the vesicular stomatitis virus. They both d to be proteins of low molecular weight, trypsin sensitive, and at a temperature of 70 C and over a wide range of pH (1–11).

luenza Virus. Many virus diseases, in essence, have been con- d or well controlled without the need really to understand the ate mechanics of the virus. If malaria, for example, can be con- by the eradication of mosquitos, if yellow fever, smallpox, clitis, and measles can be controlled by isolation of the virus the production of vaccines, there does not exist an immediate to solve the problem at the level of molecular biology. However, nted out later, the relationship between what have appeared to ntrollable viruses and later appearance of serious diseases by a *slow virus* series of events, may point to the fact that a person ering from measles, mumps, etc., may have only partially con- d the devastation of the virus and suffer some years later from conditions provoked by an earlier virus infection.

In contrast with the aforementioned common virus diseases, it appears that the solution to the problem of periodic pandemics of influenza may come only from a much better understanding of the virus forms which cause the disease. The persistence of influenza appears to derive from a unique genetic plasticity, allowing the viral agent to undergo at least two kinds of antigenic shift. There is the frequent shift, occurring once about every year or so which appears to stem from minor mutations, thus providing the new variant with an increased resistance to prevailing antibodies. And there is the less frequent (once in 10 to 12 years) antigenic shift that, unfortunately, overcomes all prior immunities. Over 50 million cases of influenza in the United States were reported during the 1968–1969 winter. These cases were attributed to a hitherto unknown variant, first isolated in Hong Kong (hence Hong Kong "flu"). Some 20,000 and possibly as many as 80,000 deaths resulted from this influenza invasion and the side effects which it produced. In the 1972–1973 winter season, a much milder and minor variant, called the London "flu," caused well over 2,000 deaths in the United States, particularly from side effects, mainly pneumonia. When combined with influenza, pneumonia is the fifth most serious public health problem in the United States. In terms of absenteeism, it is the number one problem. In the influenza pandemic of the winter of 1917–1918, over 20 million persons died worldwide, with better than one-half million fatal cases in the United States.

Myxovirus influenzae is the agent of influenza, of which there are three antigenic types, A, B, and C. The first two types occur frequently. Only type A has been found to be capable of producing pandemics. It is presumed that the B virus has a reduced ability to undergo gross antigenic mutations; and that the C virus has no such capability. The influenza A virus is identified as a medium-size RNA virus, some 110 nanometers in diameter and delimited by a membrane. The latter is composed of lipids and polysaccharides derived from the host cell and virus-specific protein. Five distinct proteins have been identified, three of which are inside the virion (part of virus circumscribed by lipid membrane). A schematic diagram of the influenza virus emerging from a cell is given in the accompanying figure.



Schematic representation of an influenza virus emerging from a cell. (*After Kilbourne*)

It has been reported that the antigenic shifts are manifested in hemagglutinin and neuraminidase, two glycoproteins found on the surface of the influenza virion. It is suggested that the hemaglutinin binds the virus to the target cell and when the hemagglutinin function is inhibited (as by an antibody), the virus is no longer effective. It is believed that the neuraminidase cleaves a glycosidic bond in the host cell membrane. This action frees the newly formed virus from the cell. It is believed that this action, if inhibited, will not reduce the infectivity of the virus, but will deter the spread of virus particles to other cells.

The abrupt emergence of new influenza subtypes appears to be too marked to be explained fully by conventional concepts of mutation. It is believed that the explanation rests in the very nature of the viral genome. It has been postulated that if a host cell is infected by two different subtypes of influenza virus at the same time, the genes from the subtypes may undergo a random reassortment in the cell, resulting not only in production of the two original subtypes, but of one or

eral subtypes as well. Each hybrid, of course, will have a different, but full set of genes and recombination within the infected host can explain the large mutations which occur about once every decade. However, it is well established that only one influenza subtype can exist in humans at any given time. Thus, the question of a host in which such recombinations can take place? It has been found, for example, that the emergence of a new subtype, such as the Hong Kong strain, will be accompanied by the abrupt disappearance of the antecedent subtype—thus indicating little if any opportunity for recombinations to occur within human cells. Of considerable interest, however, is the fact that several virus strains can exist simultaneously within various animal hosts. In animals, the appearance of a new influenza virus strain is not necessarily accompanied by the disappearance of previously recognized strains. It has been established that there are at least two discrete subtypes of equine influenza, eight or more avian strains, and a couple subtypes in swine. Thus, the postulation of recombination occurring within animals which share the general environs with humans. Some evidence of this may derive from the fact that most new subtypes appear to originate in Asia, where animals and humans commonly inhabit the same buildings.

Influenza vaccines produced to date are based upon killed viruses. Some authorities believe that attenuated live viruses could be more effective in creating immunity as well as causing fewer undesirable side effects. However, a major problem in connection with influenza vaccines has been the short time allowed for the production of a new vaccine upon the emergence of a new influenza variant. Vaccines made with live viruses have been used in the U.S.S.R. for many years. They have not been licensed in the United States out of fear of over- or underattenuation of the virus. Although the vaccine problems have been largely overcome for other diseases, they have not been solved for the influenza virus because of the almost continual appearance of new variants and the need to continuously change the vaccine formulations.

Among several interesting proposals in recent years, the concept proposed by St. Groth and under study by C. Hannoun and associates at the Pasteur Institute in Paris, is of particular note. This concept, in essence, involves forcing a recent variant of influenza, such as the A_3 subtype, to undergo mutations at an accelerated rate under laboratory conditions until an end point in the evolution of the subtype is reached. It is interesting to note that discovery of the London influenza variant, first isolated in 1972, was antigenically similar to the first mutant that Hannoun and associates had "artificially" produced in the laboratory a year earlier. By gaining a year or more on the natural processes of creating mutants, possibly by way of animal source channels, vaccines could be produced well in advance of the appearance of the mutated virus.

Cytomegalovirus. Surpassing rubella virus, this is the most common viral cause of mental retardation. It has been estimated (late-1975) that cytomegalovirus (CMV) causes serious mental retardation of one of every 1,000 infants, or more than 3,000 infants annually in the United States. Immunosuppressed patients, such as those suffering from cancer, organ transplants, etc., also are prone to infection with CMV. In addition to mental retardation, the disease in infants may cause blindness and deafness. In about 90 percent of the infants, affected by CMV, the disease can be detected only through examination of the urine. In about 10 percent of the cases, the disease is typified by enlargement of the spleen and liver, blood abnormalities, and hepatitis. Microcephaly (abnormally small head) is also sometimes an indication. CMV causes enlargement of the affected cells (cytomegaly). The disease is found throughout the world. Investigators believe that congenital infections are the result of the mother having a primary infection sometime during pregnancy. Investigators believe that CMV, like herpesviruses, persist in a latent stage for long spans of time.

Slow Viruses. During the last decade or two, there has been increasing speculation and some tentative evidence that so-called *slow viruses* may be operative and may be the underlying causes of a number of degenerative diseases, long poorly understood, such as multiple sclerosis and rheumatoid arthritis, among others. More recently, there have been increasing postulations of an association between viruses and diabetes. In fact, rather positive identification of slow viruses with some rare diseases has been established. Most investigators caution that the term "slow" should not necessarily be fully interpreted in terms of a virus per se, but equally if not completely with the manifestations of the virus. So-called slow virus infections are characterized by a long incubation period, followed by a protracted course of disease. The slowness may arise in some cases from the virus itself, but the slow pace also may be the result of weak but prolonged interactions between the virus and the host's immune system. It is also possible that these characterizations of slowness may not be attributable to viruses at all, but to some other unknown causative factors. Obviously as of this juncture, investigators are following a source of suspicion rather than a chain of hard evidence. Nevertheless, the case for the slow viruses is becoming increasingly convincing. The causative agents for at least four rare diseases, two in humans and two in animals, are sometimes referred to as "unconventional viruses."

One of these diseases in humans is *kuru*, encountered only in the Fore people and their neighbors in New Guinea. The disease for many years was considered a genetic disease. However, it has been established that the disease can be transmitted to chimpanzees by injection of extracts from the brains of human kuru victims into the brains of chimpanzees. Kuru is a neurological disease with brain lesions located mainly in the gray matter. The cerebral cortex takes on a spongy appearance. The other human disease is Creutzfeldt-Jakob disease, rare but of worldwide distribution. It involves the premature development of the mental deterioration sometimes seen in old age. It also has been established that it is caused by a transmissible agent that can infect chimpanzees and lower primates. One of the animal diseases referred to is *scrapie*, known for over two centuries as a fatal disease among sheep. The other animal disease is *transmissible mink encephalopathy*, first discovered in Wisconsin in the late 1940s. A puzzling aspect of the unconventional slow viruses is the fact that they cannot be observed with an electron microscope. Another puzzling aspect is their apparent lack of antigenicity. To date, it has not been possible to demonstrate that any of these four "agents" will evoke production of antibodies. These unconventional slow viruses are not destroyed by ultraviolet radiation, and they are highly resistant to treatment with formalin or heat, but infectivity is destroyed by phenol or ether. Some investigators believe that these agents may incorporate a very small nucleus of the size range of the viroids (self-replicating infectious RNA molecules known to produce certain plant diseases).

Two slow infections of the human central nervous system, *progressive multifocal leukoencephalopathy* (PML) and *subacute sclerosing panencephalitis* (SSPE) are thought to be associated with conventional viruses. Although PML does not cause inflammation of the brain, it does produce demyelination, i.e., destruction of the layers of membranes surrounding nerve axons. Some investigators believe that the virus is a papovavirus (group of small viruses including human wart virus, simian virus 40, and the polyoma virus of mice). It is reasoned that in PML the virus destroys the cells needed for formation and maintenance of the myelin sheath. A conventional virus has been isolated from the brains of persons suffering from SSPE. An association between measles (occurring in patients under two years of age) and later development of SSPE (approximately within six years) has been shown by one study.

Slow viruses are becoming increasingly suspect in the instances of much more common diseases, particularly the autoimmune diseases. An autoimmune disease may be defined as a disease wherein the immune system of the body does not direct its attack on an invading foreign substance, but instead at the body's own tissue. Many authorities consider rheumatoid arthritis and multiple sclerosis as autoimmune diseases. The precise causes of these diseases have remained obscure. Multiple sclerosis is a demyelinating disease and has variously been described as an autoimmune disease, a viral disease, or an autoimmune disease provoked by a virus. Epidemiological studies indicate that from 3 to 23 years may elapse between the time of exposure to the virus and the onset of symptoms. Further evidence points to involvement of a myxovirus. Measles virus is of this kind.

Possible Viral Connection to Diabetes. A Norwegian physician (J. Stang) in 1864 noted that diabetes developed in one of his patients within a short period after a mumps infection and was probably the first person to indicate a possible connection between viruses and diabetes. Over the years, numerous other connections have been attempted to relate diabetes with mumps, hepatitis, rubella, coxsackie and influenza viruses, adenoviruses, enteroviruses, and cytomegalovirus. One of the presumptions made is that viruses are understood

to replicate in the pancreas. Commencing in the late 1950s, more substantive evidence has been given. Reports from Sweden in 1958 link juvenile diabetes with mumps infection. Reports from New York State in 1974 relate closely the cycles of incidence of mumps and those of juvenile diabetes. The study was based upon investigation of records for the period 1946–1971. Tentative conclusions indicate an average lag period of about 3.8 years between onset of diabetes and exposure to mumps and it is reasoned that this represents the time required for the virus to produce permanent damage to the pancreas. Other investigators have statistically linked diabetes to rubella (German measles). Some authorities suggest that the pancreas, along with other embryonic organs, may be damaged by the virus that causes congenital rubella. The records of nearly 3,000 juvenile diabetics treated at King's College Hospital in London (1955–1968) have been studied and reveal a seasonal pattern to the onset of juvenile diabetes, striking a low incidence in June and a high incidence in October. Without presenting the details, conclusions are suggested that an association of viral infections with the juvenile form of diabetes is evident. However, the relationship, if any, has not been determined in the case of the maturity-onset form of diabetes.

Phage. Bacteriophages are viruses that invade bacterial cells and are replicated within the bacterial cells. The presence of phage in live virus vaccines has precipitated concern among some authorities. It has been established that phage are introduced into vaccines when viruses for the vaccines are grown in tissue culture. To eliminate these phage, vaccine producers would have to use only sterilely collected serum. This, of course, is difficult and costly. There is far from full agreement that phage-contaminated vaccines are harmful to humans. Some situations, however, have been postulated. Some human diseases, such as scarlet fever and diphtheria are caused indirectly by bacteria, i.e., by bacteria that are infected with phage, the human disease resulting from toxins produced by the bacteria as a result of their virus infection. It is theorized that an individual might take an oral polio virus vaccine that was contaminated with phage that infects corynebacteria and thus cause them to secrete diphtheria toxin. Thus, if the intestinal bacteria included susceptible corynebacteria, that person could contract diphtheria. Another effect of phage is that they can transmit genes to human cells in tissue culture. Phage can carry a specific gene lacking in human cells. If exposed to such phage, the human cells would start to synthesize the protein coded by that gene. It has been suggested that it is in the realm of possibility for phage to transmit genes to human cells and thus cause cancer or degenerative diseases in humans.

A link between viruses and cancer has been debated for a number of years. See also Cancer.

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VIRUS INSECTICIDES. Insect Control and Insecticides.

VISBREAKING. Petroleum.

VISCACHA. Rodentia.

VISCERA. Organs lying more or less freely in the cavities of the body. Usually applied to the heart and lungs as thoracic viscera and to the stomach, intestines, spleen, liver and pancreas, and some of the reproductive organs as abdominal viscera.

VISCERAL ARCH. The column of tissues persisting between adjacent gill slits in the wall of the vertebrate pharynx. The arch is lined with endodermal tissue and covered outside with ectodermal. It contains a bony or cartilaginous support belonging to the visceral skeleton and an aortic arch. In the fishes the gills are supported by these arches. See also Fishes.

VISCERAL MASS. A compact mass of tissue containing some of the internal organs of the mollusks. It forms the main part of the body.

VISCOELASTICITY. Mechanical behavior of material which exhibits viscous and delayed elastic response to stress in addition to instantaneous elasticity. Such properties can be considered to be associated with rate effects—time derivatives of arbitrary order of both stress and strain appearing in the constitutive equation—or hereditary or memory influences which include the history of the stress and strain variation from the undisturbed state.

VISCOSITY. A property of fluids which appears as a dissipative resistance to flow. A solid which is subjected to external forces can attain a condition of elastic equilibrium with elastic stresses balancing the applied forces. A fluid subject to external forces can be in static equilibrium only if the forces are derivable from a potential function and the usual result is steady flow resisted by viscous stresses set up by distortion of fluid elements. The mechanism and nature of the viscous effect may be very different in gases and in liquids.

In a gas, viscous stresses arise from migration of molecules which carry with them momentum relative to their starting-points. To the extent that the gas may be treated as a continuous fluid, i.e., on scales large compared with the mean free path and for time intervals large compared with the collision frequency, Newton's law of fluid friction is obeyed. The elementary form of the law is that, in simple shearing motion, the shear stress is proportional to the rate of shear. More generally, the stress tensor p_{ij} is linearly related to the rate of deformation tensor

$$s_{ij} = \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}$$

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the mercury contamination already present in the bottom, but would also prevent any problems associated with sediment migrations. The disadvantages are the cost, the permanence of the plastic seal, and the unknown ancillary ecological effects that would result form the destruction of the benthic ecosystem.

8. **Remove the mercury contamination by amalgamating it with aluminum or other active metals[911]** – This method involves adding aluminum or some other metal which will actively react with mercury to form an amalgam and thereby remove it from the biological methylation cycle. The primary disadvantage of this proposal is that it adds another metal to the aquatic ecosystem, while the unknown parameters of this proposal are its cost and the possible ecological damage from the introduction of the amalgamating metal.

9. **Decontamination of streams and lakes through the use of clams to "biologically mine" the mercury contaminants[961]** – Under this proposal, clams would be used to remove the mercury contamination biologically from an aquatic ecosystem. The great advantage of this method of mercury removal is that it would cause the least ecological damage to the aquatic environment. Among the disadvantages, the possibility exists that mercury contamination might increase because the clams disturb the bottom sediments. Also, the effectiveness of this method must be questioned. For example, assuming that clams could concentrate as much as 20 ppm of mercury in their flesh, the harvesting of each million pounds of clams would result in the removal of only 20 lb of mercury from that aquatic ecosystem. Moreover, once the clams have been harvested, they would represent a costly solid waste disposal problem.

Chapter VIII

EPIDEMIOLOGY AND TOXICOLOGY OF MERCURY

Summary

During the last two centuries an estimated 1,800 to 2,000 individuals have been poisoned by some form of mercury with an estimated 120 to 150 deaths. Among these poisonings, the number attributed to organomercurials is estimated at between 700 and 800 people, including over 125 deaths. Furthermore, the vast majority of the organomercurial poisonings are due to alkylmercurials such as methyl or ethylmercury. The potency of the alkylmercurials as poisons is reflected in the fact that they were responsible for the disasters which occurred at Minamata, Japan (1953 – 1959), Niigata, Japan (1964-1965), Iraq (1956 and 1960), Pakistan (1961), Guatemala (1964-1965), and the U.S. (1969-1970). Alkylmercurials afflicted about 700 individuals and caused about 120 deaths. Therefore, while it is important to recognize that all forms of mercury are powerful poisons, the alkylmercurials are many times more effective poisons than either the inorganic or arylmercurials.

From a toxicological point of view, the pharmacological activity of inorganic and organic forms of mercury differs greatly, not only in the extent to which they are absorbed by the body but also in the degree of injury they inflict on the body. Furthermore, it appears that the distribution of various forms of mercury in animal tissues is a function of the metabolic process of the animal. If all factors were equal, the relative concentrations of inorganic, aryl and alkyltype mercury compounds in the blood, brain, kidney, and liver tissue would be present in the following declining order

alkyl > aryl > inorganic,

while the concentrations of inorganic, aryl, and alkylmercury found in the different organ tissues are present in the following declining order

kidney > liver > blood > brain.

Inorganic forms of mercury taken orally are not absorbed very quickly by the body. And once absorbed, approximately 50% of the mercury is transported by the blood plasma and it is quickly excreted in the urine in this form. Conversely, the organic mercury compounds, especially the alkylmercurials, are more toxic than the other kinds of mercury compounds because the human body absorbs more and excretes less of them. Therefore, larger amounts of the organomercurials are stored in the various tissues of the body. In addition, alkylmercurials, such as methylmercury, easily pass the blood-brain barrier to accumulate in the brain where they destroy selected brain cells and thereby produce the specific symptoms associated with alkylmercurial poisoning. Alkylmercurials also pass easily across the placental barrier causing mercury levels in the fetal red blood cells to be 20 to 30% higher than the mother's red blood cells. It has been established that the developing fetal nerve tissue is very sensitive to the destructive effects of alkylmercurials and congenital neurological damage has been reported in human fetuses at levels that have not produced alkylmercury poisoning symptoms in the mother.

Therefore, it appears that inorganic or arylmercurials pose no real threat to man or the environment directly. However, since almost any form of mercury entering the aquatic environment can be biologically converted to methylmercury, it may ultimately become necessary to control all forms of mercury pollution.

EPIDEMIOLOGY OF MERCURY

While the cumulative poisonous effects of mercury have been known for centuries, it was not until 1557 that Jean Fernel provided the first description of industrial mercury poisoning.[1] By the end of the 16th century, mercurialism associated with the cinnabar mines at Almaden[183] and Idria[183] prompted the Spanish and Austrian governments to grant the miners shorter working hours and longer vacations.

One of the first recorded and a most unusual mass mercury intoxication occurred at Idria, Austria in 1804. As a result of a fire in a local mercury mine,[184] 900 inhabitants who were exposed to mercury vapors in the air developed mercurial tremors. Besides the people, cows and other domestic animals showed similar symptoms. In 1810, another extraordinary wholesale poisoning by metallic mercury vapor occurred on the British sloop *Triumph*. After the vessel salvaged a cargo of mercury from a disabled Spanish ship, the mercury seeped into the hold and bilges of the *Triumph*. The mercury vapors that escaped killed 3 sailors and severely poisoned 200 others.[184]

In the U. S. the first known outbreak of mercurialism occurred in New Jersey in 1860. This incident was traced to the use of carroted fur that contained excessive amounts of mercury.[185] In 1891, Adler[186] gave a clinical description of chronic mercurialism in five human males. Within the felt manufacturing industry, chronic mercury poisoning was highest among blowers and shippers, the two occupational groups that were exposed to the highest concentrations of mercury vapor.[187] Among men employed in the repair of direct current meters, the occurrence of chronic mercury poisoning was described in 1949.[188] Symptoms were found only in men who repaired mercury-containing direct current meters but not in men who tested nonmercury-containing alternating current meters. Furthermore, the incidence of mercury poisoning varied according to the atmospheric concentration of mercury in their respective working environments. Four cases of subacute or chronic mercurial poisoning were found among men who operated high frequency induction furnaces where the power was supplied by an oscillating current, high frequency converter that had a mercury discharge gap.[189,190] Other occupational intoxications occurred when policemen used mercury powder to develop fingerprints.[191-193] These incidents demonstrate that the possibility of mercurial poisoning exists whenever mercury or mercury-containing compounds are used carelessly.[190-200] Lee substantiates this with a notional examples of mercury poisoning in his discussion of the history of the statutory control of mercury poisoning in Great Britain.[200]

Isolated cases of organo-mercurial poisonings most commonly result from the accidental or ununiformed misuse of mercury in agricultural products. Since organomercurial compounds were introduced to prevent seed borne diseases in 1914, a number of people have been fatally poisoned or severely incapacitated. Individual poisonings have commonly resulted from eating food products such as bread or porridge made from cereal grains treated with some form of alkylmercury fungicide.[70-86] Another source of mercury poisoning that may well be more prevalent than has been realized previously results from the accidental, inadvertent, or intentional feeding of dressed seed grain to farm livestock. This problem came to public attention in the U.S. in December, 1969, when three members of an Almagordo, New Mexico family were stricken with classical symptoms of alkylmercury poisoning.[70,207,208] An investigation revealed that the head of the family had fed some hogs discarded waste seed grain that had been treated with an organo-mercurial fungicide. Moreover, the scientific literature contains a disturbing number of cases of livestock poisoning by organomercurials that were severe enough to warrant investigation.[81-83, 209-211] But, of course, a number of organo-mercurial poisonings that were not severe enough for the farmer to call a veterinarian are not recorded.

Kurland et al[10] have summarized 39 cases of human organomercurial poisoning that have been reported in the literature from 1865 through 1954. Some typical examples of organomercurial poisonings can be considered here. Lundgren and Swensson[201] described 9 cases of alkylmercury poisoning which not only involved ingestion of treated seeds, but also toxic human exposure to alkylmercury-treated lumber and seeds. Taylor et al[202] established higher urinary and blood mercury levels in 33 employees of an alkylmercury seed-dressing operation. Hill[203] reported that the deaths of 2 female stenographers were caused by vapors of an alkylmercurial stored in a room adjacent to their office. Ahlmark[204] described 4 cases of alkylmercury poisoning associated with seed-dressing or wood impregnation operations. There are many additional references which deal with the poisonous nature of organomercurials as fungicides.[205-209]

Several accounts of poisonings with phenylmercuric compounds have also been reported. McCord et al[408] established that phenylmercuric oleate possesses skin irritant properties. Goldwater et al[401] reported that an individual sprayed with a mixture containing 12% phenylmercuric acetate received second degree chemical burns of his skin, but had an uneventful recovery. In an earlier study, Goldwater and Jeffers[402] described the mercury poisoning of nine workers using a special antifouling marine type paint. With regard to the use of arylmercurials as water-based paint preservatives, various investigators[401,402,404] have established that the toxicological hazards involved with phenylmercuric acetate appear to be minimal.

But since antiquity, mercury-containing compounds used in medicines have also caused mercurial poisoning. For example the use of various organomercurials as diuretics has been associated on many occasions with incidents of toxicity.[405-407] The extent of the pathological changes that are induced appears to depend both on the type of mercurial used and the duration of the administration, but it is not necessarily related to the drug's efficacy as a diuretic. Thus, Mercaptomerin sodium (Thiomerin®) virtually lacks the cardiac toxicity which is common to other organomercurial diuretics.[408-411] But in high doses it is lethal and induces cortical renal necrosis without the apparent glomerular involvement that is typical of mercurial damage.[412] Several mercury preparations for diuresis in cardiac edema patients have been associated with incidents of poisoning. The toxicosis is manifested in various ways from mild cases to death. Some of the proprietary mercurial diuretics are Salyrgan®, Merbaphen®, Mercupurin®, and Esidrone®. All poisonings that have resulted from their use reflect variations in individual susceptibility to a particular mercurial. Merbaphen was the first deadly mercurial diuretic to be identified with three fatalities.[412] And Salyrgan was reported to cause death after it was administered intravenously.[410-416] Neptal®[406] and Mercupurin[412-416] have also been associated with fatalities. However, probably some of the deaths were not due to the direct toxic effects of the mercurials. Therefore, the part played by the mercurial diuretics in these cases cannot be determined directly. However, some deaths must be attributed to the drug itself.

In general, the toxic manifestations of mercurial diuretics can be grouped into three classes:

1. Symptoms related to and resulting from the associated diuresis which are essentially nonspecific.

2. Direct toxic effect of the mercury ion on specific organs. Within this class, renal lesions consist of degeneration of the proximal tubular epithelium and cause albuminuria. In immediate fatality cases following intravenous administration of mercurial diuretics, death is the result of a direct action of the mercury ion on cardiac musculature.[411-416] The effect is manifested early as a change in intraventricular conduction and later as terminal ventricular fibrillation.

3. Generalized manifestations of an idiosyncrasy or an allergic reaction which include such reactions as chills, fever, dermatosis, or leukopenia.[419-421]

Until the early 1950's, recognized [illegible] mercury poisoning usually involved individuals who were associated with industrial or occupational exposure to mercury intoxication. For example, as late as 1954, only 39 cases of organomercurial poisoning had been reported in the literature.[10] Most of these cases resulted from exposure to the organomercurials during the processing or use of seed disinfectants and a few cases resulted from laboratory exposure. But in 1953, a mysterious new type of neurological disease afflicted the inhabitants of Minamata, Japan.[11,12,426-441] After years of investigation, in 1959 the causative agent was conclusively proven to be methylmercury. The methylmercury was a by-product when mercuric sulfate and chloride were used to convert acetylene into acetaldehyde and vinyl chloride. The highly poisonous methylmercury was discharged into Minamata Bay as part of the wastewater effluent from a plastics factory. And the methylmercury subsequently accumulated in the fish and shellfish in Minamata Bay. Between 1953 and 1961, 121 cases including 46 deaths by methylmercury

poisoning were officially reported. The disease primarily afflicted fishermen and their families. Over 1% of a population of 10,000 people living in the vicinity of the Bay suffered some effect from the disease. Today the term "Minamata Disease" is used to describe the chemical and pathological characteristics of this neurological disorder. And the term "Minamata Disease" has become synonomous with methylmercury poisoning specifically and alkylmercury poisoning in general. In 1965, a similar epidemic again resulted from the discharge of methylmercury in the wastewater effluent from a chemical company into the Agano River near Nugata, Japan. This epidemic caused 47 more cases of Minamata Disease and 7 deaths.[388, 439-443] In addition, Ui and Kitamura[444] reported preliminary findings which indicate that a serious mercury pollution problem also exists in Italy. As at Minamata and Nugata, Japan, a factory in Ravenna, Italy produces acetaldehyde from acetylene with a mercury catalyst, and the wastewater effluent is discharged into a nearby lagoon. Fish taken from the lagoon near the wastewater effluent discharge point show a mercury accumulation of from 1 to 2 ppm on a wet weight basis.

Human mercury intoxication has not occurred in the local Italian population because the fish are not used for food. The fish are not consumed because they have a strong chemical smell and taste as a result of the heavy pollution in the lagoon. However, seagulls that feed on these fish have accumulated a high mercury content in their feathers. The authors of this report also established that the total mercury content of the feathers is 17 ppm, with 91% methylmercury. This value is about the same as that found by Johnels and Westermark[389] in Swedish seabirds of prey such as the Osprey (*Pandion haliaetus*) and the Great Crested Grebe (*Podiceps cristatus*), both of which are near extinction.

Whereas the Minamata and Niigata epidemics resulted when methylmercury was released into the environment as a by-product from a chemical manufacturing process, other alkylmercury poisoning epidemics were directly associated with the agricultural uses of alkylmercury-containing fungicides. Several alkylmercury poisoning epidemics have been recorded. In the Guatamalan Highlands, 45 cases of organomercurial poisoning resulted in 20 deaths in 1965.[60] In Pakistan, about 100 people were similarly afflicted in 1961.[64] The exact number of cases is difficult to determine because undetermined numbers of people were afflicted with mild symptoms in nearby villages, and the cause of their affliction was not identified and the numbers were not recorded. Also, some people died at home, while others were admitted to local hospitals or were treated as out patients. Nevertheless, of the 34 patients who were hospitalized, 4 died, and 5 seriously ill patients were removed by relatives. Their subsequent fate was not recorded. Among the remaining 25 patients, 14 had mild cases, 7 were moderately severe, and 4 were severe.

In northern Iraq in 1956 more than 100 cases of mercury poisoning and 14 deaths were diagnosed.[63,446-447] In 1960, many farmers were poisoned and 221 patients were admitted to one hospital in Baghdad, Iraq. Other patients were known to have been stricken by ethylmercuric chloride. Furthermore, scientific reports in the Russian literature identify organomercurial poisoning incidents in that country also.[62,448-449]

TOXICOLOGY OF MERCURY

As with most substances, the toxicological effects and pharmacological activity of mercury are determined by the form and quantity in which the mercury compounds are administered.[401-404] However, as with any toxic substance, the dose alone determines the poisonous nature of that substance.

Hughes[403] has shown that both the biological effect and the variation in distribution are principally due to the reaction with thiols to form mercuric mercaptides and the natural distribution of thiols in the tissues determines the degree of reaction and accumulation. This partially explains the affinity of mercury for human plasma which is rich in the thiol groupings. However, the organomercurials, especially methylmercury, have a relatively high solubility in fat although this varies with the size of the organic molecule. And these organomercurials diffuse easily through cell membranes, thus, they account for the uniform distribution throughout the body. In addition, physiological and cytological studies have established that methylmercury tends to be associated with red blood cells and the nervous system. Furthermore, methylmercury easily passes the blood-brain and placental barriers to accumulate in the brain and fetus.[405] In contrast, the inorganic salts of mercury show a strong affinity for a large number of groupings on proteins. This causes them to crowd onto a few molecules, and distribution is delayed among the available thiols throughout the body. Consequently, extreme local irritation is produced.[403]

Inorganic mercurial salts, on the other hand, characteristically show low blood levels, but with a predilation for the kidney, liver, and spleen. Evidence indicates, therefore, that pathological effects of mercury intoxication correlate very closely with the real concentration of the metal in the affected organ as well as with the sensitivity of the organ to mercury.[406] It also is evident that mercury has threshold values for the different organs which must be exceeded for the symptoms of intoxication to be observed.[407,408]

In order to assess the potential hazard of mercury and its compounds on man and the environment, it is important to distinguish among the various forms of mercury compounds. Basically, all mercury compounds can be categorized as either inorganic or organic. The inorganic mercury classification includes mercury in the form of (1) the elemental liquid metal and its vapor, (2) the mercuric ion (Hg^{++}) and its salts, (3) the mercurous ion (Hg^{+}) and its salts, and (4) mercuric ion complexes which are capable of forming reversible bonds with the thiol groups in proteins. The organomercurial classification includes chemical compounds which contain carbon atoms that are covalently bound to a mercury atom. The organomercurial compounds can be further categorized into subclassifications according to the organic functional group attached to the mercury atom. In the consideration of the toxicological effects of mercury compounds, the most important of these subclassifications are the aryl, alkyl, and alkoxyalkyl. Their generalized structures are



arylmercurial alkylmercurial alkoxyalkyl mercurial

where R is any alkyl group such as methyl, ethyl, propyl, etc.

The differentiation among these subclassifications of organomercurial compounds and their toxicological properties is primarily a function of the combined physical and pharmacological or clinical properties of each category. These toxicological differences are most important because alkylmercurial compounds show a great propensity to accumulate in nervous tissue. Therefore, they have a far greater neurotoxicity than aryl or inorganic mercury compounds.

The toxic manifestations of mercury may be acute or chronic; and, in general, industrial poisoning tends to be chronic, while nonindustrial poisoning is acute.

ACUTE MERCURY INTOXICATION[401,409-410]

The acute symptoms that result from ingestion or injection of any mercury-containing compound include: burning in the mouth and throat; eschar on the mouth and lips; extreme salivation and thirst; nausea; vomiting of blood-stained mucus; severe gastrointestinal irritation, severe abdominal pain; shock; bloody diarrhea; loss of fluids and electrolytes; rapid weak pulse; cardiac arrhythmias; cold, clammy skin; pallor; slow breathing, and peripheral vascular collapse. After from one day to two weeks, the following delayed actions occur: ulcerative colitis; salivary gland swelling; excessive salivation; metallic taste; stomatitis; foul breath; loose teeth; soft, spongy gums; and a blue-black gum line caused by mercury-sulfhydryl complex may become evident.

Oliguria is often present with anuria, uremia, albuminuria, hematuria, proteinuria, and acidosis. Death at this stage is ascribed to uremia. Autopsies reveal inflammation and extensive corrosion along the alimentary tract, severe renal tubular necrosis, and, possibly, central necrosis of the liver.

The acute symptoms that occur when inorganic mercury compounds are inhaled include stomatitis, salivation, metallic taste, abdominal cramps, diarrhea, difficulty in breathing, cough, restlessness, fever, rapid respiration, gastrointestinal and central nervous manifestation, bronchial irritation, pneumonitis, and kidney damage with renal shutdown.

CHRONIC MERCURY INTOXICATION[401,409-410]

The manifestations of chronic mercury intoxication are most commonly encountered in industry, among dentists and their patients with

mercury amalgam fillings, and in laboratory research workers. These manifestations result from prolonged exposure to excessive concentrations of mercury vapor or the dust of mercury salts.

With chronic mercury poisoning all of these symptoms may appear, but usually the onset of these symptoms is slow and insidious. While the symptoms are extremely variable, they are known to include:

1. *Central nervous system* – Headache, vertigo, vasomotor disturbance, ataxia, peripheral neuritis, muscular tremors, and pain and numbness in the extremities.

2. *Gastrointestinal* – Increased salivation, stomatitis, gingivitis with blue line, loss of appetite, weight loss, nausea, vomiting, diarrhea, swollen salivary glands, soft spongy gums, metallic taste, foul breath, and occasional liver damage.

3. *Genitourinary* – Proteinuria, hematuria, anuria, and nephritis with renal damage progressing to acute renal failure with anuria.

4. *Respiratory* – Inflammation of the nose (rhinitis), loss of smell (anosmia), cough, and fever.

5. *Skin* – Erythematous papular, vesicular lesions and urticaria progressing to weeping dermatitis.

6. *Eye* – Constrictions of the visual fields and mercurialentis which is due to the deposition of mercury on the anterior and posterior surfaces of the lens.

7. *Muscular* – Overall general muscular weakness and fatigue.

8. *Erethism* – A peculiar form of psychic disturbance that results from chronic mercury intoxication. Erethism is characterized by abnormal irritability or responsiveness to stimulation. The symptoms include irritability; stammering, blushing; shyness; anxiety; restlessness; resentment of criticism; insomnia; loss of self-confidence; fear of losing one's job; loss of concentration; loss of memory; loss of drive, energy, or interest; forgetfulness; melancholia; hallucinations; evidence of mental deterioration; mental depressions; and excessive perspiration.

Chronologically, chronic mercurialism usually begins with a progressive numbness of the distal parts of the extremities and often of the lips and tongue. This is followed by an ataxic gait, clumsiness of the hands, dysarthria, dysphagia, deafness, and blurring of vision. This blurring is associated with constriction of the visual fields. Voluntary movements are limited in most patients although muscle atrophy is rarely apparent. Spasticity and rigidity are often present; muscle stretch reflexes are usually preserved or become hyperactive, and extensor plantar responses are occasionally elicited during the later stages. Insomnia, agitation, hypomania, and the loss of emotional control are frequently noted. Stupor and coma predominate in some patients. Most patients have abnormal involuntary movements including choreoathetosis, myoclonus, and coarse resting and action tremors.[10]

The manifestations of chronic mercury poisoning in the central nervous system are associated with certain pathological features that are confined to this system.[655,677,678] These manifestations include a varying degree of cerebral edema, atrophy of the calcarine, pre- and postcentral cerebral cortex, cerebellar atrophy, and scattered punctate hemorrhages.

Histopathologically, there is a diffuse cellular degeneration with gliosis. The degeneration of nerve cells is not severe in the calcarine and precentral cortex in which the glial proliferations and extensive vacuolization are most prominent. Involvement of the rest of the central nervous system is minimal.[10] Similar histopathology of the central nervous system has been described in mink,[83] cats, crows, sea birds, and fish that spontaneously succumbed to Minamata disease,[679-685] as well as in experimental animals.[677,682,686]

In these findings on mice that were experimentally exposed to labeled mercuric chloride, Berlin and Ullberg[684] inferred that the localization of mercury at relatively high concentrations in focal areas of the brain correlated well with the areas of pathological lesion development. This appears to confirm an earlier report that mercury concentration corresponds with calcification and atrophy of the granular layer of the cerebellum in rats after their chronic exposure to mercuric chloride.[681]

ORGANOMERCURIAL INTOXICATION

While the complete syndrome of mercury intoxication can be induced by either organic or inorganic mercurials, there are some differences in the respective symptoms. Inorganic mercury poisoning victims have symptoms of stomatitis. Also, excessive salivation and erethism are usually quite pronounced while organic mercury poisoning victims usually experience more severe manifestations of the motor and sensory nerve damage symptoms. In cases of severe alkylmercurial intoxication these symptoms are not reversible, indicating that permanent brain damage has occurred. In addition, because alkylmercurials can pass the placental barrier, congenital neurological injuries can be induced in the fetus. Furthermore, even after acute exposure to toxic concentrations of methyl and other alkylmercurials, it may take weeks or months for the characteristic clinical symptoms to appear.

ALKYLMERCURY POISONING[10,105,188,301-390,830-860,874,875,877-880]

In the case of methyl or ethylmercury poisoning, the acute and chronic poisoning symptoms are quite similar. In an approximate order of mild to severe intoxication they include: excessive fatigue; headache; general overall feeling of weakness; inability to concentrate; amnesia; numbness and tingling of mouth, tongue, lips, hands, fingers, feet, and toes; and ataxia including general clumsiness, impairment of speech, unsteadiness of gait, loss of coordination, and reflex changes. In more severe cases there is a concentric narrowing of the visual field ultimately leading to tunnel vision, loss of ability to speak; impairment of hearing; severe emotional disturbances characterized by unpredictable violent outbursts of anger or fits of depression, and progressive and sometimes complete loss of muscular control, i.e., paralysis and finally death. Moreover, methylmercury salts have been shown to produce toxicity in man when they were applied to the skin in an ointment.[688-690] The lungs and the digestive tract are the most important routes of absorption, however. And the available evidence indicates that more than 90% of the methylmercury in food is absorbed.[689]

ALKOXYALKYL AND ARYLMERCURY POISONING

The organomercurials, methoxyethylmercury and phenylmercury, appear to be quickly metabolized by biological systems into inorganic mercury, which is then eliminated. Therefore, toxicity and chronic symptoms are similar to those associated with mercuric salts, i.e., diarrhea, loss of appetite, weight loss, and fatigue. Relatively few cases of methoxyethylmercury[690,691] or phenylmercury poisoning[687,691,692,693-695] have been reported, and very few cases were seriously intoxicated.[691]

ABSORPTION OF MERCURY COMPOUNDS

Mercury and its compounds have an affinity for the thiol groups found in biological protein and enzyme systems. However, the exact compositions of the complexes formed with sulfhydryl-containing substances in the body are not known. Since organic mercurials are strongly complexed by these enzyme systems, the organic mercury salts are more completely absorbed than inorganic mercury salts.

Clarkson[696] reported that only about 2% of orally administered inorganic mercury compounds are absorbed. These data appear to conflict with the findings of Fitzhugh et al.[697] that rats are capable of absorbing about 50% of the mercuric acetate fed to them.

Organomercurials can be absorbed by the respiratory tract, and gastrointestinal [illegible] Furthermore, the hazard of inhalation intoxication is increased whenever the organomercurials are highly volatile. Biological systems absorb methyl and phenylmercury compounds unchanged and in much greater quantities than the inorganic mercurials. Fitzhugh et al.[697] reported that rats had an intestinal absorption of phenylmercuric acetate of between 90 and 80% of the administered dose. In man, the intestinal absorption of alkylmercurials has been estimated at 90 to 95% of the administered dose.[691,698]

The absorption of inorganic or organic mercury vapor through the lungs poses a special intoxication problem. After exposure to mercury vapor, mercury accumulates in the brain in quantities far in excess of what is found after an equivalent amount of inorganic mercury is administered orally or intravenously.[699-708] In vitro experiments have established that whole blood is capable of absorbing mercury vapor and rapidly oxidizing the metal into the more [illegible] mercuric mercury. In any case, the brain absorbs less than 2% of the injected dose of mercury. However, when mercury

ermary excretion of about 3.3% in 49 days increased with time for 30 days after absorption.

Therefore, the considerable risk to man from methylmercury (alkylmercurials) must be a result of two parameters. First, the alkylmercurials are much more biologically stable than other forms of mercury compounds. Thus, they resist degradation to inorganic mercury which can be eliminated from the body. The 70-day biological half-life demonstrates this parameter. Second, only the alkylmercurials appear to be able to cross the blood-brain barrier and attack the central nervous system.

The information now available about human

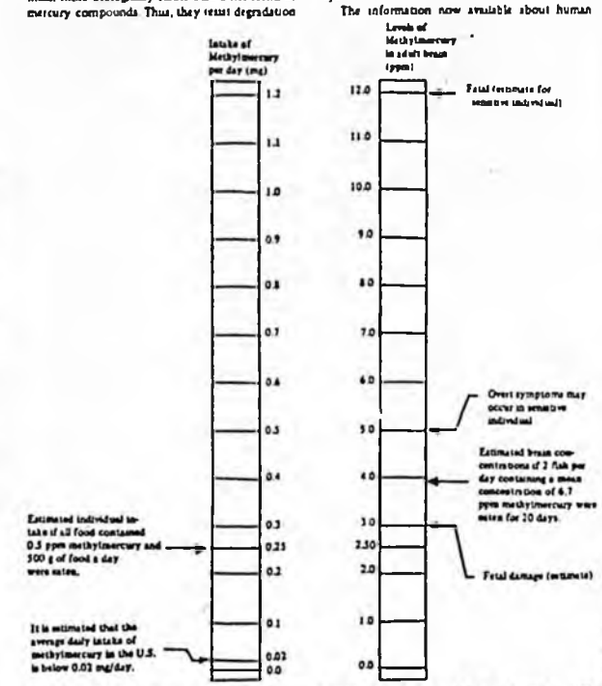


FIGURE 7. Calculated relationship between methylmercury intake and levels of methyl mercury in brain tissue[116] Calculations of brain tissue levels based on: 1. Brain distribution of 15% of total body methylmercury. It has been calculated at 10 to 15%. 2. Continuous exposure for 1 year. With an excretion rate of 1% per day of total body mercury the indicated level will almost be reached. (From Grant, N., *Environment*, 13, 14, 1971, with permission.)

beings exposed to methylmercury is summarized in Figures 7 and 8.[116]

CONGENITAL (OR FETAL) MINAMATA DISEASE

By 1960, it was evident that many children born between 1955 and 1959 in Minamata, Japan suffered from mental retardation and motoric disturbances. This new disease was puzzling initially because the clinical symptoms varied so widely from the adult cases of Minamata Disease that it was difficult to classify them. In addition, none of the afflicted children had consumed any contaminated fish or shellfish; and usually their mothers showed none of the symptoms of Minamata Disease.[119]

The clinical symptoms of children born to mothers who were exposed to alkylmercurial intoxication during their pregnancies were . . . [illegible] to symptoms experienced with severe cerebral palsy or cerebral dysfunction syndrome. These symptoms included a list of disturbances of mind, coordination, speech, and hearing, as well as constriction of the visual field, impairment of chewing and swallowing, enhanced tendon reflex, pathological reflexes, involuntary movement, primitive reflexes, superficial sensation, salivation, and forced laughing.[119] The severity of the disease ranged from children who had mild to moderate ataxia and spasticity to children with all of the listed symptoms. To date, 23 cases of Minamata Disease have been diagnosed, but only 1 of the mothers showed any outward symptoms of Minamata Disease.

The evidence that alkylmercurials cross the placental barrier and produce fetal damage is quite strong. Those infants who died were found to contain high levels of mercury in their kidneys, brain, and liver.[119] Also, Takeuchi established

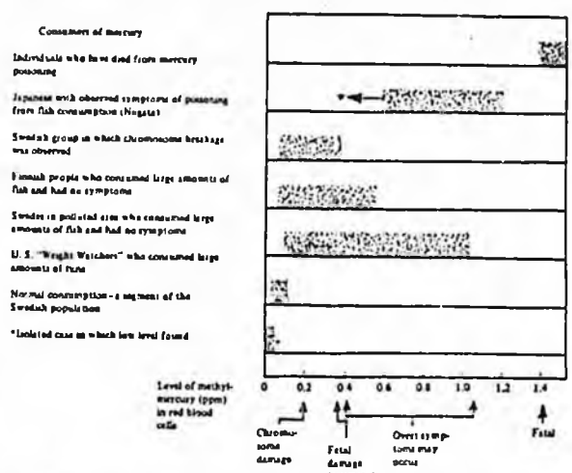


FIGURE 8. Relation of methylmercury levels in blood to physical hazard[116] (From Grant, N., *Environment*, 13, 12, 1971, with permission.)

vapor is inhaled and absorbed, because of its lipid solubility and lack of charge, more than 10% of the dissolved elemental mercury diffuses across cell membranes into the brain tissues.[488-493]

MERCURY DISTRIBUTION IN BLOOD

Inorganic mercury is absorbed into the plasma proteins in the blood. Therefore, it is more amenable to excretion from the body in the urine.[493,494] Alkyl and arylmercurials, on the other hand, are largely bound to the red blood cells, i.e., erythrocytes.[495,501] While mercury levels in the blood as a result of arylmercurials are evenly distributed between the plasma and the red blood cells, the alkylmercurials have a much greater affinity for red blood cells. Berglund and Berlin[441] reported that 90% of the methylmercury present in the blood of all species of animals studied was bound to the red blood cells. These authors also noted that the fraction of methylmercury in plasma varies according to the species as follows: 10% in man and rabbits, 4.5% in rats, and 9% in the squirrel monkey. Moreover, the alkylmercurials differ greatly from other mercurials in their ability to penetrate the blood brain and placental barriers to attack the central nervous system and the fetus. Thus, Berlin and Ullberg[486] reported that 15 to 20% of the total mercury in the body can be found in the brain.

No useful correlation factor has been found between the intake and concentration of mercury in the urine or blood after exposure to elemental or inorganic mercury compounds. However, since methylmercurials are slowly eliminated from the body, mercury levels in the blood can be used as an index of exposure to these compounds. For example, Tejning[497-510] reported that "normal mercury levels" in a 21 year-old man who never ate fish were 4.6 ppb in the blood cells. Among 58 men and 25 women in Sweden who ate fish at least once a week, the average mercury levels of the red blood cells were 9.87 ppb and 10.48 ppb, respectively. Blood plasma levels were also higher than Tejning's "normal" at 2.01 and 2.83, respectively. Sumari et al.[511] and Burke et al.[512] also confirmed that the mercury levels in the red blood cells and plasma provide at least a qualitative diagnostic index for methylmercury intoxication.

METABOLISM AND TISSUE DISTRIBUTION OF MERCURY COMPOUNDS

The two most important differences between the aryl- and alkylmercury salts are the rate at which each is eliminated from the body and their ability to penetrate the blood-brain and placental barriers to attack the brain and the fetus. Of most importance is how quickly the organic mercury compound can be metabolized into inorganic mercury which is more readily excreted from the body. Arylmercurials are rapidly metabolized by the body, whereas the more metabolically stable alkylmercurials resist degradation into inorganic mercury. Clarkson[513] theorized that perhaps the reason the alkylmercurials give no symptoms until after a latency period of one to two weeks is related to the slow rate of metabolic cleavage of these compounds. Therefore, the greater toxicity of the organomercurials, especially the alkylmercurials, could be explained largely by their greater absorption with less excretion and consequent storage in the organism.

Metabolism and tissue distribution of the various mercurials have been studied by means of radioactive tracers. With this method, a correlation has been established between the species of animal tested, the administered mercury dose, the mercury body burden, and the toxic effects of selected inorganic and organic mercurials. Moreover, it has also been established that not only are organomercurials not metabolized in the same manner as inorganic mercury compounds, but it appears that the distribution of aryl and alkylmercurials in various animals is related to their differences in metabolism. Furthermore, the rate at which organomercurials are metabolically degraded varies among different species of animals.

Differences in the metabolism of aryl and alkylmercurials have been demonstrated in various investigations of animals. For example, after a single dose of phenylmercuric acetate has been administered intravenously, intramuscularly, or orally, it is rapidly metabolized to inorganic mercury.[389,514-518] And the distribution of the metabolized phenylmercuric acetate in each organism is very similar to that produced by inorganic mercury with the highest levels found in the liver and kidneys and usually no detectable levels in the brain. In contrast, Swensson et al.[515] found that a single intramuscular injection of methylmercury dicyandiamide was uniformly distributed throughout the tissues of the body, and only a very little was detected in the brain. Later, the same authors[519] established that when this alkylmercurial was repeatedly administered, it caused an appreciable accumulation of mercury in the brain.

Investigating the distribution, metabolism, and excretion of phenylmercuric acetate and methylmercury, Gage[520] found that phenylmercuric acetate is unchanged when it is absorbed into the circulatory system. The phenylmercuric acetate is metabolized by the liver and kidneys and excreted in the feces and urine, mostly as inorganic mercury. No measurable amounts of mercury were found in the central nervous system. Furthermore, in cases where phenylmercuric acetate is continually administered, a steady condition is reached after approximately 14 days. Then the excretion of mercury nearly balances the intake. However, methylmercury accumulates in all tissues, particularly in the red blood cells. Repeated doses of methylmercury produce no clear indication that a steady state can be reached after 6 weeks. Rather, the mercury levels in the brain increase progressively. Inorganic mercury is slowly released from tissues, particularly in the intestines and muscles. Overall, however, methylmercury is much more slowly released from the tissues than phenylmercuric acetate, and the subsequent metabolism of methylmercury into inorganic mercury is low. The major route of excretion is in the feces.

Miller et al.[516] administered phenylmercuric acetate intravenously, intramuscularly, and orally to chicks, rats, and dogs. They found that the compound is absorbed unchanged with less than 10% of the initial dose excreted unmetabolized in the urine. The unchanged phenylmercuric acetate is transported by the blood into the circulatory system where it is converted into inorganic mercury through metabolism in the liver and kidneys. Then it is excreted in the feces and urine. Metabolism in the biological systems that were tested is rapid. For example, phenylmercuric acetate is detectable in the animal for only 96 hr after it is administered. In another study, Miller et al.[521] administered ethylmercuric chloride intramuscularly and orally to chicks and rats. Once again, the compound was absorbed unchanged by the organism, but in contrast to phenylmercuric acetate, ethylmercury is detectable in the livers and kidneys for at least 21 days. In addition, it was established that ethylmercury was present to a greater extent in the chick's liver than in its kidney, whereas in the rat the alkylmercurial was found predominantly in the blood and kidney. Also, while the excretion of mercury in the rat's urine was not as rapid as for phenylmercuric acetate, the mercury levels in the rat's kidneys showed a marked increase that indicated a slow metabolic conversion of ethylmercury to inorganic mercury. Furthermore, the fecal excretion of ethylmercury was minimal, and only 5% of the amount observed in the phenylmercuric acetate study was eliminated during the 7 days after its initial admission.

Ellis and Fang[522] studied the elimination, tissue accumulation, and cellular incorporation of mercury in rats that received oral doses of mercuric and phenylmercuric acetate. They showed that the highest concentrations of mercury were in the kidneys, followed by the liver, lung, and heart in declining order. The major route of excretion for both classes of mercurials was via the feces with only small amounts excreted in the urine. The average total excretion in one week reached 98 and 80% of the administered doses of mercuric acetate and phenylmercuric acetate, respectively. These elimination values show that 68 and 80% of a single dose of phenylmercuric acetate were excreted in the feces and urine while in the same period 35% of the inorganic mercury was excreted in the feces and between 1 and 4% in the urine. The similarity in these excretion patterns was related to the rapid metabolic conversion of phenylmercuric acetate to inorganic mercury.

METABOLISM, DISTRIBUTION, AND EXCRETION OF METHYLMERCURY IN MAN

In order to elucidate the mechanisms of methylmercury metabolism in man, radioactive methylmercury was administered orally to three male volunteers.[523-528] Within 15 min, their red blood cells absorbed the compound, and the mercury accumulated in the patients' livers and heads. The livers and heads accumulated about 50 and 10%, respectively, of the body burden of the methylmercury nitrate. The biological half-life for methylmercury in man was found to be between 70 and 74 days. The main excretory route was the feces with about 33% in 49 days. However, the

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AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

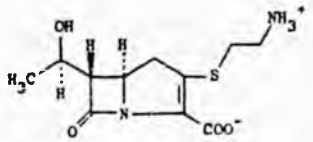
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al., Ibid. **15**, 518 (1979). Prepn of *N*-formidimidoyl thienamycin: W. J. Leanza *et al., J. Med. Chem.* **22**, 1435 (1979); T. W. Miller, Eur. pat. Appl. 6639 (1980 to Merck & Co.). *C.A.* **93**, 155845y (1980); B. G. Christensen *et al.*, U.S. pat. 4,194,047 (1980 to Merck & Co.). Evaluation of *in vitro* and *in vivo* activities: H. Kropp *et al., Antimicrob. Ag. Chemother* **17**, 993 (1980). Comparative study vs gram-positive and gram-negative aerobic and anaerobic species and β-lactamase stability: H. C. Neu, P. Labthavikul, *ibid.* **21**, 180 (1982). Pharmacokinetics, bacteriological efficacy: P. Patamasucon, G. H. McCracken, *ibid.* 390.

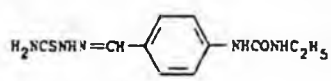


White hygroscopic solid. $[\alpha]_D^{25}$ +82.7° (c = 1.0 in water). uv max (water, pH 4-8): 296.5 nm (ε 7900). (pH 2): 309 nm; (pH 12): 300.5 nm. Freely sol in water, sparingly sol in methanol. In dilute soln, stability is optimal between pH 6-7, declining with unusual rapidity above that range. Susceptible to inactivation by dilute solns of hydroxylamine and cysteine.

N-Formamidoylthienamycin monohydrate, $C_{12}H_{17}N_3O_4S \cdot H_2O$, *6-(1-hydroxyethyl)-3-[[2-[(iminomethyl)amino]ethyl]-thio]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid monohydrate, thienamycin formamidine monohydrate, MK-0787, MK 787, imipenem, imipemide.* Cryst from water-ethanol. $[\alpha]_D^{25}$ +86.8 (c = 0.05 in 0.1 *M* phosphate, pH 7). uv max (water): 299 nm (ε 9670, 98% NH_2OH ext).

THERAP CAT: Antibacterial.

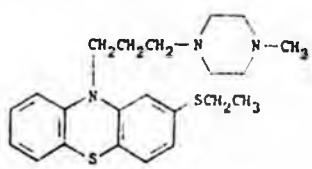
9150. Thiethazone. *2-[[4-[[(Ethylamino)carbonyl]amino]phenyl]methylene]hydrazinecarbothioamide; 1-ethyl-3-(p-formylphenyl)urea thiosemicarbazone;* ethylurcidobenzaldehyde thiosemicarbazone; thioethazone. Tebacyl. $C_{11}H_{14}N_4OS$; mol wt 265.35. C 49.79%, H 5.70%, N 26.40%, O 6.03%, S 12.09%. Prepd from ethyl thiocyanate + 4-aminobenzaldehyde thiosemicarbazone: Brit. pat. 672,370 (1952 to A. Wander).



Fine yellowish crystals, mp 220° (decompn).

THERAP CAT: Antitubercular.

9151. Thiethylperazine. *2-(Ethylthio)-10-[3-(4-methyl-1-piperazinyl)propyl]phenothiazine;* 3-ethylmercapto-10-(1'-methylpiperazinyl-4'-propyl)phenothiazine. $C_{22}H_{29}N_3S_2$; mol wt 399.62. C 66.12%, H 7.31%, N 10.51%, S 16.05%. Prepn: Bourquin *et al., Helv. Chim. Acta* **41**, 1072 (1958).



Crystals from acetone, mp 62-64° bp$_{0.01}$ 227°.

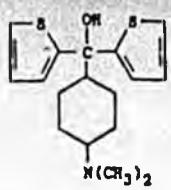
Dimaleate, $C_{30}H_{37}N_3O_8S_2$. *Forecan Maleate, Toresten, Trestén.* Crystals from methanol, dec 188-190°.

Dihydrochloride, $C_{22}H_{29}N_3S_2 \cdot 2HCl$, crystals from ethanol, mp 214-216°.

Dimalate, $C_{22}H_{29}N_3S_2 \cdot 2C_4H_6O_5$, crystals from ethanol, mp 139°.

THERAP CAT: Antiemetic.

9152. Thihexinol. *α-[4-(Diethylamino)cyclohexyl]-α-2-thienyl-2-thiophenemethanol; (4-dimethylaminocyclohexyl)-di-2-thienylmethanol; α,α'-*dithienyl-4-dimethylaminocyclohexyl carbinol; Entoquel. $C_{17}H_{23}NOS_2$; mol wt 321.51. C 63.51%, H 7.21%, N 4.36%, O 4.98%, S 19.95%. Prepn: Villani, U.S. pat. 2,764,519 (1956 to Schering).

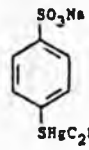


Crystals from benzene, mp 156-157°.

Methyl bromide, $C_{18}H_{26}BrNOS_2$, crystals from ethanol + ether, mp 231-232°.

THERAP CAT: Methyl bromide as anticholinergic.

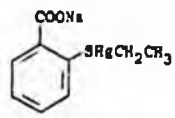
9153. Thimerfonate Sodium. *Ethyl(4-mercaptobenzenesulfonato-S⁴)mercury sodium salt;* sodium *p*-ethylmercurithiophenylsulfonate; ethyl[(*p*-sulfophenyl)thio]mercury sodium salt; Sulfo-Merthiolate. $C_8H_9HgNaO_3S_2$; mol wt 448.88. C 21.79%, H 2.06%, Hg 45.50%, Na 5.21%, O 10.89%, S 14.55%. Prepn: Waldo, *J. Am. Chem. Soc.* **53**, 992 (1931); Kharasch, U.S. pat. 1,672,615.



Powder, very sol in water. Forms a stable solution.

THERAP CAT: Topical anti-infective.

9154. Thimerosal. *Ethyl(2-mercaptobenzoato-S)mercury sodium salt; [(o-carboxyphenyl)thio]ethylmercury sodium salt;* sodium ethylmercurithiosalicylate; thiomersalate, mercurothiolate; Merthiolate; Merzonin; Mertorgan; Merlamin. $C_9H_9HgNaO_2S$, mol wt 404.84. C 26.70%, H 2.24%, Hg 49.55%, Na 5.68%, O 7.90%, S 7.92%. Prepd by reacting ethylmercuric chloride (or ethylmercuric hydroxide) with thiosalicylic acid: Kharasch, U.S. pat. 1,672,615 (1928); Trikojus, *Nature* **158**, 472 (1946); Swirska *et al., Przemysl Chem.* **39**, 371 (1960). *C.A.* **55**, 3507a (1961).

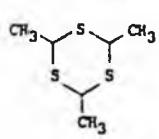


Cream-colored, cryst powder. Stable in air, but not in sunlight. One gram dissolves in about 1 ml water, in about 8 ml alcohol. Practically insol in ether and benzene. Stabilization of solns with EDTA: Davisson, U.S. pat. 2,864,838 (1958 to Lilly). pH of 1% aq soln: 6.7. LD_{50} s.c. in rats 85 mg/kg. Mason *et al., Clin. Toxicol.* **4**, 185 (1971).

THERAP CAT: Topical anti-infective; pharmaceutic aid (preservative).

THERAP CAT (VET): Antibacterial, antifungal—topical.

9155. Thioacetaldehyde. *2,4,6-Trimethyl-s-trithiane;* thioacetaldehyde. $C_6H_{12}S_3$; mol wt 180.35. C 39.95%, H 6.71%, S 53.34%. Occurs in α- and β-forms. Prepn: Baumann, Fromm, *Ber.* **22**, 2600 (1889); Fromm, Engler, *Ibid.* **58**, 1916 (1925). Molecular structure: Hassel, Viervoll, *Acta Chem. Scand.* **1**, 164 (1947). Stereochemistry: Schaberg, Barakat, *J. Chem. Soc.* 1947, 693.



α-Form, monoclinic plates, mp 101°.

...04%, H 10.41%, ...

...0.870. bp 110-11... ...ol in water; miscible with ...

...ls and essences.

Isothiocyanatoethane; ethyl ... 7.15. C 41.34%, H 5.78%, ... Obtained by the action of ... of the reaction of carbon ...

...ngent odor. d_4^{18} 1.003. bp ... 2° Insol in water; miscible ...

Caution: Vapors irritate ...

Methylbutanoic acid ethyl ... ... C 64.58%, H 10.84%, O ... I_3 ... d_{20}^{20} 0.868. bp 135°. ... 1 350 parts water; miscible ...

confectionery and beverages ...

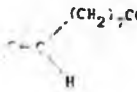
Caryopropanoic acid ethyl ... $C_5H_{10}O_3$; mol wt 118.13. C ... $H_3CHOHCOOC_2H_5$ ... odor. d_4^{14} 1.042. bp 154°, ... 117°F (47°C). Miscible ...), alcohol, ether. *Keep* ...

...lose and cellulose acetate ...

...noic acid ethyl ester. C ... H 12.36%, O 14.0... ...69°, bp_{25} 163°, n_D 1.4321 ... ether.

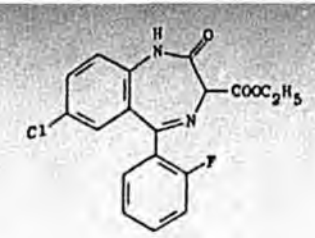
...opentanoic acid ethyl ... ...31%, H 8.39%, O 33.29%. ... n_D^{20} 1.4229. Freely sol in ...

Octadecadienoic acid ethyl ... wt 308.49%. C 77.84% ... from sunflower seed oil ... III, 526 (1955); *see* also ... (1955).



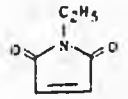
...oxidation than linoleate ... 193°, bp_{25} 175°; bp_{mm} ... value 162.5. Miscible ... oils.

...chloro-5-(2-fluorophenyl)-...azepine-3-carboxylic acid ...orophenyl)-2,3-dihydro-...carboxylate; CM-6912. ... 360.77. C 59.93%, H ... O 13.30%. Benzodia... ...pin. J. Hellerbach *et al.*, U.S. pat. 3,657,223 (1972). Analysis in plasma and ... *Biomed. Mass Spectrom.* ...tabolites: J. P. Cano. *J.* ...cologic evaluation: *G... ol. Ther. Toxicol.* 19, 453 ...



...from ether, mp 193-194°. ... CAT: Tranquilizer (minor).

3767. *N*-Ethylmaleimide. *1-Ethyl-1H-pyrrole-2,5-dione.* $C_6H_7NO_2$; mol wt 125.12. C 57.59%, H 5.64%, N 11.20%, O ... mp 45°. Prepd by heating *N*-ethylmaleamic acid in paraffin ... *J. Chem. Soc.* 1949, 1515.



Crystals, mp 45°. Lacrimator when liquid. ... In cancer research (possible antimitotic activity.) ... Strong irritant.

3768. Ethyl Malonate. *Propanedioic acid diethyl ester;* ...ethyl malonate; malonic ester. $C_7H_{12}O_4$; mol wt 160.17. C ... H 7.55%, O 39.96%. $C_2H_5OOCCH_2COOC_2H_5$. ... Prepd from chloroacetic acid and sodium cyanide followed ... esterification with ethanol and H_2SO_4: L. Gattermann, ... Berlin. *Praxis des Organischen Chemikers* (de Gruyter, ... 40th ed., 1961) pp 220-221.

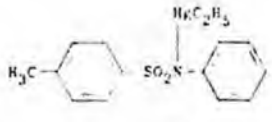
Liquid. Slightly aromatic, pleasant odor. d 1.055. bp ... bp_{12} 95°. mp −50°. n_D^{20} 1.4143. One gram dissolves in about 50 ml of water. Miscible with alcohol, ether ... Manuf of barbiturates.

3769. Ethylmercuric Chloride. *Chloroethylmercury;* ... C_2H_5ClHg; mol wt 265.13. C 9.06%, H 1.90%, ... Cl 13.37%, Hg 75.66%. CH_3CH_2HgCl. Prepd from ethylmercuric bromide by treating with methanolic KOH, filtering and neutralizing with HCl: Slotta, Jacobi, *J. Prakt. Chem.* [2] 120, 249 (1929). Prepn from $HgCl_2$ and tetraethyl ... Whelen, *Advances in Chemistry Series* 23, entitled ... *Organic Compounds* (ACS, Washington, D.C., 1960) ... 12-30. For the prepn of the bromide from ethylmagnesium bromide and mercuric bromide *see* Slotta, Jacobi, *loc. cit.* Marvel *et al.*, *J. Am. Chem. Soc.* 47, 3009 (1925). *Review:* Krause, von Grosse, *Die Chemie der Metall-organischen Verbindungen* (Berlin, 1937).

White silvery leaflets from ethanol, mp 192°. Sublimes ... Solubility in water at 18° = 1.4 × 10⁻⁴ g/100 ml; at ... = 2.5 × 10⁻⁴ g/100 ml; in ethanol at 18° = 0.75 g; at 78° = 3.5 g/100 g; in chloroform at 18° = 2.6 g; ... g. Slightly sol in ether.

USE: Applied at 2% strength (soln or mixed with solids) as a fungicide for treating seeds. *Caution:* Highly toxic ... causes skin burns; is absorbed through the skin. Chronic exposure has caused permanent injury to brain. *Note:* A ... analog *chloro(2-methoxyethyl)mercury, Ceresan Wet*, ... also used as seed fungicide.

3770. *N*-(Ethylmercuri)-*p*-toluenesulfonanilide. *Ethyl-...methyl-N-phenylbenzenesulfonamidato-N)mercury; ethyl-...phenyl-p-toluenesulfonamido)mercury;* Ceresan M. $C_{15}H_{17}HgNO_2S$; mol wt 475.99. C 37.85%, H 3.60%, Hg ... N 2.94%, O 6.72%, S 6.74%.



Crystals. Pungent odor, somewhat reminiscent of garlic. ... insol in water. LD_{50} orally in rats 100 mg/kg. ... Substances List.* H. E. Christensen, Ed. (1973) p 585.

USE: To control the various smuts which befall grain. Reduces bulb rot in gladiolus. *Caution:* Almost as toxic as mercuric chloride *(q.v.)*; less irritating to the skin than ethyl mercury phosphate. Symptoms confined to CNS and consist of deafness, ataxia, dysarthria, progressive visual deterioration; dysphagia; sphincteric incontinence, mental confusion, stupor, death: Gleason *et al.*, *Clinical Toxicology of Commercial Products* (Williams & Wilkins, Baltimore, 3rd ed., 1969) p 68, sect. II.

3771. Ethyl Methanesulfonate. *Methanesulfonic acid ethyl ester;* ethyl methanesulfonic acid; ethyl mesylate; EMS; NSC 26805. $C_3H_8O_3S$; mol wt 124.15. C 29.02%, H 6.49%, O 38.66%, S 25.82%. $CH_3SO_2OCH_2CH_3$. Prepn: O. C. Billeter, *Ber.* 38, 2015 (1905). Mutagenicity studies: T. Alderson, *Nature* 207, 164 (1965); J. B. Jenkins, *Mutat. Res.* 4, 90 (1967); A. P. Schalet, *ibid.* 49, 313 (1978). Review of carcinogenicity studies: *IARC Monographs* 7, 245-252 (1974). Review of comparative mutagenicity of EMS and methyl methanesulfonate, *q.v.*: S. Kondo, *Environ. Sci. Res.* 24, 743-785 (1981).

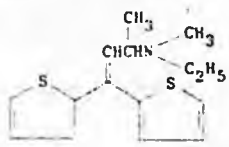
Liquid. bp_{761} 213-213.5°; bp_{10} 85-86°. d_4^{22} 1.1452.

USE: Exptlly as mutagen.

3772. Ethyl Methyl Ether. *Methoxyethane;* methyl ethyl ether. C_3H_8O; mol wt 60.09. C 59.96%, H 13.42%, O 26.62%. $C_2H_5OCH_3$.

Liquid. d_0^0 0.725. bp 10.8°. Sol in water; miscible with alcohol, ether.

3773. Ethylmethylthiambutene. *N-Ethyl-N,1-dimethyl-3,3-di-2-thienyl-2-propenamine; N*-ethyl-*N*,1-dimethyl-3,3-di-2-thienylallylamine; 3-ethylmethylamino-1,1-di(2'-thienyl)but-1-ene; ethylmethiambutene; 1C50; N1H-5145; Emethibutin. $C_{15}H_{19}NS_2$; mol wt 277.46. C 64.94%, H 6.91%, N 5.05%, S 23.11%. Prepn: Adamson, U.S. pat. 2,561,899 (1951 to Burroughs Wellcome). Toxicology: N. B. Eddy, D. Leimbach, *J. Pharmacol. Exp. Ther.* 107, 385 (1953).



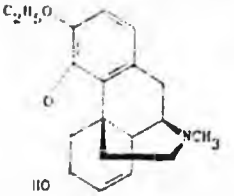
$bp_{0.01}$ 110-113°. bp_{10} 75-76°.

Hydrochloride, $C_{15}H_{19}NS_2 \cdot HCl$, crystals, mp 137-138°. LD_{50} in mice: 192 mg/kg orally; 88 mg/kg s.c., N. B. Eddy, D. Leimbach, *loc. cit.*

Caution: Abuse leads to habituation or addiction.

THERAP CAT: Narcotic analgesic.

3774. Ethylmorphine. *7,8-Didehydro-4,5-epoxy-3-ethoxy-17-methylmorphinan-6-ol.* $C_{19}H_{23}NO_3$; mol wt 313.38. C 72.82%, H 7.40%, N 4.47%, O 15.32%. Prepd by ethylation of morphine: Baizer, Ellner, *J. Am. Pharm. Assoc.* 39, 581 (1950); Gorecki, *Ann. Pharm. (Poznan)* 7, 21 (1969).



Crystals from ethanol, mp 199-201°.

Hydrochloride dihydrate, $C_{19}H_{24}ClNO_3 \cdot 2H_2O$, *Codethyline, Dionin.* White to faintly yellow cryst powder, mp about 123° (dec); anhydrous form, mp about 170° (dec). One gram dissolves in 10 ml water and in 25 ml alcohol; slightly sol in chloroform, ether. LD s.c. in mice 200 mg/kg. *RTECS* Vol. II, R. J. Lewis, R. L. Tatken, Eds. (1979) p 98.

Methiodide, $C_{20}H_{26}INO_3$, *ethyl-N-methylmorphinium iodide, Trachyl.*

Caution: Abuse leads to habituation or addiction.

Life Gets Better

A 1986 survey by The Gallup Poll indicates that only 31 percent of Americans now say they smoke—the smallest percentage of the adult population since the survey began in 1944. At that time, 41 percent of the American population smoked. Smoking reached a high in 1954, when 45 percent of the population smoked. The rate of smoking has been steadily declining since the late sixties.

A recent study of the Nielsen ratings made by the National Coalition on Television Violence (NCTV) shows that the popularity of primetime TV violence is at its lowest point in 20 years. This year only one action program is in the TV top 20.

NCTV believes that this trend is a result of increased public awareness of TV violence and the resurgence of the nonviolent situation comedy.



A Larger View of Abduction

What are the *real* numbers behind the "missing children" statistics? In 1984, the FBI listed 350,000 cases of missing children. Of these, it turns out that 67 were actually kidnapped by strangers. The remaining children were either abducted by parents or relatives engaged in custody battles or else were runaways.

The American Academy of Pediatrics now cautions that fingerprinting and other child identification programs are of limited value and tend to create unhealthy and unnecessary anxiety. Parents may be transmitting fears of stranger abduction to their children, and are advised to consider the "whole story" of the missing children statistics and the possibility of suppressing the child's developing social skills. (*Pediatrics*, 78: 369)

In addition, the "excessive and frightening" use of photographs of missing children on milk cartons, posters, and shopping bags has been under question by a congressional panel. Misleading statistics, bureaucratic infighting, and increasing numbers of businesses hoping to profit from parental fears are under scrutiny. "Public awareness has become public hysteria," says the executive director of a group called Services for the Missing. (*Houston Chronicle*, sect. 1, p. 3, 5 Aug 1986)

Vaccine Update

Confusion surrounds the vaccination question, and the debate continues. Some illnesses that we routinely vaccinate against are virtually nonexistent in this country. Diphtheria is apparently absent from the United States, with no cases reported in 1986. Only three cases had been reported in the two years previous to that. Reported tetanus cases totaled 61 in 1986, and only two cases of paralytic poliomyelitis were reported in 1986.

Pertussis, however, despite near universal vaccination, was more prevalent in 1986 than in any year since 1970. The 1986 total number of pertussis cases was approximately 4,500, with nearly a third of them—1,300 cases—reported in a major outbreak in Kansas. (All 1986 statistics cited above are from the provisional data compiled by the Centers for Disease Control and reported in *Vaccine Bulletin*, Feb 1987, pp. 11-12.)

This outbreak of pertussis in Kansas occurred in a highly immunized population: "Some 90 percent of the pertussis patients whose immunization status was known, appear to have been adequately immunized." (*Vaccine Bulletin*, Feb 1987, p. 11) The outbreak affected all age groups—from 0 to 79 years—with most cases concentrated in those under 20 years



of age. More cases than would usually be expected occurred in the five to nine age group, and less than would be expected occurred among infants.

Vaccine complications continue to receive national press coverage. Some attention has been given to the development of a different type of vaccination for pertussis, one that is associated with fewer vaccine-related complications. The pertussis vaccine currently in use in this country is a *whole-cell* vaccine, which contains dead pertussis toxin—that remains biologically active after the bacteria that secrete it have been killed—as well as endotoxin, a protein secreted by a virus or bacteria that can, in large enough quantities, affect the brain or produce shock. Developed several years ago in Japan, the *acellular* pertussis vaccine has all of the bacteria and most of the toxins removed or rendered harmless, and is considered more pure and specific. Although the acellular vaccine must undergo testing in this country and physicians will not have legal access to it for two to three years, some physicians who are concerned about side effects from the whole-cell preparation are using test batches of the new vaccine for their own children or are traveling to Japan or Hong Kong to have their children vaccinated. (*The New Mexican*, 5 April 1987)

Two preliminary studies of the acellular vaccine in the United States show promising results. Vanderbilt University School of Medicine and the UCLA School of Medicine have thus far conducted studies on 80 children from 18 to 24 months and from

 Illustrations: Ashisha

four to six years of age. Both age groups showed antibody production comparable to the old vaccine, but far fewer adverse reactions in terms of fever, fretfulness, abnormal gait, and redness, tenderness, and swelling at the vaccination site. (*Healthfacts*, vol. XI, no. 90, Nov 1986)

Among the non-Communist countries, only the United States, Australia, and Iceland have mandatory pertussis vaccination programs. And yet, the pertussis inoculation is the most toxic of all protective vaccines routinely given to children in their first five years of life. Each year, this vaccine is linked to the deaths of at least 44, and possibly as many as 900, otherwise healthy children. It also causes more lasting brain damage than whooping cough would if children were not immunized. Most of the whooping cough in America now occurs in vaccinated children or in those too young to immunize. (*The New Mexican*, 5 April 1987)

Both Sweden and Japan experienced an increase in cases of whooping cough after discontinuing mass whole-cell vaccination programs. Japan, now using the acellular vaccine and waiting until two years of age to begin vaccination, has witnessed a dramatic decline in both minor and severe reactions to the vaccine and in cases of whooping cough in general. (*The People's Medical Journal*, Dec 1986)

Many questions remain to be answered regarding the relationship between vaccinations and the decline of an illness in the general population over time; the effect of vaccinations on the immune system; and the safety of administering particular vaccines in a country in which diseases from the conditions vaccinated against are on the decline and in which large numbers of vaccinated people still contract the disease.

Meningitis Vaccine Update

In issue #39, we printed a letter from a reader inquiring about the Hib vaccine, licensed in the United States in April 1985 to protect against the leading bacterial cause of meningitis. Since then, more research has shed light on the problem and on the vaccine. Two recent studies have concluded that *Hemophilus influenza* type b does not seem to spread from child to child as readily as doctors suspected. (*New England Journal of Medicine*) Earlier studies indicated that the infant brothers or sisters of a child with meningitis are up to 400 times more likely to contract this illness; however, one of the more recent studies showed that only one child out of 587 who had regular contact with an infected toddler went on to develop the illness.

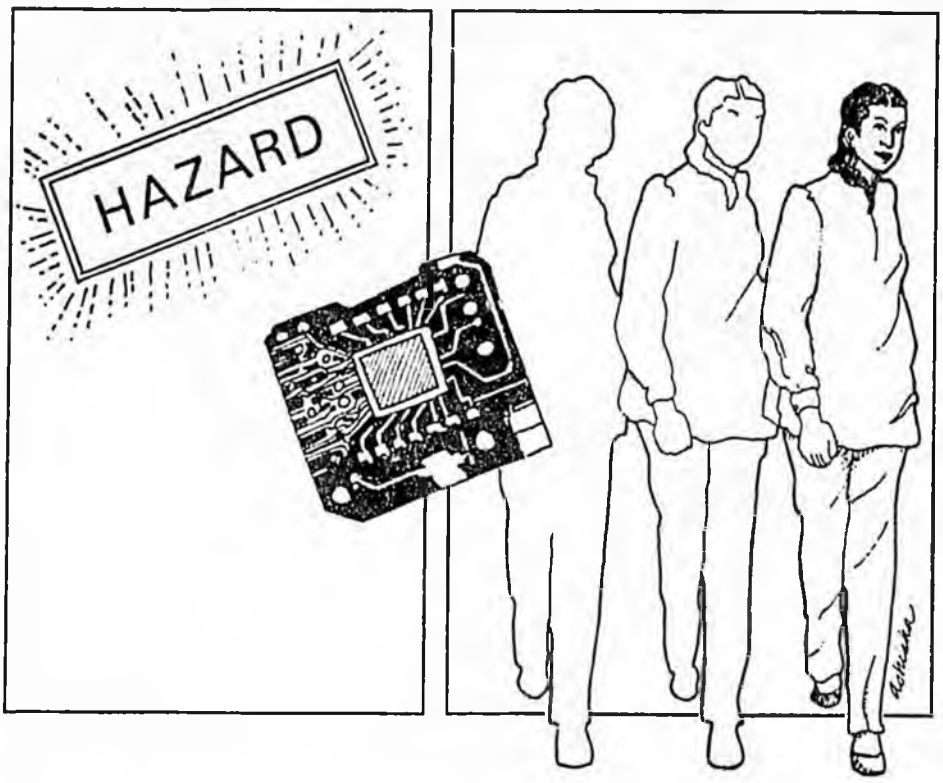
Vaccine failure is also being investigated. Work is under way to determine why it is that some children who receive the preparation go on to develop meningitis. (*New England Journal of Medicine 315*, 18 Dec 1986)

All we can conclude at this point is that contact with meningitis is less "risky" than was formerly believed; that the other causes of meningitis (such as pneumococcus, meningococcus, some viruses, and other agents) are not inoculated against in the current vaccine; that the Hib vaccine is not effective in the under-two age group, in which 75 percent of all meningitis cases occur; and that the current vaccine will not protect all children who receive it.

When the Chips Are Down

Several microelectronics firms are now offering their pregnant employees the opportunity to transfer out of production areas where they may be exposed to chemicals and gases. AT&T has taken this one step further: as of January 1987, they no longer *allow* pregnant women to work on semiconductor production lines.

This concern in the computer manufacturing industry was sparked by a University of Massachusetts at Amherst study conducted since 1984—but not yet formally published—on employees at Digital Equipment Corporation's Massachusetts plant. Results show that women in the micro-



chip etching area had nearly twice the miscarriage rate (39 percent in the first trimester) found in the general population (10 to 20 percent). (*Science News*, vol. 131, no. 5, 31 Jan 1987)

Although the researchers insist that the Digital study does not prove a causal relationship between chip production and miscarriage, and although they are calling for "more extensive exposure measurements," the industry's sensitive response to the data accumulated is to be commended.

CENTERS FOR DISEASE CONTROL

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

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Current Trends

Measles — United States, First 26 Weeks, 1985

Through December 28, 2,704 measles cases in the United States were reported to the *MMWR* for 1985. Results of detailed analyses are available for cases reported during the first 26 weeks, when a provisional total of 1,802 cases was reported, a 2.4% increase over the 1,759 cases reported during the same period in 1984 (1). The overall incidence rate in both years was 0.8 cases per 100,000 population for the 26-week period. Eight states accounted for 1,333 (73.9%) cases: Illinois (259 cases), Texas (236), Arizona (194), California (143), Montana (139), Idaho (126), New York (124), and Massachusetts (112). Ten states had incidence rates greater than 1/100,000 population: Arizona, Hawaii, Idaho, Illinois, Maryland, Massachusetts, Montana, Texas, West Virginia, and Wisconsin. During the first half of 1984 and 1985, 19 and 20 states, respectively, reported measles cases (indigenous or imported). For each year, 2.5% of the nation's 3,139 counties reported measles cases during the period.

Detailed information was provided to the Division of Immunization, Center for Prevention Services, CDC, on 1,801 of the cases reported during the first 26 weeks of 1985. Of these, 1,750 (97.2%) met the standard case definition for measles,* and 661 (36.7%) were serologically confirmed. In most cases (72%), onset of rash occurred between weeks 8 and 20 (weeks ending February 23 and May 25, respectively). There was a biphasic distribution of cases during this period (figure 1).

In the first half of 1984, the highest incidence rate was reported among children 10-14 years of age (Table 1). By comparison, in the first half of 1985, the highest incidence rate was reported among 15- to 19-year-olds (3.1/100,000), followed by preschool-aged children (2.5/100,000). The incidence rate among 10- to 14-year-olds decreased from 2.9/100,000 in 1984 to 1.8/100,000 in 1985. Of the 466 preschool-aged children with measles, 137 (29.4%) were infants under 1 year of age; 81 (17.4%) were 12-14 months of age; 24 (5.2%) were 15 months of age; and 224 (48.1%) were 16 months-4 years of age.

Of the 1,256 (69.7%) patients for whom the setting of transmission was reported, 903 (71.9%) acquired measles in school†, 126 (10.0%), at home, 63 (5.0%), in medical settings; 41 (3.3%), in daycare centers, 18 (1.4%), in church, and 105 (8.4%), in a variety of other settings, including sporting events and summer camp.

Seventy cases (3.9%) were international importations. An additional 128 (7.1%) cases

*Fever (38.3°C [101.9°F] or higher if measured), generalized rash of 3 days' or longer duration, and at least one of the following: cough, coryza (conjunctivitis).

†Includes kindergarten through college.

Measles — Continued

were epidemiologically linked to an international importation within two generations of infection. Therefore, 198 (11.0% of all cases) were classified as international importations during this period (2).

Vaccination status of patients in 1984 and 1985 was similar. Of the 1,801 cases reported during the first 26 weeks of 1985, 859 of the patients had been vaccinated on or after the first birthday; 247 had been vaccinated at 12-14 months of age (Table 2). A total of 846 measles patients were unvaccinated, and 96 had histories of inadequate vaccination (vaccinated before the first birthday).

FIGURE 1. Reported measles cases, by week of rash onset — United States, first 26 weeks, 1985

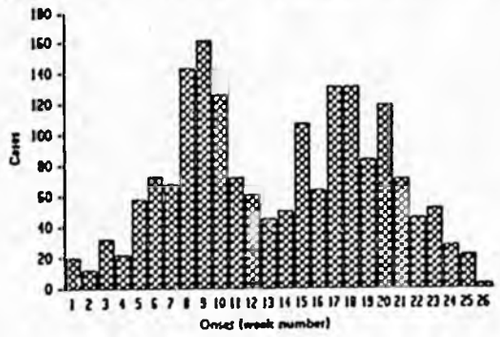


TABLE 1. Age distribution and estimated incidence rates of measles — United States, first 26 weeks, 1984 and 1985*

Age group (yrs.)	1984 No.	1984 (%)	1984 Rate†	1985 No.	1985 (%)	1985 Rate†	Rate change (%)
0-4	351	(19.9)	2.0	466	(25.9)	2.5	+25.0
5-9	201	(11.4)	1.3	152	(8.4)	0.9	-30.8
10-14	515	(29.2)	2.9	315	(17.7)	1.8	-37.9
15-19	470	(26.6)	2.4	603	(33.5)	3.1	+29.2
20-24	137	(7.8)	0.6	175	(9.7)	0.8	+33.3
≥ 25	91	(5.1)	0.1	88	(4.8)	0.1	0.0
Total	1,765§	(100.0)	0.8	1,901	(100.0)	0.8	0.0

*Provisional data.
†Per 100,000 population.
§The difference between this number and that in the text reflects differences between summary data reported to *MMWR* and more detailed data available to CDC's Division of Immunization.

Measles — Continued

Of the 1,801 cases, 466 (25.9%) were classified as preventable (2) (Table 3). The highest proportion of preventable cases occurred among persons who were not of school age: 69.2% of cases among children 18 months-4 years of age were preventable. Only 20.4% of cases among persons 5-19 years of age were preventable; however, 47.0% of all preventable cases occurred in this age group.

Of the 1,335 persons with nonpreventable cases, 242 (18.1%) were too young for routine vaccination (under 18 months of age), and 42 (3.1%) were too old (born before 1957) (Table 4). Of the 1,051 who were between 18 months and 28 years of age, 842 (80.1%) had been vaccinated on or after the first birthday, 11 (1.0%) had a prior physician diagnosis of measles; 34 (3.2%) were not U.S. citizens; and 163 (15.5%) had medical contraindications or exemptions under state law. One person (0.1%) had laboratory evidence of immunity.

Reported by Div of Immunization, Center for Prevention Svcs, CDC.

Editorial Note: In the prevaccine era, an average of 500,000 measles cases was reported

TABLE 2. Ages of measles patients at most recent vaccination — United States, first 26 weeks, 1984 and 1985*

Age at vaccination	1984 No.	1984 (%)	1985 No.	1985 (%)
< 12 mos.	135	(7.6)	96	(5.3)
12-14 mos.	255	(14.4)	247	(13.7)
15 mos.	34	(1.9)	46	(2.6)
16 mos.-4 yrs.	303	(17.2)	335	(18.6)
5-9 yrs.	139	(7.9)	165	(9.2)
10-14 yrs.	32	(1.8)	70	(3.9)
15-19 yrs.	8	(0.5)	5	(0.3)
≥ 20 yrs.	2	(0.1)	1	(0.1)
Unknown (> 12 mos.)	3	(0.2)	8	(0.4)
Unvaccinated	854	(48.4)	848	(47.0)
Total	1,765	(100.0)	1,901	(100.0)

*Provisional data.

TABLE 3. Age distribution and preventability of measles cases — United States, first 26 weeks, 1985*

Age group	Preventable No.	Preventable (%)	Nonpreventable No.	Nonpreventable (%)	Total
< 15 mos.	0	(0.0)	242	(100.0)	242
16 mo.-4 yrs.	155	(69.2)	69	(30.8)	224
5-9 yrs.	32	(21.1)	120	(78.9)	152
10-14 yrs.	52	(16.3)	267	(83.7)	319
15-19 yrs.	135	(22.4)	468	(77.6)	603
20-24 yrs.	60	(34.3)	115	(65.7)	175
25-29 yrs.	32	(60.4)	21	(39.6)	53
≥ 30 yrs.	0	(0.0)	33	(100.0)	33
Total	466	(25.9)	1,335	(74.1)	1,901

*Provisional data.

Measles — Continued

each year (3). After measles vaccine was licensed in 1963, the incidence of measles markedly declined. Since 1981, the number of reported measles cases has remained relatively consistent: 3,124 in 1981, 1,714 in 1982, 1,497 in 1983, and 2,534 in 1984. The number of cases reported during the first half of 1985 is similar to that reported during the first half of 1984 (1). As in recent years, measles was geographically restricted: 97.5% of the nation's counties were free of measles during this period.

While incidence rates during the first 26 weeks of 1984 and 1985 were comparable, there were differences in the age characteristics of patients. In 1984, persons 10-14 years of age accounted for approximately 29% of cases, compared with only 18% of cases in 1985. The incidence rate for 15- to 19-year-olds was higher in 1985. Over a third of measles patients were in this age group, due in part to the large number of outbreaks on college campuses in 1985 (4). Colleges and universities are now beginning to require evidence of immunity to measles for matriculation; this requirement should result in a decrease in measles in this population.

As the measles elimination strategy is successfully implemented, the proportion of preventable cases should decrease. The decrease in the percentage of preventable cases from 34.6% in 1984 (1) to 25.2% during the first half of 1985 is encouraging. As in 1984, preschool-aged children over 15 months of age had the highest proportion of preventable cases. Because these children are not reached by existing school laws, greater efforts need to be directed to this age group. School-aged persons accounted for the largest percentage of all preventable cases, and schools were the setting of transmission for the majority of cases. Therefore, continued enforcement of current school immunization laws is important for further reduction of measles in the United States.

References

1 CDC. Measles — United States, first 26 weeks, 1984. *MMWR* 1984;33:485-6, 491-4.
2 CDC. Classification of measles cases and categorization of measles elimination programs. *MMWR* 1982;31:707-11.
3 CDC. Measles surveillance report no. 11, 1977-1981. Atlanta, Georgia: Centers for Disease Control, 1982.
4 CDC. Measles on college campuses — United States, 1985. *MMWR* 1985;34:445-9.

TABLE 4. Reasons measles cases were classified as nonpreventable — United States, first 26 weeks, 1985*

Causes of nonpreventability	No. cases (%)		Percentage of total cases
< 15 months	242	(18.1)	13.4
Born before 1957	42	(3.1)	2.3
16 mos.-28 yrs	1,051	(77.7)	58.4
Adequately vaccinated	842	(80.1)	
Prior physician diagnosis	11	(1.0)	
Non-U.S. citizens	34	(3.2)	
Exemptions†	163	(15.5)	
Laboratory evidence of immunity	1	(0.1)	
Total	1,335	(100.0)	74.1

*Provisional data.
†Medical exemptions — 8, religious — 150, philosophic — 5.

IMPORTANT INFORMATION ABOUT POLIO AND ORAL POLIO VACCINE

Please read this carefully

OP 3/1/83

WHAT IS POLIO? Polio is a virus disease that may cause permanent crippling (paralysis) and occasionally death. There used to be thousands of cases and hundreds of deaths from polio every year in the United States. Because of the widespread use of polio vaccines, which became available beginning in the mid-1950's, polio disease has nearly been eliminated from the United States. Although thousands of cases continue to occur each year in the rest of the world, in the United States during the past 5 years there have been only 67 cases of polio reported, an average of 13 cases per year. Our success in preventing the spread of wild polio virus has been so great that most of the recent cases (approximately nine per year) have resulted from the rare side effects of oral polio vaccine (see below). Because of this fact, some people have asked why we should continue to use polio vaccine. The reason is that, even though we may not have much wild polio virus spreading here now, there is so much of it in the rest of the world that there is a great risk of its being reestablished if our children are not vaccinated.

ORAL LIVE POLIO VACCINE: Immunization with oral live polio vaccine (OPV) is one of the best ways to prevent polio. It is given by mouth starting in early infancy. Several doses are needed to provide good protection. Young children should get two or more doses in the first year of life and another dose at about 18 months of age. An additional dose is important for children when they enter school or when there is a high risk of polio, for example, during an epidemic or when traveling to a place where polio is common. The vaccine is easy to take and is effective in preventing the spread of polio. In over 90 percent of people, OPV gives protection for a long time, probably for life. Because OPV viruses live for a time in the intestinal tract of the person who is vaccinated, some of the viruses pass in the stool and can spread from the vaccinated person to those in close contact (usually household members). This may help to immunize these persons and is one of the advantages of OPV. The Immunization Practices Advisory Committee of the Public Health Service and the American Academy of Pediatrics recommend oral live polio vaccine as the preferred polio vaccine for people up to the 18th birthday.

POSSIBLE SIDE EFFECTS FROM THE VACCINE: OPV very rarely (once in about every 8.1 million doses of OPV distributed) causes paralytic polio in the person who is vaccinated. The risk may be slightly higher in adults being vaccinated and substantially higher in persons with abnormally low resistance to infection. Also very rarely (once in about every 5 million doses of OPV distributed) paralytic polio may develop in a close contact of a recently vaccinated person. Even though these risks are very low, they should be recognized. The risk of side effects from the vaccine must be balanced against the risk of the disease, both now and in the future.

(PLEASE READ OTHER SIDE)

PREGNANCY: Polio vaccine experts do not think oral polio vaccine can cause special problems for pregnant women or their unborn babies. However, doctors usually avoid giving any drugs or vaccines to pregnant women unless there is a specific need. Pregnant women should check with a doctor before taking oral polio vaccine.

WARNING—SOME PERSONS SHOULD NOT TAKE ORAL POLIO VACCINE WITHOUT CHECKING WITH A DOCTOR:

- Anyone with cancer, leukemia, or lymphoma.
- Anyone with a disease that lowers the body's resistance to infection.
- Anyone taking a drug that lowers the body's resistance to infection, such as cortisone or prednisone.
- Anyone who lives in the same household with anyone who has one of the conditions listed above.
- Anyone who is sick right now with something more serious than a cold.
- Pregnant women.
- Most persons age 18 and older because adults have a slightly bigger risk of developing paralysis from oral polio vaccine than children (However, if the risk of polio is increased-as may occur, for example, when there is an outbreak in your community-most polio experts recommend that unprotected persons receive oral polio vaccine regardless of age.)

NOTE ON INJECTABLE (KILLED) POLIO VACCINE: Besides the oral polio vaccine (OPV), there is also a killed polio vaccine (IPV) given by injection which protects against polio after several shots. This killed polio vaccine has no known risk of causing paralytic polio. Because OPV may provide lifetime protection, seems to provide stronger immunity in the intestinal tract (where infection first occurs), is simpler to administer, and is more effective in preventing the spread of polio virus than IPV, most polio experts feel that oral vaccine is more effective for controlling polio in the United States. Injectable polio vaccine is recommended for persons needing polio vaccination who have low resistance to serious infections or who live with persons with low resistance to serious infections. It may also be recommended for previously unvaccinated adults who plan to travel to a place where polio is common or for previously unvaccinated adults whose children are to be vaccinated with OPV. It is not widely used in this country at the present time, but it is available. If you would like to know more about this type of polio vaccine, or wish to receive this vaccine, please ask us.

QUESTIONS: If you have any questions about polio or polio vaccination, please ask us now or call your doctor or health department before you sign this form.

REACTIONS: If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after vaccination, please report it to the facility which provided the vaccine.

PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

I have read the information on this form about polio and the oral vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of oral polio vaccine and request that it be given to me or to the person named below for whom I am authorized to make this request.

OP 3/1/83

INFORMATION ON PERSON TO RECEIVE VACCINE (Please Print)				
Last Name	First Name	MI	Birthdate	Age
Address				
City	County		State	Zip
X				
Signature of person to receive vaccine or person authorized to make the request.				Date

FOR CLINIC USE
Clinic Ident.
Date Vaccinated
Manuf. and Lot No.
Site of Injection

FOR DATA PROCESSING USE ONLY (OPTIONAL)

VACCINE HISTORY: PLACE CHECK ☐ IN BOX IF HISTORY PREVIOUSLY SUBMITTED

DTP:	m/d/yr	m/d/yr	m/d/yr	m/d/yr	m/d/yr	MEASLES: m/d/yr	MUMPS: m/d/yr	
POLIO:	m/d/yr	m/d/yr	m/d/yr	m/d/yr	m/d/yr	RUBELLA: m/d/yr		

IMPORTANT INFORMATION ABOUT MEASLES, MUMPS, AND RUBELLA AND MEASLES, MUMPS, AND RUBELLA VACCINES

WHAT IS MEASLES? Measles is the most serious of the common childhood diseases. Usually it causes a rash, high fever, cough, runny nose, and watery eyes lasting 1 to 2 weeks. Sometimes it is more serious. It causes an ear infection or pneumonia in nearly 1 out of 10 children who get it. Approximately 1 child out of every 1,000 who get measles has an inflammation of the brain (encephalitis). This can lead to convulsions, deafness, or mental retardation. About 2 children in every 10,000 who get measles die from it. Measles can also cause a pregnant woman to have a miscarriage or give birth to a premature baby.

Before measles vaccine shots were available, there were hundreds of thousands of cases and hundreds of deaths each year. Nearly all children got measles by the time they were 15. Now, wide use of measles vaccine has nearly eliminated measles from the United States. However, if children are not vaccinated they have a high risk of getting measles, either now or later in life.

WHAT IS MUMPS? Mumps is a common disease of children. Usually it causes fever, headache, and inflammation of the salivary glands, which causes the cheeks to swell. Sometimes it is more serious. It causes a mild inflammation of the coverings of the brain and spinal cord (meningitis) in about 1 child in every 10 who get it. More rarely, it can cause inflammation of the brain (encephalitis) which usually goes away without leaving permanent damage. Mumps can also cause deafness. About 1 out of every 4 adolescent or adult men who get mumps develops painful inflammation and swelling of the testicles. While this condition usually goes away, on rare occasions it may cause sterility.

Before mumps vaccine shots were available, there were more than 150,000 cases each year. Now, because of the wide use of mumps vaccine, the number of cases of mumps is much lower. However, if children are not vaccinated, they have a high risk of getting mumps.

WHAT IS RUBELLA? Rubella is also called German measles. It is a common disease of children and may also affect adults. Usually it is very mild and causes a slight fever, rash, and swelling of glands in the neck. The sickness lasts about 3 days. Sometimes, especially in adult women, there may be swelling and aching of the joints for a week or two. Very rarely, rubella can cause inflammation of the brain (encephalitis) or cause a temporary bleeding disorder (purpura).

The most serious problem with rubella is that if a pregnant woman gets this disease, there is a good chance that she may have a miscarriage or that the baby will be born crippled, blind, or with other defects. The last big rubella epidemic in the United States was in 1964. Because of that epidemic, about 25,000 children were born with serious problems such as heart defects, deafness, blindness, or mental retardation because their mothers had rubella during the pregnancy.

Before rubella vaccine shots were available, rubella was so common that most children got the disease by the time they were 15. Now, because of the wide use of rubella vaccine, the number of cases of rubella is much lower. However, if children are not vaccinated, they have a high risk of getting rubella and possibly exposing a pregnant woman to the disease. If an unvaccinated woman later becomes pregnant and catches rubella, she may have a defective baby.

Since rubella is a mild illness, many women of childbearing age do not recall if they had rubella as a child. A simple blood test can show whether a person is immune to rubella or is not protected against the disease. Overall, about one in five women of childbearing age is not protected against rubella.

Please read this carefully

MMR 3/1/83

(PLEASE READ OTHER SIDE.)

MEASLES, MUMPS, AND RUBELLA VACCINES: The vaccines are given by injection and are very effective. Ninety percent or more of people who get the shot will have protection, probably for life. Since protection is not as likely to occur if the vaccines are given very early in life, these vaccines should be given to children after their first birthday; measles vaccine should be given at 15 months of age or older. Measles, mumps, and rubella vaccines can be given one at a time or in a combined vaccine (measles-rubella [MR], measles-mumps-rubella [MMR]) by a single shot. If they are given in combined vaccine, they should be given at 15 months of age or older.

Experts recommend that adolescents and adults—especially women of childbearing age—who are not known to be immune to rubella should receive rubella vaccine (or MMR if they might also be susceptible to measles or mumps). Women should not receive the shot if they are pregnant or might become pregnant within 3 months. There is no known risk in being vaccinated against any or all three of these diseases if you are already immune to any of them.

POSSIBLE SIDE EFFECTS FROM THE VACCINES: About 1 out of every 5 children will get a rash or slight fever lasting for a few days, 1 or 2 weeks after getting measles vaccine. Occasionally there is mild swelling of the salivary glands after mumps vaccination.

About 1 out of every 7 children who get rubella vaccine will get a rash or some swelling of the glands of the neck 1 or 2 weeks after the shot. About 1 out of every 20 children who get rubella vaccine will have some aching or swelling of the joints. This may happen anywhere from 1-3 weeks after the shot. It usually lasts only 2 or 3 days. Adults are more likely to have these problems with their joints—as many as 1 in 4 may have them. Other temporary side effects, such as pain, numbness, or tingling in the hands and feet have also occurred but are very uncommon.

Although experts are not sure, it seems that *very rarely* children who get these vaccines may have a more serious reaction, such as inflammation of the brain (encephalitis), convulsions with fever, or nerve deafness.

With any vaccine or drug, there is a possibility that allergic or other more serious reactions or even death could occur.

WARNING—SOME PERSONS SHOULD *NOT* TAKE THESE VACCINES WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who had an allergic reaction to eating eggs so serious that it required medical treatment (does not apply to rubella vaccine).
- Anyone with cancer, leukemia, or lymphoma.
- Anyone with a disease that lowers the body's resistance to infection.
- Anyone taking a drug that lowers the body's resistance to infection (such as cortisone, prednisone or certain anticancer drugs)
- Anyone who has received a gamma globulin (immune globulin) within the preceding 3 months.
- Anyone who had an allergic reaction to an antibiotic called neomycin so serious that it required medical treatment.

PREGNANCY: Measles, mumps, and rubella vaccines are not known to cause special problems for pregnant women or their unborn babies. However, doctors usually avoid giving any drugs or vaccines to pregnant women unless there is a specific need. To be safe, pregnant women should not get these vaccines. A woman who gets any of these vaccines should wait 3 months before getting pregnant.

Vaccinating a child whose mother is pregnant is not dangerous to the pregnancy.

QUESTIONS: If you have any questions about measles, mumps, or rubella vaccination, please ask us now or call your doctor or health department before you sign this form.

REACTIONS: If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after vaccination, please report it to the facility which provided the vaccine.

PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

I have read the information on this form about measles, mumps, and rubella and measles, mumps, and rubella vaccines. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of measles, mumps and rubella vaccines and request that the vaccine checked below be given to me or to the person named below for whom I am authorized to make this request.

VACCINE TO BE GIVEN: ☐ *Measles* ☐ *Mumps* ☐ *Rubella* ☐ *Measles-Rubella* ☐ *Measles-Mumps-Rubella* **MMR 3/1/83**

INFORMATION ON PERSON TO RECEIVE VACCINE (Please Print)

Last Name _____ First Name _____ MI _____ Birthdate _____ Age _____

Address _____

City _____ County _____ State _____ Zip _____

X _____

Signature of person to receive vaccine or person authorized to make the request _____ Date _____

FOR CLINIC USE

Clinic Ident. _____

Date Vaccinated _____

Manufacturer and Lot No. _____

Site of injection _____

FOR DATA PROCESSING USE ONLY (OPTIONAL)

VACCINE HISTORY: ☐ PLACE CHECK IN BOX IF HISTORY PREVIOUSLY SUBMITTED

DTP: _____ _____ _____ _____ _____ MEASLES: _____ MUMPS: _____
m/d/yr m/d/yr m/d/yr m/d/yr m/d/yr m/d/yr m/d/yr

POLIO: _____ _____ _____ _____ _____ RUBELLA: _____
m/d/yr m/d/yr m/d/yr m/d/yr m/d/yr m/d/yr

IMPORTANT INFORMATION ABOUT DIPHTHERIA, TETANUS, AND PERTUSSIS AND DTP, DT, AND Td VACCINES

Please read this carefully

DTP 2/1/86

WHAT IS DIPHTHERIA? Diphtheria is a very serious disease which can affect people in different ways. It can cause an infection in the nose and throat which can interfere with breathing. It can also cause an infection of the skin. Sometimes it causes heart failure or paralysis. About 1 person out of every 10 who get diphtheria dies of it.

WHAT IS TETANUS? Tetanus, or lockjaw, results when wounds are infected with tetanus bacteria, which are often found in dirt. The bacteria in the wound make a poison which causes the muscles of the body to go into spasm. Four out of every 10 persons who get tetanus die of it.

WHAT IS PERTUSSIS? Pertussis, or whooping cough, causes severe spells of coughing which can interfere with eating, drinking, and breathing. In the United States, more than 75 percent of reported pertussis cases occur in children younger than 5 years. Pertussis is a more serious disease in young children and more than half of the children less than 1 year of age reported to have pertussis are hospitalized. In recent years, an average of 1,700 cases of pertussis have been reported each year in the United States. Complications occur in a substantial proportion of reported cases. Pneumonia occurs in one of every four children with pertussis. For every 1,000 reported pertussis cases, 22 develop convulsions and/or have more severe problems of the brain. In recent years, an average of eight deaths due to pertussis occurred annually.

Before vaccines were developed, these three diseases were all very common and caused a large number of deaths each year in the United States. If children are not vaccinated, the risk of getting these diseases will go back up again.

DTP, DT, AND Td VACCINES: Immunization with DTP vaccine is one of the best ways to prevent these diseases. DTP vaccine is actually three vaccines combined into one shot to make it easier to get protection. The United States Public Health Service and the American Academy of Pediatrics recommend DTP vaccine be used in children up to their seventh birthday. The vaccine is given by injection starting early in infancy. At least three shots are needed to provide initial protection. Young children should get three doses in the first year of life and a fourth dose at about 18 months of age. A booster shot is important for children who are about to enter school and should be given between their fourth and seventh birthdays. The vaccine is very effective at preventing tetanus—over 95 percent of those who get the vaccine are protected if the recommended number of shots is given. Although the diphtheria and pertussis parts of the vaccine are not quite as effective, they still prevent most children from getting disease and they make the disease milder for those who do get it.

Because pertussis is not very common or severe in older children, those 7 years of age and older should take a vaccine that does not contain the pertussis part. Also, because reactions to the diphtheria part of the vaccine may be more common in older children, those 7 years of age and older should take a form of the vaccine that has a lower concentration of the diphtheria part. This vaccine which contains no pertussis part and a lower concentration of the diphtheria part is called Td vaccine. Boosters with the Td vaccine should be received every 10 years throughout life.

(PLEASE READ OTHER SIDE)

DEFERRAL OF DTP IMMUNIZATION: Children who have had a serious reaction to previous DTP shots should not receive additional pertussis vaccine (see WARNING). A preparation called DT vaccine is available for them which does not contain the pertussis part. Also, children who have previously had a convulsion or are suspected to have a problem of the nervous system should not receive DTP vaccine until a full medical evaluation has been made.

POSSIBLE SIDE EFFECTS FROM THE VACCINE: With DTP vaccine, most children will have a slight fever and be irritable within 2 days after getting the shot. One half of children develop some soreness and swelling in the area where the shot was given. More serious side effects can occur. A temperature of 105°F or greater may follow 1 out of 330 DTP shots. Continuous crying lasting 3 or more hours may occur after 1 in every 100 shots and unusual, high-pitched crying may occur after 1 in every 900 shots. Convulsions or episodes of limpness and paleness may each occur after 1 in every 1,750 shots. Children who have previously had a convulsion may be more likely to have another one after pertussis shots. Rarely, about once in every 110,000 shots, other more severe problems of the brain may occur, and permanent brain damage may occur about once in every 310,000 shots. Side effects from DT or Td vaccine are not common and usually consist only of soreness and slight fever. As with any drug or vaccine, there is a rare possibility that allergic or more serious reactions or even death could occur.

Although some people have questioned whether DTP shots might cause Sudden Infant Death Syndrome (SIDS), in careful studies DTP shots have not been shown to cause SIDS.

PREGNANCY: Babies born under unsanitary conditions to unimmunized women have a risk of developing tetanus during the newborn period (neonatal tetanus). Neonatal tetanus can be prevented by immunization of adult women. Women who have not received Td earlier and who are thought to be at risk of delivering their babies under unsanitary conditions should be immunized during pregnancy.

Td is not known to cause special problems for pregnant women or their unborn babies. Doctors usually do not recommend giving any drugs or vaccines to pregnant women unless there is a specific need. Pregnant women who need Td should receive it, preferably during the second and/or third trimesters.

WARNING—SOME PERSONS SHOULD *NOT* TAKE THESE VACCINES WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who has had a convulsion or is suspected to have a problem of the nervous system.
- Anyone who has had a serious reaction to DTP, DT, or Td shots before, such as: an allergic reaction to any vaccine component; a temperature of 105°F or greater; an episode of limpness and paleness; prolonged continous crying; an unusual, high-pitched cry; or a convulsion or other more severe problem of the brain.
- Anyone taking a drug or undergoing a treatment that lowers the body's resistance to infection, such as: cortisone, prednisone, certain anticancer drugs, or irradiation.

QUESTIONS: If you have any questions about diphtheria, tetanus, or pertussis or DTP, DT, or Td vaccination, please ask us now or call your doctor or health department before you sign this form.

REACTIONS: If the person who received the vaccine develops a temperature of 105°F or greater, continuous crying lasting 3 or more hours, an unusual high-pitched cry, a convulsion, an episode of limpness and paleness, or a severe problem of the brain, the person should be evaluated promptly by a doctor.

If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after vaccination, please report it to the facility which provided the vaccine.

PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

I have read the information on this form about diphtheria, tetanus, and pertussis and DTP, DT, and Td vaccines. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of DTP, DT, and Td vaccines and request that the vaccine checked below be given to me or to the person named below for whom I am authorized to make this request.

VACCINE TO BE GIVEN: ☐ DTP ☐ DT ☐ Td

DTP 2/1/93

INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)				
Last Name	First Name	MI	Birthdate	Age
Address				
City	County		State	Zip
X				
Signature of person to receive vaccine or person authorized to make the request.				Date

FOR CLINIC USE
Clinic Ident.
Date Vaccinated
Manuf. and Lot No.
Site of Injection

FOR DATA PROCESSING USE ONLY (OPTIONAL)

VACCINE HISTORY: PLACE CHECK ☐ IN BOX IF HISTORY PREVIOUSLY SUBMITTED

DTP:	m/d/yr	m/d/yr	m/d/yr	m/d/yr	m/d/yr	MEASLES: m/d/yr	MUMPS: m/d/yr	
POLIO:	m/d/yr	m/d/yr	m/d/yr	m/d/yr	m/d/yr	RUBELLA: m/d/yr	HAEMOPHILUS b:	

BILL SHEFFIELD, GOVERNOR

DEPT. OF HEALTH AND SOCIAL SERVICES

DIVISION OF PUBLIC HEALTH
SECTION OF COMMUNICABLE DISEASE CONTROL

3601 "C" STREET, SUITE 576
POUCH 6333
ANCHORAGE, AK 99502-0333
(907) 561-4235

November 14, 1986

Ms. Shannon Kohler
Alaska Chapter-DPT
Box 1746
Soldotna, AK 99669

Dear Ms. Kohler:

Thank you for the information relative to the pertussis poster containing incorrect information. We are not aware of any state-wide department offices displaying such a poster.

The "Dear Health Care Provider" contains information which has been in existence for at least two years and is considered common knowledge by most health care providers who administer vaccine. However, it maybe appropriate to reiterate the information in an upcoming edition of the Epidemiology Bulletin (a news bulletin sent to health care providers and other interested parties). Also, we will be rewriting the immunization standing orders for the Public Health Nurses and, if not already part of their standing orders, we will include this important information.

The State does not have any specific regulations regarding the reporting of adverse reactions following immunizations. Health care provders who administer vaccines are encouraged to report possible adverse reactions to this office. This is a passive surveillance system which relies on the integrity of the health care providers to comply.

The answers to your remaining questions are as follows:

1. Report Gathering

   A. How are adverse reactions gathered from parents? from public health officials administering vaccine? from doctors?

      Parents are to notify the provider of the vaccine if the vaccinee visits a doctor, hospital, or clinic within 4 weeks of vaccination, as requested on every Important Information Form. A public provider who is made aware of a possible adverse reaction completes the MSAEFI report form and submits it to this office. A private physician who is made aware of a possible adverse reaction notifies this office and the MSAEFI Coordinator completes the MSAEFI report form.

B. What is the estimated rate of compliance?

C. How exactly is the rate of compliance determined?

No estimated rate of compliance is determined.

2. Handling Reports

A. Once a report is received, where and how is it recorded?

All submitted MSAEFI report forms are entered onto a MSAEFI report form log sheet by the MSAEFI Coordinator. All submitted MSAEFI report forms which meet the minimal criteria for submission to the Centers for Disease Control are forwarded.

B. Is the original or copy of report kept by State office?

A typed carbon copy is retained by the State office.

C. Is the original or copy of report sent to the National Center of Disease Control (CDC) in Atlanta Georgia?

A typed copy is forwarded to the CDC.

3. Approximately how many adverse reaction reports does your office receive per year from public health officials?

1985 - 12 (2 of which were military)
1986 - 9

from doctors?

1985 - 3
1986 - 1

from parents?

1985 - 0
1986 - 0

(The numbers listed above indicate adverse reaction reports forwarded to the CDC, not the number received by this office.)

B. What are the symptoms and diagnosis included in reports?

See enclosed MSAEFI report form.

And, finally, your last request to "send me a copy of the annual Alaska State reports regarding immunizations and reactions that were sent to Atlanta, Georgia CDC in 1984 and 1985," will have to be more specific.

There are no annual reaction reports, however, there a quite a few immunization reports sent to the CDC quarterly and annually by this office. If the specific information you want is available, we will send it to you.

Sincerely,

Michael Klatt

Michael Klatt, Manager
Alaska Immunization Program

Robert I. Fraser, M.D. Chief
Sec. of Comm. Disease Control

MK+RIF:ew

Enclosure

cc: Elizabeth Ward, Director
Division of Public Health

STATE OF ALASKA

BILL SHEFFIELD, GOVERNOR

DEPT. OF HEALTH AND SOCIAL SERVICES

DIVISION OF PUBLIC HEALTH
SECTION OF COMMUNICABLE DISEASE CONTROL

3601 "C" STREET, SUITE 576
POUCH 6333
ANCHORAGE, AK 99502-0333
(907) 561-4235

May 1, 1986

The information you requested about DTP vaccine and whooping cough was not easily retrievable. The major reason being that I have only been on the job three months, therefore, I didn't know who to ask or where to look. However, this is what I have found.

1. There were five cases of whooping cough in 1984 and 30 cases in 1985.

2. Four of the five cases were confirmed in 1984 and nine of the 30 cases were confirmed in 1985.

3. A total of four of the 35 cases were hospitalized with no deaths.

4.

Age	1984	1985
unknown	0	4
<1	2	10
1	1	6
2	0	4
5-9	0	2
10-19	0	3
20-24	0	1
25-29	1	0
30-39	1	0

Approximately half of the cases had received pertussis vaccine at some point in their life , however, whether they were appropriately immunized for age I am unable to ascertain.

5. The parents/guardians of recipients who see a physician or who are hospitalized within one month of an immunization are supposed to notify the Alaska Immunization Program. When I receive notification of an adverse event following an immunization, I contact the parents/guardians, the immunization provider, and the attending physician. It is the physician's responsibility to determine whether or not the patient's problems are vaccine-related. All vaccine-related adverse reactions are documented on an official report form and sent to the Centers for Disease Control in Atlanta, Georgia.

I hope the enclosures are of help to you.

Sincerely,

Michael Klatt

Michael Klatt, Manager
Alaska Immunization Program

MK:db

(For Adult Use) is recommended.[1-8]

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

HOW SUPPLIED

Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed, Aluminum Phosphate Adsorbed, is available in vials of 7.5 ml. Product 1948-33

STORAGE

Keep between 2 and 8° C (35-46° F). DO NOT FREEZE.

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Lederle

LABORATORIES DIVISION
American Cyanamid Company, Pearl River, N.Y. 10965

REV. 11/84

16042
DX12

DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE ADSORBED TRI-IMMUNOL®

Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed, TRI-IMMUNOL® Lederle, is a combination of *Purogenated* Diphtheria Toxoid Aluminum Phosphate-Adsorbed, *Purogenated* Tetanus Toxoid Aluminum Phosphate-Adsorbed, and Pertussis Vaccine.

DESCRIPTION

The diphtheria toxin is produced according to the method of Mueller and Miller and is detoxified by use of formaldehyde. The tetanus toxin is produced by the method of Mueller and Miller and is detoxified by the use of formaldehyde. The toxoids are refined by the Pillemer alcohol fractionation method and are diluted with a solution containing potassium phosphate monobasic, sodium phosphate dibasic, glycine, and thimerosal (mercury derivative) as a preservative. Pertussis Vaccine is prepared by growing Phase I *B. pertussis* in a modified Cohen-Wheeler broth containing acid hydrolysate of casein. The *B. pertussis* culture is harvested, inactivated, and then suspended in a solution containing potassium phosphate monobasic, sodium phosphate dibasic, sodium chloride, and thimerosal (mercury derivative) as a preservative and is then combined with the refined Diphtheria and Tetanus Toxoids in physiological saline (NaCl) diluent containing thimerosal (mercury derivative) as a preservative. The final concentration of thimerosal (mercury derivative) in the combined vaccine is 1:10,000. The aluminum content of the final product does not exceed 0.80 mg per 0.5 ml dose.

The total immunizing dose contains 12 units of pertussis vaccine.

The primary immunization against diphtheria, tetanus, and pertussis consists of four 0.5 ml doses when administered as recommended.[1-8]

CLINICAL PHARMACOLOGY

Simultaneous immunization against diphtheria, tetanus, and pertussis during infancy and childhood has been a routine practice in the United States since the late 1940's. It has played a major role in markedly reducing the incidence of cases and deaths from each of these diseases.

Diphtheria is primarily a localized and generalized intoxication caused by diphtherial toxin, an extracellular protein metabolite of toxinogenic strains of *Corynebacterium diphtheriae*. While the incidence of diphtheria has decreased from about 20 cases per 100,000 population before the general use of diphtheria toxoid[1-3] to about 56 cases reported between 1976 and 1981, the ratio of fatalities to attack rate has remained constant at about 5%-10%. The highest case fatality rates are in the very young and the elderly. Diphtheria toxoid induces antitoxin. Following adequate immunization with diphtheria toxoid is thought to protect for at least 10 years.[1]

It significantly reduces both the risk of developing diphtheria and the severity of clinical illness. It does not, however, eliminate carriage of *C. diphtheriae* in the pharynx or on the skin.[1] A serum level ≥0.01 toxin neutralization units/ml is generally considered protective.[1]

Tetanus is an intoxication manifested primarily by neuromuscular dysfunction caused by a potent exotoxin elaborated by *Clostridium tetani*. The incidence of tetanus has dropped dramatically with the routine use of tetanus toxoid, remaining relatively constant over the last decade at about 100 cases reported annually. Spores of *C. tetani* are ubiquitous and there is essentially no natural immunity to tetanus toxin. Thus, universal primary immunization with tetanus toxoid with subsequent maintenance of adequate antitoxin levels by means of timed boosters is necessary to protect all age groups.[1] Tetanus toxoid is highly effective, with a failure rate in fully immunized persons of less than 4 per 100 million.[1] Protective levels of serum antitoxin (≥0.01 toxin neutralization units/ml)[4] are achieved which persist for at least 10 years after full immunization.[1]

Pertussis is a disease of the respiratory tract caused by *Bordetella pertussis*. This gram-negative coccobacillus produces an array of biologically active components that escape from the site of infection and produce systemic effects, including an endotoxin-related febrile response, attenuation of the host's febrile and inflammatory responses, lymphocytosis, leukocytosis, effects on glucose homeostasis, and possible neurotoxicity. The role of each of the different components in the pathogenesis of and immunity to pertussis is not well understood.

Pertussis is a highly communicable disease which, unique for a bacterial disease, has an attack rate in unimmunized populations of over 90%.[3] As a result of immunization with pertussis vaccine, the number of reported cases and associated mortality has de-

clined from about 120,000 cases and 1,100 deaths in 1950[4] to an annual average of abou 2,300 cases and 10 fatalities over the last 10 years.[1] Accurate data do not exist as bacteriological confirmation of pertussis can be obtained in less than half of the cases reported. Illnesses from *B. pertussis* occur in infants and young children. two-thirds of reported deaths occur in children less than one year old. Older children and adults in whom classic signs are often absent, may go undiagnosed and serve as reservoirs of disease.[1]

Evidence of the efficacy of pertussis vaccine can be provided by the recent British experience, where a reduction in the number of immunized individuals from 79% in 1973, to 31% in 1978 resulted in an epidemic of 102,500 pertussis cases and 36 deaths between late 1977 and 1980, and 1,440 cases per week reported during the winter of 1981-82. A similar situation occurred in Japan.[4]

Because the incidence and severity of pertussis decrease with age, routine pertussis immunization is not recommended for persons 7 years of age or older.[1]

INDICATION AND USAGE

Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed is indicated for active immunization of infants and children through 6 years of age against diphtheria, tetanus, and pertussis.[1-3]

CONTRAINDICATIONS

IMMUNIZATION SHOULD BE DEFERRED DURING THE COURSE OF ANY ACUTE ILLNESS. THE OCCURRENCE OF ANY TYPE OF NEUROLOGICAL SYMPTOMS OR SIGNS, INCLUDING ONE OR MORE CONVULSIONS (SEIZURES) FOLLOWING ADMINISTRATION OF THIS PRODUCT IS A CONTRAINDICATION TO FURTHER USE. USE OF THIS PRODUCT IS ALSO CONTRAINDICATED IF THE CHILD HAS A PERSONAL OR FAMILY HISTORY OF CENTRAL NERVOUS SYSTEM DISORDERS.

THE PRESENCE OF ANY EVOLVING OR CHANGING DISORDER AFFECTING THE CENTRAL NERVOUS SYSTEM IS A CONTRAINDICATION TO ADMINISTRATION OF DTP REGARDLESS OF WHETHER THE SUSPECTED NEUROLOGICAL DISORDER IS ASSOCIATED WITH OCCURRENCE OF SEIZURE ACTIVITY OF ANY TYPE.

The Committee on Infectious Diseases of the American Academy of Pediatrics recommends that pertussis vaccine should be withheld when a previous dose has been followed by convulsion, encephalitis, focal neurological signs, or collapse. Nor should infants who experience excessive somnolence, excessive screaming (persistent crying or screaming for three or more hours duration) or temperature more than 105° F (40.5° C) receive additional doses of the vaccine.[1]

The Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service recommends that hypersensitivity to vaccine components, presence of an evolving neurologic disorder, or a history of a severe reaction (usually within 48 hours) following a previous dose all remain definitive contraindications to the receipt of pertussis vaccine. Severe reactions include collapse or shock, persistent screaming episode, temperature 40.5° C (105° F) or greater, convulsion(s) with or without accompanying fever, severe alterations of consciousness, generalized and/or local neurologic signs, or systemic allergic reactions.[1]

Immunosuppressive therapy, including irradiation, corticosteroids, antimetabolites, alkylating agents, and cytotoxic agents may result in aberrant responses to active immunization procedures. Administration should be deferred in individuals receiving such therapy.

The clinical judgement of the attending physician should prevail at all times.

Elective immunization of patients over the age of 6 months should be deferred during an outbreak of poliomyelitis.

WARNING

THIS PRODUCT IS NOT RECOMMENDED FOR IMMUNIZING PERSONS AFTER THEIR SEVENTH BIRTHDAY. DO NOT ATTEMPT ROUTINE IMMUNIZATION IF THE CHILD HAS A PERSONAL OR FAMILY HISTORY OF CENTRAL NERVOUS SYSTEM DISORDERS. SHOULD ANY SYMPTOMATOLOGY RELATED TO NEUROLOGICAL DISORDERS DEVELOP FOLLOWING ADMINISTRATION, DO NOT ATTEMPT FURTHER ADMINISTRATION OF PERTUSSIS VACCINE. CONVULSION, ENCEPHALITIS, FOCAL NEUROLOGIC SIGNS, COLLAPSE, SHOCK, EXCESSIVE SCREAMING (PERSISTENT CRYING OR SCREAMING FOR THREE OR MORE HOURS DURATION), EXCESSIVE SOMNOLENCE, SEVERE ALTERATION OF CONSCIOUSNESS, SYSTEMIC ALLERGIC REACTIONS OR TEMPERATURE MORE THAN 105° F (40.5° C) ARE CONTRAINDICATIONS FOR ANY FURTHER USE OF PERTUSSIS VACCINE.

If such disorders are found, the infants or children should be given diphtheria and tetanus toxoids (DT) instead of DTP. If DT is used, three doses at least 4 weeks apart, followed by a fourth dose 6-12 months later, are recommended for infants. For children 1 year of age or older, two doses of DT at least 4 weeks apart followed by a third dose 6-12 months later, are recommended.[1]

The occurrence of sudden-infant-death syndrome (SIDS) has been reported following administration of DTP.[10-11] A causal relationship between DTP immunization and the syndrome has not been established.[12-14]

Prior to administration of this vaccine, health care personnel should inform the parent, guardian, or other responsible adult of the benefits and risks to the child of DTP vaccine. For recent information about the estimated range of risks of severe reactions following DTP administration, consult references 1, 15, 16, 17, 18, and 21.

DTP should not be given to infants or children with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration.

If the vaccine is used in persons receiving immunosuppressive therapy, the expected antigenic response may not be obtained.

Special care should be taken so the injection is not made into a blood vessel.

PRECAUTIONS

A. *General*

1. This product should be used for the age group between 2 months and the 7th birthday.
2. A separate sterile syringe and needle or a sterile disposable unit should be used for each individual patient to prevent transmission of hepatitis or other infectious agents from one person to another.
3. *Since this product contains both a bacterial suspension and an adjuvant, shake vigorously before withdrawing each dose from multiple dose vials.*
4. Before the injection of any biological, the physician should take all precautions known for prevention of allergic or any other side reactions. This should include: A review of the patient's history regarding possible sensitivity; the ready availability of epinephrine 1:1000 and other appropriate agents used for control of immediate allergic reactions; and a knowledge of the recent literature pertaining to use of the biological concerned, including the nature of side effects and adverse reactions that may follow its use.

B. *Information for Parent*

1. Prior to administration of any dose of DTP, the parent or guardian should be asked about the recent health status of the infant or child to be injected.
2. WHEN AN INFANT OR CHILD IS RETURNED FOR THE NEXT DOSE IN THE SERIES, THE PARENT SHOULD BE QUESTIONED CONCERNING OCCURRENCE OF ANY SYMPTOM AND/OR SIGNS OF AN ADVERSE REACTION AFTER THE PREVIOUS DOSE (SEE CONTRAINDICATIONS, ADVERSE REACTIONS).

ADVERSE REACTIONS

Local reactions, manifested by erythema and induration with or without tenderness, are common after administration of DTP. Such local reactions are usually self-limited and require no therapy. A nodule may be palpable at the injection site for a few weeks.

Abscess formation at the site of injection has been reported.[1,19,20] Cervical lymphadenopathy has been reported following DTP injections into the arm.[19]

Mild to moderate temperature elevations frequently follow DTP administration and are often accompanied by irritability, drowsiness, vomiting, and anorexia.[1,10,19] Approximately 50% of DTP recipients will develop temperature elevations ≥ 38° C (100.4° F) after one or more doses of the series, approximately 6% ≥ 39° C (102.2° F), and approximately 1.5% ≥ 40° C (104° F). Some data suggest that febrile reactions are more likely to occur in those who have experienced such responses after prior doses.[19]

SIGNIFICANT REACTIONS ATTRIBUTED TO THE PERTUSSIS VACCINE COMPONENT HAVE BEEN: HIGH FEVER OF 40.5° C (105° F), A TRANSIENT SHOCK-LIKE EPISODE, EXCESSIVE SCREAMING (PERSISTENT CRYING OR SCREAMING FOR THREE OR MORE HOURS DURATION), SOMNOLENCE, CONVULSIONS, AND ENCEPHALOPATHY. THESE REACTIONS HAVE BEEN REPORTED TO OCCUR RARELY FOLLOWING THE INJECTION OF THIS PRODUCT AND THEY MAY BE FATAL OR RESULT IN PERMANENT DAMAGE TO THE CENTRAL NERVOUS SYSTEM. PERTUSSIS VACCINE HAS BEEN ASSOCIATED WITH A GREATER PROPORTION OF ADVERSE REACTIONS THAN MANY OTHER CHILDHOOD IMMUNIZATIONS.[1,19] SHOULD SYMPTOMATOLOGY REFERABLE TO THE CENTRAL NERVOUS SYSTEM DEVELOP FOLLOWING ADMINISTRATION, FURTHER IMMUNIZATION WITH THIS PRODUCT IS CONTRAINDICATED (SEE CONTRAINDICATIONS). SUCH REACTIONS ALMOST ALWAYS APPEAR WITHIN 24 TO 48 HOURS AFTER INJECTION, BUT HAVE BEEN THOUGHT TO OCCUR AFTER AN INTERVAL AS LONG AS SEVEN DAYS.

NEUROLOGICAL COMPLICATIONS FOLLOWING TETANUS TOXOID ADMINISTRATION, SUCH AS PARALYSIS OF THE RADIAL NERVE,[21] RECURRENT PHARYNGEAL NERVE,[22] COCHLEAR LESION,[23] BRACHIAL PLEXUS NEUROPATHY,[21,24] AND A CASE OF DIFFICULTY IN SWALLOWING, ACCOMMODATION PARESIS, AND EEG DISTURBANCES[25] HAVE BEEN REPORTED. IN THE DIFFERENTIAL DIAGNOSIS OF POLYRADICULONEUROPATHIES FOLLOWING ADMINISTRATION OF TETANUS TOXOID, TETANUS TOXOID SHOULD BE CONSIDERED AS A POSSIBLE ETIOLOGY.[21]

DOSAGE AND ADMINISTRATION

Shake vigorously before withdrawing each dose from the multiple dose vials.

Before injection, the skin over the site to be injected should be cleansed and prepared with a suitable germicide. After insertion of the needle, aspirate to help avoid inadvertent injection into a blood vessel. Expel the dose slowly and terminate the dose with a small bubble of air (0.1 to 0.2 ml).

The basic immunizing course for infants and children through 6 years of age consists of three doses of 0.5 ml each at 4- to 8-week intervals, followed by a fourth dose of 0.5 ml approximately one year after the third dose.

It is recommended that active immunization against diphtheria, tetanus, and pertussis be started at 2 months of age.[1,3] All doses should be injected intramuscularly, preferably into the mediateral muscles of the thigh or deltoid, with care to avoid major peripheral nerve trunks.

Interruption of the recommended schedule with a delay between doses does not interfere with the final immunity achieved; nor does it necessitate starting the series over again, regardless of the length of time elapsed between doses.[1]

A recall (booster) dose of 0.5 ml is indicated at age 4-6 years, preferably prior to entrance into kindergarten or elementary school. However, if the fourth dose of the basic immunizing series was administered after the fourth birthday, a recall (booster) of DTP prior to school entry is not considered necessary.[1]

For either basic or recall (booster) immunization against tetanus and diphtheria of individuals 7 years of age and older, the use of Tetanus and Diphtheria Toxoids Adsorbed

STORAGE

To maintain potency it is necessary to store this vaccine at a temperature which will maintain ice continuously in a solid state. This vaccine may remain fluid at temperatures above -14° C (+7° F) because of its sorbitol content. If frozen, the vaccine must be completely thawed prior to use. An *unopened* container of vaccine that has been frozen and then is thawed may be carried through a maximum of 10 freeze-thaw cycles, provided the temperature does not exceed 8° C (46° F) during the periods of thaw, and provided the total cumulative duration of thaw does not exceed 24 hours. If the 24-hour period is exceeded, the vaccine then must be used within 30 days, during which time it must be stored at a temperature between 2-8° C (36-46° F).

DISCLAIMER OF REPRESENTATIONS AND WARRANTIES

This vaccine has been produced and tested in accordance with the regulations of the United States Food and Drug Administration for the production of Poliovirus Vaccine, Live, Oral Trivalent. The manufacturer makes no representation or warranty, expressed or implied, with respect to the merchantability or fitness for use of this vaccine other than that the vaccine has been produced in accordance with the standards for its production prescribed by the United States Food and Drug Administration and applicable thereto at the time of its release by the manufacturer. While the use of this preparation and other measures described herein are consistent with accepted standards of medical practice, their use as described cannot be expected necessarily to assure a specific result.

HOW SUPPLIED

2084-08 - 10 (0.5 ml) DISPETTES® Disposable Pipettes
2084-12 - 50 (0.5 ml) DISPETTES®

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REV. 12/82

80:12

POLIOVIRUS VACCINE, LIVE, ORAL TRIVALENT ORIMUNE®

0.5 ml Dose

Contains Sorbitol

SABIN STRAINS TYPES 1, 2 and 3

FOR ORAL ADMINISTRATION - NOT FOR INJECTION

DESCRIPTION

Manufacture and Composition: ORIMUNE® TRIVALENT VACCINE is a mixture of three types of attenuated polioviruses which have been propagated in cercopithecus monkey kidney cell culture. The cells are grown in the presence of Eagle's Basal Medium consisting of Earle's Balanced Salt Solution containing amino acids, antibiotics and calf serum. After cell growth, the medium is removed and replaced with fresh medium containing the inoculating virus but no calf serum. The final vaccine is diluted with a modified cell culture maintenance medium containing sorbitol. Each dose (0.5 ml) contains less than 25 micrograms of each of the antibiotics, streptomycin and neomycin.

The potency is expressed in terms of the amount of virus contained in the recommended dose as tissue culture infective doses ($TCID_{50}$). The human dose of vaccine containing all three virus types shall be constituted to have infectivity titers in the final container material of $10^{5.4}$ to $10^{6.4}$ for Type 1, $10^{4.5}$ to $10^{5.5}$ for Type 2 and $10^{5.2}$ to $10^{6.2}$ for Type 3.[1]

Color Change: This vaccine contains phenol red as a pH indicator. The usual color of the vaccine is pink, although some containers of vaccine, shipped or stored in dry ice, may exhibit a yellow coloration due to the very low temperature or possible absorption of carbon dioxide. The color of the vaccine prior to use (red -pink - yellow) has no effect on the virus or efficacy of the vaccine.

INDICATIONS AND USAGE

The purpose of administering any attenuated, live, virus vaccine is to stimulate the body mechanism to produce an active immunity by simulating the natural infection without producing untoward symptoms of the disease. To accomplish this with live poliovirus vaccine, it is necessary for the virus to multiply in the intestinal tract. A primary series of this vaccine is designed to produce an antibody response to poliovirus Types 1, 2 and 3. This response is comparable to the immunity induced by the natural disease. The antibodies thus formed help protect the individual against clinical poliomyelitis infection by any of the three types of poliovirus. When used in the prescribed manner for primary immunization, type specific neutralizing antibodies will be induced in 90% or more of susceptibles.

This vaccine is indicated for use in the prevention of poliomyelitis caused by poliovirus Types 1, 2 and 3.

Infants starting at six to twelve weeks of age, *all unimmunized children* and *adolescents* through age 18 are the usual candidates for routine prophylaxis.

The Immunization Practices Advisory Committee (IPAC) of the Public Health Service states that trivalent oral poliovirus vaccine (TOPV) and inactivated poliovirus vaccine (IPV) are both effective in preventing poliomyelitis. TOPV is the vaccine of choice for primary immunization of children in the United States when the benefits and risks for the entire population are considered. TOPV is preferred because it induces intestinal immunity, is simple to administer, is well accepted by patients, results in immunization of some contacts of vaccinated persons, and has a record of having essentially eliminated disease associated with wild poliovirus in this country.[2] The choice of TOPV as the preferred poliovirus vaccine in the United States has also been made by the Committee on Infectious Diseases of the American Academy of Pediatrics and a special expert committee of the Institute of Medicine, National Academy of Science.[3,4] TOPV is also recommended for control of epidemic poliomyelitis.[2,3]

Past history of clinical poliomyelitis or prior vaccination with IPV in otherwise healthy individuals does not preclude the administration of TOPV when otherwise indicated.

Serologic evidence indicates that measles and rubella vaccines or combinations (measles-mumps-rubella vaccine) given simultaneously with trivalent oral poliovirus vaccine can be expected to give adequate antibody response.[5]

Routine poliomyelitis immunization for adults residing in the continental United States is not necessary because of extreme unlikelihood of exposure. However, primary immunization with IPV is recommended whenever feasible for those unimmunized adults subject to *increased risk* of exposure, as by travel to or contact

with epidemic or endemic areas and for those employed in hospitals, medical laboratories, clinics or sanitation facilities. If less than 4 weeks are available before protection is needed, a single dose of TOPV is recommended, with IPV given later if the person remains at increased risk. Immunization with IPV may be indicated for unimmunized parents and those in other special situations where, in the judgement of the attending physician, protection may be needed.[3] (see CONTRAINDICATIONS and ADVERSE REACTIONS.)

CONTRAINDICATIONS

Under no circumstances should this vaccine be administered parenterally

Administration of the vaccine should be postponed or avoided in those experiencing any acute illness and in those with any advanced debilitated condition or persistent vomiting or diarrhea.

ORIMUNE *must not* be administered to patients with immune deficiency diseases such as combined immunodeficiency, hypogammaglobulinemia and agammaglobulinemia. It would also be prudent to withhold ORIMUNE from siblings of a child known to have an immunodeficiency syndrome. Further, ORIMUNE *must not* be administered to patients with altered immune states such as those occurring in thymic abnormalities, leukemia, lymphoma or generalized malignancy or by lowered resistance from therapy with corticosteroids, alkylating drugs, antimetabolites or radiation. All persons with altered immune status should avoid close household-type contact with recipients of the vaccine for at least 6-8 weeks. IPV is preferred for immunizing all persons in this setting.[2,3,4,6,7]

PRECAUTIONS

Other viruses (including poliovirus and other enterovirus) may interfere with the desired response to this vaccine, since their presence in the intestinal tract may interfere with the replication of the attenuated strains of poliovirus in the vaccine.

It would seem prudent not to administer TOPV shortly after Immune Serum Globulin (ISG) unless such a procedure is unavoidable, for example, with unexpected travel to or contact with epidemic areas or endemic areas. If TOPV is given with or shortly after ISG, the dose probably should be repeated after three months, if immunization is still indicated.[8] However, ISG may not interfere with immunization with TOPV.[9]

The vaccine is not effective in modifying or preventing cases of existing and/or incubating poliomyelitis.

Use in Pregnancy

Although there is no convincing evidence documenting adverse effects of either TOPV or IPV on the developing fetus or pregnant woman, it is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, TOPV is recommended.[3] (See CONTRAINDICATIONS and ADVERSE REACTIONS.)

ADVERSE REACTIONS

Paralytic disease following the ingestion of live poliovirus vaccines has been, on rare occasion, reported in individuals receiving the vaccine, (see for example CONTRAINDICATIONS) and in persons who were in close contact with vaccinees.[2,3,4,10,11,12,13] The vaccine viruses are shed in the vaccinee's stools for at least 6 to 8 weeks as well as via the pharyngeal route. Most reports of paralytic disease following ingestion of the vaccine or contact with a recent vaccinee are based on epidemiological analysis and temporal association between vaccination or contact and the onset of symptoms. Most authorities believe that a causal relationship exists.[2,10,14,15]

The risk of vaccine-associated paralysis is extremely small for vaccinees, susceptible family members and other close personal contacts.[2] However, prior to administration of the vaccine, the attending physician should warn or specifically direct personnel acting under his authority to convey the warnings to the vaccinee, parent, guardian or other responsible person of the possibility of vaccine-associated paralysis. The Centers for Disease Control report that during the years 1969 through 1980 approximately 290 million doses of TOPV were distributed in the United States. In the same 12 years, 25 "vaccine-associated" and 55 "contact vaccine-associated" paralytic cases were reported. Twelve other "vaccine-associated" cases have been reported in persons (recipients or contacts) with immune deficiency conditions.[2] These statistics do not provide a satisfactory basis for estimating these risks on a per person basis.[14]

When the attenuated vaccine strains are to be introduced into a household with adults who have not been adequately vaccinated or whose immune status cannot be determined, the risk of vaccine-associated paralysis can be minimized by giving these adults three doses of IPV a month apart before the children receive ORIMUNE.[2] The CDC reports that no paralytic reactions to IPV are known to have occurred since the 1955 cluster of poliomyelitis cases caused by vaccine that contained live polioviruses that had escaped inactivation.[2]

The Immunization Practices Advisory Committee of the U.S. Public Health Service states:

"Because of the overriding importance of ensuring prompt and complete immunization of the child and the extreme rarity of OPV-associated disease in contacts, the Committee recommends the administration of OPV to a child regardless of the poliovirus-vaccine status of adult household contacts. This is the usual practice in the United States. The responsible adult should be informed of the small risk involved. An acceptable alternative, if there is strong assurance that ultimate, full immunization of the child will not be jeopardized or unduly delayed, is to immunize adults according to the schedule outlined above before giving OPV to the child."[2]

The Immunization Practices Advisory Committee has concluded that "Oral polio vaccine remains the vaccine of choice for primary immunization of Children."[2]

ADMINISTRATION

ORIMUNE is to be administered *orally, under the supervision of a physician. Under no circumstances should this vaccine be administered parenterally.* For convenience, the vaccine is supplied in a disposable pipette containing a single dose of 0.5 ml. The vaccine can be administered directly or mixed with distilled water, tap water free of chlorine, simple syrup USP or milk. Alternatively, it may be adsorbed on any one of a number of foods such as bread, cake or cube sugar.

Community Programs

Poliovirus Vaccine, Live, Oral Trivalent has been recommended for epidemic control. Within an epidemic area, TOPV should be provided for all persons over 6 weeks of age who have not been completely immunized or whose immunization status is unknown, with the exceptions noted under immunodeficiency.[2,3]

DOSAGE

Dose. Each single dose consists of 0.5 ml of Poliovirus Vaccine, Live, Oral Trivalent ORIMUNE.

Initial Administration (Primary Series)

Infants: The primary series is three doses. The Immunization Practices Advisory Committee (Public Health Service) recommends that the three dose immunization series be started at 6 to 12 weeks of age, commonly with the first DTP inoculation. The second dose should be given not less than 6 and preferably 8 weeks later. The third dose is an integral part of the primary immunization and should be administered 8 to 12 months after the second dose.[3]

The American Academy of Pediatrics recommends that the vaccine be administered at 2 months, 4 months, and at approximately 18 months of age. An optional dose of TOPV may be given at 6 months in areas where poliomyelitis is endemic.[3]

Administration to the newborn (under 6 weeks) is not generally recommended because of the varying persistence of maternal antibodies. However, in certain tropical endemic areas, where poliomyelitis has been increasing in recent years, the physician may wish to administer TOPV to the infant at birth, and complete the basic course during the first six months of life.[3] If the physician chooses to immunize the infant at birth, it may be wise to wait until the child is three days old, and it may be prudent to recommend abstention from breast-feeding for two to three hours before and after oral vaccination to permit establishment of the vaccine viruses in the gut.[16]

Older Children and Adolescents (through age 18): Two doses, given not less than 6 and preferably 8 weeks apart and the third dose 6 to 12 months after the second dose.[3]

Adults: See INDICATIONS and ADVERSE REACTIONS. Where ORIMUNE is given to unimmunized adults, the dosage is as indicated for children and adolescents.

Booster Doses - School Entrance: On entering elementary school, all children who have completed the primary series should be given a single follow-up dose of trivalent oral poliovirus vaccine.[2,3] All others should complete the primary series.

The Public Health Service Advisory Committee does not recommend routine booster doses of vaccine on the basis of current information, beyond that given at the time of entering school.[2] Recent data indicates that over 95% of children studied five years after full immunization with oral poliovirus vaccine had protective antibodies to all three types of poliovirus.[17]

Increased risk: If an individual who has completed a primary series is subjected to a substantially increased risk by virtue of contact, travel or occupation, a single dose of TOPV has been suggested.[2]

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MSD | M-M-R® II (MEASLES, MUMPS, and RUBELLA VIRUS VACCINE LIVE, MSD)

M-M-R® II
(Measles, Mumps, and Rubella Virus Vaccine Live, MSD)

DESCRIPTION

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live, MSD) is a live virus vaccine for immunization against measles (rubeola), mumps and rubella (German measles).

M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX® (Measles Virus Vaccine Live, MSD), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and grown in cell cultures of chick embryo, (2) MUMPSVAX® (Mumps Virus Vaccine Live, MSD), the Jeryl Lynn (B level) strain of mumps virus grown in cell cultures of chick embryo, and (3) MERUVAX® II (Rubella Virus Vaccine Live, MSD), the Wistar RA 27 3 strain of live attenuated rubella virus grown in human diploid cell (WI-38) culture.[1,2] The vaccine viruses are the same as those used in the manufacture of ATTENUVAX (Measles Virus Vaccine Live, MSD), MUMPSVAX (Mumps Virus Vaccine Live, MSD) and MERUVAX II (Rubella Virus Vaccine Live, MSD). The three viruses are mixed before being lyophilized. The product contains no preservative.

The reconstituted vaccine is for subcutaneous administration. When reconstituted as directed, the dose for injection is 0.5 mL and contains not less than the equivalent of 1,000 $TCID_{50}$ (tissue culture infectious doses) of the U.S. Reference Measles Virus; 5,000 $TCID_{50}$ of the U.S. Reference Mumps Virus, and 1,000 $TCID_{50}$ of the U.S. Reference Rubella Virus. Each dose contains approximately 25 mcg of neomycin. The product contains no preservative. Sorbitol and hydrolyzed gelatin are added as stabilizers.

CLINICAL PHARMACOLOGY

Clinical studies of 279 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95 percent, mumps neutralizing antibodies in 96 percent, and rubella HI antibodies in 99 percent of susceptible persons.

The RA 27 3 rubella strain in M-M-R II elicits higher immediate post-vaccination HI, complement-fixing and neutralizing antibody levels than other strains of rubella vaccine[3-9] and has been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies.[10,11] The RA 27 3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses.[11-13] The increased levels and broader profile of antibodies produced by RA 27 3 strain rubella virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild virus,[11,13-15] and provide greater confidence for lasting immunity.

Vaccine induced antibody levels following administration of M-M-R II have been shown to persist for at least two years without substantial decline.[16] Antibody levels after immunization with M-M-R (Measles, Mumps, and Rubella Virus Vaccine Live, MSD), containing the HPV-77 strain of rubella, have persisted for 10.5 years without substantial decline.[17] If the present pattern continues, it will provide a basis for the expectation that immunity following vaccination will be permanent. However, continued surveillance will be required to demonstrate this point.

INDICATIONS AND USAGE

M-M-R II is indicated for simultaneous immunization against measles, mumps, and rubella in persons 15 months of age or older. A booster is not needed.

Infants who are less than 15 months of age may fail to respond to the measles component of the vaccine due to presence in the circulation of residual measles antibody of maternal origin, the younger the infant, the lower the likelihood of seroconversion. In geographically isolated or other relatively inaccessible populations for whom immunization programs are logistically difficult, and in population groups in which natural measles infection may occur in a significant proportion of infants before 15 months of age, it may be desirable to give the vaccine to infants at an earlier age. Infants vaccinated under these conditions at less than 12 months of age should be revaccinated after reaching 15 months of age. There is some evidence to suggest that infants immunized at less than one year of age may not develop sustained antibody levels when later reimmunized. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.[18]

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reviously unimmunized children of susceptible pregnant women should ive live attenuated rubella vaccine, because an immunized child will be likely to acquire natural rubella and introduce the virus into the house-d.

Pregnant Adolescent and Adult Females

mmunization of susceptible non-pregnant adolescent and adult females hildbearing age with live attenuated rubella virus vaccine is indicated if tain precautions are observed (see below and PRECAUTIONS). Vaccinat susceptible postpubertal females confers individual protection against sequently acquiring rubella infection during pregnancy, which in turn vents infection of the fetus and consequent congenital rubella injury.[19] Women of childbearing age should be advised not to become pregnant for te months after vaccination and should be informed of the reasons for precaution.*

is recommended that rubella susceptibility be determined by serologic ting prior to immunization.** If immune, as evidenced by a specific ella antibody titer of 1:8 or greater (hemagglutination-inhibition test), cination is unnecessary. Congenital malformations do occur in up to ren percent of all live births.[20] Their chance appearance after vaccination uld lead to misinterpretation of the cause, particularly if the prior rubella-mune status of vaccinees is unknown.

Postpubertal females should be informed of the frequent occurrence of -limited arthralgia and possible arthritis beginning 2 to 4 weeks after cination (see ADVERSE REACTIONS).

ostpartum Women

t has been found convenient in many instances to vaccinate rubella-sceptible women in the immediate postpartum period. (See *Nursing others.*)

Revaccination: Children vaccinated when younger than 12 months of age ould be revaccinated. Based on available evidence, there is no reason to utinely revaccinate persons who were vaccinated originally when 12 onths of age or older. However, persons should be revaccinated if there is idence to suggest that initial immunization was ineffective.

ion with other Vaccines

Routine administration of DTP (diphtheria, tetanus, pertussis) and or OPV ral poliovirus vaccine) concomitantly with measles, mumps and rubella ccines is not recommended because there are insufficient data relating to e simultaneous administration of these antigens. However, the American cademy of Pediatrics has noted that in some circumstances, particularly hen the patient may not return, some practitioners prefer to administer all ese antigens on a single day. If done, separate sites and syringes should be sed for DTP and M-M-R □.[21]

M-M-R □ should not be given less than one month before or after administration of other virus vaccines.

CONTRAINDICATIONS

Do not give M-M-R □ to pregnant females; the possible effects of the acc ne on fetal development are unknown at this time. If vaccination of ostpubertal females is undertaken, pregnancy should be avoided for three onths following vaccination. (See PRECAUTIONS, *Pregnancy*.)

Anaphylactoid reaction to neomycin (each dose of reconstituted vaccine ontains approximately 25 mcg of neomycin).

History of anaphylactoid reaction to eggs (see HYPERSENSITIVITY TO GGS below).

Any febrile respiratory illness or other active febrile infection.

Active untreated tuberculosis.

Patients receiving immunosuppressive therapy. This contraindication oes not apply to patients who are receiving corticosteroids as replacement herapy, e.g., for Addison's disease.

Individuals with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic sys-ems.

Primary immunodeficiency states, including cellular immune deficien-ies, hypogammaglobulinemic and dysgammaglobulinemic states.

Individuals with a family history of congenital or hereditary immunodefi-iency, until the immune competence of the potential vaccine recipient is demonstrated.[22]

*NOTE: The Immunization Practices Advisory Committee (ACIP) has rec-ommended "In view of the importance of protecting this age group against rubella, reasonable precautions in a rubella immu-nization program include asking females if they are pregnant, excluding those who say they are, and explaining the theoretical risks to the others."[19]

**NOTE: The Immunization Practices Advisory Committee (ACIP) has stated "When practical, and when reliable laboratory services are available, potential vaccinees of childbearing age can have serologic tests to determine susceptibility to rubella. . . . However, routinely performing serologic tests for all females of childbear-ing age to determine susceptibility so that vaccine is given only to proven susceptibles is expensive and has been ineffective in some areas. Accordingly, the ACIP believes that rubella vaccina-tion of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing."[19]

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M-M-R® □
(Measles, Mumps, and Rubella Virus Vaccine Live, MSD)

HYPERSENSITIVITY TO EGGS

Live measles vaccine and live mumps vaccine are produced in chick embryo cell culture. Persons with a history of anaphylactic or other immedi-ate reactions (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion should not be vaccinated. Evidence indicates that persons are not at increased risk if they have egg allergies that are not anaphylactic in nature. Such persons may be vaccinated in the usual manner. There is no evidence to indicate that persons with allergies to chickens or feathers are at increased risk of reac-tion to the vaccine.[19]

PRECAUTIONS

General

Adequate treatment provisions including epinephrine, should be avail-able for immediate use should an anaphylactoid reaction occur.

Due caution should be employed in administration of M-M-R □ to persons with a history of febrile convulsions, cerebral injury or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur following vaccination. (See ADVERSE REACTIONS.)

Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin.

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7-28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact, while accepted as a theoretical possibility, is not regarded as a significant risk.[19] However, transmission of the rubella vaccine virus to infants via breast milk has been documented (see *Nursing Mothers*).

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

It has been reported that live attenuated measles, mumps and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either before or simultaneously with M-M-R □.

As for any vaccine, vaccination with M-M-R □ may not result in seroconversion in 100% of susceptible persons given the vaccine.

Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with M-M-R □. It is also not known whether M-M-R □ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for three months following vaccination (see CONTRAINDICATIONS).

In counseling women who are inadvertently vaccinated when pregnant or who become pregnant within 3 months of vaccination, the physician should be aware of the following: (1) In a 10 year survey involving over 700 pregnant women who received rubella vaccine within 3 months before or after con-ception (of whom 189 received the Wistar RA 27/3 strain), none of the newborns had abnormalities compatible with congenital rubella syn-drome;[23] (2) Although mumps virus is capable of infecting the placenta and fetus, there is no good evidence that it causes congenital malformations in humans. Mumps vaccine virus also has been shown to infect the placenta, but the virus has not been isolated from the fetal tissues from susceptible women who were vaccinated and underwent elective abortions;[24] and (3) Reports have indicated that contracting of natural measles during preg-nancy enhances fetal risk. Increased rates of spontaneous abortion, still-birth, congenital defects and prematurity have been observed subsequent to natural measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects.

Nursing Mothers

It is not known whether measles or mumps vaccine virus is secreted in human milk. Recent studies have shown that lactating postpartum women immunized with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants.[25] In the infants with serological evidence of rubella infection, none exhibited severe disease; however, one exhibited mild clinical illness typical of acquired rubella.[26,27] Caution should be exercised when M-M-R □ is administered to a nursing woman.

ADVERSE REACTIONS

Because of the slightly acidic pH (6.2-6.6) of the vaccine, patients may complain of burning and or stinging of short duration at the injection site.

The adverse clinical reactions associated with the use of M-M-R II are those expected to follow administration of the monovalent vaccines given separately. These may include malaise, sore throat, headache, fever and rash; mild local reactions such as erythema, induration, tenderness and regional lymphadenopathy, parotitis, orchitis; nerve deafness; thrombocy-topenia and purpura; allergic reactions such as wheal and flare at the injection site or urticaria; and arthritis, arthralgia and polyneuritis.

syringe to be used for reconstitution. Inject all the ...luent in the syrir into the vial of lyophilized vaccine, and agitate to mix thoroughly. Wi draw the entire contents into a syringe and inject the total volume of restored vaccine subcutaneously.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

10 Dose Vial (available only to government agencies/institutions)

Withdraw the entire contents (7 mL) of the diluent vial into the sterile syringe to be used for reconstitution, and introduce into the 10 dose vial of lyophilized vaccine. Agitate to ensure thorough mixing. The outer labeling suggests "For Jet Injector or Syringe Use". Use with separate sterile syringes is permitted for containers of 10 doses or less. The vaccine and diluent do not contain preservatives; therefore, the user must recognize the potential contamination hazards and exercise special precautions to protect the sterility and potency of the product. The use of aseptic techniques and proper storage prior to and after restoration of the vaccine and subsequent withdrawal of the individual doses is essential. Use 0.5 mL of the reconstituted vaccine for subcutaneous injection.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

Each dose contains not less than the equivalent of 1,000 $TCID_{50}$ of the U.S. Reference Measles Virus, 5,000 $TCID_{50}$ of the U.S. Reference Mumps Virus and 1,000 $TCID_{50}$ of the U.S. Reference Rubella Virus.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. M-M-R II, when reconstituted, is clear yellow.

HOW SUPPLIED

No. 4749 — M-M-R II is supplied as a single-dose vial of lyophilized vaccine, NDC 0006-4749-00, and a vial of diluent.

No. 4681/4309 — M-M-R II is supplied as follows: (1) a box of 10 single-dose vials of lyophilized vaccine (package A), NDC 0006-4681-00; and (2) a box of 10 vials of diluent (package B). To conserve refrigerator space, the diluent may be stored separately at room temperature.

Available only to government agencies/institutions:

No. 4682X — M-M-R II is supplied as one 10 dose vial of lyophilized vaccine.

NDC 0006-4682-00, and one 7 mL vial of diluent.

Storage

It is recommended that the vaccine be used as soon as possible after reconstitution. Protect vaccine from light at all times, since such exposure may inactivate the virus. Store reconstituted vaccine in the vaccine vial in a dark place at 2 - 8°C (35.6 - 46.4°F) and discard if not used within 8 hours.

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REPORT OF ADVERSE EVENT FOLLOWING IMMUNIZATION
DEPARTMENT OF HEALTH & HUMAN SERVICES, PUBLIC HEALTH SERVICE, Centers for Disease Control, Atlanta, Georgia 30333

PATIENT ID

Immunization Project Area _____ | State Code ☐☐ | Seq. No. ☐☐☐☐ | County Where Administered: _____ County Code ☐☐☐ | MSAEFI REPORT NO. FOR CDC USE ONLY

Date of Birth ☐☐ Mo. ☐☐ Day ☐☐ Yr. | Sex M ☐ F ☐ | Date of Initial Report ☐☐ Mo. ☐☐ Day ☐☐ Yr. | Source of Information MD/DO ☐ Nurse ☐ Family ☐ Other ☐ _____

VACCINE HISTORY

Date of Immunization ☐☐ Mo. ☐☐ Day ☐☐ Yr.

Vaccine Administered By: Pub. ☐ Pvt. ☐ Mil. ☐ Other ☐

Vaccine Purchased By: Pub. ☐ Pvt. ☐ Mil. ☐ Other ☐

Enter Below All Vaccines Given on the Date of Immunization:

	Vaccine Type	Mfgr.	Lot Number	Route	Site	No. Prior Doses
A						
B						
C						
D						

CLINICAL DESCRIPTION OF PRESENT ILLNESS

SIGNS AND SYMPTOMS OF PRESENT ILLNESS

Onset of 1st Sign or Symptom: ☐☐ Mo. ☐☐ Day ☐☐ Yr.

	Yes	No	Unk
1. Fever: Temp ≥(100°F (37.8°C) (7806)	☐	☐	☐
Felt Hot, But Temperature Not Measured: (7800)	☐		
Highest Measured Temperature ☐☐☐.☐ F/C			
2. Local Reaction: Site _____			
Pain, Swelling, Increased Warmth, Induration or Lump Without Abscess (9993)	☐	☐	☐
Abscess Formation — Required Drainage or Drained Spontaneously (6829)+(9993)	☐	☐	☐
Results of Culture _____			
3. Rash: Other Than at Injection Site (7821)	☐	☐	☐
4. Adenopathy:			
Local (Injection Site Area) (7856)	☐	☐	☐
Generalized (7856)	☐	☐	☐
5. Allergic Event: (9995)	☐	☐	☐
Hives (7080)	☐	☐	☐
Angioneurotic Edema (9951)	☐	☐	☐
Wheezing/Asthma (4939)	☐	☐	☐
Anaphylaxis (9994)	☐	☐	☐
If "Yes," Interval from Vaccination to Onset: < 30 min ☐ 30 min-6 hrs ☐ > 6 hrs ☐			
Was Blood Pressure Measured?	☐	☐	☐
If "Yes," Lowest B.P. ☐☐☐/☐☐☐			
6. Arthralgia/Arthritis:			
Pain in Joints (7194)	☐	☐	☐
Inflammation of Joints (Redness, Swelling, Tenderness) (7109)	☐	☐	☐
7. Convulsions: (7803)	☐	☐	☐
If "Yes," How many Episodes Following Immunization ☐☐			
8. Encephalitis and/or Encephalopathy: (3483)	☐	☐	☐
Abnormal Lumbar Puncture (Enter Results in Laboratory subsection) (7920)	☐	☐	☐
Signs of Increased Intracranial Pressure (3481)	☐	☐	☐
Focal Neurologic Signs (3409)	☐	☐	☐
Coma or Marked Alteration in Level of Consciousness (7800)	☐	☐	☐

	Yes	No	Unk
9. Guillain–Barré Syndrome: (3570)	☐	☐	☐
10. Reye's Syndrome: (3318)	☐	☐	☐
11. Polio: (0469)	☐	☐	☐
12. Paralysis other than GBS, Reye's Syndrome or Polio (3449)	☐	☐	☐
13. Other Neurologic Symptoms and Diagnoses:			
Aseptic Meningitis (3479)	☐	☐	☐
Infantile Spasms (Hypsarrhythmia, drop seizures) (3456)	☐	☐	☐
Bell's Palsy (3510)	☐	☐	☐
Hearing Loss (3899)	☐	☐	☐
Neuritis, Neuralgia (7292	☐	☐	☐
Paresthesias (7820)	☐	☐	☐
Screaming Episode (High-Pitched Abnormal Cry or Screaming Lasting ≥ 3 Hours) (7998)	☐	☐	☐
Neurologic Symptoms not cited above (specify) _____	☐	☐	☐
14. Miscellaneous:			
Hypotonic, Hyporesponsive Episode (7859)	☐	☐	☐
Idiopathic Thrombocytopenic Purpura	☐	☐	☐
If "Yes," Lowest Platelet count (2873) ☐☐☐☐☐			
Pancreatitis (5770)	☐	☐	☐
Parotitis (5272)	☐	☐	☐
15. Death:			
Sudden Infant Death Syndrome (SIDS) (7980)	☐	☐	☐
Non-SIDS Death (7981)	☐	☐	☐
If "Yes," Cause(s): _____			

LABORATORY:

	Performed Yes	No	Unk	Results Normal	Abnormal
EEG	☐	☐	☐	☐	☐ (7940)
BRAIN SCAN	☐	☐	☐	☐	☐ (7940)
LUMBAR PUNCTURE	☐	☐	☐	☐	☐ (7920)

Results if Abnormal:
WBC's _____ Opening Pressure _____
Lymphs (%) _____ Culture Results _____
Glucose _____ Other _____
Total Protein _____

Other Pertinent Information: _____

Signature of MSAEFI Coordinator: _____

Seen by Health Care Provider: ☐ Yes ☐ No ☐ Unk ☐ Number of Visits | Hospitalized ☐ Yes ☐ No ☐ Unk ☐☐ Number of Days

PAST HISTORY

Previous Illness Following Immunization: Yes ☐ No ☐ If "Yes," Date: ☐☐ Mo. ☐☐ Day ☐☐ Yr.
Vaccine _____
Describe Illness _____

Previous Convulsions in Patient: Yes ☐ No ☐ Unk ☐
If "Yes," ☐ With Fever ☐ Without Fever

History of Convulsions in Siblings or Parents: Yes ☐ No ☐ Unk ☐
If "Yes," ☐ With Fever ☐ Without Fever

FOLLOWUP

SEVEN DAY FOLLOWUP: If recovered, send to State Office — ☐☐ Mo. ☐☐ Day ☐☐ Yr.

30 DAY FOLLOWUP: If not recovered at 7 days, carry out 30 Day Followup and send to State Office — ☐☐ Mo. ☐☐ Day ☐☐ Yr.

	Duration of Illness	Recovered	Partially Recovered*	Not Recovered*	Not Located	Dead
SEVEN DAY FOLLOWUP	Days ☐☐	☐	☐	☐	☐	☐
30 DAY FOLLOWUP	Days ☐☐	☐	☐	☐	☐	☐

*Comments _____

Reviewed By Immunization Project Physician (Items 7 - 15 and Anaphylaxis): ☐ Yes ☐ No ☐ Unk
Signature of Reviewing M.D. _____

CDC USE

Results of One-Year Followup: Recovered ☐ Partially Recovered* ☐ Not Recovered* ☐ Dead ☐ Not Located ☐ *Comments _____

This rep[illegible] law (42 USC 247b; 42 CFR 51 b). Its submission is needed to monitor possible reactions to vaccination and [illegible] volume[illegible] ed as a condition of immunization grant awards.

CDC 71.19

LECTURE 8

IMMUNIZATIONS

A Dissenting View

Richard Moskowitz, M.D.

INTRODUCTION OF THE SPEAKER

Lori Andrews: Thank you. Next, we'll be hearing from Dr. Richard Moskowitz, who will talk to us about immunizations. Dr. Moskowitz graduated Phi Beta Kappa from Harvard University and received his medical degree at New York University, but he has not taken a narrow-minded approach to his professional interest. From 1963 to 1965 he was a graduate fellow in the department of philosophy at the University of Colorado graduate school. He studied homeopathy in Athens, Greece, as well as at the National Center for Homeopathy in Washington, D.C., where he currently serves as the director of publications and is a member of the permanent teaching faculty. He has also practiced in a variety of settings. He was the founder and medical director of the Boulder Free Clinic and a volunteer physician on the Medical Committee for Human Rights in New York. He's now in the private practice of classical homeopathy and has published extensively in journals such as *Homeopathy Today*, *Homeotherapy*, and *The Journal of the American Institute of Homeopathy*. Thank you, Dr. Moskowitz.

LECTURE

Dr. Moskowitz: For the past 10 years or so, I have felt a deep and growing compunction against giving routine immunizations to children. It began with the fundamental belief that people have the right to make that choice for themselves. Soon I discovered that I could no longer bring myself to give the injections even when the parents wished me to.

At bottom, I have always felt that the attempt to eradicate entire microbial species from the biosphere must inevitably upset the balance of nature in fundamental ways that we can as yet scarcely imagine. Such concerns loom ever larger as new vaccines continue to be developed, seemingly for no better reason than that we have the technical capacity to make them and thereby to demonstrate our power, as a civilization, to manipulate the evolutionary process itself.

Purely from the viewpoint of our own species, even if we could be sure that the vaccines were harmless, the fact remains that they are compulsory, that all children are required to undergo them without any sensitive regard for basic differences in individual susceptibility, to say nothing of the wishes of the parents or the children themselves.

Most people can readily accept the fact that, from time to time, certain laws that some of us strongly disagree with may be necessary for the public good. But the issue in this case involves nothing less than the introduction of foreign proteins or even live viruses into the bloodstream of entire populations. For that reason alone, the public is surely entitled to convincing proof, beyond any reasonable doubt, that artificial immunization is in fact a safe and effective procedure, in no way injurious to health, and that the threat of the corresponding natural diseases remains sufficiently clear and urgent to warrant mass inoculation of everyone, even against their will if necessary.

Unfortunately, such proof has never been given; and, even if it could be, continuing to employ vaccines against diseases that are no longer prevalent or no longer dangerous hardly qualifies as an emergency.

Finally, even if such an emergency did exist, and artificial immunization could be shown to be an appropriate response to it, the decision would remain essentially a *political* one, involving issues of public health and safety that are far too important to be settled by any purely scientific or technical criteria, or indeed by *any* criteria less authoritative than the clearly articulated sense of the community about to be subjected to it.

For all of these reasons, I want to present the case against routine

immunization as clearly and forcefully as I can. What I have to say is not quite a formal theory capable of rigorous proof or disproof. It is simply an attempt to explain my own experience, a nexus of interrelated facts, observations, reflections and hypotheses which, taken together, are more or less coherent and plausible and make intuitive sense to me.

I offer them to the public in part because the growing refusal of parents to vaccinate their children is so seldom articulated or taken seriously. The fact is that we have been taught to accept vaccination as a sort of involuntary communion, a sacrament of our own participation in the unrestricted growth of scientific and industrial technology, utterly heedless of the long-term consequences to the health of our own species, let alone to the balance of nature as a whole. For that reason alone, the other side of the case urgently needs to be heard.

1. Are the Vaccines Effective?

There is widespread agreement that the time period since the common vaccines were introduced has seen a remarkable decline in the incidence and severity of the corresponding natural infections. But the customary assumption that the decline is *attributable* to the vaccines remains unproven, and continues to be seriously questioned by eminent authorities in the field. The incidence and severity of whooping cough, for example, had already begun to decline precipitously long before the pertussis vaccine was introduced,[1] a fact which led the epidemiologist C. C. Dauer to remark, as far back as 1943:

> If mortality (from pertussis) continues to decline at the same rate during the next 15 years, it will be extremely difficult to show statistically that (pertussis immunization) had any effect in reducing mortality from whooping cough.[2]

Much the same is true not only of diphtheria and tetanus, but also of TB, cholera, typhoid, and other common scourges of a bygone era, which began to disappear toward the end of the nineteenth century, perhaps partly in response to improvements in public health and sanitation, but in any case long before antibiotics, vaccines, or any specific medical measures designed to eradicate them.[3]

Reflections such as these led the great microbiologist René Dubos to observe that microbial diseases have their own natural history, indepen-

dent of drugs and vaccines, in which asymptomatic infection and symbiosis are far more common than overt disease:

> It is barely recognized, but nevertheless true, that animals and plants, as well as men, can live peacefully with their most notorious microbial enemies. The world is obsessed by the fact that poliomyelitis can kill and maim several thousand unfortunate victims every year. But more extraordinary is the fact that millions upon millions of young people become infected by polio viruses, yet suffer no harm from the infection. The dramatic episodes of conflict between men and microbes are what strike the mind. What is less readily apprehended is the more common fact that infection can occur without producing disease.[4]

The principal evidence that the vaccines are effective actually dates from the more recent period, during which time the dreaded polio epidemics of the 1940s and 1950s have never reappeared in the developed countries, and measles, mumps, and rubella, which even a generation ago were among the commonest diseases of childhood, have become far less prevalent, at least in their classic acute forms, since the triple MMR vaccine was introduced into common use.

Yet how the vaccines actually accomplish these changes is not nearly as well understood as most people like to think it is. The disturbing possibility that they act in some other way than by producing a genuine immunity is suggested by the fact that the diseases in question have continued to break out even in highly immunized populations, and that in such cases the observed differences in incidence and severity between immunized and unimmunized persons have tended to be far less dramatic than expected, and in some cases not measurably significant at all.

In a recent British outbreak of whooping cough, for example, even fully immunized children contracted the disease in fairly large numbers, and the rates of serious complications and death were reduced only slightly.[5] In another recent outbreak of pertussis, 46 of the 85 fully immunized children studied eventually contracted the disease.[6]

In 1977, 344 new cases of measles were reported on the campus of UCLA in a population that was supposedly 91 percent immune, according to careful serological testing.[7] Another 20 cases of measles were reported in the Pecos, New Mexico, area within a period of a few months in 1981, and 75 percent of them had been fully immunized, some

of them quite recently.[8] A survey of sixth-graders in a well-immunized urban community revealed that about 15 percent of this age group are still susceptible to rubella, a figure essentially identical with that of the prevaccine era.[9]

Finally, although the overall incidence of typical acute measles in the U.S. has dropped sharply from about 400,000 cases annually in the early 1960s to about 30,000 cases by 1974–76, the death rate remained exactly the same;[10] and, with the peak incidence now occurring in adolescents and young adults, the risk of pneumonia and demonstrable liver abnormalities has actually increased substantially, according to one recent study, to well over 3 percent and 20 percent, respectively.[11]

The simplest way to explain these discrepancies would be to postulate that the vaccines confer only partial or temporary immunity, which sounds reasonable enough given the fact that they are either live viruses rendered less virulent by serial passage in tissue culture, or bacteria or bacterial proteins that have been killed or denatured by heat, such that they can still elicit an antibody response but no longer initiate the full-blown disease.

Because the vaccine is a "trick," in the sense that it simulates the true or natural immune response developed in the course of recovering from the actual disease, it is certainly realistic to expect that such artificial immunity will in fact "wear off" quite easily, and even require additional "booster" doses at regular intervals throughout life to maintain peak effectiveness.

Such an explanation would be disturbing enough for most people. Indeed, the basic fallacy inherent in it is painfully evident in the fact that there is no way to know how long this partial or temporary immunity will last in any given individual, or how often it will need to be restimulated, because the answers to these questions clearly depend on precisely the same individual variables that would have determined whether or how severely the same person, unvaccinated, would have contracted the disease in the first place.

In any case, a number of other observations suggests equally strongly that this simple explanation cannot be the correct one. In the first place, a number of investigators have shown that when a person vaccinated against the measles, for example, again becomes susceptible to it, even repeated booster doses will have little or no effect.[12]

In the second place, the vaccines do not act merely by producing pale or mild copies of the original disease; all of them also commonly produce

a variety of symptoms of their own. Moreoever, in some cases, these illnesses may be considerably more serious than the original disease, involving deeper structures, more vital organs, and less of a tendency to resolve spontaneously. Even more worrisome is the fact that they are almost always more difficult to recognize.

Thus, in a recent outbreak of mumps in supposedly immune schoolchildren, several developed atypical symptoms, such as anorexia, vomiting, and erythematous rashes, without any parotid involvement, and the diagnosis required extensive serological testing to rule out other concurrent disease.[13] The syndrome of "atypical measles" can be equally difficult to diagnose, even when it is thought of,[14] which suggests that is is often overlooked entirely. In some cases, atypical measles can be much more severe than the regular kind, with pneumonia, petechiae, edema, and severe pain,[15] and likewise can often go unsuspected.

In any case, it seems virtually certain that other vaccine-related syndromes will be described and identified, if only we take the trouble to look for them, and that the ones we are aware of so far represent only a very small part of the problem. But even these few make it less and less plausible to assume that the vaccines produce a normal, healthy immunity that lasts for some time but then *wears off*, leaving the patient miraculously unharmed and unaffected by the experience.

2. *Some Personal Experiences with Vaccine-Related Illness*

I would like now to present a few of my own vaccine cases, both to give a sense of their variety and chronicity, and to show how difficult it can be to trace them, and also to begin to address the crucial question that is too seldom even asked, namely, how the vaccines actually *work*, i.e., what effects they do in fact produce in the human body.

My first case was that of an eight-month-old girl with recurrent fevers of unknown origin. I first saw her in January of 1977, a few weeks after her third such episode. These were brief, lasting 48 hours at most, but very intense, with the fever typically reaching 105°F. During the second episode, she was hospitalized for diagnostic evaluation, but her pediatrician found nothing out of the ordinary. Apart from these episodes, the child felt quite well, and appeared to be growing and developing normally.

I could get no further information from the mother, except for the fact that the episodes had occurred almost exactly one month apart; and, upon

consulting her calendar, we learned that the first episode had come exactly one month after the last of her DPT injections, which had also been given at monthly intervals. At this point, the mother remembered that the child had had similar febrile episodes immediately after each injection, but that she had been instructed to ignore them, inasmuch as they are "common reactions" to the vaccine. I therefore gave the child a single *oral* dose of dilute homeopathic DPT vaccine; and I am happy to report that the child has remained well since, with no further episodes of any kind.

This case illustrates how homeopathic remedies prepared from vaccines can be used for *diagnosis* as well as treatment of vaccine-related illnesses, which, no matter how strongly they are suspected, might otherwise be almost impossible to substantiate.

Secondly, because fever is the commonest known complication of the pertussis vaccine, and inasmuch as the child seemed quite well between the attacks, her response to the vaccine appeared to be a relatively strong and healthy one, disturbing because of its recurrence and periodicity, but in any case relatively simple to cure, as indeed it proved to be. But one cannot help wondering what happens to the vaccine in those tens of millions of children who show no obvious reponse to it at all.

Since that time, I have seen numerous cases of children with recurrent fevers of unknown origin, associated with a variety of other chronic complaints, chiefly irritability, temper tantrums, and increased susceptibility to colds, tonsillitis, and ear infections, which were similarly traceable to the pertussis vaccine, and which responded successfully to treatment with the homeopathic DPT nosode. Indeed, I would have to say, on the basis of that experience, that the DPT vaccine is probably one of the major causes of recurrent fevers of unknown origin in small children today.

My second case was that of a 9½-month-old girl, who presented acutely with a fever of 105° F., and very few other symptoms. Like the first, this child had had two similar episodes previously, but at irregular intervals; and the parents, who felt ambivalent about vaccinations in general, had given her only one dose of the DPT vaccine so far, although the first episode occurred a few weeks afterwards.

I first saw the child in June of 1978. The fever remained high and unremitting for 48 hours, despite the usual acute remedies and supportive measures. A CBC revealed a white count of 32,100 per mm.3, with 43 percent lymphocytes, 11 percent monocytes, 25 percent neutrophilis

(many with toxic granulations), and 1 percent metamyelocytes and other immature forms. When I asked a pediatrician about these findings, "pertussis" was his immediate reply. After a single oral dose of homeopathic DPT vaccine, the fever came down abruptly within a few hours, and the child has remained well since.

This case was disturbing mainly because of the hematological abnormalities, which were in the leukemoid range, together with the absence of any cough or distinctive respiratory symptoms, which suggested that introducing the vaccine directly into the blood may actually promote deeper or more systematic pathology than allowing the pertussis organism to set up typical symptoms of local inflammation at the normal portal of entry.

The third case was a five-year-old boy with chronic lymphocytic leukemia, whom I happened to see in August of 1978, while visiting an old friend and teacher, a family physician with over 40 years' experience. Well out of earshot of either the boy or his parents, he told me that the leukemia had first appeared following a DPT vaccination, and that, although he had treated the child successfully with natural remedies on two previous occasions, with shrinking of the liver and spleen to approximately normal size, and dramatic improvement in the blood picture, full relapse had occurred soon after each successive DPT booster.

The idea that vaccinations might also be implicated in some cases of childhood leukemia was shocking enough in itself, but it also completed the line of reasoning opened up by the previous case. For leukemia is a cancerous process of the blood and the blood-forming organs, the liver, the spleen, the lymph nodes, and the bone marrow, which are also the basic anatomical units of the immune system. Insofar as the vaccines are capable of producing serious complications at all, the blood and the immune organs would certainly be the logical place to begin looking for them.

But perhaps even more shocking to me is the fact that the boy's own physician dared not communicate his suspicion of vaccine-related illness to the parents, let alone to the general public. It was this case that convinced me, once and for all, of the need for serious, public discussion of our collected experiences with vaccine-related illness, precisely because rigorous experimental proof will require years of investigation and a firm public commitment that has not even been made yet.

I will now present two cases from my limited experience with MMR vaccine.

> In December of 1980 I saw a three-year-old boy with a four-week history of loss of appetite, stomachaches, indigestion, and swollen glands. The stomach pains were quite severe, and often accompanied by belching, flatulence, and explosive diarrhea. The nose was also congested, and the lower eyelids were quite red. The mother also reported some unusual behavior changes, such as extreme untidiness, "wild" and "noisy" playing, and waking at 2 A.M. to get into bed with the parents.
>
> The physical examination was unremarkable except for some large, tender left posterior auricular and suboccipital nodes, and marked enlargement of the tonsils. I then learned that the child had received the MMR vaccine in October, about two weeks before the onset of symptoms, with no apparent reaction to it at the time. I gave the child a single dose of the homeopathic rubella vaccine, and the symptoms promptly disappeared within 48 hours.
>
> In April 1981, the parents brought him back for a slight fever, and another three-week history of intermittent pain in and behind the right ear, stuffy nose, etc. On examination, the whole right side of the face appeared to be swollen, especially the cheek and the angle of the jaw. The right eye was red and infected. He responded well to acute homeopathic remedies and has remained well since.

This boy was typical of my rubella vaccine cases. At an interval of a few weeks after the MMR vaccine, which is about the same as the normal incubation period of rubella, a rather nondescript illness develops, which becomes subacute and rather more severe than rubella in the same age group, with, e.g., abdominal or joint pains and marked adenopathy, but no rash. Usually the diagnosis is suspected because of the characteristic posterior auricular and suboccipital nodes, and confirmed by a favorable response to the homeopathic rubella nosode.

As I read over this case, I am struck by the possibility that his second illness, and especially the parotid enlargement, may have represented continuing activity of the mumps component of the vaccine, inasmuch as I did not have the triple MMR nosode, but only those derived from the individual components. We must therefore also consider the probability that a variety of "mixed" or composite syndromes may occur, representing the patient's responses to two or all three of the vaccine components, either simultaneously or over time.

In April of 1981 I first saw a four-year-old boy for bilateral chronic enlargement of the posterior auricular nodes, which were also occasionally tender. The mother had noticed the swelling for about one year, during which time he had become more susceptible to various upper respiratory infections, none of them especially severe. The mother had also noticed recurrent parotid swelling at irregular intervals over the same time period, which began shortly after the MMR vaccine was given at the age of three.

At the time of the first visit, the child was not ill, and because the mother was about two months pregnant at the time, I elected to observe the child and do nothing if possible until the pregnancy was over. He did develop a mild laryngitis in the last trimester, which responded well to bed rest and simple homeopathic remedies.

In April of 1982, he came down with acute bronchitis. I noticed that the posterior auricular nodes were once again swollen and tender and decided to give him the homeopathic rubella nosode at that point. The cough promptly subsided, and the nodes regressed in size and were no longer tender. Two weeks later, however, he returned with a noticeably hard, tender swelling on the outside of the right cheek, near the angle of the jaw, and some pain on chewing or opening the mouth. A single dose of the homeopathic mumps nosode was given, and the child has been well since.

In this case also, we see the subacute pattern of the disease, with a strong tendency to chronicity and increased susceptibility to weaker, low-grade responses, in contrast to the vigorous, acute responses typically associated with diseases like the measles and the mumps when acquired naturally.

3. *How Do the Vaccines Work?*

It is dangerously misleading, and, indeed, the exact opposite of the truth to claim that a vaccine makes us "immune" or *protects* us against an acute disease, if in fact it only drives the disease deeper into the interior and causes us to harbor it *chronically*, with the result that our responses to it become progressively weaker, and show less and less tendency to heal or resolve themselves spontaneously.

What I propose, then, is simply to investigate as thoroughly and objectively as we can how the vaccines actually *work* inside the human body, and to begin by paying attention to the implications of what we already know. In particular, I would like to consider in detail the process

of falling ill with and recovering from a typical acute disease, such as the measles, in contrast with what we can observe following the administration of the measles vaccine.

We all know that measles is primarily a virus of the respiratory tract, both because it is inhaled by susceptible persons upon contact with infected droplets in the air, and because these droplets are produced by the coughing and sneezing of a person with the disease.

Once inhaled by a susceptible person, the measles virus then undergoes a long period of silent multiplication, first in the tonsils, adenoids, and accessory lymphoid tissues of the nasopharynx; later in the regional lymph nodes of the head and neck; and, eventually, several days later, it passes into the blood and enters the spleen, the liver, the thymus, and the bone marrow, the visceral organs of the immune system.[16] Throughout this incubation period, which lasts from 10 to 14 days, the patient usually feels quite well and experiences few or no symptoms.[17]

By the time that the first symptoms of measles appear, circulating antibodies are already detectable in the blood, and the height of the symptomatology coincides with the peak of the antibody response.[18] In other words, the "illness" is simply the definitive effort of the immune system to clear the virus from the blood. Equally noteworthy is the fact that the virus is eliminated by sneezing and coughing, i.e., via the same route through which it entered in the first place.

It is evident that the process of *mounting* an acute illness like the measles, no less than recovering from it, involves a general mobilization of the entire immune system, including inflammation of the previously sensitized tissues at the portal of entry, activation of leukocytes and macrophages, liberation of the serum complement system, and a host of other mechanisms, of which the production of circulating antibody is only one, and by no means the most important.

Such a splendid outpouring leaves little doubt that such illnesses are in fact the decisive experiences in the normal physiological maturation of the immune system as a whole in the life of a healthy child. For not only will the child who recovers from the measles never again be susceptible to it;[19] such an experience also cannot fail to prepare the individual to respond even more promptly and effectively to any infections he may acquire in the future. The ability to mount a vigorous acute response to organisms of this type must therefore be reckoned among the most fundamental requirements of general health and well-being.

In contrast, when an artificially attenuated virus such as measles is

injected directly into the blood, bypassing the normal portal of entry, at most a brief inflammatory reaction may be noted at the injection site, or in the regional lymph nodes, but there is no "incubation period" of local contact at the normal portal of entry, and consequently very little possibility of eliminating the virus via the same route.

Even more important is the fact that the virus has been artificially "attenuated," so that it will no longer initiate a generalized inflammatory response, or indeed any of the nonspecific defense mechanisms that help us to respond to infection generally. By "tricking" the body in this fashion, we have accomplished what the entire immune system seems to have evolved in order to prevent: We have placed the virus directly into the blood, and given it free and immediate access to the major immune organs, without any obvious way of getting rid of it.

The result is, indeed, the production of circulating antibodies against the virus; but the antibody response now occurs as an isolated technical feat, without any generalized inflammatory response, or any noticeable improvement in the general health of the organism. Exactly the opposite, in fact: The price that we have to pay for those antibodies is the persistence of virus elements in the blood for prolonged periods of time, perhaps permanently, which in turn presupposes a systematic weakening of our ability to mount an effective response not only to measles, but also to other acute infections as well.

Far from producing a genuine immunity, then, the vaccines may act by actually interfering with or *suppressing* the immune response as a whole, in much the same way that radiation, chemotherapy, and corticosteroids and other anti-inflammatory drugs do. Artificial immunization focuses on *antibody production*, a single aspect of the immune process, and disarticulates it and allows it to stand for the whole, in much the same way as chemical suppression of an elevated blood pressure is accepted as a valid substitute for a genuine *cure* of the patient whose blood pressure has risen. Worst of all, by making it difficult or impossible to mount a vigorous, acute response to infection, artificial immunization substitutes for it a much weaker, *chronic* response with little or no tendency to heal itself spontaneously.

Moreover, adequate models already exist for predicting and explaining what sorts of chronic disease are likely to result from the chronic, long-term persistence of viruses and other foreign proteins within the cells of the immune system. It has long been known that live viruses, for example, are capable of surviving or remaining latent within the host

cells for years, without continually provoking acute disease. They do so simply by attaching their own genetic material as an extra particle or "episome" to the genome of the host cell, and replicating along with it, which allows the host cell to continue its own normal funtions for the most part, but imposes on it additional instructions for the synthesis of viral proteins.[20]

Latent viruses of this type have already been implicated in three distinct types of chronic disease, namely (1) *recurrent or episodic acute diseases* such as herpes, shingles, warts, etc.[21]; (2) *"slow-virus" diseases*, i.e., subacute or chronic, progressive, often fatal conditions, such as kuru, Creutzfeldt-Jakob disease, subacute sclerosing panencephalitis (SSPE), AIDS, and possibly Guillain-Barre syndrome[22]; and (3) *tumors*, both benign and malignant.[23]

In any case, the latent virus survives as a clearly "foreign" element within the cell, which means that the immune system must continue to try to make antibodies against it, insofar as it can still respond to it at all. Because the virus is now permanently incorporated within the genetic material of the cell, these antibodies will now have to be directed against the cell itself.

The persistence of live viruses or other foreign antigens within the cells of the host therefore cannot fail to provoke *auto-immune* phenomena, because destroying the infected cells is now the only possible way that this constant antigenic challenge can be removed from the body. Since routine vaccination introduces live viruses and other highly antigenic material into the blood of virtually every living person, it is difficult to escape the conclusion that a significant harvest of auto-immune diseases will automatically result.

Sir Macfarlane Burnet has observed that the components of the immune system all function as if they were collectively designed to help the organism to discriminate "self" from "nonself," i.e., to help us to recognize and tolerate our own cells, and to identify and eliminate foreign or extraneous substances as completely as possible.[24] This concept is exemplified not only by the acute response to infection, but also by the rejection of transplanted tissues, or "homografts," both of which result in the complete and permanent removal of the offending substance from the body.

If Burnet is correct, then latent viruses, auto-immune phenomena, and cancer would seem to represent different aspects of the same basic dilemma, which the immune system can neither escape nor resolve. For

all of them presuppose a certain degree of *chronic immune failure*, a state in which it becomes difficult or impossible for the body either to recognize its own cells as unambiguously its own, or to eliminate its parasites as unequivocally foreign.

In the case of the attenuated measles virus, it is not difficult to imagine that introducing it directly into the blood would continue to provoke an antibody response for a considerable period of time, which is doubtless the whole point of giving the vaccine; but that eventually, as the virus succeeded in attaining a state of latency within the cell, the antibody response would wane, both because circulating antibodies cannot normally cross the cell membrane, and also because they are powerful immunosuppressive agents in their own right.[25]

The effect of circulating antibody will thereafter be mainly to keep the virus *within* the cell, i.e., to continue to prevent any acute inflammatory response, until eventually, perhaps under circumstances of accumulated stress or emergency, this precarious balance breaks down, antibodies begin to be produced in large quantities against the cells themselves, and frank auto-immune phenomena of necrosis and tissue destruction supervene. Latent viruses, in this sense, are like biological "time bombs," set to explode at an indeterminate time in the future.[26]

Auto-immune diseases have always seemed obscure, aberrant, and bizarre, because it is not intuitively obvious why the body should suddenly begin to attack and destroy its own tissues. They make a lot more sense, and, indeed, must be reckoned as "healthy," if destroying the chronically infected cells is the only possible way of eliminating an even more serious threat to life, namely, the persistence of the foreign antigenic challenge within the cells of the host.

Tumor formation could then be understood as simply a more advanced stage of chronic immune failure, according to the same model. For, as long as the host is subjected to enormous and unremitting pressure to make antibodies against itself, that response will automatically tend to become less and less effective.

Eventually, under stress of this magnitude, the auto-immune mechanism could easily break down to the point that the chronically infected and genetically transformed cells, no longer clearly "self" or "nonself," begin to free themselves from the normal restraints of "histocompatibility" within the architecture of the surrounding cells, and begin to multiply autonomously at their expense.

A tumor could then be described as "benign" insofar as the break-

down of histocompatibility remains strictly localized to the tissue of [illegible] can be spread to other cell types, tissues, and organs, even to more remote areas. Malignancy might simply [illegible] into a more acute, florid form with less chronicity and more rapid [illegible] original victim.

If what I am saying turns out to be true, then what we have done by artificial immunizations is essentially to trade off our acute, epidemic disease of the past century for the weaker and far less curable chronic diseases of the present, with their amortizable suffering and disability. In doing so, we have also opened up limitless evolutionary possibilities for the future of ongoing *in vivo* genetic recombination within the cells of the race.

4. *The Individual Vaccines Reconsidered*

I want next to consider each of the vaccines on an individual basis, in relation to the infectious diseases from which they are derived.

The MMR is composed of attenuated live measles, mumps, and rubella viruses administered in a single intramuscular injection at about 15 months of age. Subsequent reimmunization is no longer recommended, except for young women of childbearing age, in whom the risk of congenital rubella syndrome (CRS) is thought to warrant it, even though the effectiveness of reimmunization is questionable at best.

Prior to the vaccine era, measles, mumps, and rubella were reckoned among the "routine childhood diseases," which most schoolchildren contracted before the age of puberty, and from which nearly all recovered with permanent, lifelong immunity, and no complications or sequelae.

But they were not always so harmless. Measles, in particular, can be a devastating disease when a population encounters it for the first time. Its importation from Spain, for instance, undoubtedly contributed to Cortez' conquest of the great Aztec Empire: Whole villages were carried off by epidemics of measles and smallpox, leaving only a small remnant of cowed, superstitious warriors to face the bearded *conquistadores* from across the sea.[27] In more recent outbreaks among isolated, primitive people, the case fatality rate from measles averaged 20 to 30 percent.[28]

In these so-called "virgin-soil" epidemics, not only measles but also polio and many other similar diseases take their highest toll of death and

serious complications among adolescents and young adults, healthy and vigorous people in the prime of life, and leave relatively unharmed the group of school-age children before the age of puberty.[29]

This means that the evolution of a disease such as measles from a dreaded killer to an ordinary disease of childhood presupposes the development of nonspecific or "herd" immunity in young children, such that, when they are finally exposed to the disease, it activates defense mechanisms already prepared and in place, resulting in the long incubation period and the usually benign, self-limited course described above.

Under these circumstances, the rationale for wanting to vaccinate young children against measles is limited to the fact that a very small number of deaths and serious complications have continued to occur, chiefly pneumonia, encephalitis, and the rare but dreaded subacute sclerosing panencephalitis (SSPE), a slow-virus disease with a reported incidence of 1 per 100,000 cases.[30] Pneumonia, by far the commonest complication, is usually benign and self-limited, even without treatment[31]; and, even in those rare cases in which bacterial pneumonia supervenes, adequate treatment is currently available.

By all accounts, then, the death rate from wild-type measles is very low, the incidence of serious sequelae is insignificant, and the general benefit to the child who recovers from the disease and to his contacts and descendants, is very great. Consequently, even if the measles vaccine could be shown to reduce the risk of death or serious complications from the disease, it still could not justify the high probability of auto-immune diseases, cancer, and whatever else may result from the propagation of latent measles virus in human tissue culture for life.

Ironically, what the measles vaccine certainly has done is to reverse the historical or evolutionary process to the extent that measles is once again a disease of adolescents and young adults,[32] with a correspondingly higher incidence of pneumonia and other complications and a general tendency to be a more serious and disabling disease than it usually is in younger children.

As for the claim that the vaccine has helped to eliminate measles encephalitis, I myself, in my own relatively small general practice, have already seen two children with major seizure disorders which the parents clearly ascribed to the measles vaccine, although they would never have been able to prove the connection in a court of law, and never considered the possibility of compensation.

Such cases therefore never make the official statistics, and are accordingly omitted from conventional surveys of the problem. Merely injecting the virus into the blood would naturally favor a higher incidence of deep or visceral complications affecting the lungs, liver, and brain, for which the measles virus has a known affinity.

The case for immunizing against mumps and rubella seems *a fortiori* even more tenuous, for exactly the same reasons. Mumps is also essentially a benign, self-limited disease in children before the age of puberty, and recovery from a single attack confers lifelong immunity. The principal complication is meningoencephalitis, mild or subclinical forms of which are relatively common, although the death rate is extremely low,[33] and sequelae are rare.

The mumps vaccine is prepared and administered in much the same way as the measles, usually in the same injection; and the dangers associated with it are likewise comparable. Again, like the measles, mumps is fast becoming a disease of adolescents and young adults,[34] age groups which do not tolerate the disease as well. The chief complication is acute epididymo-orchitis, which occurs in 30 to 40 percent of the males affected past the age of puberty, and usually results in atrophy of the testicle on the affected side[35]; but it also shows a strong tendency to attack the ovary and the pancreas.

For all of these reasons, the greatest favor we could do for our children would be to expose them all to the measles and mumps when they are young, which would not only protect them against contracting more serious forms of these diseases when they grow older, but would also greatly assist in their immunological maturation with minimal risk. I need hardly add that this is very close to the actual evolution of these diseases before the MMR vaccine was introduced.

The same discrepancy is evident in the case of rubella, or "German measles," which in young children is a disease so mild that it frequently escapes detection,[36] but in older children and adults not infrequently produces arthritis, purpura, and other severe, systemic signs.[37] The main impetus for the development of the vaccine was certainly the recognition of the congenital rubella syndrome (CRS) resulting from damage to the developing embryo in utero during the first trimester of pregnancy,[38] and the relatively high incidence of CRS traceable to the rubella outbreak of 1964.

But here again, we have an almost entirely benign, self-limited disease transformed by the vaccine into a considerably less benign disease of

adolescents and young adults of reproductive age, which is, ironically, the group that most needs to be protected against it. Moreover, as with measles and mumps, the simplest and most effective way to prevent CRS would be to expose everybody to rubella in elementary school; reinfection does sometimes occur after recovery from rubella, but much less commonly than after vaccination.[39]

The equation looks somewhat different for the diphtheria and tetanus vaccines. First of all, both diphtheria and tetanus are serious, sometimes fatal diseases, even under the best of treament; this is especially true of tetanus, which still carries a mortality of anywhere from 20 to 50 percent.

Furthermore, these vaccines are not made from living diphtheria and tetanus organisms, but only from certain "toxins" elaborated by them; these poisonous substances are still highly antigenic even after being inactivated by heat. Diphtheria and tetanus "toxoids" therefore do not protect against infection per se, but only against the systemic action of the original poisons in the absence of which both infections are of minor importance clinically.

Consequently, it is easy to understand why parents might want their children protected against diphtheria and tetanus, if safe and effective protection were available. Moreover, both vaccines have been in use for a long time, and the reported incidence of serious problems has remained very low, so that there has never been much public outcry against them.

On the other hand, both diseases are quite readily controlled by simple sanitary measures and careful attention to wound hygiene; and, in any case, both have been steadily disappearing from the developing countries, since long before the vaccines were introduced.

Diphtheria now occurs sporadically in the United States, often in areas with significant reservoirs of unvaccinated children. But the claim that the vaccine is "protective" is once again belied by the fact that, when the disease does break out, the supposedly "susceptible" children are in fact no more likely to develop clinical diphtheria than their fully immunized contacts. In a 1969 outbreak in Chicago, for example, the Board of Health reported that 25 percent of the cases had been fully immunized and that another 12 percent had received one or more doses of the vaccine and showed serological evidence of full immunity, whereas 18 percent had been partly immunized according to the same criteria.[40]

So, once again, we are faced with the probability that what the diphtheria toxoid has produced is not a genuine immunity to diphtheria at all, but rather some sort of chronic immune *reaction* to it, by harboring highly antigenic residues somewhere within the cells of the

immune system, presumably with long-term suppressive effects on the immune mechanism generally.

This suspicion is further aggravated by the fact that all of the DPT vaccines are alum-precipitated and preserved with thimerosal, an organomercury derivative, to prevent them from being metabolized too rapidly, so that the antigenic challenge will continue for as long as possible. The fact is that we do not know and have never even attempted to discover what actually becomes of these foreign substances once they are inside the human body.

Exactly the same problems complicate the record of the tetanus vaccine, which almost certainly has had at least some impact in reducing the incidence of tetanus in its classic acute form, yet presumably also survives for years or even decades as a potent foreign antigen within the body, with long-term effects on the immune system and elsewhere that are literally incalculable.

"Whooping cough," much like diphtheria and tetanus, began to decline as a serious epidemiological threat long before the vaccine was introduced. Moreover, the vaccine has not been particularly effective, even according to its proponents; and the incidence of known side effects is disturbingly high.

The power of the pertussis vaccine to damage the central nervous system, for example, has received growing attention since Stewart and his colleagues reported an alarmingly high incidence of encephalopathy and severe convulsive disorders in British children that were traceable to the vaccine.[41] My own cases, a few of which were reported above, suggest that hematological disturbances may be even more prevalent, and that, in any case, the *known* complications almost certainly represent a small fraction of the total.

In any case, the pertussis vaccine has become controversial even in the United States, where medical opinion has remained almost unanimously in favor of immunizations generally, and several countries, such as West Germany, have discontinued routine pertussis vaccination entirely.[42]

Pertussis is also extremely variable clinically, ranging in severity from asymptomatic, mild, or inapparent infections, which are quite common actually, to very rare cases in young infants less than five months of age, in which the mortality is said to reach 40 percent.[43] Indeed, the disease is rarely fatal or even that serious in children over a year old, and antibiotics have very little to do with the outcome.[41]

A good deal of the pressure to immunize at the present time thus seems to be attributable to the higher death rate in very young infants,

which has led to the terrifying practice of giving this most clearly dangerous of the vaccines to infants at two months of age, when their mother's milk would normally have protected them from all infection about as well as it can ever be done,[45] and the effect on the still developing blood and nervous system could be catastrophic.

For all of these reasons, the practice of routine pertussis immunization should be discontinued as quickly as possible and more studies done to assess and compensate the damage that it has already done.

Poliomyelitis and the polio vaccines present an entirely different situation. The standard Sabin vaccine is trivalent, consisting of attenuated, live polioviruses of each of the three strains associated with poliomyelitis; but it is administered orally, in much the same way as the infection is acquired in nature. The oral or noninjectable route, which leaves the recipient free to develop a natural immunity at the normal portal of entry, i.e., the GI tract, would therefore appear to represent a considerable safety factor.

On the other hand, the wild-type poliovirus produces no symptoms whatsoever in over 90 percent of the people who contact it, even under epidemic conditions[46]; and, of those people who do come down with recognizable clinical disease, perhaps only 1 or 2 percent ever progress to the full-blown neurological picture of "poliomyelitis," with its characteristic lesions in the anterior horn cells of the spinal cord or medulla oblongata.[47]

Poliomyelitis thus presupposes peculiar conditions of susceptibility in the host, even a specific *anatomical* susceptibility, since, even under epidemic conditions, the virulence of the poliovirus is so low, and the number of cases resulting in death or permanent disability was always remarkably small.[48]

Given the fact that the poliovirus was ubiquitous before the vaccine was introduced, and could be found routinely in samples of raw sewage wherever it was looked for,[49] it is evident that effective natural immunity to poliovirus was already as close to being universal as it can ever be, and a fortiori that no artificial substitute could ever equal or even approximate that result. Indeed, because the virulence of the poliovirus was so low to begin with, it is difficult to see what further attenuation of it could possibly accomplish, other than to abate as well the full vigor of the natural immune response to it.

For the fact remains that even the attenuated virus is still alive, and that the people who were anatomically susceptible to it before are still susceptible to it now. This means, of course, that at least *some* of these

same people will develop paralytic polio from the vaccine,[50] and that the others may still be harboring the virus in latent form, perhaps within those same cells.

The only obvious advantage of giving the vaccine, then, would be to introduce the population to the virus when they are still infants, and the virulence is normally lowest anyway[51]; and even this benefit could be more than offset by the danger of weakening the immune response, as we have seen. In any case, the whole matter is clearly one of enormous complexity, and illustrates only too well the hidden dangers and miscalculations that are inherent in the virtually irresistible attempt to beat nature at her own game, to eliminate a problem that cannot be eliminated, i.e., the susceptibility to disease itself.

So even in the case of the polio vaccine, which appears to be about as safe as any vaccine ever *can* be, the same fundamental dilemma remains. Perhaps the day will come when we can face the consequences of deliberately feeding live polioviruses to every living infant, and admit that we should have left well enough alone, and addressed ourselves to the art of healing the sick when we have to, rather than to the technology of eradicating the *possibility* of sickness, when we don't have to, and can't possibly succeed in any case.

5. *Vaccination and the Path of Medical Technology*

In conclusion, I want to go back to the beginning, to the essentially political aspects of vaccination, that oblige us all to reason and deliberate together about matters of common concern, and to reach a clear decision about how we choose to live. I have stated my own views regarding the safety and effectiveness of the vaccines, and I hope that others of differing views will do the same.

That is why I am deeply troubled by the atmosphere of fanaticism with which the vaccines are imposed on the public, and serious discussion of them is ignored or stifled by the medical authorities, as if the question had already been settled definitively and for all time. In the words of Sir Macfarlane Burnet:

> It is our pride that in a civilized country the only infectious diseases which anyone is likely to suffer are either trivial or easily cured by available drugs. The diseases that killed in the past have in one way or another been rendered impotent, and, in the process, general principles of control have been developed which should be applicable to any unexpected outbreak in the future.[52]

Quite apart from the truth of these claims, they exemplify the smugness and self-righteousness of a profession and a society that worships its own ability to manipulate and control the processes of nature itself. That is why, as Robert Mendelsohn has said, "We are quick to pull the trigger, but slow to examine the consequences of our actions."[53]

Indeed, one would have to say, *methodically* slow. In 1978, for example, the American Academy of Pediatrics, which had been charged by Congress with responsibility to formulate guidelines for federal compensation of "vaccination-related injuries," issued the following eligibility restrictions:

> 1. Compensation should be made available to any child or young person under the age of 18 years, or a contact of such person of any age, who suffers a major reaction to a vaccine mandated for school entry or continuation in his or her state of residence.
> 2. Such a reaction should have been previously recognized as a possible consequence of the vaccine given.
> 3. Such a reaction should have occurred no more than 30 days following the immunization.[54]

These restrictions would automatically exclude all of the chronic diseases, or indeed anything other than the very few adverse reactions that have so far been identified, which clearly represent only a tiny fraction of the problem.

Still less can either the government or the medical establishment be considered ignorant of the possibility that lurks in every parent's mind and heart, namely, that the vaccines cause cancer and other chronic diseases. Precisely that possibility was raised by Professor Robert Simpson of Rutgers in a 1976 seminar for science writers sponsored by the American Cancer Society:

> Immunization programs against flu, measles, mumps, polio, and so forth, may actually be seeding humans with RNA to form latent proviruses in cells throughout the body. These latent proviruses could be molecules in search of diseases; when activated, under proper conditions, they could cause a variety of diseases, including rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, Parkinson's disease, and perhaps cancer.[55]

Unfortunately, this is the sort of warning that very few people are willing or able to hear at this point, least of all the American Cancer Society or the American Academy of Pediatrics. The fact is, as Dubos points out, that all of us still want to believe in the "miracle," regardless of the evidence:

> The faith in the magical power of drugs often blunts the critical senses, and comes close at times to a mass hysteria, involving scientists and laymen alike. Men want miracles as much today as in the past. If they do not join one of the newer cults, they satisfy this need by worshipping at the altar of modern science. This faith in the magical power of drugs is not new. It helped to give medicine the authority of a priesthood and to recreate the glamour of ancient mysteries.[56]

The idea of eradicating measles or polio has come to seem attractive to us simply because the power of medical science makes it seem technically *possible;* we worship every victory of technology over nature, just as the bullfight celebrates the triumph of human intelligence over the brute beast.

That is why we do not begrudge the drug companies their enormous profits, and gladly volunteer our own bodies and those of our children for their latest experiments. Vaccination is essentially a religious sacrament of our own participation in the miracle, a veritable auto-da-fe in the name of modern civilization itself.

Nobody in his right mind would seriously entertain the idea that if we could somehow eliminate, one by one, measles and polio and all the known diseases of mankind, we would be any the healthier for it, or that other even more serious diseases would not quickly take their places.

Still less would a rational being suppose that the illnesses from which he suffered were "entities" somehow separable from the patients who suffer them, and that, with the appropriate chemical or surgical sacrament, this separation can literally be carried out.

Yet these are precisely the "miracles" we are taught to believe in, and the idolatries to which we aspire. We prefer to forget the older and simpler truths, that the propensity or susceptibility to illness is deeply rooted in our biological nature and that the phenomena of disease are the expression of our own life energy, trying to overcome whatever it is trying to overcome, trying, in short to *heal itself.*

The myth that we can find technical solutions for all human ailments seems attractive at first, precisely because it bypasses the problem of

healing, which is a genuine miracle in the sense that it can always *fail* to occur. We are all genuinely at risk of illness and death at every moment; no amount of technology can change that. Yet the mission of technical medicine is precisely to try to change that: to stand at all times in the front lines against disease, and to attack and destroy it whenever and wherever it shows itself.

That is why, with all due respect, I cannot have faith in the miracles or accept the sacraments of Merck, Sharp, and Dohme and the Center for Disease Control. I prefer to stay with the miracle of life itself, which has given us illness and disease, but also the arts of medicine and healing, through which we can acknowledge and experience our pain and our vulnerability, and sometimes, with the grace of God and the help of our fellow men, an awareness of health and well-being that transcends all boundaries. That is *my* religion; and, while I would willingly share it, I would not *force* it on anyone.

Postscript on Immunizations: Directions for Future Research

In "Immunizations—A Dissenting View," my intention was simply to understand my own experience, to develop a coherent and plausible line of reasoning that could explain what I had read and felt and thought about, and what my patients were telling me.

The next step is to address the issue of *experimental verification*, to try to sketch out where and how we might look for valid, repeatable evidence for the efficacy, safety, and mode of action of the common vaccines.

As I reread the argument, I realized that even the more speculative ideas in it could in fact be tested quite easily with the standard research techniques now in common use. Because I myself have very little research training or experience, I am doubly curious why such tests were not carried out long ago.

A number of scholars have certainly *entertained* these ideas before, as I indicated in the text, and even considered them publicly. The only obstacle that I can see to taking them seriously is that they are "heretical," that it would be impossible even to take the time to study them without a "paradigm shift" of some magnitude.[57]

1. How Effective Are the Vaccines?

If the vaccines act by *suppressing* the ability of the organism to mount

an effective acute inflammatory response, then we can no longer accept a simple drop in the incidence of the acute disease as a measure of true immunity. I also argued that the mere presence of circulating antibody cannot suffice either, because the diseases in question do continue to break out, even in serologically highly "immune" populations.

What strikes me as a far more interesting and relevant measurement is the degree to which the vaccine "protects" against the acute disease when the latter actually does break out. This could be determined relatively easily by studying the incidence and morbidity of each disease in fully and partly immunized populations, as compared with those of their nonimmunized neighbors. Such a study would still have nothing to say about the possibility of immunosuppression. But it would at least give a truer perspective on the ability of the vaccines to do what their proponents seem to *want* them to do.

I cannot resist pointing out that such research obviously requires a sizable cohort of unimmunized people, which is now being provided by those parents who have refused to immunize their children, despite the concerted efforts of the medical and public health authorities to intimidate and punish them. The same result could of course be achieved much more efficiently by simply making the vaccines *optional*, as they are in West Germany, Sweden, the United Kingdom, and some other places, which would allow the experimental and control groups to select themselves. Our frantic efforts to secure 100 percent compliance with the present mandatory program evidently succeeds only in making such studies impossible.

A closely related type of study would be to measure the effectiveness of *reimmunization* at varying intervals after the original course. In this case, there would be *two* control groups:

1. the same unimmunized cohort, as before; and
2. a group of children previously vaccinated, whose parents decided not to give them a "booster" dose.

This study would also measure the incidence and morbidity of the acute disease when it *does* break out, rather than simply the circulating antibody titer, which is probably far less relevant.

My conjecture, based on the preliminary studies I cited in the text, is that both primary and booster vaccinations tend to give considerably less protection against the corresponding acute disease when it does break out than the simple drop in incidence, or the rise in antibody titer, would indicate.

Both of these studies could also be carried out in suitable animal populations, using vaccines developed against disease peculiar to each species, such as canine distemper, leptospiro and the like, inasmuch as what we are concerned with includes the effectiveness and mode of action of the vaccines in general.

A third possibility would be to investigate the relationship between circulating antibody and "immunity" in the above sense. This could be done by measuring antibody titer periodically in a large pooled sample, and then retrospectively comparing baseline titers in an immunized group that subsequently developed the disease with another immunized group that was exposed to the disease but did not develop it. Both could then be compared with the corresponding nonimmunized groups, who would be expected to show no measurable titers at all prior to exposure.

2. *How Do the Vaccines Act?*

The problem with all of these studies is that they systematically ignore the crucial possibility that the vaccines may act immunosuppressively, and may therefore produce or at least promote a variety of obscure chronic diseases over long periods of time. This is why the "effectiveness" of the vaccines cannot really be studied in isolation without first understanding their mode of action in a more comprehensive fashion.

Indeed, the issue of effectiveness is actually misleading, insofar as it leads us to focus on the typical acute disease, rather than the broad spectrum of biological effects that can be associated with bacteria, viruses, and the vaccines derived from them, a spectrum that includes latent, subclinical, and chronic phenomena as well. We certainly know of situations in which *inability* to develop acute disease represents the exact opposite of good health, i.e., the consequences of chronic immune tolerance rather than true immunity.

At the crudest level, then, we need to study the effects of the vaccines, both acutely and long-term, on various clinical and laboratory parameters of health and disease. In the case of the pertussis vaccine, for example, we need good prospective studies on the incidence and severity of various hematological and CNS abnormalities over time, following the administration of the single vaccine at the usual time (and at routine intervals before and after). This could be done simply and inexpensively by performing CBCs, brief neurological exams, and behavioral assessments on the same self-selected groups of immunized and unimmunized children.

Another method would be to follow certain obvious *clinical* variables at the time of the normal well-child and other pediatric visits, such as the incidence and severity of acute and recurrent URI, tonsillitis, pharyngitis, otitis media, cervical adenopathy, and the like, in both immunized and unimmunized children over a period of years.

The same experimental format should also make it possible to sort out the various patterns of chronic morbidity following each individual vaccine. Again, the crucial importance of the unimmunized cohort becomes obvious. With regard to pertussis, for example, my clinical experience to date strongly suggests that the immunized group will have a significantly higher incidence and morbidity from chronic and recurrent infections, with higher rates of complications and disability, such as myringotomies, hearing loss, etc.

A long-term study could then follow these same children through older childhood and adolescence, to determine the incidence and morbidity of various chronic disease, such as eczema, asthma, rheumatoid arthritis, SLE, ulcerative colitis, multiple sclerosis, and other idiopathic degenerative, CNS, or connective-tissue diseases, as well as mental retardation, hyperactivity, school and behavior problems, convulsive disorders, leukemia, and other forms of cancer. Once again, my suspicion is that the immunized group would show a significantly higher increase in the incidence and morbidity in all these categories. I *hope* I'm wrong, but I don't think I am.

Another interesting and useful study would be to measure the effect of the common vaccines on the incidence and morbidity of other acute infections to which the individual was definitely or probably exposed (influenza, hepatitis, genital herpes, Colorado tick fever, etc.). The point here would be to see if the vaccination process has any effect on the capacity of the immune system to deal with acute infection generally, which seems quite probable.

In this case there would be two control groups:

1. one group of children not previously immunized (against measles, mumps, or whatever), who were subsequently exposed to influenza, hepatitis, or some other acute infection; and
2. a group of similar children who contracted and recovered from acute measles, mumps, or whatever, some time before their exposure to influenza, hepatitis, etc.

Again, my conjecture is that both groups, while perhaps no less likely

to *contract* the second disease, would show significantly less acute and chronic *morbidity* as a result of it.

Along these same lines, it would not be very difficult to design some good animal studies investigating the possibility of immunosuppression by the vaccines. This could be done by measuring leukocyte and macrophage activity both in vivo and in vitro, in response to various challenges, such as exposure to unrelated infections, allergens, and chemicals. Various liver function tests, as well as the ability of the spleen and bone marrow to respond to hemorrhage and blood transfusion could also be followed. Finally, the ability of both immunized and unimmunized animals to reject homografts could be measured quite easily.

Careful cytogenetic studies could also be made, to show the effects of vaccination on karyotype and chromosome morphology, beginning with typical "target" cells for which the vaccine in question has a known affinity (e.g., liver parenchymal cells in hepatitis, parotid acinar cells in mumps, cells of the nasal mucosa in measles). Careful virological studies of these same cells should also make it possible to recover or at least demonstrate the existence of episomes or viral nucleoprotein moieties within the DNA or RNA of the host, which would confirm the suspicion of latency and chronic infection, at least in the case of the live vaccine.

But, whichever studies are done, the point is that the technology to do them already exists; and the only thing that prevents them from being done is our own ideological resistance to the self-evident truth that vaccines are not simply "wonder drugs" that produce specific antibodies and nothing more, but complex, biologically active substances whose effects on the human organism urgently need to be investigated.

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QUESTION AND ANSWER PERIOD

Q: Why does the American Academy of Pediatrics draft a bill for compensation of vaccine-damaged children that we taxpayers will have to pay for? Why don't the pharmaceutical companies and the doctors and legislators pay for this damage?

Lori Andrews: Before you answer the questions, I'm going to make a suggestion, since I know that the subject of immunization evokes a lot

of interest. I wonder if we could get a number of questions and comments first and then you might answer them as a group, and then everybody can have their chance to talk.

Q: How many cases have you found that had cancer developed at the site of the injection? Can you elaborate on Senate Bill S.2117, as to why the taxpayer should not be used to compensate the vaccine-damaged children? In my opinion, epidemics are pharmaceutical clearance sales. Epidemics are seasonal events. All vaccines are iatrogenic. Today's immunized children are tomorrow's asthmatics, diabetics, and cancer victims.

Q: I'd like to make a comment: I recently met a man who had vaccinations 60 years ago. The left half of his body is completely raw and they determined it's all vaccination, just growing in his body. My question is: Since laws on immunizations are enforced more and more, it is our legislators that pass these laws after the lobbyists have talked them into passing the laws. Who are the people who pay the lobbyists to force the immunizations?

Q: Are you familiar at all with John Chris Hofman's work, University of Maryland? He has speculated that vaccine-induced immunity commits more of the body's immune system to that particular antigen, which means they are less available for nonspecific reactions. Have you in your research come across any support for that speculation, and what are your own feelings on that?

Q: I've read some of your other articles on immunizations, and I'd like to know exactly how, in your opinion, a homeopathically prepared remedy would work as opposed to immunization shots. What is the physiology of what actually takes place biologically?

Q: I'd like to know if you know of any cases where the breast on the opposite side of where the vaccination was to be removed? We know of a lot of them that were on the same side where the vaccine was, but haven't found anybody yet that really had it on the opposite side.

Q: Your talk has been very educational for me, and my question is: What if you refuse shots? I know last year Chicago had a big thing about if you didn't have shots you couldn't get back into the school, and I want to know what options you have if you definitely refuse to have your children vaccinated.

Q: Dr. Moskowitz, from the credits that we heard at the beginning of your speech, I take it that you're not a resident of Illinois, but live in Massachusetts. In response to the question that was just asked—what do parents do for enforced immunizations perpetrated by the school system

and the public health authority?—the answer is simple. You have to fight the bastards in court. That's it; it just has to be done that way. I apologize for being so rude, but that, in fact, is the case, because the laws are such that you just have no choice. That's why I think, Dr. Mendelsohn, that immunizations evoke such response from the public, because it is the area in which the freedom of choice of the people is really being taken away from them and they can do very little about it.

Dr. Moskowitz: Maybe I can address some of those questions now. First of all, the lady who asked about cancer at the injection site: No, I have never seen such a thing. It may be possible, but I personally have not seen it or heard of it. In fact, I'd be interested in knowing any documentation you might have of that.

As far as the bill compensating victims of vaccination, I'm opposed to that bill because I think that basically the bill is an attempt to maintain the system as we have it. The American Academy of Pediatrics was challenged by Congress to come up with some guidelines to compensate vaccine-injured people and basically what they came up with is that in order to prove that the victim was injured by the vaccine, they have to show first of all that the effect happened within 30 days of the administration of the vaccine and, secondly, that it has to be an effect that's already been studied or already been discovered. That eliminates immediately the whole concern of my paper, which is precisely those chronic things that happen later, that may be very insidious and very difficult to trace, and for which we as yet have no adequate experimental evidence. So, I think that's a very shortsighted bill and I think really the purpose of it is simply to continue compulsory immunization. I think the bill is paying off a few, a very, very few people, just the very tip of that iceberg there, and the rest of it is being left not only unpaid but uninvestigated as well. That's the whole point of what I'm trying to say, that we need new laws to make those vaccines voluntary. They are in some states; some states have changed the laws in this respect.

As far as the third question goes, I'm not familiar with Dr. Hotman's work, and I'd be very interested in it; but my feeling is that that's only a very small part of what happens because I think the nonspecific immunity is also very important and is probably the reason why measles evolved from a killer disease, which it was at one time. When it was introduced by Cortez into the Americas as the secret weapon of the conquistadores, it decimated whole populations of Mexican villages. It's been estimated to kill about 20 percent of the people infected with it

when it meets a population for the first time. The evolution of a disease like measles from a killer into a more or less common disease of childhood which is handled very effectively by the vast majority of people in a population requires generations and generations of what you might call nonspecific or herd immunity, such that when the disease actually strikes, the immune mechanism is already in place waiting for it. So, I think those nonspecific responses are very, very important for the development of what we call true immunity, lifelong immunity, such as you get from recovering from a natural disease.

As far as the homeopathic remedies are concerned, I honestly do not know how the homeopathic remedies work and cannot as yet give you a convincing explanation of how substances as dilute as that can work. We know that they work; we've had the *experience* that they work, and it's a very beautiful, elegant, and safe method. But it implies the existence of a science that in a sense has not been discovered yet, although we're working on it, and trying very hard to elaborate it. I certainly would not say that it's a panacea for every patient with vaccine-related illness, but it certainly can help in many cases.

Someone alluded to the possibility of using a homeopathic remedy in lieu of vaccine. There were homeopaths who advocated that, and indeed there are some people who still do. I myself do not do it because I think the immunization laws are concerned with *long-term* immunity. In order to do that with a homeopathic remedy you would have to give it many, many times, and that's a usage that I would not support. I don't think that long-term immunity is really possible, or even desirable, using artificial means.

As far as the vaccine on the same side as the breast cancer, there again, you've got me; I've never heard of that before. It's very interesting, and I'd like very much to see the information you've collected about it.

As far as the question about the school requirements, I would say that it varies quite a bit from state to state and even from school district to school district. For example, Indiana is one of the many states that, partly in response to public outcry, changed its law so that people may waive the requirement for their children to be immunized if they have a strong philosophical objection to it. They have to sign a waiver that the state gives them; but, even in a state like that, where the law is on the books, to get a school board to allow that may be very difficult. It may take a telephone call from a lawyer or something to let them know that you're really serious to honor the law that exists.

In many other states, in Maryland, for example, the law is quite rigid and without exception: There are no exceptions, except in some cases, if the doctor writes a letter of exemption for very strong medical reasons, such as for a child who has a high fever or convulsions at the time of the test. In that case everyone would agree that the immunization should not be given. If there was a strong history of neurological disease, they might also entertain such a letter; but this whole area that we were getting into here about the connection between vaccines and chronic disease would not be allowed at present in a state such as Maryland.

It is the intent of the Legislature that the Department of Health and Social Services shall report to the 16th Legislature no later than April 1, 1989 as to the federal regulations promulgated by both the Federal Drug Administration and Department of Health and Human Services regarding the use of vaccines and the resulting Alaska program; its requirements regarding specific information which must be provided to the guardians of minors to be vaccinated and the manner in which adverse reactions must be reported.

ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
RESEARCH AGENCY

P.O. Box Y, State Capitol
Juneau, Alaska 99811-3100
Mail Stop 3100
(907) 465-3991

April 19, 1988

MEMORANDUM

TO: Representative Niilo Koponen

ATTN: Lisa McLaren

FROM: Patricia Brawley pb
Legislative Analyst

RE: Vaccination Information Requirements
Research Request 88.240

You wished to know 1) if any states require both public and private sector health care providers to inform vaccine recipients, their parents, or legal guardians about the vaccines and their potential adverse effects, and 2) if statutes of states which require dissemination of information include provisions for enforcement and penalties for noncompliance. As background for this question, I will discuss access to and control of vaccines, as well as current and future requirements for health care providers who administer them.

Vaccines--Access and Control

In the United States, vaccines are either publicly or privately purchased. Privately purchased vaccines can be bought directly from drug manufacturers. Adverse reactions resulting from privately purchased vaccines are reported to the Food and Drug Administration (FDA). According to Ken Allman, Public Health Advisor at the Centers for Disease Control (CDC) in Atlanta, vaccines are generally purchased by states through a contract with the federal government. State or local money is used, and vaccines are distributed throughout the public sector. One stipulation of this contract is that public health care providers who administer these vaccines also dispense an "important information statement" which provides background information on the disease and the antigen, risks and benefits of the vaccine, contraindication, signs and symptoms of possible adverse reactions, and what to do and who to call in case of adverse reactions. Another stipulation involves use of the Monitoring System for Adverse Events Following Immunization (MSAEFI) developed by the Centers for Disease Control.

The contract between the federal and state governments requires that public sector health care providers comply with these stipulations as a condition of receiving vaccines from the state agency which purchased them. According to Elfrida Nord, Chief of Nursing, Department of Health and Social Services (DHSS), Alaska was one of the last states to accept the federal vaccine program and its attendant regulations. Until January 1985, when the federal contract became more attractive due to state funding considerations, Alaska purchased vaccines directly from manufacturers.

In some states--such as Alaska--private sector providers may receive publicly purchased vaccines from the public sector agencies. In Alaska, vaccines are made available at no cost to public health care providers, and to private physicians who request them. Private sector health care providers have been encouraged to use the information statements and reporting forms, but because the public sector has no jurisdiction over the private sector, there has been no enforcement. Although not required to use the information statements, many physicians obtain vaccines directly from the manufacturers, preferring direct access to low cost.

State Legislation Requiring Information Prior to Vaccinations

Information and reporting requirements were incorporated into the federal contract largely as a result of lobbying efforts by Dissatisfied Parents Together (DPT), a group opposed to mandatory DPT vaccinations--specifically, to the pertussis (P) component of the vaccination. Because the federal regulations did not adequately extend to private sector providers, both Maryland and New Jersey addressed this problem (for pertussis vaccinations only) by requiring that all health care providers give written information to the parents or legal guardians of children prior to their children receiving immunizations for pertussis. Neither statute contains provisions for enforcement or penalties for noncompliance.

Recent Federal Regulations

As you may know, the National Childhood Vaccine Injury Act of 1986, which established the National Vaccine Injury Compensation Program, became effective on March 22, 1988. Intended to assure a safer childhood vaccination program in the U.S., this Act will improve the systems for reporting adverse reactions and standardize the use of important information statements prior to the administration of the vaccines. Under the new law, all health care providers will permanently record certain vital information, and will report any adverse reaction or event described in the Vaccine

Injury Tables which occurs within a specified time after the date of vaccination.[1] Information requirements are being developed and will include the following:

> . . . each health care provider who administers a vaccine set forth in the Vaccine Injury Table shall provide to the legal representatives of any child to whom such provider intends to administer such vaccine a copy of the information materials developed . . . or other written information which meets the requirements of this section. Such materials or other information shall be provided prior to the administration of such vaccine. . . . The information in such materials shall be presented in understandable terms and shall include--
>
> 1) the frequency, severity, and potential long-term effects of the disease to be prevented by the vaccine,
>
> 2) the symptoms or reactions to the vaccine which, if they occur, should be brought to the immediate attention of the health care provider,
>
> 3) precautionary measures legal representatives should take to reduce the risk of any major adverse reactions to the vaccine that may occur,
>
> 4) early warning signs or symptoms to which legal representatives should be alert as possible precursors to such major adverse reactions,
>
> 5) a description of the manner in which legal representatives should monitor such major adverse reactions, including a form on which reactions can be recorded to assist legal representatives in reporting information to appropriate authorities,

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[1]Memorandum from Alan R. Hinman, Director, Center for Prevention Services, CDC, to Immunization Project Directors, March 21, 1988, and CDC, "National Childhood Vaccine Injury Act: Requirements for Permanent Vaccination Records and for Reporting of Selected Events After Vaccination," Morbidity and Mortality Weekly Report, April 8, 1988, pp. 197 - 200, Attachment A.

6) a specification of when, how, and to whom legal representatives should report any major adverse reaction,

7) the contraindications to (and bases [sic] for delay of) the administration of the vaccine,

8) an identification of the groups, categories, or characteristics of potential recipients of the vaccine who may be at significantly higher risk of major adverse reaction to the vaccine than the general population,

9) a summary of relevant State and Federal laws concerning the vaccine, including information on--

   A) the number of vaccinations required for school attendance and the schedule recommended for such vaccinations, and

   B) the availability of the Program, and

10) such other relevant information as may be determined by the Secretary. [See Attachment B for full text.]

There are no provisions in the new federal law for enforcement or penalties for noncompliance, other than for manufacturers who intentionally misrepresent information. According to representatives of the CDC, however, the injury compensation program and growing public awareness of problems associated with vaccines make the use of both information statements and reporting systems more desirable for all health care providers.

I have requested that the CDC send copies of both current and future "important information statements" to your office. I hope this information is useful to you. If you need further information, please call.

Attachments

ATTACHMENT A

Memorandum from Alan R. Hinman, Director,
Center for Prevention Services, CDC, to Immunization
Project Directors, March 21, 1988, and CDC, "National Childhood Vaccine
Injury Act: Requirements for Permanent Vaccination Records
and for Reporting of Selected Events After Vaccination,"
Morbidity and Mortality Weekly Report, April 8, 1988

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MAR 29 1988
Dept. of Health & S.S.
Section of Epidemiology

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
Atlanta GA 30333

March 21, 1988

TO : Immunization Project Directors

SUBJECT: National Vaccine Injury Compensation Program: Legal Requirements for Reporting of Events Following Vaccination Beginning March 22, 1988

As a result of the National Vaccine Injury Act of 1986, which established the National Vaccine Injury Compensation Program, and amendments enacted as of December 22, 1987, all providers of vaccinations will be required to report selected adverse events for selected vaccines to the Federal government. The requirement becomes effective March 22, 1988.

Attached to this memorandum is a draft of an article describing Program reporting requirements and the system(s) to use for reporting adverse events. This article will be published in the Morbidity and Mortality Weekly Report (MMWR) and most likely in the Food and Drug Administration (FDA) Bulletin. For public sector immunization programs nationwide, the most important point to be extracted from the article, is that, at least for the interim, adverse events following immunization with selected publicly-funded vaccines that require reporting under the Program are to be reported through the Monitoring System for Adverse Events Following Immunization (MSAEFI) using the current Adverse Event Following Immunization form (CDC form 71.19) available in each State. The current MSAEFI program encompasses the reporting requirements of the National Vaccine Injury Compensation Program. While no punitive measures for nonreporting are designated within the law, increased reporting of events (including those following publicly-funded vaccines) can be anticipated because of increased awareness of the law among providers of vaccine and among the public. How great this increase might be in the public sector is difficult to envision at this time, but the Division of Immunization will monitor this closely.

The attachment also outlines the system to be used by providers of privately purchased vaccines to report selected events following selected vaccines. Basically, such reports are to be made directly to the FDA on its Adverse Reaction Report (FDA form 1639). This form is currently in use for adverse event reporting after receipt of drugs and biologics such as vaccines. The FDA, like the Division of Immunization, will be quantitating the impact of the reporting requirement on its workload.

Some confusion will arise among some vaccine providers concerning the systems for reporting both publicly and privately purchased vaccines. Local, county, and State immunization and other public health personnel are likely to be contacted by vaccine providers to clarify the what, the how, and the where of reporting. The content and tables of the attachment can be used for this purpose.

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Active consideration is being given to developing a single reporting system to accommodate reports of events after both publicly and privately purchased vaccines. Several options have been outlined, and the costs and logistics of each are being developed and discussed. It will be some time before a decision is made and such a system made available to replace the systems outlined in this memorandum and this attachment.

Finally, we want to emphasize that the Adverse Event Following Immunization form should continue to be completed and sent by States to CDC for any adverse event following receipt of any publicly purchased vaccine that had onset within 28 days of vaccination and for which the vaccine recipient was seen by a health care provider. We continue to be most appreciative of the ongoing support given to MSAEFI by public health personnel at all levels.

Your help in distributing the content of this memorandum to pertinent immunization personnel who may be responsible for the current public sector adverse event reporting system, and to other health department personnel who may be in a position to answer health care provider and public inquiries would be most appreciated. Any questions concerning reporting from program personnel should be addressed to Edward W. Brink, M.D., (404) 639-1867.

Alan Hinman

Alan R. Hinman, M.D.
Director
Center for Prevention Services

Attachment (Draft of MMWR. April 8, 1988, pp. 197-200.)

cc:
Regional Offices
Immunization Program Managers
MSAEFI Coordinators
Association of State and Territorial
Health Officers
Conference of State and Territorial Epidemiologists

CENTERS FOR DISEASE CONTROL

April 8, 1988 / Vol. 37 / No. 13

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

197 National Childhood Vaccine Injury Act: Requirements for Permanent Vaccination Records and for Reporting of Selected Events After Vaccination
200 High Prevalence of Iron Deficiency Anemia Among Alaskan Native Children
207 Influenza – United States
210 CDC Symposium on Statistics in Surveillance

Current Trends

National Childhood Vaccine Injury Act: Requirements for Permanent Vaccination Records and for Reporting of Selected Events After Vaccination

Since March 21, 1988, health-care providers who administer certain vaccines and toxoids are required by law to record permanently certain information and to report certain events.* The vaccines and toxoids to which these requirements apply follow: diphtheria and tetanus toxoids and pertussis vaccine (DTP); pertussis vaccine (P); measles, mumps, and rubella single-antigen vaccines and combination vaccines (MMR, MR); diphtheria and tetanus toxoids (DT); tetanus and diphtheria toxoids (Td); tetanus toxoid (T); poliovirus vaccine live, oral (OPV); and poliovirus vaccine inactivated (IPV) (Table 1). The requirements also will apply to DTP combined with inactivated poliovirus vaccine (DTP/Polio combined) if it becomes available.

Requirements for Recording

Specifically, all health-care providers who administer one or more of these vaccines or toxoids are required to ensure that there is recorded in the vaccine recipient's permanent medical record (or in a permanent office log or file) the date the vaccine was administered, the manufacturer and lot number of the vaccine, and the name, address, and title of the person administering the vaccine. The term health-care provider is defined as any licensed health-care professional, organization, or institution, whether private or public (including federal, state, and local departments and agencies), under whose authority a specified vaccine is administered.

Requirements for Reporting

Health-care providers are required to report to the U.S. Department of Health and Human Services (DHHS) selected events occurring after vaccination. Reportable events applicable to the previously mentioned vaccines and toxoids are shown in Table 1 and include events described in the vaccine manufacturer's package insert as contraindications to receiving additional doses of the vaccine.

*The National Childhood Vaccine Injury Act of 1986, at Section 2125 of the Public Health Service Act as codified at 42 U.S.C. § 300aa-25 (Supp. 1987).

Vaccine – Continued

TABLE 1. Reportable events following vaccination

Vaccine/Toxoid	Event	Interval from Vaccination
DTP, P, DTP/Polio Combined	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)*	7 days
	C. Shock-collapse or hypotonic-hyporesponsive collapse*	7 days
	D. Residual seizure disorder*	(See Aids to Interpretation*)
	E. Any acute complication or sequela (including death) of above events	No limit
	F. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine† (such as convulsions)	(See package insert)
Measles, Mumps, and Rubella; DT, Td, Tetanus Toxoid	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)*	15 days for measles, mumps, and rubella vaccines; 7 days for DT, Td, and T toxoids
	C. Residual seizure disorder*	(See Aids to Interpretation*)
	D. Any acute complication or sequela (including death) of above events	No limit
	E. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine†	(See package insert)
Oral Polio Vaccine	A. Paralytic poliomyelitis	
	—in a non-immunodeficient recipient	30 days
	—in an immunodeficient recipient	6 months
	—in a vaccine-associated community case	No limit
	B. Any acute complication or sequela (including death) of above events	No limit
	C. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine†	(See package insert)
Inactivated Polio Vaccine	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Any acute complication or sequela (including death) of above event	No limit
	C. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine†	(See package insert)

*Aids to Interpretation:

Shock-collapse or hypotonic-hyporesponsive collapse may be evidenced by signs or symptoms such as decrease in or loss of muscle tone, paralysis (partial or complete), hemiplegia, hemiparesis, loss of color or turning pale white or blue, unresponsiveness to environmental stimuli, depression of or loss of consciousness, prolonged sleeping with difficulty arousing, or cardiovascular or respiratory arrest.

Residual seizure disorder may be considered to have occurred if no other seizure or convulsion unaccompanied by fever or accompanied by a fever of less than 102° F occurred before the first seizure or convulsion after the administration of the vaccine involved.

AND, if in the case of measles-, mumps-, or rubella-containing vaccines, the first seizure or convulsion occurred within 15 days after vaccination OR in the case of any other vaccine, the first seizure or convulsion occurred within 3 days after vaccination,

AND, if two or more seizures or convulsions unaccompanied by fever or accompanied by a fever of less than 102° F occurred within 1 year after vaccination.

The terms seizure and convulsion include grand mal, petit mal, absence, myoclonic, tonic clonic, and focal motor seizures and signs. Encephalopathy means any significant acquired abnormality of, injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurologic signs, increased intracranial pressure, or changes lasting at least 6 hours in level of consciousness, with or without convulsions. The neurologic signs and symptoms of encephalopathy may be temporary with complete recovery, or they may result in various degrees of permanent impairment. Signs and symptoms such as high-pitched and unusual screaming, persistent unconsolable crying, and bulging fontanel are compatible with an encephalopathy, but in and of themselves are not conclusive evidence of encephalopathy. Encephalopathy usually can be documented by slow wave activity on an electroencephalogram.

†The health-care provider must refer to the CONTRAINDICATION section of the manufacturer's package insert for each vaccine.

Vaccine – Continued

Methods for Reporting

In the United States, vaccines are either publicly or privately purchased. Publicly purchased vaccines are bought with federal, state, and/or local government funds. At present, the method and route for reporting adverse events depend on whether the vaccine administered is publicly or privately purchased. Events occurring after receipt of publicly purchased vaccines are reported through local, county, and/or state health departments to the Centers for Disease Control (CDC) on its Report of Adverse Events Following Immunization (CDC form 71.19). Events occurring after receipt of a privately purchased vaccine usually are reported directly to the Food and Drug Administration (FDA) on its Adverse Reaction Report (FDA form 1639) by the health-care provider or the manufacturer.

For the time being, these two systems for reporting adverse events are to be used to implement the requirement of Title XXI of the Public Health Service Act for reporting adverse events to DHHS (Table 2).

Reportable events occurring after receipt of a publicly purchased vaccine shall be reported to local, county, and/or state health departments through channels currently in place at those institutions. The Report of Adverse Events Following Immunization, available at each state health department, shall be completed and sent by the state health department to CDC.

TABLE 2. Reporting of events occurring after vaccination

	Vaccine Purchased with Public Money	Vaccine Purchased with Private Money
Who Reports:	Health-care provider who administered the vaccine	Health-care provider who administered the vaccine
What Products To Report:	DTP, P, Measles, Mumps, Rubella, DT, Td, T, OPV, IPV, and DTP/Polio Combined	DTP, P, Measles, Mumps, Rubella, DT, Td, T, OPV, IPV, and DTP/Polio Combined
What Reactions To Report:	Events listed in Table 1 including contraindicating reactions specified in manufacturers' package inserts	Events listed in Table 1 including contraindicating reactions specified in manufacturers' package inserts
How To Report:	Initial report taken by local, county, or state health department. State health department completes CDC form 71.19	Health-care provider completes Adverse Reaction Report-FDA form 1639 (include interval from vaccination, manufacturer, and lot number on form)
Where To Report:	State health department sends CDC form 71.19 to MSAEFI/IM (E05) Centers for Disease Control Atlanta, GA 30333	Completed FDA form 1639 is sent to Food and Drug Administration (HFN-730) Rockville, MD 20857
Where To Obtain Forms:	State health departments	FDA and publications such as *FDA Drug Bu...*

ATTACHMENT B

The National Childhood Vaccine Injury Act of 1986

Legislative History. For legislative history and purpose of Pub.L. 98–512, see 1984 U.S.Code Cong. and Adm.News, p. 4095.

Library References
United States ⇐82.
C.J.S. United States § 122.

§ 300z–10. Restrictions

Library References
United States ⇐82.
C.J.S. United States § 122.

SUBCHAPTER XIX—VACCINES

PART 1—NATIONAL VACCINE PROGRAM

§ 300aa–1. Establishment

The Secretary shall establish in the Department of Health and Human Services a National Vaccine Program to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines. The Program shall be administered by a Director selected by the Secretary.

(July 1, 1944, c. 373, Title XXI, § 2101, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3756.)

Effective Date. Section 323 of Pub.L. 99–660 provided that:

"(a) **General rule.**—Part 1 of title XXI of the Public Health Service Act [part 1 of this subchapter] shall take effect on the date of the enactment of this Act [Nov. 14, 1986] and Subtitle 2 of such title [part 2 of this subchapter] and this title [see Short Title note under section 201 of this title] shall take effect on the effective date of a tax enacted after the date of the enactment of this Act to provide funds for compensation paid under such subtitle 2.

"(b) **Insufficiency of funds.**—If at any time there are insufficient funds to pay all of the claims payable under subtitle 2 of title XXI of the Public Health Service Act [part 2 of this subchapter] for 180 days, such subtitle shall cease to be in effect until sufficient funds to pay all of the claims under such subtitle become available."

Study of Relationship between Vaccines Containing Pertussis and Certain Illnesses. Section 312 of Pub.L. 99–660 provided that:

"(a) **Review of pertussis vaccines and related illnesses and conditions.**—Not later than 3 years after the effective date of this title [see section 323 of Pub.L. 99–660 set out as a note under this section], the Secretary of Health and Human Services shall complete a review of all relevant medical and scientific information (including information obtained from the studies required under subsection (e)) on the nature, circumstances, and extent of the relationship, if any, between vaccines containing pertussis (including whole cell, extracts, and specific antigens) and the following illnesses and conditions:

"(1) Hemolytic anemia.

"(2) Hypoarrhythmia.

"(3) Infantile spasms.

"(4) Reye's syndrome.

"(5) Peripheral mononeuropathy.

"(7) Aseptic meningitis.

"(8) Juvenile diabetes.

"(9) Autism.

"(10) Learning disabilities.

"(11) Hyperactivity.

"(12) Such other illnesses and conditions as the Secretary may choose to review or as the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [section 300aa–19 of this title] recommends for inclusion in such review.

"The review under this subsection shall include notice and opportunity for a public hearing, consideration of written information submitted by the public, and consultation with such Advisory Commission.

"(b) **Findings with respect to pertussis.**—Not later than 3 years after the effective date of this title, the Secretary shall make, and publish in the Federal Register, the following specific findings:

"(1) Whether each of the illnesses or conditions set forth in subsection (a) can reasonably be determined in some circumstances to be caused or significantly aggravated, by pertussis-containing vaccines.

"(2) For each illness or condition for which a finding of causation or aggravation related to vaccines containing pertussis is made under paragraph (1), the circumstances under which such causation or aggravation can reasonably be determined to occur.

"(3) For each illness or condition for which a finding of causation or aggravation related to vaccines containing pertussis is made under paragraph (1), and for each illness or condition set forth in the Vaccine Injury Table under section 2114 of the Public Health Service Act [section 300aa–14 of this title] the time periods within which the first symptom or manifestation of onset or aggravation of each such illness [illegible] determined to

"(c) **Revision of table with respect to pertussis vaccines.**—At the same time the Secretary publishes in the Federal Register findings under subsection (b), the Secretary shall propose regulations to amend the Vaccine Injury Table under section 2114 of the Public Health Service Act [section 300aa–14 of this title] as a result of such findings. Not later than 42 months after the effective date of this title, the Secretary shall promulgate such proposed regulations with such modifications as may be necessary after opportunity for public hearing.

"(d) **Review of MMR vaccines and related illnesses and conditions.**—Not later than 3 years after the effective date of this title, the Secretary of Health and Human Services shall complete a review similar to the review conducted under subsection (a) with respect to the potential relationship between vaccines containing rubella (including MMR) and radiculoneuritis. The review under this subsection shall include notice and opportunity for a public hearing, consultation with the Advisory Commission on Childhood Vaccines and consideration of written information submitted by the public. Not later than 3 years after the effective date of this title, the Secretary shall make and publish in the Federal Register findings similar to those required by subsection (b) and shall, if appropriate, propose similar regulations (and thereafter promulgate such regulations) to those required by subsection (c), with respect to compensation under the National Vaccine Injury Compensation Program established under section 2110 of the Public Health Service Act [section 300aa–10 of this title] for radiculoneuritis caused, contributed to, or significantly aggravated by vaccines containing rubella.

"(e) **Pertussis and MMR studies.**—

"(1) In order to assist the Secretary in making the findings required under subsections (b) and (d), the Secretary shall, in accordance with subparagraph (B), arrange for the conduct of studies of—

"(A) the relationship between vaccines containing pertussis (including whole cell, extracts, and specific antigens) and the illnesses or conditions set forth in paragraphs (1) through (11) of subsection (a),

"(B) the relationship between vaccines containing pertussis and any other illnesses and conditions, as selected by the Secretary or the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [section 300aa–19 of this title], and

"(C) the relationship between vaccines containing rubella (including MMR) and radiculoneuritis.

"(2)(A) The Secretary shall request the Institute of Medicine of the National Academy of Sciences to conduct the studies required by paragraph (1) under an arrangement by which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary.

"(B) If the Institute of Medicine is unwilling to conduct such study under such an arrangement, the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study and prepare and submit the reports thereon as

"(C) The Institute of Medicine or other group or association conducting the studies required by paragraph (1) shall conduct such studies in consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [section 300aa–19 of this title].

"(3) Reports on the results of the studies required by paragraph (1) shall be completed and submitted to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the State and to the Secretary not later than 32 months after the effective date of this title. Upon submission to the Secretary, the reports shall be made available to the public.

"(4) There are authorized to be appropriated such sums as are necessary for the purpose of making payments for the conduct of the studies required under this subsection.

"(f) **Definitions.**—For purposes of this section:

"(1) The term 'medical and scientific information' includes epidemiologic, clinical, biostatistical, pathological, toxicologic, and other laboratory data and case study information, observations, studies, and reports in peer-reviewed literature or official Government publications, as well as relevant unpublished information, data, studies, and observations.

"(2) The term 'MMR' means a vaccine containing material intended to prevent or confer immunity against measles, mumps, and rubella disease."

Study of Other Vaccine Risks. Section 313 of Pub.L. 99–660 provided that:

"(a) **Study.**—

"(1) Not later than 3 years after the effective date of this title [see section 323 of Pub.L. 99–660, set out as a note under this section] the Secretary shall, after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [section 300aa–19 of this title]—

"(A) arrange for a broad study of the risks (other than the risks considered under section 102) to children associated with each vaccine set forth in the Vaccine Injury Table under section 2114 of such Act [section 300aa–14 of this title] and

"(B) establish guidelines, after notice and opportunity for public hearing and consideration of all relevant medical and scientific information, respecting the administration of such vaccines which shall include—

"(i) the circumstances under which any such vaccine should not be administered,

"(ii) the circumstances under which administration of any such vaccine should be delayed beyond its usual time of administration, and

"(iii) the groups, categories, or characteristics of potential recipients of such vaccine who may be at significantly higher risk of major adverse reactions to such vaccine than the general population of potential recipients.

"(2)(A) The Secretary shall request the Institute of Medicine of the National Academy of

graph (1) under an arrangement by which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary.

"(B) If the Institute of Medicine is unwilling to conduct such study under such an arrangement, the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study.

"(C) The Institute of Medicine or other group or association conducting the study required by paragraph (1) shall conduct such studies in consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [section 300aa–19 of this title].

"(b) **Revision of guidelines.**—The Secretary shall periodically, but at least every 3 years after establishing guidelines under subsection (a), review and revise such guidelines after notice and opportunity for public hearing and consideration of all relevant medical and scientific information, unless the Secretary finds that on the basis of all relevant information no revision of such guidelines is warranted and publishes such finding in the Federal Register.

"(c) **Factors affecting guidelines.**—Guidelines under subsection (a) shall take into account—

"(1) the risk to potential recipients of the vaccines with respect to which the guidelines are established,

"(2) the medical and other characteristics of such potential recipients, and

"(3) the risks to the public of not having such vaccines administered.

"(d) **Dissemination.**—The Secretary shall widely disseminate the guidelines established under subsection (a) to—

"(1) physicians and other health care providers,

"(2) professional health associations,

"(3) State and local governments and agencies, and

"(4) other relevant entities."

Review of Warnings, Use Instructions and Precautionary Information Issued by Vaccine Manufacturers. Section 314 of Pub.L. 99-660 provided that: "Not later than 1 year after the effective date of this title [see section 323 of Pub.L. 99-660, set out as a note under this section] and after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [section 300aa-19 of this title] and with other appropriate entities, the Secretary of Health and Human Services shall review the warnings, use instructions, and precautionary information presently issued by manufacturers of vaccines set forth in the Vaccine Injury Table set out in section 2114 of the Public Health Service Act [section 300aa-14 of this title] and shall by rule determine whether such warnings, instructions, and information adequately warn health care providers of the nature and extent of dangers posed by such vaccines. If the Secretary determines that any such warning, instruction, or information is inadequate for such purpose in any respect, the Secretary shall at the same time require the manufacturers to revise and reissue such warning, instruction, or information as expeditiously as practical, but not later than 18 months after the effective date of this title."

Waiver of Paperwork Reduction. Section 321 of Pub.L. 99-660 provided that: "Chapter 35 of title 44, United States Code [44 U.S.C.A. § 3501 et seq.] shall not apply to information required for purposes of carrying out this title [Title III of Pub.L. 99-660, see Short Title of 1986 Amendment note set out under section 201 of this title] and implementing the amendments made by this title."

Nonseverability. Section 322 of Pub.L. 99-660 provided that: "If any provision of this title [Title III of Pub.L. 99-660, see Short Title of 1986 Amendment note set out under section 201 of this title] or the application of any provision of this title to any person or circumstance is held invalid by reason of a violation of the Constitution, the entire title shall be considered invalid."

Legislative History. For legislative history and purpose of Pub.L. 99-660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–2. Program responsibilities

(a) The Director of the Program shall have the following responsibilities:

(1) Vaccine research

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, coordinate and provide direction for research carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development on means to induce human immunity against naturally occurring infectious diseases and to prevent adverse reactions to vaccines.

(2) Vaccine development

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, coordinate and provide direction for activities carried out in or through the National Institutes of Health, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development to develop the techniques needed to produce safe and effective vaccines.

(3) Safety and efficacy testing of vaccines

The Director of the Program shall, through the plan issued under section

300aa–3 of this title, coordinate and provide direction for testing of vaccines carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development.

(4) Licensing of vaccine manufacturers and vaccines

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, coordinate and provide direction for the allocation of resources in the implementation of the licensing program under section 263a of this title.

(5) Production and procurement of vaccines

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, ensure that the governmental and non-governmental production and procurement of safe and effective vaccines by the Public Health Service, the Department of Defense, and the Agency for International Development meet the needs of the United States population and fulfill commitments of the United States to prevent human infectious diseases in other countries.

(6) Distribution and use of vaccines

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, coordinate and provide direction to the Centers for Disease Control and assistance to States, localities, and health practitioners in the distribution and use of vaccines, including efforts to encourage public acceptance of immunizations and to make health practitioners and the public aware of potential adverse reactions and contraindications to vaccines.

(7) Evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, coordinate and provide direction to the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the National Center for Health Statistics, the National Center for Health Services Research and Health Care Technology Assessment, and the Health Care Financing Administration in monitoring the need for and the effectiveness and adverse effects of vaccines and immunization activities.

(8) Coordinating governmental and non-governmental activities

The Director of the Program shall, through the plan issued under section 300aa–3 of this title, provide for the exchange of information between Federal agencies involved in the implementation of the Program and non-governmental entities engaged in the development and production of vaccines and in vaccine research and encourage the investment of non-governmental resources complementary to the governmental activities under the Program.

(9) Funding of federal agencies

The Director of the Program shall make available to Federal agencies involved in the implementation of the plan issued under section 300aa–3 of this title funds appropriated under section 300aa–6 of this title to supplement the funds otherwise available to such agencies for activities under the plan.

(b) In carrying out subsection (a) of this section and in preparing the plan under section 300aa–3 of this title, the Director shall consult with all Federal agencies involved in research on and development, testing, licensing, production, procurement, distribution, and use of vaccines.

(July 1, 1944, c. 373, Title XXI, § 2102, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3756.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–3. Plan

The Director of the Program shall prepare and issue a plan for the implementation of the responsibilities of the Director under section 300aa–2 of this title. The plan shall establish priorities in research and the development, testing, licensing, production, procurement, distribution, and effective use of vaccines, describe an optimal use

of resources to carry out such priorities, and describe how each of the various departments and agencies will carry out their vaccine functions in consultation and coordination with the Program and in conformity with such priorities. The first plan under this section shall be prepared not later than January 1, 1987, and shall be revised not later than January 1 of each succeeding year.

(July 1, 1944, c. 373, Title XXI, § 2103, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3757.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–4. Report

The Director shall report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate not later than January 1, 1988, and annually thereafter on the implementation of the Program and the plan prepared under section 300aa–3 of this title.

(July 1, 1944, c. 373, Title XXI, § 2104, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3757.)

Study of Impact on Supply of Vaccines. Section 316 of Pub.L. 99–660 provided that: "On June 30, 1987, and on June 30 of each second year thereafter, the Secretary of Health and Human Services shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate—

"(1) an assessment of the impact of the amendments made by this title on the supply of vaccines listed in the Vaccine Injury Table under section 2114 of the Public Health Service Act [42 U.S.C.A. § 300aa–14], and

"(2) an assessment of the ability of the administrators of vaccines (including public clinics and private administrators) to provide such vaccines to children."

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–5. National Vaccine Advisory Committee

(a) There is established the National Vaccine Advisory Committee. The members of the Committee shall be appointed by the Director of the Program, in consultation with the National Academy of Sciences, from among individuals who are engaged in vaccine research or the manufacture of vaccines or who are physicians, members of parent organizations concerned with immunizations, or representatives of State or local health agencies or public health organizations.

(b) The Committee shall—

(1) study and recommend ways to encourage the availability of an adequate supply of safe and effective vaccination products in the States,

(2) recommend research priorities and other measures the Director of the Program should take to enhance the safety and efficacy of vaccines,

(3) advise the Director of the Program in the implementation of sections 300aa–2, 300aa–3, and 300aa–4 of this title, and

(4) identify annually for the Director of the Program the most important areas of government and non-government cooperation that should be considered in implementing sections 300aa–2, 300aa–3, and 300aa–4 of this title.

(July 1, 1944, c. 373, Title XXI, § 2105, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3758.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–6. Authorization of appropriations

(a) To carry out this part other than section 300aa–2(9) of this title there are authorized to be appropriated $2,000,000 for fiscal year 1987, $2,500,000 for fiscal year 1988, $3,000,000 for fiscal year 1989, $3,500,000 for fiscal year 1990, $4,000,000 for fiscal year 1991.

(b) To carry out section 300aa–2(9) of this title there are authorized to be

$25,000,000 for fiscal year 1989, $27,500,000 for fiscal year 1990, $30,000,000 for fiscal year 1991.

(July 1, 1944, c. 373, Title XXI, § 2106, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3758.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

PART 2—NATIONAL VACCINE INJURY COMPENSATION PROGRAM

Subpart A—Program Requirements

§ 300aa–10. Establishment of program

(a) Program established

There is established the National Vaccine Injury Compensation Program to be administered by the Secretary under which compensation may be paid for a vaccine-related injury or death.

(b) Attorney's obligation

It shall be the ethical obligation of any attorney who is consulted by an individual with respect to a vaccine-related injury or death to advise such individual that compensation may be available under the program for such injury or death.

(July 1, 1944, c. 373, Title XXI, § 2110, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3758.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm. News, p. 6287.

§ 300aa–11. Petitions for compensation

(a) General rule

(1) A proceeding for compensation under the Program for a vaccine-related injury or death shall be initiated by service upon the Secretary and the filing of a petition with the United States district court for the district in which the petitioner resides or in which the injury or death occurred.

(2)(A) No person may bring a civil action for damages in an amount greater than $1,000 or in an unspecified amount against a vaccine manufacturer in a State or Federal court for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this part, and no such court may award damages in an amount greater than $1,000 in a civil action for damages for such a vaccine-related injury or death, unless—

(i) a petition has been filed, in accordance with section 300aa–16 of this title, under subsection (b) of this section for compensation under the Program for such injury or death,

(ii) a district court of the United States has issued a judgment under section 300aa–12 of this title on such petition, and

(iii) such person elects under section 300aa–21(a) of this title to file such an action.

(B) If a civil action which is barred under subparagraph (A) is filed in a State or Federal court, the court shall dismiss the action. If a petition is filed under this section with respect to the injury or death for which such civil action was brought, the date such dismissed action was filed shall, for purposes of the limitations of actions prescribed by section 300aa–16 of this title, be considered the date the petition was filed if the petition was filed within one year of the date of the dismissal of the civil action.

(3) No vaccine manufacturer may be made a party to a civil action (other than a civil action which may be brought under paragraph (2)) for damages for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle.

(4) If in a civil action brought against a vaccine manufacturer before the effective date of this part damages were denied for a vaccine-related injury or death or if such civil action was dismissed with prejudice, the person who brought such action may file a petition under subsection (b) of this section for such injury or death.

(5)(A) A plaintiff who on the effective date of this subtitle has pending a civil action for damages for a vaccine-related injury or death may, at any time within 2 years after the effective date of this part or before judgment, whichever occurs first, elect to withdraw such action without prejudice and file a petition under subsection (b) of this section for such injury or death.

(B) If a plaintiff who on the effective date of this part had pending a civil action for damages for a vaccine-related injury or death does not withdraw the action under subparagraph (A), such person may not file a petition under subsection (b) of this section for such injury or death.

(6) If a person brings a civil action after the effective date of this part for damages for a vaccine-related injury or death associated with the administration of a vaccine before the effective date of this part, such person may not file a petition under subsection (b) of this section for such injury or death.

(7) If in a civil action brought against a vaccine manufacturer for a vaccine-related injury or death damages are awarded under a judgment of a court or a settlement of such action, the person who brought such action may not file a petition under subsection (b) of this section for such injury or death.

(b) Petitioners

(1)(A) Except as provided in subparagraph (B), any person who has sustained a vaccine-related injury, the legal representative of such person if such person is a minor or is disabled, or the legal representative of any person who died as the result of the administration of a vaccine set forth in the Vaccine Injury Table may file a petition for compensation under the Program.

(B) No person may file a petition for a vaccine-related injury or death associated with a vaccine administered before the effective date of this part if compensation has been paid under this part for 3500 petitions for such injuries or deaths.

(2) Only one petition may be filed with respect to each administration of a vaccine.

(c) Petition content

A petition for compensation under the Program for a vaccine-related injury or death shall contain—

(1) an affidavit, and supporting documentation, demonstrating that the person who suffered such injury or who died—

(A) received a vaccine set forth in the Vaccine Injury Table or, if such person did not receive such a vaccine, contracted polio, directly or indirectly, from another person who received an oral polio vaccine,

(B)(i) if such person received a vaccine set forth in the Vaccine Injury Table—

(I) received the vaccine in the United States or in its trust territories,

(II) received the vaccine outside the United States or a trust territory and at the time of the vaccination such person was a citizen of the United States serving abroad as a member of the Armed Forces or otherwise as an employee of the United States or a dependent of such a citizen, or

(III) received the vaccine outside the United States or a trust territory and the vaccine was manufactured by a vaccine manufacturer located in the United States and such person returned to the United States not later than 6 months after the date of the vaccination,

(ii) if such person did not receive such a vaccine but contracted polio from another person who received an oral polio vaccine, was a citizen of the United States or a dependent of such a citizen,

(C)(i) sustained, or had significantly aggravated, any illness, disability, injury, or condition set forth in the Vaccine Injury Table in association with the vaccine referred to in subparagraph (A) or died from the administration of such vaccine, and the first symptom or manifestation of the onset or of the significant aggravation of any such illness, disability, injury, or condition or the death occurred within the time period after vaccine administration set forth in the Vaccine Injury Table, or

(ii)(I) sustained, or had significantly aggravated, any illness, disability, injury, or condition not set forth in the Vaccine Injury Table but which was caused by a vaccine referred to in subparagraph (A), or

(II) sustained, or had significantly aggravated, any illness, disability, injury, or condition set forth in the Vaccine Injury Table the first symptom or manifestation of the onset or significant aggravation of which did not occur within the time period set forth in the Table but which was caused by a vaccine referred to in subparagraph (A),

(D)(i) suffered the residual effects or complications of such illness, disability, injury, or condition for more than 1 year after the administration of the vaccine, (ii) incurred unreimbursable expenses due in whole or in part to such illness, disability, injury, or condition in an amount greater than $1,000, or (iii) died from the administration of the vaccine, and

(E) has not previously collected an award or settlement of a civil action for damages for such vaccine-related injury or death,

(2) all available relevant medical records (including autopsy reports, if any) relating to the person who suffered such injury or who died from the administration of the vaccine and an identification of any unavailable records known to the petitioner and the reasons for their unavailability, and

(3) appropriate assessments, evaluations, and prognoses and such other records and documents as are reasonably necessary for the determination of the amount of compensation to be paid to, or on behalf of, the person who suffered such injury or who died from the administration of the vaccine.

(July 1, 1944, c. 373, Title XXI, § 2111, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3758.)

References in Text. The effective date of this part, referred to in subsec. (a)(2)(A), (3), (4), (5)(A), (B), (6), (b)(1)(B), is the effective date of part II of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm. News, p. 6287.

§ 300aa–12. Court jurisdiction

(a) General rule

The district courts of the United States shall have jurisdiction (1) over proceedings to determine if a petitioner under section 300aa–11 of this title is entitled to compensation under the Program and the amount of such compensation, and (2) to issue and enforce such orders as the courts deem necessary to assure the prompt payment of any compensation awarded.

(b) Parties

(1) The Secretary shall be named as the respondent in all proceedings brought by the filing of a petition under section 300aa–11(b) of this title. Except as provided in paragraph (2), no other person may intervene in any such proceeding.

(2) Within 30 days after the Secretary receives service of any petition filed under section 300aa–11 of this title the Secretary shall publish notice of such petition in the Federal Register. The special master designated with respect to such petition under subsection (c) of this section shall afford all interested persons an opportunity to submit relevant, written information—

(A) relating to the existence of the evidence described in section 300aa–13(a)(1)(B) of this title, or

(B) relating to any allegation in a petition with respect to the matters described in section 300aa–11(c)(1)(C)(ii) of this title.

(c) Special masters

(1) Following receipt of a petition under subsection (a) of this section, the district court of the United States in which the petition is filed shall designate a special master to carry out the functions authorized by paragraph (2).

(2) A special master shall serve as an adjunct to the court and may—

(A) require such evidence as may be appropriate for the preparation of proposed findings of fact and conclusions of law with respect to whether compensation is to be provided under the Program and the amount of any such compensation,

(B) require the submission of such information as may be reasonable and necessary to determine if the petitioner is entitled to compensation,

(C) require the testimony of any person and the production of any document as may be reasonable and necessary to determine if the petitioner is entitled to compensation,

(D) conduct such hearings as may be appropriate, and

(E) prepare and submit to the court proposed findings of fact and conclusions of law.

Information submitted to a special master in a proceeding on a petition may not be disclosed to a person who is not a party to the proceeding without the express, written consent of the person who submitted the information. There may be no discovery in a proceeding on a petition other than the discovery required under this paragraph.

(d) Action by the court

(1) Upon objection by the petitioner or respondent to the proposed findings of fact or conclusions of law prepared by the special master or upon the court's own motion, the court shall undertake a review of the record of the proceedings and may thereafter make a de novo determination of any matter and issue its judgment accordingly, including findings of fact and conclusions of law, or remand for further proceedings.

(2) If no objection is filed under paragraph (1) or if the court does not choose to review the proceeding, the court shall adopt the proposed findings of fact and conclusions of law of the special master as its own and render judgment thereon.

(3) The court shall render its judgment on any petition filed under the Program as expeditiously as practicable but not later than 365 days after the date on which the petition was filed.

(e) Administration of award

The Program shall administer the payments of such compensation. The Program shall audit the payments of compensation under a judgment. A petitioner awarded compensation shall notify the Program of any changes which significantly affect the compensation to be paid.

(f) Revision of award

(1) If the court issues a judgment awarding to a petitioner compensation described in section 300aa–15(a)(1)(A) of this title for unreimbursable expenses and the compensation is insufficient to meet such expenses, such petitioner may petition the court to (A) review such award, and (B) increase the award to make it sufficient to meet such expenses or amend the periodic payment schedule established under section 300aa–15 of this title, or both.

(2) If an audit conducted under subsection (e) of this section discloses the improper use of compensation awarded under a judgment or the termination of a need for an item of compensation, the Program shall petition the court which awarded the compensation to make an appropriate revision in the compensation.

(g) Appeals

The findings of fact and conclusions of law of a district court of the United States on a petition shall be final determinations of the matters involved, except that the Secretary or any petitioner aggrieved by the findings or conclusions of the court may obtain review of the judgment of the court in the United States court of appeals for the circuit in which the court is located upon petition filed with such court of appeals.

(July 1, 1944, c. 373, Title XXI, § 2112, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3761.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm. News, p. 6287.

§ 300aa–13. Determination of eligibility and compensation

(a) General rule

(1) Compensation shall be awarded under the Program to a petitioner if the court finds on the record as a whole—

(A) that the petitioner has demonstrated by a preponderance of the evidence the matters required in the petition by section 300aa–11(c)(1) of this title, and

(B) that there is not a preponderance of the evidence that the illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition.

The court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion.

(2) For purposes of paragraph (1), the term "factors unrelated to the administration of the vaccine"—

(A) does not include any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness, or condition, and

(B) may, as documented by the petitioner's evidence or other material in the record, include infection, toxins, trauma (including birth trauma and related anoxia), or metabolic disturbances which have no known relation to the vaccine involved, but which in the particular case are shown to have been the agent or agents principally responsible for causing the petitioner's illness, disability, injury, condition, or death.

(b) Matters to be considered

(1) In determining whether to award compensation to a petitioner under the Program, the court shall consider, in addition to all other relevant medical and scientific evidence contained in the record—

(A) any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death, and

(B) the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions.

Any such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the court. In evaluating the weight to be afforded to any such diagnosis, conclusion, judgment, test result, report, or summary, the court shall consider the entire record and the course of the injury, disability, illness, or condition until the date of the judgment of the court.

(2) The court may find the first symptom or manifestation of onset or significant aggravation of an injury, disability, illness, condition, or death described in a petition occurred within the time period described in the Vaccine Injury Table even though the occurrence of such symptom or manifestation was not recorded or was incorrectly recorded as having occurred outside such period. Such a finding may be made only upon demonstration by a preponderance of the evidence that the onset or significant aggravation of the injury, disability, illness, condition, or death described in the petition did in fact occur within the time period described in the Vaccine Injury Table.

(c) Record defined

For purposes of this section, the term "record" means the record established by a district court of the United States in a proceeding on a petition filed under section 300aa–11 of this title.

(July 1, 1944, c. 373, Title XXI, § 2113, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3763.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code

§ 300aa–14. Vaccine injury table

(a) Initial table

The following is a table of vaccines, the injuries, disabilities, illnesses, conditions, and deaths resulting from the administration of such vaccines, and the time period in which the first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths is to occur after vaccine administration for purposes of receiving compensation under the Program:

VACCINE INJURY TABLE

	Illness, disability, injury, or condition covered:	Time period for first symptom or manifestation of onset or of significant aggravation after vaccine administration:
I.	DTP; P; DTP/Polio Combination; or Any Other Vaccine Containing Whole Cell Pertussis Bacteria, Extracted or Partial Cell Bacteria, or Specific Pertussis Antigen(s).	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)	3 days
	C. Shock-collapse or hypotonic-hyporesponsive collapse	3 days
	D. Residual seizure disorder in accordance with subsection (c)(2)	3 days
	E. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
II.	Measles, mumps, rubella, or any vaccine containing any of the foregoing as a component; DT; Td; or Tetanus Toxoid.	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)	15 days (for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component). 3 days (for DT, Td, or tetanus toxoid).
	C. Residual seizure disorder in accordance with subsection (c)(2)	15 days (for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component). 3 days (for DT, Td, or tetanus toxoid).
	D. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
III.	Polio Vaccines (other than Inactivated Polio Vaccine).	
	A. Paralytic polio	
	—In a non-immunodeficient recipient	30 days
	—In an immunodeficient recipient	6 months
	—In a vaccine-associated community case	Not applicable
	B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
IV.	Inactivated Polio Vaccine.	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable

(b) Qualifications and aids to interpretation

(1) A shock-collapse or a hypotonic-hyporesponsive collapse may be evidenced by indicia or symptoms such as decrease or loss of muscle tone, paralysis (partial or complete, hemiplegia or hemiparesis, loss of color or turning pale white or blue, unresponsiveness to environmental stimuli, depression of consciousness, loss of consciousness, prolonged sleeping with difficulty arousing, or cardiovascular or respiratory arrest.

(2) A petitioner may be considered to have suffered a residual seizure disorder if the petitioner did not suffer a seizure or convulsion unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit before the first seizure or convulsion after the administration of the vaccine involved and if—

(A) in the case of a measles, mumps, or rubella vaccine or any combination of such vaccines, the first seizure or convulsion occurred within 15 days after administration of the vaccine and 2 or more seizures or convulsions occurred within 1 year after the administration of the vaccine which were unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit, and

(B) in the case of any other vaccine, the first seizure or convulsion occurred within 3 days after administration of the vaccine and 2 or more seizures or convulsions occurred within 1 year after the administration of the vaccine which were unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit.

(3)(A) The term "encephalopathy" means any significant acquired abnormality of, or injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurologic signs, increased intracranial pressure, or changes lasting at least 6 hours in level of consciousness, with or without convulsions. The neurological signs and symptoms of encephalopathy may be temporary with complete recovery, or may result in various degrees of permanent impairment. Signs and symptoms such as high pitched and unusual screaming, persistent unconsolable crying, and bulging fontanel are compatible with an encephalopathy, but in and of themselves are not conclusive evidence of encephalopathy. Encephalopathy usually can be documented by slow wave activity on an electroencephalogram.

(B) If in a proceeding on a petition it is shown by a preponderance of the evidence that an encephalopathy was caused by infection, toxins, trauma, or metabolic disturbances the encephalopathy shall not be considered to be a condition set forth in the table. If at the time a judgment is entered on a petition filed under section 300aa–11(b) of this title for a vaccine-related injury or death it is not possible to determine the cause, by a preponderance of the evidence, of an encephalopathy, the encephalopathy shall be considered to be a condition set forth in the table. In determining whether or not an encephalopathy is a condition set forth in the table, the court shall consider the entire medical record.

(4) For purposes of paragraphs (2) and (3), the terms "seizure" and "convulsion" include grand mal, petit mal, absence, myoclonic, tonic-clonic, and focal motor seizures and signs. If a provision of the table to which paragraph (1), (2), (3), or (4) applies is revised under subsection (c) or (d) of this section, such paragraph shall not apply to such provision after the effective date of the revision unless the revision specifies that such paragraph is to continue to apply.

(c) Administrative revision of the table

(1) The Secretary may promulgate regulations to modify in accordance with paragraph (3) the Vaccine Injury Table. In promulgating such regulations, the Secretary shall provide for notice and opportunity for a public hearing and at least 180 days of public comment.

(2) Any person (including the Advisory Commission on Childhood Vaccines) may petition the Secretary to propose regulations to amend the Vaccine Injury Table. Unless clearly frivolous, or initiated by the Commission, any such petition shall be referred to the Commission for its recommendations. Following—

(A) receipt of any recommendation of the Commission, or

(B) 180 days after the date of the referral to the Commission

whichever occurs first, the Secretary shall conduct a rulemaking proceeding on the matters proposed in the petition or publish in the Federal Register a statement of reasons for not conducting such proceeding.

(3) A modification of the Vaccine Injury Table under paragraph (1) may add to, or delete from, the list of injuries, disabilities, illnesses, conditions, and deaths for which compensation may be provided or may change the time periods for the first symptom or manifestation of the onset or the significant aggravation of any such injury, disability, illness, condition, or death.

(4) Any modification under paragraph (1) of the Vaccine Injury Table shall apply only with respect to petitions for compensation under the Program which are filed after the effective date of such regulation.

(d) Role of commission

Except with respect to a regulation recommended by the Advisory Commission on Childhood Vaccines, the Secretary may not propose a regulation under subsection (c) of this section or any revision thereof, unless the Secretary has first provided to the Commission a copy of the proposed regulation or revision, requested recommendations and comments by the Commission, and afforded the Commission at least 90 days to make such recommendations.

(e) Recommendation

The Secretary may recommend to Congress revisions of the table to change the vaccines covered by the table.

(July 1, 1944, c. 373, Title XXI, § 2114, as added Nov. 14, 1986, Pub.L. 99-660, Title III, § 311(a), 100 Stat. 3764.)

Legislative History. For legislative history and purpose of Pub.L. 99-660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa-15. Compensation

(a) General rule

Compensation awarded under the Program to a petitioner under section 300aa-11 of this title for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this part shall include the following:

(1)(A) Actual unreimbursable expenses incurred from the date of the judgment awarding such expenses and reasonable projected unreimbursable expenses which—

(i) result from the vaccine-related injury for which the petitioner seeks compensation,

(ii) have been or will be incurred by or on behalf of the person who suffered such injury, and

(iii)(I) have been or will be for diagnosis and medical or other remedial care determined to be reasonably necessary, or

(II) have been or will be for rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary.

The amount of unreimbursable expenses which may be recovered under this subparagraph shall be limited to the amount in excess of the amount set forth in section 300aa-11(e)(1)(D)(ii) of this title.

(B) Subject to section 300aa-16(a)(2) of this title, actual unreimbursable expenses incurred before the date of the judgment awarding such expenses which—

(i) resulted from the vaccine-related injury for which the petitioner seeks compensation,

(ii) were incurred by or on behalf of the person who suffered such injury,

(iii) were for diagnosis, medical or other remedial care, rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary.

The amount of unreimbursable expenses which may be recovered under this subparagraph shall be limited to the amount in excess of the amount set forth in section 300aa-11(e)(1)(D)(ii) of this title.

(2) In the event of a vaccine-related death, an award of $250,000 for the estate of the deceased.

(3)(A) In the case of any person who has sustained a vaccine-related injury after attaining the age of 18 and whose earning capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded, compensation for actual and anticipated loss of earnings determined in accordance with generally recognized actuarial principles and projections.

(B) In the case of any person who has sustained a vaccine-related injury before attaining the age of 18 and whose earning capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded and whose vaccine-related injury is of sufficient severity to permit reasonable anticipation that such person is likely to suffer impaired earning capacity at 18 and beyond, compensation after attaining the age of 18 for loss of earnings determined on the basis of the average gross weekly earnings of workers in the private, non-farm sector, less appropriate taxes and the average cost of a health insurance policy, as determined by the Secretary.

(4) For actual and projected pain and suffering and emotional distress from the vaccine-related injury, an award not to exceed $250,000.

Payments for projected expenses shall be paid on a periodic basis (but no payment may be made for a period in excess of 1 year). Payments for pain and suffering and emotional distress and incurred expenses may be paid in a lump sum.

(b) Vaccines administered before the effective date

Compensation awarded under the Program to a petitioner under section 300aa-11 of this title for a vaccine-related injury or death associated with the administration of a vaccine before the effective date of this part shall only include the compensation described in paragraphs (1)(A) and (2) of subsection (a) of this section.

(c) Residential and custodial care and service

The amount of any compensation for residential and custodial care and service expenses under subsection (a)(1) of this section shall be sufficient to enable the compensated person to remain living at home.

(d) Types of compensation prohibited

Compensation awarded under the Program may not include the following:

(1) Punitive or exemplary damages.

(2) Except with respect to compensation payments under paragraphs (2) and (3) of subsection (a) of this section, compensation for other than the health, education, or welfare of the person who suffered the vaccine-related injury with respect to which the compensation is paid.

(e) Attorneys' fees

(1) The judgment of a court on a petition filed under section 300aa-11 of this title awarding compensation shall include an amount to cover—

(A) reasonable attorneys' fees, and

(B) other costs,

incurred in any proceeding on such petition. If the judgment of a court on such a petition does not award compensation, the court may include in the judgment an amount to cover petitioner's reasonable attorneys' fees and other costs incurred in any proceeding on such petition if the court determines that the civil action was brought in good faith and there was a reasonable basis for the claim for which the civil action was brought

(2) If the petitioner, before the effective date of this part, filed a civil action for damages for any vaccine-related injury or death for which compensation may be awarded under the Program, and elected under section 300aa-11(a)(4) of this title to withdraw such action and to file a petition for compensation under the Program, the judgment of the court on such petition may include an amount limited to the costs and expenses incurred by the petitioner and the attorney of the petitioner before the effective date of this part in preparing, filing, and prosecuting such civil action (including the reasonable value of the attorney's time if the civil action was filed under contingent fee arrangements).

(3) No attorney may charge any fee for services in connection with a petition filed under section 300aa-11 of this title which is in addition to any amount included under paragraph (1) in a judgment on such petition.

(f) Payment of compensation

(1) Except as provided in paragraph (2), no compensation may be paid until an election has been made, or has been deemed to have been made, under section 300aa-21(a) of this title to receive compensation.

(2) Compensation described in subsection (a)(1)(A)(iii) of this section shall be paid from the date of the judgment of the district court of the United States under section 300aa-12 of this title awarding the compensation. Such compensation may not be paid after an election under section 300aa-21(b) of this title to file a civil action for damages for the vaccine-related injury or death for which such compensation was awarded.

(3) Payments of compensation shall be exempt from reduction under any order issued under part C of the Balanced Budget and Emergency Deficit Control Act of 1985.

(f) Program not primarily liable.

Payment of compensation under the Program shall not be made for any item or service to the extent that payment has been made, or can reasonably be expected to be made, with respect to such item or service (1) under any State compensation program, under an insurance policy, or under any Federal or State health benefits program, or (2) by an entity which provides health services on a prepaid basis.

(g) Liability of health insurance carriers, prepaid health plans, and benefit providers

No policy of health insurance may make payment of benefits under the policy secondary to the payment of compensation under the Program and—

(1) no State, and

(2) no entity which provides health services on a prepaid basis or provides health benefits,

may make the provision of health services or health benefits secondary to the payment of compensation under the Program.

(July 1, 1944, c. 373, Title XXI, § 2115, as added Nov. 14, 1986, Pub.L. 99-660, Title III, § 311(a), 100 Stat. 3767.)

References in Text. The effective date of this part, referred to in subsec. (a), (b), (e)(2), is the effective date of part II of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation under such part 2, see section 323 of Pub.L. 99-660, set out as an Effective Date note under section 300aa-1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99-660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa-16. Limitations of actions

(a) General rule

In the case of—

(1) a vaccine set forth in the Vaccine Injury Table which is administered before the effective date of this subchapter, if a vaccine-related injury or death occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such injury or death after the

(2) a vaccine set forth in the Vaccine Injury Table which is administered after the effective date of this subchapter, if a vaccine-related injury occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such injury after the expiration of 36 months after the date of the occurrence of the first symptom or manifestation of onset or of the significant aggravation of such injury, and

(3) a vaccine set forth in the Vaccine Injury Table which is administered after the effective date of this subchapter, if a death occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such death after the expiration of 24 months from the date of the death and no such petition may be filed more than 48 months after the date of the occurrence of the first symptom or manifestation of onset or of the significant aggravation of the injury from which the death resulted.

(b) Effect of revised table

If at any time the Vaccine Injury Table is revised and the effect of such revision is to permit an individual who was not, before such revision, eligible to seek compensation under the Program, such person may file a petition for such compensation not later than 2 years after the effective date of the revision, except that no compensation may be provided under the Program with respect to a vaccine-related injury or death covered under the revision of the table if—

(1) the vaccine-related death occurred more than 8 years before the date of the revision of the table, or

(2) the vaccine-related injury occurred more than 8 years before the date of the revision of the table.

(c) State limitations of actions

If a petition is filed under section 300aa-11(b) of this title for a vaccine-related injury or death, limitations of actions under State law shall be stayed with respect to a civil action brought for such injury or death for the period beginning on the date the petition is filed and ending on the date a final judgment is entered on the petition.

(July 1, 1944, c. 373, Title XXI, § 2116, as added Nov. 14, 1986, Pub.L. 99-660, Title III, § 311(a), 100 Stat. 3769.)

References in Text. For effective date of this subchapter, referred to in subsec. (a)(1), (2), (3), see section 323 of Pub.L. 99-660, set out as an Effective Date note under section 300aa-1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99-660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa-17. Subrogation

(a) General rule

(1) Upon payment of compensation to any petitioner under the Program, the trust fund which has been established to provide such compensation shall be subrogated to all rights of the petitioner with respect to the vaccine-related injury or death for which compensation was paid, except that the trust fund may not recover under such rights an amount greater than the amount of compensation paid to the petitioner.

(2) In any case in which it deems such action appropriate, a district court of the United States may, after entry of a final judgment providing for compensation to be paid under section 300aa-15 of this title for a vaccine-related injury or death, refer the record of such proceeding to the Secretary and the Attorney General with such recommendation as the court deems appropriate with respect to the investigation or commencement of a civil action by the Secretary under paragraph (1).

(b) Disposition of amounts recovered

Amounts recovered under subsection (a) of this section shall be collected on behalf of, and deposited in, the trust fund which has been established to provide compensation under the Program.

(July 1, 1944, c. 373, Title XXI, § 2117, as added Nov. 14, 1986, Pub.L. 99-660, Title III, § 311(a), 100 Stat. 3770.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa–18. Increase for inflation

The compensation under subsections (a)(2) and (a)(4) of section 300aa–15 of this title the civil penalty under section 300aa–27(b) of this title shall, effective December 1 of each year beginning 1 year after the effective date of this subchapter, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest 1/10 of 1 percent. For purposes of this section, the term "base quarter", as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

(July 1, 1944, c. 373, Title XXI, § 2118, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3771.)

References in Text. For the effective date of this subchapter, referred to in text, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.)

§ 300aa–19. Advisory Commission on Childhood Vaccines

(a) Establishment

There is established the Advisory Commission on Childhood Vaccines. The Commission shall be composed of:

(1) Nine members appointed by the Secretary as follows:

(A) Three members who are health professionals, who are not employees of the United States, and who have expertise in the health care of children, the epidemiology, etiology, and prevention of childhood diseases, and the adverse reactions associated with vaccines, of whom at least two shall be pediatricians.

(B) Three members from the general public, of whom at least two shall be legal representatives of children who have suffered a vaccine-related injury or death.

(C) Three members who are attorneys, of whom at least one shall be an attorney whose specialty includes representation of persons who have suffered a vaccine-related injury or death and of whom one shall be an attorney whose specialty includes representation of vaccine manufacturers.

(2) The Director of the National Institutes of Health, the Assistant Secretary for Health, the Director of the Centers for Disease Control, and the Commissioner of Food and Drugs (or the designees of such officials), each of whom shall be a nonvoting ex officio member.

The Secretary shall select members of the Commission within 90 days of the effective date of this part. The members of the Commission shall select a Chair from among the members.

(b) Term of office

Appointed members of the Commission shall be appointed for a term of office of 3 years, except that of the members first appointed, 3 shall be appointed for a term of 1 year, 3 shall be appointed for a term of 2 years, and 3 shall be appointed for a term of 3 years, as determined by the Secretary.

(c) Meetings

The Commission shall first meet within 60 days after all members of the Commission are appointed, and thereafter shall meet not less often than four times per year and at the call of the chair. A quorum for purposes of a meeting is 5. A decision at a meeting is to be made by a ballot of a majority of the voting members of the

(d) Compensation

Members of the Commission who are officers or employees of the Federal Government shall serve as members of the Commission without compensation in addition to that received in their regular public employment. Members of the Commission who are not officers or employees of the Federal Government shall be compensated at a rate not to exceed the daily equivalent of the rate in effect for grade GS–18 of the General Schedule for each day (including traveltime) they are engaged in the performance of their duties as members of the Commission. All members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703, Title 5, for employees serving intermittently.

(e) Staff

The Secretary shall provide the Commission with such professional and clerical staff, such information, and the services of such consultants as may be necessary to assist the Commission in carrying out effectively its functions under this section.

(f) Functions

The Commission shall—

(1) advise the Secretary on the implementation of the Program,

(2) on its own initiative or as the result of the filing of a petition, recommend changes in the Vaccine Injury Table,

(3) advise the Secretary in implementing the Secretary's responsibilities under section 300aa–27 of this title regarding the need for childhood vaccination products that result in fewer or no significant adverse reactions,

(4) survey Federal, State, and local programs and activities relating to the gathering of information on injuries associated with the administration of childhood vaccines, including the adverse reaction reporting requirements of section 300aa–25(b) of this title, and advise the Secretary on means to obtain, compile, publish, and use credible data related to the frequency and severity of adverse reactions associated with childhood vaccines, and

(5) recommend to the Director of the National Vaccine Program research related to vaccine injuries which should be conducted to carry out this part.

(July 1, 1944, c. 373, Title XXI, § 2119, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3771.)

References in Text. The effective date of this part, referred to in subsec. (a) is the effective date of part II of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

Subpart B—Additional Remedies

§ 300aa–21. Authority to bring actions

(a) Election

After the judgment of a district court of the United States under section 300aa–11 of this title on a petition filed for compensation under the Program for a vaccine-related injury or death has become final, the person who filed the petition shall file with the court—

(1) if the judgment awarded compensation, an election in writing to receive the compensation or to file a civil action for damages for such injury or death, or

(2) if the judgment did not award compensation, an election in writing to accept the judgment or to file a civil action for damages for such injury or death.

An election shall be filed under this subsection not later than 90 days after the date of the entry of the court's judgment with respect to which the election is to be made. If a person required to file an election with a court under this subsection does not file the election within the time prescribed for filing the election, such person shall be deemed to have filed an election to accept the judgment of the court. If a person elects to receive compensation under a judgment of a court or is deemed to have

accepted the judgment of a court, such person may not bring or maintain a civil action for damages against a vaccine manufacturer for the vaccine-related injury or death for which the judgment was entered.

(b) Limitations of actions

A civil action for damages arising from a vaccine-related injury or death for which a petition was filed under section 300aa–11 of this title shall, except as provided in section 300aa–16(b) of this title, be brought within the period prescribed by limitations of actions under State law applicable to such civil action.

(July 1, 1944, c. 373, Title XXI, § 2121, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3772.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–22. Standards of responsibility

(a) General rule

Except as provided in subsections (b), (c), and (e) of this section State law shall apply to a civil action brought for damages for a vaccine-related injury or death.

(b) Unavoidable adverse side effects; warnings

(1) No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this part if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.

(2) For purposes of paragraph (1), a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with all requirements under the Federal Food, Drug, and Cosmetic Act and section 262 of this title (including regulations issued under such provisions) applicable to the vaccine and related to vaccine-related injury or death for which the civil action was brought unless the plaintiff shows—

(A) that the manufacturer engaged in the conduct set forth in subparagraph (A) or (B) of section 300aa–23(d)(2) of this title, or

(B) by clear and convincing evidence that the manufacturer failed to exercise due care notwithstanding its compliance with such Act and section (and regulations issued under such provisions).

(c) Direct warnings

No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this part solely due to the manufacturer's failure to provide direct warnings to the injured party (or the injured party's legal representative) of the potential dangers resulting from the administration of the vaccine manufactured by the manufacturer.

(d) Construction

The standards of responsibility prescribed by this section are not to be construed as authorizing a person who brought a civil action for damages against a vaccine manufacturer for a vaccine-related injury or death in which damages were denied or which was dismissed with prejudice to bring a new civil action against such manufacturer for such injury or death.

(e) Preemption

No State may establish or enforce a law which prohibits an individual from bringing a civil action against a vaccine manufacturer for damages for a vaccine-related injury or death if such civil action is not barred by this part.

(July 1, 1944, c. 373, Title XXI, § 2122, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3773.)

References in Text. The effective date of this part, referred to in subsecs. (b)(1) and (c), is the effective date of part II of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–23. Trial

(a) General rule

A civil action against a vaccine manufacturer for damages for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this part which is not barred by section 300aa–11(a)(2) of this title shall be tried in three stages.

(b) Liability

The first stage of such a civil action shall be held to determine if a vaccine manufacturer is liable under section 300aa–22 of this title.

(c) General damages

The second stage of such a civil action shall be held to determine the amount of damages (other than punitive damages) a vaccine manufacturer found to be liable under section 300aa–22 of this title shall be required to pay.

(d) Punitive damages

(1) If sought by the plaintiff, the third stage of such an action shall be held to determine the amount of punitive damages a vaccine manufacturer found to be liable under section 300aa–22 of this title shall be required to pay.

(2) If in such an action the manufacturer shows that it complied, in all material respects, with all requirements under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act applicable to the vaccine and related to the vaccine injury or death with respect to which the action was brought, the manufacturer shall not be held liable for punitive damages unless the manufacturer engaged in—

(A) fraud or intentional and wrongful withholding of information from the Secretary during any phase of a proceeding for approval of the vaccine under section 262 of this title,

(B) intentional and wrongful withholding of information relating to the safety or efficacy of the vaccine after its approval, or

(C) other criminal or illegal activity relating to the safety and effectiveness of vaccines,

which activity related to the vaccine-related injury or death for which the civil action was brought.

(e) Evidence

In any stage of a civil action, the Vaccine Injury Table, any finding of a district court of the United States or a master appointed by such court in a proceeding on a petition filed under section 300aa–11 of this title and the final judgment of a district court of the United States on such a petition shall not be admissible.

(July 1, 1944, c. 373, Title XXI, § 2123, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3774.)

References in Text. The effective date of this part, referred to in subsec. (a), is the effective date of part II of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

PART C—ASSURING A SAFER CHILDHOOD VACCINATION PROGRAM IN THE UNITED STATES

§ 300aa–25. Recording and reporting of information

(a) General rule

Each health care provider who administers a vaccine set forth in the Vaccine Injury Table to any person shall record, or ensure that there is recorded, in such person's permanent medical record (or in a permanent office log or file to which a legal representative shall have access upon request) with respect to each such vaccine—

(1) the date of administration of the vaccine,

(2) the vaccine manufacturer and lot number of the vaccine,

(3) the name and address and, if appropriate, the title of the health care provider administering the vaccine, and

(4) any other identifying information on the vaccine required pursuant to regulations promulgated by the Secretary.

(b) Reporting

(1) Each health care provider and vaccine manufacturer shall report to the Secretary—

(A) the occurrence of any event set forth in the Vaccine Injury Table, including the events set forth in section 300aa–14(b) of this title which occur within 7 days of the administration of any vaccine set forth in the Table or within such longer period as is specified in the Table or section,

(B) the occurrence of any contraindicating reaction to a vaccine which is specified in the manufacturer's package insert, and

(C) such other matters as the Secretary may by regulation require.

Reports of the matters referred to in subparagraphs (A) and (B) shall be made beginning 90 days after the effective date of this part. The Secretary shall publish in the Federal Register as soon as practicable after such date a notice of the reporting requirement.

(2) A report under paragraph (1) respecting a vaccine shall include the time periods after the administration of such vaccine within which vaccine-related illnesses, disabilities, injuries, or conditions, the symptoms and manifestations of such illnesses, disabilities, injuries, or conditions, or deaths occur, and the manufacturer and lot number of the vaccine.

(3) The Secretary shall issue the regulations referred to in paragraph (1)(C) within 180 days of the effective date of this part.

(c) Release of information

(1) Information which is in the possession of the Federal Government and State and local governments under this section and which may identify an individual shall not be made available under section 552 of Title 5, or otherwise, to any person except—

(A) the person who received the vaccine, or

(B) the legal representative of such person.

(2) For purposes of paragraph (1), the term "information which may identify an individual" shall be limited to the name, street address, and telephone number of the person who received the vaccine and of that person's legal representative and the medical records of such person relating to the administration of the vaccine, and shall not include the locality and State of vaccine administration, the name of the health care provider who administered the vaccine, the date of the vaccination, or information concerning any reported illness, disability, injury, or condition resulting from the administration of the vaccine, any symptom or manifestation of such illness, disability, injury, or condition, or death resulting from the administration of the vaccine.

(3) Except as provided in paragraph (1), all information reported under this section shall be available to the public.

(July 1, 1944, c. 373, Title XXI, § 2125, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a),

References in Text. The effective date of this part, referred to in subsec. (b)(1), (2), is the effective date of part II of subchapter XIX of this chapter which shall become effective on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S.Code Cong. and Adm.News, p. 6287.

§ 300aa–26. Vaccine information

(a) General rule

Not later than 1 year after the effective date of this part, the Secretary shall develop and disseminate vaccine information materials for distribution by health care providers to the legal representatives of any child receiving a vaccine set forth in the Vaccine Injury Table. Such materials shall be published in the Federal Register and may be revised.

(b) Development and revision of materials

Such materials shall be developed or revised by rule—

(1) after notice to the public, opportunity for a public hearing, and 90 days of comment thereon, and

(2) in consultation with the Advisory Commission on Childhood Vaccines, appropriate health care providers and parent organizations, the Centers for Disease Control, and the Food and Drug Administration.

(c) Information requirements

The information in such materials shall be presented in understandable terms and shall include—

(1) the frequency, severity, and potential long-term effects of the disease to be prevented by the vaccine,

(2) the symptoms or reactions to the vaccine which, if they occur, should be brought to the immediate attention of the health care provider,

(3) precautionary measures legal representatives should take to reduce the risk of any major adverse reactions to the vaccine that may occur,

(4) early warning signs or symptoms to which legal representatives should be alert as possible precursors to such major adverse reactions,

(5) a description of the manner in which legal representatives should monitor such major adverse reactions, including a form on which reactions can be recorded to assist legal representatives in reporting information to appropriate authorities,

(6) a specification of when, how, and to whom legal representatives should report any major adverse reaction,

(7) the contraindications to (and bases for delay of) the administration of the vaccine,

(8) an identification of the groups, categories, or characteristics of potential recipients of the vaccine who may be at significantly higher risk of major adverse reaction to the vaccine than the general population,

(9) a summary of relevant State and Federal laws concerning the vaccine, including information on—

(A) the number of vaccinations required for school attendance and the schedule recommended for such vaccinations, and

(B) the availability of the Program, and

(10) such other relevant information as may be determined by the Secretary.

(d) Health care provider duties

On and after a date determined by the Secretary which is—

(1) after the Secretary develops the information materials required by subsection (a), and

(2) not later than 6 months after the date such materials are published in the Federal Register,

each health care provider who administers a vaccine set forth in the Vaccine Injury Table shall provide to the legal representatives of any child to whom such provider intends to administer such vaccine a copy of the information materials developed

pursuant to subsection (a) of this section, or other written information which meets the requirements of this section. Such materials or other information shall be provided prior to the administration of such vaccine.

(July 1, 1944, c. 373, Title XXI, § 2126, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3775.)

References in Text. The effective date of this part, referred to in subsec. (a), is the effective date of part 2 of subchapter XIX of this chapter which shall become effective on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa–27. Mandate for safer childhood vaccines

(a) General rule

In the administration of this part and other pertinent laws under the jurisdiction of the Secretary, the Secretary shall—

(1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on the effective date of this part and promote the refinement of such vaccines, and

(2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.

(b) Report

Within 2 years after the effective date of this part, and periodically thereafter, the Secretary shall prepare and transmit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report describing the actions taken pursuant to subsection (a) of this section during the preceding 2-year period.

(July 1, 1944, c. 373, Title XXI, § 2127, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3777.

References in Text. The effective date of this part, referred to in subsecs. (a) and (b), is the effective date of part 2 of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa–28. Manufacturer recordkeeping and reporting

(a) General rule

Each vaccine manufacturer of a vaccine set forth in the Vaccine Injury Table or any other vaccine the administration of which is mandated by the law or regulations of any State, shall, with respect to each batch, lot, or other quantity manufactured or licensed after the effective date of this part—

(1) prepare and maintain records documenting the history of the manufacturing, processing, testing, repooling, and reworking of each batch, lot, or other quantity of such vaccine, including the identification of any significant problems encountered in the production, testing, or handling of such batch, lot, or other quantity,

(2) if a safety test on such batch, lot, or other quantity indicates a potential imminent or substantial public health hazard is presented, report to the Secretary within 24 hours of such safety test which the manufacturer (or manufacturer's representative) conducted, including the date of the test, the type of vaccine tested, the identity of the batch, lot, or other quantity tested, whether the batch, lot, or other quantity tested is the product of repooling or reworking of previous [illegible] the identity of the previous batches,

lots, or other quantities which were repooled or reworked), the complete test results, and the name and address of the person responsible for conducting the test,

(3) include with each such report a certification signed by a responsible corporate official that such report is true and complete, and

(4) prepare, maintain, and upon request submit to the Secretary product distribution records for each such vaccine by batch, lot, or other quantity number.

(b) Sanction

Any vaccine manufacturer who intentionally destroys, alters, falsifies, or conceals any record or report required under paragraph (1) or (2) of subsection (a) shall—

(1) be subject to a civil penalty of up to $100,000 per occurrence, or

(2) be fined $50,000 or imprisoned for not more than 1 year, or both.

Such penalty shall apply to the person who intentionally destroyed, altered, falsified, or concealed such record or report, to the person who directed that such record or report be destroyed, altered, falsified, or concealed, and to the vaccine manufacturer for which such person is an agent, employee, or representative. Each act of destruction, alteration, falsification, or concealment shall be treated as a separate occurrence.

(July 1, 1944, c. 373, Title XXI, § 2128, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3777.)

References in Text. The effective date of this part, referred to in subsec. (a), is the effective date of part 2 of subchapter XIX of this chapter which shall take effect on the effective date of a tax enacted after Nov. 14, 1986 to provide funds for compensation paid under such part 2, see section 323 of Pub.L. 99–660, set out as an Effective Date note under section 300aa–1 of this title.

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. Adm. News, p. 6287.

PART D—GENERAL PROVISIONS

§ 300aa–31. Citizen's actions

(a) General rule

Except as provided in subsection (b) of this section, any person may commence in a district court of the United States a civil action on such person's own behalf against the Secretary where there is alleged a failure of the Secretary to perform any act or duty under this part.

(b) Notice

No action may be commenced under subsection (a) of this section before the date which is 60 days after the person bringing the action has given written notice of intent to commence such action to the Secretary.

(c) Costs of litigation

The court, in issuing any final order in any action under this section, may award costs of litigation (including reasonable attorney and expert witness fees) to any party, whenever the court determines such award is appropriate.

(July 1, 1944, c. 373, Title XXI, § 2131, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3778.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa–32. Judicial review

A petition for review of a regulation under this part may be filed in a court of appeals of the United States within 60 days from the date of the promulgation of the regulation or after such date if such petition is based solely on grounds arising after such 60th day.

(July 1, 1944, c. 373, Title XXI, § 2132, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3778.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

§ 300aa–33. Definitions

For purposes of this part:

(1) The term "health care provider" means any licensed health care professional, organization, or institution, whether public or private (including Federal, State, and local departments, agencies, and instrumentalities) under whose authority a vaccine set forth in the Vaccine Injury Table is administered.

(2) The term "legal representative" means a parent or an individual who qualifies as a legal guardian under State law.

(3) The term "manufacturer" means any corporation, organization, or institution, whether public or private (including Federal, State, and local departments, agencies, and instrumentalities), which manufactures, imports, processes, or distributes under its label any vaccine set forth in the Vaccine Injury Table, except that, for purposes of section 300aa–28 of this title, such term shall include the manufacturer of any other vaccine covered by that section. The term "manufacture" means to manufacture, import, process, or distribute a vaccine.

(4) The term "significant aggravation" means any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health.

(5) The term "vaccine-related injury or death" means an illness, injury, condition, or death associated with one or more of the vaccines set forth in the Vaccine Injury Table, except that the term does not include an illness, injury, condition, or death associated with an adulterant or contaminant intentionally added to such a vaccine.

(6)(A) The term "Advisory Commission on Childhood Vaccines" means the Commission established under section 300aa–19 of this title.

(B) The term "Vaccine Injury Table" means the table set out in section 300aa–14 of this title.

(July 1, 1944, c. 373, Title XXI, § 2133, as added Nov. 14, 1986, Pub.L. 99–660, Title III, § 311(a), 100 Stat. 3778.)

Legislative History. For legislative history and purpose of Pub.L. 99–660, see 1986 U.S. Code Cong. and Adm. News, p. 6287.

SUBCHAPTER XX—REQUIREMENTS FOR CERTAIN GROUP HEALTH PLANS FOR CERTAIN STATE AND LOCAL EMPLOYEES

§ 300bb–1. State and local governmental group health plans must provide continuation coverage to certain individuals

(a) In general

In accordance with regulations which the Secretary shall prescribe, each group health plan that is maintained by any State that receives funds under this chapter, by any political subdivision of such a State, or by any agency or instrumentality of such a State or political subdivision, shall provide, in accordance with this subchapter, that each qualified beneficiary who would lose coverage under the plan as a result of a qualifying event is entitled, under the plan, to elect, within the election period, continuation coverage under the plan.

(b) Exception for certain plans

Subsection (a) of this section shall not apply to—

(1) any group health plan for any calendar year if all employers maintaining such plan normally employed fewer than 20 employees on a typical business day during the preceding calendar year, or

(2) any group health plan maintained for employees by the government of the District of Columbia or any territory or possession of the United States or any

Under regulations, rules similar to the rules of subsections (a) and (b) of section 52 of Title 26 (relating to employers under common control) shall apply for purposes of paragraph (1).

(July 1, 1944, c. 373, Title XXII, § 2201, as added Apr. 7, 1986, Pub.L. 99–272, Title X, § 10003(a), 100 Stat. 232.)

Effective Date. Section 10003(b) of Pub.L. 99–272 provided that:

"(1) General rule.—The amendments made by this section [enacting this subchapter and enacting a provision set out as a note under section 300bb–7 of this title] shall apply to plan years beginning on or after July 1, 1986.

"(2) Special rule for collective bargaining agreements.—In the case of a group health plan maintained pursuant to one or more collective bargaining agreements between employee representatives and one or more employers ratified before the date of the enactment of this Act [Apr. 7, 1986], the amendments made by this section shall not apply to plan years beginning before the later of—

"(A) the date on which the last of the collective bargaining agreements relating to the plan terminates (determined without regard to any extension thereof agreed to after the date of the enactment of this Act) [Apr. 7, 1986], or

"(B) January 1, 1987.

For purposes of subparagraph (A), any plan amendment made pursuant to a collective bargaining agreement relating to the plan which amends the plan solely to conform to any requirement added by this section shall not be treated as a termination of such collective bargaining agreement."

Legislative History. For legislative history and purpose of Pub.L. 99–272, see 1986 U.S.Code Cong. and Adm.News, p. 42.

§ 300bb–2. Continuation coverage

For purposes of section 300bb–1 of this title, the term "continuation coverage" means coverage under the plan which meets the following requirements:

(1) Type of benefit coverage

The coverage must consist of coverage which, as of the time the coverage is being provided, is identical to the coverage provided under the plan to similarly situated beneficiaries under the plan with respect to whom a qualifying event has not occurred. If coverage is modified under the plan for any group of similarly situated beneficiaries, such coverage shall also be modified in the same manner for all individuals who are qualified beneficiaries under the plan pursuant to this part in connection with such group.

(2) Period of coverage

The coverage must extend for at least the period beginning on the date of the qualifying event and ending not earlier than the earliest of the following:

(A) Maximum required period.—

(i) General rule for terminations and reduced hours.—In the case of a qualifying event described in section 300bb–3(2) of this title, except as provided in clause (ii), the date which is 18 months after the date of the qualifying event.

(ii) Special rule for multiple qualifying events.—If a qualifying event occurs during the 18 months after the date of a qualifying event described in section 300bb–3(2) of this title, the date which is 36 months after the date of the qualifying event described in section 300bb–3(2) of this title.

(iii) General rule for other qualifying events.—In the case of a qualifying event not described in section 300bb–3(2) of this title, the date which is 36 months after the date of the qualifying event.

(B) End of plan

The date on which the employer ceases to provide any group health plan to any employee.

(C) Failure to pay premium

The date on which coverage ceases under the plan by reason of a failure to make timely payment of any premium required under the plan with respect to the qualified beneficiary. The payment of any premium (other than any payment referred to in the last sentence of paragraph (3)) shall be considered to be timely if made within 30 days after the date due or within such longer period as applies to or under the plan.

ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
RESEARCH AGENCY

P.O. Box Y, State Capitol
Juneau, Alaska 99811-3100
Mail Stop 3100
(907) 465-3991

January 28, 1988

MEMORANDUM

TO: Representative Mike Navarre

FROM: Patricia Brawley
Legislative Analyst

RE: **Personal Exemption from Mandatory Immunization**
Research Request 88.075 (Supplemental Information)

You requested that we provide information about personal exemptions from mandatory immunization laws in Colorado, Wisconsin and Utah. Specifically, you wanted to know the following:

1. Historically, how did this personal exemption come about in those states, and what was the reason for the change in existing law?

2. What happened to the vaccination compliance rate as a result of these waivers? What is the current compliance rate?

3. What is the before and after frequency of the "serious seven" diseases in those states, and in what percentage of cases, if any, were the persons vaccinated?

4. Do parents have the opportunity to "pick and choose" which vaccinations their children will receive, or is it an "all or nothing" proposition?

The Center for Disease Control in Atlanta indicates that all states have mandatory immunization laws. The following exemptions have been incorporated into law: every state allows a medical exemption; every state, except Mississippi and West Virginia, allows a religious exemption; and 22 states allow a philosophical (personal) exemption. Responses to your specific questions concerning Colorado, Wisconsin and Utah follow.

COLORADO

According to Judy Canner, Immunization Program Director, Colorado Department of Health, the state's mandatory immunization law was in place by 1975. The original version covered only kindergartners, transfer students through grade 6, and child care facility enrollees. An amendment in 1978 extended coverage to all students in public schools and added the personal exemption. The push for inclusion of a personal exemption was based on the argument that the law was an infringement of personal rights. Colorado officials believe that the amendment would not have passed without the addition of the personal exemption.

The Colorado Department of Health does not consider the personal exemption to have significantly affected compliance rates. Statistics showing percentage of compliance and percentage of personal exemptions suggest, however, that the compliance rate is in a slight downward trend while the personal exemption rate is climbing.

School Year	Compliance Rate (%)	Personal Exemption Rate (%)
78-79	90	0.3
79-80	97.7	0.5
80-81	unavailable	unavailable
81-82	97.4	0.6
82-83	97.8	0.7
83-84	97.4	0.8
84-85	97.2	0.8
85-86	97.4	0.8
86-87	97.1	0.9

There is little correlation between the personal exemption and the frequency of disease outbreak. Frequency has continued to decline during the last decade, except in the case of pertussis (whooping cough), which has been on the increase. This is a reflection of the law rather than the exemption, however, because Colorado does not require immunization against pertussis. Colorado currently has a an outbreak of measles in a college community; most of the involved individuals had been vaccinated. While this year's incidence far exceeds the frequency typical of the last decade, it is still considered to be "well within the five percent failure rate common in vaccines, and is typical of measle transmission."

Parents are allowed to choose which vaccines their children will be exempt from taking. In practice, parents generally object to all vaccines if they object to any.

WISCONSIN

Craig Leutzinger, Immunization Program Director, Wisconsin Department of Public Health, indicated that Wisconsin's mandatory immunization law included medical and religious exemptions when it was instituted in 1975. It was ineffective in that it covered only kindergartners, and the wording did not require parents to have children vaccinated. Amendments in 1980 expanded coverage to grades K - 12 (to be implemented gradually), changed the wording to require vaccinations, and added the personal exemption. In spite of Department of Health opposition, the exemption was included through lobbying efforts of a group known as Dissatisfied Parents Together (DPT), which was led by a woman whose son had been severely injured by the DPT vaccine.

Immunization is a widely accepted practice in Wisconsin as reflected by a 99 percent compliance rate. Since 1977, the total percentage of exemptions has remained constant at 0.8 percent to one percent. Prior to 1980, the one percent reflected equal numbers of religious and medical exemptions; since 1980, religious and medical exemptions have dropped to 0.1 percent each while personal exemptions have remained steady at 0.6 percent. It appears that individuals who might previously have claimed religious exemptions now call their objections philosophical rather than religious.

In spite of the high compliance rate, Wisconsin had the highest state rate of mumps in 1987. The incidence of measles in Wisconsin was also high (284 in Wisconsin compared to 12 in Colorado). This does not necessarily correlate to the personal exemption, however, because Wisconsin's mandatory immunization law was set up to be implemented in stages. For example, vaccination for mumps was required beginning in 1982, and only grades K - 4 are currently covered; if an unvaccinated fifth-grader from another state enters a Wisconsin school, there is no requirement that the child be vaccinated against mumps. Another important factor in the high incidence of disease in Wisconsin is that until 1987 there was a strong reluctance on the part of schools to exclude unvaccinated individuals from school during disease outbreaks, even though the law allowed for it. In 1987, during an outbreak of measles, the need to protect unvaccinated children and to interrupt the transmission cycle overcame that reluctance. Since then, exclusion from school has become widely accepted. Outbreaks have "certainly included uncovered children," but no statistics are available on the percentages.

As in Colorado, parents have the right to select which vaccinations their children will be exempt from taking; however, generally there is an all or nothing attitude.

UTAH

According to Rick Crankshaw, Immunization Program Coordinator, Utah Department of Health, Utah's mandatory immunization law included only entering kindergartners when it was enacted in 1976. An amendment in 1982 expanded the coverage to grades K - 12, included all licenced child care facilities, and incorporated the personal exemption. The inclusion of the personal exemption was based on other states' experience with the DPT controversy over vaccinations for pertussis--which sometimes causes extremely serious adverse reactions.

The compliance rate in Utah is very high; exemptions during the last several years have been approximately one percent. Of that, 0.8 percent are personal exemptions and the other 0.2 percent are medical exemptions. No statistics directly comparing compliance rates before and after incorporation of the personal exemption are available.

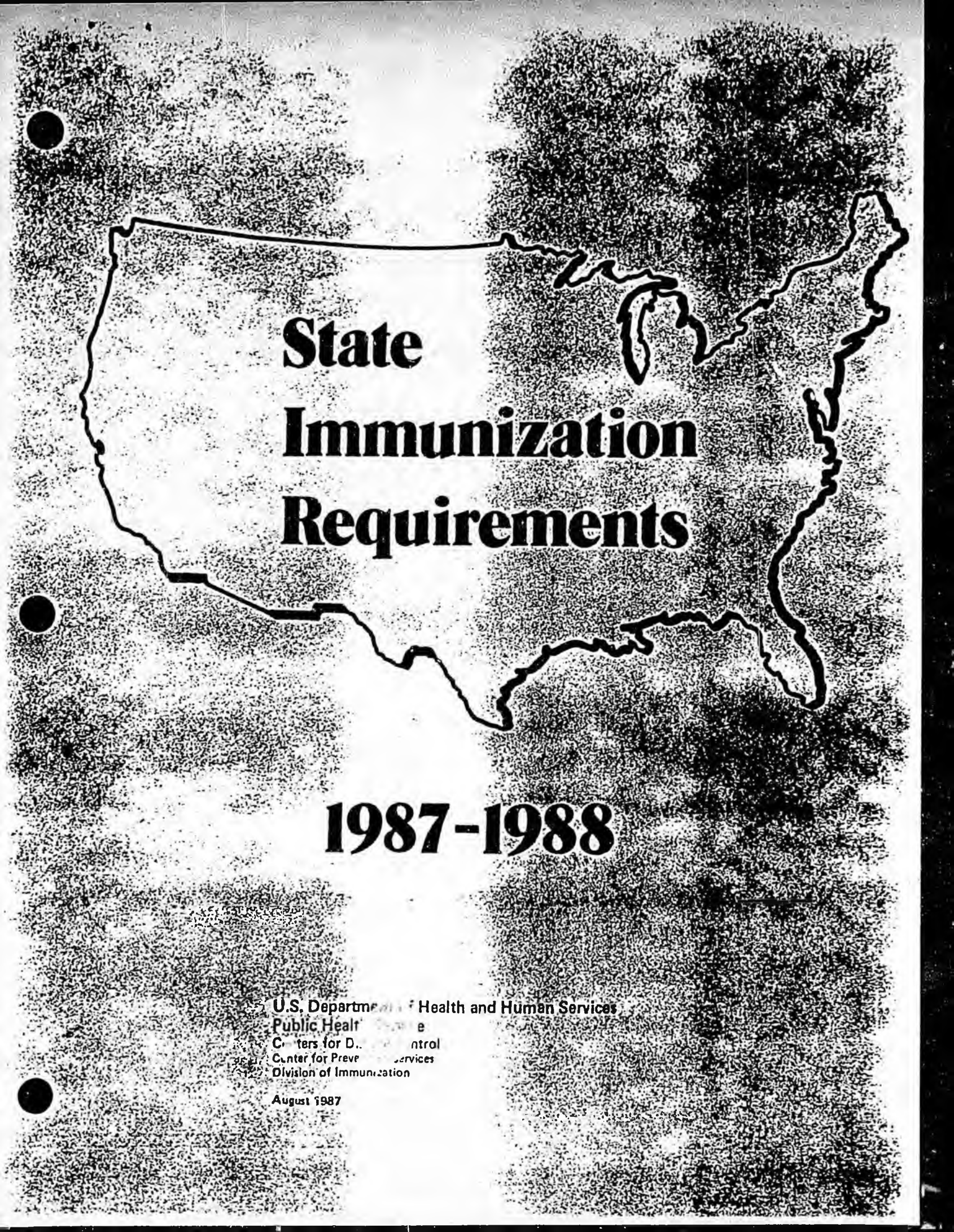
No statistics are available on the frequency of disease before and after incorporation of the personal exemption. Because of the law, Utah schools now have an accurate tracking system so that each school can make an immunization assessment. During an outbreak of disease, the Department of Health orders that any unprotected children be excluded from school until the outbreak is over.

As in Colorado and Wisconsin, parents can choose individual vaccinations to which they are philosophically opposed. In practice, however, parents generally object to all vaccinations or to none.

According to the results of this sample, and the Center for Disease Control, the availability of the personal exemption appears to have had relatively little significance. Feared problems have not materialized; the philosophical exemption does, however, weaken the force of immunization laws inasmuch as it provides some potential for sustaining transmission of disease.

I have requested a copy of the Center for Disease Control's most recent update of State Immunization Requirements, which I will forward to you.

I hope you find this information useful. Please contact me if you have any questions.



State Immunization Requirements

1987-1988

U.S. Department of Health and Human Services
Public Health Service
Centers for Disease Control
Center for Prevention Services
Division of Immunization

August 1987

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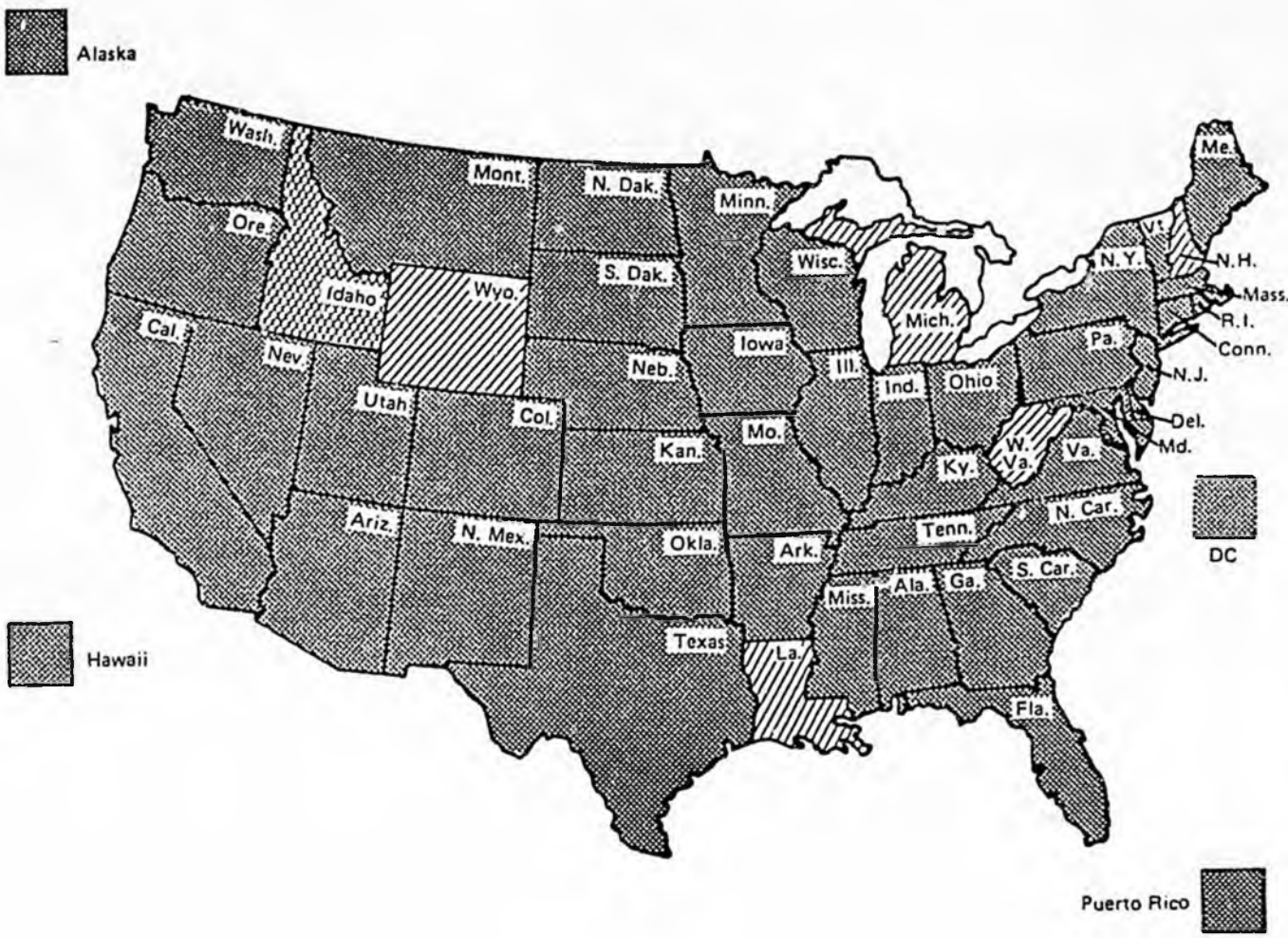
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State Immunization Requirements
Applicable to Any or All of Grades K-12

State	Diphtheria	Tetanus	Pertussis	Measles	Mumps	Rubella	Polio
Alabama	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Alaska	K-12	K-12	K-6 yrs	K-12	Not Required	K-11 yrs	K-12
Arizona	K-12	Not Required	Not Required	K-12	Not Required	K-12	K-12
Arkansas	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
California	K-12	K-12	K-6 yrs	K-12	K-6 yrs	K-12	K-12
Colorado	K-12	K-12	K-6 yrs	K-12	K	K-6	K-12
Connecticut	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Delaware	K-12	K-12	K-6 yrs	K-12	K-8	K-12	K-12
Dist. of Col.	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Florida	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Georgia	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Hawaii	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Idaho	K-5	K-5	Not Required	K-5	K-5	K-5	K-5
Illinois	K-12	K-12	K-5 yrs	K-12	K-12	K-12	K-12
Indiana	K-12	K-12	K-6 yrs	K-12	K-1	K-12	K-12
Iowa	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
Kansas	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Kentucky	K-12	K-12	Not Required	K-12	Not Required	K-12	K-12
Louisiana	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers
Maine	K-12	K-12	K-6 yrs	K-12	K-8	K-12	K-12
Maryland	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
Massachusetts	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Michigan	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers
Minnesota	K-12	K-12	K-6 yrs	K-12	K-6 yrs	K-12	K-12
Mississippi	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
Missouri	K-12	Not Required	Not Required	K-12	Not Required	K-12	K-12
Montana	K-12	K-12	Not Required	K-12	Not Required	K-12	K-12
Nebraska	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Nevada	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
New Hampshire	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers	New Enterers
New Jersey	K-12	K-12	K-6 yrs	K-12	K-14 yrs	K-12	K-12
New Mexico	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
New York	K-12	Not Required	Not Required	K-12	K-12	K-12	K-12
North Carolina	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
North Dakota	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Ohio	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Oklahoma	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
Oregon	K-12	K-12	Not Required	K-12	New Enterers	K-12	K-12
Pennsylvania	K-12	K-12	Not Required	K-12	K-12	K-12	K-12
Puerto Rico	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Rhode Island	K-12	K-12	Not Required	K-12	K-6 yrs	K-12	K-12
South Carolina	K-12	K-12	K-5 yrs	K-12	Not Required	K-12	K-12
South Dakota	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Tennessee	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
Texas	K-12	K-12	Not Required	K-12	K-15 yrs	K-11 yrs	K-12
Utah	K-12	K-12	K-6 yrs	K-12	K-12	K-12	K-12
Vermont	K-12	K-12	K-6 yrs	K-12	Not Required	K-12	K-12
Virginia	K-12	K-12	K-6 yrs	K-12	New Enterers	K-12	K-12
Washington	K-12	K-12	Not Required	K-12	K1	K-12	K-12
West Virginia	New Enterers	New Enterers	New Enterers	New Enterers	Not Required	New Enterers	New Enterers
Wisconsin	K-12	K-12	K-6 yrs	K-12	K-4	K-11 yrs	K-12
Wyoming	New Enterers	New Enterers	K-6 yrs	New Enterers	New Enterers	New Enterers	New Enterers

DIPHTHERIA
Immunization Requirements
(For Any or All of Grades K-12)



New Enterers

K-5th Grade

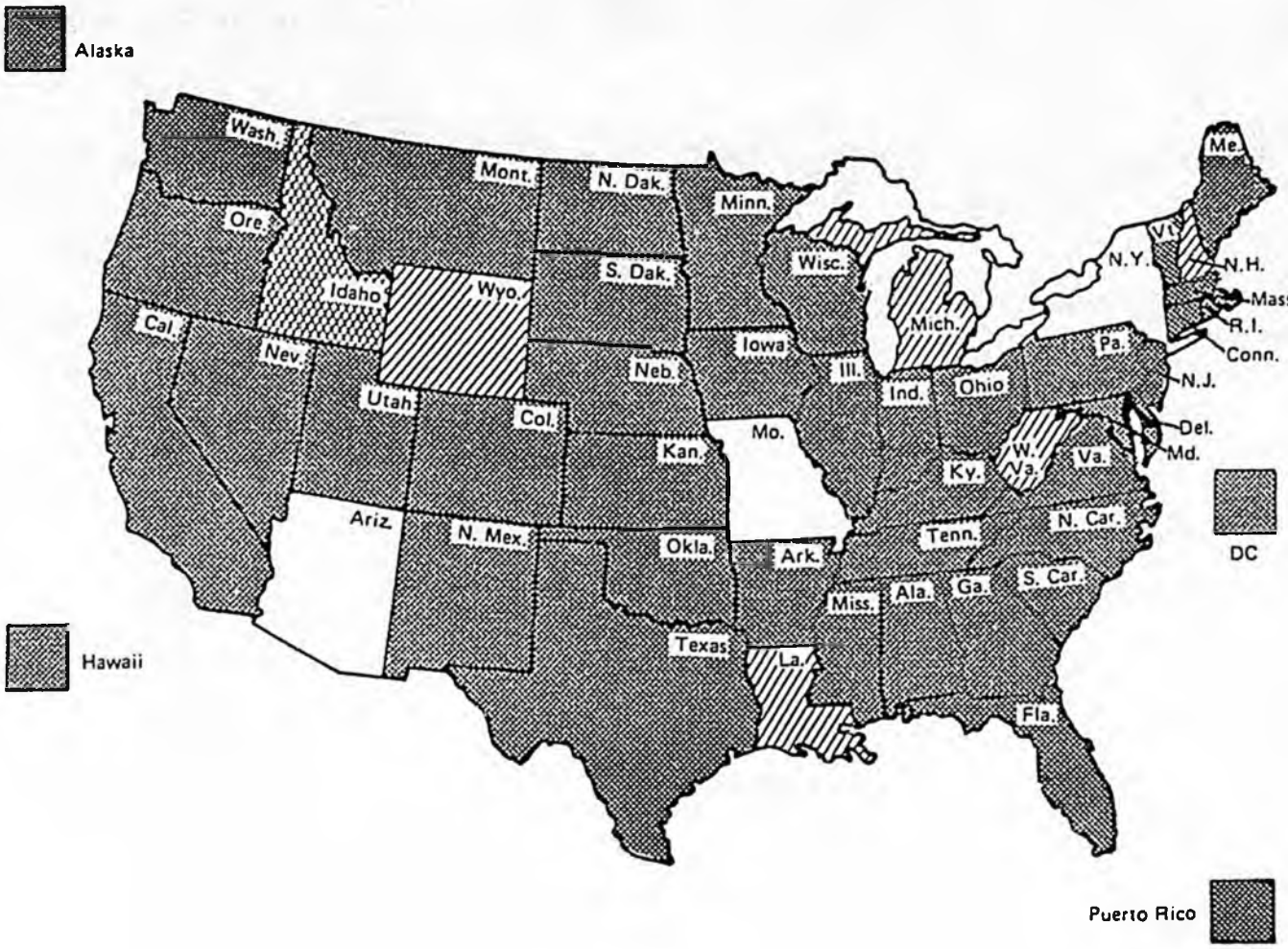
K-12th Grade

DIPHTHERIA

State Immunization Requirements
Applicable to Any or All of Grades K-12

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-12	3 dose minimum required
Alaska	K-12	5 doses unless 4th dose after 4th birthday, then 4; 3 doses if 7 years and older
Arizona	K-12	5 doses unless 4th dose after 4th birthday
Arkansas	K-12	3 doses; last must have been after 4th birthday
California	K-12	4 doses; 4th dose after 2nd birthday
Colorado	K-12	4 doses
Connecticut	K-12	3 doses
Delaware	K-12	3 doses
Dist. of Col.	K-12	3 doses plus booster if series started as infant; a 5th dose is recommended; also required of college students
Florida	K-12	5 doses unless 4th dose after 4th birthday, then 4; 3 doses if 7 yrs & older
Georgia	K-12	3 doses minimum; the last dose given after 4th birthday
Hawaii	K-12	As recommended by American Academy of Pediatrics
Idaho	K-5	4 doses
Illinois	K-12	4 doses; the last a booster on or after 4th birthday plus a 10 year booster
Indiana	K-12	4 doses for K-1, 3 doses for grades 2 and above
Iowa	K-12	3 doses, one must be after age 4 years
Kansas	K-12	4 doses if series is begun before age 7 years; 3 if begun after 6 years
Kentucky	K-12	3 to 5 doses—the last a booster on or after 4th birthday plus a 10 year booster
Louisiana	New Enterers	4 to 5 doses; at least 1 dose after age 4 years
Maine	K-12	3 doses
Maryland	K-12	4 doses minimum, with 1 after 4 years of age
Massachusetts	K-12	4 doses for K; 3 doses plus 10 year booster for 1-12
Michigan	New Enterers	4 doses, only 3 if series started after 6 years, plus booster every 10 years
Minnesota	K-12	4 doses
Mississippi	K-12	4 doses if before 7 years; 3 if after 7 years; at least 1 booster dose after 4 years
Missouri	K-12	3 doses, at least 1 after age 3 years
Montana	K-12	4 doses if 6 years old or less; 3 if 7 years or older; last dose after 4th birthday
Nebraska	K-12	3 doses
Nevada	K-12	4 to 5 dose.
New Hampshire	New Enterers	5 doses; 4 if 4th is on or after 4th birthday; 3 if over 6 years and 3rd dose given on or after 4th birthday
New Jersey	K-12	4 doses including booster for ages 1-6; 3 doses for 7 years and older
New Mexico	K-12	4 doses if begun before age 7 years; 3 if after age 7 years; at least 1 dose after 4th birthday
New York	K-12	3 doses
North Carolina	K-12	5 doses; 3 doses by 1 yr of age, 1 booster dose in 2nd yr, 1 booster dose on or after 4th birthday
North Dakota	K-12	4 doses
Ohio	K-12	4 doses; 3 if 3rd on or after 6th birthday
Oklahoma	K-12	3 doses
Oregon	K-12	4 doses; 5 if 4th was before age 4 years; 3 for grades 2-12 if in Oregon Schools on 3 14 82 unless 1 or more before 6 months, then 4 doses
Pennsylvania	K-12	3 doses
Puerto Rico	K-12	3 - doses, provided the 3rd is given after 4th birthday
Rhode Island	K-12	3 doses
South Carolina	K-12	3 doses, at least 1 must have been on or after 4th birthday
South Dakota	K-12	4 doses, at least 1 must have been after 4th birthday
Tennessee	K-12	4 doses
Texas	K-12	3 doses, 1 dose after 4th birthday plus 1 within 10 years
Utan	K-12	4 doses
Vermont	K-12	3 doses, with 6 months between 2nd dose and any thereafter
Virginia	K-12	3 doses, with 3rd after 4th birthday
Washington	K-12	3 doses, last dose must be at or after age 4 years
West Virginia	New Enterers	3 doses minimum, with at least 1 after 4th birthday
Wisconsin	K-12	4 doses, only 3 if 3rd received after 4th birthday

TETANUS
Immunization Requirements
(For Any or All of Grades K-12)



Not Required

New Enterers

K-5th Grade

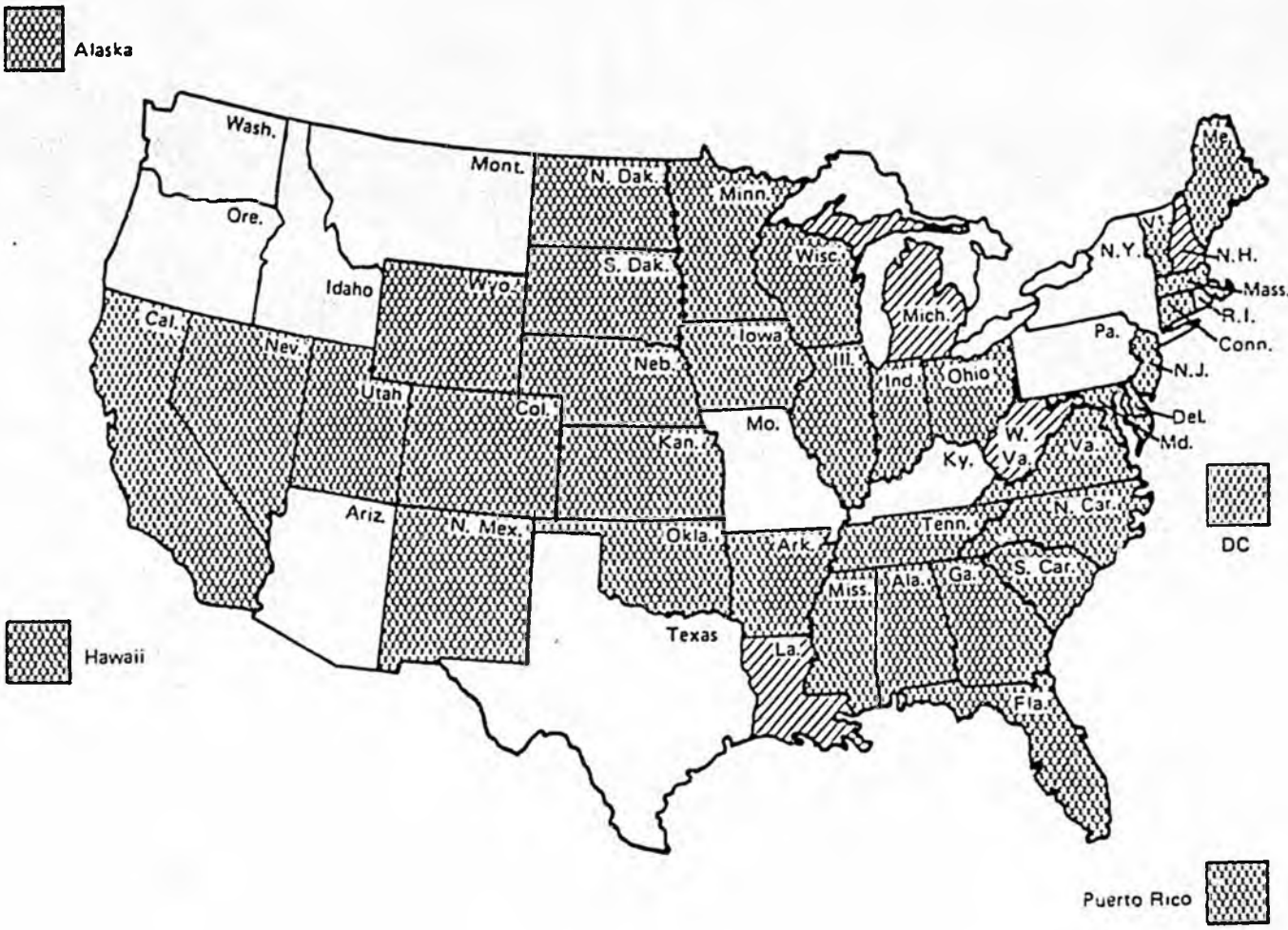
K-12th Grade

TETANUS

State Immunization Requirements
Applicable to Any or All of Grades K-12

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-12	3 dose minimum required
Alaska	K-12	5 doses unless 4th dose after 4th birthday, then 4 doses; 3 doses if 7 years and older
Arizona	Not Required	Usually given with diphtheria
Arkansas	K-12	3 doses, but last must have been since 4th birthday
California	K-12	4 doses, 4th dose after 2nd birthday
Colorado	K-12	4 doses
Connecticut	K-12	3 doses
Delaware	K-12	3 doses
Dist. of Col.	K-12	3 doses plus booster if series started as infant; a 5th dose is recommended; also required of college students
Florida	K-12	5 doses unless 4th dose after 4th birthday, then 4; 3 doses if 7 yrs & older
Georgia	K-12	3 doses minimum; the last dose given after the 4th birthday
Hawaii	K-12	As recommended by American Academy of Pediatrics
Idaho	K-5	4 doses
Illinois	K-12	4 doses; the last a booster on or after 4th birthday plus a 10 year booster
Indiana	K-12	4 doses for K-1, 3 doses for grades 2 and above
Iowa	K-12	3 doses, 1 must be after age 4 years
Kansas	K-12	4 doses if started before age 7 years; 3 if begun after 7 years
Kentucky	K-12	3 to 5 doses—the last a booster on or after 4th birthday plus a 10 year booster
Louisiana	New Enterers	4 to 5 doses; at least 1 dose after age 4 years
Maine	K-12	3 doses
Maryland	K-12	4 doses minimum, with 1 after 4 years of age
Massachusetts	K-12	4 doses for K; 3 doses plus 10 year booster for 1-12
Michigan	New Enterers	4 doses, only 3 if series started after 6 years of age, plus booster every 10 years
Minnesota	K-12	4 doses
Mississippi	K-12	4 doses if before 7 years; 3 if after 7 years; at least 1 booster dose after 4 years
Missouri	Not Required	3 doses, at least 1 after age 3 years recommended
Montana	K-12	4 doses if 6 years or less; 3 if 7 years or older; last dose after 4th birthday
Nebraska	K-12	3 doses
Nevada	K-12	4 to 5 doses
New Hampshire	New Enterers	5 doses; 4 if 4th is on or after 4th birthday, 3 if over 6 years and 3rd given on or after 4th birthday
New Jersey	K-12	4 doses including booster for ages 1-6; 3 doses for 7 years and older
New Mexico	K-12	4 doses if begun before age 7 years; 3 if begun at age 7 years or older; at least 1 dose after 4th birthday
New York	Not Required	
North Carolina	K-12	5 doses; 3 doses by 1 yr of age, 1 booster dose in 2nd yr, 1 booster dose on or after 4th birthday
North Dakota	K-12	4 doses
Ohio	K-12	4 doses; 3 if 3rd received on or after 6th birthday
Oklahoma	K-12	3 doses
Oregon	K-12	4 doses; 5 if 4th was before age 4 years; 3 for grades 2-12 if in Oregon Schools on 3 14 82 unless 1 or more before 6 months, then 4 doses
Pennsylvania	K-12	3 doses
Puerto Rico	K-12	3 + doses, provided the 3rd is given after 4th birthday
Rhode Island	K-12	3 doses
South Carolina	K-12	3 doses, at least 1 must have been on or after 4th birthday
South Dakota	K-12	4 doses, at least 1 must have been after 4th birthday
Tennessee	K-12	4 doses
Texas	K-12	3 doses, 1 dose after 4th birthday plus 1 within 10 years
Utah	K-12	4 doses
Vermont	K-12	3 doses, with 6 months between 2nd dose and any thereafter; plus booster in 10 years
Virginia	K-12	3 doses, with 3rd after 4th birthday
Washington	K-12	3 doses, last dose must be at or after age 4 years
West Virginia	New Enterers	3 doses minimum, with at least 1 after 4th birthday
Wisconsin	K-12	4 doses, only 3 doses if 3rd received after 4th birthday

PERTUSSIS
Immunization Requirements
(For Any or All of Grades K-12)



Not Required

New Enterers

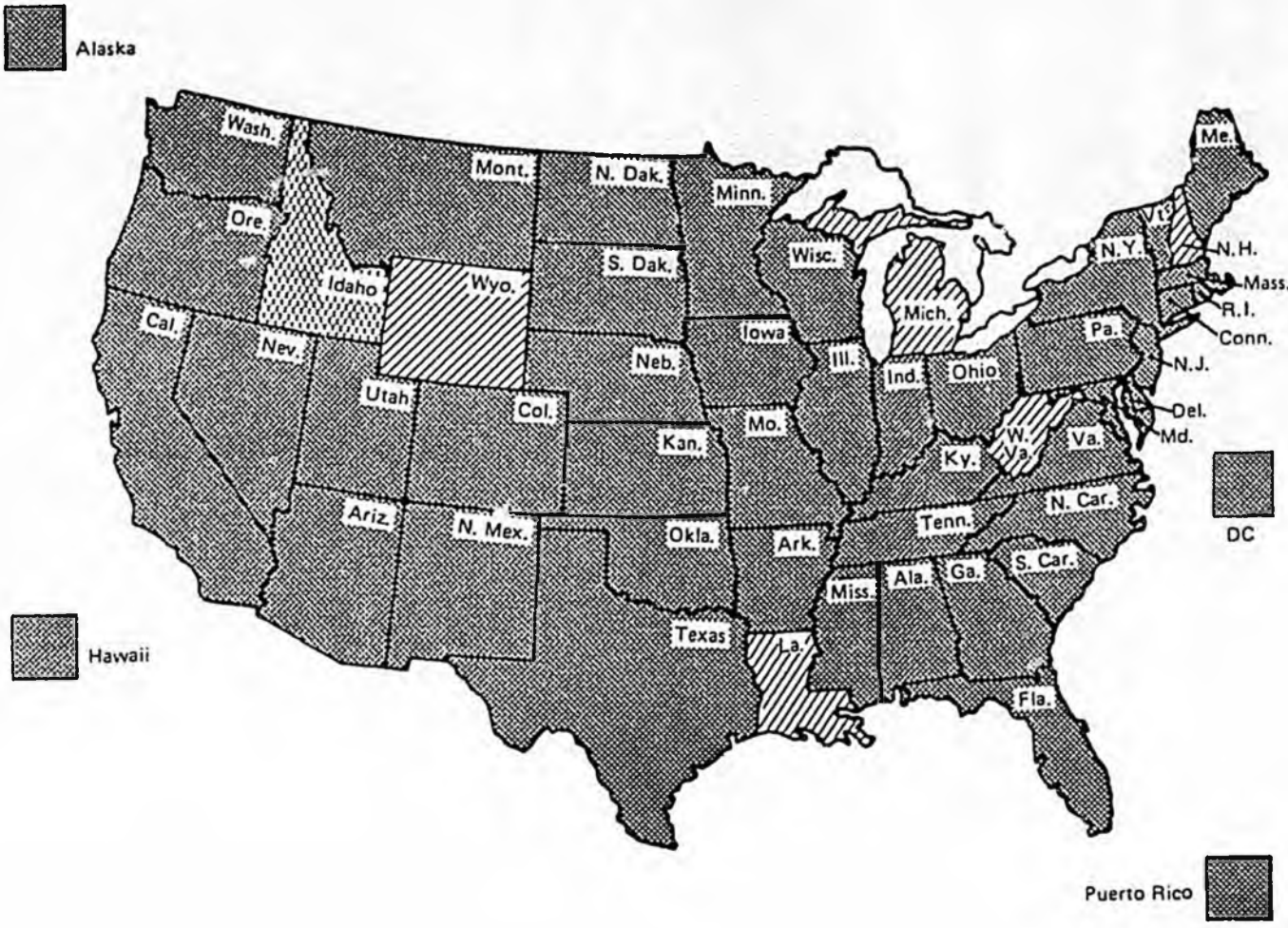
K-5 yrs or K-6 yrs

PERTUSSIS

State Immunization Requirements
Applicable to Any or All of Grades K-12

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-6 yrs	3 dose minimum required
Alaska	K-6 yrs	5 doses unless 4th dose after 4th birthday, then 4 doses
Arizona	Not Required	Usually given with diphtheria
Arkansas	K-6 yrs	3 doses, but last must have been after 4th birthday
California	K-6 yrs	4 doses, 4th dose after 2nd birthday
Colorado	K-6 yrs	4 doses
Connecticut	K-6 yrs	3 doses
Delaware	K-6 yrs	3 doses
Dist. of Col.	K-6 yrs	3 doses
Florida	K-6 yrs	5 doses unless 4th dose after 4th birthday; then 4 doses
Georgia	K-6 yrs	3 doses minimum; the last dose given after the 4th birthday
Hawaii	K-6 yrs.	As recommended by American Academy of Pediatrics
Idaho	Not Required	
Illinois	K-5 yrs	4 doses; the last a booster on or after 4th birthday
Indiana	K-6 yrs	4 doses
Iowa	K-6 yrs	3 doses, 1 must be after age 4 years
Kansas	K-6 yrs	4 doses
Kentucky	Not Required	
Louisiana	New Enterers	4 to 5 doses; at least 1 after age 4 years; required to age 7 years
Maine	K-6 yrs	3 doses
Maryland	K-6 yrs	Minimum 4 doses with 1 after 4 years of age
Massachusetts	K-6 yrs	4 doses
Michigan	New Enterers	4 doses, not required after 6th birthday
Minnesota	K-6 yrs	4 doses
Mississippi	K-6 yrs	4 doses if before 7 years; at least 1 booster after 4th birthday
Missouri	Not Required	3 doses, at least 1 after age 3 years recommended
Montana	Not Required	Usually given with diphtheria-tetanus
Nebraska	K-6 yrs	3 doses
Nevada	K-6 yrs	4 to 5 years
New Hampshire	New Enterers	5 doses; 4 if 4th given on or after 4th birthday; not required to be given if 7 years or older
New Jersey	K-6 yrs	4 doses
New Mexico	K-6 yrs	4 doses
New York	Not Required	
North Carolina	K-6 yrs	5 doses; 3 doses by 1 yr of age, 1 booster dose in 2nd yr, 1 booster dose on or after 4th birthday
North Dakota	K-6 yrs	4 doses
Ohio	K-6 yrs	4 doses; 3 if 3rd dose required on or after 6th birthday
Oklahoma	K-6 yrs	3 doses
Oregon	Not Required	
Pennsylvania	Not Required	
Puerto Rico	K-6 yrs	3 doses, if 3rd is given after 4th birthday; not required after 7th birthday
Rhode Island	Not Required	
South Carolina	K-5 yrs	3 doses, at least 1 received on or after 4th birthday
South Dakota	K-6 yrs	4 doses, at least 1 received after 4th birthday
Tennessee	K-6 yrs	4 doses
Texas	Not Required	
Utah	K-6 yrs	4 doses
Vermont	K-6 yrs	3 doses, 6 months between 2nd and any thereafter
Virginia	K-6 yrs	3 doses, with 3rd dose after 4th birthday
Washington	Not Required	
West Virginia	New Enterers	3 doses minimum, with at least 1 after 4th birthday; not required after 6 years of age
Wisconsin	K-6 yrs	4 doses, only 3 doses if 3rd received after 4th birthday
Wyoming	K-6 yrs	4 doses; required up to but not including 7th birthday

MEASLES
Immunization Requirements
(For Any or All of Grades K-12)



New Enterers

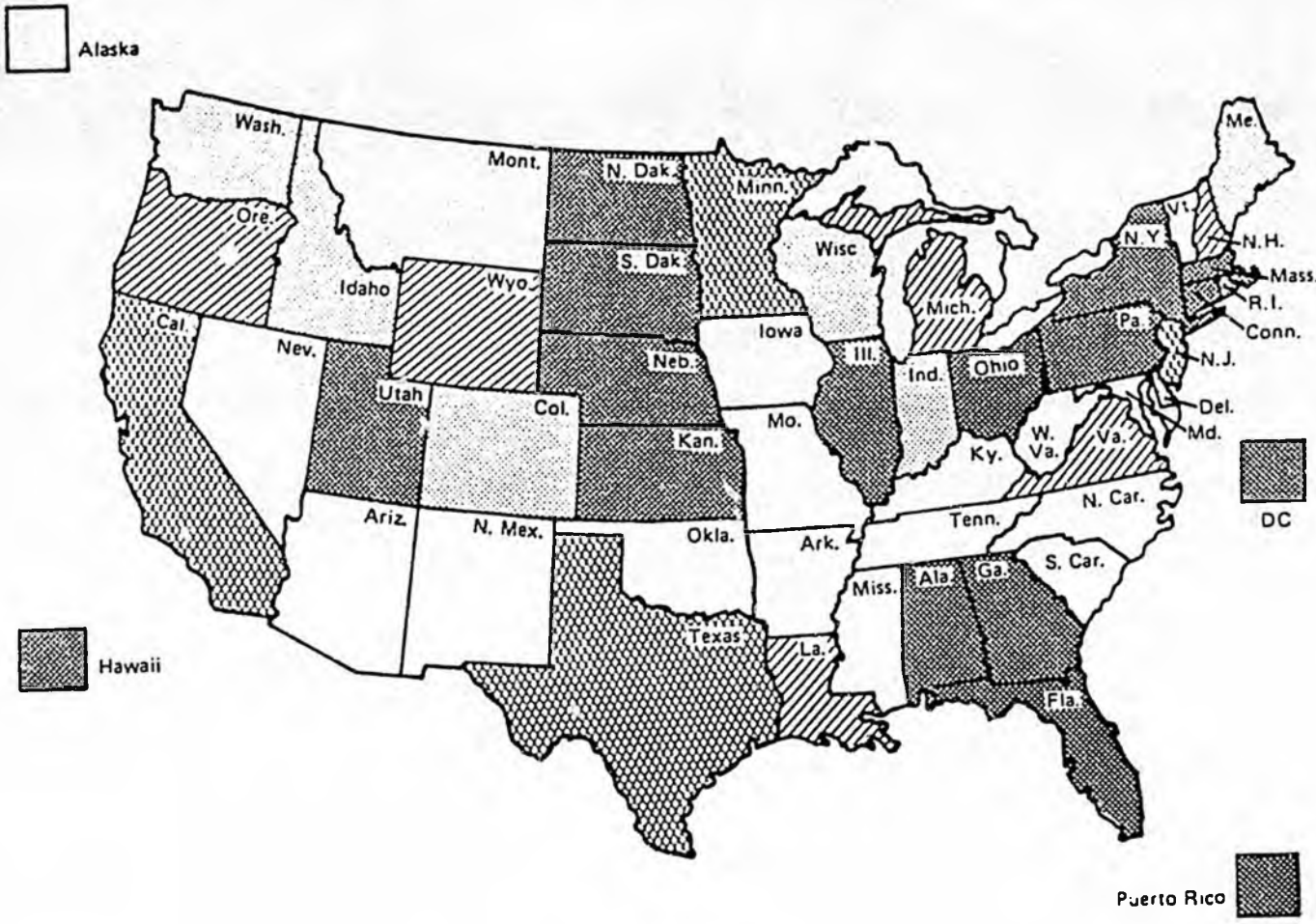
K-5th Grade

K-12th Grade

State Immunization Requirements Applicable to Any or All of Grades K-12

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-12	1 dose after 15 months of age
Alaska	K-12	1 dose on or after 1st birthday
Arizona	K-12	1 dose live measles vaccine given on or after 1st birthday
Arkansas	K-12	1 dose given after 1st birthday and after January 1968
California	K-12	1 dose of live virus vaccine administered on or after 1st birthday
Colorado	K-12	1 dose on or after 1st birthday
Connecticut	K-12	1 dose after age 1 and vaccine did not include gamma globulin
Delaware	K-12	1 dose after 1 year of age
Dist. of Col.	K-12	1 dose, must be repeated if given before 1969; also required of college students
Florida	K-12	1 dose at 15 months recommended, over 12 months accepted; and in 1968 or later
Georgia	K-12	1 dose of live virus vaccine given after the 1st birthday and after 1968; or positive serology
Hawaii	K-12	1 dose as recommended by American Academy of Pediatrics
Idaho	K-5	1 dose after 1st birthday; MD diagnosis of disease or laboratory confirmation of immunity accepted
Illinois	K-12	1 dose at 15 months of age or later; MD diagnosis of disease or laboratory confirmation accepted
Indiana	K-12	1 dose at or after 12 months of age
Iowa	K-12	1 dose after 15 months of age or physician's diagnosis
Kansas	K-12	1 dose given after 12 months of age
Kentucky	K-12	1 dose on or after 12 months of age, recommended 15 months
Louisiana	New Enterers	1 dose given on or after 15 months, 12 to 15 months also accepted
Maine	K-12	1 dose at 12 months of age or older or serologic confirmation of immunity
Maryland	K-12	1 dose live vaccine at 1 year or older or titer of 1:4 or greater
Massachusetts	K-12	1 dose at or after 12 months of age
Michigan	New Enterers	1 dose after 1st birthday; MD diagnosis of disease accepted
Minnesota	K-12	1 dose after 11 months 15 days of age
Mississippi	K-12	1 dose after 1st birthday
Missouri	K-12	1 dose given after 12 months of age; children born in or after 1982 at 15 months
Montana	K-12	1 dose given after 12 months of age
Nebraska	K-12	1 dose at or after 12 months of age
Nevada	K-12	1 dose after 12 months of age
New Hampshire	New Enterers	1 dose live vaccine on or after 1st birthday
New Jersey	K-12	1 dose live virus vaccine given after 12 months of age
New Mexico	K-12	1 dose live virus given on or after 12 months of age
New York	K-12	1 dose live vaccine administered after 12 months of age, but recommended at 15 months
North Carolina	K-12	1 dose live vaccine on or after 1st birthday
North Dakota	K-12	1 dose if given after 15 months of age; 12 months accepted
Ohio	K-12	1 dose live virus vaccine on or after 1st birthday
Oklahoma	K-12	1 dose, received on or after 1st birthday
Oregon	K-12	1 dose at or after 12 months of age, but recommended at 15 months
Pennsylvania	K-12	1 dose live vaccine on or after 1st birthday, or positive serology
Puerto Rico	K-12	1 dose live virus vaccine recommended to be given at or after 15 months of age
Rhode Island	K-12	1 dose after 12 months of age; also required of college students
South Carolina	K-12	1 dose, must have been on or after 1st birthday
South Dakota	K-12	1 dose after 12 months of age or MD's diagnosis of disease; also required by State funded colleges
Tennessee	K-12	1 dose given after 12 months of age
Texas	K-12	1 dose on, after, or during the calendar month of the 1st birthday or physician verified history of disease
Utah	K-12	1 dose given after 12 months of age
Vermont	K-12	1 dose administered on or after 1st birthday or a MD diagnosed disease history
Virginia	K-12	1 dose after 12 months of age
Washington	K-12	1 dose of live vaccine after 1st birthday
West Virginia	New Enterers	1 dose given after 12 months of age
Wisconsin	K-12	1 dose on or after 1st birthday

MUMPS
Immunization Requirements
(For Any or All of Grades K-12)



Not Required

New Enterers

K, K-1st, K-4th, K-5th, or K-8th Grade

K-6yrs, K-14yrs, or K-15yrs

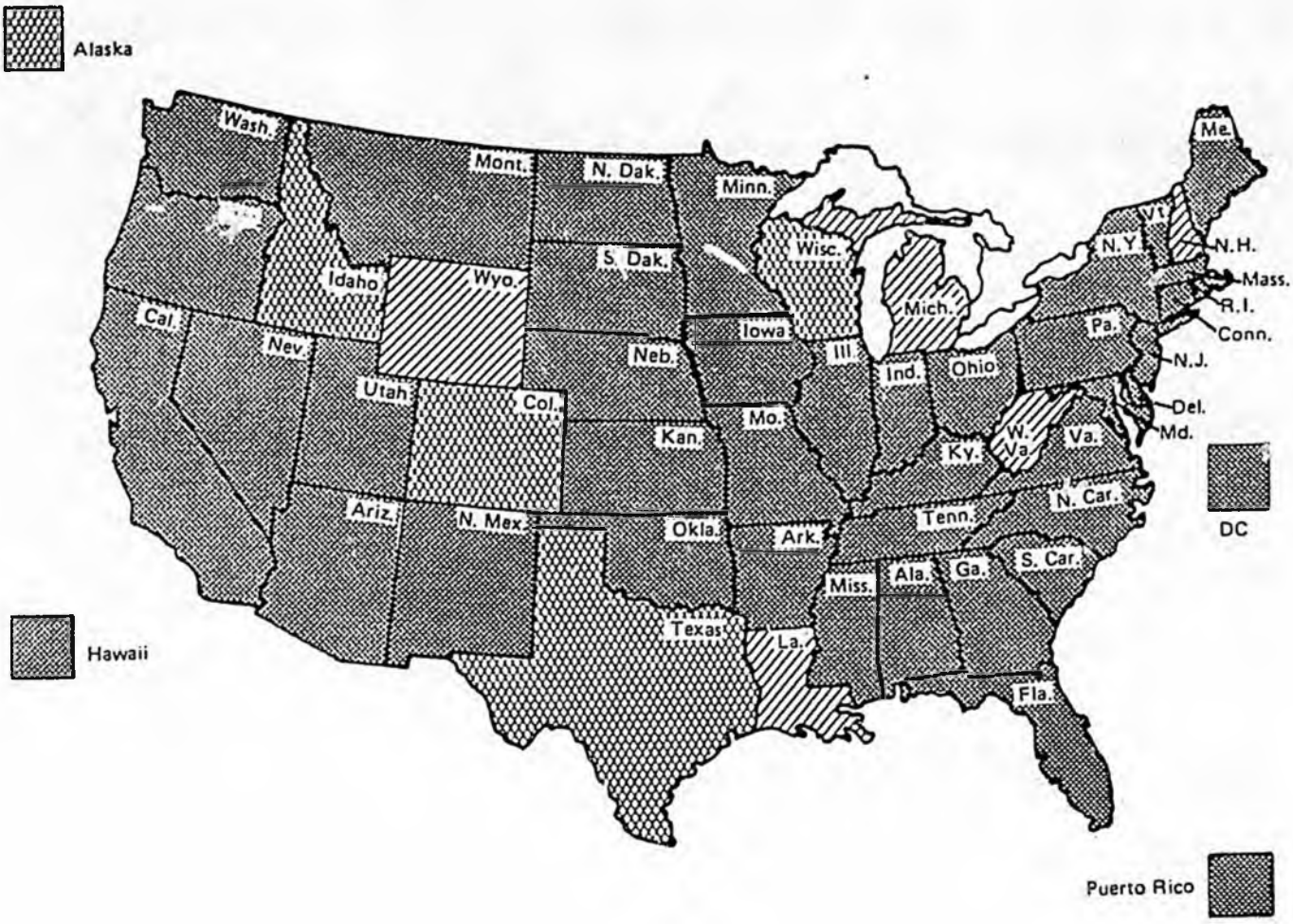
K-12th Grade

MUMPS

State Immunization Requirements
Applicable to Any or All of Grades K-12

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-12	1 dose after 15 months of age
Alaska	Not Required	
Arizona	Not Required	Usually given with measles and rubella vaccine
Arkansas	Not Required	
California	K-6 yrs	1 dose administered on or after 1st birthday
Colorado	K	1 dose on or after 1st birthday, not required after K
Connecticut	K-12	1 dose given after age 1 year
Delaware	K-8	1 dose after 1 year of age; K-9 in 88-89, K-10 in 89-90 etc.
Dist. of Col.	K-12	1 dose, also required of college students
Florida	K-12	1 dose at 15 months recommended, over 12 months accepted
Georgia	K-12	1 dose of live virus vaccine given after the 1st birthday
Hawaii	K-12	1 dose as recommended by American Academy of Pediatrics
Idaho	K-5	1 dose after 1st birthday; MD diagnosis of disease or laboratory confirmation of immunity accepted
Illinois	K-12	1 dose at 1 year of age or later, or MD diagnosis of disease
Indiana	K-1	1 dose at or after 12 months of age; 1 additional grade each year
Iowa	Not Required	
Kansas	K-12	1 dose given after 12 months of age
Kentucky	Not Required	
Louisiana	New Enterers	1 dose given on or after 15 months; 12 to 15 months also accepted
Maine	K-8	1 dose at 12 months of age or older or serologic confirmation of immunity
Maryland	Not Required	
Massachusetts	K-12	1 dose at or after 12 months of age
Michigan	New Enterers	1 dose, only in K-4 and entered K in 1979 or later
Minnesota	K-6 yrs	1 dose
Mississippi	Not Required	
Missouri	Not Required	1 dose, given on or after 15 months; recommended
Montana	Not Required	Highly recommended
Nebraska	K-12	1 dose at or after 12 months of age
Nevada	Not Required	
New Hampshire	New Enterers	1 dose
New Jersey	K-14 yrs	1 dose; required of those born on or after 1 1 73
New Mexico	Not Required	1 dose strongly recommended
New York	K-12	1 dose live vaccine given after 12 months of age
North Carolina	K-12	1 dose live vaccine by 2 yrs of age; not required for children who entered 1st grade before July 1, 1987
North Dakota	K-12	1 dose if given after 15 months of age — 12 months accepted
Ohio	K-12	1 dose live virus vaccine on or after 1st birthday
Oklahoma	Not Required	
Oregon	New Enterers	1 dose includes all out-of-state transferees but not students in grades 2-12 in Oregon schools on 3/14/82
Pennsylvania	K-12	1 dose on or after 1st birthday or MD diagnosis of disease
Puerto Rico	K-12	1 dose live virus vaccine recommended to be given at or after 15 months of age
Rhode Island	K-6 yrs	1 dose after 12 months of age
South Carolina	Not Required	
South Dakota	K-12	1 dose given after 12 months of age
Tennessee	Not Required	
Texas	K-15 yrs	1 dose or physician verified disease; an additional year of age to be added each year until K-12 coverage reached
Utah	K-12	1 dose given after 12 months of age
Vermont	Not Required	
Virginia	New Enterers	1 dose given at 12 months of age or older; required of all new enterers since 8 1 81
Washington	K-1	1 dose
West Virginia	Not Required	
Wisconsin	K-4	1 dose on or after 1st birthday; applied to one additional grade until K-12 coverage reached
		[illegible] entering Wyoming schools

RUBELLA
Immunization Requirements
(For Any or All of Grades K-12)



New Enterers

K-11 yrs, K-5th, or K-6th Grade

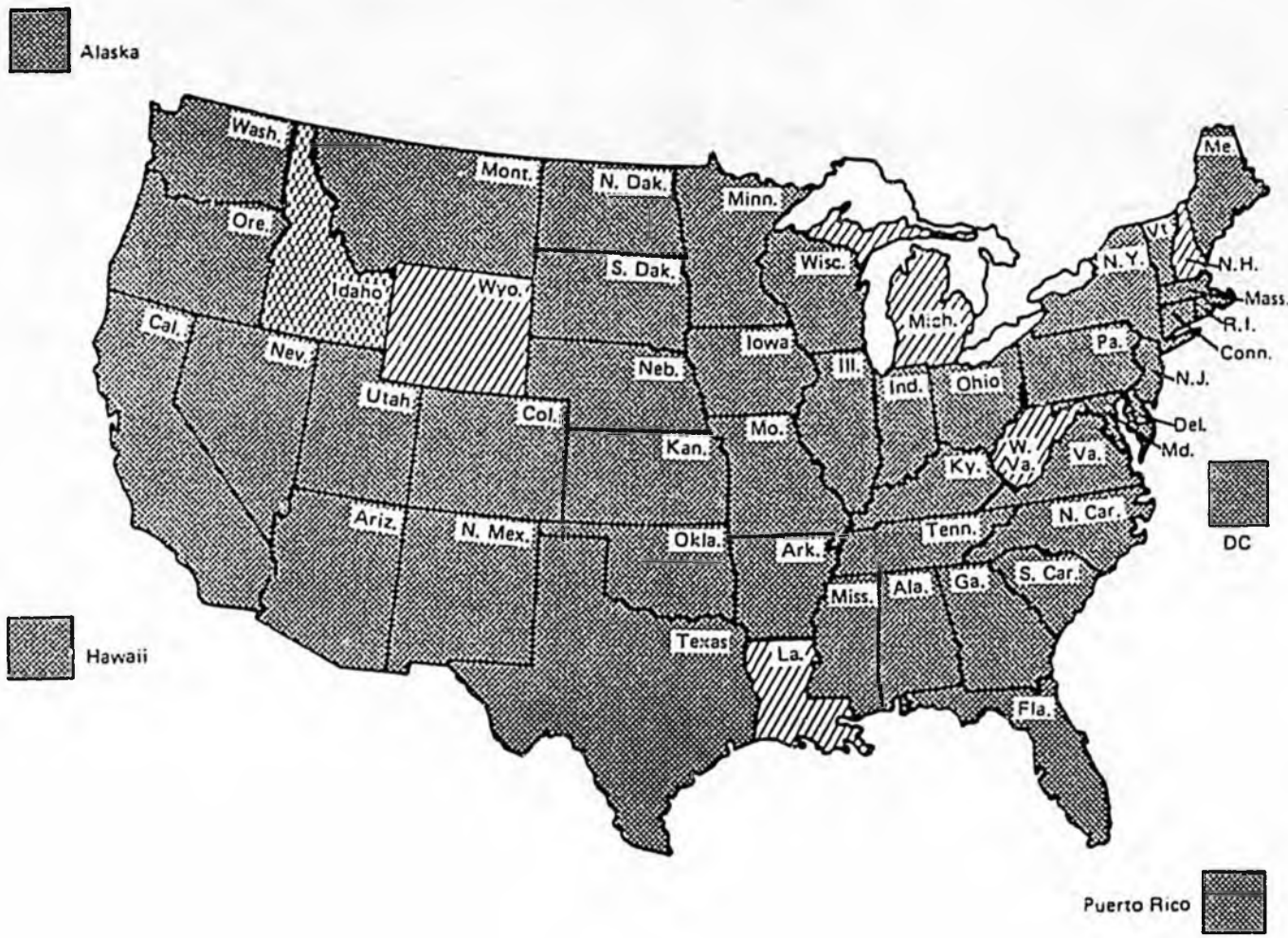
K-12th Grade

RUBELLA

State Immunization Requirements
Applicable to Any or All of Grades K-12

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-12	1 dose administered after 15 months of age
Alaska	K-11 yrs	1 dose administered on or after 1st birthday
Arizona	K-12	1 dose given on or after 1st birthday
Arkansas	K-12	1 dose given after the 1st birthday and after 6/1/69
California	K-12	1 dose administered on or after 1st birthday
Colorado	K-6	1 dose on or after 1st birthday; post pubertal females exempt
Connecticut	K-12	1 dose given after 1 year of age
Delaware	K-12	1 dose given after 1 year of age
Dist. of Col.	K-12	1 dose; also required of college students
Florida	K-12	1 dose at 15 months of age recommended, over 12 months accepted
Georgia	K-12	1 dose of live virus vaccine given after the 1st birthday
Hawaii	K-12	1 dose, as recommended by American Academy of Pediatrics
Idaho	K-5	1 dose after 1st birthday; laboratory confirmation of immunity accepted
Illinois	K-12	1 dose at 1 year of age or later, or laboratory confirmation
Indiana	K-12	1 dose at or after 12 months of age
Iowa	K-12	1 dose after 15 months of age, or laboratory confirmation
Kansas	K-12	1 dose given after 12 months of age
Kentucky	K-12	1 dose on or after 12 months of age
Louisiana	New Enterers	1 dose given on or after 15 months of age; 12 to 15 months also accepted
Maine	K-12	1 dose at 12 months of age or older; or serologic confirmation of immunity
Maryland	K-12	1 dose of live vaccine or a titer of 1:8 or greater; in K-2, must have been administered on or after 1st birthday
Massachusetts	K-12	1 dose at or after 12 months of age
Michigan	New Enterers	1 dose given after the 1st birthday
Minnesota	K-12	1 dose; not required of females 12 years of age or older
Mississippi	K-12	1 dose after 12 months of age
Missouri	K-12	1 dose given after 12 months of age; children born in or after 1982, at 15 months
Montana	K-12	1 dose after 12 months of age; not required of females 12 years old or older
Nebraska	K-12	1 dose at or after 12 months of age
Nevada	K-12	1 dose after 12 months
New Hampshire	New Enterers	1 dose
New Jersey	K-12	1 dose
New Mexico	K-12	1 dose at 12 months of age
New York	K-12	1 dose live vaccine after 12 months of age; may be waived for females 11 years old and up
North Carolina	K-12	1 dose of live vaccine by age 2 years
North Dakota	K-12	1 dose, if given after 15 months of age — 12 months accepted
Ohio	K-12	1 dose live virus vaccine on or after 1st birthday
Oklahoma	K-12	1 dose; not required of females ages 12 years and above
Oregon	K-12	1 dose at or after 12 months of age, but recommended at 15 months
Pennsylvania	K-12	1 dose on or after 1st birthday, or positive serology
Puerto Rico	K-12	1 dose live virus vaccine recommended to be given at or after 15 months of age
Rhode Island	K-12	1 dose after 12 months of age; also required of college students
South Carolina	K-12	1 dose on or after 1st birthday; not required of females after onset of puberty
South Dakota	K-12	1 dose given after 12 months of age; or positive serology; also required by State funded colleges
Tennessee	K-12	1 dose on or after 12 months of age; females 13 years old and up are exempt
Texas	K-11 yrs	1 dose
Utah	K-12	1 dose given after 12 months of age
Vermont	K-12	1 dose given on or after 1st birthday, or positive serology
Virginia	K-12	1 dose given after 12 months of age or older
Washington	K-12	1 dose after 1 year; or positive serology
West Virginia	New Enterers	1 dose given after 12 months of age
Wisconsin	K-11 yrs	1 dose given on or after 1st birthday
Wyoming	New Enterers	1 dose after 12 months of age, entering Wyoming schools through age 10 years

POLIO
State Immunization Requirements
Applicable to Any or All of Grades K-12



New Enterers

K-5th Grade

K-12th Grade

POLIO
Immunization Requirements
(For Any or All of Grades K-12)

State	Grade	Dosage Requirements and Additional Comments
Alabama	K-12	3 dose minimum required
Alaska	K-12	4 doses unless 3rd dose after 4th birthday, then 3 doses
Arizona	K-12	5 doses unless 4th dose after 4th birthday, then 4 doses
Arkansas	K-12	3 doses, last must have been given after 4th birthday
California	K-12	3 doses, 3rd dose after 2nd birthday
Colorado	K-12	3 doses
Connecticut	K-12	3 doses TOPV or IPV-3 virus types plus 1 TOPV; or IPV with 2 year boosters
Delaware	K-12	3 doses required
Dist. of Col.	K-12	3 OPV plus booster if series started before 4 years of age
Florida	K-12	4 doses; unless 3rd dose after 4th birthday, then 3 doses
Georgia	K-12	3 doses minimum of TOPV or 4 of IPV given after 1968; last dose must have been given after 4th birthday
Hawaii	K-12	As recommended by American Academy of Pediatrics
Idaho	K-5	3 doses
Illinois	K-12	3 doses; the last a booster on or after 4th birthday
Indiana	K-12	3 doses, oral polio vaccine specified
Iowa	K-12	3 doses, 1 must be after 4 years of age; not required after 18 years of age
Kansas	K-12	3 doses
Kentucky	K-12	3 to 4 doses, the last a booster on or after 4th birthday
Louisiana	New Enterers	4 to 5 doses; at least 1 dose after age 4 years
Maine	K-12	3 doses, 1 of which is given after the 1st birthday
Maryland	K-12	3 dose minimum with 1 after age 4 years
Massachusetts	K-12	3 doses
Michigan	New Enterers	3 doses, not required after 18th birthday
Minnesota	K-12	3 doses
Mississippi	K-12	3 doses, 1 must have been after 4th birthday
Missouri	K-12	3 doses TOPV, at least 1 after age 3 years
Montana	K-12	3 dose minimum o live TOPV, last dose after 4th birthday
Nebraska	K-12	3 doses
Nevada	K-12	3 to 4 doses
New Hampshire	New Enterers	4 doses; 3 if 3rd is on or after 4th birthday
New Jersey	K-12	3 doses OPV including booster; IPV 4 doses including booster 1968 and after
New Mexico	K-12	3 doses, at least 1 dose after 4th birthday
New York	K-12	3 or more doses of TOPV, or 4 or more doses of IPV, and administered after 1968
North Carolina	K-12	4 doses oral vaccine; 3 doses by age 2 yrs; 1 dose on or after 4 years
North Dakota	K-12	4 doses
Ohio	K-12	3 doses OPV or 4 IPV through 17 years of age
Oklahoma	K-12	3 doses
Oregon	K-12	4 doses; 3 for grades 2-12 in Oregon schools on 3/14 82 unless 1 or more received before 6 months, then 4 doses
Pennsylvania	K-12	3 doses OPV or 4 doses IPV
Puerto Rico	K-12	3 doses, provided the 3rd is given after 4th birthday
Rhode Island	K-12	3 doses
South Carolina	K-12	3 doses, at least 1 must be on or after 4th birthday
South Dakota	K-12	3 doses OPV or 4 doses IPV, at least 1 received after the 4th birthday
Tennessee	K-12	4 doses, 1 dose given on or after the 6th birthday
Texas	K-12	3 doses, 1 dose since 4th birthday; through 17 years old
Utah	K-12	3 doses
Vermont	K-12	3 doses, with 6 months between 2nd dose and any thereafter
Virginia	K-12	3 doses, with 3rd after 4th birthday
Washington	K-12	3 doses, last dose must be at or after age 4 years
West Virginia	New Enterers	3 doses minimum, with 1 after 4th birthday, not given after 18 years of age
Wisconsin	K-12	4 doses, only 3 if 3rd received after 4th birthday
Wyoming	New Enterers	4 doses, entering Wyoming schools

Physician Diagnosis of Disease Accepted as Evidence of Immunity (K-12)

■ Accepted ☐ Not Accepted ⊟ Not Applicable (Immunity not required)

State	Diphtheria	Tetanus	Pertussis	Measles	Mumps	Rubella	Polio
Alabama		■			■		
Alaska					⊟		
Arizona		⊟	⊟		⊟		
Arkansas	■	■	■	■	⊟	■	■
California				■			
Colorado				■	■		
Connecticut				■	■		
Delaware							
Dist. of Col.	■	■	■		■		■
Florida				■			
Georgia							
Hawaii				■	■		
Idaho			⊟	■	■		
Illinois				■	■		
Indiana				■	■		
Iowa				■	⊟		
Kansas				■	■	■	
Kentucky			⊟	■	⊟		
Louisiana	■	■	■	■	■	■	■
Maine							
Maryland					⊟		
Massachusetts	■	■	■	■	■		■
Michigan				■		■	
Minnesota				■			
Mississippi				■	⊟	■	
Missouri	■	⊟	⊟	■	⊟	■	■
Montana			⊟	■	⊟		
Nebraska							
Nevada				■	⊟		
New Hampshire				■	■		
New Jersey				■	■		
New Mexico					⊟		
New York		⊟	⊟	■	■		
North Carolina				■			
North Dakota							
Ohio				■	■		
Oklahoma				■	⊟		
Oregon			⊟	■	■	■	
Pennsylvania			⊟		■		
Puerto Rico		■	■	■	■	■	■
Rhode Island			⊟				
South Carolina					⊟		
South Dakota				■			
Tennessee				■	⊟		
Texas			⊟	■	■		
Utah				■	■		
Vermont				■	⊟		
Virginia							
Washington			⊟	■			
West Virginia		■	■	■	⊟		■
Wisconsin							
Wyoming					■		

Immunization Date and Dose Documentation Required (K-12)

■ Single date/dose documentation required ▩ Mixed date/dose documentation used

State	Dose Only	Applicable Vaccines	Dose & Year	Applicable Vaccines	Dose & Mo/Yr	Applicable Vaccines	Dose & M/D/Y	Applicable Vaccines
Alabama					■	ALL		
Alaska							■	ALL
Arizona					▩	D,PO,R	▩	MEASLES
Arkansas							■	ALL
California					■	ALL		
Colorado					▩	DTP,PO	▩	MMR
Connecticut							■	ALL
Delaware					■	ALL		
Dist. of Col.	■	ALL						
Florida							▩	ALL
Georgia					▩	ALL		
Hawaii							▩	ALL
Idaho							■	ALL
Illinois							■	ALL
Indiana					▩	DTP,PO	▩	MMR
Iowa							■	ALL
Kansas							■	ALL
Kentucky					■	ALL		
Louisiana					▩	DTP,PO,MU,R	▩	MEASLES
Maine					■	ALL		
Maryland							▩	ALL
Massachusetts					▩	ALL		
Michigan					▩	DTP,PO	▩	MMR
Minnesota					▩	DTP,PO,MU,R	▩	MEASLES
Mississippi					■	ALL		
Missouri					■	ALL		
Montana					▩	DT,PO,R	▩	MEASLES
Nebraska					■	ALL		
Nevada					■	ALL		
New Hampshire							■	ALL
New Jersey					▩	DTP,PO	▩	MMR
New Mexico							■	ALL
New York			▩	D,PO			▩	MMR
North Carolina							■	ALL
North Dakota					■	ALL		
Ohio							▩	ALL
Oklahoma					■	ALL		
Oregon					■	ALL		
Pennsylvania					■	ALL		
Puerto Rico					■	ALL		
Rhode Island					■	ALL		
South Carolina					▩	DTP,PO	▩	ME,R
South Dakota					■	ALL		
Tennessee					■	ALL		
Texas					■	ALL		
Utah					■	ALL		
Vermont			■	ALL				
Virginia							▩	ALL
Washington					■	ALL		
West Virginia							▩	ALL
Wisconsin							■	ALL
Wyoming							■	ALL

ALL = All vaccines required by individual states

Exemptions from Immunization Requirements (K-12)

■ Allowed ☐ Not Allowed

State	Medical	Religious	Philosophical
Alabama	■	■	
Alaska	■	■	
Arizona	■	■	■
Arkansas	■	■	
California	■	■	■
Colorado	■	■	■
Connecticut	■	■	
Delaware	■	■	■
Dist. of Col.	■	■	
Florida	■	■	
Georgia	■	■	
Hawaii	■	■	
Idaho	■	■	■
Illinois	■	■	
Indiana	■	■	■
Iowa	■	■	
Kansas	■	■	
Kentucky	■	■	
Louisiana	■	■	■
Maine	■	■	■
Maryland	■	■	
Massachusetts	■	■	
Michigan	■	■	■
Minnesota	■	■	■
Mississippi	■		
Missouri	■	■	■
Montana	■	■	■
Nebraska	■	■	■
Nevada	■	■	
New Hampshire	■	■	
New Jersey	■	■	
New Mexico	■	■	
New York	■	■	
North Carolina	■	■	
North Dakota	■	■	■
Ohio	■	■	■
Oklahoma	■	■	■
Oregon	■	■	
Pennsylvania	■	■	■
Puerto Rico	■	■	
Rhode Island	■	■	■
South Carolina	■	■	
South Dakota	■	■	
Tennessee	■	■	
Texas	■	■	
Utah	■	■	■
Vermont	■	■	■
Virginia	■	■	
Washington	■	■	
West Virginia	■		
Wisconsin	■	■	■
Wyoming	■	■	

Immunization Requirements Applicable to Any or All Students Enrolled in K-12, Day-Care, and College

▨ Required ☐ Not Required ⊟ Not Applicable (no law or requirement)

	Diphtheria			Tetanus			Pertussis			Measles			Mumps			Rubella			Polio		
	K-12	Day Care	College	K-12	Day Care	College	K-12	Day Care	College	K-12	Day Care	College	K-12	Day Care	College	K-12	Day Care	College	K-12	Day Care	College
Alabama	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Alaska	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	▨	▨	⊟
Arizona	▨	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	☐	⊟	☐	☐	⊟	▨	☐	⊟	▨	☐	⊟
Arkansas	▨	▨	☐	▨	▨	☐	▨	▨	☐	▨	▨	▨	☐	☐	☐	▨	▨	▨	▨	▨	☐
California	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Colorado	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Connecticut	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Delaware	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟
Dist. of Col.	▨	▨	▨	▨	▨	▨	☐	☐	☐	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	☐
Florida	▨	▨	☐	▨	▨	☐	▨	▨	☐	▨	▨	▨	▨	▨	☐	▨	▨	▨	▨	▨	☐
Georgia	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Hawaii	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Idaho	▨	⊟	⊟	▨	⊟	⊟	☐	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟
Illinois	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Indiana	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	☐	⊟	▨	▨	⊟	▨	▨	⊟
Iowa	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	▨	▨	⊟
Kansas	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Kentucky	▨	▨	⊟	▨	▨	⊟	☐	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	▨	▨	⊟
Louisiana	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Maine	▨	▨	▨	▨	▨	▨	▨	▨	☐	▨	▨	▨	▨	▨	☐	▨	▨	▨	▨	▨	☐
Maryland	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	▨	▨	⊟
Massachusetts	▨	▨	▨	▨	▨	▨	▨	▨	☐	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	☐
Michigan	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Minnesota	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟
Mississippi	▨	▨	☐	▨	▨	☐	▨	▨	☐	▨	▨	▨	☐	▨	☐	▨	▨	▨	▨	▨	☐
Missouri	▨	⊟	⊟	☐	⊟	⊟	☐	⊟	⊟	▨	⊟	⊟	☐	⊟	⊟	▨	⊟	⊟	▨	⊟	⊟
Montana	▨	▨	⊟	▨	☐	⊟	☐	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	▨	▨	⊟
Nebraska	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟
Nevada	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	☐	☐	⊟	▨	▨	⊟	☐	☐	⊟
New Hampshire	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	☐	⊟	☐	☐	⊟
New Jersey	☐	☐	⊟	▨	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	☐	⊟	☐	☐	⊟
New Mexico	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	☐	⊟	☐	☐	⊟
New York	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	☐	⊟	☐	☐	⊟
North Carolina	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
North Dakota	▨	▨	⊟	▨	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	▨	⊟	☐	☐	⊟
Ohio	▨	▨	⊟	▨	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	▨	⊟	☐	☐	⊟
Oklahoma	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
Oregon	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
Pennsylvania	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
Puerto Rico	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Rhode Island	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
South Carolina	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
South Dakota	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Tennessee	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
Texas	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Utah	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
Vermont	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
Virginia	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Washington	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟
West Virginia	▨	▨	⊟	▨	☐	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	▨	⊟	☐	☐	⊟
Wisconsin	▨	▨	⊟	▨	▨	⊟	☐	☐	⊟	☐	☐	⊟	☐	☐	⊟	▨	▨	⊟	☐	☐	⊟

Enforcement of Immunization Requirements

▩ Law/requirement contains clause ☐ Law/requirement does not contain clause
⊟ Not Applicable (No law or requirement)

State	Penalty Clause for Noncompliance			Exclusion Clause for Noncompliance		
	K-12	Day-Care	College	K-12	Day-Care	College
Alabama	▩	▩	⊟	▩	☐	⊟
Alaska	☐	☐	⊟	▩	▩	⊟
Arizona	☐	☐	⊟	▩	▩	⊟
Arkansas	▩	▩	☐	▩	☐	☐
California	☐	☐	⊟	▩	▩	⊟
Colorado	☐	☐	⊟	▩	▩	⊟
Connecticut	▩	▩	⊟	☐	☐	⊟
Delaware	☐	⊟	⊟	▩	⊟	⊟
Dist. of Col.	☐	▩	☐	▩	▩	☐
Florida	☐	☐	☐	▩	▩	▩
Georgia	▩	▩	⊟	▩	▩	⊟
Hawaii	▩	▩	⊟	▩	▩	⊟
Idaho	☐	⊟	⊟	☐	⊟	⊟
Illinois	▩	▩	⊟	▩	☐	⊟
Indiana	☐	☐	⊟	▩	☐	⊟
Iowa	▩	▩	⊟	☐	☐	⊟
Kansas	☐	▩	⊟	▩	☐	⊟
Kentucky	▩	▩	⊟	▩	☐	⊟
Louisiana	▩	▩	⊟	▩	▩	⊟
Maine	☐	☐	☐	▩	▩	▩
Maryland	☐	☐	⊟	▩	▩	⊟
Massachusetts	☐	▩	☐	▩	▩	☐
Michigan	▩	▩	⊟	▩	▩	⊟
Minnesota	☐	☐	⊟	▩	▩	⊟
Mississippi	▩	▩	☐	▩	▩	▩
Missouri	☐	⊟	⊟	▩	⊟	⊟
Montana	▩	☐	⊟	▩	▩	⊟
Nebraska	▩	▩	⊟	▩	▩	⊟
Nevada	▩	▩	⊟	▩	▩	⊟
New Hampshire	☐	▩	⊟	▩	▩	⊟
New Jersey	▩	▩	⊟	▩	▩	⊟
New Mexico	▩	▩	⊟	▩	▩	⊟
New York	▩	☐	⊟	▩	▩	⊟
North Carolina	▩	☐	☐	▩	▩	☐
North Dakota	▩	▩	⊟	▩	▩	⊟
Ohio	☐	☐	⊟	▩	▩	⊟
Oklahoma	▩	▩	⊟	▩	▩	⊟
Oregon	☐	☐	⊟	▩	▩	⊟
Pennsylvania	▩	▩	⊟	▩	☐	⊟
Puerto Rico	▩	▩	☐	▩	▩	▩
Rhode Island	☐	☐	☐	▩	▩	▩
South Carolina	▩	▩	⊟	▩	▩	⊟
South Dakota	☐	▩	☐	▩	☐	☐
Tennessee	▩	▩	⊟	☐	☐	⊟
Texas	☐	☐	☐	☐	☐	☐
Utah	▩	☐	⊟	▩	▩	⊟
Vermont	☐	☐	⊟	▩	☐	⊟
Virginia	▩	☐	☐	☐	▩	☐
Washington	☐	☐	⊟	▩	▩	⊟
West Virginia	▩	☐	⊟	☐	☐	⊟
Wisconsin	▩	☐	⊟	▩	▩	⊟
Wyoming	☐	☐	☐	▩	▩	▩

Rubella Susceptibility Testing

■ Required ☐ Not Required

State	Premarital	Hospital Employee
Alabama		
Alaska		■
Arizona		
Arkansas		
California	■	
Colorado	■	
Connecticut	■	
Delaware		
Dist. of Col.		
Florida		
Georgia	■	
Hawaii	■	
Idaho	■	
Illinois		
Indiana	■	
Iowa		
Kansas		
Kentucky		
Louisiana		
Maine		■
Maryland		■
Massachusetts		
Michigan		
Minnesota		
Mississippi		
Missouri		
Montana	■	
Nebraska	■	
Nevada		
New Hampshire		■
New Jersey		
New Mexico	■	
New York	■	■
North Carolina		
North Dakota		
Ohio		
Oklahoma		
Oregon		
Pennsylvania		
Puerto Rico		
Rhode Island	■	■
South Carolina		
South Dakota		
Tennessee		
Texas		
Utah		
Vermont		
Virginia		
Washington		
West Virginia		
Wisconsin		
Wyoming	■	

Immunization of Rubella Susceptibles

■ Required ☐ Not Required

State	Premarital	Hospital Employee
Alabama		
Alaska		■
Arizona		
Arkansas		
California		
Colorado		
Connecticut	■	
Delaware		
Dist. of Col.		
Florida		
Georgia		
Hawaii		
Idaho		
Illinois		
Indiana		
Iowa		
Kansas		
Kentucky		
Louisiana		
Maine		■
Maryland		
Massachusetts		
Michigan		
Minnesota		
Mississippi		
Missouri		
Montana		
Nebraska		
Nevada		
New Hampshire		■
New Jersey		
New Mexico		
New York		■
North Carolina		
North Dakota		
Ohio		
Oklahoma		
Oregon		
Pennsylvania		
Puerto Rico		
Rhode Island		■
South Carolina		
South Dakota		
Tennessee		
Texas		
Utah		
Vermont		
Virginia		
Washington		
West Virginia		
Wisconsin		
Wyoming		

Alaska State Legislature
House of Representatives
COMMITTEE ON HEALTH, EDUCATION
AND SOCIAL SERVICES

OFFICIAL BUSINESS

POUCH V
JUNEAU, AK 99811
465-3759

March 8, 1988

Honorable Ted Stevens
United State Senate
522 Hart Building
Washington, D.C. 20510

Dear Senator Stevens:

As the Co-Chairs of the Alaska House Health, Education, and Social Services Committee, we would like to recommend Shannon Kohler be appointed to the federal Commission being created in conjunction with the National Childhood Vaccine Injury Compensation Act.

Ms Kohler has a strong viewpoint on the subject of mandatory immunization and has put considerable effort into researching and organizing around it. We believe the federal Commission to be an appropriate place for someone with her concerns to serve. She would undoubtedly make a hard working member of such a commission.

It is our understanding that Shannon is also being recommended by the Alaska Department of Health and Social Services, by the Senate HESS Chair, Senator Paul Fischer, and by Representative Mike Navarre.

Thank you for your attention to this matter. We will continue to monitor discussions around the subjects of immunization and public health.

Sincerely,

Rep. Niilo Koponen, Co-Chair

Rep. Johnny Ellis, Co-Chair

CC: Shannon Kohler
NK/JE/ljm

POSITION PAPER/Department of Health & Social Services

Position Paper

HB 277

For an Act entitled: "An Act relating to the immunization of minors."

HB 277 proposes the following changes in statutes pertaining to the immunization of minors in Alaska:

1. Section 1 amends AS 14.30.125 by removing the requirements for immunization against specific diseases as a condition for admission to schools, preschools, nurseries, or day care or child care when a parent or legal guardian states that immunization is contrary to the parent's or guardian's philosophical beliefs. (The Alaska Administrative Code currently exempts children whose parents object to immunizations because of religious beliefs.)

2. Section 2 requires that an individual or facility administering vaccine must provide the following information to the parent or guardian prior to the immunization: (a) a written explanation of the risks and benefits associated with the immunization; (b) a copy of the product insert required by the Food and Drug Administration; (c) a list of symptoms of adverse reactions to the immunization; and (d) a copy of the pertinent legislation and regulations. Moreover, the person who administers the immunization must ascertain that the parent or guardian has received and understands the materials provided.

3. Proposed Section AS 18.15.310 requires that health care providers submit and the Department of Health and Social Services investigate any reports of adverse reactions to immunizations and requires the department to report annually to the legislature on the incidence of infectious disease and the incidence of serious reactions and permanent or long-term damage to minors that results from immunization.

4. Proposed Section AS 18.15.320 requires that records of lot numbers and vaccine manufacturers be maintained for three years after immunization.

The first three of these provisions are discussed below.

1. <u>Exemption from mandatory immunization requirements based on philosophical beliefs of parent or guardian</u>

AS 14.30.125 authorizes the Department of Health and Social Services to require that children entering school be immunized against diseases

specified by the commissioner. Currently, regulations (7 AAC 50.255) require immunizations against diphtheria, tetanus, polio, measles, rubella, and if the child is under seven years of age, pertussis. Regulations allow a child to be exempted from immunization requirements if receiving the immunization is contrary to the religious beliefs of the parent or guardian or if there are medical reasons to exempt the child. 7 AAC 50.255, adopted under the authority of AS 47.35.030, requires that a child receive immunizations "appropriate to his age as prescribed in the Alaska Division of Public Health's schedule for active immunization" as a condition of admission to day care.

Although "childhood diseases" are commonly thought to be benign, complications do occur and can be severe. For example, inflammation of the heart muscle can complicate diphtheria; pneumonia is one of the chief complications of both measles and pertussis; and neurological damage can occur with diphtheria, measles, mumps, and pertussis. Rubella can cause a wide spectrum of congenital disorders when acquired by the mother during pregnancy. The goal of rubella immunization programs is to assure immunity of all females before they reach childbearing age and to limit the accidental exposure of pregnant women to the virus.

Vigorous immunization efforts aimed particularly at very young children have virtually eliminated most of the vaccine-preventable diseases, as seen in the following table:

	Diphtheria	Measles	Mumps	Pertussis	Rubella
1976	8	14	39	0	2
1977	2	60	35	5	1
1978	3	1	15	18	8
1979	0	17	15	10	4
1980	0	6	15	5	12
1981	1	0	20	1	1
1982	0	1	6	0	1
1983	0	1	10	0	0
1984	0	0	8	3	1
1985	0	0	10	30	1
1986	0	0	8	5	0

Unfortunately, vaccines are not perfect. Vaccines are not 100 per cent effective, and therefore some people who are immunized may not be protected. Also, vaccines are not perfectly safe, and some people who receive them may be damaged by them. The question is one of balancing the benefits to the individual receiving the vaccine and the benefits to society in general against the risk of damage.

In recent years, debate on benefit v. risk has centered on the pertussis vaccine. (Pertussis is a component of the DPT vaccine, one of the "baby shots.") Reactions to the vaccine are relatively common since about 40 per cent of vaccinated children develop minor redness, swelling, and pain at the site of injection. Fever, vomiting, and drowsiness occur in about 20 per cent of vaccines. Convulsions or collapse with complete recovery occur at a rate of about one episode per 1,750 vaccine doses given. Encephalitis occurs at a rate of one case per 110,000 doses

given, and encephalitis with residual defect at a rate of one case per 310,000 doses administered. Sudden infant death syndrome is not related to pertussis vaccine use.

Given the relatively low incidence of pertussis, the adverse effects associated with the vaccine seem prominent. However, for perspective, the effects of the disease itself should be considered. The death rate from pertussis for previously unvaccinated patients who develop the disease is one in 1,000; among affected children less than one year of age, the death rate is one per cent. Permanent brain damage from whooping cough afflicts one child in 10,000 cases. Consensus among health authorities is that the benefit from immunization outweighs the risk. This view has been expressed by the American Medical Association, the Public Health Service, the American Academy of Pediatrics, and the American Public Health Association.

The department believes that because the proposed exemption includes individuals with philosophical objections to immunization, a serious health threat for many Alaskan children will be created. There will be increased risk for those whose parents or guardians elect to exclude them from immunization. There will be increased risk to very young children in other families who have not had a chance to complete the entire series of injections. There will be increased risk to the 10 to 20 per cent of completely immunized children who are incompletely protected because the vaccine is not 100 per cent effective. The decision not to immunize has effects that extend beyond the individual.

Since the decision not to immunize is likely to be unevenly distributed across the population, it is thought that there will be geographic areas in which significant numbers of children will be unimmunized and where the likelihood of disease occurrence will be great.

The recent upswing in reported cases of pertussis in Alaska is directly attributable to the nonimmunized or inadequately immunized status of the cases.

2. Immunization Information

Much of the intent of this portion of the proposed bill is already required by the department as a part of its agreement with the federal Centers for Disease Control, through whom the state's vaccine supply is purchased. The department provides the major portion of vaccines used in the state, with the exception of vaccines used by the military. A written explanation of risks and benefits called the Important Information Statement is used in the public sector. By signing the statement, the parent or guardian states that he or she has read the statement and has had an opportunity to ask questions of the person administering the vaccine. The manufacturer's name and vaccine lot number are recorded and retained. Private physicians who receive vaccine from the state can use the Important Information Statement system or exercise their professional judgement in informing parents or guardians of the risks and benefits of immunization. Written descriptions of potential adverse reactions are also provided. Copies of applicable statutes and regulations are not distributed or discussed.

POSITION PAPER/Department of Health & Social Services

3. Reporting of adverse reactions

7 AAC 27.005 currently requires health care providers to report "severe reactions to any vaccine" to the department. These reports are investigated according to strict protocol required by the national Centers for Disease Control. The investigation and reporting of adverse reactions to vaccinations are required as a condition of the immunization grant awards the department receives from the Centers for Disease Control. The department believes that the current regulatory language is sufficiently directive with regard to the reporting of adverse reactions and the statutory changes proposed in HB 277 are unnecessary.

In addition, Congress has recently adopted a federal vaccine liability law, and the federal government is currently writing regulations for its implementation. This law states: "The Secretary shall establish in the Department of Health and Human Services a National Vaccine Program to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines."

This new law does not allow states to use any discretion regarding the reporting and investigation of reactions to vaccinations. This law also requires that each health care provider who administers a vaccine shall provide to any legal representative of any child to whom such provider intends to administer a vaccine a copy of written information about the vaccine.

Departmental Position

The department opposes this bill for three reasons: (1) Extending exemption from immunization requirements to individuals with philosophical opposition to such requirements will create a serious public health threat to Alaskan children. (2) HB 277's requirement to inform the parent or guardian of an immunization's risks and benefits is unnecessary, as this is already required by the department and by recently enacted federal law. (3) The department will be required to conform with the stringent new federal law governing reporting of adverse reactions. The statutory changes proposed in HB 277 are thus unnecessary and, if adopted, may have to be changed to meet the new federal requirements.

Recommended by: Elizabeth Ward
Elizabeth Ward, Director
Division of Public Health

Date: January 26 1988

Approved by: Myra M. Munson
Myra M. Munson, Commissioner
Department of Health and
Social Services

Date: Feb 10, 1988

STATE OF ALASKA
1988 LEGISLATIVE SESSION

BILL VERSION: HB 277
PUBLISH DATE: _____

FISCAL NOTE

REQUEST:

Revision Date: 4/29/87
Title: An Act relating to the immunization of minors.
Sponsor: _____
Requestor: Navarre

Agency Affected: Health & Social Services
BRU: State Health Services
Components: Section of Epidemiology

EXPENDITURES/REVENUES: (Thousands of Dollars)

OPERATING	FY 88	FY 89	FY 90	FY 91	FY 92	FY 93
PERSONAL SERVICES		45.2	46.9	48.7	50.5	52.4
TRAVEL		6.0	6.0	6.0	6.0	6.0
CONTRACTUAL						
SUPPLIES						
EQUIPMENT						
LAND & STRUCTURES						
GRANTS, CLAIMS						
MISCELLANEOUS						
TOTAL OPERATING		51.2	52.9	54.7	56.5	58.4
CAPITAL						
REVENUE						

FUNDING: (Thousands of Dollars)

GENERAL FUND		51.2	52.9	54.7	56.5	58.4
FEDERAL FUNDS						
OTHER						
TOTAL		51.2	52.9	54.7	56.5	58.4

POSITIONS:

FULL-TIME		1.0	1.0	1.0	1.0	1.0
PART-TIME						
TEMPORARY						

ANALYSIS: (Attach a separate page if necessary)

Personal services and travel costs are for one PFT Public Health Representative, range 16, to assure public information and reporting requirements are met. See attached.

Prepared by: Elizabeth Ward, Director
Division: Public Health
Phone: 465-3090
Date: 2-09-88

(R) Approved by Commissioner: Myra M Munson
Agency: Department of Health & Social Services
Date: 2-10-88

Distribution (by preparer):
Legislative Finance
Legislative Sponsor
Requestor
Office of Management and Budget
Impacted Agency(ies)

HB 277 Fiscal Note Analysis

To meet the requirements of Section 2 of HB 277, which requires individuals or facilities administering immunizations to provide detailed immunization information, a PFT Public Health Representative, range 16, will be needed. This person will be responsible for monitoring the individuals and agencies providing immunizations to assure compliance with the public information requirements of this bill. This person will educate providers on public information and reporting requirements, and will develop and maintain a centralized data bank regarding compliance.

The incumbent will also serve as the intial investigator for the proposed AS 18.15.310 and will develop the annual report for submission to the legislature.

This legislation will cause a reduction in immunization levels in Alaska. Increased disease outbreaks will follow, requiring additional staff time to perform follow-up investigations and outreach information services.

Position Title	No. of Positions	Range/Step	Barg. Unit
Public Health Representative	1	16B	GGU

Time Status	Staff Months	Location	Election District
PFT	12	Anchorage	HD 10/SD F

Type of Expenditure		Amount
1	2	3
Salary	33.6	
Benefits	11.6	
Premium Pay	0	
Other	0	
Total Personal Services		45.2
Travel		6.0
Contractual		
Commodities		
Equipment		
Other		
Total Cost		51.2

Funding Source for Total Cost		
Federal Receipts	1002	
G. F. Match	1003	
General Fund	1004	51.2
GF Program Receipts	1005	
Other		

Justification

A Public Health Representative, range 16, in Anchorage is necessary to assure compliance with the public information requirements of this legislation. This position will monitor the individuals and agencies providing immunizations and will educate them on public information and reporting requirements. The position will develop and maintain a centralized data bank on compliance. The incumbent will also be the initial investigator for the proposed AS 18.15.310 and will develop the annual report to the legislature.

Request For New Position

Agency: Health & Social Services

BRU: State Health Services

Component: Epidemiology

Revised Date

FY 89

From the Governor's Interim Commission on Children and Youth Report

1. Quality: *Health*

BACKGROUND RECOMMENDATION

Child Care Revolving Loan Fund: 31

Centers and homes that provide child care and education must be healthy for our children. But many programs are located in inadequate, makeshift spaces, sometimes poorly heated and often with minimal outdoor play space and equipment. When children spend so much of their time indoors, the space must be adequate for the number of children as well as well-lit, heated and maintained.

Child care is labor intensive and capital poor. Alaska used to have a Child Care Revolving Loan Fund for capital improvement. The maximum loan per facility was $50,000. By banking standards the loans were small. Loans were only available to property owners who often did not run the programs. These factors make it extremely difficult for child care programs to find needed capital to improve existing buildings and make them healthy places for children.

Alaska should reinstate the low interest Child Care Revolving Loan Fund, increase its previous level of funding and simplify the required paperwork. This loan program provides funding support so child care facilities can meet all codes and ensure a healthy environment for our children.

Child care is labor intensive and capital poor.

Comprehensive Health Screening: 32

Comprehensive health screenings assure parents and practitioners that the care for young children is appropriate to their needs. Screenings that check height and weight, blood pressure, teeth and include a random check for scoliosis promote normal growth and development. Regular attention to each child's physical health is essential to all children's well-being. The only funding presently available for comprehensive health screening of children in the Department of Health and Social Services is for children who have already been identified as developmentally disabled.

Required immunizations, adequate nutrition and access to medical, dental and mental health services are the right of all of Alaska's children and part of any quality early childhood system.

Comprehensive health screenings should be guaranteed to all Alaska's infants, toddlers, preschoolers and students, to identify problems as soon as possible to prevent more expensive treatment later.

Regular attention to each child's physical health is essential to all children's well-being.

Pertinent correspondence from State Health Dept. as referred to in Briefing Paper

STATE OF ALASKA

DEPT. OF HEALTH AND SOCIAL SERVICES

DIVISION OF PUBLIC HEALTH
SECTION OF COMMUNICABLE DISEASE CONTROL

May 1, 1986

The information you requested about DTP vaccine and whooping cough was not easily retrievable. The major reason being that I have only been on the job three months, therefore, I didn't know who to ask or where to look. However, this is what I have found.

1. There were five cases of whooping cough in 1984 and 30 cases in 1985.

2. Four of the five cases were confirmed in 1984 and nine of the 30 cases were confirmed in 1985.

3. A total of four of the 35 cases were hospitalized with no deaths.

4.

Age	1984	1985
unknown	0	4
<1	2	10
1	1	6
2	0	4
5-9	0	2
10-19	0	3
20-24	0	1
25-29	1	0
30-39	1	0

Approximately half of the cases had received pertussis vaccine at some point in their life , however, whether they were appropriately immunized for age I am unable to ascertain.

5. The parents/guardians of recipients who see a physician or who are hospitalized within one month of an immunization are supposed to notify the Alaska Immunization Program. When I receive notification of an adverse event following an immunization, I contact the parents/guardians, the immunization provider, and the attending physician. It is the physician's responsibility to determine whether or not the patient's problems are vaccine-related. All vaccine-related adverse reactions are documented on an official report form and sent to the Centers for Disease Control in Atlanta, Georgia.

I hope the enclosures are of help to you.

Sincerely,

Michael Klatt

Michael Klatt, Manager
Alaska Immunization Program

MK:db

BILL SHEFFIELD, GOVERNOR

DEPT. OF HEALTH AND SOCIAL SERVICES

DIVISION OF PUBLIC HEALTH
SECTION OF COMMUNICABLE DISEASE CONTROL

3601 "C" STREET, SUITE 576
POUCH 6333
ANCHORAGE, AK 99502-0333
(907) 561-4235

November 14, 1986

Ms. Shannon Kohler
Alaska Chapter-DPT
Box 1746
Soldotna, AK 99669

Dear Ms. Kohler:

Thank you for the information relative to the pertussis poster containing incorrect information. We are not aware of any state-wide department offices displaying such a poster.

The "Dear Health Care Provider" contains information which has been in existence for at least two years and is considered common knowledge by most health care providers who administer vaccine. However, it maybe appropriate to reiterate the information in an upcoming edition of the Epidemiology Bulletin (a news bulletin sent to health care providers and other interested parties). Also, we will be rewriting the immunization standing orders for the Public Health Nurses and, if not already part of their standing orders, we will include this important information.

The State does not have any specific regulations regarding the reporting of adverse reactions following immunizations. Health care provders who administer vaccines are encouraged to report possible adverse reactions to this office. This is a passive surveillance system which relies on the integrity of the health care providers to comply.

The answers to your remaining questions are as follows:

1. Report Gathering

   A. How are adverse reactions gathered from parents? from public health officials administering vaccine? from doctors?

      Parents are to notify the provider of the vaccine if the vaccinee visits a doctor, hospital, or clinic within 4 weeks of vaccination, as requested on every Important Information Form. A public provider who is made aware of a possible adverse reaction completes the MSAEFI report form and submits it to this office. A private physician who is made aware of a possible adverse reaction notifies this office and the MSAEFI Coordinator completes the MSAEFI report form.

B. What is the estimated rate of compliance?

C. How exactly is the rate of compliance determined?

No estimated rate of compliance is determined.

2. Handling Reports

A. Once a report is received, where and how is it recorded?

All submitted MSAEFI report forms are entered onto a MSAEFI report form log sheet by the MSAEFI Coordinator. All submitted MSAEFI report forms which meet the minimal criteria for submission to the Centers for Disease Control are forwarded.

B. Is the original or copy of report kept by State office?

A typed carbon copy is retained by the State office.

C. Is the original or copy of report sent to the National Center of Disease Control (CDC) in Atlanta Georgia?

A typed copy is forwarded to the CDC.

3. Approximately how many adverse reaction reports does your office receive per year from public health officials?

1985 - 12 (2 of which were military)
1986 - 9

from doctors?

1985 - 3
1986 - 1

from parents?

1985 - 0
1986 - 0

(The numbers listed above indicate adverse reaction reports forwarded to the CDC, not the number received by this office.)

B. What are the symptoms and diagnosis included in reports?

See enclosed MSAEFI report form.

And, finally, your last request to "send me a copy of the annual Alaska State reports regarding immunizations and reactions that were sent to Atlanta, Georgia CDC in 1984 and 1985," will have to be more specific.

There are no annual reaction reports, however, there a quite a few immunization reports sent to the CDC quarterly and annually by this office. If the specific information you want is available, we will send it to you.

Sincerely,

Michael Klatt, Manager
Alaska Immunization Program

Robert I. Fraser, M.D. Chief
Sec. of Comm. Disease Control

MK+RIF:ew

Enclosure

cc: Elizabeth Ward, Director
Division of Public Health

HB 277
REFERENCE MATERIALS
FROM
ALASKA DISSATISFIED PARENTS TOGETHER

TURNING POINT
Family Wellness Center

Edward H. Chapman, M.D.
Dolores Heeb, Reg. Ac.
Richard P. Ingrasci, M.D., M.P.H.
Richard Moskowitz, M.D.
Geri Schumacher, R.N.

November 25, 1987

Alaska State Legislature
Health Education and Social Affairs Committee
c/o Glenda Landua, Alaska DPT
39918 Dawn Avenue
Kenai, Alaska 99611

Dear Sir:

I am writing in support of House Bill No. 277, "An Act Relating to the Immunization of Minors."

I am a family physician and have been practising medicine for the past twenty years. During that time I have been impressed with the number and variety of chronic diseases that can be provoked or exacerbated by the various childhood vaccines in general use. My thoughts and observations on this subject are summarized in the articles enclosed herewith.

I am especially troubled by the fact that investigations of vaccine-related illness have generally been limited to acute complications occurring within thirty (30) days of the administration of the vaccine, thus excluding any condition occurring more gradually or not evident until months or years later.

Requiring all children to be vaccinated with foreign proteins or live viruses clearly presupposes the moral and legal obligation to prove both that the corresponding natural diseases constitute a serious public health hazard, and that the vaccines themselves are in no way detrimental to health. Furthermore, it implies full legal and financial liability for any illness or injury sustained by those vaccinated against their will.

Adequate investigation of chronic vaccine-related illness will necessarily be prolonged and difficult. It will require following large numbers of both vaccinated and unvaccinated children for at least a decade or more, to determine any differences in their overall health patterns, and in the incidence and severity of various chronic diseases (recurrent otitis media, asthma, epilepsy, behavior disorders, etc.).

Until these studies are completed, it would be reckless indeed to continue routine childhood vaccination on a compulsory or statutory basis. I personally favor making all vaccines completely optional, i.e., freely available to all who want them, and allowing parents to make the choice with and for their children, as is now being done in West Germany and many other countries. This practice will effectively reduce the liability of the state, if and when complications do occur. Furthermore, it will create a sizeable control group of unvaccinated children for the long-term studies that urgently need to be done.

For all of these reasons, I urge you to support H. B. 277, and to make it as simple as possible for parents not to vaccinate their children. I would suggest, for example, amending the opening section so as to allow parents to accept some vaccines, and to reject others, without having to give a reason, and without any discrimination or penalty. The term "religious or philosophical beliefs" implies a principled, across-the-board repudiation, while many parents actually prefer to obtain the tetanus and oral polio vaccines, for example, but not the others. The right to make such choices should perhaps be stated explicitly.

But, even in its present form, the proposed law is an important step forward, bringing Alaska abreast of the other states that have been most progressive in this respect. It deserves your full support.

Thank you.

Truly yours,

Richard Moskowitz, M.D.

The Nevada Clinic
6105 W. Tropicana Ave., Las Vegas, NV 89103
(702) 871-2700

January 13, 1988

Shannon Kohler, President
Alaska Dissatisfied Parents Together
Box 1746
Soldotna, Alaska 99669

Dear Shannon:

I have received your letter and am in complete sympathy with your efforts to modify the immunization laws as they exist in your state. Thank you very much for sending me a copy of the House Bill No. 277. I wish you all the success in the world in getting it passed.

I am enclosing a photocopy of a fairly recent article from the April, 1987 issue of the British Homeopathic Journal that deals with the use of pertussin as a prophylactic treatment to prevent whooping cough. As you can see from the articles enclosed, the battle goes on in other countries, as well as in various states in the United States.

I believe that homeopathy offers tremendous advantages over the standard and routine immunization programs, which have been pushed by allopathic medicine since the beginning of time (Pasteur's time, that is).

Our clinic has seen several infants and children who have not had a good response as a result of D.P.T. immunizations. I can recall three small children who developed "infantile spasms" and seizures as a result of the pertussin part of the D.P.T. immunization. Of course, none of the physicians who administered the injections, nor the company that made the serum, would in any way admit any kind of a connection between the immunization and the child's problems. Nevertheless, when treated homeopathically to remove the pertussin from the brains and nervous systems of these infants, they all have totally recovered without any further seizures or spasms.

There has not been a great deal of research done that I am aware of in this country with regards to an immunization program based on the treatments utilized by homeopathic physicians for the past 150 years. Nevertheless, these programs have proven very effective. In fact, during the 1917 flu epidemic in this country, the only patients who survived were those who were fortunate enough to find a homeopathic physician and be treated homeopathically.

I hope this information is of some help to you. There are obviously other journals and articles that could be sent, but I don't have them in hand at the present time.

Sincerely,

F. Fuller Royal, M.D.

FFR/elm

IMMUNIZATION COMPLIANCE RATES OF SCHOOL AGE CHILDREN (K-1ST GRADE) AND INCIDENCE OF VACCINE PREVENTABLE DISEASES (1986)

ALL STATES INCLUDED IN SURVEY HAVE PHILOSOPHICAL OBJECTION TO STATE MANDATED IMMUNIZATIONS IN STATUTES

	compliance rate:	reported cases of: measles	rubella	mumps	pertussis	tetanus	diptheria	polio
Michigan	91%	185	24	467	36	1	INA	INA
1971 (approx.) - mandatory law implemented 1971 (approx.) - philosophical objection allowed								
Utah	93%	13 [38.5%] {61.5%}	15	16	44 [65.9%] {34.1%}	0	0	0
197[illegible] - mandatory law implemented **1982 (approx.) - philosophical exemption allowed**								
Washington	95.7%	176 [65%] {35%}	15	30	163 [56%] {44%}	0	0	0
Missouri	98.3%	32	1	23*	32*	2(2)*	0	0
California	93.4%	497 [50%] {50%}	242	336	310 [40%] {60%}	3	0	1
1961-mandatory law implemented 1961-philosophical exemption allowed								
Pennsylvania	99.2%	28	1	63	52	1	0	0
Oklahoma	97.6%	39	0	INA	134	1	0	0
1976-mandatory law implemented 1976-philosophical exemption allowed								
Nebraska	96.5%	1	0	2	10	INA	INA	INA
1973-mandatory law implemented 1973-philosophical exemption allowed								
Indiana	97%	39	0	339	39	2	0	0
1976-mandatory law implemented 1976-philosophical exemption allowed								
Delaware	98%	35	INA	INA	INA	INA	INA	INA
1982-mandatory law implemented 1982-philosophical exemption allowed								

(6)

COMPLIANCE RATES CONT'D.

	compliance rate:	reported cases of: measles	rubella	mumps	pertussis	tetanus	diptheria	polio
Ohio	95%	1(0) [80%] {20%}	0	150	170	0	0	2
1959-mandatory law implemented **1970 (approx.)-philosophical exemption allowed**								
Arizona	95.1%	252	2	209	78	1	0	0
1976-mandatory law implemented **1981-philosophical exemption allowed**								
Minnesota	99%	50 [89%] {21%}	1	86 [88.8%] {11.2%}	50	0	0	0
1967-mandatory law implemented **1978-philosophical exemption allowed**								
Colorado	96.3%	11	1	17	84(2)	0	0	0
1974-mandatory law implemented **1979-philosophical exemption allowed**								
Maine	INFORMATION NOT AVAILABLE							
1977-mandatory law implemented 1977-philosophical exemption allowed								
Wisconsin	96.5%	287	1	325	111	0	0	0
1975-mandatory law implemented **1980-philosophical exemption allowed**								
Vermont	98%	0	1	6	5	0	0	0
1979-mandatory law implemented 1979-philosophical exemption allowed								

INA: information not available
*: immunization not mandatory in state
(n): fatalities
[n]: percent of ill fully immunized
{n}: percent of ill unimmunized

Data received from State Health Departments of states listed
22 states contacted - 17 states responded to date - January 20, 1988

All states implement exclusion of unimmunized children from school during vaccine preventable disease occurances.

13 of 17 states have mandatory disease reporting laws; 7 of those have penalties for non-reporting of contagious diseases

Data compiled by the Alaska Chapter of Dissatisfied Parents Together

(7)

Box 118
Columbus, Ohio 43266-0118

Telephone (614) 466-3543

RICHARD F. CELESTE
Governor

November 4, 1987

Shannon Kohler
Alaska Chapter-DPT
Box 1746
Soldotna, Alaska 99669

Dear Ms. Kohler:

I am responding to your July 27 letter regarding immunization exemptions. I am sorry for the delay, but the mail had apparently been misrouted.

While immunization exemptions are a concern, immunization-exempt children have not contributed to disease initiation or propagation in Ohio.

In Ohio immunization levels exceed 95 percent in schools; in fact, in kindergarten they are 97 percent or greater. Immunization exemptions have not exceeded Ø.3 percent - Ø.5 percent among children new to Ohio schools. (The table enclosed gives you information regarding immunization levels, exemptions and reported cases of the vaccine-preventable diseases you requested.)

The measles cases in Ohio (1Ø last year) can virtually all be attributed to importations and spread from importations among persons either inadequately vaccinated or vaccine failures, but not persons who are immunization exempt. In 1986, only two of the 1Ø cases were not previously vaccinated. Because of their small number, exemptions have not played a major part in outbreaks.

In 1986 Ohio reported 17Ø cases of pertussis. Of these we were able to determine the age and vaccine status of 115. Most of these cases were just too young to have completed a full series of DTP immunizations. While an analysis of immunization exemptions was not made, only two of the cases were of school age.

Mumps cases have been declining in Ohio since the inclusion of mumps in the school immunization law beginning in 1984. The 15Ø cases reported in 1986 can not be attributed to immunization exemptions.

I hope this answers most of your questions, please let me know if I can provide any further information.

Sincerely,

Thomas J. Halpin, M.D., M.P.H.
Chief
Bureau of Preventive Medicine

KOHLERLE.PRN
Enclosure:

(9)

November 12, 1987

SUMMARY OF SEVERE ADVERSE REACTIONS TO STATE MANDATED IMMUNIZATIONS

Data collected by: Dissatisfied Parents Together, Alaska Chapter

Dates of survey: October 1986-October 1987

Method used: Alaska "DPT" vaccine adverse reaction questionnaire

Number of subjects (reactions) - 25: 24 DPT
1 MMR

Range of survey: State of Alaska

1- College, AK.	1- Anchorage, AK.
1- Gustavis, AK.	1- Anchor Point, AK.
1- Sterling, AK.	1- Homer, AK.
4- Kenai, AK.	3- Fairbanks, AK.
2- Juneau, AK.	7- Soldotna, AK.
1- Palmer, AK.	2- Kasilof, AK.

Ages of subjects at date of response:

2- 4 months	1- 4 years
1- 6 months	2- 5 years
1-10 months	3- 6 years
1- 14 months	1- 8 years
1- 18 months	1- 17 years
5- 2 years	1- 20 years
4- 3 years	1- 23 years

Return to: Dissatisfied Parents Together (11)
Box 1746
Soldotna, AK 99669
Shannon Kohler 262-3825

DPT SHOT REACTION QUESTIONNAIRE

Directions: Please place an "X" before the answer(s) you select or fill in the spaces when appropriate.

1. Before your child received his DPT shot(s), did a health professional inform you of the possible serious reactions to the shot?

   5 Yes (1) 19 No (2) 1 Don't Know (3)

2. Did the health professional who gave your child the DPT shot(s) tell you to look for and report severe reactions such as a high temperature, excessive crying or high pitched screaming, excessive sleepiness, etc.?

   6 Yes (1) 18 No (2) 1 Don't Know (3)

3. Before giving your child the DPT shot(s) did a health professional tell you when the shot should not be given (i.e. if the child has an active infection or a fever, if the child reacted severely to a previous DPT shot, etc.)?

   6 Yes (1) 16 No (2) 3 Don't Know (3)

4. Did you sign a consent form containing information about the DPT shot and its possible reactions before your child received his DPT shot?

   2 Yes (1) 15 No (2) 8 Don't Know (3)

5. Before your child received his DPT shot(s), did a health professional question you about your family's and your child's medical history?

   ___ Yes (1) 23 No (2) 2 Don't Know (3)

6. Do you believe your child reacted severely to any of his DPT shots? (Answer yes only if the reaction was more serious than a low fever, mild crying, or slight redness or puffiness around the site of the shot)

   25 Yes (1) ___ No (2) ___ Don't Know (3)

If you answered yes to question #6, please answer the rest of the questionnaire. If you answered no to question #6, skip the rest of the questions and fill in your name, address and telephone number at the end of the questionnaire.

7. After the DPT shot that caused your child to react severely, did he have:
   most children had more than one symptom of reaction

   4 convulsions (1)
   16 fever of more than 103 degrees (2)
   13 excessive crying or high pitched screaming for long periods (3)
   6 extreme sleepiness (4)
   ___ collapse or shock (5)
   5 loss of muscle control (temporary or pemanent paralysis) (6)
   ___ death (7) 1-nerve damage deafness 1-severe allergies & eczema
   2-permanent partial paralysis 1-chronic cold sores
   ___ other (please explain) 1-severe congestion 1-whooping-like cough (8)
   1-limping 1-severe swelling of arm 1-severe leg swelling
   1-severe swelling of glands in head
   1-temporary loss of hearing 1-temporary fever blister

(12)

8. How long after the shot did the reaction begin to occur?

24 Within 24 hours after the shot (1)
1 24-48 hours after the shot (2)
___ 2 days - 7 days after the shot (3)
___ 1 week - 2 weeks after the shot (4)
___ more than 2 weeks after the shot (5)

9. After which DPT shot did your child react severely? Some children reacted to more than 1 shot

15 First shot (1)
4 Second shot (2)
3 Third shot (3)
2 Fourth shot (4)
___ Fifth shot (5)
1 all shots

10. How old was your child when he was given the DPT shot that caused the severe reaction?

8 2-3 months old (1)
6 4-5 months old (2)
4 6-7 months old (3)
3 8-12 months old (4)
1 13-18 months old (5)
1 19-24 months old (6)
___ 25 months - 3 years old (7)
___ over 3 years old (8)
1 all
1 Dont Know

11. How old is your child now?

See 1st page attachment

12. Did you report your child's severe reaction to the DPT shot to a health professional?

21 Yes (1) 4 No (2) ___ Don't Know (3)

13. If you did not report your child's severe reaction to the DPT shot, was it because you were not aware that the reaction was serious and should have been reported?

4 Yes (1) No ___ (2) ___ Don't Know (3)

* 14. If you did report your child's severe reaction to the DPT shot to a health professional, did that person report your child's severe reaction orally or in writing to: NO: 10

___ drug manufacturer (1)
___ federal government (2)
3 state health department (3)
___ any local health agency (4)
8 Don't Know (5) none of these parents had an official MSAEFI form completed

15. Was your child's severe reaction to the DPT shot written on his medical record?

6 Yes (1) 8 No (2) 11 Don't Know (3)

16. After your child reacted severely to a DPT shot, was he given another shot that contained the pertussis vaccine?

6 Yes (1) 17 No (2) 1 Don't Know (3) 1 n/a mmr shot

17. Was your child mentally and physically normal before he received the DPT shot to which he reacted severely?

25 Yes (1) ___ No (2) ___ Don't Know (3)

18. Prior to the DPT shot to which your child reacted severely, did your child have a history of convulsions or neurologic disease?

____ Yes (1) 24 No (2) 1 Don't know

19. Does your family have a history of convulsions or neurologic disease?

1 Yes (1) 23 No (2) 1 Don't Know (3)

20. Did you or your husband ever have whooping cough?

1 Yes (1) 22 No (2) 2 Don't Know (3)

21. Is there a significant history of allergies in your family or has your child ever been diagnosed as having allergies?

9 Yes (1) 12 No (2) 4 Don't Know (3)

22. If your child has allergies, were the allergies apparent before or after the DPT shot to which he reacted severely?

3 Before (1) 5 After (2) N/A 17

23. At the time your child had a severe reaction to the DPT shot, was he primarily bottle-fed?

9 Yes (1) 11 No (2) 5 Both

24. Has your child had a continuing physical or mental health problem since the DPT shot that caused the severe reaction?

12 Yes (1) 12 No (2) 1 dont know yet

If you answered yes to question #24, please answer the rest of the questions.

25. Is your child now:

1 experiencing motor delay
mentally retarded (1)

4 physicially handicapped (2)

3 experiencing convulsions (3)

4 exhibiting learning difficulties (4)

____ in an institution (5)

____ other (please explain) 1-nerve damage deafness 1-epilepsy 2-permanent partial paralysis 1-speech problem 2-cerebral palsy 1-severe allergies (6)

26. Has a physician confirmed your belief that your child's present health problems were caused by the DPT shot?

7 Yes (1) 7 No (2)

27. Has your child required special medical treatment, medicine, hospitalization, or therapy since the DPT shot that caused the severe reaction?

11 Yes (1) 14 No (2)

28. The cost of your child's special medical treatment is estimated to have been:

1 Under $2,000

10 $2,000 - $7,000

____ $7,000 - $12,000

____ $12,000 - $20,000 (4)

____ $20,000 - $40,000 (5)

____ Over $40,000 (6)

29. Please feel free to use the back of this page to tell us your story of what happened to your child as a result of his severe reaction to a DPT shot. Try to be as specific as possible, giving names, dates, and places.

Name: See next page for Emergency Treatment Information

Address: _____

Telepone Numbers: _____ (home) _____ (work)

Date: _____

(19)

4 visits to emergency room
2 telephone contact only

a) 1st parent
b) 2nd parent
c) 3rd parent
d) 4th parent
e) 5th parent
f) 6th parent

30. Emergency room treatment of adverse reaction, if applicable

a) What hospital did you go to?
a) Central Pen Gen. Hospital
B) Kenai Emergency medical Clinic
c) Central Peninsula Gen Hospital
D) Tanana, Alaska
e) Central Pen. Gen. Hospital
f) Homer South Peninsula Hospital

b) Did you call the emergency room?
5 yes a) B) C) D) e) 1 no f)

c) Did you go to the emergency room?
4 yes a) B) D) f) 2 no c) e)

d) How were you treated? (if more room needed, use back of sheet)
a) told not to worry; give cold bath & tylenol
B) O.K.
c) told not to worry; give cold bath & tylenol
D) hospital did not even record visit
e) Give cold bath & tylenol
f) good

e) Were you advised to tell your doctor of reaction?
___yes 6 no a) B) c) D) e) f)

f) Were you advised to tell Health Dept. of reaction?
___yes 6 no a) B) c) D) e) f)

31. Was your child hospitalized?
1 yes f) 5 no a) B) c) D) e)

a) Where? Homer South Peninsula General Hospital

b) For how long? 3 days

c) How was reaction treated? not treated as vaccine reaction

Attachment 3

COMPREHENSIVE CHILD CARE COMMITTEE

Public Comment
July 10, 1987

loyd Richmond, Executive Director of Women in Safe Homes, (WISH). ox 6552, Ketchikan, AK, 99901, 225-9474. Richmond expressed that the overnment has a role in providing freedom of choice to work outside the ome or in the home. This can only be achieved through a system of ffordable, qua ty child care. Note: Written testimony from Richmond s available by ontacting the office.

hannon Kohler, President of the Alaska chapter of Dissatisfied Parents ogether (DPT), Box 1746, Soldotna, AK 99669, 262-3825. Kohler poke on behalf of AK-DPT. This organization is actively working for he passage of HB 277, sponsored by Rep. Navarre. This legislation ould 1) require all public health officials to report all adverse eactions to immunizations, 2) require that prior to vaccination that ll parents are given accurate benefit/risk information with regard to accine safety, and 3) amend Alaska statues to allow a parent to enroll child in public schools with out vaccinating the child. Note: Written estimony and supporting documents presented by Kohler are available in he office.

Margeret Green, Tom Thumb Montessori Schools, 1901 Spenard Road, nchorage, AK 99503, 272-5033
n has b
een involved with this private school since 1956. Their rogram works with children from three years old through sixth grade. She attributes their success to emphasizing developmentally appropriate curriculum. Green shared that she is apprehensive about creating new statutes and regulations that would impact their successful program.

leather Heames, DPT, Box 73, Clam Gulch, AK 99568, 262-6287
leames is the mother of a child that suffered a severe reation to a DPT vaccine. She urged the Committee to do what it could from subjecting others to the problems that her child has faced.

Mary Wilson, Tom Thumb Montessori Schools, 1823 Beaver Pl., Anchorage, AK, 338-1669. Wilson is a teacher/supervisor at the Montessori school and is a certified elementary and montessori teacher. This school is self supporting. In response to questions it was calculated that the typical cost per child per month, for the full day program is $295.

Cheryl Rykaczewski, DPT, Box 311, Kasilof, AK. She is a parent concerned about vaccine safety. She urge the Committee to support the passage of HB 277- The Alaska Vaccine Reform Act.

Terry Victor, DPT, Box 1752, Fairbanks, AK 99708, 488-9531. Victor is the parent of a 15 month old child that suffered a severe reactio to a vaccine. She urged the Committee to support passage of HB 277, which ld require health care providers to report adverse reactions.

Mary Jo Hotchkiss, Instructor at Anchorage Community College, 2333 Providence Dr., 99508. She explained that in 1980 the University deleted their degree program in Early Childhood Education. This was a

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result of there being few graduates in the program, which she attributed to the lack of incentives with in the field for pursuing a degree. She urged the Committee to support changes in the University that would establish training and possibly degrees in Early Childhood Education.

Regina Olszewski, 4003 Garfield , Anchorage, AK. She has a niece that suffered a stroke following a DPT vaccination. She urge the Committee to support the passage of HB 277.

Cecelia Bumanglage, Box 2708, Palmer, AK, 745-2528. She is the parent of a child that suffered a stroke following a DPT vaccination. Since there is no pediatric neurologist in Alaska, they have had to make medical trips to Seattle. The process of treating her now handicapped child is financially difficult. She urges the Committee to support the passage of HB 277, and possibly save one family this pain as the result of mandatory vaccination.

Susan Adams, Illilgaat Tupqaat, Inc., Box 1130, Kotzebue, AK, 442-3157. Adams is the Director of Illilgaat Tupqaat, a day care center. She agreed with the statements shared by Floyd Richmond of Ketchikan with regard to the State's responsibility in assisting in providing affordable, quality child care. She shared the story of a mother of four children, ages 4 months to 6 years, who wants to work outside the home, but can not afford a babysitter and does not qualify for day care assistance. Adams urged the Committee to assist the government in taking a leadership role in establishing quality day care in Alaska.

Carolyn Barnes, 5131 Hatcher, Anchorage, AK, 333-6028.
She is the parent of a child that became deaf after a DPT vaccine. She urged the Committee to support the passage of HB 277.

Dianne Gerber, DPT, St. Rt. 2, Box 560-Z, Kasiloff, AK 99610, 262-1714. She is the parent of a child that had severe reactions to the DPT vaccine and to the MMR vaccine. The child suffered fours days of high fever following the MMR vaccine. She urged the Committee to support the passage of HB 277.

Sharon Wells, 9340 Stratamore, Anchorage, AK, 243-4148. She is a medical foster parent for infants and premature babies. She is very concerned that many infants stay in foster care too long. Because of problems in the Indian Child Welfare Act, many infants that are adoptable stay in foster care past the point of being easily adoptable.

Kathy Boucha-Roberts, Director of Child Development at Providence Hospital, 3200 Providence Dr., Anchorage, AK, 99519, 261-3075. Roberts directs the corporate sponsored child care facility at Providence Hospital. The program cares for approximately 500 children and has a staff of 65. The fee for a child is based on age and the type of care, (i.e. daytime, night time, full time, drop in). They provide services 18 hours a day, 7 days a week, 365 days a year. This program also provides parenting education through classes taught at the hospital that provide interaction between parents and teachers.

Dee Ann Mueller, DPT, 501 Cole Dr., Kenai, AK 99611, 283-7459. She expressed her strong concern that parents should have a choice in deciding to vaccinate a child. Her child had adverse reactions to two DPT vaccines. She was not given any precautionary information, nor was the reaction reported. As a result of the vaccine her child now suffers with mild cerebral palsy.

Pertussis Whooping Cough

definition: an infectious disease typically of children marked by paroxysms of violent coughing followed by a shrill, whooping drawing in of breath. from: Nelson's Medical Dictionary

the following from: Vaccine Preventable Diseases - manual published by CDC

diagnosis: It has fastidious growth requirements that make it difficult to isolate with multiple serotypes. There are other causes of paroxysmal coughing that may also be confused with pertussis. These include bronchiolitis, bronchopneumonia, Bordetella parapertussis, B. bronchiseptica infections, adenovirus infections, chlymydia trachomatis, and others. Difficult to diagnose. Some success with swabs taken from posterior nasopharynx or immunoflourescent antibody testing.

treatment: erythromycin antibiotic of choice to decrease communicability and treat bacteriological secondary infections such as bronchopneumonia (most common and most severe secondary infection). Intensive nursing care essential. Pertussis immune globulin may help shorten illness.

complications: 10% of all pertussis cases may be hospitalized. 1982-1983 encephalopathy occurred in 371,000 cases, 2.5% of cases in children less than 1 year may have convulsion. Average of 6 deaths per year in United States due to pertussis.

Diptheria

definition: highly contagious bacterial disease spread by coughing and sneezing. Patches can be observed in throat that cause swelling, may obstruct breathing in severe cases and cause victim to choke to death.

diagnosis: usually made based on clinical presentation; swab of pharangeal area. variety of types: nasal, tonsillar, pharyngeal, laryngeal, etc.

treatment: antibiotics and antitoxin. respitory support and airway maintenance if needed

complications: respiratory diseases. 9% respiratory diptheria fatal. approx. 1 death per year in U.S. 1983; 5 cases, 0 deaths

Tetanus

definition: an acute infectious disease characterized by spasms of the muscles especially of the jaw caused by a baccillic toxin introduced through a wound. not contagious.

diagnosis: many medical conditions simulate tetanus. no laboratory findings characteristic of tetanus. Diagnosis is entirely clinical.

complications: spasms, coma, aspiration pneumonia. 20% of tetanus deaths attributed to tetanus toxoid. average 91 cases, 30 deaths per year in U.S. (no information as to vaccination rate of inflicted)

NOTES ABOUT TETANUS:
1) "...the mortality in reported cases of tetanus is higher in the U.S. than in developing countries." (Am J. Dis. Child, Vol 135, June 1981, pg. 571)
2) "nosocomial" (hospital acquired pneumonia) pneumonia is a major cause of death in these patients that come to autopsy." (J. Arkansas Med. Soc., Vol 80, No. 3, Aug. 1983, pg. 136)

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GENERAL DPT (DIPTHERIA, PERTUSSIS, AND TETANUS) VACCINE INFORMATION

All vaccines come combined unless specifically requested separate via medical prescription. The following is from Lederle and Connaught manufacturer's inserts.

Ingredients: Lederle Co.: FORMALDEHYDE, potassium phosphate monobasic, sodium phosphate dibasis, glycine, THIMEROSAL (mercury derivative), sodium chloride, ALUMINUM, inactivated diptheria and tetanus toxoids, inactivated pertussis bacteria. Connought Co.: basically the same but no mention of formaldehyde.

Minor-Moderate Adverse Reactions: (See manufacturer's product insert for complete list)
1) local reactions, adscess formation at sight of injection, fretfulness, drowsiness, vomiting, anorexia

Severe Adverse Reactions: (See manufacturer's product insert insert for those recognized by manufacturer. Read large print under ADVERSE REACTIONS.)

ADVERSE REACTIONS

Local reactions manifested by erythema and induration with or without tenderness are common after administration of DTP. Such local reactions are usually self-limited and require no therapy. A nodule may be palpable at the injection site for a few weeks.

Abscess formation at the site of injection has been reported [illegible]. Cervical lymphadenopathy has been reported following DTP injections into the arm.

Mild to moderate temperature elevations frequently follow DTP administration and are often accompanied by fretfulness, drowsiness, vomiting, and anorexia. Approximately 50% of DTP recipients will develop temperature elevations > 38° C (100.4° F) after one or more doses of the series, approximately 6% > 39° C (102.2° F), and approximately 1.5% > 40° C (104° F). Some data suggest that febrile reactions are more likely to occur in those who have experienced such responses after prior doses.

SIGNIFICANT REACTIONS ATTRIBUTED TO THE PERTUSSIS VACCINE COMPONENT HAVE BEEN: HIGH FEVER OF 40.5° C (105° F), A TRANSIENT SHOCK-LIKE EPISODE, EXCESSIVE SCREAMING (PERSISTENT CRYING OR SCREAMING FOR THREE OR MORE HOURS DURATION), SOMNOLENCE, CONVULSIONS, AND ENCEPHALOPATHY. THESE REACTIONS HAVE BEEN REPORTED TO OCCUR RARELY FOLLOWING THE INJECTION OF THIS PRODUCT AND THEY MAY BE FATAL OR RESULT IN PERMANENT DAMAGE TO THE CENTRAL NERVOUS SYSTEM. PERTUSSIS VACCINE HAS BEEN ASSOCIATED WITH A GREATER PROPORTION OF ADVERSE REACTIONS THAN MANY OTHER CHILDHOOD IMMUNIZATIONS. SHOULD SYMPTOMATOLOGY REFERABLE TO THE CENTRAL NERVOUS SYSTEM DEVELOP FOLLOWING ADMINISTRATION, FURTHER IMMUNIZATION WITH THIS PRODUCT IS CONTRAINDICATED (SEE CONTRAINDICATIONS). SUCH REACTIONS ALMOST ALWAYS APPEAR WITHIN 24 TO 48 HOURS AFTER INJECTION, BUT HAVE BEEN THOUGHT TO OCCUR AFTER AN INTERVAL AS LONG AS SEVEN DAYS.

NEUROLOGICAL COMPLICATIONS FOLLOWING TETANUS TOXOID ADMINISTRATION, SUCH AS PARALYSIS OF THE RADIAL NERVE, RECURRENT PHARYNGEAL NERVE, COCHLEAR LESION, BRACHIAL PLEXUS NEUROPATHY, AND A CASE OF DIFFICULTY IN SWALLOWING, ACCOMMODATION PARESIS, AND EEG DISTURBANCES, HAVE BEEN REPORTED. IN THE DIFFERENTIAL DIAGNOSIS OF POLYRADICULONEUROPATHIES FOLLOWING ADMINISTRATION OF TETANUS TOXOID, TETANUS TOXOID SHOULD BE CONSIDERED AS A POSSIBLE ETIOLOGY.

CONTRAINDICATIONS

IMMUNIZATION SHOULD BE DEFERRED DURING THE COURSE OF ANY ACUTE ILLNESS. THE OCCURRENCE OF ANY TYPE OF NEUROLOGICAL SYMPTOMS OR SIGNS, INCLUDING ONE OR MORE CONVULSIONS (SEIZURES) FOLLOWING ADMINISTRATION OF THIS PRODUCT IS A CONTRAINDICATION TO FURTHER USE. USE OF THIS PRODUCT IS ALSO CONTRAINDICATED IF THE CHILD HAS A PERSONAL OR FAMILY HISTORY OF CENTRAL NERVOUS SYSTEM DISORDERS.

THE PRESENCE OF ANY EVOLVING OR CHANGING DISORDER AFFECTING THE CENTRAL NERVOUS SYSTEM IS A CONTRAINDICATION TO ADMINISTRATION OF DTP REGARDLESS OF WHETHER THE SUSPECTED NEUROLOGICAL DISORDER IS ASSOCIATED WITH OCCURRENCE OF SEIZURE ACTIVITY OF ANY TYPE.

The Committee on Infectious Diseases of the American Academy of Pediatrics recommends that pertussis vaccine should be withheld when a previous dose has been followed by convulsion, encephalitis, focal neurological signs or collapse. Nor should infants who experience excessive somnolence, excessive screaming (persistent crying or screaming for three or more hours duration) or temperature more than 105° F (40.5° C) receive additional doses of the vaccine.

The Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service recommends that hypersensitivity to vaccine components, presence of an evolving neurologic disorder, or a history of a severe reaction (usually within 48 hours) following a previous dose all remain definitive contraindications to the receipt of pertussis vaccine. Severe reactions include collapse or shock, persistent screaming episode, temperature 40.5° C (105° F) or greater, convulsion(s) with or without accompanying fever, severe alterations of consciousness, generalized and/or focal neurologic signs, or systemic allergic reactions.

Immunosuppressive therapy, including irradiation, corticosteroids, antimetabolites, alkylating agents, and cytotoxic agents may result in aberrant responses to active immunization procedures. Administration should be deferred in individuals receiving such therapy.

The clinical judgement of the attending physician should prevail at all times.

Elective immunization of patients over the age of 6 months should be deferred during an outbreak of poliomyelitis.

PARTIAL LIST OF POSSIBLE SEVERE LONG-TERM ADVERSE REACTIONS TO DPT VACCINE (USUALLY PERTUSSIS COMPONENT IMPLICATED)

* article available from Alaska Dissatisfied Parents Together

*1) **Cervical lymphadenopathy** . Omokoku, B: "Post DPT inoculation caused lymphadenitis in children." N.Y. State Journa. ' 'cine 81:1667, 1981

2) **Thrombocytopenia** (blood disease). Connaught manufacturer's insert* Pertussis. Report of Committee on Infectious Diseases. AAP, Evanston, Illinois, p. 205. 1977

*3) **hemolytic anemia** (blood disease). Haneberg B.; "Acute hemolytic anemia related to DPT vaccination": ACTA Pae diatr. Scand. 67:347-350, 1978

*4) **death, encephalopathy, Reyes syndrome, tracheo bronchitis. convulsions with and without residual brain damage** . Griffith A.H: "Reactions after Pertussis vaccine; a manufacturer's experiences and difficulties since 1964", British Medical Journal: April 1, 1978, pg. 809-814

*5) **destructive encephalopathys, convulsions, hypsarrhythmia, shock, serious meningitis** . Incidence of neurological reactions 1:3,600 children. Strom, Justus M.D., "Further Experience of Reactions, Especially of a Cerebral Nature, in Conjunction w/Triple Vaccine: Swedish Study, 1959-1965", British Medical Journal, 1967, 320-323

*6) **recurrent seizures, severe developmental delays** . Murphy, Jerome. "Recurrent Seizures after DPT Vaccine Immunization", AJDC, Vol 138, Oct. 984

*7) **blindness, cerebral palsy, death, mental retardation, chronic convulsions** Byers, Randolph. "Encephalopathies Following Prophylactic Pertussis Vaccine", Pediatrics, Vol. 1, #4, April 1948.

*8) **recurring convulsions, paralysis, mental retardation, allergies** Berg, J.M "Neurological Complications of Pertussis Immunization", British Medical Journal, July 5, 1958

*9) **death, sudden death, convulsions, paresis, rhinopharyngitis, rapid mental deterioration, coma, cerebral palsy, deafness, epilepsy** Neurological reactions after vaccination-1 in 6,000 children; death or permanent defect-1 in 17,000. "Is Universal Vaccination Against Pertussis Always Justified?" Justus Strom, M.D., British Medical Journal. Oct. 22, 1960.

*10) **allergic form of encephalopathy, death** . "Encephalopathy Following Pertussis Vaccine Prophylaxis", Joseph H. Globus, M.D., J.A.M.A., October 22, 1949

*11) **cerebral degeneration, blindness** . "Neurological Complications of Pertussis Inoculation", M. Kulenkanpff, Archives of Disease in Children, 1974, pg. 46, 49

*12) **sudden death, seizures, convulsions, respiratory infection** . John A. Toomey, "Reactions to Pertussis Vaccine", J.A.M.A., February

13) "**Post vaccinal lymphadenitis developing into Hodgkins Disease**". Bichel, J. ACTA Med. Scand., 199:523, 1976

*14) **anaphylaxis** (extreme, sometimes fatal allergic reaction). Howard Orens, M.D. "Anaphylaxis due to vaccination in the Office". Can. Med. Assoc. Journal

*15) **paroxysmal supra ventricular tachycardia** . Joon M. Park, M.D. "Paroxysmal Supra ventricular tachycerdia precipitated by pertussis vaccine", Journal of Pediatrics, June 1983

SIDS AND DPT VACCINATION

STUDIES THAT SHOW CORRELATION BETWEEN SIDS/DPT

*1) BARAFF GRAPH. "Possible Temporal Association between DPT Vaccination and Sudden Infant Death" Pediatric Infectious Disease, 1983, 2,7-11

*2) TORCH STUDY summary & graph. DPT Immunization, a Potential Cause of the Sudden Infant Death Syndrome. Neurology 1982, 32 A No 3

(20)

*3) BERNIER STUDY GRAPH. "DTP Vaccination and SIDS in Tennessee." Journal of Pediatrics, 1982, 101:419-421
*4) "DTP Immunization and Sudden Infant Death Syndrome." Alexander M. Walker, et. al., AJPH, August 1987, Vol. 77, #8

TETANUS VACCINE REACTIONS (PARTIAL LIST)

1) "Abnormal T-Lymphocyte Subpopulations in Healthy Subjects After Tetanus Booster Immunization." Martha Eibe, New England Journal of Medicine, 310(3) 1307-1313, November 26, 1981. Report pointed out that similar drops in helper/suppressor ratio of T-lymphcytes are characteristic of AIDS.
2) **neuralgic amyotophy** . J. Neurology, Neurosurgy & Psych, Vol. 47; 320, March 1984
3) **transverse myelitis.** Br. Med Journal 1977; 1: 1430-1431
4) **demyelinating neuropathy** . J Neur. Sci. 1978; 37: 113-125
5) **peripheral neuropathy** . Arch Phys Med Rehab Vol 63, July 1982, 332-334. (detailing many cases)
6) **calcifying dermatomyositis** . Arch Int Med Vol 143, July 1983, 1457-8
7) **mono and polyneuritis** (22 cases). Int. Symnos. on Imm. Dev. Biol Stands, Vol. 43, pg. 25-32, 1979
8) **Guillain Barre Syndrome** . N.Z. Med J., Nov 11, 1981 , Akt Neurol 1980: 7;195-200
9) **hemolytic anemia** . Acta Pediatric Scand, May 1978
10) **anaphylactic shock** . Harefuah, Nov 1975 - Dtsch Med Wochenschr, Jan 1973 - Annals of Allergy, Vol 49, August 1982, pg 107
11) **nerve damage, inner ear** . Munch Med. Wochen Schr., Nov 1965
12) **foreign body granuloma** . Rocky Mountain Medical Journal, Jan, 1966
13) **seizure activity** . Neurol Neurochir Pol., Sept 1981
14) **recurrent abscess formatio n.** Pediatric, May 1985
15) **brachial plexus neuropathy** . Archives of Neurology, 1972
(which can lead to paralysis of the arm)

DIPTHERIA VACCINE REACTIONS

(all from Center of Disease Control Manual: "Vaccine Preventable Diseases; Epedemiology, Prevention and Control", pg 38-39.)

1) local reactions, abscess at the site of injection
2) arthus-type hypersensitivity reactions, characterized by severe local reactions
3) severe systemic reactions such as generalized urticaria (allergic rash and hives), anaphylaxis, neurological complications

DPT VACCINE INGREDIENTS

*data available from Alaska Dissatisfied Parents Together

FORMALDEHYDE

"Formaldehyde (ingredient in Lederle DPT vaccine) is also mutagenic in bacteria, viruses, fungi, insects and mouse lymphoma cells with or without metabolic activation. It induces chromosomal recombination in yeast, insects, and cultured mammalian cells, as well as cellular transformation in mouse Balb/C 3T3 cells (Griesemer, et al., 1980). These results indicate that formaldehyde is capable of binding to, and altering, genetic material."
Formaldehyde: Review of Scientific Basis of EPA's Carcinogenic Risk Assessment Peter W. Preuss Ph. D., May 20, 1987 page 21-

"Immunologic. (physiological effect): The characteristics of an allergic mechanism are that the response can be evoked in sensitized individuals with very small amounts of formaldehyde. Symptoms usually develop some time after the initial exposure rather than on initial contact. Usually only a proportion of the exposed will be affected. In the documented cases there is typically a delayed response, although there may be a brief immediate reaction as well (dual response), and the late reaction may be prolonged." Formaldehyde Toxicity, James E. Gibson, 1983*

"Carcinogenic Effect: Of additional concern is the carcinogenic potential of formaldehyde in humans. This concern is based on metabolism, mutagenicity, and carcinogenicity studies which were reviewed in the Report of the Federal Panel on Formaldehyde, Griesemer, et. al., 1980. In brief, the panel reported that these studies showed that formaldehyde reacts readily with biological chemical, including proteins and nucleic acids." page 395, Formaldehyde: Review of Scientific Basis of EPA's Carcinogenic Risk Assessment, May 20, 1982*

Aluminum

(another ingredient in all DPT vaccines)

"...In Canada (researchers) found that after a latent period of 10 to 20 days, animals receiving a single intracerebral injection of aluminum incurred a progressive decline in learning and memory." Physiol Behav, Crapper DR, Dalton AJ, 1973

"Crapper also found that aluminum accumulates preferentially on the chromatin of various cell nuclei, including brain cell nuclei from patients with SDAT... (Senile Dementia of the Alaheimer's Type)." Frontiers in Neurology and Neuroscience Research, "Dementia: Recent observations on Alzheimer's disease and experimental aluminum encephalopathy." Crapper, Dr., 1974

Thimerosal (mercury derivative)

definition: prepared by reacting ethylmercuric chloride (or ethymercuric hydroxide) with thiosalicylic acid. The Merck Index, 1983*

ethylmercuric chloride: caution: Highly toxic. causes skin burns, is absorbed through the skin, chronic exposure has caused permanent injury to brain, applied at 2% strength as a fungicide for treating seeds. The Merck Index, 1983*

the following from: "Epidemiology & Toxicology of Mercury" The Environmental Mercury Problem*

"Furthermore, the vast majority of the organomercurial poisonings are due to alkylmercurials such as methyl or ethylmercury."

"Therefore while it is important to recognize that all forms of mercury are powerful poisons, the akylmercurials are many times more effective poisons than either the inorganic or arylmercurials."

"...the organic mercury compounds, especially the alkymercurials (ethymercury) are more toxic than the other kinds of mercury compounds because the human body absorbs more and excretes less of them."

"Several alkylmercury poisoning epidemics have been recorded." Guatamala, Pakistan, Iraq: "In 1960 many farmers were poisoned and 221 patients were admitted to hospital in Baghdad, Iraq. Other patients were known to have been stricken by ETHYLMERCURIC CHLORIDE

POLIO

definition : a viral disease marked by inflammation of the nerve cells of the spinal cord, deformity, and paralysis. 95% of all polio infections are inapparent or subclinical, but may still be able to transmit infection to others (CDC Manual)

diagnosis : A) 4%-8% nonspecific illness of influenza-like illness B) 1%-2% of polio infections result in major illness w/complete recovery C) 0.1%-0.2% of all polio infections result in flaccid paralysis. Many persons w/paralytic polio recover completely. Deathrate: 2-5% in children 15-30% in adults

treatment : 1) early ambulation 2) muscular relaxation 3) controlled and prolonged medical observation 4) special nutrition program Virginia Medical Monthly, June 1956, Nutrition; "Nutrition as Treatment for Polio Victims", Prevention, November 1960

complications: See diagnosis

POLIOVIRUS VACCINE

all information from manufacturer's product insert unless specified

Ingredients: mixture of 3 types of attenuated polioviruses propagated in cercopithecus MONKEY KIDNEY CELLS, amino acids, antibiotics, CALF SERUM, sorbitol, streptomycin, NEOMYCIN

CONTRAINDICATION MUST NOT BE ADMINISTERED TO PATIENTS WITH IMMUNE DEFICIENCY

Question: Since no mechanisms are employed by health care providers to determine immune deficiency (especially public health providers who have never seen 2 month old infants before vaccine clinics), how is this to be determined?

ALL PERSONS WITH ALTERED IMMUNE STATUS SHOULD AVOID CLOSE HOUSEHOLD-TYPE CONTACT WITH RECIPIENTS FOR AT LEAST 6-8 WEEKS.

Question: Most people aren't aware of the health status of everyone their child comes in contact with (especially other infants in day care), so how is this to be accomplished and what are the other health implications?

Adverse Reactions: 1) paralytic disease, vaccine associated paralysis in healthy vaccines, susceptible family members, and other close personal contacts 2) transverse myletis (inflammation of spinal cord or bone marrow) "Transverse myletis after diptheria, tetanus, and polio immunization." case history British Medical Journal, June 4, 1977

NOTES:

1) "Many physicians and health workers will be surprised to learn that the Sabin vaccine is now the chief cause of polio in the world today and that it was introduced without any controlled field trials." J. and D. Salk, Science 4/4/77

2) Current Trends: Average of 10 cases per year reported 1980-1985, no wild virus cases since 1979; one imported case per year. REMAINING CASES IN VACCINE RECIPIENTS OR CONTACTS. page 88, CDC manual Note: speaker at seminar Neil Livengood stated that no "natural cases" of polio have occurred in U.S. since 1979

(2-4)

3) "A defect either in the humoral (B-cell) mediated (T-cell) system appears to increase the risk of vaccine associated polio myelitis. T-cell dysjunction from any cause must therefore be assumed to confer greater risk for vaccine related poliomyelitis." Elena Nightengale, Ph. D, et al, Committee for the Study of Poliomyelitis Vaccines, Institute of Medicine. Correspondence New England Journal of Medicine, Dec. 8, 1977

4) "The poliovirus isolated from a patient with paralytic disease may not always be the virus causing the patients disease." Lancet, Dec. 8, 1984, pg 1315

*5) "The DBS (Division of Biological Sciences) requires monkey kidney cells used in growing polio vaccine be held for only 28 days in order to ensure that they contain no SV 40 virus According to A. Girandi of the Wistar Institute SV 40 may remain latent for up to 35 days. Nor does the DBS require monkey kidney cells to be screened for chromosomal abnormalities - a possible indicator of cancerous tendencies - a test they would probably fail in large numbers." "The Boat That Never Rocked", Science, March 17, 1977

CONTRAINDICATIONS

Under no circumstances should this vaccine be administered parenterally

Administration of the vaccine should be postponed or avoided in those experiencing an acute illness and in those with any advanced debilitated condition or persistent vomiting or diarrhea

ORIMUNE *must not* be administered to patients with immune deficiency diseases such as combined immunodeficiency, hypogammaglobulinemia and agammaglobulinemia. It would also be prudent to withhold ORIMUNE from siblings of a child known to have an immunodeficiency syndrome. Further, ORIMUNE *must not* be administered to patients with altered immune states such as those occurring in thymic abnormalities, leukemia, lymphoma or generalized malignancy or by lowered resistance from therapy with corticosteroids, alkylating drugs, antimetabolites or radiation. All persons with altered immune status should avoid close household-type contact with recipients of the vaccine for at least 6-8 weeks. IPV is preferred for immunizing all persons in this setting.[2,3,4,6,7]

PRECAUTIONS

Other viruses (including poliovirus and other enterovirus) may interfere with the desired response to this vaccine since their presence in the intestinal tract may interfere with the replication of the attenuated strains of poliovirus in the vaccine

It would seem prudent not to administer TOPV shortly after Immune Serum Globulin (ISG) unless such a procedure is unavoidable, for example, with unexpected travel to or contact with epidemic areas or endemic areas. If TOPV is given with or shortly after ISG, the dose probably should be repeated after three months if immunization is still indicated.[8] However, ISG may not interfere with immunization with TOPV.[9]

The vaccine is not effective in modifying or preventing cases of existing and/or incubating poliomyelitis.

ADVERSE REACTIONS

Paralytic disease following the ingestion of live poliovirus vaccines has been, on rare occasion, reported in individuals receiving the vaccine, (see for example CONTRAINDICATIONS) and in persons who were in close contact with vaccinees.[2,3,4,10,11,12,13] The vaccine viruses are shed in the vaccinee's stools for at least 6 to 8 weeks as well as via the pharyngeal route. Most reports of paralytic disease following ingestion of the vaccine or contact with a recent vaccinee are based on epidemiological analysis and temporal association between vaccination or contact and the onset of symptoms. Most authorities believe that a causal relationship exists.[2,10,14,15]

The risk of vaccine-associated paralysis is extremely small for vaccinees, susceptible family members and other close personal contacts.[7] However, prior to administration of the vaccine, the attending physician should warn or specifically direct personnel acting under his authority to convey the warnings to the vaccinee, parent, guardian or other responsible person of the possibility of vaccine-associated paralysis. The Centers for Disease Control report that during the years 1969 through 1980 approximately 290 million doses of TOPV were distributed in the United States. In the same 12 years, 25 "vaccine-associated" and 55 "contact vaccine-associated" paralytic cases were reported. Twelve other "vaccine-associated" cases have been reported in persons (recipients or contacts) with immune deficiency conditions.[7] These statistics do not provide a satisfactory basis for estimating these risks on a per person basis."[14]

When the attenuated vaccine strains are to be introduced into a household with adults who have not been adequately vaccinated or whose immune status cannot be determined, the risk of vaccine-associated paralysis can be minimized by giving these adults three doses of IPV a month apart before the children receive ORIMUNE.[7] The CDC reports that no paralytic reactions to IPV are known to have occurred since the 1955 cluster of poliomyelitis cases caused by vaccine that contained live polioviruses that had escaped inactivation.[7]

The Immunization Practices Advisory Committee of the U.S. Public Health Service states:

"Because of the overriding importance of ensuring prompt and complete immunization of the child and the extreme rarity of OPV-associated disease in contacts, the Committee recommends the administration of OPV to a child regardless of the poliovirus-vaccine status of adult household contacts. This is the usual practice in the United States. The responsible adult should be informed of the small risk involved. An acceptable alternative, if there is strong assurance that ultimate, full immunization of the child will not be jeopardized or unduly delayed, is to immunize adults according to the schedule outlined above before giving OPV to the child."[7]

The Immunization Practices Advisory Committee has concluded that "Oral polio vaccine remains the vaccine of choice for primary immunization of Children

from: How to Raise a Healthy Child in Spite of Your Doctor, Dr. Robert Mendelsohn

MUMPS

definition and diagnosis: relatively innocous viral disease, usually experienced in childhood, causes swelling of one or both of the salivary glands. Symptoms; temp of 100-104 degrees, appetite loss, headache, back pain. Infection confers lifetime immunity.

treatment: does not require medical treatment - bed rest, lots of fluids, ice packs to reduce swelling.

complications: very rarely in adult males with mumps infection, orchitis (mumps condition that affects testicles) may occur. Orchitis rarely causes sterility and when it does usually only one testicle is affected

In 1981, 1,491 cases in U.S..; 1 death (MMWR 1983 summary)

MEASLES

definition and diagnosis: rubeola, contagious viral disease that can be contracted by touching an object used by infected person, slight fever at first to high (103-104 degrees) in few days-sometimes small white spots occur inside mouth - rash occurs below hairline and spreads downward to cover body in about 36 hours

treatment: bedrest, fluids, Calamine lotion or cornstarch to relieve itching, may be light sensitive (darken room), Vitamin A supplements in malnourished. "Vitamin A Supplements and Mortality Related to Measles: A Randemised Clinical Trial", Andrew J.G. Barclay, British Medical Journal, Jan. 31, 1987, Volume 294

RUBELLA

definition and diagnosis: non-threatening disease in children that does not require medical treatment- fever, slight cold w/sore throat - rash appears on face and spreads to body, spot do not run together (as in measles), confers lifetime immunity

treatment: rest and fluids

complications: none to child. Threat posed by rubella is the possibility it may cause damage to fetus if a women contracts disease during first three months of pregnancy

In 1981, 2,077 cases of rubella in U.S.; 5 deaths (MMWR 1983 Summary)

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MEASLES, MUMPS, RUBELLA (MMR)
VACCINE INFORMATION AND ADVERSE REACTIONS

NOTE: Since all three vaccines in combined shot, it's difficult to ascertain what vaccine causes what reaction. Any live virus vaccine is capable of producing the same syptoms, reactions, etc. as the virus.

Ingredients: CELL CULTURES OF CHICK EMBRYO (measles and mumps), HUMAN DIPLOID CELL culture (rubella), neomycin, sorbitol, hydorlized gelatin.
Adverse Reactions: (from Manufacturer's insert)

CONTRAINDICATIONS

Do not give M·M·R II to pregnant females; the possible effects of the vaccine on fetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy must be avoided for three months following vaccination.

Hypersensitivity to neomycin (each dose of reconstituted vaccine contains approximately 25 mcg of neomycin).

Any febrile respiratory illness or other active febrile infection.

Active untreated tuberculosis.

Patients receiving therapy with ACTH, corticosteroids, irradiation, alkylating agents or antimetabolites. This contraindication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Individuals with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Primary immuno-deficiency states, including cellular immune deficiencies, hypogammaglobulinemic and dysgammaglobulinemic states.

HYPERSENSITIVITY TO EGGS, CHICKEN, OR CHICKEN FEATHERS

This vaccine is essentially devoid of potentially allergenic substances derived from host tissues (chick embryos).* However, because the attenuated measles and mumps viruses in this vaccine are propagated in cell cultures of chick embryo, there is a potential risk of hypersensitivity reactions in patients allergic to eggs, chicken or chicken feathers. Widespread use of the vaccine for more than a decade has resulted in only rare, isolated reports of minor allergic reactions attributed to allergens of this kind, possibly related to the vaccine. Significantly, when children with known allergies to eggs, chicken and chicken feathers were given a similarly prepared vaccine in a clinical study,[20] none experienced reactions other than those reactions previously observed in non-allergic children.

PRECAUTIONS

Administer M·M·R II subcutaneously; *do not give intravenously.*

Epinephrine should be available for immediate use in case an anaphylactoid reaction occurs.

M·M·R II may be given simultaneously with monovalent or trivalent poliovirus vaccine, live, oral. M·M·R II should not be given less than one month before or after administration of other live virus vaccines.

Due caution should be employed in administration of M·M·R II to children with a history of febrile convulsions, cerebral injury or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur 5 to 12 days following vaccination.

Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin.

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7-28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission, while accepted as a theoretical possibility, is not regarded as a significant risk.**

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

It has been reported that live attenuated measles, mumps and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either before or simultaneously with M·M·R II.

As for any vaccine, vaccination with M·M·R II may not result in seroconversion in 100% of susceptible subjects given the vaccine.

ADVERSE REACTIONS

Because of the slightly acidic pH (6.2-6.6) of the vaccine, patients may complain of burning and/or stinging of short duration at the injection site.

The adverse clinical reactions associated with the use of M·M·R II are those expected to follow administration of the monovalent vaccines given separately. These may include malaise, sore throat, headache, fever, and rash; mild local reactions such as erythema, induration, tenderness and regional lymphadenopathy; parotitis; orchitis; thrombocytopenia and purpura; allergic reactions such as wheal and flare at the injection site or urticaria; and arthritis, arthralgia and polyneuritis.

Moderate fever (101-102.5°F [38.3-39.4°C]) occurs occasionally, and high fever (above 103°F [39.4°C]) occurs less commonly. On rare occasions, children developing fever may exhibit febrile convulsions. Rash occurs infrequently and is usually minimal, but rarely may be generalized.

Clinical experience with live attenuated measles, mumps and rubella virus vaccines given individually indicates that encephalitis and other nervous system reactions have occurred very rarely. These might occur also with M·M·R II.

Experience from more than 80 million doses of all live measles vaccines given in the U.S. through 1975 indicates that significant central nervous system reactions such as encephalitis and encephalopathy, occurring within 30 days after vaccination, have been temporally associated with measles vaccine approximately once for every million doses. In no case has it been shown that reactions were actually caused by vaccine. The Center for Disease Control has pointed out that "a certain number of cases of encephalitis may be expected to occur in a large childhood population in a defined period of time even when no vaccines are administered". However, the data suggest the possibility that some of these cases may have been caused by measles vaccines. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy with natural measles (one per thousand reported cases).

There have been isolated reports of ocular palsies and Guillain-Barre syndrome occurring after immunization with vaccines containing live attenuated measles virus. The ocular palsies have occurred approximately 3-24 days following vaccination. No definite causal relationship has been established between either of these events and vaccination.

There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of natural measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed. This is far less than the association with natural measles, 5-10 cases of SSPE per million cases of measles. The results of a retrospective case-controlled study conducted by the Center for Disease Control suggest that the overall affect of measles vaccine has been to protect against SSPE by preventing measles with its inherent higher risk of SSPE.

Local reactions characterized by marked swelling, redness and vesiculation at the injection site of attenuated live measles virus vaccines have occurred in children who received killed measles vaccine previously. M·M·R II was not given under this condition in clinical trials.

Transient arthritis, arthralgia and polyneuritis are features of natural rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. This type of involvement has also been reported following administration of MERUVAX II (Rubella Virus Vaccine, Live, MSD). In children, joint reactions are rare and of brief duration if they do occur. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0-3%; women: 12-20%),[21] and the reactions tend to be more marked and of longer duration. Rarely, symptoms may persist for a matter of months. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35-45 years), these reactions are generally well tolerated and rarely interfere with normal activities.

NOTES:

MEASLES

1) subacute scleros panencephalitis "SSPE" (fatal hardening of brain) Modern Medicine, 1/7/74 and "Occurence of Measles in Previously Vaccinated Individuals, 1979", American Society for Microbiology meeting at Ft. Detrick, Md., April 27, 1987

*2) toxic epidermal nercrolysis (dying of skin "scalded skin") also reported to occur secondary to polio, diptheria, and tetanus vaccinations. "Toxic Epidermal Nercrolysis Following Measles Vaccination", Robert G. Shoss, M.D. Arch Dermatol, Vol 110, Nov. 1974

*3) ataxia (inability to coordinate muscle movements), mental retardation, aseptic meningitis, seizure disorders, hemiparesis (paralysis affecting one side of body), multiple sclerosis, Reyes syndrome, juvenile-onset diabetes. How to Raise a Healthy Child In Spite of Your Doctor, Robert S. Mendelsohn, M.D., 1984, Contemporary Books, Inc.

RUBELLA

*1) thrombocytopenia (blood clotting problem) "Thrombocytopenia Associated With Rubella Vaccination", Henry R. Bartos M.D., F.A.C.P; New York State Journal of Medicine, Feb. 15, 1972

2) arthritis and arthralgia. In United States, 87 cases of congenital rubella syndrome were reported, 12 in New Jersey. 17% of all children vaccinated in N. Jersey developed arthritis and arthralgia. Science, March 26, 1977

(29)

Boffins claim the cure can kill

By HARRY NELSON

ST PETERSBURG, (Florida).— New findings about the way viruses ebave once more point to their possible role in causing cancer — and, perhaps diseases such as arthritis and multiple sclerosis.

The findings, reported here at a seminar for science writers spnsored by the American Cancer Society, raise questions about the possible harmful effects of immunization programmes to prevent influenza, measles and polio.

The new findings came from Dr Robert W. Simpson, of Rutgers University in New Jersey, and Dr Wendell D. Winters, a University of California at Los Angeles virologist now working at the University of Texas in San Antonio.

Last year, the Nobel Prize for medicine was given to David Baltimore and Howard Temin for discovering that viruses that cause cancer in animals are equipped with a very special enzyme called reverse transcriptase.

The viruse that carry the enzyme are called RNA viruses. Possession of the enzyme allows the RNZ viruses to form strands of DNA, thus enabling them to become cftegrated with the DNA of the cells they infect.

It is this integration of the DNA transcribed by the virus with the cell's DNA that somehow triggers cancer, at least in animals.

(The genetic material of all living things, includin viruses, is either RNA (ribonucleic acid) or DNA (deoxyribonucleic acid). Before the discovery of reverse transcriptase, which enables RNA viruses to transcribe their genetic material into a DNA form, scientists had trouble understanding how RNA cancer viruses could transform DNA cells.)

in cells without expressing themselves in any way.

Simpson raised the question whether immunization programmes against flu, measles, mumps and polio may actually be seeding humans with RNA to form proviruses which will then becme latent in cells throughout the body.

He said some of these latent proviruses could be "molecules in search of disease" which under proper conditions become activated and cause a variety of diseases.

Of diseases that could be caused in this manner, the chief possibilities are rheumatoid arthritis, multiple sclerosis, lupus erythematosus, Parkinson's disease and, perhaps cancer.

Winters, the UCLA virologist, has added a new dimension to the subject of viruses being a possible cause of human cancer.

Cells grown

He has been working in the laboratory with tumour cells removed frm UCLA surgery patients. The cells were then grown in dishes.

When he added a common respiratory virus known as Adenovirus 5 to the cells, the Adenovirus caused large numbers of latent RNA particles to be released.

It is possible but not proven that the RNA particles were the cause of the human tumours. Perhaps they are also the seeds released into the bloodstream which float to other parts of the body where they infect cells and start cancer viruses into action.— Los Angeles Times service.

More recently, Simpson has found that RNA viruses which do not cause cancer also can form DNA, even though they lack reverse transcriptase.

DNA formed in this way from an RNA virus is called a provirus.

No effect

It is known from earlier work that some non-cancerous viruses have a tendency to exist as proviruses for long periods of time in cells without causing any apparent disease.

Some examples of common RNA viruses that do not cause cancer but may have the capacity to form proviruses are influenza, measles, mumps and polio viruses.

Simpson showed in laboratory experiments that proviruses derived from the measles virus and the respiratory syncytial virus (a cause of respiratory disease in newborn babies) can exist

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Expert links AIDS to bovine viruses

By PHILIP M. BOFFEY
New York Times

WASHINGTON — Jeremy Rifkin, an outspoken critic of genetic engineering and other biotechnologies, Monday asked three federal agencies to determine whether cattle viruses play a role in causing AIDS.

In a petition submitted to the Agriculture Department, the Federal Centers for Disease Control and the National Institutes of Health, Rifkin called the cattle viruses "an extraordinary potential threat to public health."

Rifkin speculated in an interview that the AIDS virus might have evolved from cattle viruses, or that the cattle viruses might themselves play a role in the development of acquired immune deficiency syndrome in humans.

The petition cited scientific papers indicating a "close correlation" between the HIV, or human immunodeficiency virus, that causes AIDS in humans, and a virus found in cattle called bovine visna-like virus or bovine immunodeficiency-like virus. The petition warned that a range of viruses "exist in domestic animal herds in the U.S. and thus could pose a potential health hazard."

It also speculated that the cattle virus, BIV, might have infected cell cultures used to make some human vaccines, perhaps thereby contributing to the global spread of AIDS.

However, two of the scientists whose papers were cited by Rifkin expressed doubt in interviews that the cattle viruses played any role in causing AIDS.

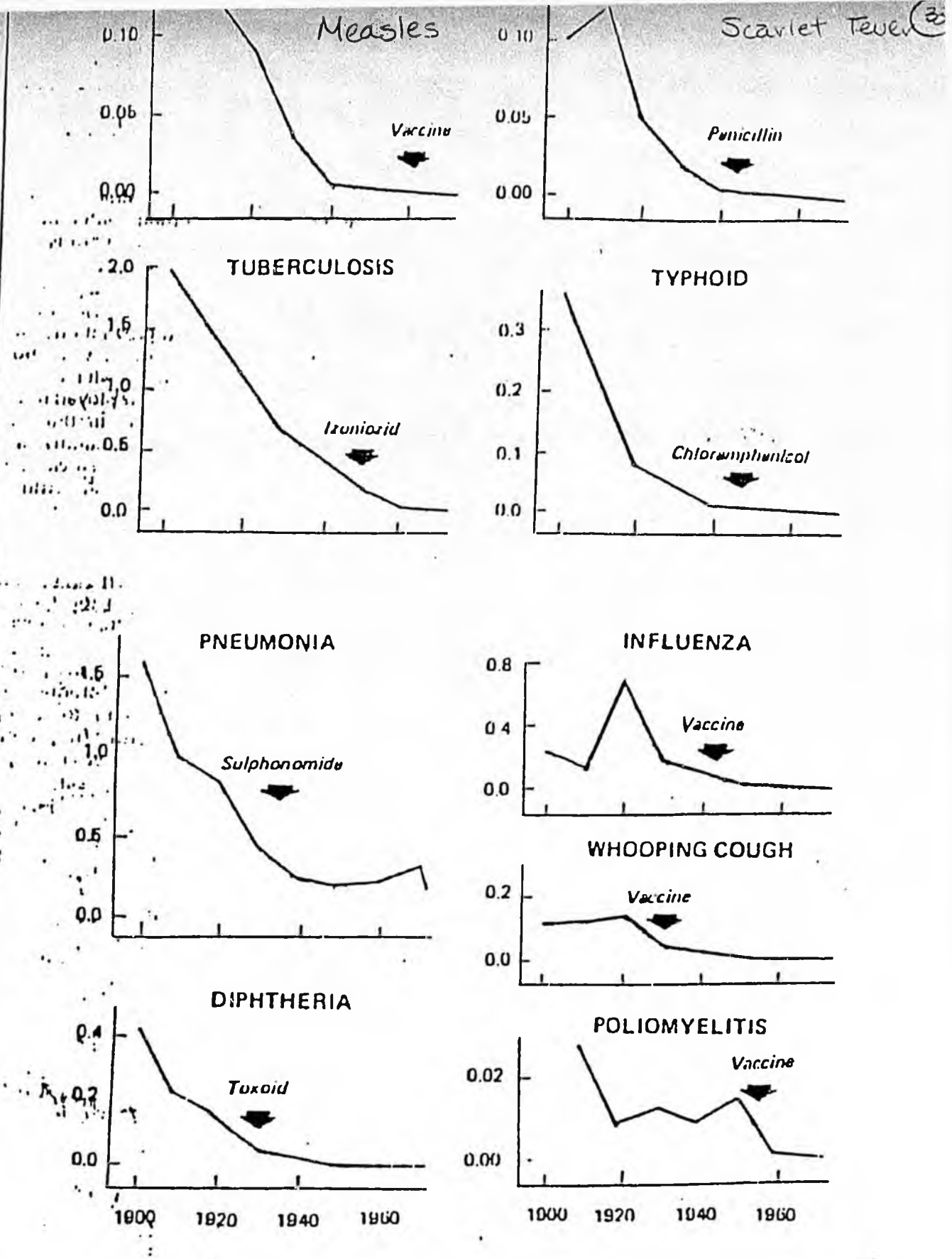
One of them, Dr. Matthew A. Gonda, a virus expert who has performed detailed studies of the structural and genetic makeup of BIV as compared to the AIDS virus, said that the two were close enough to be considered members of the same family of viruses, called lentiviruses.

In fact, Gonda and his colleagues at Program Resources, Inc., which conducts research for the National Cancer Institute in Frederick, Md., have proposed that the cattle virus be used as a model for studying the AIDS virus. But the cattle virus is not close enough to be considered the progenitor of the AIDS virus or the cause of AIDS, Gonda said.

"I don't think that BIV could cause AIDS in humans," he said. "I don't want people to say this is an AIDS virus. It's not something that somebody should be afraid will jump into humans or that should make people fear cows."

The second expert, Dr. Martin J. Van der Maaten, of the Agriculture Department's National Animal Disease Laboratory in Ames, Iowa., who first isolated BIV from cattle, said he believed there was "very little chance of it infecting humans."

[redacted]



The Fall in the Standardized Death Rate (per 1,000 Population) for Nine Common Infectious Diseases in Relation to Specific Medical Measures, for the United States, 1900-1977.

From "Contribution of Medical Measures to Mortality Decline", by John B. McKinlay and Sonja M. McKinlay

Children's Diseases Increase As Vaccinations Decline

Officials are worried about minor problems becoming major

By Michael Specter
Washington Post Staff Writer

Cases of measles, mumps and whooping cough have risen steadily over the past several years while the percentage of young children receiving vaccines has dropped, according to a recent report by the Children's Defense Fund.

Public health officials have become worried that if the trend continues, childhood diseases that are now considered minor problems in the United States could return in force.

"Anytime you have a disease that can be prevented by a vaccine, the effort of the nation should be to eliminate it," says Surgeon General C. Everett Koop. "Compare the cost of the vaccine—in pain as well as money—to the cost of the disease. We need to reach the children we are missing."

Health experts say that diminished federal funds have been responsible for at least part of the problem. As funds have been cut during the past five years, it has become increasingly difficult for poorer children to gain access to vaccines, according to the report.

The surgeon general has set as a health objective for 1990 that at least 90 percent of the nation's children have vaccines before they are 2 years old. But general levels of immunization for preschool children declined between 1980 and 1985, according to federal statistics.

Progress toward the surgeon general's vaccination goals slowed or fell off for most major childhood diseases in the past five years, the Children's Defense Fund report says. For polio, measles, rubella, mumps and DPT (diphtheria, pertussis and tetanus), the percentage of children under 2 who received full immunization declined between 1980 and 1985.

During those years, the last for which there are complete statistics, the proportion of 1- to 4-year-olds receiving no doses of polio vaccine rose by 40 percent for children of all races and 80 percent for nonwhite children, according to the report. In addition, cases of mumps rose in 1986 after a 15-year decline, and in 1985 there were 3,589 reported cases of whooping cough, or pertussis, the highest number since 1970.

"This is becoming a very serious problem," says Dr. Richard Narkewicz, president of the American Academy of Pediatrics. "The immunization program in this country is a bulwark for the future health of our children. It has been built over years and it is beginning to erode."

Narkewicz cites several reasons for the drop in the percentage of children seeking immunization. The liability risks have driven the costs of vaccines up and pushed many drug companies out of the business. Also, because vaccines pose an inherent—but incredibly small—risk to children under 2, some parents decide to avoid them.

"Many American pediatricians have never even seen whooping cough," Narkewicz says. "Because the disease is so rare a certain complacency begins to settle in. But as long as the disease is still out there, it cannot be ignored."

Many health officials believe that parental fears about bad reactions to vaccines have been blown out of proportion. Nearly 11 million children are immunized in America each year and about 30 to 50—at most one out of 220,000—have reactions that cause permanent damage.

But health officials agree that benefits of vaccines far outweigh possible risks. The Children's Defense Fund report, which used figures compiled by the federal Centers for Disease Control, says the number of measles cases reported has risen dramatically since 1983 and that more than 80 percent could have been prevented through adequate immunization.

The development of successful vaccines for most major childhood diseases has been regarded as a hallmark of modern medicine. Vaccines routinely protect children against seven diseases: polio, measles, mumps, rubella, diphtheria, tetanus and pertussis.

Statistics suggest that the decline in vaccinations can be attributed at least partially to access problems rather than parental decisions to avoid the shots. Poor and minority children consistently had the biggest drop in vaccination rates.

Vaccines against DPT give some illustration of the small but growing problem. The percentage of children from 1 to 4 years old with no reported dosages rose only slightly from 0.7 to 0.8 percent between 1980 and 1985, according to the report.

Complete protection requires a series of shots. The number of children younger than 1 only partially immunized against DPT climbed by 10 percent, from 15.8 to 17.3, while the percentage of nonwhite infants not fully immunized climbed 68 percent from 21.0 to 35.2 percent.

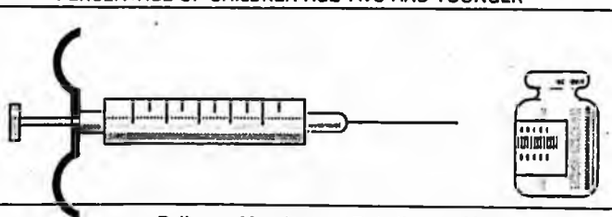
The final appropriation for the program in fiscal 1988 has been set at $86 million, $8 million below the full authorization level. That figure is slightly higher than current levels, but the price per dose of vaccine for measles, mumps and rubella has risen sharply over the past decade from $2.42 in 1975 to $8.47 last year, according to the report.

"By 1986 it took three times as many federal immunization grant dollars to purchase the same number of vaccine doses that were purchased in 1981," the report says.

The number of children younger than 6 has also increased over the past several years, from 18.8 million in 1979 to 21.7 million in 1986, and the number of poor and uninsured children rose dramatically. Between 1982 and 1985 the number of uninsured children increased by more than 16 percent. "It all boils down to dollars," Narkewicz says. "But this makes sense economically as well as medically." ■

HOW MANY CHILDREN ARE IMMUNIZED?

PERCENTAGE OF CHILDREN AGE TWO AND YOUNGER



Year	Polio	Measles	Rubella	Mumps	DPT*
1980	80.7%	83.0%	83.2%	80.2%	87.0%
1981	80.9	81.5	83.9	79.1	87.6
1982	78.6	84.3	81.1	79.0	88.4
1983	78.6	83.9	81.9	78.1	88.4
1984	74.2	81.7	76.7	78.4	85.8
1985	76.7	81.7	77.3	78.9	85.8
1990 Objective	90.0	90.0	90.0	90.0	90.0

*Diphtheria, pertussis and tetanus
NOTE: Full immunization for DPT and polio at this age is defined as three or more vaccinations.
SOURCE: Centers for Disease Control

THE WASHINGTON POST

Diphtheria-Tetanus-Pertussis Immunization and Sudden Infant Death Syndrome

ALEXANDER M. WALKER, MD, DrPH, HERSHEL JICK, MD, DAVID R. PERERA, MD, MPH, ROBERT S. THOMPSON, MD, AND THOMAS A. KNAUSS, MD, PhD

Abstract: We compared the recency of diphtheria-tetanus-pertussis (DTP) immunization in healthy children with birthweights greater than 2500 gms who died of sudden infant death syndrome (SIDS) to that of age-matched reference children, using a modified case-control analysis. Focusing on very narrow time intervals following immunization, we found the SIDS mortality rate in the period zero to three days following DTP to be 7.3 times that in the period beginning 30 days after immunization (95 per cent confidence interval, 1.7 to 31). The mortality rate of non-immunized infants was 6.5 times that of immunized infants of the same age (95 per cent CI, 2.2 to 19). The latter result and to some extent the former appear to be ascribable to known risk factors for SIDS. Although the mortality ratios for SIDS following DTP, as estimated from this study, are high the period of apparently elevated risk was very short, so that only a small proportion of SIDS cases in infants with birthweights greater than 2500 gms could be associated with DTP. (*Am J Public Health* 1987; 77:945–951.)

Introduction

Sudden infant death syndrome (SIDS) has been reported as a possible complication of pertussis immunization on a number of occasions and despite studies which have been interpreted as unsupportive of the idea, a causal relation has not been ruled out.[1–7] There is some *a priori* credibility to the hypothesis that pertussis vaccination might induce a fatal disorganization of respiratory control in susceptible infants. Minor systemic reactions are common,[8] and pertussis vaccine is thought to have rare but serious neurologic sequellae.[9] Neither vital statistics on infant death nor case reports are entirely helpful for the elucidation of a link between SIDS and pertussis vaccine, since the period of highest risk for SIDS coincides in the United States with the recommended dates for the first two diphtheria-tetanus-pertussis (DTP) immunizations. Formal analyses must moreover contend with the potential distortive effect of risk factors for SIDS that in themselves influence pertussis immunization schedules: poverty and low birthweight[10] are prominent in this category.

The present study was designed to re-examine the hypothesis that DTP vaccine might be associated with an increased risk of SIDS in the first year of life. We have been fortunate in having access to complete medical records and notifications of death in a well-defined population. In order to clarify the examination of an outcome thought to have many possibly independent causes,[10] we further focused attention on children possessing no obvious medical risk factors for SIDS.

Methods

Group Health Cooperative of Puget Sound (GHC) is a consumer-owned health maintenance organization founded in 1945 which provides its members with full coverage for virtually all aspects of outpatient and inpatient medical care. According to internal surveys, the GHC population is 90 per cent non-Hispanic White; 92 per cent of members over the age of 18 have completed high school, and two-thirds have had *more* than 12 years of education. Unemployment among GHC members was 4 per cent in 1985. GHC maintains its own clinics, hospitals, and a centralized pharmacy to serve its membership, which now exceeds 309,000 persons. Since 1972, all hospital discharges have been recorded in a machine-readable format and can be linked with GHC's membership file and with computerized death records from the State of Washington. All pharmacy prescriptions and refills have been recorded since July 1976 and can be similarly linked to the other GHC data bases. Coded abstracts of GHC's computerized files, including archival records, are maintained by the Boston Collaborative Drug Surveillance Program to facilitate joint research.

The study population for the present report consists of all apparently healthy infants of birthweight greater than 2500 grams born in GHC hospitals from 1972 to 1983, who were subsequent users of GHC services, and for whom all medical records were retrievable in 1985 and 1986, the period during which this investigation was carried out. There were 35,581 deliveries at GHC hospitals during the period of study. An analysis of a random sample of records (see below) indicates that 75 per cent of these deliveries were of infants eligible for the present investigation. The surveyed population experience thus comprises the immunization and mortality of approximately 26,500 infants. These infants remained under surveillance, and therefore in the study population, for the duration of their families' membership in GHC.

All deaths occurring from 1972 through 1983 among GHC members from 30 to 365 days of age were identified by linkage of GHC membership files to State records. These deaths were reviewed in a two-step process. First, all deaths which on the basis of death certificate diagnosis, hospital discharge data, and pharmacy use taken together could be clearly ascribed to causes not related to immunization were excluded. All remaining records were then abstracted in order to determine cause of death in cases in which computerized data left room for doubt. Copies of death certificates and autopsy results were sought whenever cause of death was not evident from attending physicians' notes.

SIDS was defined as any death for which no cause could be discerned among infants of normal birthweight and without predisposing medical conditions born at GHC hospitals in the years 1972 through 1983. The case series consisted of all 29 SIDS deaths, so defined. Although an autopsy compatible with SIDS was not required for eligibility for this study, all but one of the eligible cases had been autopsied, and the

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Editor's Note: See also related editorial p 925 this issue.

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autopsy diagnosis was in every case SIDS. An additional 14 deaths certified as SIDS occurred among GHC members over the age of 30 days. These have been retained for some of the descriptive material, as described below, and are presented in some detail in the Appendix, but they did not enter into formal analyses.

The overall incidence of SIDS was estimated by dividing the number of deaths (including low birthweight and medically predisposed cases) by the number of infant years at risk in the age range 30 to 365 days.

The timing of DTP administration was determined for the case group by abstracting each infant's lifetime outpatient record. The timing of immunization in the population giving rise to the cases was estimated by examining 262 records of infants with birthweight >2500 grams, without medical conditions placing them at high risk for SIDS, and receiving their primary medical care at GHC during the period under review. These reference records were the complete set of eligible records identified out of 350 randomly selected records of children born at GHC hospitals. (The list of 350 records reviewed comprised 50 records identified at random from computerized files of children born in each of the years 1972, 1974, 1976, 1978, 1980, 1982 and 1984.) The sampled target population may be estimated to constitute about 75 per cent (262/350) of all births at GHC. Most of the first two DTP immunizations were accompanied by oral polio vaccine (OPV) through 1979. From 1980 the first OPV appears to have been given often in conjunction with the second DTP. All DTP and OPV administrations took place in a GHC clinic.

Each case was compared to all the reference children born in the calendar year closest to the case's date of birth, and immunization status was evaluated from the primary medical record for the case and all of the corresponding reference children as of the case's age in days at death. Immunization status was categorized as "No pertussis vaccine to date," "Last immunization within the past three days," "Last immunization within four to seven days," "Last immunization within eight to 29 days," and "Last immunization 30 or more days earlier." Split vaccine doses were counted as separate immunizations.

Variation in mortality from SIDS in relation to DTP immunization status was calculated by means of a matched case-control analysis[11] performed in GLIM,[12] using Whitehead's[13] algorithm. All analyses were carried out both with and without matching on calendar period, with essentially identical results. Analyses presented in what follows retain the period matching. Since no SIDS victim studied was born after June 30, 1983, the 1984 reference group was not invoked for the period-matched analyses, and the reference series used in the period-matched analyses numbered 225 infants. All reference series children were counted for the graphical displays.

Confidence intervals for the relative mortalities in the crude analyses of Tables 2 through 4 were derived by considering pairs of case counts to be distributed as binomial variables and obtaining the binomial counterpart of Cornfield's[14] limits, without continuity correction. A product-limit estimate[15] was used to calculate the cumulative probability of immunization in children excluded from the study.

Results

Case Characteristics

Some details of the 29 case histories are listed in Table 1. Corresponding data for 14 deaths ascribed to SIDS in GHCmembers who were not part of the study population are listed in Appendix Table A1. Thirty-nine of the total 43 cases identified on their death certificates as SIDS occurred in children born at GHC hospitals, during a period that encompassed 27,940.8 infant years of observation, giving an overall mortality of 1.4 cases per 1,000 infant years at risk.

Never Immunized Infants

Six of the 29 infants had not received pertussis vaccine at the time of their death (Table 1). This proportion is compared to that expected (1.56 out of 29) and further analyzed in Table 2. The relative mortality can be approximated by the cross product of Table 2, giving $(6 \times 27.44)/(23 \times 1.56) = 4.6$. The formal matched analysis yields an estimate of 6.5 fold increase in mortality of never-immunized over ever-immunized infants (95 per cent CI 2.2 and 19).

At the time of their deaths, all but one of the non-immunized had passed the 95th percentile of the population distribution of age at first DTP (Figure 1). In order to determine whether any common circumstances related to risk of SIDS affected their immunization schedules, we reabstracted the charts of the non-immunized SIDS victims for data on social characteristics and utilization of medical care. Four out of six mothers were single parents, three of whom were unemployed, and two of whom were receiving public assistance. Physical abuse, at least of the mother, appears to have characterized one other family.

Although at least five of these infants who died before recorded DTP immunization (and/or their mothers) appeared to be using GHC services in the interval between delivery and the infant's death, it is conceivable that the mother might have sought infant immunizations elsewhere. We identified and contacted all well child clinics operating near the homes of these children or near the homes of other possible caretakers listed in the chart, such as grandparents. None of these clinics had any record of visits of any kind by any of the children in question.

Immunized Children

We analyzed SIDS mortality among immunized children by a procedure analogous to that above, except that non-immunized cases were deleted and non-immunized reference group members were omitted from every matched set. There was an important decline in SIDS mortality rates over the days following immunization (Table 3). Four infants died within three days of DTP (three following the first immunization, one following the second) yielding an estimated age- and period-adjusted relative mortality rate of 7.3 (95 per cent CI 1.7 to 31) by comparison to children immunized at least 30 days earlier. Age-adjusted mortality declined gradually over the four weeks following immunization. It should be noted that the confidence intervals for relative mortality in the fourth through 29th days following immunization extend well below one and therefore into the range of a mortality deficit. The overall mortality in the period 0 to 29 days following DTP was 2.9 times that in the period 30 or more days after immunization; the 95 per cent CI was 0.93 to 9.1. The data therefore do not rule out the possibility of a compensatory decline in SIDS mortality after a brief post-immunization rise.

Reabstraction of the medical records of the four children dying soon after immunization for indications of non-medical risk factors for SIDS was not productive of the kinds of indicators of risk found with the non-immunized cases. However, an indirect indicator of postnatal care, the date of first DTP immunization, was somewhat delayed in three of

TABLE 1—SIDS Deaths in Children without Predisposing Medical Conditions Born at Group Health Cooperative of Puget Sound

Patient #	Sex	Race[a]	Birth Weight	Month/Year of Death	Age at Death (days)	Days Since Last DTP	No. of DTPs Preceding Death	Autopsy Diagnosis	Observations
1	F	W	2982	8/72	160	—	0	(SIDS)[b]	post mature
2	M	W	3863	10/72	167	6	3	SIDS[c]	
3	F	W	3579	12/72	102	3	2	(SIDS)	
4	F	W	3124	1/74	117	25	2	(SIDS)	
5	F	A	3323	1/74	60	14	1	SIDS	
6	M	W	3295	10/74	78	25	1	(SIDS)	twin
7	M	W	3380	11/74	133	20	2	(SIDS)	history of fracture of right humerus. ?child abuse
8	M	W	3240	12/75	52	5	2	SIDS	
9	F	B	3039	12/76	87	—	0	SIDS	
10	M	W	3721	4/77	80	14	1	SIDS	
11	M	W	4346	7/77	77	49	1	SIDS	
12	F	W	2897	11/77	87	42	1	SIDS	
13	M	W	3607	12/77	115	44	1	SIDS	
14	M	W	3493	2/78	175	28	1	SIDS	
15	F	W	2812	7/78	56	13	1	SIDS	
16	F	W	3636	8/78	277	137	2	SIDS	
17	F	W	3437	12/79	60	31	1	SIDS	
18	F	AI	3266	2/80	78	—	0	SIDS	fever, vomiting, 2 days before death
19	M	W	4090	4/80	84	—	0	SIDS	
20	M	W	3238	6/80	114	72	1	SIDS	
21	M	W	3266	7/80	81	37	1	Refused	
22	F	W	3550	8/80	134	—	0	(SIDS)	
23	M	W	3777	8/81	58	2	1	SIDS	
24	M	W	3181	11/81	59	—	0	SIDS	
25	M	W	4573	1/82	103	2	1	SIDS	
26	M	W	3181	7/82	134	95	1	SIDS	
27	M	W	3493	8/82	46	0	1	SIDS	family disruption
28	F	A	2925	9/82	53	9	1	SIDS	
29	M	W	4402	1/83	178	45	2	SIDS	

[a]Race: A—Asian, AI—American Indian, B—Black, W—White
[b](SIDS) autopsy performed and recorded on Death Certificate as supportive of diagnosis of SIDS, but original documentation no longer available.
[c]SIDS full autopsy results available and supportive of diagnosis.

TABLE 2—SIDS Mortality in Relation to DTP

	DTP Immunization Status		
	Never	Ever	Total
Observed Case Distribution	6	23	29
Age- and Period-Matched Expected Case Distribution[a]	1.56	27.44	29
Relative Mortality			
Crude Analysis[b]	4.6	1.0	
95% Confidence Limits	(1.9,11)		
Matched Analysis[c]	6.5	1.0	
95% Confidence Limits	(2.2,19)		

[a]Based on immunization histories in a random sample of children born at Group Health Hospitals.
[b]Calculated as: (6/1.56)/(23/27.44) = 4.6.
[c]Age- and period-matching accounted for in analysis (see text).

these children (including Case 3, whose death followed the second DTP administration). Figure 1 plots these ages at first DTP and those of the remaining SIDS infants.

Three of the cases dying shortly after immunization did so during a 13-month span beginning in August 1981. For these children, it was possible to identify the lot numbers of the vaccines used. The infants had each received vaccine from a different lot; the lots came from two different manufacturers. Of the four children dying shortly after DTP, only Case 3 had had a concurrent OPV.

Discussion

The major finding of the present study is an apparent 7.3 fold elevation in the risk for SIDS in the first four days following immunization with DTP in the first year of life. In addition, children without any DTP immunization had a SIDS mortality more than six times higher than those who had been immunized. All of the children who died without immunization had already passed the normal ages of first DTP immunization at Group Health, as had a majority of those children who died within a few days of immunization.

Delay in immunization of high-risk infants might lead both to an elevated risk in the never-immunized and to a foreshortening of the interval between immunization and SIDS in the immunized. Both phenomena could operate in the absence of any causal connection between immunization and risk of SIDS death, and could account at least in part for the results obtained here. Review of the individual non-immunized cases suggested a high prevalence of factors that might well lead to a delay in immunization and which are known to predispose to SIDS. Although these elements are not in themselves entirely sufficient to explain the observed risk elevation, both the pattern itself (high risk of SIDS associated with absence of immunization) and probable confounding by socioeconomic factors have been observed previously.[4,6] Data reported from a prospective study of SIDS in Sheffield, United Kingdom,[4] yield a crude SIDS

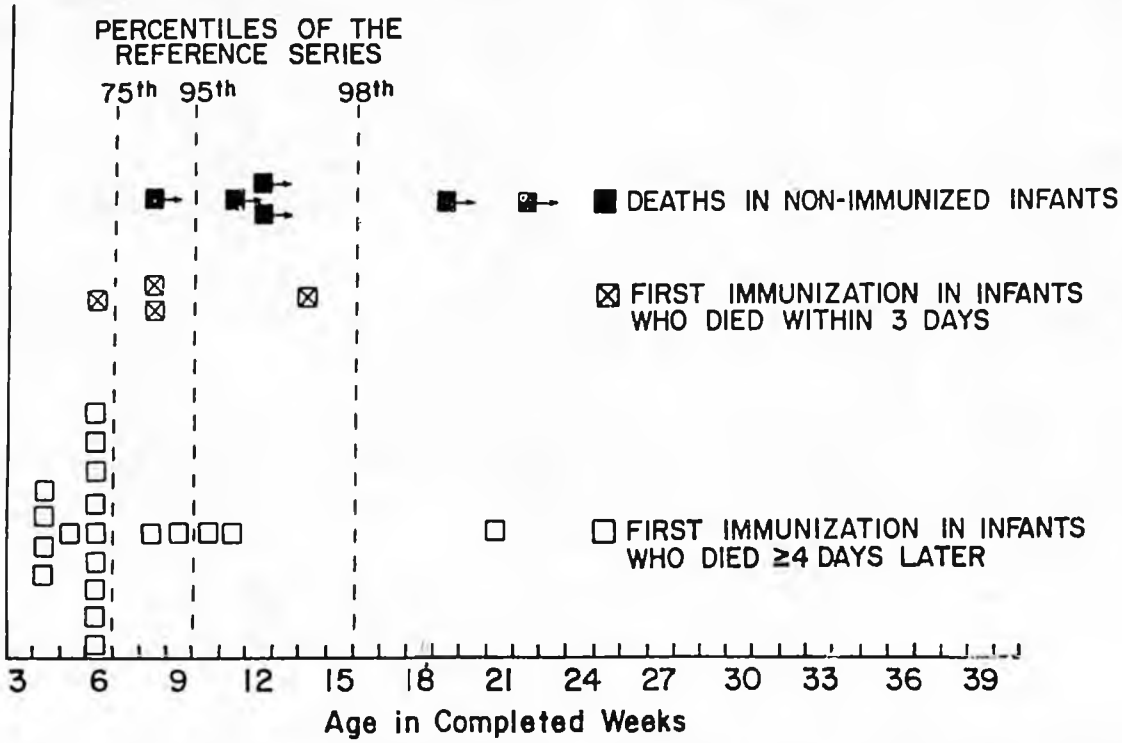


FIGURE 1—Timing of first DTP in immunized SIDS cases, and of death in the non-immunized. Arrows are on the non-immunized to emphasize that date of first DTP would have been later than the date indicated for death. Vertical lines give the percentiles of the cumulative distribution of age at first DTP in the reference series. Time of first DTP serves here as an index of timeliness of postnatal care. The proportions of cases beyond the 75th percentile of the reference distribution are: non-immunized, 100%; recently immunized, 75%; others, 26%. The first two categories of infants experienced delays in their postnatal care.

TABLE 3—SIDS Mortality among the Immunized in Relation to Post-Immunization Interval

	Days Since Last DTP				
	0–3	4–7	8–29	30+	Total
Observed Case Distribution	4	2	8	9	23
Age- and Period-Matched Expected Case Distribution[a]	1.36	1.56	8.23	11.85	23
Relative Mortality					
Crude Analysis[a]	3.9	1.7	1.2	1.0	
95% Confidence Limits	(1.3,12)	(0.41,6.9)	(0.51,3.2)		
Matched Analysis[a]	7.3	3.1	1.9	1.0	
95% Confidence Limits	(1.7,31)	(0.52,19)	(0.53,6.9)		
		2.9			
		(0.93,9.1)			

[a]Non-immunized excluded from reference series.

relative risk of 2.4 for never immunized as compared to age-matched immunized children. The NICHD Cooperative Epidemiological Study of Sudden Infant Death Syndrome[6] found crude relative risks of about two for SIDS in unimmunized infants compared to those who had received DTP in both Whites and Blacks.

All candidate explanations for the observation of increased risk of SIDS in nonimmunized infants hinge on an artifact of some sort. SIDS rates in the UK did not rise and fall with the mass abandonment of pertussis vaccination, nor with the ensuing epidemics of pertussis.[17] It seems therefore unlikely that pertussis immunization protects against SIDS, as for example by aborting an idiosyncratic, fatal reaction to *Bordetella pertussis*.

Several factors mitigate also against acceptance of the data on immunized children (Table 3) as evidence for a simple causal association. A delay in the immunization schedule among high-risk infants could produce an increase in the number of short intervals between immunizations and death, if immunizations were postponed from an age of lower risk (six weeks) to one of higher risk (eight to 16 weeks). The relatively small number of SIDS cases in the present study also admits the possibility of substantial random error.

Preceding investigations of the relation between SIDS and DTP have been subject to a variety of interpretations, partly because of differences in methodology. Table 4 presents an attempt to abstract elements common to this earlier work. For various time intervals following immunization, Table 4 gives the number of SIDS cases reported and the durations of the intervals. A crude relative mortality has been calculated in Table 4 as the ratio of two ratios: (deaths in interval/duration of interval) divided by (deaths in last reported interval/duration of last reported interval). The rationale for this comparison is that the number of child days at risk in the populations giving rise to the SIDS cases in various time intervals must be, to a very close approximation, proportional to the length of the interval. Thus, for example, Baraff, *et al*,[6] reported five cases in the 3.5-day period 0–3 days following DTP and nine cases in the 22-day period 8–29 days following DTP. If the number of children at risk is N, then the ratio of SIDS daily mortality rates in the two periods is $[5/(3.5 \times N)]/[9/(22 \times N)] = (5/3.5)/(9/22) = 5.4$. To the extent that immunizations occur in periods of declining risk for SIDS, the comparisons in Table 4 are somewhat biased toward higher relative mortality in the earlier intervals. Two of the studies tabulated were undertaken in response to reported deaths; the index deaths and the mortality ratios obtained by the inclusion of the deaths that

TABLE 4—Case Series of SIDS Preceded by Pertussis Vaccine Relative Mortality Inferred from Ratios of Cases to Days-at-Risk

Source	Period I			Period II			Period III		
	Definition	Duration[a]	Cases	Definition	Duration	Cases	Definition	Duration	Cases
ner, et al. (ref 2)									
sla	0–3 days	3.5	3(+4)[c]	4–7 days	4	5	8–29 days	22	11
lative Mortality[b]		1.7 (4.0)			2.5			1.0	
% CI		0.52–5.7 (1.6–10)			0.91–6.9				
(ref 3)									
a	0–3 days	3.5	9(+3)	4–7 days	4	5	8–21 days	14	16
tive Mortality		2.3 (3.0)			1.0			1.0	
CI		1.0–5.0 (1.4–6.2)			0.37–2.5				
n et al. (ref 4)									
	24 hours	1	2	1–14 days	14	33			
ve Mortality		0.85			1.0				
CI		0.23–3.2							
and Emery (ref 5)									
	0–2 days	2.5	1	3–7 days	5	0	8–28 days	21	3
ve Mortality		2.8			0			1.0	
CI		0.41–20			0–5.4				
et al. (ref 6)									
	0–3 days	3.5	9	4–7 days	4	8	8–28 days	21	10
ve Mortality		5.4			4.2			1.0	
CI		2.3–13			1.7–10				
(ref 7)									
	0–3 days	3.5	4	4–7 days	4	11	8–28 days	21	38
ve Mortality		0.63			1.5			1.0	
CI		0.24–1.7			0.79–2.9				
Study									
	0–3 days	3.5	5	4–7 days	4	2	8–29 days	22	9
ve Mortality		3.5			1.4			1.0	
CI		1.2–9.9			0.33–5.7				

[a] 0 counted as 0.5 days unless authors state to contrary.
[b] ative mortality [(deaths in interval) (days in interval)] [(deaths in last interval) (days in last interval)]
[c] ers in parentheses are based on inclusion of additional cases that prompted the investigation in question.
[d] e entries derived from percentages reported in the original.
[e] e entries derived from graphical presentation in the original.

ipted the studies are given in parentheses. In the line sponding to the present study, the otherwise eligible s who were excluded for not having been born at a GHC ital are reintroduced.

The studies presented in Table 4 vary enormously in the tail of data acquisition and in the thoroughness of analysis, rmation which is not reflected in the table. Although, fortunately, the full text of Solberg's[7] report has had only ited distribution in English (in the form of an NIH Library anslation), its negative result should be given especially erious consideration. Of all the investigations listed, only at one is comparable to the present study in that: 1) analysis the DTP-SIDS relation was a primary initial objective of e research; 2) case identification and exposure ascertainent were based on medical and vital statistics data of a latively standard format and accessibility for all the popuation covered; and 3) the data have been fully reported (i.e., t only in an abstract or letter form).

While the results of the present study are worrisome, ey do not constitute an appropriate basis for any specific tion other than a thorough examination of data from other urces. First, the study is confined to children at a low seline risk for SIDS. There were not enough births at GHC permit an approach to the question of vaccine risks in low rthweight or ill children, but the sparse data available do not dicate an elevated risk in that group (see the Appendix). ven if all the SIDS occurring within three days after mmunization were due to DTP, immunization practice ould not have accounted for more than about 10 per cent of SIDS cases at GHC. The possibility of compensatory decline in mortality after an initial rise cannot be ruled out.

In the absence of infant immunization programs there would have been a substantial risk of pertussis itself,[18] a serious illness requiring hospitalization for the great majority of infected children under six months of age and resulting in death for about one infant in a hundred.[19] Even a six-month postponement in the currently recommended US schedule for DTP immunizations is thought to entail serious potential consequences.[20]

The present study was one whose logistics were not complex, given the health maintenance organization (HMO) in which it was carried out. It should be replicable in any population with a defined infant membership, clear immunization records, linked death files, and reasonably complete autopsy data on children. Since many HMOs and governmental programs meet these minimal criteria, it should be possible to organize routine administrative data into vaccine surveillance systems capable of addressing the questions raised here.

Reevaluation of the immunization status of a single reference group at different ages for different cases produces a variant of case-control studies which has been termed a "case-cohort" design, since the evolving exposure status of the reference series mirrors that of the underlying cohort.[11] When the cases are few by comparison to the size of the reference series or when the exposure status at one time is a weak predictor of exposure status at another time, the appropriate analysis is just that of a matched case-control

TABLE A1—Sudden Unexplained Death In GHC Infants Who Were Not Members of the Study Population

Patients	Sex	Race[a]	Birth Weight	Month/Year of Death	Age at Death (days)	Days Since Last DTP	No. of DTPs Preceding Death	Death Certificate Diagnosis	Autopsy Diagnosis	Reason for Ineligibility
x1	F	AI	1647	10/73	161	—	0	SIDS	SIDS[b]	Low birthweight
x2	M	W	1619	8/74	93	—	0	SIDS	(SIDS)[c]	Low birthweight
x3	M	W	2727	5/77	76	—	0	SIDS	SIDS	Failure to thrive, PDA, hospitalized for pneumonitis × 22 days, discharged 2 days before death
x4	M	B	2101	10/78	47	18	1	SIDS	SIDS	Low birthweight
x5	F	W	n/a	12/78	182	3	3	SIDS	Refused	Not born GHC
x6	M	W	1220	10/80	52	—	0	SIDS	Not performed	Low birthweight
x7	F	W	2100	12/80	228	78	1	SIDS	SIDS	Low birthweight
x8	F	W	n/a	1/81	217	148	2	SIDS	Not available	Not born GHC
x9	M	W	n/a	10/81	124	71	1	SIDS	Not available	Not born GHC
x10	M	W	n/a	11/81	64	17	1	SIDS	SIDS	Not born GHC
x11	M	W	2868	12/81	88	45	1	SIDS	SIDS	Severe birth asphyxia, Neonatal Group B strep sepsis
x12	F	B	2073	3/82	76	34	1	SIDS	SIDS	Low birthweight
x13	M	W	1350	5/82	77	49	1	SIDS	Not performed	Low birthweight
x14	F	W	2329	9/83	91	43	1	SIDS	SIDS	Low birthweight

[a]Race: AI = American Indian, B = Black, W = White
[b]SIDS full autopsy results available and supportive of diagnosis.
[c](SIDS) autopsy performed and recorded on Death Certificate as supportive of diagnosis of SIDS, but original documentation no longer available.

study (R. L. Prentice, personal communication). The variance of estimates arising from a case-cohort study tend to be smaller than those of more traditional designs. In the present instance, however, all error estimates were determined principally by the relatively small numbers of cases, and so the advantage was small.

APPENDIX

SIDS Deaths in Children Not Members of the Study Population

Fourteen GHC members who were not from the study population were certified as having died of SIDS at age 30 days or older during the years 1972–83. Eight had birthweights below 2500 grams, two had life-threatening medical conditions, and four were not born at GHC hospitals. Although these children could not be entered into the formal comparisons, some of their case data are presented in Table A1 in order to provide a complete portrait of SIDS at GHC.

The prevalence of immunization among the SIDS cases excluded for medical reasons exceeded 50 per cent only at 150 days of life. This observation tends to confirm the anticipated relation between medical risk factors for SIDS and delay in immunization. As a group, very high-risk infants may therefore not be exposed to pertussis vaccine at an age comparable to that of lower risk children. None of the 10 high-risk children who died of SIDS at GHC had had a DTP in the two weeks preceding death.

The four cases ineligible because of not having been born at a GHC hospital (cases x5, x8, x9 and x10) had unremarkable DTP immunization histories. The intervals between DTP and death in these children (3, 17, 71, and 148 days) were similar to those of the eligible cases, and addition of these deaths to the case series would have strengthened the associations documented in Table 3.

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The *AIDS KNOWLEDGE BASE*, a unique, new database on AIDS from San Francisco General Hospital, to be available this summer online on BRS, is designed for use by clinicians, researchers, nurses, public health personnel, hospital administrators, educators, and others working to combat AIDS. The *AIDS KNOWLEDGE BASE* will evolve through continuous updating as new developments and practices emerge in this rapidly changing area, allowing users to keep current with all aspects of clinical practice and research.

For further information about this or other Colleague Program activities, contact BRS Colleague, BRS Information Technologies, 555 East Lancaster Avenue, St. Davids, PA 19087, or check the newsletter *On Call*, published bimonthly at BRS/Colleague, 1350 Avenue of the Americas, New York, NY 10019.

DTP and SIDS: When Data Differ

The question of the possible relationship of certain serious events and the administration of diphtheria and tetanus toxoids and pertussis vaccine (DTP) to infants has resulted in considerable consternation among parents and health professionals, particularly in the United Kingdom, Japan, and the United States. Resolution of these questions is not easily achieved, and all of the answers are not available in spite of considerable effort. The questions in particular revolve around the reactivity of the pertussis component of DTP. The probable reason for this reactivity is that pertussis vaccine is not as refined as one would like, largely because the relationship of the organism's biologic anatomy to immunity in man eluded investigators for many years, and only recently shows prospects of being elucidated. It is to be anticipated that a more refined vaccine, limited to those components of the organism that are responsible for immunity, will ameliorate some of the concerns about DTP.[1]

Reports of severe neurologic damage and death associated with the administration of DTP date back many years.[2] To most physicians during the early years of pertussis vaccine these reported events were probably deemed to be a small price to pay for protection from a disease of high mortality and morbidity. Only as the disease has nearly disappeared in the United States and other developed countries, largely because of the vaccine, have these untoward reactions loomed larger in importance.

The occasional untoward events temporally associated with DTP that have been of greatest concern are acute encephalopathy with permanent brain damage and the sudden infant death syndrome (SIDS).[3] For three reasons, sorting out of cause and effect relationships between these disorders and DTP has been most difficult epidemiologically.

- First, seizures with or without permanent brain damage in infancy occur for many reasons, known and unknown. Because the vast majority are not related to DTP, to determine whether a small fraction may be attributable to the vaccine is a complex task. The same may be said for SIDS; the vast majority of these unfortunate events clearly bear no relationship to DTP, and determining that a very few are due to the vaccine, if such is the case, is very difficult.
- Second, DTP is given to infants at 2, 4 and 6 months of age, a time in life when inherent, underlying neurologic disorders often become apparent or manifest as the child's neurologic development proceeds or fails to proceed. The peak age-specific incidence of SIDS is also between 2 and 4 months.
- Third, it is possible that fever and other systemic effects of DTP may prematurely induce inevitable manifestations of underlying central nervous system disease, such as seizures.

Several attempts to answer these questions have been made in recent years. The remarkable National Childhood Encephalopathy Study (NCES), conducted in Britain in 1976–79, compared the frequency of receipt of DTP in the recent past in 1,182 children with acute encephalopathy with the frequency in a group of matched control children.[4] During the week prior to onset of encephalopathy, there was a slight excess of affected children who had received DTP compared to the control group. Because the study population included all children in Britain and because the numbers of doses of DTP distributed were known, the investigators were able to estimate that encephalopathy with permanent brain damage occurred approximately once in a third of a million doses administered. However, in this study there was also a small excess of encephalopathy following DT and a deficit of encephalopathy one to four weeks following DTP. Although neither of these achieved statistical significance, they do suggest that at least some of the episodes of acute encephalopathy associated with DTP comprised the premature precipitation of inevitable manifestations of an underlying disorder. Further, because the final risk estimates were based on only four children who may have had other unrecognized causes for their disorders, the authors concluded that encephalopathy resulting from DTP, if it ever occurs, is extremely rare.[5]

The NCES also shed light on the possible relationship of DTP to infantile spasms.[6] This disorder strikes approximately 1,200 children in the United States annually: its onset is usually between 2 and 8 months of age. The NCES clearly demonstrated that DTP either brings out, or attracts the parents' attention to, the characteristic symptoms of infantile spasms a week or two earlier than they otherwise would have occurred, but does not cause the problem.

Similar approaches to the possible relationship of DTP to SIDS have been undertaken. In the US for each of the three years, 1982–84, an average of 5,276 SIDS deaths occurred, for a rate of 1.44 per 1,000 live births.[7] Because the peak age incidence for SIDS is 8–10 weeks of age, it is to be expected that a proportion would occur in temporal proximity to receipt of DTP by simple chance. Nonetheless, although SIDS existed long before DTP, it is reasonable to suppose that in some instances SIDS might be precipitated by a systemic effect of DTP, a supposition that is not easily studied.

Other than anecdotal evidence there have been reports of five prior studies of this question;[8–12] a sixth by Walker, *et al*, appears in this issue of the Journal.[13] Two of the first five reports showed a relationship between SIDS and DTP. However, that of Torch is available only as an abstract and the data cannot be independently analyzed. Moreover, the report suggests considerable potential for ascertainment and/or recall bias. That of Baraff, *et al*, has also been discounted because of potential recall bias, plus the fact that the data were not adjusted for week by week changes in the age incidence of SIDS.[14] The other three studies, if anything, show a reverse association of DTP with SIDS, i.e., infants who experienced SIDS are less likely to be immunized than control infants, perhaps in part due to socioeconomic factors.

The most recent of these is a large, multicenter case-control study conducted by the National Institute of Child Health and Human Development (NICHHD).[12] The purpose of this study was to pursue clues as to the etiology of SIDS, including vaccine administration. In this study each of 757 infants succumbing to SIDS was matched with two control infants, one matched by birth date (control A), and one by birth date, birth weight and race. The results of this large study showed no relationship between DTP and SIDS:

indeed, if anything, SIDS infants were less likely to have been immunized in the recent past or at any time than controls.

The present report by Walker, *et al.* suggests a small but significant excess of SIDS in the three days following DTP. How can the disparity between the results of this study and those of others, particularly the large cooperative study conducted in the US, be explained? This is an important question, given the legal issues involved and the fact that DTP, like fluoridation, receives the blame for a great many of our woes in certain circles. Three possibilities exist, all noted by the authors:

- The first is that DTP does, in rare instances, trigger SIDS.
- The second and most likely is that of simple random chance, given the fact that the number of infants succumbing to SIDS within three days of DTP is only four.
- The third relates to delay in immunization in higher-risk infants for socioeconomic reasons and consequent administration of DTP at the peak age of SIDS incidence.

As these authors note,[13] even in the extreme their results are compatible with only 10 per cent of SIDS cases being attributable to DTP, but this would implicate DTP in up to 500 infant deaths annually, all occurring within three days of receiving the vaccine. It is difficult to believe that such would not have been recognized in the NICHHD study. In that study, five (0.7 per cent) of 757 SIDS deaths occurred within 24 hours and 12.9 per cent within two weeks of receiving DTP. In this regard, using age-specific SIDS rates[15] and assuming 80 per cent of infants receive DTP on schedule, among the average of 5,276 deaths from SIDS observed annually, 1982–84, 48 (0.09 per cent) and 679 (12.9 per cent) would have been expected by chance alone within 24 hours and 14 days respectively following DTP. Thus, in the context of other data, if DTP causes SIDS, it must do so sufficiently infrequently to be nearly immeasurable.

The authors of the present study are appropriately cautious. They advise no change in immunization policy on the basis of their data and note the established benefits of DTP. Instead, they suggest pursuit of similar information from other sources. We should heed that advice.

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People

Klatt urges parents to immunize children

By JANET HEVLY
Staff Writer

Parents who aren't immunizing their children because of concern about the safety of the pertussis vaccine are encouraged to consider the risks of the disease, says Michael Klatt, manager of the Alaska Immunization Program.

"The real risks of the pertussis disease far outweigh the theoretical risks of the pertussis vaccine," Klatt said in a recent interview. "The best way to protect your child and society from the disease is to immunize your child on schedule."

Pertussis, also called whooping cough, can be a fatal disease for children. According to information Klatt provided from various medical journals, the disease claims an estimated 600,000 lives a year throughout the world. The vast majority of these fatalities are children under six months of age.

For children, whooping cough is characterized by a distinctive wheezing gasp for air in coughing episodes that can last several minutes. The gasp is coupled by a choking build-up of thick mucus — appearing as a froth from the nose and mouth — that restricts the child's ability to breathe. Children may turn blue from lack of oxygen.

Several epidemics of whooping cough were reported in 1985, resulting in 30 reported cases of the disease in Alaska. During that year, 18 cases were reported in the Kenai-Soldotna area, with 13 of those cases occurring in children under the age of five, Klatt said.

Of the 13 preschoolers, four of the children were less than six months old, four were between the ages of six and 12 months, and five were reported in children between one and five years of age.

Klatt said 11 of the 13 children afflicted with the disease had not been properly immunized. Those children either hadn't received any immunizations, or hadn't been immunized according to the mandated immunization schedule. State and federal laws require children in public schools, in state day-care centers and in the federally funded Headstart program to be immunized at two, four and six months, and between 15 and 18 months of age. A booster shot is also recommended before entering school.

Klatt said five cases of whooping cough were reported in 1986, and three cases have been reported so far this year.

Many of the parents who aren't immunizing their children are worried about the adverse effects of the pertussis vaccine. Klatt said 15 adverse reactions were reported in Alaska in 1985. An adverse reaction is defined as anything more than a fever or minor reaction at the site of the injection.

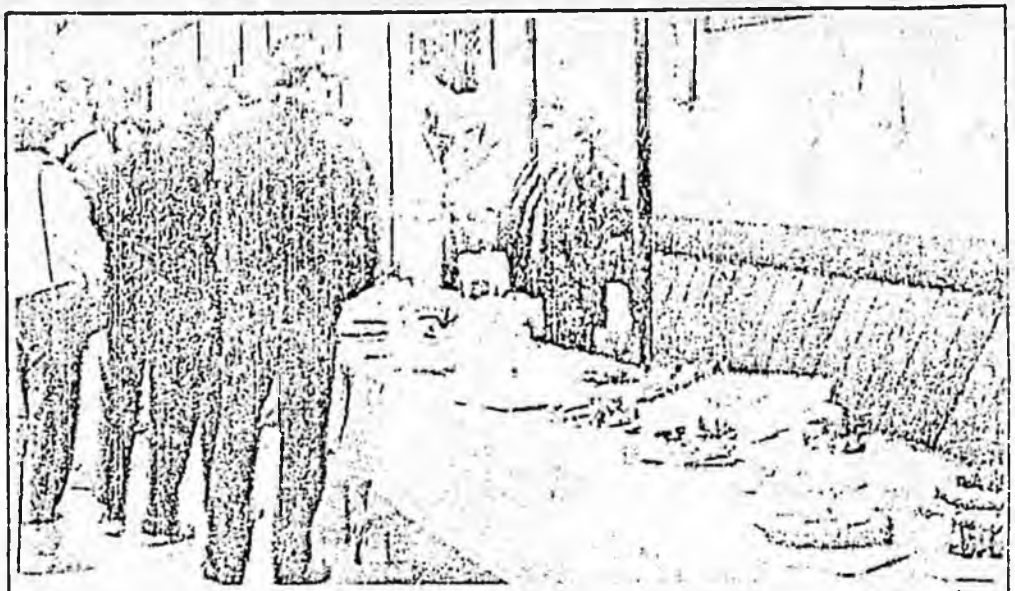
He acknowledges that the reaction reporting system hasn't been effective in the past, and that many parents may not have associated illnesses occurring after a vaccination as related to the vaccine. "I have no doubt that the adverse reactions were under-reported," Klatt said.

As of mid-1986, Klatt said the state is using vaccines purchased from the federal government which require parents to receive written information about the potential hazards of the vaccines. Parents must sign a form stating they understand the possible adverse reactions, and that any adverse reactions should be reported to the health-care provider.

Prior to the written warnings, parents having their children immunized only received verbal warnings about the potential adverse reactions to the shots, Klatt said.

"I anticipate an increase in reported adverse reactions," Klatt said, "And that's good because we want accurate reporting."

According to information from Klatt's medical journals, whooping cough is an extremely contagious disease. The odds indicate that if one of your children brings it home, the rest of the kids will get it. Recovery takes weeks; the Japanese name for whooping cough is translated to "the hundred-days cough."



Neva Black, a judge in the 4-H Council's Chocolate Lovers Contest, talks to passersby who were looking at entries to the contest this weekend at the Kenai Mall. (Photo by Nicky Donald)

Children have about a 50-50 chance of developing minor redness, swelling and pain at the site of the DTP injection. Fever, vomiting and drowsiness after a DTP vaccination occur about one in five times. One in 310,000 vaccinated children suffers brain damage, according to information supplied by Klatt. Despite the alarming number of side affects, he emphasized that a study in the United States indicates that SIDS victims were no more likely than non victims to have received a DTP vaccine.

Parents who delay having their children immunized until after six months of age are actually missing their prime opportunity to immunize against pertussis when it is most effective, Klatt said. Whooping cough is most fatal to children under six months of age.

Klatt said public health nurses are receiving an increasing number of requests for just a DT vaccine, without the "P" for pertussis. "They won't honor that request unless they have a written request from a physician," Klatt said. Only a private physician will give just a DT vaccine because a parent philosophically objects to the pertussis vaccine.

A more safe pertussis vaccine may be introduced in the near future, Klatt said. The United States is currently helping finance a study being conducted in Sweden on an acellular pertussis vaccine. The pertussis vaccine administered here is a whole cell vaccine, using all parts of the pertussis bacteria, Klatt said. The acellular vaccine separates the bacteria, attempting to use just the immune qualities of the bacteria and eliminate the other ingredients that may be causing the adverse reactions, he explained.

"The study should be done by the end of the summer, and the results written up by the end of the year," Klatt said. "If it is determined to be as effective at protecting against pertussis with less side affects, I would assume the U.S. would go for that vaccine."

Klatt said he obtained his information from articles on pertussis in Public Health Reports, Journal of the American Medical Association, the American Journal of Diseases of Children, the John Hopkins University School of Hygiene and Public Health and Mothers Today.

Letters to the editor

DPT parent responds to report on interview of health official

To the editor:

This is in regard to the article, "Klatt urges parents to immunize children," by Janet Hevly, Jan. 18.

I am president of the Alaska chapter of Dissatisfied Parents Together (DPT), parents concerned with vaccine safety, efficacy and awareness. We are not anti-vaccine, but stress that each parent should be educated as to all the risks as well as the benefits of any vaccine to be administered to their child. We also stress that each parent should be allowed to choose what vaccines their child is to receive without threat of exclusion from public school.

I wish to clarify and comment on several of the misleading statemets made by Mr. Klatt, so that local parents will not fall prey to the scare tactics so willingly employed by our public health department.

As it is true that the pertussis disease can be fatal, the high death rate (600,000 yearly worldwide) does not exist in developed countries. In Sweden and West Germany, where mandatory pertussis vaccinations have been discontinued due to high reaction rates, the death rate is virtually nonexistent. According to the official Annual Summary 1983 of Morbidity and Mortality Weekly Report, distributed by the U.S. Department of Health and Human Services, only six fatalities due to the pertussis disease occurred in the U.S. in 1981. According to this publication, six deaths per year due to pertussis is the average in our country. An interesting note: the only part of Europe where pertussis vaccination is universally imposed is in the communist countries, such as the Soviet Union, East Germany, Poland and Czechoslovakia.

In regards to the 1985 whooping cough epidemic, I have correspondence from Michael Klatt stating that only 9 of the 30 reported whooping cough cases were actually confirmed pertussis. Approximately half had received pertussis vaccinations. There were no deaths. According to this letter and future correspondence, Mr. Klatt stated that he "was unable to ascertain the immunization histories, because immunization histories were not gotten (for whatever reasons) for all reported cases." How did he manage to come up with the in-depth information then for his interview with Ms. Hevly?

While our group of concerned parents is glad to see that the health department is finally allowing that their adverse-reaction reporting system is inefficient and has been underreporting both immediate severe reactions and long-term illnesses suffered from vaccinations, it is not heartening to realize that this same health department expects parents to disregard these facts and keep on injecting our children with this highly reactive pertussis vaccine. Also, Mr. Klatt failed to mention that his office does not accept an adverse-reaction form unless it meets minimum criteria. One of these is that the reaction must have been severe enough to require a visit to a doctor, health-care facility or hospital. None of these places are required to report any reaction, however.

If a report form does not include this visit, it is shredded. According to the 1987 Goals and Objectives, published by our health department, this criteria is not scheduled to change.

In regard to the statistics Mr. Klatt quoted in relation to reported adverse reactions, they are not only questionable because they are admittedly underreported, but they do not begin to address the long-term damage associated with many immediate adverse reactions; epilepsy, chronic blood diseases, deafness, blindness, cerebral palsy, severe retardation, death, etc.

Our organization finds it amazing that though there have been four studies published in the 1980s in the Unites State showing a direct causal relationship between DPT vaccinations and SIDS, our government and public officials (e.g., Mr. Klatt) have chosen to disregard these findings in favor of another study that shows only a temporal relation. I have correspondence from our Alaska Health Department that states that no vaccine information is collected on SID victims, supposedly because such information is too hard to analyze!

Also, Mr. Klatt failed to mention that the DPT vaccination series is not effective until all three shots of that first series are completed at the age of six months (if the vaccination schedule is strictly adhered to), so by the time child is "protected," he's already out of the danger zone. "Whooping cough is most fatal to children under six months of age," Klatt, quoted from Clarion article.

As a last comment, I'd like to let Alaskan parents know that there is legislation being drafted to require mandatory adverse-reaction reporting by all sectors, to require accurate parent information, extensive long-term followup and to allow Alaskan parents to object to any or all state mandated vaccines without exclusion from public school is allowed in 22 other states.

Shannon Kohl
Soldotna

PEDIATRIC CONSULTANTS OF ALASKA, INC.
Clinton B. Lillibridge, M.D., F.A.A.P.
Peter H. Michelson, M.D., F.A.A.P.

December 10, 1987

Representative Kay Brown
3111 C Street, Suite 435
Anchorage, Alaska 99503

RE: HOUSE BILL 277 (Amendment to immunization regulations, making them optional)

Dear Kay:

I am terribly upset at the amount of misinformation and emotionalism exhibited by the proponents of this bill. The facts which are pertinent have been ignored. Specifically, pertussis, diphtheria, and tetanus organisms are widespread throughout the community and are easily caught. The rate of death for even something as simple as pertussis is about 10%. One out of a thousand children who catch pertussis will survive, but be permanently brain-damaged. The shot itself causes brain-damage in 1 out of 310,000 people. There have been six infants in Alaska this year who caught whooping cough (they were not immunized) and nearly died. The parents had huge hospital bills because of that, but luckily their children survived.

I strongly urge you to do everything you can to work against House Bill 277.

Sincerely,

Clint

Clinton B. Lillibridge, M.D.
Pediatrician

CBL:pm

1200 Airport Heights Drive, Suite 230 • Anchorage, Alaska 99508
Telephone (907) 276-5517

May 3, 1987

Representative Kopanen
Alaska State Legislature
Pouch V (MS 3100)
Juneau, Alaska 99811

Dear Representative Kopanen:

I am writing to you to let you know how important I feel House Bill 277 is.

I support House Bill 277 and I would like you to support it too.

I had know idea of the problems that could arise from the DPT shots until I contacted my local Chapter of Dissatisfied Parents Together. I was very thankful for the information I received because my daughter did have a reaction to the shot and I was able to know what to look out for and stop any damage that could have been done.

It seems a shame that we carry these children so carefully for 9 months; we eat well, take vitamins, and watch out for hazards in our environment that might affect them, and then we turn around and inject them with something that can cause so much harm.

Please pass House Bill 277 through the committee without change.

Sincerely,

Kika Hutto
3955 Nichols
Soldotna, Alaska 99669

Alaska State Legislature

Please enter into the record my testimony to the HHS
committee name

committee on House Bill No. 277, dated 11 Feb 88.
bill/subject

I would like to respond to several points. Number one, I agree that better information could be made available to parents. I spend many hours adding to the information parents have.

Many studies are available showing both the long Term effects of no vaccinations and also the great value of immunizations. The incidence of severe effects of measles such as subacute sclerosing panencephalitis has fallen remarkably since measles vaccine became available. The issue of whether boosters are needed is still uncertain, but since giving the vaccine to children aged 15 months rather than 9 months should make immunity more certain. This will need continuing study.

Signed: Richard C. Reem, M.D.
Testifier

Representing (Optional)

1001 Noble Street, Fairbanks
Address

452-1611
Phone No.

It has been demonstrated over and over that the more pertusis vaccine one has had, the milder is the disease. Whooping cough is unheard of in children who have had all doses of the vaccine.

No doubt, vaccines need improvement, especially pertussis vaccine. New vaccines are needed such as vaccine against Hemophyllus influenza, AIDS, and other diseases.

MY NAME IS JUDY AMES, BOX 824, SOLDOTNA

I am a concerned parent who takes health issues very seriously. We all know there are new findings happening daily concerning all aspects of the human body, particularly the immune system. After receiving all the information regarding vaccinations provided by a health care provider, I am left feeling very unassured and helpless. My additional research on this issue has given me more reason to doubt a "safe" system. I want the personal choice of taking charge of my child's health care and am looking forward to a change in the present immunization system.

Please take a positive approach to hb 277.

Judy Ames
2-11-88

Alaska State Legislature

(1)

Please enter into the record my testimony to the Health Education & Social Services + Judiciary committee name committee on House Bill No. 277 bill/subject, dated February 11, 1988.

"An act relating to the immunization of minors"

As a concerned citizen and currently employed as a Public Health nurse I am opposed to House Bill No 277 because:

1) a child who is not required to be immunized before entry into school, preschool, nursery or day care facility puts the public at risk for increase of incidence of disease & will create a serious health problem for Alaska students.
2) The state of Alaska already requires informed parental consent before administering vaccines.
   ie: Parent (important) information forms plus parental signature
   Also at the time of birth, all new parents receive a booklet called - "Parents Guide to Immunizations."
3) The current alaska immunization Program requires health professionals to report any adverse reactions to vaccines.
4) Adverse reactions secondary to administration of vaccines is rarely fatal.
5) Communities should become more involved in public awareness of the benefits vs risks of vaccination.

Signed: Leslie Callaway (Travis)
Testifier

Representing (Optional)

PO Box 1125 Kotzebue AK 99752
Address

442-2608
Phone No.

udget cuts add to girl's whooping cough

He baby was only 5 weeks old

INIE CHAPPELL
ws reporter

ER — Sabrina Kvas- is no longer gasping ith or coughing so vio- that the tiny blood in her eyes burst. Her doesn't worry any bout her choking to n her own vomit. The spasms that left her is shade of blue have

worst is over. After a the hospital, she has returned to her home village of Port Graham.

Sabrina suffers from pertussis, a highly infectious, sometimes fatal respiratory disease that is commonly known as whooping cough. She is also the victim of state budget cuts that kept her from getting a vaccine that could have prevented her from contracting the disease.

Lydia Kvasnikoff tried to have her daughter innoculated.

"We were unable to get the shot because the state had cut the travel budget of the public health nurse," she said.

The nurse, based in Homer, used to visit Port Graham on a monthly basis to administer shots, render prenatal care to pregnant women and see to other needs beyond the ability of the village health aide.

That changed when the price of oil plummeted.

Now the nurse gets to the village about six times a year. She was there in October when Kvasnikoff first inquired about having her daughter innoculated. Sabrina, who was then 6 weeks old, was too young for the shot.

In Alaska, children receive three DPT (diptheria, pertussis and tetanus) shots. The first is administered at age 2 months, the second at 4 months and the third at 6 months.

The nurse didn't return to Port Graham in November or December. In January, she tried to fly into the village, but was weathered out. By then, Sabrina, had started to cough.

"This particular case is very tragic," said Almeda Amoureux, regional supervisor for the public health nurses who work in southcentral Alaska. "I wish the baby had been two weeks older when we were there. It would have made so much difference in her life. It was just a quirk of fate that the child was too young that first time."

Amoureux acknowledges that her nurses are traveling less. Several were laid off in the aftermath of a drastic budget cut in 1986 and visits to many villages had to be curtailed. Some of that money was restored by the legislature in 1987, but there still isn't enough to resume monthly visits to the villages around Kachemak Bay.

So Amoureux and the nurses who work for her are forced to ration their services.

See Page C-3, COUGH

COUGH: Cuts add

Continued from Page C-1

Villages with large numbers of infants and pregnant women receive the most attention. The schedule for Port Graham was established to allow immunization clinics every two months, she said.

For Sabrina, however, that wasn't enough.

Her sickness "began like a regular cold," said Kvasnikoff, who has two other children. "We waited about a week but she never got over it. She kept getting worse. The health aide gave us medicine, but it didn't help. We kept her in a mist tent and everything. She just couldn't catch her breath."

By late January, Sabrina was making the whooping sound for which the disease is known. Kvasnikoff flew to Homer to see a doctor. Three days later, lab tests confirmed that the baby girl was suffering from pertussis.

Sabrina was admitted to South Peninsula General Hospital and put in respiratory isolation. She lived in an oxygen tent.

After a difficult week her symptoms subsided. Dr. Paul Raymond sent Sabrina home Tuesday after ascertaining that she was no longer capable of infecting others.

In the meantime, public health officials have been scrambling to contain an outbreak of the highly contagious disease. As soon as Sabrina's diagnosis was confirmed, a nurse flew to Port Graham and to English Bay to check the vaccination records of every child in both villages and to innoculate those who needed shots. The nurse also contacted everyone who came in contact with Sabrina.

Village health aides have been instructed to report everyone who complains of a persistant cough and fever.

"The big concern we have is that a lot of families have not got DPT shots," said Dr. Paul Eneboe. "So now there is a pool of susceptible children in the villages around Kachemak Bay has declined, Eneboe said.

who eigh- early w, a

(4) Hold hearings, in accordance with section 205(a), in areas of the United States with high infant mortality rates.

(b) RECOMMENDATIONS.—The Commission shall—

(1) recommend a national policy designed to reduce and prevent infant mortality, including recommendations concerning populations at risk of high infant death rates and recommendations concerning appropriate roles for the Federal Government, States, local governments, and private sector;

(2) recommend to the Congress and the President the specific changes needed within Federal laws and Federal programs to achieve an effective Federal role in preventing infant mortality, including the programs specified in subparagraphs (A) and (B) of subsection (a)(1);

(3) recommend to the Congress and the President the specific changes needed to improve the national vital statistics registration system with respect to infant death statistics; and

(4) present such recommendations to the President, the Committee on Energy and Commerce of the House of Representatives, and the Committees on Finance and Governmental Affairs of the Senate no later than one year after enactment of this Act.

42 USC 285g note.

SEC. 205. POWERS OF THE COMMISSION.

(a) HEARINGS.—The Commission, or at its direction, any subcommittee or member thereof, may for the purpose of carrying out the provisions of this title, hold such hearings, sit and act at such times and places, take such testimony, receive such evidence and administer such oaths, as the Commission or such subcommittee or member may deem advisable. Any member of the Commission may administer oaths or affirmations to witnesses appearing before the Commission, subcommittee, or member thereof.

(b) INFORMATION.—The Commission may secure directly from any Federal department or agency such information as may be necessary to enable the Commission to carry out this title. Upon request of the Chairman of the Commission, the head of such department or agency shall furnish such information to the Commission.

(c) CONTRACTS.—To carry out this title, the Commission may enter into such contracts and other arrangements to such extent or in such amounts as are provided in appropriation Acts, and without regard to the provisions of section 3709 of the Revised Statutes (41 U.S.C. 5). Contracts and other arrangements may be entered into under this subsection with or without consideration or bond.

(d) APPLICABILITY OF FEDERAL ADVISORY COMMITTEE ACT.—The provisions of the Federal Advisory Committee Act shall not apply to the Commission.

5 USC app.

42 USC 285g note.

SEC. 206. COMMISSION STAFF.

(a) EXECUTIVE DIRECTOR.—The Chairperson and Vice Chairperson of the Commission shall appoint an executive director. The employment of such executive director shall be subject to confirmation by the Commission.

(b) OTHER PERSONNEL.—The Commission may appoint and terminate the executive director selected under subsection (a) and such other personnel as it considers appropriate to assist in the performance of its duties under this title, without regard to the provisions of title 5, United States Code, governing appointments in the competitive service, and may pay such executive director and other personnel without regard to the provisions of chapter 51 and subchapter III of chapter 53 of such title relating to classification and General Schedule pay rates, except that the rate of pay for such executive director and other personnel may not exceed the rate payable for GS-18 of the General Schedule under section 5332 of such title.

(c) APPLICABILITY OF OTHER FEDERAL LAWS.—Service of an individual as a member of the Commission or employment of an individual by the Commission on a part-time or full-time basis and with or without compensation shall not be considered as service or employment bringing such individual within the provisions of any Federal law relating to conflicts of interest or otherwise imposing restrictions, requirements, or penalties in relation to the employment of persons, the performance of services, or the payment or receipt of compensation in connection with claims, proceedings, or matters involving the United States. Service as a member of the Commission or as an employee of the Commission, shall not be considered service in an appointive or elective position in the Government for purposes of section 8344 of title 5, United States Code, or comparable provisions of Federal law.

(d) EXPERTS AND CONSULTANTS.—Subject to such rules as may be prescribed by the Commission, the Chairman of the Commission may procure temporary and intermittent services under section 3109 of title 5, United States Code, at rates for individuals not to exceed the daily rate payable for GS-18 of the General Schedule under section 5332 of such title.

SEC. 207. SUNSHINE PROVISION.

The Commission shall establish procedures to ensure its proceedings are open to the public to the maximum extent practicable.

SEC. 208. TERMINATION OF THE COMMISSION.

Ninety days after the Commission submits its recommendations as required by section 204(b)(4) the Commission shall terminate.

SEC. 209. AUTHORIZATION OF APPROPRIATIONS.

There are authorized to be appropriated to the Commission such sums as may be necessary. Amounts appropriated under this section shall remain available until the day on which the Commission terminates under section 208.

TITLE III—VACCINE COMPENSATION

SEC. 301. SHORT TITLE.

This title may be cited as the "National Childhood Vaccine Injury Act of 1986".

PART A—VACCINES

SEC. 311. AMENDMENT TO PUBLIC HEALTH SERVICE ACT.

(a) NEW TITLE.—The Public Health Service Act is amended by redesignating title XXI as title XXIII, by redesignating sections 2101 through 2116 as sections 2301 through 2316, respectively, and by inserting after title XX the following new title:

"TITLE XXI—VACCINES

"Subtitle 1—National Vaccine Program

"ESTABLISHMENT

42 USC 300aa-1. "SEC. 2101. The Secretary shall establish in the Department of Health and Human Services a National Vaccine Program to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines. The Program shall be administered by a Director selected by the Secretary.

"PROGRAM RESPONSIBILITIES

42 USC 300aa-2. "SEC. 2102. (a) The Director of the Program shall have the following responsibilities:

"(1) VACCINE RESEARCH.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for research carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development on means to induce human immunity against naturally occurring infectious diseases and to prevent adverse reactions to vaccines.

"(2) VACCINE DEVELOPMENT.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for activities carried out in or through the National Institutes of Health, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development to develop the techniques needed to produce safe and effective vaccines.

"(3) SAFETY AND EFFICACY TESTING OF VACCINES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for safety and efficacy testing of vaccines carried out in or through the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development.

"(4) LICENSING OF VACCINE MANUFACTURERS AND VACCINES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction for the allocation of resources in the implementation of the licensing program under section 353.

42 USC 263a.

"(5) PRODUCTION AND PROCUREMENT OF VACCINES.—The Director of the Program shall, through the plan issued under section 2103, ensure that the governmental and non-governmental production and procurement of safe and effective vaccines by the Public Health Service, the Department of Defense, and the Agency for International Development meet the needs of the United States population and fulfill commitments of the United States to prevent human infectious diseases in other countries.

"(6) DISTRIBUTION AND USE OF VACCINES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction to the Centers for Disease Control and assistance to States, localities, and health practitioners in the distribution and use of vaccines, including efforts to encourage public acceptance of immunizations and to make health practitioners and the public aware of potential adverse reactions and contraindications to vaccines.

"(7) EVALUATING THE NEED FOR AND THE EFFECTIVENESS AND ADVERSE EFFECTS OF VACCINES AND IMMUNIZATION ACTIVITIES.—The Director of the Program shall, through the plan issued under section 2103, coordinate and provide direction to the National Institutes of Health, the Centers for Disease Control, the Office of Biologics Research and Review of the Food and Drug Administration, the National Center for Health Statistics, the National Center for Health Services Research and Health Care Technology Assessment, and the Health Care Financing Administration in monitoring the need for and the effectiveness and adverse effects of vaccines and immunization activities.

"(8) COORDINATING GOVERNMENTAL AND NON-GOVERNMENTAL ACTIVITIES.—The Director of the Program shall, through the plan issued under section 2103, provide for the exchange of information between Federal agencies involved in the implementation of the Program and non-governmental entities engaged in the development and production of vaccines and in vaccine research and encourage the investment of non-governmental resources complementary to the governmental activities under the Program.

"(9) FUNDING OF FEDERAL AGENCIES.—The Director of the Program shall make available to Federal agencies involved in the implementation of the plan issued under section 2103 funds appropriated under section 2106 to supplement the funds otherwise available to such agencies for activities under the plan.

"(b) In carrying out subsection (a) and in preparing the plan under section 2103, the Director shall consult with all Federal agencies involved in research on and development, testing, licensing, production, procurement, distribution, and use of vaccines.

"PLAN

42 "SEC. 2103. The Director of the Program shall prepare and issue a plan for the implementation of the responsibilities of the Director under section 2102. The plan shall establish priorities in research and the development, testing, licensing, production, procurement, distribution, and effective use of vaccines, describe an optimal use of resources to carry out such priorities, and describe how each of the various departments and agencies will carry out their vaccine functions in consultation and coordination with the Program and in conformity with such priorities. The first plan under this section shall be prepared not later than January 1, 1987, and shall be revised not later than January 1 of each succeeding year.

"REPORT

42 "SEC. 2104. The Director shall report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate not later than January 1, 1988, and annually thereafter on the implementation of the Program and the plan prepared under section 2103.

"NATIONAL VACCINE ADVISORY COMMITTEE

42 USC 300aa-5.

"SEC. 2105. (a) There is established the National Vaccine Advisory Committee. The members of the Committee shall be appointed by the Director of the Program, in consultation with the National Academy of Sciences, from among individuals who are engaged in vaccine research or the manufacture of vaccines or who are physicians, members of parent organizations concerned with immunizations, or representatives of State or local health agencies or public health organizations.

"(b) The Committee shall—

"(1) study and recommend ways to encourage the availability of an adequate supply of safe and effective vaccination products in the States,

"(2) recommend research priorities and other measures the Director of the Program should take to enhance the safety and efficacy of vaccines,

"(3) advise the Director of the Program in the implementation of sections 2102, 2103, and 2104, and

"(4) identify annually for the Director of the Program the most important areas of government and non-government cooperation that should be considered in implementing sections 2102, 2103, and 2104.

"AUTHORIZATIONS

42 USC 300aa-6.

"SEC. 2106. (a) To carry out this subtitle other than section 2102(9) there are authorized to be appropriated $2,000,000 for fiscal year 1987, $2,500,000 for fiscal year 1988, $3,000,000 for fiscal year 1989, $3,500,000 for fiscal year 1990, $4,000,000 for fiscal year 1991.

"(b) To carry out section 2102(9) there are authorized to be appropriated $20,000,000 for fiscal year 1987, $22,500,000 for fiscal year 1988, $25,000,000 for fiscal year 1989, $27,500,000 for fiscal year 1990, $30,000,000 for fiscal year 1991.

"Subtitle 2—National Vaccine Injury Compensation Program

"PART A—PROGRAM REQUIREMENTS

"ESTABLISHMENT OF PROGRAM

42 USC 300aa-10.

"SEC. 2110. (a) PROGRAM ESTABLISHED.—There is established the National Vaccine Injury Compensation Program to be administered by the Secretary under which compensation may be paid for a vaccine-related injury or death.

"(b) ATTORNEY'S OBLIGATION.—It shall be the ethical obligation of any attorney who is consulted by an individual with respect to a vaccine-related injury or death to advise such individual that compensation may be available under the program for such injury or death.

"PETITIONS FOR COMPENSATION

42 USC 300aa-11.

"SEC. 2111. (a) GENERAL RULE.—

"(1) A proceeding for compensation under the Program for vaccine-related injury or death shall be initiated by service upon the Secretary and the filing of a petition with the United States district court for the district in which the petitioner resides or in which the injury or death occurred.

"(2)(A) No person may bring a civil action for damages in an amount greater than $1,000 or in an unspecified amount against a vaccine manufacturer in a State or Federal court for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle, and no such court may award damages in an amount greater than $1,000 in a civil action for damages for such a vaccine-related injury or death, unless—

"(i) a petition has been filed, in accordance with section 2116, under subsection (b) for compensation under the Program for such injury or death,

"(ii) a district court of the United States has issued a judgment under section 2112 on such petition, and

"(iii) such person elects under section 2121(a) to file such an action.

"(B) If a civil action which is barred under subparagraph (A) is filed in a State or Federal court, the court shall dismiss the action. If a petition is filed under this section with respect to the injury or death for which such civil action was brought, the date such dismissed action was filed shall, for purposes of the limitations of actions prescribed by section 2116, be considered the date the petition was filed if the petition was filed within one year of the date of the dismissal of the civil action.

"(3) No vaccine manufacturer may be made a party to a civil action (other than a civil action which may be brought under paragraph (2)) for damages for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle.

"(4) If in a civil action brought against a vaccine manufacturer before the effective date of this subtitle damages were denied for a vaccine-related injury or death or if such civil action was dismissed with prejudice, the person who brought such action may file a petition under subsection (b) for such injury or death.

"(5)(A) A plaintiff who on the effective date of this subtitle has pending a civil action for damages for a vaccine-related injury or death may, at any time within 2 years after the effective date of this title or before judgment, whichever occurs first, elect to withdraw such action without prejudice and file a petition under subsection (b) for such injury or death.

"(B) If a plaintiff who on the effective date of this subtitle had pending a civil action for damages for a vaccine-related injury or death does not withdraw the action under subparagraph (A), such person may not file a petition under subsection (b) for such injury or death.

"(6) If a person brings a civil action after the effective date of this subtitle for damages for a vaccine-related injury or death associated with the administration of a vaccine before the effective date of this subtitle, such person may not file a petition under subsection (b) for such injury or death.

"(7) If in a civil action brought against a vaccine manufacturer for a vaccine-related injury or death damages are awarded under a judgment of a court or a settlement of such action, the person who brought such action may not file a petition under subsection (b) for such injury or death.

"(b) PETITIONERS.—

"(1)(A) Except as provided in subparagraph (B), any person who has sustained a vaccine-related injury, the legal representative of such person if such person is a minor or is disabled, or the legal representative of any person who died as the result of the administration of a vaccine set forth in the Vaccine Injury Table may file a petition for compensation under the Program.

"(B) No person may file a petition for a vaccine-related injury or death associated with a vaccine administered before the effective date of this subtitle if compensation has been paid under this subtitle for 3500 petitions for such injuries or deaths.

"(2) Only one petition may be filed with respect to each administration of a vaccine.

"(c) PETITION CONTENT.—A petition for compensation under the Program for a vaccine-related injury or death shall contain—

"(1) an affidavit, and supporting documentation, demonstrating that the person who suffered such injury or who died—

"(A) received a vaccine set forth in the Vaccine Injury Table or, if such person did not receive such a vaccine, contracted polio, directly or indirectly, from another person who received an oral polio vaccine,

"(B)(i) if such person received a vaccine set forth in the Vaccine Injury Table—

"(I) received the vaccine in the United States or in its trust territories,

"(II) received the vaccine outside the United States or a trust territory and at the time of the vaccination such person was a citizen of the United States serving abroad as a member of the Armed Forces or otherwise as an employee of the United States or a dependent of such a citizen, or

"(III) received the vaccine outside the United States or a trust territory and the vaccine was manufactured by a vaccine manufacturer located in the United States and such person returned to the United States not later than 6 months after the date of the vaccination,

"(ii) if such person did not receive such a vaccine but contracted polio from another person who received an oral polio vaccine, was a citizen of the United States or a dependent of such a citizen,

"(C)(i) sustained, or had significantly aggravated, any illness, disability, injury, or condition set forth in the Vaccine Injury Table in association with the vaccine referred to in subparagraph (A) or died from the administration of such vaccine, and the first symptom or manifestation of the onset or of the significant aggravation of any such illness, disability, injury, or condition or the death occurred within the time period after vaccine administration set forth in the Vaccine Injury Table, or

"(ii)(I) sustained, or had significantly aggravated, any illness, disability, injury, or condition not set forth in the Vaccine Injury Table but which was caused by a vaccine referred to in subparagraph (A), or

"(II) sustained, or had significantly aggravated, any illness, disability, injury, or condition set forth in the Vaccine Injury Table the first symptom or manifestation of the onset or significant aggravation of which did not occur within the time period set forth in the Table but which was caused by a vaccine referred to in subparagraph (A),

"(D)(i) suffered the residual effects or complications of such illness, disability, injury, or condition for more than 1 year after the administration of the vaccine, (ii) incurred unreimbursable expenses due in whole or in part to such illness, disability, injury, or condition in an amount greater than $1,000, or (iii) died from the administration of the vaccine, and

"(E) has not previously collected an award or settlement of a civil action for damages for such vaccine-related injury or death,

"(2) all available relevant medical records (including autopsy reports, if any) relating to the person who suffered such injury or who died from the administration of the vaccine and an identification of any unavailable records known to the petitioner and the reasons for their unavailability, and

"(3) appropriate assessments, evaluations, and prognoses and such other records and documents as are reasonably necessary for the determination of the amount of compensation to be paid to, or on behalf of, the person who suffered such injury or who died from the administration of the vaccine.

"COURT JURISDICTION

"SEC. 2112. (a) GENERAL RULE.—The district courts of the United States shall have jurisdiction (1) over proceedings to determine if a petitioner under section 2111 is entitled to compensation under the Program and the amount of such compensation, and (2) to issue and enforce such orders as the courts deem necessary to assure the prompt payment of any compensation awarded.

"(b) PARTIES.—

"(1) The Secretary shall be named as the respondent in all proceedings brought by the filing of a petition under section 2111(b). Except as provided in paragraph (2), no other person may intervene in any such proceeding.

"(2) Within 30 days after the Secretary receives service of any petition filed under section 2111 the Secretary shall publish notice of such petition in the Federal Register. The special master designated with respect to such petition under subsection (c) shall afford all interested persons an opportunity to submit relevant, written information—

"(A) relating to the existence of the evidence described in section 2113(a)(1)(B), or

"(B) relating to any allegation in a petition with respect to the matters described in section 2111(c)(1)(C)(ii).

"(c) SPECIAL MASTERS.—

"(1) Following receipt of a petition under subsection (a), the district court of the United States in which the petition is filed shall designate a special master to carry out the functions authorized by paragraph (2).

"(2) A special master shall serve as an adjunct to the court and may—

"(A) require such evidence as may be appropriate for the preparation of proposed findings of fact and conclusions of law with respect to whether compensation is to be provided

under the Program and the amount of any such compensation,

"(B) require the submission of such information as may be reasonable and necessary to determine if the petitioner is entitled to compensation,

"(C) require the testimony of any person and the production of any document as may be reasonable and necessary to determine if the petitioner is entitled to compensation,

"(D) conduct such hearings as may be appropriate, and

"(E) prepare and submit to the court proposed findings of fact and conclusions of law.

Information submitted to a special master in a proceeding on a petition may not be disclosed to a person who is not a party to the proceeding without the express, written consent of the person who submitted the information. There may be no discovery in a proceeding on a petition other than the discovery required under this paragraph.

"(d) ACTION BY THE COURT.—

Records.

"(1) Upon objection by the petitioner or respondent to the proposed findings of fact or conclusions of law prepared by the special master or upon the court's own motion, the court shall undertake a review of the record of the proceedings and may thereafter make a de novo determination of any matter and issue its judgment accordingly, including findings of fact and conclusions of law, or remand for further proceedings.

"(2) If no objection is filed under paragraph (1) or if the court does not choose to review the proceeding, the court shall adopt the proposed findings of fact and conclusions of law of the special master as its own and render judgment thereon.

"(3) The court shall render its judgment on any petition filed under the Program as expeditiously as practicable but not later than 365 days after the date on which the petition was filed.

"(e) ADMINISTRATION OF AWARD.—The Program shall administer the payments of such compensation. The Program shall audit the payments of compensation under a judgment. A petitioner awarded compensation shall notify the Program of any changes which significantly affect the compensation to be paid.

"(f) REVISION OF AWARD.—

"(1) If the court issues a judgment awarding to a petitioner compensation described in section 2115(a)(1)(A) for unreimbursable expenses and the compensation is insufficient to meet such expenses, such petitioner may petition the court to (A) review such award, and (B) increase the award to make it sufficient to meet such expenses or amend the periodic payment schedule established under section 2115, or both.

"(2) If an audit conducted under subsection (e) discloses the improper use of compensation awarded under a judgment or the termination of a need for an item of compensation, the Program shall petition the court which awarded the compensation to make an appropriate revision in the compensation.

"(g) APPEALS.—The findings of fact and conclusions of law of a district court of the United States on a petition shall be final determinations of the matters involved, except that the Secretary or any petitioner aggrieved by the findings or conclusions of the court may obtain review of the judgment of the court in the United States court of appeals for the circuit in which the court is located upon petition filed with such court of appeals.

"DETERMINATION OF ELIGIBILITY AND COMPENSATION

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"SEC. 2113. (a) GENERAL RULE.—

"(1) Compensation shall be awarded under the Program to a petitioner if the court finds on the record as a whole—

"(A) that the petitioner has demonstrated by a preponderance of the evidence the matters required in the petition by section 2111(c)(1), and

"(B) that there is not a preponderance of the evidence that the illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition.

The court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion.

"(2) For purposes of paragraph (1), the term 'factors unrelated to the administration of the vaccine'—

"(A) does not include any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness, or condition, and

"(B) may, as documented by the petitioner's evidence or other material in the record, include infection, toxins, trauma (including birth trauma and related anoxia), or metabolic disturbances which have no known relation to the vaccine involved, but which in the particular case are shown to have been the agent or agents principally responsible for causing the petitioner's illness, disability, injury, condition, or death.

"(b) MATTERS TO BE CONSIDERED.—

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"(1) In determining whether to award compensation to a petitioner under the Program, the court shall consider, in addition to all other relevant medical and scientific evidence contained in the record—

"(A) any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death, and

"(B) the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions.

Any such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the court. In evaluating the weight to be afforded to any such diagnosis, conclusion, judgment, test result, report, or summary, the court shall consider the entire record and the course of the injury, disability, illness, or condition until the date of the judgment of the court.

"(2) The court may find the first symptom or manifestation of onset or significant aggravation of an injury, disability, illness, condition, or death described in a petition occurred within the time period described in the Vaccine Injury Table even though the occurrence of such symptom or manifestation was not recorded or was incorrectly recorded as having occurred outside such period. Such a finding may be made only upon demonstration by a preponderance of the evidence that the onset or significant aggravation of the injury, disability, illness, condi-

tion, or death described in the petition did in fact occur within the time period described in the Vaccine Injury Table.

"(c) RECORD DEFINED.—For purposes of this section, the term 'record' means the record established by a distict court of the United States in a proceeding on a petition filed under section 2111.

"VACCINE INJURY TABLE

42 USC 300aa-14.

"SEC. 2114. (a) INITIAL TABLE.—The following is a table of vaccines, the injuries, disabilities, illnesses, conditions, and deaths resulting from the administration of such vaccines, and the time period in which the first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths is to occur after vaccine administration for purposes of receiving compensation under the Program:

"VACCINE INJURY TABLE

I.	DTP; P; DTP/Polio Combination; or Any Other Vaccine Containing Whole Cell Pertussis Bacteria, Extracted or Partial Cell Bacteria, or Specific Pertussis Antigen(s).	
	Illness, disability, injury, or condition covered:	Time period for first symptom or manifestation of onset or of significant aggravation after vaccine administration:
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)	3 days
	C. Shock-collapse or hypotonic-hyporesponsive collapse	3 days
	D. Residual seizure disorder in accordance with subsection (c)(2)	3 days
	E. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
II.	Measles, mumps, rubella, or any vaccine containing any of the foregoing as a component; DT; Td; or Tetanus Toxoid.	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Encephalopathy (or encephalitis)	15 days (for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component). 3 days (for DT, Td, or tetanus toxoid).
	C. Residual seizure disorder in accordance with subsection (c)(2)	15 days (for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component). 3 days (for DT, Td, or tetanus toxoid).
	D. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable
III.	Polio Vaccines (other than Inactivated Polio Vaccine).	
	A. Paralytic polio	
	—in a non-immunodeficient recipient	30 days
	—in an immunodeficient recipient	6 months
	—in a vaccine-associated community case	Not applicable
	B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not apolicable
IV.	Inactivated Polio Vaccine.	
	A. Anaphylaxis or anaphylactic shock	24 hours
	B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed	Not applicable

"(b) QUALIFICATIONS AND AIDS TO INTERPRETATION.—The following qualifications and aids to interpretation shall apply to the Vaccine Injury Table in subsection (a):

"(1) A shock-collapse or a hypotonic-hyporesponsive collapse may be evidenced by indicia or symptoms such as decrease or loss of muscle tone, paralysis (partial or complete), hemiplegia or hemiparesis, loss of color or turning pale white or blue, unresponsiveness to environmental stimuli, depression of consciousness, loss of consciousness, prolonged sleeping with difficulty arousing, or cardiovascular or respiratory arrest.

"(2) A petitioner may be considered to have suffered a residual seizure disorder if the petitioner did not suffer a seizure or convulsion unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit before the first seizure or convulsion after the administration of the vaccine involved and if—

"(A) in the case of a measles, mumps, or rubella vaccine or any combination of such vaccines, the first seizure or convulsion occurred within 15 days after administration of the vaccine and 2 or more seizures or convulsions occurred within 1 year after the administration of the vaccine which were unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit, and

"(B) in the case of any other vaccine, the first seizure or convulsion occurred within 3 days after administration of the vaccine and 2 or more seizures or convulsions occurred within 1 year after the administration of the vaccine which were unaccompanied by fever or accompanied by a fever of less than 102 degrees Fahrenheit.

"(3)(A) The term 'encephalopathy' means any significant acquired abnormality of, or injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurologic signs, increased intracranial pressure, or changes lasting at least 6 hours in level of consciousness, with or without convulsions. The neurological signs and symptoms of encephalopathy may be temporary with complete recovery, or may result in various degrees of permanent impairment. Signs and symptoms such as high

pitched and unusual screaming, persistent unconsolable crying, and bulging fontanel are compatible with an encephalopathy, but in and of themselves are not conclusive evidence of encephalopathy. Encephalopathy usually can be documented by slow wave activity on an electroencephalogram.

"(B) If in a proceeding on a petition it is shown by a preponderance of the evidence that an encephalopathy was caused by infection, toxins, trauma, or metabolic disturbances the encephalopathy shall not be considered to be a condition set forth in the table. If at the time a judgment is entered on a petition filed under section 2111(b) for a vaccine-related injury or death it is not possible to determine the cause, by a preponderance of the evidence, of an encephalopathy, the encephalopathy shall be considered to be a condition set forth in the table. In determining whether or not an encephalopathy is a condition set forth in the table, the court shall consider the entire medical record.

"(4) For purposes of paragraphs (2) and (3), the terms 'seizure' and 'convulsion' include grand mal, petit mal, absence, myoclonic, tonic-clonic, and focal motor seizures and signs. If a provision of the table to which paragraph (1), (2), (3), or (4) applies is revised under subsection (c) or (d), such paragraph shall not apply to such provision after the effective date of the revision unless the revision specifies that such paragraph is to continue to apply.

"(c) ADMINISTRATIVE REVISION OF THE TABLE.—

gulations.

"(1) The Secretary may promulgate regulations to modify in accordance with paragraph (3) the Vaccine Injury Table. In promulgating such regulations, the Secretary shall provide for notice and opportunity for a public hearing and at least 180 days of public comment.

"(2) Any person (including the Advisory Commission on Childhood Vaccines) may petition the Secretary to propose regulations to amend the Vaccine Injury Table. Unless clearly frivolous, or initiated by the Commission, any such petition shall be referred to the Commission for its recommendations. Following—

"(A) receipt of any recommendation of the Commission, or

"(B) 180 days after the date of the referral to the Commission,

whichever occurs first, the Secretary shall conduct a rulemaking proceeding on the matters proposed in the petition or publish in the Federal Register a statement of reasons for not conducting such proceeding.

"(3) A modification of the Vaccine Injury Table under paragraph (1) may add to, or delete from, the list of injuries, disabilities, illnesses, conditions, and deaths for which compensation may be provided or may change the time periods for the first symptom or manifestation of the onset or the significant aggravation of any such injury, disability, illness, condition, or death.

"(4) Any modification under paragraph (1) of the Vaccine Injury Table shall apply only with respect to petitions for compensation under the Program which are filed after the effective date of such regulation.

"(d) ROLE OF COMMISSION.—Except with respect to a regulation recommended by the Advisory Commission on Childhood Vaccines, the Secretary may not propose a regulation under subsection (c) or any revision thereof, unless the Secretary has first provided to the Commission a copy of the proposed regulation or revision, requested recommendations and comments by the Commission, and afforded the Commission at least 90 days to make such recommendations.

"(e) RECOMMENDATION.—The Secretary may recommend to Congress revisions of the table to change the vaccines covered by the table.

"COMPENSATION

"SEC. 2115. (a) GENERAL RULE.—Compensation awarded under the Program to a petitioner under section 2111 for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle shall include the following:

"(1)(A) Actual unreimbursable expenses incurred from the date of the judgment awarding such expenses and reasonable projected unreimbursable expenses which—

"(i) result from the vaccine-related injury for which the petitioner seeks compensation,

"(ii) have been or will be incurred by or on behalf of the person who suffered such injury, and

"(iii)(I) have been or will be for diagnosis and medical or other remedial care determined to be reasonably necessary, or

"(II) have been or will be for rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary.

The amount of unreimbursable expenses which may be recovered under this subparagraph shall be limited to the amount in excess of the amount set forth in section 2111(c)(1)(D)(ii).

"(B) Subject to section 2116(a)(2), actual unreimbursable expenses incurred before the date of the judgment awarding such expenses which—

"(i) resulted from the vaccine-related injury for which the petitioner seeks compensation,

"(ii) were incurred by or on behalf of the person who suffered such injury, and

"(iii) were for diagnosis, medical or other remedial care, rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary.

The amount of unreimbursable expenses which may be recovered under this subparagraph shall be limited to the amount in excess of the amount set forth in section 2111(c)(1)(D)(ii).

"(2) In the event of a vaccine-related death, an award of $250,000 for the estate of the deceased.

"(3)(A) In the case of any person who has sustained a vaccine-related injury after attaining the age of 18 and whose earning

capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded, compensation for actual and anticipated loss of earnings determined in accordance with generally recognized actuarial principles and projections.

"(B) In the case of any person who has sustained a vaccine-related injury before attaining the age of 18 and whose earning capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded and whose vaccine-related injury is of sufficient severity to permit reasonable anticipation that such person is likely to suffer impaired earning capacity at age 18 and beyond, compensation after attaining the age of 18 for loss of earnings determined on the basis of the average gross weekly earnings of workers in the private, non-farm sector, less appropriate taxes and the average cost of a health insurance policy, as determined by the Secretary.

"(4) For actual and projected pain and suffering and emotional distress from the vaccine-related injury, an award not to exceed $250,000.

Payments for projected expenses shall be paid on a periodic basis (but no payment may be made for a period in excess of 1 year). Payments for pain and suffering and emotional distress and incurred expenses may be paid in a lump sum.

"(b) VACCINES ADMINISTERED BEFORE THE EFFECTIVE DATE.—Compensation awarded under the Program to a petitioner under section 2111 for a vaccine-related injury or death associated with the administration of a vaccine before the effective date of this subtitle shall only include the compensation described in paragraphs (1)(A) and (2) of subsection (a).

"(c) RESIDENTIAL AND CUSTODIAL CARE AND SERVICE.—The amount of any compensation for residential and custodial care and service expenses under subsection (a)(1) shall be sufficient to enable the compensated person to remain living at home.

"(d) TYPES OF COMPENSATION PROHIBITED.—Compensation awarded under the Program may not include the following:

"(1) Punitive or exemplary damages.

"(2) Except with respect to compensation payments under paragraphs (2) and (3) of subsection (a), compensation for other than the health, education, or welfare of the person who suffered the vaccine-related injury with respect to which the compensation is paid.

"(e) ATTORNEYS' FEES.—

Courts, U.S.

"(1) The judgment of a court on a petition filed under section 2111 awarding compensation shall include an amount to cover—

"(A) reasonable attorneys' fees, and

"(B) other costs,

incurred in any proceeding on such petition. If the judgment of a court on such a petition does not award compensation, the court may include in the judgment an amount to cover petitioner's reasonable attorneys' fees and other costs incurred in any proceeding on such petition if the court determines that the civil action was brought in good faith and there was a reasonable basis for the claim for which the civil action was brought.

"(2) If the petitioner, before the effective date of this title, filed a civil action for damages for any vaccine-related injury or death for which compensation may be awarded under the Program, and elected under section 2111(a)(4) to withdraw such action and to file a petition for compensation under the Program, the judgment of the court on such petition may include an amount limited to the costs and expenses incurred by the petitioner and the attorney of the petitioner before the effective date of this subtitle in preparing, filing, and prosecuting such civil action (including the reasonable value of the attorney's time if the civil action was filed under contingent fee arrangements).

"(3) No attorney may charge any fee for services in connection with a petition filed under section 2111 which is in addition to any amount included under paragraph (1) in a judgment on such petition.

"(f) PAYMENT OF COMPENSATION.—

"(1) Except as provided in paragraph (2), no compensation may be paid until an election has been made, or has been deemed to have been made, under section 2121(a) to receive compensation.

"(2) Compensation described in subsection (a)(1)(A)(iii) shall be paid from the date of the judgment of the district court of the United States under section 2112 awarding the compensation. Such compensation may not be paid after an election under section 2121(b) to file a civil action for damages for the vaccine-related injury or death for which such compensation was awarded.

"(3) Payments of compensation shall be exempt from reduction under any order issued under part C of the Balanced Budget and Emergency Deficit Control Act of 1985.

"(f) PROGRAM NOT PRIMARILY LIABLE.—Payment of compensation under the Program shall not be made for any item or service to the extent that payment has been made, or can reasonably be expected to be made, with respect to such item or service (1) under any State compensation program, under an insurance policy, or under any Federal or State health benefits program, or (2) by an entity which provides health services on a prepaid basis.

"(g) LIABILITY OF HEALTH INSURANCE CARRIERS, PREPAID HEALTH PLANS, AND BENEFIT PROVIDERS.—No policy of health insurance may make payment of benefits under the policy secondary to the payment of compensation under the Program and—

"(1) no State, and

"(2) no entity which provides health services on a prepaid basis or provides health benefits,

may make the provision of health services or health benefits secondary to the payment of compensation under the Program.

"LIMITATIONS OF ACTIONS

"SEC. 2116. (a) GENERAL RULE.—In the case of—

"(1) a vaccine set forth in the Vaccine Injury Table which is administered before the effective date of this title, if a vaccine-related injury or death occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such injury or death after the expiration of 24 months after the effective date of this title,

"(2) a vaccine set forth in the Vaccine Injury Table which is administered after the effective date of this title, if a vaccine-related injury occurred as a result of the administration of such

vaccine, no petition may be filed for compensation under the Program for such injury after the expiration of 36 months after the date of the occurrence of the first symptom or manifestation of onset or of the significant aggravation of such injury, and

"(3) a vaccine set forth in the Vaccine Injury Table which is administered after the effective date of this title, if a death occurred as a result of the administration of such vaccine, no petition may be filed for compensation under the Program for such death after the expiration of 24 months from the date of the death and no such petition may be filed more than 48 months after the date of the occurrence of the first symptom or manifestation of onset or of the significant aggravation of the injury from which the death resulted.

"(b) EFFECT OF REVISED TABLE.—If at any time the Vaccine Injury Table is revised and the effect of such revision is to permit an individual who was not, before such revision, eligible to seek compensation under the Program, such person may file a petition for such compensation not later than 2 years after the effective date of the revision, except that no compensation may be provided under the Program with respect to a vaccine-related injury or death covered under the revision of the table if—

"(1) the vaccine-related death occurred more than 8 years before the date of the revision of the table, or

"(2) the vaccine-related injury occurred more than 8 years before the date of the revision of the table.

"(c) STATE LIMITATIONS OF ACTIONS.—If a petition is filed under section 2111(b) for a vaccine-related injury or death, limitations of actions under State law shall be stayed with respect to a civil action brought for such injury or death for the period beginning on the date the petition is filed and ending on the date a final judgment is entered on the petition.

"SUBROGATION

42 USC 300aa–17.

"SEC. 2117. (a) GENERAL RULE.—

"(1) Upon payment of compensation to any petitioner under the Program, the trust fund which has been established to provide such compensation shall be subrogated to all rights of the petitioner with respect to the vaccine-related injury or death for which compensation was paid, except that the trust fund may not recover under such rights an amount greater than the amount of compensation paid to the petitioner.

Courts, U.S. Records. Claims.

"(2) In any case in which it deems such action appropriate, a district court of the United States may, after entry of a final judgment providing for compensation to be paid under section 2115 for a vaccine-related injury or death, refer the record of such proceeding to the Secretary and the Attorney General with such recommendation as the court deems appropriate with respect to the investigation or commencement of a civil action by the Secretary under paragraph (1).

"(b) DISPOSITION OF AMOUNTS RECOVERED.—Amounts recovered under subsection (a) shall be collected on behalf of, and deposited in the trust fund which has been established to provide compensation under the Program.

"SEC. 2118. The compensation under subsections (a)(2) and (a)(4) of section 2115 and the civil penalty under section 2127(b) shall, effective December 1 of each year beginning 1 year after the effective date of this title, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest 1/10 of 1 percent. For purposes of this section, the term 'base quarter', as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

"ADVISORY COMMISSION ON CHILDHOOD VACCINES

"SEC. 2119. (a) ESTABLISHMENT.—There is established the Advisory Commission on Childhood Vaccines. The Commission shall be composed of:

"(1) Nine members appointed by the Secretary as follows:

"(A) Three members who are health professionals, who are not employees of the United States, and who have expertise in the health care of children, the epidemiology, etiology, and prevention of childhood diseases, and the adverse reactions associated with vaccines, of whom at least two shall be pediatricians.

"(B) Three members from the general public, of whom at least two shall be legal representatives of children who have suffered a vaccine-related injury or death.

"(C) Three members who are attorneys, of whom at least one shall be an attorney whose specialty includes representation of persons who have suffered a vaccine-related injury or death and of whom one shall be an attorney whose specialty includes representation of vaccine manufacturers.

"(2) The Director of the National Institutes of Health, the Assistant Secretary for Health, the Director of the Centers for Disease Control, and the Commissioner of Food and Drugs (or the designees of such officials), each of whom shall be a nonvoting ex officio member.

The Secretary shall select members of the Commission within 90 days of the effective date of this subtitle. The members of the Commission shall select a Chair from among the members.

"(b) TERM OF OFFICE.—Appointed members of the Commission shall be appointed for a term of office of 3 years, except that of the members first appointed, 3 shall be appointed for a term of 1 year, 3 shall be appointed for a term of 2 years, and 3 shall be appointed for a term of 3 years, as determined by the Secretary.

"(c) MEETINGS.—The Commission shall first meet within 60 days after all members of the Commission are appointed, and thereafter shall meet not less often than four times per year and at the call of the chair. A quorum for purposes of a meeting is 5. A decision at a meeting is to be made by a ballot of a majority of the voting members of the Commission.

"(d) COMPENSATION.—Members of the Commission who are officers or employees of the Federal Government shall serve as members of the Commission without compensation in addition to that received in their regular public employment. Members of the

5 USC 5332.

Government shall be compensated at a rate not to exceed the daily equivalent of the rate in effect for grade GS-18 of the General Schedule for each day (including travel time) they are engaged in the performance of their duties as members of the Commission. All members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703, title 5, United States Code, for employees serving intermittently.

"(e) STAFF.—The Secretary shall provide the Commission with such professional and clerical staff, such information, and the services of such consultants as may be necessary to assist the Commission in carrying out effectively its functions under this section.

"(f) FUNCTIONS.—The Commission shall—

"(1) advise the Secretary on the implementation of the Program,

"(2) on its own initiative or as the result of the filing of a petition, recommend changes in the Vaccine Injury Table,

"(3) advise the Secretary in implementing the Secretary's responsibilities under section 2127 regarding the need for childhood vaccination products that result in fewer or no significant adverse reactions,

"(4) survey Federal, State, and local programs and activities relating to the gathering of information on injuries associated with the administration of childhood vaccines, including the adverse reaction reporting requirements of section 2125(b), and advise the Secretary on means to obtain, compile, publish, and use credible data related to the frequency and severity of adverse reactions associated with childhood vaccines, and

"(5) recommend to the Director of the National Vaccine Program research related to vaccine injuries which should be conducted to carry out this subtitle.

"PART B—ADDITIONAL REMEDIES

"AUTHORITY TO BRING ACTIONS

2 USC 300aa-21.

"SEC. 2121. (a) ELECTION.—After the judgment of a district court of the United States under section 2111 on a petition filed for compensation under the Program for a vaccine-related injury or death has become final, the person who filed the petition shall file with the court—

"(1) if the judgment awarded compensation, an election in writing to receive the compensation or to file a civil action for damages for such injury or death, or

"(2) if the judgment did not award compensation, an election in writing to accept the judgment or to file a civil action for damages for such injury or death.

An election shall be filed under this subsection not later than 90 days after the date of the entry of the court's judgment with respect to which the election is to be made. If a person required to file an election with a court under this subsection does not file the election within the time prescribed for filing the election, such person shall be deemed to have filed an election to accept the judgment of the court. If a person elects to receive compensation under a judgment of a court or is deemed to have accepted the judgment of a court, against a vaccine manufacturer for damages for a vaccine-related injury or death for which the judgment was entered.

"(b) LIMITATIONS OF ACTIONS.—A civil action for damages arising from a vaccine-related injury or death for which a petition was filed under section 2111 shall, except as provided in section 2116(c), be brought within the period prescribed by limitations of actions under State law applicable to such civil action.

"STANDARDS OF RESPONSIBILITY

"SEC. 2122. (a) GENERAL RULE.—Except as provided in subsections (b), (c), and (e) State law shall apply to a civil action brought for damages for a vaccine-related injury or death.

"(b) UNAVOIDABLE ADVERSE SIDE EFFECTS; WARNINGS.—

"(1) No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.

"(2) For purposes of paragraph (1), a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with all requirements under the Federal Food, Drug, and Cosmetic Act and section 351 of the Public Health Service Act (including regulations issued under such provisions) applicable to the vaccine and related to vaccine-related injury or death for which the civil action was brought unless the plaintiff shows—

"(A) that the manufacturer engaged in the conduct set forth in subparagraph (A) or (B) of section 2123(d)(2), or

"(B) by clear and convincing evidence that the manufacturer failed to exercise due care notwithstanding its compliance with such Act and section (and regulations issued under such provisions).

"(c) DIRECT WARNINGS.—No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle solely due to the manufacturer's failure to provide direct warnings to the injured party (or the injured party's legal representative) of the potential dangers resulting from the administration of the vaccine manufactured by the manufacturer.

"(d) CONSTRUCTION.—The standards of responsibility prescribed by this section are not to be construed as authorizing a person who brought a civil action for damages against a vaccine manufacturer for a vaccine-related injury or death in which damages were denied or which was dismissed with prejudice to bring a new civil action against such manufacturer for such injury or death.

"(e) PREEMPTION.—No State may establish or enforce a law which prohibits an individual from bringing a civil action against a vaccine manufacturer for damages for a vaccine-related injury or death if such civil action is not barred by this subtitle.

"TRIAL

42 USC 300aa-23.

"SEC. 2123. (a) GENERAL RULE.—A civil action against a vaccine manufacturer for damages for a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this subtitle which is not barred by section 2111(a)(2) shall be tried in three stages.

"(b) LIABILITY.—The first stage of such a civil action shall be held to determine if a vaccine manufacturer is liable under section 2122.

"(c) GENERAL DAMAGES.—The second stage of such a civil action shall be held to determine the amount of damages (other than punitive damages) a vaccine manufacturer found to be liable under section 2122 shall be required to pay.

"(d) PUNITIVE DAMAGES.—

"(1) If sought by the plaintiff, the third stage of such an action shall be held to determine the amount of punitive damages a vaccine manufacturer found to be liable under section 2122 shall be required to pay.

and.

"(2) If in such an action the manufacturer shows that it complied, in all material respects, with all requirements under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act applicable to the vaccine and related to the vaccine injury or death with respect to which the action was brought, the manufacturer shall not be held liable for punitive damages unless the manufacturer engaged in—

21 USC 301 note.
42 USC 201 note.

"(A) fraud or intentional and wrongful withholding of information from the Secretary during any phase of a proceeding for approval of the vaccine under section 351,

42 USC 262.

"(B) intentional and wrongful withholding of information relating to the safety or efficacy of the vaccine after its approval, or

fety.

"(C) other criminal or illegal activity relating to the safety and effectiveness of vaccines,

which activity related to the vaccine-related injury or death for which the civil action was brought.

"(e) EVIDENCE.—In any stage of a civil action, the Vaccine Injury Table, any finding of a district court of the United States or a master appointed by such court in a proceeding on a petition filed under section 2111 and the final judgment of a district court of the United States on such a petition shall not be admissible.

"PART C—ASSURING A SAFER CHILDHOOD VACCINATION PROGRAM IN THE UNITED STATES

"RECORDING AND REPORTING OF INFORMATION

42 USC 300aa-25.

"SEC. 2125. (a) GENERAL RULE.—Each health care provider who administers a vaccine set forth in the Vaccine Injury Table to any person shall record, or ensure that there is recorded, in such person's permanent medical record (or in a permanent office log or file to which a legal representative shall have access upon request) with respect to each such vaccine—

"(1) the date of administration of the vaccine,

"(2) the vaccine manufacturer and lot number of the vaccine,

"(3) the name and address and, if appropriate, the title of the health care provider administering the vaccine, and

"(4) any other identifying information on the vaccine required pursuant to regulations promulgated by the Secretary.

"(b) REPORTING.—

"(1) Each health care provider and vaccine manufacturer shall report to the Secretary—

"(A) the occurrence of any event set forth in the Vaccine Injury Table, including the events set forth in section 2114(b) which occur within 7 days of the administration of any vaccine set forth in the Table or within such longer period as is specified in the Table or section,

"(B) the occurrence of any contraindicating reaction to a vaccine which is specified in the manufacturer's package insert, and

"(C) such other matters as the Secretary may by regulation require.

Reports of the matters referred to in subparagraphs (A) and (B) shall be made beginning 90 days after the effective date of this subtitle. The Secretary shall publish in the Federal Register as soon as practicable after such date a notice of the reporting requirement.

"(2) A report under paragraph (1) respecting a vaccine shall include the time periods after the administration of such vaccine within which vaccine-related illnesses, disabilities, injuries, or conditions, the symptoms and manifestations of such illnesses, disabilities, injuries, or conditions, or deaths occur, and the manufacturer and lot number of the vaccine.

"(3) The Secretary shall issue the regulations referred to in paragraph (1)(C) within 180 days of the effective date of this subtitle.

"(c) RELEASE OF INFORMATION.—

"(1) Information which is in the possession of the Federal Government and State and local governments under this section and which may identify an individual shall not be made available under section 552 of title 5, United States Code, or otherwise, to any person except—

"(A) the person who received the vaccine, or

"(B) the legal representative of such person.

"(2) For purposes of paragraph (1), the term 'information which may identify an individual' shall be limited to the name, street address, and telephone number of the person who received the vaccine and of that person's legal representative and the medical records of such person relating to the administration of the vaccine, and shall not include the locality and State of vaccine administration, the name of the health care provider who administered the vaccine, the date of the vaccination, or information concerning any reported illness, disability, injury, or condition resulting from the administration of the vaccine, any symptom or manifestation of such illness, disability, injury, or condition, or death resulting from the administration of the vaccine.

"(3) Except as provided in paragraph (1), all information reported under this section shall be available to the public.

"VACCINE INFORMATION

"SEC. 2126. (a) GENERAL RULE.—Not later than 1 year after the effective date of this subtitle, the Secretary shall develop and

of this section. Such materials or other information shall be provided prior to the administration of such vaccine.

"MANDATE FOR SAFER CHILDHOOD VACCINES

"SEC. 2127. (a) GENERAL RULE.—In the administration of this subtitle and other pertinent laws under the jurisdiction of the Secretary, the Secretary shall—

"(1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on the effective date of this subtitle and promote the refinement of such vaccines, and

"(2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.

"(b) REPORT.—Within 2 years after the effective date of this subtitle, and periodically thereafter, the Secretary shall prepare and transmit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report describing the actions taken pursuant to subsection (a) during the preceding 2-year period.

"MANUFACTURER RECORDKEEPING AND REPORTING

"SEC. 2128. (a) GENERAL RULE.—Each vaccine manufacturer of a vaccine set forth in the Vaccine Injury Table or any other vaccine the administration of which is mandated by the law or regulations of any State, shall, with respect to each batch, lot, or other quantity manufactured or licensed after the effective date of this subtitle—

"(1) prepare and maintain records documenting the history of the manufacturing, processing, testing, repooling, and reworking of each batch, lot, or other quantity of such vaccine, including the identification of any significant problems encountered in the production, testing, or handling of such batch, lot, or other quantity,

"(2) if a safety test on such batch, lot, or other quantity indicates a potential imminent or substantial public health hazard is presented, report to the Secretary within 24 hours of such safety test which the manufacturer (or manufacturer's representative) conducted, including the date of the test, the type of vaccine tested, the identity of the batch, lot, or other quantity tested, whether the batch, lot, or other quantity tested is the product of repooling or reworking of previous batches, lots, or other quantities (and, if so, the identity of the previous batches, lots, or other quantities which were repooled or reworked), the complete test results, and the name and address of the person responsible for conducting the test,

"(3) include with each such report a certification signed by a responsible corporate official that such report is true and complete, and

"(4) prepare, maintain, and upon request submit to the Secretary product distribution records for each such vaccine by batch, lot, or other quantity number.

Fraud.

"(b) SANCTION.—Any vaccine manufacturer who intentionally destroys, alters, falsifies, or conceals any record or report required under paragraph (1) or (2) of subsection (a) shall—

"(1) be subject to a civil penalty of up to $100,000 per occurrence, or

"(2) be fined $50,000 or imprisoned for not more than 1 year, or both.

Such penalty shall apply to the person who intentionally destroyed, altered, falsified, or concealed such record or report, to the person who directed that such record or report be destroyed, altered, falsified, or concealed, and to the vaccine manufacturer for which such person is an agent, employee, or representative. Each act of destruction, alteration, falsification, or concealment shall be treated as a separate occurrence.

"PART D—GENERAL PROVISIONS

"CITIZEN'S ACTIONS

42 USC 300aa-31.

"SEC. 2131. (a) GENERAL RULE.—Except as provided in subsection (b), any person may commence in a district court of the United States a civil action on such person's own behalf against the Secretary where there is alleged a failure of the Secretary to perform any act or duty under this subtitle.

"(b) NOTICE.—No action may be commenced under subsection (a) before the date which is 60 days after the person bringing the action has given written notice of intent to commence such action to the Secretary.

Courts, U.S.

"(c) COSTS OF LITIGATION.—The court, in issuing any final order in any action under this section, may award costs of litigation (including reasonable attorney and expert witness fees) to any party, whenever the court determines such award is appropriate.

"JUDICIAL REVIEW

Regulations. 42 USC 300aa-32.

"SEC. 2132. A petition for review of a regulation under this subtitle may be filed in a court of appeals of the United States within 60 days from the date of the promulgation of the regulation or after such date if such petition is based solely on grounds arising after such 60th day.

"DEFINITIONS

42 USC 300aa-33.

"SEC. 2133. For purposes of this subtitle:

"(1) The term 'health care provider' means any licensed health care professional, organization, or institution, whether public or private (including Federal, State, and local departments, agencies, and instrumentalities) under whose authority a vaccine set forth in the Vaccine Injury Table is administered.

"(2) The term 'legal representative' means a parent or an individual who qualifies as a legal guardian under State law.

"(3) The term 'manufacturer' means any corporation, organization, or institution, whether public or private (including Federal, State, and local departments, agencies, and instrumentalities), which manufactures, imports, processes, or distributes under its label any vaccine set forth in the Vaccine Injury Table, except that, for purposes of section 2128, such

ered by that section. The term 'manufacture' means to manufacture, import, process, or distribute a vaccine.

"(4) The term 'significant aggravation' means any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health.

"(5) The term 'vaccine-related injury or death' means an illness, injury, condition, or death associated with one or more of the vaccines set forth in the Vaccine Injury Table, except that the term does not include an illness, injury, condition, or death associated with an adulterant or contaminant intentionally added to such a vaccine.

"(6)(A) The term 'Advisory Commission on Childhood Vaccines' means the Commission established under section 2119.

"(B) The term 'Vaccine Injury Table' means the table set out in section 2114.".

(b) CONFORMING AMENDMENTS.—

(1) Sections 217(c), 465(f), and 497 of the Public Health Service Act (42 U.S.C. 218(c), 286(f), 289(f)) are each amended by striking out "2101" and inserting in lieu thereof "2301".

(2) Section 305(h) of such Act (42 U.S.C. 242c(h)) is amended by striking out "2113" each place it occurs and inserting in lieu thereof "2313".

SEC. 312. RELATED STUDIES.

(a) REVIEW OF PERTUSSIS VACCINES AND RELATED ILLNESSES AND CONDITIONS.—Not later than 3 years after the effective date of this title, the Secretary of Health and Human Services shall complete a review of all relevant medical and scientific information (including information obtained from the studies required under subsection (e)) on the nature, circumstances, and extent of the relationship, if any, between vaccines containing pertussis (including whole cell, extracts, and specific antigens) and the following illnesses and conditions:

(1) Hemolytic anemia.
(2) Hypsarrhythmia.
(3) Infantile spasms.
(4) Reye's syndrome.
(5) Peripheral mononeuropathy.
(6) Deaths classified as sudden infant death syndrome.
(7) Aseptic meningitis.
(8) Juvenile diabetes.
(9) Autism.
(10) Learning disabilities.
(11) Hyperactivity.
(12) Such other illnesses and conditions as the Secretary may choose to review or as the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act recommends for inclusion in such review.

The review under this subsection shall include notice and opportunity for a public hearing, consideration of written information submitted by the public, and consultation with such Advisory Commission.

(b) FINDINGS WITH RESPECT TO PERTUSSIS.—Not later than 3 years after the effective date of this title, the Secretary shall make, and publish in the Federal Register, the following specific findings:

(1) Whether each of the illnesses or conditions set forth in subsection (a) can reasonably be determined in some circumstances to be caused or significantly aggravated, by pertussis-containing vaccines.

(2) For each illness or condition for which a finding of causation or aggravation related to vaccines containing pertussis is made under paragraph (1), the circumstances under which such causation or aggravation can reasonably be determined to occur.

(3) For each illness or condition for which a finding of causation or aggravation related to vaccines containing pertussis is made under paragraph (1), and for each illness or condition set forth in the Vaccine Injury Table under section 2114 of the Public Health Service Act, the time periods within which the first symptom or manifestation of onset or aggravation of each such illness or condition can reasonably be determined to occur after pertussis vaccination.

Ante, p. 3764.

Regulations.

(c) REVISION OF TABLE WITH RESPECT TO PERTUSSIS VACCINES.—At the same time the Secretary publishes in the Federal Register findings under subsection (b), the Secretary shall propose regulations to amend the Vaccine Injury Table under section 2114 of the Public Health Service Act as a result of such findings. Not later than 42 months after the effective date of this title, the Secretary shall promulgate such proposed regulations with such modifications as may be necessary after opportunity for public hearing.

(d) REVIEW OF MMR VACCINES AND RELATED ILLNESSES AND CONDITIONS.—Not later than 3 years after the effective date of this title, the Secretary of Health and Human Services shall complete a review similar to the review conducted under subsection (a) with respect to the potential relationship between vaccines containing rubella (including MMR) and radiculoneuritis. The review under this subsection shall include notice and opportunity for a public hearing, consultation with the Advisory Commission on Childhood Vaccines and consideration of written information submitted by the public. Not later than 3 years after the effective date of this title, the Secretary shall make and publish in the Federal Register findings similar to those required by subsection (b) and shall, if appropriate, propose similar regulations (and thereafter promulgate such regulations) to those required by subsection (c), with respect to compensation under the National Vaccine Injury Compensation Program established under section 2110 of the Public Health Service Act for radiculoneuritis caused, contributed to, or significantly aggravated by vaccines containing rubella.

Federal Register, publication.

Ante, p. 3758.

(e) PERTUSSIS AND MMR STUDIES.—

(1) In order to assist the Secretary in making the findings required under subsections (b) and (d), the Secretary shall, in accordance with subparagraph (B), arrange for the conduct of studies of—

(A) the relationship between vaccines containing pertussis (including whole cell, extracts, and specific antigens) and the illnesses or conditions set forth in paragraphs (1) through (11) of subsection (a),

(B) the relationship between vaccines containing pertussis and any other illnesses and conditions, as selected by the Secretary or the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act, and

Ante, p. 3771.

(C) the relationship between vaccines containing rubella (including MMR) and radiculoneuritis.

(2)(A) The Secretary shall request the Institute of Medicine of the National Academy of Sciences to conduct the studies required by paragraph (1) under an arrangement by which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary.

(B) If the Institute of Medicine is unwilling to conduct such study under such an arrangement, the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study and prepare and submit the reports thereon as provided in paragraph (3).

(C) The Institute of Medicine or other group or association conducting the studies required by paragraph (1) shall conduct such studies in consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act.

(3) Reports on the results of the studies required by paragraph (1) shall be completed and submitted to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate and to the Secretary not later than 32 months after the effective date of this title. Upon submission to the Secretary, the reports shall be made available to the public.

(4) There are authorized to be appropriated such sums as are necessary for the purpose of making payments for the conduct of the studies required under this subsection.

(f) DEFINITIONS.—For purposes of this section:

(1) The term "medical and scientific information" includes epidemiologic, clinical, biostatistical, pathological, toxicologic, and other laboratory data and case study information, observations, studies, and reports in peer-reviewed literature or official Government publications, as well as relevant unpublished information, data, studies, and observations.

(2) The term "MMR" means a vaccine containing material intended to prevent or confer immunity against measles, mumps, and rubella disease.

SEC. 313. STUDY OF OTHER VACCINE RISKS.

(a) STUDY.—

(1) Not later than 3 years after the effective date of this title, the Secretary shall, after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act—

(A) arrange for a broad study of the risks (other than the risks considered under section 102) to children associated with each vaccine set forth in the Vaccine Injury Table under section 2114 of such Act, and

(B) establish guidelines, after notice and opportunity for public hearing and consideration of all relevant medical and scientific information, respecting the administration of such vaccines which shall include—

(i) the circumstances under which any such vaccine should not be administered,

(ii) the circumstances under which administration of any such vaccine should be delayed beyond its usual time of administration, and

(iii) the groups, categories, or characteristics of potential recipients of such vaccine who may be at significantly higher risk of major adverse reactions to such vaccine than the general population of potential recipients.

(2)(A) The Secretary shall request the Institute of Medicine of the National Academy of Sciences to conduct the study required by paragraph (1) under an arrangement by which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary.

(B) If the Institute of Medicine is unwilling to conduct such study under such an arrangement, the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study.

(C) The Institute of Medicine or other group or association conducting the study required by paragraph (1) shall conduct such studies in consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act.

Ante, p. 3771.

(b) REVISION OF GUIDELINES.—The Secretary shall periodically, but at least every 3 years after establishing guidelines under subsection (a), review and revise such guidelines after notice and opportunity for public hearing and consideration of all relevant medical and scientific information, unless the Secretary finds that on the basis of all relevant information no revision of such guidelines is warranted and publishes such finding in the Federal Register.

Federal Register, publication.

(c) FACTORS AFFECTING GUIDELINES.—Guidelines under subsection (a) shall take into account—

(1) the risk to potential recipients of the vaccines with respect to which the guidelines are established,

(2) the medical and other characteristics of such potential recipients, and

(3) the risks to the public of not having such vaccines administered.

(d) DISSEMINATION.—The Secretary shall widely disseminate the guidelines established under subsection (a) to—

Physicians. Hospitals. Nurses. State and local governments.

(1) physicians and other health care providers,

(2) professional health associations,

(3) State and local governments and agencies, and

(4) other relevant entities.

42 USC 300aa-1 note.

SEC. 314. REVIEW OF WARNINGS, USE INSTRUCTIONS, AND PRECAUTIONARY INFORMATION.

Not later than 1 year after the effective date of this title and after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act and with other appropriate entities, the Secretary of Health and Human Services shall review the warnings, use instructions, and precautionary information presently issued by manufacturers of vaccines set forth in the Vaccine Injury Table set out in section 2114 of the Public Health Service Act and shall by rule determine whether such warnings, instructions, and information adequately warn health care providers of the nature and extent of dangers posed by such vaccines. If the Secretary determines that any such warning, instruction, or information is inadequate for such purpose in any respect, the Secretary shall at the same time require the manufacturers to revise and reissue such warning, instruction, or information as expeditiously as practical, but not later than 18 months after the effective date of this title.

Ante, p. 3764.

SEC. 315. RECALL AUTHORITY.

Subsection (d) of section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) by inserting "(1)" after "(d)", and

(2) by adding at the end thereof the following new paragraph:

"(2)(A) Upon a determination that a batch, lot, or other quantity of a product licensed under this section presents an imminent or substantial hazard to the public health, the Secretary shall issue an order immediately ordering the recall of such batch, lot, or other quantity of such product. An order under this paragraph shall be issued in accordance with section 554 of title 5, United States Code.

"(B) Any violation of subparagraph (A) shall subject the violator to a civil penalty of up to $100,000 per day of violation. The amount of a civil penalty under this subparagraph shall, effective December 1 of each year beginning 1 year after the effective date of this subparagraph, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest 1/10 of 1 percent. For purposes of this subparagraph, the term 'base quarter', as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.".

SEC. 316. STUDY OF IMPACT ON SUPPLY OF VACCINES.

On June 30, 1987, and on June 30 of each second year thereafter, the Secretary of Health and Human Services shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate—

(1) an assessment of the impact of the amendments made by this title on the supply of vaccines listed in the Vaccine Injury Table under section 2114 of the Public Health Service Act, and

(2) an assessment of the ability of the administrators of vaccines (including public clinics and private administrators) to provide such vaccines to children.

PART B—MISCELLANEOUS

SEC. 321. WAIVER OF PAPERWORK REDUCTION.

Chapter 35 of title 44, United States Code, shall not apply to information required for purposes of carrying out this title and implementing the amendments made by this title.

SEC. 322. NONSEVERABILITY.

If any provision of this title or the application of any provision of this title to any person or circumstance is held invalid by reason of a violation of the Constitution, the entire title shall be considered invalid.

SEC. 321. EFFECTIVE DATE.

(a) GENERAL RULE.—Subtitle 1 of title XXI of the Public Health Service Act shall take effect on the date of the enactment of this Act and Subtitle 2 of such title and this title shall take effect on the effective date of a tax enacted after the date of the enactment of this Act to provide funds for compensation paid under such subtitle 2.

Ante, p. 3756.
Ante, p. 3758.

Claims.

(b) INSUFFICIENCY OF FUNDS.—If at any time there are insufficient funds to pay all of the claims payable under subtitle 2 of title XXI of the Public Health Service Act for 180 days, such subtitle shall cease to be in effect until sufficient funds to pay all of the claims under such subtitle become available.

TITLE IV—ENCOURAGING GOOD FAITH PROFESSIONAL REVIEW ACTIVITIES

Health Care Quality Improvement Act of 1986.

42 USC 11101 note

SEC. 401. SHORT TITLE.

This title may be cited as the "Health Care Quality Improvement Act of 1986".

42 USC 11101.

SEC. 402. FINDINGS.

The Congress finds the following:

(1) The increasing occurrence of medical malpractice and the need to improve the quality of medical care have become nationwide problems that warrant greater efforts than those that can be undertaken by any individual State.

(2) There is a national need to restrict the ability of incompetent physicians to move from State to State without disclosure or discovery of the physician's previous damaging or incompetent performance.

(3) This nationwide problem can be remedied through effective professional peer review.

(4) The threat of private money damage liability under Federal laws, including treble damage liability under Federal antitrust law, unreasonably discourages physicians from participating in effective professional peer review.

(5) There is an overriding national need to provide incentive and protection for physicians engaging in effective professional peer review.

PART A—PROMOTION OF PROFESSIONAL REVIEW ACTIVITIES

42 USC 11111.

SEC. 411. PROFESSIONAL REVIEW.

State and local governments.

(a) IN GENERAL.—

(1) LIMITATION ON DAMAGES FOR PROFESSIONAL REVIEW ACTIONS.—If a professional review action (as defined in section 431(9)) of a professional review body meets all the standards specified in section 412(a), except as provided in subsection (b)—

(A) the professional review body,

(B) any person acting as a member or staff to the body,

(C) any person under a contract or other formal agreement with the body, and

(D) any person who participates with or assists the body with respect to the action,

shall not be liable in damages under any law of the United States or of any State (or political subdivision thereof) with respect to the action. The preceding sentence shall not apply to damages under any law of the United States or any State relating to the civil rights of any person or persons, including the Civil Rights Act of 1964, 42 U.S.C. 2000e, et seq. and the Civil Rights Acts, 42 U.S.C. 1981, et seq. Nothing in this paragraph shall prevent the United States or any Attorney General of a State from bringing an action, including an action under section 4C of the Clayton Act, 15 U.S.C. 15C, where such an action is otherwise authorized.

(2) PROTECTION FOR THOSE PROVIDING INFORMATION TO PROFESSIONAL REVIEW BODIES.—Notwithstanding any other provision of law, no person (whether as a witness or otherwise) providing information to a professional review body regarding the competence or professional conduct of a physician shall be held, by reason of having provided such information, to be liable in damages under any law of the United States or of any State (or political subdivision thereof) unless such information is false and the person providing it knew that such information was false.

(b) EXCEPTION.—If the Secretary has reason to believe that a health care entity has failed to report information in accordance with section 423(a), the Secretary shall conduct an investigation. If after providing notice of noncompliance, an opportunity to correct the noncompliance, and an opportunity for a hearing, the Secretary determines that a health care entity has failed substantially to report information in accordance with section 423(a), the Secretary shall publish the name of the entity in the Federal Register. The protections of subsection (a)(1) shall not apply to an entity the name of which is published in the Federal Register under the previous sentence with respect to professional review actions of the entity commenced during the 3-year period beginning 30 days after the date of publication of the name.

(c) TREATMENT UNDER STATE LAWS.—

(1) PROFESSIONAL REVIEW ACTIONS TAKEN ON OR AFTER OCTOBER 14, 1989.—Except as provided in paragraph (2), subsection (a) shall apply to State laws in a State only for professional review actions commenced on or after October 14, 1989.

(2) EXCEPTIONS.—

(A) STATE EARLY OPT-IN.—Subsection (a) shall apply to State laws in a State for actions commenced before October 14, 1989, if the State by legislation elects such treatment.

(B) STATE OPT-OUT.—Subsection (a) shall not apply to State laws in a State for actions commenced on or after October 14, 1989, if the State by legislation elects such treatment.

(C) EFFECTIVE DATE OF ELECTION.—An election under State law is not effective, for purposes of subparagraphs (A) and (B), for actions commenced before the effective date of the State law, which may not be earlier than the date of the enactment of that law.

SEC. 412. STANDARDS FOR PROFESSIONAL REVIEW ACTIONS.

(a) IN GENERAL.—For purposes of the protection set forth in section 411(a), a professional review action must be taken—

Name: Michael E. Jones, M.D.

Title: Medical Epidemiologist
State of Alaska Department of Health and Social Services,
Division of Public Health, Section of Epidemiology, Immunization Program

Subject: Testimony Presented to the House HESS Committee on February 11, 1988, in Opposition to House Bill 277

Many of us consider the vaccine-preventable diseases of childhood a thing of the past; some of us may think they no longer exist. Except for smallpox, which was eradicated from the world in 1977, those diseases do still exist, but in relatively small numbers. The decline in the incidence rates of childhood diseases is largely attributable to the development of effective vaccines. For example, 21,000 cases of paralytic polio were reported in the USA in 1952; in 1986, only 2 cases were reported. Cases of diphtheria peaked at 207,000 cases in 1921; no cases were reported in 1986. We forget not only how common those diseases were, but also how serious they were and are. As many as 20 percent of children under 5 years of age died after contracting respiratory diphtheria. Measles can be complicated by pneumonia, convulsions, or an inflammatory brain disease. For whooping cough (also known as pertussis), the death rate for children under 6 months of age is 1%.

Although vaccines are extremely effective in preventing certain diseases and their complications, they are not without side effects. The side effects, or adverse events, associated with vaccine administration may be mild or severe. However, permanent, serious adverse events associated with vaccines are quite rare. In order for a vaccine to be useful, its benefits must outweigh its risks. For example, pertussis disease is complicated by encephalopathy--an inflammatory brain condition--once in every 250 cases. Although pertussis vaccine is associated with encephalopathy once in every 110,000 doses, the use of this vaccine has resulted in a 93% decline in the number of cases of this potentially fatal disease during the past 50 years. The vast majority of United States scientists, physicians, and public health officials believe that the benefits of immunization far outweigh the risks, and that the savings outweigh the costs.

In order to collect detailed information about vaccine-associated side-effects, the Alaska Immunization Program uses the Monitoring System for Adverse Events Following Immunization, or MSAEFI, established by the Centers for Disease Control in late 1978. This monitoring system is used to collect reports from public and private providers of publicly funded vaccines concerning adverse events following immunization.

Under MSAEFI, each parent or guardian of a child who receives publicly funded vaccine is to be instructed to report any illness that occurs within 28 days of receiving vaccine and that is severe enough to require a visit to a doctor, clinic, or hospital. This instruction is accomplished in the public medical sector by a notice in writing on every Important Information Statement. Important Information Statements (developed by the Centers for Disease Control) are to be given to all parents/guardians of children who receive an immunization in a public medical facility as a condition for receipt of publicly funded vaccine.

Important Information Statements discuss the risks and benefits of the specific vaccine and the risks of the specific vaccine-preventable disease. By signing the Statement the parent/guardian states that they have read the Important Information Statement and have had an opportunity to ask questions of the health care provider administering the vaccine. Signed Important Information Statements must be kept 10 years beyond the end of the calendar year in which the signature was obtained.

In addition to the parent's/guardian's signature, the vaccine manufacturer's name, the vaccine lot number, the date of the Important Information Statement, and the date of the immunization are documented and retained. Private providers of publicly funded vaccines can either use the Important Information Statement system or use their professional medical judgment to inform parents/guardians of the risks and benefits of the vaccines. Reporting of adverse events following immunization by health care providers has been required in Alaska by regulation since 1974.

Reports of adverse events following immunization which meet minimum reporting criteria are investigated by the Alaska Immunization Program and the pertinent information forwarded to the Centers for Disease Control in Atlanta. A one year follow-up is conducted by the Alaska Immunization Program to determine the health status of the vaccinee.

An integral component of the Alaska Immunization Program is the hospital-based maternal education/immunization program for new mothers. New mothers are to be given a Parents Guide to Immunization (some hospitals distribute their own immunization literature) either during prenatal classes or at the time of discharge. Not only are all of Alaska's hospitals with OB/GYN services part of a maternal education/immunization program, but so are Alaska's lay midwives.

The Alaska Immunization Program has mechanisms in place for informing in print the parents/guardians of the risks and benefits of vaccine(s), ascertaining that the parents/guardians receive and understand the vaccine information, documenting the vaccine manufacturer's name and the vaccine lot number, reporting and investigating adverse events following immunization, and educating mothers of newborns about immunizations.

The current Immunization Program in Alaska traces its roots to the epidemics of diptheria and measles in Alaska in 1975 and 1977. Investigation of the measles epidemic in 1977 revealed that it occurred because Alaska's school immunization law was not being enforced and children were not being vaccinated. A massive, state-wide vaccination campaign was effective in stopping the measeles epidemic. Since March 1, 1977, the daycare and school immunization regulations have been enforced with great success. Cases of rubella and pertussis have been documented in Alaska among individuals who were not appropriately vaccinated or who have recently arrived in Alaska bringing the diseases with them. For 10 years our program has worked well, has achieved our goals of preventing these diseases among Alaskans, and has been accepted by almost all Alaskans.

My name is Cheryl Rykaczewski, I am a concerned parent and a member of the Alaska Chapter of Dissatisfied Parents Together.

I support HB277 because I am concerned about the risk of adverse reaction that we take when we are required to immunize our children. Currently parents are not given enough information about the diseases that can occur as a long term result of an adverse reaction. This bill requires that extensive information be given to parents well in advance of the date of immunization, allowing them to examine their child's and their family's health history and decide whether their child could have a serious reaction to the immunization.

Only a philosophical objection allowance will give parents the confidence and right to exclude their child from immunization if they are at serious risk.

Thank you,

Cheryl Rykaczewski
Box 311
Kasilof, AK 99610
262-4937

Testimony before the Alaska House Committee on Health, Education, and Social Services
February 11, 1988

Shannon M. Kohler, President
Alaska Dissatisfied Parents Together (AK-DPT)

Rep. Koponen, Rep. Ellis and members of the committee:

My name is Shannon Kohler. I am President of the Alaska Chapter of Dissatisfied Parents Together and am here on behalf of that group. AK-DPT is part of a national, non-profit educational organization consisting of parents concerned with vaccine safety and efficacy. We are not anti-vaccine. Alaska DPT has four simple goals that are effectively addressed in H.B. 277, sponsored by Rep. Mike Navarre at the request of Alaska DPT.

Before I go into a quick and concise presentation of some of the supporting data for H.B. 277, I'd like to express my sincere appreciation for the convening of today's hearing (especially since it was arranged to be as convenient as possible for my situation.) I'd also like to convey my and the Alaska DPT group's thanks to Rep. Mike Navarre for sponsorship of this bill, thus giving us the chance to bring to light many of the problems existing in the state's current vaccine program.

I do understand the limited time available for this hearing and the need to lay factual groundwork for this bill. Many parents are willing to tell their stories and express their support of H.B. 277 and have asked me to convey their desire for a statewide teleconference. AK DPT did participate in a teleconference sponsored by The Governors Interim Commission on Youth in July 1987. A copy of that testimony is included in the packets I have distributed.

I would also like to add that it is not the intention of AK-DPT to dismantle the AK Immunization Program. Alaska Law currently mandates that each child receive 5 DPT (Diptheria, Pertussis and Tetanus) shots, recommended at 2,4, 6 & 15 months and 5 years. It mandates 3 oral live polio vaccines recommended at 2,4,and 18 months and one Measles, Mumps and Rubella shot recommended at 15 months. We view the major parts of HB 277 (i.e. Sections 2,3 & 4) as desperately needed information and accountability improvements to the existing program. The first section which relates to choice I will discuss now.

House Bill 277, An Act Relating to the Immunization of Minors
Section I: Philosophical Objection

As H.B. 277 is constructed the first section refers to parental choice (philosophical objection) to vaccination. I will discuss this briefly, then since the remainder of the bill also adds support to this concept, I will return to summarize the necessity of this section.

To allow a parent to choose whether their child is to be vaccinated with a variety of bacteria, viruses, preservatives, additives, etc. should ideally be a simple matter of CHOICE. But since many view choosing not to vaccinate as negligence, I view my task here as one that shows some of the reasons why a responsible loving parent may choose not to vaccinate. It is not my intention or the intention of AK-DPT, to convince parents to vaccinate or not, but in this instance to advocate a choice. Currently state law allows for exemption on medical or religious grounds. It seems ironic that people may currently object to vaccines if they are a member of a religious organization whose beliefs forbid immunizations (i.e. it is their "GOD GIVEN RIGHT" to refuse to immunize their child) but it is unacceptable legally to say "I read 25 articles in medical journals, three newspaper articles, and saw on 20/20 that pertussis vaccine has serious side effects and for this reason I don't want my child to have pertussis vaccine." This statement is not reason enough to refuse to immunize your child against pertussis, at least it is not currently acceptable by law. This is one of the most serious problems with immunization policy: in order to legally refuse any single immunization it is necessary to be opposed to all immunizations on religious grounds.

Alaska DPT has written letters to the twenty-two states that already allow a philosophical objection or parental discretion to vaccination. We asked a variety of questions, including questions about their rates of compliance and rates of disease. Seventeen of the states responded. We have compiled a chart that shows the pertinent data they provided. Please open your packet to this chart. Note that 6 of the 17 states have added a philosophical exemption since 1970, most since 1979, and all have very high vaccine compliance rates. This data should effectively address the possible argument that if AK allows for choice that parents may become lazy or disinterested and discontinue vaccination. This **has not** occurred in the 17 states on this chart, why should it happen in Alaska? This chart also shows that we would not be setting a precedent, we would be joining a growing list of states that obviously decided personal choice in this matter is a distinct priority.

(Discuss disease rates: Vaccinated/Unvaccinated)

Please note the letter from the State of Ohio stating that exemptions cause no disease implication concern there.

Section II. IMMUNIZATION INFORMATION

A) Safety of Vaccines

Though the AK Immunization Program does provide parent information handouts written by the National Center of Disease Control, our group stresses that this information is not nearly adequate at addressing the spectrum of adverse events that may follow routine vaccination. This Immunization Program material never mentions the ingredients contained in any vaccine. Since the state provides the vaccines, it follows that the state should make every effort to give complete information about the ingredients, contraindications (who should not be vaccinated and why), as well as recognized adverse reactions. This requirement could easily be met by providing parents with the manufacturers product insert from each vaccine. Also in this section of H.B. 277 is the provision that hospitals provide all vaccination information to parents of newborns. This is to insure that the parents have ample time to ingest this information before vaccination time 2 months later.

We have heard the argument from health care providers that giving people information will frighten them, that the risks should be minimized, not accentuated. That the benefits out weigh the risks. We have compiled a lot of information that points to the contrary. That pertussis is no longer the dread disease of the early 1900's. That it had declined in frequency by 70% by the time the vaccine was introduced in 1940 [from Pertussis Immunization: Problems, Perspectives, Prospects, Edward A Mortimer Jr. Case Western Reserve Univ., Hospital Practice, Oct 1980, pp103] There is increasing medical evidence and opinion that the vaccine may cause more encephalopathy (and consequent brain damage) than could be expected from the disease itself. [Vaccine Roulette, Dr. Robert Mendelsohn & Dr. Gordon Stewart, Vaccination Against Whooping-Cough, Efficacy versus Risks, Gordon T. Stewart, The Lancet, January 29, 1977, pp237] We realize that this is all currently controversial and do not put ourselves before you as experts, only as people who have a valid concern. We contend that parents as well as health care professionals should be as informed as possible to help initially screen for high risk infants who otherwise might slide through the screening process. No one knows a child's or family's history better than the parent. Information about adverse side effects is also very important to the child who has exhibited a serious reaction with a prior immunization and may be at (in the instance of Pertussis vaccine) substantially increased risk of brain damage. We have experience with parents who didn't realize that the reaction their child had should have been considered serious (because they were not provided information on what constitutes a "serious" reaction or because the seriousness was denied or minimized by their health care provider) and subsequent shots actually did permanent damage. If the reporting of reactions to the shots were encouraged and taken seriously, these children would not be dealing with life long disability today. [See Testimony of Gov. Interim

Commission on Youth, and the Summary of Severe Adverse Reactions.]

Also in the packet provided, AK DPT has prepared a list of severe adverse reactions that may occur after vaccination all with references as to source from medical literature. I must stress that these listings are partial. **[READ SOME OF LISTINGS]**

New information as to the possible long term effects of vaccination is surfacing all the time. Also in these packets are descriptions of some of the ingredients in these vaccines. Did you know that formaldehyde, thimerosal (mercury derivative) and aluminum are ingredients found in the DPT vaccine? As described in your packet, formaldehyde is a highly suspected carcinogen and worse. Thimerosal is made of ethymercuric chloride which happens to belong to the alkylmercuric family which is the most poisonous of mercury families. This mercury is easily absorbed by the body and not easily excreted. It causes brain damage. Aluminum toxicity has been associated with the occurence of Altzheimer's disease. I am not saying that these vaccine ingredients are the only source of these contaminants in our world. Nonetheless, due to the route of exposure (i.e. frequent injection) and time of exposure (early infancy and youth) they can not be discounted as having no possible affect on the general and long term health of our children.

As regards live virus vaccines; measles, mumps, rubella, polio, there are many questions as to the long term implications of their use. I have included a newspaper clipping in your packets that addresses this. In summary this article states that live virus vaccines may be seeding humans with RNA to form proviruses which will then become latent in cells throughout the body. These proviruses could under proper conditions become activated and cause rheumatoid arthritis, multiple sclerosis, allergies and perhaps cancer. I have many medical articles with me that describe the variety of other problems that may exist with the use of live virus vaccines. One very interesting tidbit of info is found on page 25 of the handbook "Surgeon Generals Report on AIDS" provided to all United States households. Under Testing of Military Personnel: I quote about AIDS testing of military recruits: "...They also need to protect new recruits (who unknowingly may be AIDS virus carriers) from receiving live virus vaccines. These vaccines could activate disease and be potentially life-threatening to the recruits."

Question: What other as yet unknown virus may be activated by live virus vaccines?

The fact that there are an infinite number of viruses in the world and these are constantly mutating leads to another question: What kinds of undetected viruses are included in these live virus vaccines that should not be injected into humans? Such an incident was discovered to be occurring in 1961. Simion virus 40, a monkey virus occuring in the monkey kidney ingredient of the polio vaccine, was found to be contaminating the

polio vaccines being injected world wide. Simion virus 40 is known to cause leukemia and cancerous tumors in hamsters. [Division of Biologics Standards. The Boat that Never Rocked; March 1972 Science. Near Disaster With The Salk Vaccine Dec 1963 Science Digest; Development of S and T Antigens and Oncogenicity in Hamster Embryonic Cell Lines Exposed to SV40 Virology 34 1968.] It was reported in the Survey of Childhood Malignancies, Feb 1962 *that children, between the ages of 2 and 4, were being adversely affected by an unfavorable trend of leukemia mortality in technically advanced countries.* [Survey of Childhood Malignancies" Alice Stewart M.D. Public Health Reports Vol 77, No. 2, Feb 1962]

I have the articles describing these incidents and others. Another quote about live virus vaccines from Van Nostrand's Scientific Encyclopedia' Fifth Edition; part of the defintion of virus:

"Phage: Bacteriophages are viruses that invade bacterial cells and are replicated within the bacterial cells. The presence of phage in live virus vaccines has precipitated concern among some authorities. It has been established that phage are introduced into vaccines when viruses for the vaccines are grown in tissue culture... It has been suggested that it is in the realm of possibility for phage to transmit genes to human cells and thus cause cancer or degenerative disease in humans".

VACCINE EFFICACY

According to the vaccine compliance chart we looked at earlier, on the average during a pertussis epidemic 50% of those stricken are vaccinated; 50% are not. During measles outbreaks usually more are vaccinated than are not.

More Facts:

*Some 90% of the pertussis patients whose immunization status was known, appear to have been adequately vaccinated" From the Vaccine Bulletin, Feb 1987, pp11-12, Center for Disease Control publication in regard to the 1986 pertussis outbreak of 1300 cases in Kansas.

*Approximately half of the cases of pertussis (whooping cough) in 1984/85 epidemic had received pertussis vaccine at some point in their life (from correspondence of May 1, 1986 with the AK Public Health Dept.)

Measles:

**Nationally, of the 1,051 affected with measles who were between the ages of 16 months and 28 years of age, 842 (80.1%) had been vaccinated on or after their first birthday which is the currently recommended timetable for measles vaccination".* (from Morbidity and Mortality Weekly, CDC Report, Jan 10, 1986)

The following measles and rubella quotes are from "The 'New' Epidemiology of Measles and Rubella", by James D. Cherry M.D., Univ of Calif, L.A., published in Hospital Practice July 1980, pp49-57.

Direct Quote from Cherry article " *Both Diseases have been effectively controlled in the pediatric population that, in the prevaccine era, harbored them. However, with the shift in prevalence to adolescents and young adults, it is possible the diseases may be "time bombs".*

Spring 1977- outbreak of measles on the UCLA campus. "When 506 students underwent serologic screening 9% had HIA titers of less than 5 and thus, presumably, were susceptible to measles: in other words, the outbreak had developed in a population that appeared to be 91% immune".

Testing done in 1976 and 1977 in Los Angeles County and also on the UCLA campus suggest that booster shots might not have any lasting effect on waning measles immunity.

RUBELLA:
Since 1969 Rubella activity has declined about 70% (aprox administration of 83 million doses). But as with measles there has been a shift in age groups susceptible to rubella. Before rubella immunization less than 25% of reported rubella involved patients 15 or older. By 1975 62% was in the 15 or older age group and by 1976 and 1977 70% was in 15 and older age group (with 15-19 yrs having the highest incidence) Direct Quote from Cherry: *"The decline in congenital rubella is curious because the number of infections in women of child bearing age has remained the same. Anyway, it is clear that the apparent stability in the control of congenital rubella is precarious".*

Along with the problem of waning immunity which leaves an older, more vulnerable age group at risk for serious illness from childhood diseases there is also the problem of Atypical measles. According to James Cherry M.D., in the 1980 article 'The 'New' Epidemiology of Measles and Rubella, atypical measles started showing up in 1965 and were traced to the Killed measles vaccine. It was a serious illness that led into pneumonia and because of the atypical symptoms proved to be a diagnostic challence for physicians. Quote: *"Since "only" about 1.8 million doses of killed vaccine were distributed between 1963 and 1967, and since "only" an estimated 600,000 to 900,00 children received two or three doses of killed vaccine in those years, it was expected in the early 1970's that the problem would disappear quickly. Eventually (If its pathogenesis involves killed vaccine) it will, but in the meantime, atypical measles is still very much with us. It is a disease of significant morbidity in young adults and some adolescents..."*

Vaccinations apparent effect on mortality rates occurring from measles, diptheria, polio can be questioned via another chart in your packet: "Contribution of Medical Measure to Mortality Decline". Vaccination in these instances were introduced when mortalities from these diseases

were already steadily declining.

SECTION III: Adverse Reaction Reports

HB277 would mandate that **all** health care providers report to the Public Health Dept. **all** occurences of serious adverse reactions to vaccinations and also asks for long term follow-up investigations.

A major problem with the federal MSAEFI reporting system is that a report is not accepted if the parent and child do not physically visit a clinic or hospital within 4 weeks of vaccination to report an adverse event or seek treatment. Here is an often occuring scenario: The child receives their shot of vaccine at the Public Health Department, eight hours later is suffering from a high fever and prolonged high pitched screaming. The health department is closed, their doctor is gone for the day so the parent calls the emergency room and is told to give the child Tylenol and is reassured that this is not an unusual reaction to a shot. The child is never seen by a doctor or health professional. This serious adverse reaction just slipped through the reporting system. By the next morning, or whenever next the parent can get in to see the family doctor the child appears to be better. The health dept. does not hear about the reaction, the hospital nor the doctor report the reaction and although the parent and health provider need to carefully consider whether giving additional doses of the vaccine is a good idea, no one catches that. Obviously, loopholes abound! What about a convulsion and or high fever that occurs during the night and apparently resolves itself by morning... perhaps a Saturday morning when clinics and doctors offices are closed? What about a parent who can't necessarily afford an emergency room or doctor visit to seek treatment? Accessability and affordability play key roles here. All reactions should be reported to accurately ascertain just what is happening to our children after vaccination both immediately and in the long term. Parents should be believed and encouraged to report regardless of time elapsed and professional assistance sought.

The State's apparent attitude as regards adverse reaction reporting can be summed up in one statement from correspondence with AK Public Health Dept. *"The State does not have any specific regulations regarding the reporting of adverse reactions following immunizations. Health care providers who administer vaccines are encouraged to report possible adverse reactions to this office. This is a passive surveillance system that relies on the integrity of the health care providers to comply"* correspondence with Michael Klatt, manager AK Immunization Program, Nov 14, 1986

Add this quote to the apparent lack of health care provider integrity shown in the summary of adverse reactions (in your packet) Page 2 of the questionnaire shows that of the 21 who reported the adverse reaction to a health care provider 18 never had a MSAEFI form completed for them (This means they were not effectively reported if they were reported at all)

(NOTE - Discuss Summary)
This system must be improved now! Alaskan children are reacting to these vaccinations! They are not, however being counted in vaccine safety statistics. It is ironic to me that that health providers quote statistics on the safety of the vaccines when statistics are something that are currently so poorly kept. How will the problems with the vaccines ever be defined and resolved if they continue to be ignored and denied? Just look at this summary and at the testimony at the children's commission for the specifics!

IV. IMMUNIZATION RECORDS

This part of HB 277 is to insure that the vaccination manufacturer and lot number be kept on file for at least three years and to insure that any severe reaction be recorded in the minors permanent record. Obviously this section is necessary to avoid dangerous revaccination of any adversely affected child, even if location of administration varies. It will also help determine tainted batches of vaccine should they occur.

This all brings us full circle back to the first section of HB277.
I have talked about how other states have been adding this exemption without undue loss of vaccine compliance, and without apparent disease implications. I have shown this committee that the short term and long term safety of all of these vaccines is indeed questionable. More questions and uncertainties arise almost daily especially as regards live virus vaccines and the ingredients of all vaccines. I have shown this committee how vaccination does not guarantee immunity from these diseases. I have shown, too, the variety of other known and suspected ailments that can be contracted via vaccination. I feel I have provided the evidence necessary to show this committee why a responsible parent might intelligently question vaccination. Because one parent may choose not to vaccinate should not reflect on another parents right to choose immunization. AK-DPT does not want to imply that we advocate against the immunization program. We do not wish to interfere with the accessibility and affordibility of the vaccine program but rather wish to encourage the safest and most effective program that can be made available. We are asking quite simply for accountability.

I end this testimony feeling frustrated because I have barely touched the tip of the iceberg as regards this issue. The time element and repect for this committee's already overloaded agenda does not allow me to expound any further. All the material I have referred to, if not already in your individual packets, will be on file as reference material with the chairmen

or available by request from AK-DPT. Within your packets, the materials with asterisks are available from me on request.

I will be in Juneau through Saturday Feb 13 and available to discuss this further. Copies of this testimony are at the end of your packets for easy reference.

I and the members of Alaska's DPT chapter urge you to support HB277.

I'd like to finish with this quote by Edward Bradley who is a researcher with the Cetus Corporation: *"We probably know as little about the immune system now as Columbus knew about the Americas after his first voyage."* Edward Bradley researcher, Cetus Corporation from the article: Our Immune Systerm: The Wars Within, National Geographic magazine June 1986:

Once again I thank you for your time and consideration of this important matter.

Official Business

COMMITTEE: HOUSE HESS

DATE: 2-11-88

SIGN-IN

Subject of meeting:
HB 277 Immunization of Minors
HCR 4 Children's Law Task Force
HB 332 Burn Injuries
HB 409 WAMI

NAME	ADDRESS	PHONE	REPRESENTING	DO YOU WANT TO TESTIFY? if yes, which one
CHRIS CLERK		2828	REP. COLLINS	HCR 4 ✓
Elizabeth A Ward	Box H-06 Juneau	5-3090	HSS	277 yes
Jan Maynard	Box FP	234	ACPE	no
Shannon Hohlo	Box 1746 Soldotna, AK	262-3825		YES 217 ✓
David B Alexander	9601 Prospect Anchorage 99516	346 2447	ASMA	HB @ 1:30 277 yes
Gayle Horetski	Box N Juneau 99811	465-4322	DPS	HB 332 yes
CHARLES STEINER Steiner	1001 Noble FBX AK	452-1611	Self, ASMA	HB277 Here @ 9:30 yes
Nina Keeler Kinney	Dept of Public Safety PO Box N Juneau 99811	465-4356	Dept. of Public Safety	HCR 4 Available for questions ✓
DAVID JOHNSON	3612 TONGASS AVE KETCHIKAN	225-5146	ALASKA STATE MEDICAL ASSOCIATION	YES HB 332
Commissioner Munson Yvonne Chrisel	Box H-05 Juneau	465-3030	DHSS	YES

English 111 Scott Manchee

December 10, 1987

"No Shots, No School"

Janet, a licenced practical nurse, took her two-month-old son. Ritchie, to the pediatrician for a check up. He was found to be in good health and was given his first DPT shot (diphtheria, pertussis, tetanus vaccine) and oral polio vaccine. By evening, the site of the injection was dark purple and spreading causing him to cry when it was touched. The next morning "`...he started screaming off and on. He sounded like a cat in pain. His scream was high and forceful, and then he would fall asleep,'" Janet remembers (Coulter 6). All through the day Ritchie's condition worsened. He had explosive diarrhea, stopped responding to voices and sweated excessively. "`When I picked him up, he was completely soaked through two receiving blankets. I have never seen a baby soaked like that. The order was musty and pungent, a smell I will never forget'" (6). As Janet and her husband were getting Ritchie ready to take to the hospital, he stopped breathing. Janet administered CPR until the ambulance came and took over. Thirty-three hours after his first DPT shot, Ritchie was dead. Ritchie's case is a classic example of some of the documented side effects of the DPT vaccine.

Deborah a new mother, began to cough. A month later her coughs made her feel like her insides were turning out (Coulter 154). About this time her new daughter, Sarah began to cough slightly. The doctors diagnosed a flu bug. Sarah's cough worsened to such an extent that she would turn blue

when she coughed. The doctors finally suspected pertussis or whooping cough, as it is commonly known and sent both of them to the hospital (155). Sarah was admitted to ICU (intensive care unit). They both were put on antibiotics to alleviate the secondary complications from whooping cough. Sarah continued to have fits of coughing and turning blue. After leaving ICU, Sarah stopped breathing once and was revived by the nurses (156). Ten days after entering the hospital Sarah was discharged the cough having become a shadow of itself. During Sarah's stay in the hospital, Deborah's other daughter Miriam developed a cough that cultured positive for whooping cough. Although she had whooping cough her case was mild and it was difficult to tell she was really sick (157). Sarah was too young to have received a vaccination against the disease but, Miriam had received four vaccinations and Deborah had received her full complement of five shot to be fully immunized against whooping cough (158).

Immunization is the process of protecting a population from plagues and epidemics of diseases such as pertussis. A vaccine is used to trick the immune system, causing antibodies to be released that remain in the system protecting us from a particular disease. Polio, rubella, diphtheria and many other dreaded diseases of the past have been virtually eliminated by using vaccines to immunize a population. Although, there are drawbacks to some vaccines. Many cases of polio today are caused by the vaccine rather than exposure to the disease itself. The most controversial of the vaccines today is the DPT shot, a combination of the diphtheria, pertussis and tetanus vaccines.

The controversy surrounding the DPT vaccine primarily focuses on the pertussis portion of the vaccine. The documented side effects range from

mild fever to death. "NO shots,no school," is a slogan used by local school districts to inform parents that DPT shots are required before admission to schools. This forms another controversy surrounding the shots. Parents should be allowed to weigh the risks of pertussis against the risks of the vaccine and base their decision on these risks, rather being forced into vaccinating their children so they can attend public schools.

Pertussis has been with us for centuries. The disease reached its highest levels in the nineteenth century. The overcrowding and poor sanitation in the cities of America and Europe contributed to the spread of pertussis and other diseases. The death rates from pertussis declined steadily from this point until the vaccine gained widespread use after World War II. There were 210 deaths per million in the 1870s in the U.S. dropping to 21 per million in 1940. European countries saw a similar decline. In Sweden during the five years prior to World War I, 800 children died annually from pertussis. The decline continued with 10 deaths between 1951 and 1955. Even though there is no cure for pertussis, the overall improved health of babies and the use of medical skills to alleviate the secondary complications from the disease, such as pneumonia, starvation, and suffocation has contributed to the decline in deaths from pertussis

The pertussis bacterium is very complex and unstable. It was not until 1906 when Jules Bordet and Octave Gengou of the Pasteur Institute announced they had isolated the toxic Bacterium. Today, there is still much to learn of the of B. pertussis bacterium (*Bordetella pertussis*, named after Jules Bordet). John Robbins M.D. of the FDA (Food and Drug Administration) stated, "'Unfortunately, we do not know the toxic component responsible for central nervous system injury in pertussis disease,'" in 1978 (Coulter 20).

Even though little was known about the Bacterium, once it was isolated, Jules Bordet and Octave Gengou were able to make a vaccine in 1912. They grew the bacteria in large pots, then killed the bacteria with heat, using formaldehyde to preserve it. This process is very similar today, creating the crudest vaccine produced today. Whole cell pertussis vaccine is termed crude because it is not known which part of the pertussis bacterium produces immunity, or causes brain damage, or if it is the same agent that causes both reactions. The pertussis vaccine in not completely effective. Gordon Stewart of the University of Glasgow, Rutchill Hospital (an infectious disease hospital), states that, "about 30% of cases of whooping cough have been confirmed in fully vaccinated children (Stewart 135)." There have been several cases of so called epidemics initially attributed to declines in vaccination, upon further investigations the cases were from babies under two months of age (first DPT shot given at two months of age in U.S) and from the immunized population.

The side effects from the DPT vaccine are numerous. In the CDC (Center for Disease Control, the federal agency that monitors the quality of vaccines and promotes immunization) pamphlet for parents about childhood immunization it states about possible side effects, "with DTP vaccine, most children will have a slight fever and will be irritable within two days after getting the shot. More than one half of children develop some soreness and swelling in the area where the shot was given. More serious side effects can occur. A temperature greater than 102°F may follow 1 of 20 DTP shots. Unusual high-pitched crying may occur after 1 in 1,000 shots. Convulsions or episodes of limpness and paleness may occur after 1 in 1,750 shots. Children who have previously had a convulsion may be more likely to have another

after pertussis shots. Rarely, about once in 110,000 shots, inflammation of the brain (encephalitis) may occur, and permanent brain damage may occur about once in 310,000 shots" (U.S. 6).

This excerpt from the CDC pamphlet doesn't tell the whole story of side effects of the pertussis vaccine. In Britain a pronounced local skin reaction is considered a contraindication (to make further treatment inadvisable) to further injections of pertussis vaccine. The product insert for the pertussis vaccine from Lerdle Laboratories and Connaught Laboratories (manufacturers of DPT vaccine) states that fever over 103°F contraindicates further pertussis vaccine (Coulter 55).

Vomiting and diarrhea are possible side effects, as one mother reported after her three month old daughter received her first DPT shot, "Once at home, she started having terrible gas. About every couple of minutes, she would have violent, explosive gas. I have never heard a human sound like that. Maybe a 300 pound pig in a barnyard, but never a human (Coulter 57)."

The CDC pamphlet fails to warn parents of some side effect and when serious side effects do occur, the DPT shots should be discontinued. Blood disorders, excessive sleepiness and the side effects listed by the CDC as excessive fever, convulsions and high pitched screaming are absolutely contraindicated by the makers of the DPT vaccine.

SIDS (sudden infant death syndrome) has been linked to the DPT vaccine in some cases. William C. Torch M.D., former director of Child Neurology, Department of Pediatrics, at University of Nevada School of Medicine, presented a paper linking SIDS and DPT vaccination. He states that out seventy cases of SIDS studied 6.5% died twelve hours after receiving DPT vaccination, 13% after twenty-four hours, 26% within three days. He found in

the non-DPT group deaths peaked at 2 months and in the DPT group deaths peaked at 2 and 4 months. He also discovered in the non-DPT group deaths occurred most often in the fall\winter season and in the DPT group deaths were nonseasonal (Coulter 94). With 1 in every 600 live births dying annually from SIDS (Mendelsohn 4) and 45% of SIDS cases occurring within 3 days of DPT vaccination (Coulter 94), using 3.7 million births per year (Funkhauser 1342) I conclude that approximately 2700 more deaths annually might be attributed to the DPT vaccine. Or, at the very least these deaths are misrepresented as SIDS deaths if not related.

In light of the SIDS statistics, let us take a closer look at the CDC figures in their pamphlet stating that 1 in 110,000 for encephlapathy and 1 in 330,000 for brain damage from the vaccine. These statistics were derived from the British National Childhood Encephalopathy Study (NCES). The study encompassed all cases of acute neurological illness in British children from two to thirty six months of age who were admitted to hospitals between 1976 and 1979. The NCES only included those patients admitted to a hospital and those who had a convulsion lasting 30 minutes or longer (Stewart 136). In the thirty-five cases receiving compensation, for 100% disability, caused by pertussis vaccinations, from the West German Health Authority there were six that had encephalopathy without convulsions and twenty-two with convulsion lasting less than 30 minutes. In comparing this data, we might assume that the NCES missed the 80% of the cases where brain damage occurred. In using the NCES figures, the CDC ignored that Britain uses a milder vaccine and British children are vaccinated at a older age. These discrepancies could raise the incidence of permanent brain damage much higher (Coulter 373).

The NCES study also gives us estimates of the incidence of damage

caused by whooping cough. The NCES estimated that acute encephalopathy occurred once every 300,000 cases of whooping cough. When compared to the NCES figures for damage from the vaccine, the chance of neurological damage from the vaccine and the disease are equal (Stewart 136).

In America the first DPT shot is given at two months of age, then four months, then six months, eighteen months, then a final shot between four and six years of age. This is in sharp contrast to other industrialized countries: Sweden and West Germany, without pertussis vaccinations; England, with shots starting at six months of age; Japan, DPT shots starting at two years of age. Between 1946 and 1957 the Medical Research Council in England conducted field trail of the pertussis vaccine involving 50,000 children between six months and eighteen months of age, with 80% fourteen months of age or older. There were 44 cases of convulsions reported during these tests. Even though these test were designed to test the effectiveness of the vaccine not the safety, the U.S. uses the data collected from Britain to justify the safety of the vaccine in newborns. George Dick M.D. asks, "'How did it come about that it was assumed that babies of only a few months of age would react the same way as babies twice their weight? Why was immunization with pertussis-containing vaccines recommended in babies a few moths of age with no adequate toxicity tests having being done? (Coulter 33)'"

The DPT issue is filled with may cases of reserchers omiting or discounting data, because of the source. A recent article in the Journal of American Medical Association (JAMA) estimates the effects of delaying the U.S. pertussis vaccination schedule to 8, 10 and 12 months of age. They concluded that the increased incidence of whooping cough in children under the age of two, would outweigh the risks from the vaccine in the same group.

In their conclusion they considered SIDS deaths as associated by chance with the pertussis vaccine, therefore not valid for their conclusion (Funkhauser 1345). They also discounted the Japanese experience of delaying the pertussis vaccination until children are two years old. They did not use this data for their conclusion, even though they stated it "might support use of the new schedule over the current one,(1346)" because the data was not "collected in a controlled clinical setting,"by the japanese compensation system and covered a different age group (1346). Instead they cited the NCES study as being "collected using carefully designed methods. (1346)" A related article in the same issue of JAMA recommends the use of acellular pertussis vaccine currently being used in Japan. When referring to possible under reporting by the Japanese compensation system they state the chances are minimal (Noble 1355).

In deciding whether to vaccinate their children parents must also consider Alaska statute. In Alaska all children entering school, public or private, are required to be vaccinated including the DPT vaccination. This law was implemented, as all laws are, for the common good of the public. This law was designed to protect the public through mandatory vaccination from epidemics of these diseases. But, are healthy, well fed children living in a clean, sanitary environment in Juneau at risk? We know the vast majority of pertussis cases occurring world wide are from third word countries with a low standard of living and primitive sanitary conditions. These same condition prevailed in the U.S. during the major pertussis epidemics of the 1870s.

With 30 cases (9 confirmed) of pertussis in 1985 and only 5 cases (4 confirmed) in 1985 reported in Alaska, there were only 4 cases hospitalized,

without any deaths (Klatt). There is not any regulations governing the reporting of reactions from the pertussis vaccine in Alaska (Klatt and Frazier). Without a larger group of cases in Alaska, we cannot fi[illegible]re the risks of the vaccine against the risks of the disease.

Just as there is not complete data in Alaska on whooping cough or the reactions from the vaccine, parents must make a decision for their children on incomplete or distorted information. There has not been a major clinical study of the risks of the vaccine or the risks to society from the disease, without flaws. The NCES study, from which our government bases it decision to promote the DPT vaccine, omits pertinent cases, causing the data to be flawed. Even if the data was not flawed, the NCES finds the incidence of permanent brain damage from the vaccine approximately equal to the incidence of permanent brain damage from pertussis. With all the conflicting data and controversy surrounding the DPT vaccine, for there to be statute requiring immunization is shameful. Parents should be allowed to choose whether their children brave the risks of the vaccine or the disease, without the education of their children held hostage.

MEMORANDUM State of Alaska

TO: Elizabeth Ward
Director, Division of Public Health

DATE: March 4, 1988

FILE NO:

TELEPHONE NO: 561-4406

FROM: Michael E. Jones
Medical Epidemiologist

SUBJECT: Review of MSAEFI Reports and Philosophical Exemptions to Immunization

I have reviewed all MSAEFI (Monitoring System for Adverse Events Following Immunization) reports submitted to the Section of Epidemiology during the three years from 1985 through 1987. During this period, there were eighty-one reports of adverse events occurring in persons vaccinated within the preceding 28 days. Of these events, twenty-seven (33%) were classified either as anaphylaxis or as one of the illnesses listed in subsections 7-15 of the MSAEFI form (attached); reports of such events require review by the Immunization Project physician to verify the clinical information.

The vaccines associated with these reported adverse events and the number of instances in which they were associated with such reactions were as follows: diphtheria-pertussis-tetanus (DPT) vaccine, 22 instances; oral polio vaccine (OPV), 7; measles-mumps-rubella (MMR) vaccine, 4; hepatitis B vaccine (Heptavax), 1; and Hemophilus influenzae type b (Hib) vaccine, 1. (Numbers total more than 27 because some individuals received two or more vaccines concurrently.) The disproportionate number of DPT-associated adverse events may be related in part to the fact that DPT is the most frequently administered vaccine in Alaska: a total of 5 doses of DPT vaccine are recommended for adequate immunization, compared with 4 doses of OPV and one dose of MMR vaccine.

The serious reactions reported, and the number of times they were associated with individual vaccines or with vaccine combinations, are listed in the table which follows:

1988 RECEIVED Division of Public Health

TABLE 1

VACCINE(S) ADMINISTERED PRIOR TO ADVERSE EVENT

Adverse Event	DPT	DPT/OPV	DPT/OPV/Hib	MMR	Heptavax	Total
Convulsions/Seizures	7	-	-	4	-	11
Screaming Episodes	3	4	1	-	-	8
Hypotonic/Hyporesponsive Episodes ("Collapse")	3	-	-	-	-	3
Encephalitis (without residual defect)	-	1	-	-	-	1
Weakness of Extremities	-	1	-	-	-	1
Anaphylaxis	1	-	-	-	-	1
Infantile Spasms	1	-	-	-	-	1
Neonatal Apnea	-	-	-	-	1	1
All Adverse Events	15	6	1	4	1	27

None of these reactions was fatal. Except for one child who had persistent, mild weakness of his extremities one year following onset of the adverse event, all patients recovered fully.

It is important to remember that these adverse events are defined as being temporally related to vaccination (that is, they have occurred within 28 days following vaccine administration). It is not possible, in any individual case, to establish a cause-effect relationship between immunization and an adverse event, nor is it possible always to exclude such a relationship. Of the eleven individuals who had seizures, four (36%) had had histories of seizures prior to vaccine administration. The child with encephalitis was clinically diagnosed as having "viral meningoencephalitis" (an inflammatory brain condition caused by a virus). The child with persistent weakness of his extremities was examined by a neurologist who did not believe that his impairment was related to immunization. However, since the possibility that such adverse events are related to vaccination cannot be discounted, it is important that they be included in Alaska's MSAEFI reports and be analyzed with nation-wide data by the Centers for Disease Control.

Table 2 illustrates the frequency with which certain adverse events were reported to follow DPT vaccination in Alaska during the 3-year period, 1985-1987. Based on the number of doses (33,073) of DPT vaccine known to have been administered during 1987, it is estimated that a minimum of 99,000 doses of the vaccine were administered during that 3-year period. Thus, on average, seizure activity occurred following one of every 14,143 doses of DPT vaccine; a hypotonic/hyporesponsive episode (transient "collapse") after one in every 33,000 doses; and encephalitis following one of the 99,000 doses. It is evident from the data in table 2 that the reported frequency of these events in Alaska is less than, or approximately equal to, the published frequency with which such events can be expected to occur within very large populations. Of course, these frequency estimates depend upon the completeness of reporting of vaccine-associated adverse events by health care providers; and reporting of "severe reactions to any vaccination" has been required (7 AAC 27.005) in Alaska since at least 1975. It is not possible, from existing data, to estimate completeness of reporting.

The National Childhood Vaccine Injury Act of 1986 requires that each health care provider who administers a vaccine containing tetanus toxoid or diphtheria, pertussis, measles, mumps, rubella, or polio components shall record in a permanent record the date of administration of the vaccine, the vaccine manufacturer and lot number of the vaccine, the name and address of the health care provider administering the vaccine, and any other identifying information on the vaccine required pursuant to regulations promulgated by the Secretary of the Department of Health and Human Services. In addition, each health care provider and vaccine manufacturer are to report certain adverse events or reactions, set forth in a vaccine injury table, which occur within specified time intervals following vaccine administration. These adverse events, which

vary according to the vaccine(s) specified, include anaphylaxis or anaphylactic shock, encephalopathy (or encephalitis), shock-collapse or hypotonic-hyporesponsive collapse, residual seizure disorder, paralytic polio, or any acute complication or sequela (including death) of these illnesses, disabilities, injuries, or conditions. As of October, 1988, federal law, as well as existing state statutes, will require Alaska's health care providers to record information about the vaccines they administer and to report any adverse events following administration of vaccines.

Finally, there are no published reports which document the effects of philosophical exemptions from immunization in states which have such an exemption nor is any organized information about this issue available from the Centers for Disease Control's Immunization Division. The American Medical Association's recommendation (American Medical News, August 14, 1987) that both philosophical and religious exemptions be removed from statutes requiring mandatory immunizations was prompted, in part, by reports of two large outbreaks of measles which originated in, and were facilitated by, infection of persons with religious exemptions to immunization. These outbreaks resulted in three fatalities and affected individuals without such exemptions. Thus, the concern that vaccine-preventable diseases occurring in persons with exemptions from immunization might have deleterious effects on the general population is clearly more than a theoretical consideration. However, no body of data exists that would allow a reliable assessment of the public health impact of philosophical or religious exemptions.

MJ/jh
Attachment

TABLE 2

ANALYSIS OF SELECTED ADVERSE EVENTS ASSOCIATED
WITH DPT VACCINE, 1985-1987, ALASKA

Adverse Event	Number of Adverse Events Reported	Estimated Number of Doses of Vaccine Administered 1985-1987	Observed Incidence of Adverse Event	Expected Incidence of Adverse Event *
Seizure/Convulsion	7	99,000	1 in 14,143 Doses	1 in 1,750 Doses
Hypotonic/Hyporesponsive Episode	3	"	1 in 33,000 Doses	1 in 1,750 Doses
Encephalitis				
- Total	1	"	1 in 99,000 Doses	1 in 110,000 Doses
- With Residual Neurologic Defect	0	"	0	1 in 310,000 Doses

* Hinman and Koplan, JAMA 1984, 251:3109-3133

REPORT OF ADVERSE EVENT FOLLOWING IMMUNIZATION

FORM APPROVED
OMB NO. 0920-0039
EXP. DATE 9/87

PERSONAL IDENTIFIERS

Patient:	Form Completed By:	Vaccine Administered By:	Physician or Health Facility Visited for Treatment of Adverse Event:
Name	Name	Name	Name
Address	Address	Address	Address
Telephone No.	Telephone No.	Telephone No.	Telephone No.

REPORT OF ADVERSE EVENT FOLLOWING IMMUNIZATION
DEPARTMENT OF HEALTH & HUMAN SERVICES, PUBLIC HEALTH SERVICE, Centers for Disease Control, Atlanta, Georgia 30333

PATIENT ID

Immunization Project Area | State Code | Seq. No. | County Where Administered: | County Code | MSAEFI REPORT NO. FOR CDC USE ONLY

Date of Birth: Mo. Day Yr. | Sex: M F | Date of Initial Report: Mo. Day Yr. | Source of Information: MD/DO Nurse Family Other

VACCINE HISTORY

Date of Immunization: Mo. Day Yr.

Vaccine Administered By: Pub. Pvt. Mil. Other

Vaccine Purchased By: Pub. Pvt. Mil. Other

Enter Below All Vaccines Given on the Date of Immunization:

	Vaccine Type	Mfgr.	Lot Number	Route	Site	No. Prior Doses
A						
B						
C						
D						

CLINICAL DESCRIPTION OF PRESENT ILLNESS

SIGNS AND SYMPTOMS OF PRESENT ILLNESS

Onset of 1st Sign or Symptom: Mo. Day Yr.

	Yes	No	Unk
1. Fever: Temp ≥(100°F (37.8°C) (7806)			
Felt Hot, But Temperature Not Measured: (7806)			
Highest Measured Temperature ____ . ____ F/C			
2. Local Reaction: Site ____			
Pain, Swelling, Increased Warmth, Induration or Lump Without Abscess (9993)			
Abscess Formation — Required Drainage or Drained Spontaneously (6829)+(9993)			
Results of Culture ____			
3. Rash: Other Than at Injection Site (7823)			
4. Adenopathy:			
Local (Injection Site Area) (7856)			
Generalized (7856)			
5. Allergic Event: (9995)			
Hives (7060)			
Angioneurotic Edema (9951)			
Wheezing/Asthma (4939)			
Anaphylaxis (9994)			
If "Yes," Interval from Vaccination to Onset: < 30 min / 30 min-6 hrs / > 6 hrs			
Was Blood Pressure Measured?			
If "Yes," Lowest B.P. ___/___			
6. Arthralgia/Arthritis:			
Pain in Joints (7194)			
Inflammation of Joints (Redness, Swelling, Tenderness) (7169)			
7. Convulsions: (7803)			
If "Yes," How many Episodes Following Immunization			
8. Encephalitis and/or Encephalopathy: (3483)			
Abnormal Lumbar Puncture (Enter Results in Laboratory subsection) (7920)			
Signs of Increased Intracranial Pressure (3482)			
Focal Neurologic Signs (3499)			
Coma or Marked Alteration in Level of Consciousness (7800)			

	Yes	No	Unk
9. Guillain–Barré Syndrome: (3570)			
10. Reyo's Syndrome: (3318)			
11. Polio: (0459)			
12. Paralysis other than GBS, Reyo's Syndrome or Polio: (3449)			
13. Other Neurologic Symptoms and Diagnoses:			
Aseptic Meningitis (0479)			
Infantile Spasms (Hypsarrhythmia, drop seizures) (3456)			
Bell's Palsy (3510)			
Hearing Loss (3899)			
Neuritis, Neuralgia (7292)			
Paresthesias (7820)			
Screaming Episode (High-Pitched Abnormal Cry or Screaming Lasting ≥ 3 Hours) (7998)			
Neurologic Symptoms not cited above (specify) ____			
14. Miscellaneous:			
Hypotonic, Hyporesponsive Episode (7859)			
Idiopathic Thrombocytopenic Purpura			
If "Yes," Lowest Platelet count (2873) ____			
Pancreatitis (5770)			
Parotitis (5272)			
15. Death:			
Sudden Infant Death Syndrome (SIDS) (7980)			
Non–SIDS Death (7981)			
If "Yes," Cause(s): ____			

LABORATORY:	Performed Yes	Performed No	Performed Unk	Results Normal	Results Abnormal
EEG (7940)					
BRAIN SCAN (7940)					
LUMBAR PUNCTURE (7920)					

Results if Abnormal:
WBC's ____ Opening Pressure ____
Lymphs (%) ____ Culture Results ____
Glucose ____ Other ____
Total Protein ____

Other Pertinent Information:

Signature of MSAEFI Coordinator:

PAST HISTORY

Seen by Health Care Provider: Yes No Unk Number of Visits | Hospitalized Yes No Unk Number of Days

Previous Illness Following Immunization: Yes No If "Yes," Date: Mo. Day Yr.
Vaccine ____
Describe Illness ____

Previous Convulsions in Patient: Yes No Unk.
If "Yes," With Fever Without Fever

History of Convulsions in Siblings or Parents: Yes No Unk.
If "Yes," With Fever Without Fever

FOLLOWUP

SEVEN DAY FOLLOWUP: Mo. Day Yr.
If recovered, send to State Office

30 DAY FOLLOWUP:
If not recovered at 7 days, carry out 30 Day Followup and send to State Office

	Duration of Illness	Recovered	Partially Recovered*	Not Recovered*	Not Located	Dead
SEVEN DAY FOLLOWUP	Days					
30 DAY FOLLOWUP	Days					

* Comments ____

Reviewed By Immunization Physician (Items 7 - 15 and Anaphylaxis): Yes No Unk
Signature of Reviewing M.D.

CDC USE

Results of One-Year Followup: Recovered Partially Recovered* Not Recovered* Dead Not Located *Comments ____

This report is authorized by law (42 USC 247b; 42 CFR 51 b). Its submission is needed to monitor possible reactions to vaccination and is voluntary except when required as a condition of immunization grant awards.

CDC 71.19 REV. 9-85

CDC Copy

Please enter as testimony
3/10 - HHESS - HB277: IMMUNIZATION of MINOR

H. E. S. S. TELECONFERENCE

I support HB 277 which would provide more information on the benefits and risks if the D.P.T. program.

I as a parent am uninformed of the risks and benifits of these shots, manditory by the State with no garantee or liabelity by the State in case of mental, physical, or mortal damage to my child.

I as a parent have become alarmed to see the negative reaction my child has had from these D.P.T. shots.

I as a parent demand to know the risk factor of the diseases. Are they in remission, currently life threatning or readily treatable by modern medicine? Does the D.P.T. vaccine garantee safe protection or in fact cause illness itself ?

Please help answer these questions. SUPPORT HB 277.

Eastham

Sincerly Terry Eastham Nancy Eastham

Terry and Nancy Eastham

Soldotna

My name is Eileen Wagner. I am the parent of a 3 1/2 year old boy who has severe allergies which began right after his first DPT shot. I think the shot triggered the allergies. Doctors do not think so. Onset of allergies is not considered a contraindication to further shots. There is a great gray area of vaccine reactions, there are many children who don't collapse, die, or suffer brain damage from the shot, but who are "slightly" injured, and never reported.

John seemed to be a normal baby at the time of his first DPT shot at 3 1/2 months of age. As the public health nurse prepared the shot, I asked "Don't I have to sign something?" "oh no, we don't do that," she replied. I remember being surprised, since we had lived in Wisconsin when one of my older children was getting her shots, and each time I had had to read and sign a lengthy warning about vaccine risk. (I have 2 older fully vaccinated children.)

I was given no information of any kind. After the shot, John went to sleep for 16 hours It was a profound, deathlike sleep - he didn't move a muscle during that time, even when I felt his head for fever.

Within 2 weeks the skin trouble had started.

It was the beginning of a year of agony for my son. He itched intensely at all times, clawed himself bloody, even had hives on the soles of his feet. His nose and eyes ran constantly, his body was swollen all over. He writhed in my arms as I nursed him. He was completely breastfed, and exquisitely sensitive to the foods I was eating. Gradually we have learned what makes John tick, and he is now living a normal life, though his diet and environment are rigidly controlled. We carry an injection of epinephrine for emergencies. He still has occasional swelling of the windpipe, as well as many lesser allergic reactions.

The important thing for you to know is that the many doctors, both here and in Seatttle, I saw during that first year steadfastly denied any connection with the DPT shot. It was all so unbelievable to me that I began to do research at the State Library about vaccines, allergies, the immune system. I don't pretend to be an expert. But I found out enough to decide that further vaccination is too risky for John. And I found a Canadian doctor who had studied babies like John for 30 years. We had many phone conversations and during one he said that vaccination had triggered the allergies of many of the most severely allergic infants. "It's quite common, actually." The reason this doctor could level with me and admit that the shot triggered the allergies, whereas 4 American doctors denied it, is that Canada, although they recommend vaccination, does not mandate it.

The mandatory nature of the vaccine policy puts doctors in the position of having to deny a lot of reactions, to deny in their own minds as well as to the patient. When my dr. urged me to continue to vaccinate John, offering to withold the pertussis component, he said, "I'll admit I'll be biting my fingernails waiting to see if John has a reaction."
The fault does not lie with individual doctors but with the AAP, which provides doctors with guidelines.

I am uneasy about not having John vaccinated against tetanus and polio. I would really like to do it. I would like to be able to study state or national statistics and compare the number of children reported to have had allergic reactions after their DPT to the number of allergic reactions after DT, without pertussis. My question is, was it the pertussis component? or was it the shock of vaccination to a child who apparently had latent allergies? There is no way to get an answer to my question - no statistics exist. For this reason, I urge you to require health care providers to report <u>all</u> adverse reactions to vaccines.

There is a moral question here - can a free society require citizens to be injected with a toxic vaccine and continue to deny the full extent of risk involved? We look to you to get the facts out on the table. Only if we know the facts can we decide if the benefits really do outweigh the risks.

TESTIMONY BEFORE THE HOUSE H.E.S.S. COMMITTEE
March 10, 1988 by: Judy Ames, Box 824, Soldotna, Alaska 99669

I am a supporter of HB 277. This bill effectively addresses the vaccination issue so that I as a parent may try and raise my healthy child by known and safe health standards.

For this testimony, I would like to address one issue in particular - the questionable ingredients contained in these vaccines. Particularly, formaldehyde, mercury, and aluminum. These 3 ingredients are listed on the manufacturer's insert for the DPT vaccine with the exception of Connought Co. making no mention of formaldehyde. I am very particular about the substances I and my family consumes and I object to any level of formaldehyde, mercury or aluminum entering my child's body. It does not take many supposed or concrete findings to raise my objections to vaccinating my child with vaccines containing these potentially harmful toxins. Our state health dept. is not required to provide parents with a list of ingredients along with other vaccination information. The new Federal law, "National Childhood Vaccine Injury Act of 1986" under Sec. 2126 (c) Information Requirements, has no mention of requiring the manufacturer's product insert be presented to parents along with other pertinent vaccination information. Parents need to be informed of the ingredients entering their child's body at the time of vaccination. HB 277 would see to those requirements.

There are many uncertainties as to the rise and cause of certain diseases and immunological disorders in our society. For example, we are seeing an increase in allergies. In their article entitled "Bringing Vaccines into Perspective," Harold E. Buttram, M.D. and John Hoffmann suggest ..."current mass vaccination programs must be highly suspected as contributing to the increased incidence of allergic disorders. And from James Gibson's book, Formaldehyde Toxicity, "The characteristics of an allergic mechanism are that the response can be evoked in sensitized individuals with very small amounts of formaldehyde."

I am concerned about the possible link between aluminum (a cumulative carcinogen) and Alzheimer's disease, as reported in research entitled Physiological Behavior and Frontiers in Neurology and Neuroscience Research.

According to the Merck Index, ethylmercuric chloride used in preparation of thimerosal (another ingedient in the DPT vaccine) has a caution of being highly toxic.

I am concerned about the standards by which the ingredients used in vaccines are screened as in the monkey kidney cells used in growing the polio vaccine. Can we be guaranteed they contain no latent virus or disease harmful to the human body?

(1)

The list of questions and concerns goes on and on. The manufacturer claims the ingredients used in these vaccines are set at safe levels. What long term studies ON HUMAN BEINGS are being done to prove these safeties? If our own health department calls its vaccine reaction reporting system passive, what can be said about studies tracing the effect of the potential toxins being injected as part of our vaccines. How can any conclusive, concrete findings about the effect of these ingredients on infants and all human bodies be established when a system has obvious flaws?

From my point of view it appears that vaccine safety is not proven, however, the risks are substantial. Please consider this issue is full depth. Thank-you.

(2)

Deborah Gravel
Peter Dwyer
Rt. 2 Box 45
Ketchikan, Ak.99901

To Concerned Legislators,

We seriously question the safety of the DPT vaccine. We cannot ignore the dangers to our children's health that compulsory vaccinations represent. We feel that we must have a choice of whether to vaccinate our children or not.

We will not try to convince you of all the risks involved with vaccinations. We hope only that you will research this topic enough to acknowledge that there are good reasons to be concerned about the safety of children being vaccinated.

We feel that HB 277 is a beginning for concerned parents. We need a reporting system to document how children are reacting to the shots. Vaccines are administered with no guarantees as to their safety or effectiveness, Yet parents are urged to vaccinate despite the fact that Sudden Infant Death Syndrome, polio, encephalitis, and rheumatoid arthritis have been conclusively linked to vaccination.

We will not vaccinate our children. We are gravely concerned with their wellbeing and as responsible parents cannot take the risk to their health that vaccines represent.

We urge you to pass HB 277 as it is written. We feel it is our personal right to safe guard our children's health and we ask you to respect our rights.

Sincerely,

Deborah Gravel
Peter Dwyer

Alaska State Legislature

(1)

Please enter into the record my testimony to the HESS committee name

committee on HB 277 bill/subject, dated 3-10-88.

My Name is Cheryl Rykasaguski.

I am a supporter of HB277 for a variety of reasons. At this time, I will address one of these reasons.

It has been the experience of members of the Alaska Chapter of DPT that Doctors and Public Health Providers who administer vaccines refuse to admit that symptoms a child experiences after a vaccination can possibly be a reaction to that vaccine.

This fact leads me to Question the current system of voluntary reporting of adverse reactions first to the State Health Department and then on to the Center for Disease Control for the purpose of compiling statistics. It appears that there is a Conflict of Interest for a physician to diagnose a vaccine induced injury in a child whom they themselves vaccinated. How objective can they be when their Livlihood may be threatened

Signed: _____
Testifier

_____
Representing (Optional)

_____
Address

_____
Phone No.

Alaska State Legislature

(2)

Please enter into the record my testimony to the HESS
committee name

committee on HB 277 , dated 3-10-88 .
bill/subject

by financial liability if a lawsuit occurs. Cont'd. The emotional repercussions of watching a child suffer as a result of a drug that they administered.

Now, Put yourself in the frightening position of a parent who has a child reacting to a vaccination. No one will even acknowledge the reaction or take responsibility for treating your childs reaction. Where do you turn?

The Alaska Vaccine Reform Legislation, HB 277, strives to correct these inconsistencies in the reporting of reactions. One long term benefit will be accurate statistics on adverse reactions to vaccinations.

Signed: Cheryl Rykaczewski (RYKACZEWSKI)
Testifier

Representing (Optional)

Box 311 KASILOF, AK 99610
Address

262-4937
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the HESS
committee name

committee on HB 277, dated 3-10-88.
bill/subject

Feel HB 277 unnecessary. Many dollars and much time spent in effort toward immunized population. Prevention important! Medical and religious exemptions in place. That is enough!

Signed: Beth Taeschner
Testifier

Self - Retired School Nurse. Former PHN
Representing (Optional)

P.O. Box 56 Soldotna, AK 99669
Address

262-4287
Phone No.

Teleconference

I support bill HB277

I believe parents have the right to free choice regarding the health of their children

I feel parents in Alaska are concerned enough and informed enough to make the choice that is best for their children.

I do not feel the medical community should take this choice away from parents.

Lee Conay
PO Box 3234
Soldotna, AK 99669

MAR 10 '89 18:00 LEG. AFFAIRS - SOLDOTNA

Jacqui Conduey

I believe that all parents have the responsibility to educate themselves and to use that knowledge in making decisions regarding their children's welfare. Society has demanded that all children be immunized. However most parents are unaware there are many risks associated with all vaccines. When my daughter received her first DPT shot she cried, a loud piercing cry for 2 days. In my ignorance, I just accepted it as an inevitable side effect of the vaccine. Later, as her second DPT was approaching, I started to question how anything that could affect my healthy 2 month old so strongly, could really be beneficial. So I began reading and learning about immunizations. I found that many parents and doctors agree that mass immunization ~~are~~ are neither a guaranteed preventative against the illnesses nor were they risk free. I also found that because of this many states and other countries do not require them. I was not informed by any health care worker of any of this information. Alaska does not require that this very pertinent information be shared with parents or allow exemptions based on this knowledge. It is time for this state to adopt HB 277.

Alaska State Legislature

Please enter into the record my testimony to the HESS
committee name

committee on HB 277, dated 3/10/88.
bill/subject

I want to urge HB 277 NOT be passed. A philosophical exemption would endanger the health + lives of Alaskan children. As a society we chose to protect our children in various ways + I believe it's reasonable to continue to enforce mandatory immunization. I'm afraid many people have been lulled into complacency, forgetting the past + potential future ravages of vaccine-preventable diseases. Regarding the education component required in this bill — it's important for people to know that Public Health Nurses administer a large percentage of immunizations in the State + because of a required procedure of informing parents about risks, benefits, + adverse reactions, parents are well informed. I, too, empathize with parents + their testimony can sound convincing, however, it's important to for everyone to realize there's a big difference between temporal association of vaccine + reactions + proof of cause. The vaccines, unfortunately aren't all perfect, but a philosophical exemption is not the answer. Benefits of vaccination still outweigh risks.

Signed: Debbie Golden
Testifier

self
Representing (Optional)

P.O. Box 10533 Fairbanks, AK. 99710
Address

HM: 457-4022 WK: 452-1776
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the HESS committee name

committee on Immunizations HB 277 bill/subject, dated 4/17/87.

I support HB 277 due to the personal experience with both of my children. My son was given the measles by his measles vaxination and my daughter received an "extreme allergic reaction" - as stated by her doctor from her DPT. She had a 105° F fever and was limp & lifeless for 10 days. This happened 2 times as when we moved to another state another DPT booster was required. Again she had the same reaction. The subject of immunization needs more investigation & the public needs to be informed. I have seen illnesses come and go. Could it be that by immunizing we → (over)

Signed: M. Suzanne Rich
Testifier

Representing (Optional)

1451 Flat Mtn. Rd.
Address

457-8086
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the H&SS
committee name

committee on HB 277 , dated 03/10/88
bill/subject

there is a growing body of scientific evidence indicating that animal retro-viruses may have contaminated the live vaccines with which we have all been inoculated for the past 30 yrs. these animal viruses, injected into the human body, may have combined with human genetic material to form the AIDS virus. one of the retro viruses only 4) have been identified, all in domestic animals - is apparently the closest virus to AIDS yet discovered. we've pumped live viruses into millions of people over 3 decades, to believe there's no downside is naive. the AIDS virus is widely believed to have begun in Africa where massive small pox vaccinations were conducted from late 60s to 80-81. the standard method for developing the vaccine in Africa was to grow the pox in the bellies of cows. Most cow herds are taught to contain retro-viruses.

Signed: _____
Testifier

Dave Jones
Representing (Optional)

Box 81785
Address

456 2871
Phone No.

9/86 Legislative Information Office

Alaska State Legislature

Please enter into the record my testimony to the H.E.S.S.
committee name

committee on HB277 Vaccinations, dated 3/10/88.
bill/subject

I support HB277. The power of the state should not be used to compel people to medicate themselves or their children against their will. This is a civil rights issue.

The long-term effects of vaccines are not known. There has been a large increase in chronic degenerative diseases in countries with widespread vaccination programs. Some authorities argue that this is due to weakened immune systems in vaccinated persons.

The situation is much like that of radiation. Thirty years ago we knew little about long-term effects radiation, especially at low levels. Until medical science asks the question: what are the long term effects of vaccinations?, there will be no answers. We have asked this question about radiation, and we are beginning to get the answers now (and they are rather grim, the victims say).

People should have the right to examine the pros and cons of this issue, and make an informed choice.

Signed: Ed Berg — graduate student in biology at UAF and a parent
Testifier

Representing (Optional)

2682 Goldhill Rd, Fairbanks AK 99709
Address

479-3796
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the H.E.S.S
committee name

committee on HB 277 - Immunizations, dated 3/10/88 .
bill/subject

There is a school of medical science called Natural Hygiene. The following discussion against immunizations is from an Australian physician Alex Burton's (MHO, D.O.D.F.(2)) speech taped at the July 1987 Natural Hygiene Society's international conference at St. Catharines, Ontario.

At this conference, Burton said that generally disease is thought of as an "attack" of an "invader" - and that the physician is supposed to destroy this "attacker" or "conquer the disease." A natural hygiene physician conversely sees a disease not as something negative, but positive: disease is seen as the process of the body healing itself. For example, if you say that "on Monday I was well, but on Tuesday I was sick," the Natural Hygienist would say that on Monday you were sick and on Tuesday you were getting well.

The concept of immunization - ie. to make someone immune, →

Signed: Linda Redman LINDA REDMAN
Testifier

Representing (Optional)

21082 Goldhill Rd.
Address

479-3796
Phone No.

implies that a person can have the freedom to do as he or she pleases without any consequences. Nature is not like that, Burton says. He continued, disease has three stages: the cause, the process of healing, & the effect. Immunization suspends causality.

Immunization relates to certain foreign substances that gain entrance to the body. These foreign substances are often protein substances and are called "antigens." The body's means of resisting these antigens is to produce substances by lymphocytes called "antibodies."

[As a side note, according to Natureal Hygiene, prevention of disease is possible by optimum nutrition. Intaking "high octane-type fuels" and maximizing fitness will keep the body's energy reserve level overflowing and thus can help prevent disease. If disease occurs a high health and energy level can help the process of disease to successfully repair the body.]

The theory of auto immune disease says that the body no longer recognizes itself, and the antibodies attack the body's own tissue, destroying it. Dr. Burton continues, says that this is a process that results from a long time of ignoring causes and supressing disease. The cause of auto immune deficiency for example is that a person's body is so toxemic and enervated (from poor nutrition, and thus a low vital force) that the result is an almost total collapse of the body's mechanisms to heal itself...

Basically, I believe immunization tends to override the body's own immune system. There is growing concern that many medicines serve to inhibit the body's natural defense mechanisms and supress the full healing process thus allowing the later onset of immune deficient diseases such as cancer and AIDS. I support HB 277 as I believe people in this state should have the very important choice of deciding what to put in or keep out of their bodies.

Municipality of Anchorage

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Tom Fink
MAYOR

MUNICIPAL HEALTH & HUMAN SERVICES COMMISSION

March 9, 1988

Representative Johnny Ellis, Chair
House Health, Education and
Social Services Committee
Alaska State Legislature
POB V
Juneau, Alaska 99811

Dear Representative Ellis,

The Municipal Health and Human Services Commission can not support HB277. In fact, HB277 is entirely contrary to sound public health policy. The Municipal Health and Human Services Commission is, therefore, opposed to changes in current state policy regarding immunizations. The effects of many infectious diseases, such as whooping cough, are contagious and can be devastating. Current state policy protects the public's health by attempting to prevent an outbreak through immunization.

We do, however, see the merits of reporting adverse reactions to immunizations and maintaining records of the vaccine manufacturer and lot number. We would like to recommend such measures are taken as a means of protecting the consumer.

If you have any questions, please feel free to call me (562-2828) or our staff (343-4674).

Sincerely,

Gari B. Andreini, Chair
Municipal Health and Human Services Commission

cc: Representative Mike Navarre, Sponsor
House HESS Committee
Myra Munson, Commissioner, Department of Health and Social Services,
State of Alaska
Anchorage Municipal Assembly
Tom Fink, Mayor, Municipality of Anchorage
Ron Garzini, Manager, Municipality of Anchorage
Robert A. (Bert) Hall, Director, Department of Health and Human Services,
Municipality of Anchorage

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