SB

185

MEMBER

TENTH ALASKA LEGISLATURE
ELEVENTH ALASKA LEGISLATURE
TWELFTH ALASKA LEGISLATURE
THIRTEENTH ALASKA LEGISLATURE
FOURTEENTH ALASKA LEGISLATURE
FIFTEENTH ALASKA LEGISLATURE
SIXTEENTH ALASKA LEGISLATURE
EIGHTEENTH ALASKA LEGISLATURE
NINETEENTH ALASKA LEGISLATURE

ALASKA STATE SENATE

SENATOR TIM KELLY

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Sponsor Statement

SB 185
"An Act relating to immunization records for children under the age of seven"

SB 185 was introduced in response to a growing concern over the safety of childhood immunizations. For more than a century, childhood immunizations have been one of the foremost public health concerns. Immunization of our children has lead to the near elimination of diseases which were once devastatingly fatal. However, some vaccines including the whooping cough vaccine and the German measles vaccine typically contain small quantities of material derived from disease-causing organisms which could possibly be linked to childhood death or injury.

SB 185 requires the funeral director or the person acting as the funeral director to include a record of the dates of any immunizations a deceased child under the age of seven has received when filing the death certificate. Further, the death certificate must include the name and type of each vaccine administered, as well as the name of the vaccine's manufacturer and the lot and batch number.

If the immunization record cannot be obtained within three days of death the funeral director shall file the death certificate in compliance with existing state law and shall continue to make efforts to obtain the records from the next of kin or other source.

If the records are unavailable from these sources, the funeral director is required to request the immunization record from the Immortality Review Committee established by the commissioner of the Department of Health and Social Services. The committee must provide this information within 90 days.

There are approximately 125 deaths every year of children under the age of seven. SB 185 might help to establish a link between immunizations and childhood death.

STATE OF ALASKA
1996 LEGISLATIVE SESSION

BILL NO. SB 185.

Revision Date:
Dept. Affected: Health and Social Services
Title: An act relating to immunization records for children under the age of seven
BRU: State Health Services
Component: Bureau of Vital Statistics
Sponsor: Kelly
COMPONENT SERIAL NO. 961
Requestor: Senate HES
See also (SN#):

Expenditures/Revenues: (Thousands of Dollars)

OPERATING EXPENDITURES	FY97	FY98	FY99	FY00	FY01	FY02
PERSONAL SERVICES	8.2	8.4	8.6	8.8	9.1	9.3
TRAVEL						
CONTRACTUAL	30.0					
SUPPLIES	1.0	0.5	0.5	0.5	0.5	0.5
EQUIPMENT	1.6	0.1	0.1	0.1	0.1	0.1
LAND & STRUCTURES						
GRANTS, CLAIMS						
MISCELLANEOUS						
TOTAL OPERATING	40.8	9.0	9.2	9.4	9.7	9.9
CAPITAL EXPENDITURES						
CHANGES IN REVENUES ( )						

FUND SOURCE (Thousands of Dollars)						
1002 Federal Receipts						
1003 GF Match						
1004 GF	40.8	9.0	9.2	9.4	9.7	9.9
1005 GF/Program Receipts						
1037 GF/Mental Health						
Other (please specify)						
TOTAL	40.8	9.0	9.2	9.4	9.7	9.9

Estimate of any current year (FY96) cost: $0.0

POSITIONS:

FULL-TIME						
PART-TIME	0.25	0.25	0.25	0.25	0.25	0.25
TEMPORARY						

ANALYSIS: (Attach a separate page if necessary)

Of the approximately 2,500 deaths per year in Alaska, 125 deaths are of children who are under the age of 7 years. During the lifetime of a 7 year-old, s/he will receive 16 immunizations, most of these occurring before the age of two. Using an average of 9 immunizations per child, the cost associated with this legislation would:

Personal Services - $8.2

A quarter time administrative clerk II would be needed to key, verify, query and correct the increased workload mandated by this legislation to include the immunization record of children under the age of seven years. The assumption would be that the cost for the position would increase by 2.5% for inflation.

Contractual - $30.0

The bill requires that there be six data fields for each immunization. This will mean a maximum increase of 96 fields to the

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Approved by Com: Karen Perdue, Commissioner
Agency: Department of Health & Social Services
Date: 1-9-96

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ANALYSIS (cont.):

existing 58 fields that are now required for each death certificate. Modification would be required to all the programs that constitute the death record file.

Supplies - $1.0

The current forms would have to be redesigned and reprinted. This will cost $1.0 for the first year and $0.5 for each year thereafter.

Equipment - $1.6

Data storage requirements will double for the entire death file requiring a purchase of 16 megabytes of storage for the WANG minicomputer the first year at $100/megabyte and 1 megabyte for each following year.

Position Title	No. of Positions	Range/Step	Bargaining Unit
Administrative Clerk II	1	8A	GGU

Time Status	Staff Months	Location	Election District
PPT	3	Juneau	

TYPE of EXPENDITURE		AMOUNT
Salary		5.5
Benefits		2.7
Premium Pay		
Other		
Total Personal Services		8.2
Travel		
Contractual		
Commodities		
Equipment		
Other		
Total Cost		8.2
FUNDING SOURCE for TOTAL COST		
1002 Federal Receipts		
1003 GF Match		
1004 General Fund		8.2
1005 GF/Program Receipts		
1007 I/A Receipts		
1037 GF/MH		
1061 CIP Receipts		
Other ( )		

Justification

A quarter time administrative clerk II would be needed to assume the extra workload created by the additional fields which would need to be keyed, verified and corrected on the 125 death certificates for children under seven years of age.

REQUEST for NEW POSITION

AGENCY: Health and Social Services

BRU: State Health Services

COMPONENT: Bureau of Vital Statistics

Revised Date:

FY97

Institute of Medicine Testimony, January 16, 1993

Thank you for allowing me to speak.

My name is Sandy Mintz and I live in Alaska. I am a full-time, parent volunteer for the National Vaccine Information Center/Dissatisfied Parents Together, as well as founder of a local group called "Parents Concerned About the Safety of Vaccines".

The points I would like to raise in my testimony today revolve around 3 main areas of concern: 1) problems with the 1991 report I hope the current committee can avoid, 2) specific concerns about vaccines, using measles as a model, and 3) suggestions for the direction and design of future vaccine safety and efficacy research.

In the 1991 IOM review, the Committee quite fairly pointed out that it had been handicapped by the lack of adequate studies, including the poor design of many. The Committee also properly concluded that the absence of appropriate studies meant that there was insufficient evidence to indicate whether or not there was a causal relationship between many of the adverse reactions being studied and vaccination. Imponderably, however, similarly flawed information was cited as evidence AGAINST causality in their report in a number of instances.

The Committee's conclusions concerning SIDS and DPT vaccine are a case in point. Although they admitted in their review, and I quote, "Prior to the 1960's, little was known about the epidemiology of sudden infant death syndrome (SIDS)", they concluded, and again I quote, "Studies showing a temporal relation between these events are consistent with the expected occurence of SIDS over the age range in which DPT immunization typically occurs". Without information on the background rate of SIDS in historically, socioeconomically, and otherwise comparable never vaccinated groups, data on the expected frequency of SIDS merely reflects its incidence among vaccinated populations, rather than absent vaccination and cannot be considered accurate or meaningful. Given that such background information was not presented by the Committee, conclusions about the absence of a relationship between SIDS and vaccination were not justified.

Nor were any studies cited - in fact, to my knowledge none exist - in which the only proper control group, never vaccinated children, was used. If, as is the case in most studies, "less recently", but nonetheless vaccinated, children were used as controls, and an adverse vaccine event can be either a delayed or long-term consequence of vaccination, one would EXPECT to find no differences between the study groups, even if vaccination HAD caused an adverse event. Conclusions about causality drawn from any study with such serious limitations are not justified.

The fact is, all controls are not equal. More importantly, many groups are improperly designated as controls. The 1991 IOM statement that a nontreatment group, i.e., control, might be one using an established alternate vaccine, is an example of an improper definition of a control. In no way can any form of vaccination, whether "established" or less recently administered, be considered lack of intervention. The

extent to which various established vaccines and times since administration of vaccine are similar to non-vaccination should be studied, not assumed. Only a placebo, which in the case of vaccination studies equals the absence of vaccination, is appropriate.

As to the notion that it is unethical to withhold vaccination due to "widespread acceptance" of vaccination, I would submit that to the contrary, if anything, it is unethical to administer vaccinations of unknown safety and efficacy. It is unsound to argue we can't withhold vaccines beause of "widespread acceptance", as the 1991 IOM Committee did, when the reason there is such widespread acceptance of vaccinations is that we have been told the vaccines are safe and effective. Their argument is particularly ironic given their finding that serious consequences can result from the two vaccines, and lament about the absence of adequate information. To the contrary, the conclusion that must be drawn from their review is that randomized, long-term, placebo-controlled, prospective clinical trials are urgently needed, in spite of ethical concerns about ADMINISTERING vaccines of unknown safety. Indeed, no reassuring claims about the infrequency of any linked adverse event should be made until and unless the false premises underlying study designs and the many study design flaws, including the lack of reasonable and time appropriate controls, and reporting system inadequacies, are corrected.

Please note that in any study of long-term vaccine consequences, in which proper experimental and control groups are used, a comprehensive and longitudinal medical assessment is necessary in order to discern all observable and measurable effects of vaccination, both good and bad, known and unknown.

An insidious way in which the risks of vaccination can be incorrectly estimated is by using the number of doses of vaccine which appear to result in injury, rather than the number of children that are administered how ever many doses it takes to injure them. Since nearly all vaccines are currently being recommended to be administered in multiple doses, using doses rather than children can result in gross underestimation of actual risk. We also cannot ignore confounding which occurs when high-risk children are eliminated, either by not receiving the vaccine in question at all, or by receiving only one dose.

Take as an example convulsions resulting from either whooping cough vaccine or whooping cough. The CDC says that 1/1750 vaccinations result in convulsions but that 2/100 children who get whooping cough have convulsions. If we divide the 1750 vaccinations by the between 4 and 5 doses children are required to get, the result is 1/350 to 1/438 children getting convulsions after whooping cough vaccine, not nearly as dramatic a difference.

If we further try to factor in the impact of underreporting of adverse reactions, the actual incidence of which is unknown but presumed to be significant, it becomes clear that there may be no difference, and in fact, that it is possible convulsions are more likely to result after vaccination than after disease.

The fact is, however, that we do not know the true incidence of vaccine adverse reactions, of whooping cough itself, of convulsions after whooping cough or many other relevant and critical factors, including

the actual number of children receiving a vaccine once high-risk children have been removed. We should simply admit it and set about trying to learn what we can. We should not, however, be issuing reassuring assessments of vaccine risk.

When evaluating the risks of vaccines, it is imperative that we look at the big picture. We simply cannot accurately evaluate vaccine benefits or risks in a vacuum, nor consider the evaluation static. Among the many things which need to be considered are the following:

1) The true risk of contracting a disease, in comprable, never vaccinated populations, as well as the true risk of suffering serious consequences from a disease, must be determined. Included in any such analysis should be historical morbidity and mortality data from years prior to the introduction of vaccines, preferably smallpox vaccine. When considering the true risk of long-term serious consequences of disease, new treatment strategies, like erythromycin for whooping cough, and vitamin A for rubeola, should be factored in. The role breastfeeding plays in preventing and/or mitigating the effects of diseases needs to be better understood and factored in as well.

2) The background rate of an event occurring in comparable never vaccinated populations, should be compared to recently and not so recently vaccinated ones. However, as useful and important as background rates are, when making comparisons between groups, such rates should never be used to substantiate claims about whether or not a particular child suffered "residual effects" from some untoward event following vaccination, since a particular child's potential can never be predicted. This holds especially true when estimating an infant's potential.

3) Graphs should be presented fairly, and if they have not been, primary data, rather than graphs, should be used. Included in my submissions is a graph found in the MMWR which provides an excellent example of the dangers of their unquestioned use and "how to lie with statistics". The Y axis uses an inappropriately applied logarithmic scale, the result being that drops in both morbidity and mortality prior to vaccination are made to appear insignificant, while drops occurring post-vaccination are made to appear dramatic. In fact, the opposite is true.

We also cannot ignore the impact of vaccines on changing epidemiology when considering their risks and benefits. For instance, measles may have been made a more serious disease because of measles vaccination. Prior to widespread vaccination, once a population had been exposed to measles, few adults or infants contracted it, adults due to lifelong immunity and infants due to maternal antibodies. Now, adults AND infants are getting the measles, with serious consequences. I would like to include reference to a recent Washington Post article entitled:

"Measles Still Menace to Infants: Vaccinated Moms Pass Less Immunity to Babies". In this article it was noted that although in 1976 3% of measles cases occurred in children less than one, today, more than 25% do. The author also indicated that prior to vaccination, 3 to 4 million measles cases occurred with around 500 deaths. This would make the case-fatality ratio for that period between 1 to 2 per 10,000. In the years 1989, 1990 and 1991 combined, however, it was reported that

around 55,000 people got the measles and 165 died, making the case-fatality ratio dramatically higher at 3 out of 1,000. At this rate, fewer than 175,000 cases per year would be necessary to result in the same number of deaths which used to occur when there were millions of cases.

The CDC says that, although worrisome, the problem would be solved were all preschoolers vaccinated and measles virus eliminated from circulation. Yet I would submit that with waning measles vaccine immunity a fact of life, and subclinical cases of the measles occurring routinely among the vaccinated and considered to boost vaccine-induced immunity, vaccinating preschoolers will not prevent measles from circulating. Indeed, an obvious major source of infection for infants and unimmunized toddlers has been properly vaccinated school-age children who developed most of the clinical measles cases, as well as many subclinical ones. It is, in fact, puzzling that the CDC would offer such reassurances given that they have admitted even 100% vaccinated populations can have outbreaks.

The CDC also says that about 40% of mothers currently do not have protective antibodies and that at the end of the decade that figure will be 100%. This, of course, means that as the percentage of mothers without antibodies rises, the death rate should rise as well, since an even higher percentage of cases will be infants.

Morbidity and mortality statistics for measles should also rise as fewer and fewer adults have natural immunity and more and more adults have waning vaccine immunity. The scenario is quite believeable in which mothers would get measles and pass them on to their infants, whereas before they would never have gotten the measles, and would instead of passing the measles on to their infants, have passed on protective measles antibodies to them.

In other words, measles may not be controllable, and may have been made vastly more serious, by the use of measles vaccination. Adults, in fact, may now be faced with the unsavory prospect of getting measles or receiving a vaccine, neither of which has been proven to be safe for them. Any risk/benefit analysis should take into consideration the impact of vaccine-program induced changing epidemiology on the seriousness of any diseases vaccines are designed to prevent, as well as the consequences, including efficacy, of vaccinating adults against what were once childhood diseases.

The problems which can be overlooked if vaccine analysis is taken out of context are well exemplified in the case of rubella vaccine. A normally benign disease in childhood, usually affording lifelong immunity, it can result in devastating effects if a non-immune pregnant woman is exposed during the critical time period. As devastating as the consequences can be for an infant, it is important to not only determine the actual incidence in epidemic years of congenital rubella syndrome, but whether or not an unvaccinated child allowed exposure to rubella is more or less likely to be immune in adulthood than a previously vaccinated child, given that vaccine immunity is now generally thought to be short-lived. Indeed, it is entirely possible that the risk to the fetus is greater from once-vaccinated mothers, given waning vaccine immunity, and the overall risk to the population greater, once the risks of adult rubella vaccination have been factored

in.

Aside from my earlier recommendations concerning properly designed studies (and by long-term, I mean 20-30 years at least), I would also urge that you recommend some enforcement mechanism vis a vis doctors reporting adverse reactions. Although I realize that adverse reaction reporting is an extremely flawed method, as we all know, in theory as well as in fact, and can neither be viewed as proof of causation or as exhaustive, still we need to get some idea of the range of possible vaccine consequences, as well as to follow up on those we do know about.

Among the many other questions which need to be asked and answered, I would recommend the following:

1. Is cancer more or less likely to occur among the vaccinated? Included in any studies should be reference to SV40, other vaccine contaminants, the role of chromosomal damage as a result of vaccination, and immune system suppression. The notion that a subclinical case of a disease is preferable to a full-blown case should be studied, not assumed. Submitted is a tantalizing study by Ronne in The Lancet in which he found that subclinical cases of the measles resulted in significantly increased rates of serious disease among adults.

2. What, if anything, is the role of vaccine contaminants in causing adverse reactions and new diseases? Included in any such studies would be the role played by such contaminants in the outbreak of AIDS and other recent immune system disorders like chronic fatigue syndrome, Kawasaki's disease and others.

3. Why, during polio epidemics, do most people get polio, gaining lifelong immunity while apparently suffering no ill effects, while a small percentage of the population gains that lifelong immunity at a great price? Included in any examination of this issue should be the role provocation polio and tonsillectomy play in predisposing a person to paralytic or bulbar polio, and the extent to which they each effect the incidence of serious polio.

4. Can vaccination result in post-polio syndrome? If it can, then we need to find out if instead of the small percentage of the population who got polio being susceptible to post-polio syndrome, whether now the entire vaccinated population is at risk.

5. What is the effect of combining vaccines in vivo and in vitro? Studies of this should include clinical trials of all vaccines individually, as well as the effects of their simultaneous administration. The practice of administering vaccinations in combination without data to support their safety and effectiveness should stop until the safety and effectiveness of the practice can be firmly established. Relevant to this discussion, and included among my submissions is a paper by Javier et al in Science magazine in which it was found that two harmless herpes viruses recombined in vivo and became extremely lethal as a result.

6. Has a relatively small risk of long-term consequences from childhood diseases been traded for a vaccine-induced, larger risk of chronic childhood disease? I refer you to a New York Times article I have

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Honorable Lyda Green
Alaska State Senate
Room 423, State Capitol
Juneau, AK 99801

February 20, 1996

Dear Senator Green:

I would like to respond to as many of the points made by the Department of Health and Social Services as I can on such short notice.

1. VAERS (The Vaccine Adverse Events Reporting System) is a passive reporting system. It requires that someone make a connection between a vaccination and a possible adverse event, and that someone report it. Compared to an active surveillance system, which post-marketing surveillance is, considerable under-reporting can be expected. As Dr. James Froeschle of Connaught Laboratories (a vaccine maker) testified to the Institute of Medicine (IOM), and as reported on page 328 of "Adverse Events Associated with Childhood Vaccines - Evidence Bearing on Causality", "From a comparison of spontaneous reports with postmarketing surveillance data, the company estimates about a 50-fold underreporting of adverse events in the passive reporting system." BECAUSE OF THIS AND OTHER LIMITATIONS OF VAERS, ADDITIONAL METHODS OF DATA COLLECTION NEED TO BE DEVISED.
2. Given that neither VAERS nor post-marketing surveillance is proof of causality, ultimately it would be hoped that evidence of temporal association would be followed up by well-designed, controlled studies.
3. Data on the incidence of SIDS goes back only about 25 years. Vaccinations have been around for a lot longer than that (for instance, the first pertussis vaccination was, according to "Vaccines" by Plotkin and Mortimer, developed in 1926). NO ONE HAS ANY IDEA WHAT THE INCIDENCE OF SIDS WOULD BE IF CHILDREN WERE NOT BEING VACCINATED. IT IS ENTIRELY POSSIBLE THAT THERE WAS VERY LITTLE SIDS PRIOR TO VACCINATION. GLIB REJECTION OF THE POSSIBILITY OF A RELATIONSHIP IS BASED ON OPINION, NOT FACT.
4. Please request from the Department copies of all studies which show that "children who had recently gotten a DTP shot were less likely to get SIDS". In the only one which I am aware of, "Diphtheria-tetanus-pertussis immunization and sudden infant death: results of the National Institute of Child Health Development Cooperative Epidmiological Study of Sudden Infant Death Syndrome risk factors", by Hoffman et al in Pediatrics, April of 1987, the authors make it clear that the lesser rate among DPT vaccinated children had nothing to do with protective effects from the vaccine, contrary to what was implied by the Department.
5. The fact that "No deaths caused by anaphylaxis following DTP vaccination have been reported to the CDC since the inception of vaccine-adverse-events reporting began in 1978" merely proves that the CDC is uninformed and that SB185 is sorely needed. Why are they unaware that the IOM found a causal link between the whole cell pertussis vaccine and anaphylaxis, and the drug companies themselves report that such deaths occur (one can consult the PDR for drug company warnings), and THAT SUCH DEATHS HAVE BEEN REPORTED TO VAERS AND COMPENSATED BY THE GOVERNMENT?
6. It is not clear that the risks from the diseases are greater than the risks from the vaccines when it becomes clear that little is known about the magnitude of vaccination risks. Take the CDC's own figures regarding convulsions and DPT vaccine vs. whooping cough the disease. According to the CDC, 1/1750 vaccinations result in convulsion, whereas 2/100 children with whooping cough will have a convulsion. But children get between 4 and 5 doses of vaccine. If we divide 1750 by the

between 4 and 5 doses most children get, the result is 1/350 ro 1/438 children getting convulsions after vaccination. Furthermore if we multipy by 50 the number of incidences one might expect in a post-marketing survey, we arrive at 1/7 to 1/9 temporally associated convulsions. If only 10% of these were deemed caused by the vaccine, 1/70 to 1/90 children could be having convulsions as a result of DPT vaccine.

THE FACT IS, WE DO NOT KNOW HOW MANY TEMPORALLY ASSOCIATED EVENTS ARE ACTUALLY OCCURRING, NOR DO WE KNOW HOW MANY OF THEM ARE ACTUALLY CAUSED BY VACCINATION. SB185 WOULD BEGIN TO RECTIFY THIS SITUATION BY COLLECTING DATA ON ONLY ONE EVENT - TEMPORALLY ASSOCIATED VACCINE DEATHS.

7. It is interesting that the Department failed to note that the death rate in England in 1978 was considerably below prior whooping cough death rates. According to figures I received from the CDC, in 1920 there were 5,122 deaths and 107,473 cases in the U.S. In 1978 in England, there were only 36 deaths for 100,000 cases. It is also interesting to note that no mention was made of possible deaths due to the vaccine which might have been compared to the number of deaths from whooping cough.

Thank you for your fair-minded consideration of the points made here.

Sincerely,

Sandy Mintz

To Senator Kelly
Reference HES, STA
12th Feb. 1996

From Archivides Kalokerinos
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Born 28th Sept. 1927. Glen Innes, Australia
Graduated M.b ,B.S. Jan. 1951, University Sydney
Fellow Royal Society of Tropical Medicine, London

Retired from full-time practice.
Consultant to various organisations in Australia and overseas and Australian Aboriginal communities.
Special interests - Aboriginal infant and adult health, Vitamin and mineral supplements, nutrition, and problems associated with routine vaccine administrations.

In 1957 I commenced work as the sole medical practitioner in the remote township of Collarenebri, 500 miles north-west of Sydney. There were about 500 Caucasians in the town, 200 Aborigines on the nearby reserve and about 500 Caucasians in the surrounding district.

Before my time in Collarenebri and for the first ten years of my period there an extraordinarily high infant mortality rate, amongst Caucasians and Aborigines, was apparent. During one 24 hour period three Caucasian babies died.

The infant deaths were strange. Some infants who were apparently well or suffering from a trivial illness, were found dead in their cots - typical sudden, unexpected, infant deaths. Other infants who were apparently well, or suffering from trivial complaints, went into unexplained shock from which they could not be resuscitated. Others became excessively irritable, then unconscious and died. In all cases autopsies failed to offer satisfactory explanations for death. In some cases autopsies revealed yellow patches in the liver and it was observed, before death, that these cases displayed varying degrees of liver pain and tenderness.

All other doctors in Australia, including academic staff and State and Commonwealth Departments of Health, denied that infant death rates were high in other areas and denied the existence of the clinical patterns observed by myself. Years later I learned that the problems were widespread across Australia and, indeed, worse in many areas.

In other words, I was deliberately misinformed by some and others appeared incapable of recognising what was going on before their eyes. Sometimes, for reasons not fully understood, epidemics of one of the disease patterns occurs - for example, *The Dark Disease Of Naples,* (Italy) during the late 1970's where infants and children became suddenly unconscious, for no known reason, and died. Two thirds of these cases had upper respiratory infections, the other third had recently received routine vaccinations.

Eventually I found that intramuscular or intravenous Vitamin C, if administered early, reversed the shock state and the unconscious state. I was fortunate because I was always able to commence treatment early.

The first injection of Vitamin C was given in December 1967. From that time on, until I left the area in November 1975, there were no more infant deaths under my care. I was also able to drop the infant mortality rates in neighbouring districts. Other doctors who followed my methods achieved similar results.

However, I did observe that routine immunisations had a dreadful effect on some infants for a period of some weeks following the administration. A few suffered from an apparent immune paralysis and contracted serious bacterial infections. Others went into the strange state of shock or became excessively irritable , then unconscious. Both states could be reversed by intravenous Vitamin C. Bacterial infections were difficult to control.

Because of this routine immunisations were sometimes delayed. The percusses component was sometimes omitted and sick infants received injections of vitamin C.

It is important to note that most standard methods of medical treatment were always employed, before and after the realisation of the importance of Vitamin C and the harm sometimes done by routine vaccinations. What made the difference to mortality rates (and the figures could hardly be more dramatic) was the uses of Vitamin C and care with routine vaccinations.

I should also inform you that in the state of NSW records of vaccinations, including batch numbers, are kept and copies given to all parents.

Family Health Pataline

IN THIS ISSUE:

- Women who gave birth to an infant who died during 1992-94 had less prenatal care than the overall population of women giving birth in Alaska during 1992.
- Among women who gave birth to an infant who died, the highest rates of inadequate prenatal care were identified in young mothers and those with chart documentation of prepregnancy alcohol drinking.
- The infant mortality rate due to extreme prematurity or low birthweight declined 52% from 1979-80 to 1991-92.
- All of the decrease in mortality due to extreme prematurity or low birthweight occurred because of increased survival of premature or low birthweight infants rather than a decrease in the premature or low birthweight birth rate.
- Alaska Natives, blacks, and teenage mothers have significantly higher mortality rates due to extreme prematurity or low birthweight because of higher premature or low birthweight birth rates.

In this issue we present a description of the Alaska Maternal-Infant Mortality Review (MIMR) Process and an evaluation of data from this project regarding pregnancy related risk factors and prematurity.

The MIMR Process

The MIMR review team

The MIMR review team consists of representatives from the Section of Maternal, Child, and Family Health (MCFH), the Bureau of Vital Statistics, and the Division of Family and Youth Services; private physicians, nurses, and other medical providers; and medical and programmatic staff from the Alaska Area Native Health Service (Indian Health Service) and the Regional Native Health Corporations.

Identification of an infant death

The MIMR review team attempts to identify infant deaths through several sources.

- Deaths occurring outside the hospital and of questionable etiology are referred to one of the state coroners. The state coroners in turn call an Infant Death Hotline located at MCFH.
- The Bureau of Vital Statistics matches the death and birth certificates for any infant under one year of age and sends this information to the MIMR program.
- MIMR staff read the newspaper obituaries section to identify infant deaths.

Collecting data for each infant death

Multiple data sources are used to create a complete picture of the circumstances leading to an infant's death.

- Birth and death certificates. We collect information from matched birth and death certificates including date and time of death, number of prenatal visits, trimester prenatal care began, birthweight, and APGAR scores.
- Infant medical records. A standard abstraction tool is used to collect information from hospital and clinic records on the immediate neonatal circumstances as well as subsequent illnesses, clinic or emergency room visits, hospitalizations, treatments and immunizations, and a clinical summary of events immediately preceding death.
- Maternal medical records. A standard abstraction tool is used to collect information on the mother's medical history, previous pregnancy history, and prenatal course. If the number of prenatal care visits or the trimester prenatal care visits were initiated is not available from the birth certificate, this information is collected from the maternal medical record.
- Autopsies. Infants who die outside of the hospital usually have an autopsy. Autopsies are performed on infants who die in the hospital less frequently. A standard abstraction tool is used to collect information on the gross anatomic, organ specific, and microscopic findings.

- **Family interviews.** MIMR staff offer a home interview, administered by a public health nurse, to the familes of infants who died outside of the hospital. Information collected through the home interview includes family demographic data, maternal reproductive history and pregnancy planning, prenatal care and delivery history (including payment methods for these services), family life circumstances, infant health care, and the immediate circumstances of the infant's death.

The review process

Three steps constitute the review process.

- **Monthly mortality reviews.** Each month, a representative sample of committee members from various disciplines, including physicians, nurses, administrative staff, and public health program managers meet to review the information collected for each infant. The committee determines a consensus cause of death and identifies potentially modifiable contributing factors to the infant's death.

- **Data entry and analysis.** Information from the various sources, including the monthly mortality reviews, is entered into a computerized database and analyzed by the MIMR chairman and a pediatric epidemiologist.

- **Yearly MIMR committee meetings.** Once each year, committee members meet to discuss findings, identify problems with the review process and develop consensus recommendations.

Findings and Recommendations

General

The MIMR committee has reviewed 121 deaths: we reviewed 43 of 92 deaths which occurred during 1992, 45 of 90 deaths which occurred during 1993, and 33 of an unknown number of deaths which occurred during 1994. During 1992, we included only deaths which occurred from June forward. Failure to review a death was most commonly due to lacking complete records for a particular infant. This in turn usually resulted from a failure to obtain maternal prenatal records from the Alaska Native Health Service: 96%, 97%, and 66% of incomplete charts during 1992, 1993, and 1994, respectively, were for Alaska Native children. Home interviews were offered only for children who died outside of the hospital setting. To date, 24 interviews have been completed, 8 women declined an interview, 8 women have moved and could not be located, and 44 interviews are pending.

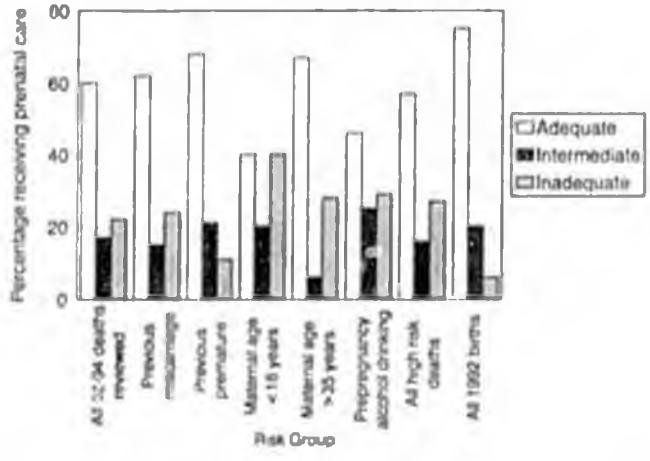
Pregnancy related risk factors

Findings

Among the cohort of mothers who gave birth to the 121 infants who died, 20% had chart documented evidence of alcohol consumption during the three months before pregnancy, 4% were younger than 18 years and 9% were older than 35 years, 16% had at least one previous preterm birth, 28% had at least one previous miscarriage, and 55% had at least one of these risk factors.

We used the Kessner Index to define adequacy of prenatal care. Women who gave birth to an infant who died during 1992-94 had less prenatal care than the overall population of women giving birth in Alaska during 1992 (Figure 1), particularly in the inadequate prenatal care category. Women in our study with risk factors identifiable before pregnancy - such as maternal age, substance use history, and previous adverse pregnancy outcomes - received no greater prenatal care than the general cohort of women. The highest rates of inadequate prenatal care were identified among young mothers and those with chart documentation of prepregnancy alcohol drinking.

Figure 1. Adequacy of prenatal care for 121 infants who died during 1992-94 by various risk groups; for comparison adequacy of prenatal care for all 1992 births is also included.



Recommendations

Identification of women with a high risk of adverse pregnancy outcomes and enrollment of these women into prenatal care programs theoretically contributes to lower rates of premature delivery and hence lower infant mortality rates[1]. Unfortunately, research has failed to document the effectiveness of this approach[2,3]. Researchers may have failed to document the efficacy of prenatal care because they measured the quantity rather than the quality of prenatal services. For example, prenatal care programs connected with substance use, nutrition, domestic violence, and financial assistance services may more effectively decrease adverse pregnancy outcomes than prenatal care programs which focus only on the physical aspect of pregnancy. Additionally, recent research indicates that identification and treatment of bacterial vaginosis during pregnancy may reduce the incidence of preterm delivery[4]. Finally, recent

research suggests that premature birth clusters in families[5], a finding supported by our data. This emphasizes the importance of early identification and monitoring of women who have had previous preterm births or who were born preterm themselves.

Based on our findings, the MIMR committee recommends:

- **Encouraging innovative approaches designed to increase prenatal care and to link prenatal care with other services. Health care providers should identify pregnant women at high risk for domestic violence, substance abuse, poverty, and pregnancy related infections AND refer them for appropriate services.**
- **Identifying and closely monitoring women who have had a previous preterm birth or who were born prematurely themselves.**
- **Using the Pregnancy Risk Assessment Monitoring System (PRAMS)[6] to determine barriers to prenatal care.**

Prematurity and Low Birthweight

Findings

From 1979-80 to 1991-92, the infant mortality rate due to extreme prematurity or low birthweight (defined as an infant born at less than 1000 g or less than 28 weeks gestation, who dies before 28 days of life, and who did not die of SIDS, trauma, congenital anomalies [except pulmonary hypoplasia], or cancer) declined from 2.9 to 1.7 per 1000 live births per year (chi-square for trend = 9.6, p=0.002) a decline of 52% (Figure 2).

A decline in mortality rate due to low birthweight or prematurity can occur for two reasons: a decline in the proportion of infants born with extreme prematurity/low birthweight or a decrease in the proportion of infants born with extreme prematurity/low birthweight who die. The proportion of infants born with extreme prematurity/low birthweight who died decreased from 44% during 1979-80 to 26% during 1991-92 (chi-square for trend, 9.1; p=0.003) (Figure 3). During the same time period, the rate of extremely premature/low birthweight births did not change.

Compared to whites, the risk ratio for mortality due to extreme prematurity/low birthweight among Alaska Natives was 1.23 (95% confidence interval [CI], 0.95 to 1.58) and among blacks was 2.96 (95% CI, 2.09 to 4.21). All of the increase in mortality for Alaska Natives and blacks resulted from higher extreme prematurity/low birthweight birth rates. Compared to whites, Alaska Natives had a risk ratio of 1.62 (95% CI, 1.42, 1.86) and blacks had a risk ratio of 3.31 (95% CI, 2.72 to 4.04) for delivering an extremely premature or low birthweight infant.

Compared to mothers 20-29 years of age, the risk ratio for mortality due to extreme prematurity/low birthweight among mothers less than 20 years of age was 1.84 (95% CI, 1.37 to 2.47) and among mothers 30 years or older was 1.09 (95% CI, 0.86 to 1.39). All of the increased risk for younger mothers occurred because of an increase in the extreme prematurity/low birthweight birth rate: compared to mothers 20-29 years of age, mothers less than 20 years had a risk ratio of 1.84 (95% CI, 1.37 to 2.47).

Figure 2. Mortality rate due to extreme prematurity or low birthweight: Alaska, 1979-92

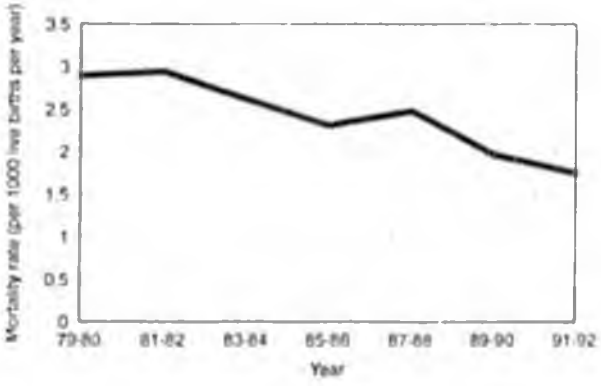
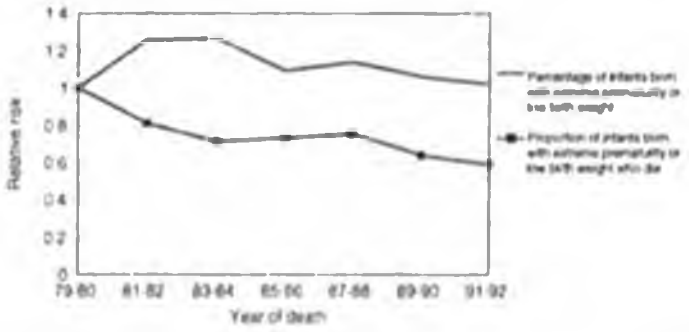


Figure 3. Using 1979-80 data as baseline, the relative risk by year for the percentage of infants born with extreme prematurity or low birth weight, and the proportion of infants born with extreme prematurity or low birthweight who die; Alaska, 1979-92



Recommendations

The cause of prematurity and low birthweight remains one of the most perplexing problems of medical research. As indicated by our data, advances have occurred in the survival of babies born with extreme prematurity or low birthweight, primarily through technology advances such as mechanical ventilation, surfactant therapy, nutritional and fluid support, and infection control. Unfortunately, no improvement has occurred in decreasing the number of children born with

prematurity or low birthweight, a trend found throughout the country[7]. Thus prematurity and low birthweight continue to cause a disproportionate amount of neonatal mortality in the U.S.[8].

In Alaska distinct racial differences exist among mortality rates due to extreme prematurity/low birthweight. These differences reflect differences in the rate of premature delivery rather than differences in survival. Similar to findings in the rest of the United States, blacks had increased rates of extreme premature/low birthweight delivery. Additionally, younger mothers had increased rates of extreme premature/low birthweight births, a result recently documented in Utah[9].

Based on our findings, the MIMR Committee recommends:

- **Directing efforts primarily toward decreasing the rate of preterm/low birthweight birth, rather than emphasizing postnatal care.**
- **Focusing efforts to decrease the rate of preterm/low birthweight birth on specific high risk groups such as blacks, Alaska Natives, and teenage mothers.**

Submitted by:
Bradford D. Gessner, M.D.

References

1. Kiely JL, Kogan MD. Prenatal care. In: Wilcox LS, Marks JS eds. From data to action: CDC's Public Health Surveillance for Women, Infants, and Children. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, 1995:107-118.
2. Bryce, R. The epidemiology of preterm birth. In: Kiely, M ed. Reproductive and Perinatal Epidemiology. Boca Raton, FL: CRC Press, 1991:437-444.
3. Rowley DL. Framing the debate: can prenatal care help to reduce the black-white disparity in infant mortality? JAMWA 1995;50:187-193.
4. Hauth JC, Goldenberg RL, Andrews WW, DuBard MB, Copper RL. Reduced incidence of preterm delivery with metronidazole and erythromycin in women with bacterial vaginosis. N Eng J Med 1995;333:1732-6.
5. Wang X, Zuckerman B, Coffman GA, Corwin MJ. Familial aggregation of low birth weight among whites and blacks in the United States. N Eng J Med 1995;333:1744-49.
6. Family Health Dataline, Section of Maternal, Child, and Family Health, Alaska Division of Public Health. May, 1995; Vol 1, No 2.
7. National Center for Health Statistics. Health, United States, 1992. Hyatsville, MD: Public Health Service. 1993.
8. Wise PH, Wampler N, Barfield W. The importance of extreme prematurity and low birthweight to US neonatal mortality patterns: implications for prenatal care and women's health. JAMWA 1995;50:152-55.
9. Fraser AM, Brocken JE, Ward RH. Association of young maternal age with adverse reproductive outcomes. N Eng J Med 1995;332:1113-7.

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Adverse Events Associated with CHILDHOOD VACCINES

Evidence Bearing on Causality

Kathleen R. Stratton, Cynthia J. Howe, and
Richard B. Johnston, Jr., *Editors*

Vaccine Safety Committee

Division of Health Promotion and Disease Prevention

INSTITUTE OF MEDICINE

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1

Executive Summary

"Our aim, therefore, must be to study these [complications] as fully as possible in the confident expectation that, as in other branches of science, knowledge will bring enlightenment" (Wilson, 1967).

Childhood immunization has been one of the foremost public health measures of the twentieth century. It has allowed control and prevention of many diseases from which morbidity and mortality can be staggering. Medical personnel in the United States currently rarely see a case of the infectious diseases against which the vaccines are directed. Yet, recent measles epidemics on college campuses and in inner cities suggest that vaccine-preventable disease is not to be ignored. The first health initiative of the new presidential administration was to increase funding for childhood immunization programs to boost vaccination rates in the United States, particularly for children under age 2 years.

BACKGROUND AND HISTORY

The public policy debate regarding immunization stretches beyond the question of how to meet the goals of universal immunization. Concern over the safety of pertussis vaccine was long-standing in Great Britain by the time of the 1982 airing in the United States of a documentary entitled "DPT: Vaccine Roulette" (WRC-TV, 1982) and the 1985 publication of *DPT: A Shot in the Dark* (Coulter and Fisher, 1985). Concern has stretched to other vaccines and has spawned the formation of groups of interested citizens throughout the United States, for example, National Vaccine Information Center/Dissatisfied Parents Together, Determined Parents to Stop Hurting Our Tots, Concerned Health Professionals and Others, and Parents

Concerned About the Safety of Vaccines. More articles and books have been published (e.g., Coulter, 1990; Miller, 1992) to alert the public to the potential risks of vaccination.

In 1986, the U.S. Congress passed the National Childhood Vaccine Injury Act (NCVIA; P.L. 99-660) in response to worries about the safety of currently licensed childhood vaccines and in response to the economic pressures that were threatening the integrity of childhood immunization programs. The litigation costs associated with claims of damage from vaccines had forced several companies to end their vaccine research and development programs as well as to stop producing already licensed vaccines. The NCVIA was an attempt to encourage and ensure vaccine production by creating a no-fault compensation program (the National Vaccine Injury Compensation Program) as a required first resort for those who believed that they or their children had been injured by certain vaccines. The need for a compensation program had long been recognized, and several groups had proposed possible mechanisms for compensating people believed to be injured by vaccination (Institute of Medicine, 1985; Office of Technology Assessment, 1980). This program was envisioned to alleviate, but not completely eliminate, manufacturer liability and encourage research and development of more and safer vaccines. The compensation program is administered by the federal government and is financed by an excise tax on the sale of vaccines covered by the program (Iglehart, 1987; Mariner, 1992).

In addition to establishing the compensation program, the NCVIA set forth other vaccine-related efforts to be carried out by the U.S. Department of Health and Human Services, including mandatory reporting of specific adverse events following childhood immunizations against diphtheria, tetanus, pertussis, measles, mumps, rubella, and polio (see box entitled The Vaccine Injury Table in Chapter 10); voluntary reporting of any reaction to any immunization to the Vaccine Adverse Event Reporting System (see Chapter 10 for a discussion of this passive surveillance system and Figure 1-1 for a copy of the reporting form); the creation of a National Vaccine Program Office to coordinate federal vaccine initiatives and to help meet immunization coverage goals; the establishment of advisory groups to the National Vaccine Program and the National Vaccine Injury Compensation Program; and better communication of the potential risks of vaccines through public information pamphlets that are distributed at the time of vaccination (under the direction of the Centers for Disease Control and Prevention) and changes in vaccine package inserts (under the direction of the U.S. Food and Drug Administration).

The NCVIA also mandated that the Secretary of the U.S. Department of Health and Human Services enlist the help of the Institute of Medicine (IOM) of the National Academy of Sciences to study the adverse effects of childhood vaccines. The NCVIA called for two specific studies. The first, mandated under Section 312 of P.L. 99-660, was to address the serious adverse effects of pertussis and rubella vaccines. The Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines published its findings in 1991 (Institute of Medicine, 1991). Appendix A contains the Executive Summary of that report.

The second study, mandated under Section 313 of P.L. 99-660, was to review adverse events associated with other vaccines commonly administered during childhood. The Vaccine Safety Committee, which was charged with performing the second study, was convened early in 1992. The results of that inquiry are provided in this report.

THE CHARGE TO THE COMMITTEE

The members of the interdisciplinary, 14-member Vaccine Safety Committee have expertise in such areas as immunology, pediatrics, internal medicine, infectious diseases, neurology, virology, microbiology, epidemiology, and public health. The committee was charged with (1) reviewing the relevant scientific and medical literature on specific risks to children associated with the vaccines or vaccine components directed against tetanus, diphtheria, measles, mumps, polio, *Haemophilus influenzae* type b, and hepatitis B currently licensed for use in the United States and (2) reviewing the available data on specific risk-modifying factors, that is, circumstances under which administration of these vaccines increases the risk of an adverse event, characteristics of groups known to be at increased risk of an adverse event, and timing of vaccination that increases the risk of an adverse event.

Risk-benefit comparisons or recommendations about immunization schedules were not within the charge to the Vaccine Safety Committee. Despite the name of the committee, many aspects of vaccine safety, such as purity standards or production techniques, also were beyond the committee's charge.

Both IOM studies mandated in P.L. 99-660 entailed the evaluation of the weight of scientific and medical evidence bearing on the question of whether a causal relation exists between certain vaccines and specific serious adverse events. Like the Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines, the Vaccine Safety Committee approached its task from a position of neutrality, presuming neither the presence nor the absence of a causal relation between the vaccines and the adverse events under consideration.

THE STUDY PROCESS

Over the course of 18 months, the committee met six times, reviewed more than 7,000 abstracts of scientific and medical studies, read more than 2,000 published books and articles (including many sources in the non-

English literature), analyzed information from U.S. Public Health Service-administered reporting systems for adverse reactions to vaccines, and considered material submitted by interested parties. The committee solicited input from scientists who were invited to participate in two open scientific meetings and from other interested parties at two open public meetings. Details regarding how the committee gathered information are given in Appendix B. All salient information from those reviews is contained in this report.

P.L. 99-660 stated that the review was to include those vaccines covered by the National Vaccine Injury Compensation Program. *Haemophilus influenzae* type b (Hib) and hepatitis B vaccines were added for consideration because of the increasing use of these vaccines and the supposition that in the near future they could be mandatory vaccines covered by the National Vaccine Injury Compensation Program. The list of adverse events investigated for this report derived primarily from negotiations with representatives of the U.S. Public Health Service. However, preliminary investigations into additional adverse events were prompted by queries from interested parties or committee members. After considering the information from these preliminary investigations, the committee added several vaccine-adverse event relations to the original list. Table B-1 in Appendix B contains a complete listing of the specific vaccine-adverse event relations under study.

The report begins with background information. Chapter 2 contains an in-depth discussion of the approach used by the committee to weigh the evidence and assess causality. Information on the neurologic disorders and immunologic reactions discussed in much of the report is contained in Chapters 3 and 4. Chapters 5 through 9 include the vaccine-specific evidence and conclusions. All information (evidence, causality argument, and conclusions) regarding death as an adverse event associated with vaccination is contained in Chapter 10.

Adverse Effects of Pertussis and Rubella Vaccines (Institute of Medicine, 1991), the report of the predecessor IOM committee, provides an in-depth review of the literature concerning the adverse events associated with diphtheria and tetanus toxoids and pertussis vaccine (DPT), as well as pertussis vaccine, and should be referred to for conclusions regarding DPT. Appendix A contains the Executive Summary of that report. The charge to the Vaccine Safety Committee was to examine adverse events associated with tetanus toxoid as well as tetanus and diphtheria toxoid combination preparations. The committee reviewed data concerning DPT if the data also concerned diphtheria and tetanus toxoids for pediatric use (DT); however, it was beyond the committee's scope to make conclusions about pertussis vaccine or DPT.

The IOM Committee to Review the Adverse Consequences of Pertussis

and Rubella Vaccines made determinations of causality only for rubella vaccine and the rubella vaccine component of multivalent vaccines, but not for measles-mumps-rubella vaccine (MMR). Thus, the Vaccine Safety Committee reviewed data regarding immunization with MMR as well as data on monovalent measles and mumps preparations. The committee has made separate determinations of causality for the measles and mumps vaccine components for the adverse events for which data were available, particularly if measles or mumps vaccine-strain virus was isolated from the patient. In circumstances in which a causality assessment specific to monovalent measles or mumps vaccine was not possible, this is stated in the conclusion regarding that specific adverse event.

In circumstances in which the committee determined that a component of a multivalent preparation was causally related to a specific adverse event, but there is no direct experience of such an adverse event being caused by the multivalent preparation, the committee states this, but judges that the combined preparation also is causally related to that adverse event.

Many case reports described an adverse event(s) in a patient who received more than one vaccine. A common combination, as a result of the immunization schedules recommended in the United States, is DPT, oral polio vaccine, and Hib vaccine. Assessment of causality in those reports was more difficult than if the patient had received only one vaccine or vaccine component, but the committee considered that the reports could be theoretically supportive of causality for the combination but not in themselves sufficient to allow a firm judgment regarding causality.

CAUSALITY AND WEIGHT OF EVIDENCE

As discussed in detail in Chapter 2, the committee considered four types of evidence: biologic plausibility; case reports, case series, and uncontrolled observational studies; controlled observational studies; and controlled clinical trials. The committee used qualitative and quantitative approaches to weigh each type of evidence. Table 1-1 contains a summary of the different types of evidence for every vaccine-adverse event relation studied. The committee believes that although it is plausible that there is a causal relation between any of the vaccine-adverse event associations under review, plausibility has been demonstrated only for certain ones of these. Therefore, information on the plausibility of a causal relation was classified in Table 1-1 as either theoretical only or as demonstrated. The other types of evidence were classified in Table 1-1 as nonexistent, indeterminate, or as weighing, on the whole, for or against a determination of a causal relation. The consideration of all four types of evidence as a whole led to a conclusion of the final weight of evidence regarding causality. Table 1-2 contains these conclusions.

Vaccine and Adverse Event	Biologic Plausibility[a]	Case Reports, Case Series, and Uncontrolled Observational Studies	Controlled Observational Studies and Controlled Clinical Trials
Diphtheria and Tetanus Toxoids[c]			
Encephalopathy	Demonstrated	Indeterminate	Against (DT) No data (Td, T)
Infantile spasms[d] (DT only)	Theoretical only	No data	Against
Residual seizure disorders other than infantile spasms	Theoretical only	Indeterminate (DT, T) No data (Td)	No data
Demyelinating diseases of the central nervous system	Demonstrated	For	No data
Guillain-Barre syndrome	Demonstrated	For (T) Indeterminate (DT, Td)	No data
Mononeuropathy	Theoretical only	Indeterminate (T, Td) No data (DT)	No data
Brachial neuritis	Theoretical only	For (T) Indeterminate (Td) No data (DT)	No data
Arthritis	Theoretical only	Indeterminate	No data
Erythema multiforme	Theoretical only	Indeterminate (DT, Td) No data (T)	No data
Anaphylaxis	Demonstrated	For (T) Indeterminate (DT, Td)	No data
Death from SIDS (DT only)[e]	Theoretical only	Indeterminate	Against
Measles Vaccine[f]			
Encephalopathy	Demonstrated	Indeterminate	Indeterminate
Subacute sclerosing panencephalitis	Demonstrated	Indeterminate	Indeterminate
Residual seizure disorder	Demonstrated	Indeterminate	No data
Sensorineural deafness	Theoretical only	Indeterminate (MMR)	No data
Optic neuritis	Demonstrated	Indeterminate	No data
Transverse myelitis	Demonstrated	Indeterminate	No data
Guillain-Barre syndrome	Demonstrated	Indeterminate	No data
Thrombocytopenia	Demonstrated	Indeterminate (measles) For (MMR)	Indeterminate (measles) No data (MMR)
Insulin-dependent diabetes mellitus	Theoretical only	Indeterminate	Indeterminate

continued

TABLE 1-1 *(continued)*

Vaccine and Adverse Event	Biologic Plausibility[b]	Case Reports, Case Series, and Uncontrolled Observational Studies	Controlled Observational Studies and Controlled Clinical Trials
Anaphylaxis	Theoretical only	For	No data
Death from vaccine-strain viral infection[c]	Demonstrated	For	No data
Mumps Vaccine[d]			
Encephalopathy	Demonstrated	Indeterminate	No data
Aseptic meningitis	Demonstrated	Indeterminate	No data
Residual seizure disorder	Theoretical only	No data	No data
Neuropathy	Theoretical only	No data	No data
Sensorineural deafness	Demonstrated	Indeterminate (MMR)	No data
Insulin-dependent diabetes mellitus	Demonstrated	Indeterminate	Indeterminate
Sterility	Demonstrated	No data	No data
Thrombocytopenia	Demonstrated	Indeterminate	No data
Anaphylaxis	Theoretical only	Indeterminate (MMR)	No data
Polio Vaccine (OPV and IPV)[e]			
Guillain-Barre syndrome	Demonstrated (OPV) Theoretical only (IPV)	For (OPV) Indeterminate (IPV)	For (OPV) No data (IPV)
Transverse myelitis	Demonstrated (OPV) Theoretical only (IPV)	Indeterminate (OPV) No data (IPV)	No data
Poliomyelitis (OPV only)	Demonstrated	For	No data
Thrombocytopenia (IPV)	Theoretical only	No data	No data
Anaphylaxis (IPV)	Theoretical only	No data	No data
Death from SIDS[c]	Theoretical only	Indeterminate	Indeterminate
Death from vaccine-strain viral infection, including from paralytic poliomyelitis (OPV only)[c]	Demonstrated	For	No data
Hepatitis B Vaccine			
Guillain-Barre syndrome	Demonstrated	Indeterminate	No data
Demyelinating diseases of the central nervous system	Demonstrated	Indeterminate	No data
Arthritis	Demonstrated	Indeterminate	No data
Anaphylaxis	Theoretical only	For	No data
Death from SIDS[c]	Theoretical only	Indeterminate	No data

(continued)

TABLE 1-1 *(continued)*

Vaccine and Adverse Event	Biologic Plausibility[2]	Case Reports, Case Series, and Uncontrolled Observational Studies	Controlled Observational Studies and Controlled Clinical Trials
Haemophilus influenzae type b Vaccine			
Guillain-Barre syndrome	Theoretical only	Indeterminate	No data
Transverse myelitis	Theoretical only	Indeterminate	No data
Thrombocytopenia	Theoretical only	Indeterminate	Indeterminate
Susceptibility to early Hib disease[n]	Demonstrated	Indeterminate	For (PRP) Against (conjugated)
Anaphylaxis	Theoretical only	Indeterminate	No data
Death from SIDS[r]	Theoretical only	Indeterminate	No data

[q]*Indeterminate* indicates that there is evidence in this category, but the committee did not consider that, on the whole, it weighed either for or against a causal relation. *No data* indicates that the committee did not find data of this type directly bearing on a causal relation between the vaccine and the adverse event.

[p]The committee considered all adverse events to be theoretically plausible and, therefore, classified plausibility in support of causality as either theoretical only or demonstrated. Demonstrated biologic plausibility refers to information on the known effects of the natural disease against which the vaccine is given and the results of animal experiments and in vitro studies.

[o]Unless noted otherwise, the classification for tetanus toxoid (T), diphtheria-tetanus toxoid for pediatric use (DT), and tetanus-diphtheria toxoid for adult use (Td) is the same. The committee was not charged with assessing monovalent diphtheria toxoid or the combined diphtheria and tetanus toxoids and pertussis vaccine (DPT). In Appendix A, see the Executive Summary of *Adverse Effects of Pertussis and Rubella Vaccines* for conclusions about DPT.

[n]Infantile spasms occur only in the age group that receives DT but not Td or T. A possible causal relation between infantile spasms and Td and T was not examined.

[r]In this table, the committee summarizes the data regarding the causal relation between the vaccine and only those deaths that are classified as sudden infant death syndrome (SIDS) or that are a consequence of vaccine-strain viral infection. SIDS occurs primarily in infants too young to receive tetanus and diphtheria toxoids for adult use, measles vaccine, mumps vaccine, or usually, tetanus toxoid. Therefore, a relation between these vaccines and SIDS was not assessed. If the evidence favors the acceptance of (or establishes) a causal relation between a vaccine and an adverse event, and if that adverse event can be fatal, then in the committee's judgment the evidence favors the acceptance of (or establishes) a causal relation between the vaccine and death from the adverse event. Direct evidence regarding death in association with a potentially fatal adverse event that itself is causally related to the vaccine is limited to tetanus-diphtheria toxoid for adult use and Guillain-Barre syndrome, tetanus toxoid and anaphylaxis, and oral polio vaccine (OPV) and poliomyelitis. Direct evidence regarding death in association with a potentially fatal adverse event that itself is causally related to the vaccine is lacking for measles vaccine and anaphylaxis, MMR and anaphylaxis, OPV and Guillain-Barre syndrome, hepatitis B vaccine and anaphylaxis, and *Haemophilus influenzae* type b unconjugated PRP vaccine and early-onset *Haemophilus influenzae* type b disease in children age 18 months or older who receive their first Hib immunization with unconjugated PRP vaccine. See Chapter 10 for details. The data are indeterminate regarding the causal relation between the vaccine and causes of death other than those discussed above. Data regarding death as an adverse consequence of the vaccines under review are discussed in Chapter 10 rather than in the vaccine-specific chapters.

[s]The committee was charged with assessing the causal relation between several adverse events and measles vaccine or mumps vaccine. The committee was not charged with assessing monovalent rubella vaccine. In Appendix A, see the Executive Summary of *Adverse Effects of Pertussis and Rubella Vaccines* for conclusions regarding rubella vaccine. [t]MMR1 indicates that the data derive exclusively from the multivalent preparation.

[u]OPV is oral polio vaccine; IPV is inactivated polio vaccine.

[v]The committee assessed data regarding the increased susceptibility to *Haemophilus influenzae* type b disease within 7 days of immunization with *Haemophilus influenzae* type b vaccine. For this adverse event only, the committee was able to separate the data regarding the unconjugated (PRP) vaccine from the data regarding the conjugated vaccines.

TABLE 1-2 Conclusions Based on the Evidence Bearing on Causality

DT/Td/T	Measles[a]	Mumps[a]	OPV/IPV[a]	Hepatitis B	*H. influenzae* type b
Category 1: No Evidence Bearing on a Causal Relation					
		Neuropathy	Transverse myelitis (IPV)		
		Residual seizure disorder	Thrombocytopenia (IPV)		
			Anaphylaxis (IPV)		
Category 2: The Evidence Is Inadequate to Accept or Reject a Causal Relation					
Residual seizure disorder other than infantile spasms	Encephalopathy	Encephalopathy	Transverse myelitis (OPV)	Guillain-Barre syndrome	Guillain-Barre syndrome
Demyelinating diseases of the central nervous system	Subacute sclerosing panencephalitis	Aseptic meningitis	Guillain-Barre syndrome (IPV)	Demyelinating diseases of the central nervous system	Transverse myelitis
Mononeuropathy	Residual seizure disorder	Sensorineural deafness (MMR)	Death from SIDS[c]	Arthritis	Thrombocytopenia
Arthritis	Sensorineural deafness (MMR)	Insulin-dependent diabetes mellitus		Death from SIDS[c]	Anaphylaxis
	Optic neuritis	Sterility			Death from SIDS[c]
Erythema multiforme	Transverse myelitis	Thrombocytopenia			
	Guillain-Barre syndrome	Anaphylaxis[d]			
	Thrombocytopenia				
	Insulin-dependent diabetes mellitus				
Category 3: The Evidence Favors Rejection of a Causal Relation					
Encephalopathy[e]					Early onset *H. influenzae* b disease (conjugate vaccines)
Infantile spasms (DT only)[f]					
Death from SIDS (DT only)[f,g]					
Category 4: The Evidence Favors Acceptance of a Causal Relation					
Guillain-Barre syndrome[h]	Anaphylaxis[d]		Guillain-Barre syndrome (OPV)		Early-onset *H. influenzae* b disease in children age 15 months or older who receive their first Hib immunization with unconjugated PRP vaccine
Brachial neuritis[h]					

(continued)

TABLE 1-2 *(continued)*

DT,Td/T	Measles[a]	Mumps[a]	OPV/IPV[b]	Hepatitis B	*H. influenzae* type b
Category 3: The Evidence Establishes a Causal Relation					
Anaphylaxis[a]	Thrombocytopenia (MMR)		Poliomyelitis in recipient or contact (OPV)	Anaphylaxis	
	Anaphylaxis (MMR)[d]				
	Death from measles vaccine-strain viral infection[c,d]		Death from polio vaccine-strain viral infection[c,d]		

[a]If the data derive from a monovalent preparation, then in the committee's judgment the causal relation extends to multivalent preparations. If the data derive exclusively from MMR, that is so indicated by (MMR). In the absence of any data on the monovalent preparation, in the committee's judgment the causal relation determined for the multivalent preparations does not extend to the monovalent components.

[b]For some adverse events, the committee was charged with assessing the causal relation between the adverse event and only oral polio vaccine (OPV) (paralytic and nonparalytic poliomyelitis) or only inactivated polio vaccine (IPV) (anaphylaxis and thrombocytopenia). If the conclusions are different for OPV than for IPV for the other adverse events, that is so noted.

[c]This table lists weight-of-evidence determinations only for deaths that are classified as SIDS and deaths that are a consequence of vaccine-strain viral infection. However, if the evidence favors the acceptance of (or establishes) a causal relation between a vaccine and an adverse event, and that adverse event can be fatal, then in the committee's judgment the evidence favors the acceptance of (or establishes) a causal relation between the vaccine and death from the adverse event. Direct evidence regarding death in association with a vaccine-associated adverse event is limited to tetanus-diphtheria toxoid for adult use (Td) and Guillain-Barré syndrome, tetanus toxoid and anaphylaxis, and OPV and poliomyelitis. Direct evidence regarding death in association with a potentially fatal adverse event that itself is causally related to the vaccine is lacking for measles vaccine and anaphylaxis, MMR and anaphylaxis, OPV and Guillain-Barré syndrome, hepatitis B vaccine and anaphylaxis, and *H. influenzae* type b unconjugated PRP vaccine and early-onset *H. influenzae* type b disease in children age 18 months or older who receive their first Hib immunization with unconjugated PRP vaccine. See Chapter 10 for details.

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[d]The evidence that establishes a causal relation for anaphylaxis derives from MMR. The evidence regarding monovalent measles vaccine favors acceptance of a causal relation, but are less convincing, mostly because of incomplete documentation of symptoms or the possible attenuation of symptoms by medical intervention.

[e]The evidence derives from studies of diphtheria-tetanus toxoid for pediatric use (DT). If the evidence favors rejection of a causal relation between DT and encephalopathy, then in the committee's judgment the evidence favors rejection of a causal relation between Td and tetanus toxoid and encephalopathy.

[f]Infantile spasms and SIDS occur only in an age group that receives DT but not Td or tetanus toxoid.

[g]The evidence derives mostly from DPT. Because there are supportive data favoring rejection of a causal relation between DT and SIDS as well, if the evidence favors rejection of a causal relation between DPT and SIDS, then in the committee's judgment the evidence favors rejection of a causal relation between DT and SIDS.

[h]The evidence derives from tetanus toxoid. If the evidence favors acceptance of (or establishes) a causal relation between tetanus toxoid and an adverse event, then in the committee's judgment the evidence favors acceptance of (or establishes) a causal relation between DT and Td and the adverse event as well.

[i]The data come primarily from individuals proven to be immunocompromised.

The committee organized these conclusions into five categories. Because some confusion has arisen over the meaning of the category descriptions used by the Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines, despite extensive explanations in both the footnotes and the text, the Vaccine Safety Committee adopted some minor modifications in wording intended to help in the interpretation of the present report. To facilitate reading by those familiar with the report of the previous committee, the present committee maintained both the number of categories (five) and the order of those categories but modified the wording in an attempt to clarify its meaning. However, the Vaccine Safety Committee (which has some overlap in committee membership and staff with the earlier committee) believes that the categories represent the same concepts intended by the predecessor committee. The categories are:

1. No evidence bearing on a causal relation
2. The evidence is inadequate to accept or reject a causal relation
3. The evidence favors rejection of a causal relation
4. The evidence favors acceptance of a causal relation
5. The evidence establishes a causal relation

Chapter 2 contains a discussion of the criteria used by the committee for each determination of the final weight of evidence.

The evidence favors rejection of, favors acceptance of, or establishes a causal relation between a vaccine and an adverse event in approximately one third of the relations studied. For the other relations the evidence was inadequate to accept or reject a causal relation or there was no evidence bearing on the relation. It is important to note that the use of the term *inadequate* does not necessarily imply that the data were scarce. In some cases the committee identified an abundance of data. However, as a whole, it did not favor either acceptance or rejection of a causal relation. In the lists below, the superscript letters refer to the appropriate notes in Table 1-2. The notes in Tables 1-1 and 1-2 are integral to interpretation of the findings. The committee reached the following conclusions regarding causality.

The evidence favors rejection of a causal relation between:

- diphtheria and tetanus toxoids and encephalopathy,[c] infantile spasms,[d] and death from sudden infant death syndrome (SIDS);[e,g] and
- conjugate Hib vaccines and early-onset Hib disease.

The evidence favors acceptance of a causal relation between:

- diphtheria and tetanus toxoids and Guillain-Barré syndrome[h] and hospital reentry,[b]
- measles vaccine and anaphylaxis,[d]

- oral polio vaccine and Guillain-Barré syndrome, and
- unconjugated (PRP) Hib vaccine and early-onset Hib disease in children age 18 months or older who receive their first Hib immunization with unconjugated (PRP) vaccine.

The evidence establishes a causal relation between:

- diphtheria and tetanus toxoids and anaphylaxis,[b]
- measles vaccine and death from measles vaccine-strain viral infection,[f]
- measles-mumps-rubella vaccine and thrombocytopenia and anaphylaxis,
- oral polio vaccine and poliomyelitis and death from polio-vaccine-strain viral infection,[f] and
- hepatitis B vaccine and anaphylaxis.

For the vast majority of vaccine-adverse event relations studied, the data came predominantly from uncontrolled studies and case reports. Most of the pathologic conditions studied are rare in the general population. The risk of developing these conditions because of vaccination would *seem* to be low. Without age-specific incidence rates and relative risk estimates, however, it is not possible to calculate the proportion of individuals whose condition is causally related to a vaccine. When the data permitted, such calculations (i.e., the risk difference or excess risk) were made and can be found in the conclusions in Chapters 5 through 9. Because age-specific incidence rates were not available for many of the pathologic conditions studied and because controlled epidemiologic studies of these relations are lacking, few such estimates could be made.

NEED FOR RESEARCH AND SURVEILLANCE

During its attempt to find evidence regarding causality, the committee identified needs for research and surveillance of adverse events. Work in these areas will help to ensure that all vaccines used are as free from the risk of causing adverse events as possible. Some of the needs identified are for increased surveillance of reports of demyelinating disease and arthritis following hepatitis B vaccination, better follow-up of reports of death and other serious adverse events following vaccination, increased use of large databases (currently used only on a small scale) to supplement passive surveillance reporting systems, and disease registries for the rare pathologic conditions studied by the committee.

REFERENCES

Fowler III, Wilson. Vaccination: Social Violence and Criminality: The Medical Assault on the American Brain. Berkeley, CA: North Atlantic Books, 1981.

Coulter HL, Fisher BL. DPT: A Shot in the Dark. San Diego: Harcourt Brace Jovanovich; 1985.
Iglehart IK. Compensating children with vaccine related injuries. New England Journal of Medicine 1987;316:1282-1288.
Institute of Medicine. Adverse Effects of Pertussis and Rubella Vaccines. Washington, DC: National Academy Press; 1991.
Institute of Medicine. Vaccine Supply and Innovation. Washington, DC: National Academy Press; 1985.
Mariner WK. The National Vaccine Injury Compensation Program: update. Health Affairs 1992(Spring):255-265.
Miller NZ. Vaccines: Are They Really Safe and Effective? A Parent's Guide to Childhood Shots. Santa Fe, NM: New Atlantean Press; 1992.
Office of Technology Assessment. Compensation for Vaccine Related Injuries: A Technical Memorandum. Washington, DC: U.S. Government Printing Office; 1980.
Wilson GS. The Hazards of Immunization. London: The Athlone Press; 1967.
WRC-TV DPT: Vaccine Roulette. Washington, DC: WRC-TV; 1982.

2

Causality and Evidence

CAUSALITY

Definitions

The concept of causality is of cardinal importance in health research, clinical practice, and public health policy. It also lies at the heart of this committee's charge: to make causal inferences about the relation between vaccines routinely administered to children in the United States and several specific adverse health outcomes. Despite its importance, however, causality is not a concept that is easy to define or understand (Kramer and Lane, 1992). Consider, for example, the relation between vaccine x and Guillain-Barré syndrome (GBS). Does the statement "Vaccine x causes GBS" mean that (1) all persons immunized with vaccine x will develop GBS, (2) all cases of GBS are caused by exposure to vaccine x, or (3) there is at least one person whose GBS was caused or will be caused by vaccine x?

The first interpretation corresponds to the notion of a *sufficient cause*; vaccine x is a sufficient cause of GBS if all vaccine x recipients develop the disease. Vaccine x is a *necessary cause* of GBS if the disease occurs only among vaccine x recipients (second interpretation above). Although the idea that a "proper" cause must be both necessary and sufficient underlies Koch's postulates of causality (see Glossary in Appendix C), it is now generally recognized that for most exposure-outcome relations, exposure (i.e., the putative cause) is neither necessary nor sufficient to cause the

A REVIEW OF SELECTED FEDERAL VACCINE AND IMMUNIZATION POLICIES

OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC

1980

NIAID (Austrian)—San Francisco (Kaiser) Trial, 1975-77

Austrian, with the cooperation of Marvin A. Fried, conducted a large clinical trial involving 13,600 subjects 45 years of age and older enrolled in the Kaiser Permanente Health Plan in San Francisco, California (Austrian, et al., 1976). A total of 6,850 subjects received a 12-valent vaccine (Types 1, 3, 4, 6, 7, 8, 9, 12, 14, 18, 19, 23) produced by Eli Lilly, and 6,750 subjects received a saline placebo.

Data from this study have not been completely analyzed, so there is as yet no conclusive evidence from this study of this vaccine's efficacy in preventing pneumococcal pneumonia. Nonetheless, two findings can be reported. First, no cases of pneumococcal bacteremia caused by the serotypes represented in the vaccine were reported among vaccine recipients, whereas four such cases were reported among controls. Second, about 60 percent of those who received pneumococcal vaccine reported no adverse reactions, about 40 percent experienced discomfort or pain at the injection site, 35 percent developed redness at the injection site, and 3.4 percent developed a mild fever (Austrian, et al., 1976).[7]

NIAID (Ammann)—San Francisco (Univ. of Calif.) Trial, 1974-76

Arthur Ammann tested the safety and efficacy of a Lilly-produced 8-valent pneumococcal polysaccharide vaccine (Types 1, 3, 6, 7, 14, 18, 19, and 23) among children believed to be at high risk of contracting pneumococcal disease (Ammann, 1977). These children, who had either sickle-cell anemia or inadequate spleen function, were vaccinated at the University of California, San Francisco Medical Center.

Ammann administered Lilly's 8-valent pneumococcal vaccine to 96 high risk children: 77 patients with sickle-cell anemia and 19 with inadequate spleen function. He then measured and compared antibody responses to the vaccine among these unhealthy children with antibody responses elicited by the vaccine among 44 healthy children.

Ammann also immunized another 38 healthy young people and observed them specifically for adverse reactions. Further, during a 2-year postimmunization period, Ammann compared the incidence of pneumococcal infection among the 77 vaccinated sickle-cell patients with that among 106 unvaccinated sickle-cell patients.

Antibody titer responses to pneumococcal vaccine among the 96 high risk children were good and did not differ significantly from the responses among the 44 healthy children. Among the 77 sickle-cell patients, the mean fold increase in indirect hemagglutination titers (i.e., the postimmunization titer divided by preimmunization titer) ranged from 1.65 (Type 19) to 12.55 (Type 3). Among the 19 asplenic children, the corresponding mean fold increase in titers ranged from 1.46 (Type 19) to 18.36 (Type 3). Among both these groups of patients, a mean fold increase of 2.00 or more was recorded 3 to 4 weeks after immunization for six of the eight types of pneumococci represented in the vaccine. A mean fold increase of 2.00 or more for six of the eight types also was recorded among both groups of patients 1 year after immunization.

The only adverse reactions Ammann found were local pain at the injection site and one case of brief fever (38° C). During a 2-year postimmunization period, he found no cases of pneumococcal infection among the 77 vaccinated sickle-cell patients and eight cases among the 106 unvaccinated sickle-cell patients who served as controls.

Based on his results, Ammann's conclusions were that 1) the 8-valent pneumococcal polysaccharide vaccine stimulates type-specific antibody formation in patients with inadequate spleen function, 2) the vaccine may help reduce the incidence of pneumococcal infection in sickle-cell patients and 3) the vaccine produces very few adverse reactions.

[7] See tables 7 and 8 in ch. 3.

Appendix 3.7
CDC'S PASSIVE, VOLUNTARY CASE REPORTING SYSTEM FOR MONITORING ADVERSE REACTIONS TO LICENSED VACCINES[1]

Introduction

Vaccinations are recommended and administered to millions of children and other individuals each year on the presumption that the benefits far outweigh the risks. The benefit side of the equation is straightforward: vaccinations can prevent serious disease. The risk side is not as straightforward, since it includes factors that are known and others that

[1] This appendix (apart from the title) is a verbatim reproduction of CDC's official written description of its system for monitoring and reporting adverse reactions to licensed vaccines.

nay exist but have not yet been discovered. It is necssary, therefore, to maintain surveillance of potential risks of vaccination to continually reevaluate whether individual vaccinations are, on balance, ;ood for people. Such surveillance is important, not nly to provide potential vaccinees with accurate information about the consequences of vaccination, ut also to stimulate improvements in the vaccination process or recommendations that will minimize r eliminate the risks.

The surveillance of these risks, or adverse reactions to vaccination, can be carried out actively or assively. In the active approach, systematic and intensive efforts are made to obtain reports of all dverse effects following vaccination. An example of his is a clinical field trial, required for licensure of a ew vaccine. In the passive approach, a mechanism s established by which individuals may voluntarily eport vaccine reactions. The active approach is comrehensive, but costly in terms of personnel time and ther resources. The passive approach is not compreensive, but it can be reasonably efficient at detecting evere and uncommon reactions without substantial xpenditures of time and resources since it makes aximum use of existing reporting mechanisms and rocedures.

The following discussion describes a passive sys:m for monitoring adverse reactions to vaccination iat should be used by all immunization projects. Included will be a form for reporting adverse reactions o the Center for Disease Control where a National dverse Reactions Monitoring System will be maintined.

ystem Description

The system description will center around these pics:

- designation of adverse reaction coordinators,
- establishment of a reporting mechanisms,
- stimulation of reporting,
- criterion for reporting, and
- submission of reaction reports to CDC.

)esignation of Adverse Reaction :oordinators

The responsibility for establishing an Adverse Re:tion Monitoring System is that of each Immuniza:on Project Office. The first step is to designate an dividual on the Immunization Project staff to serve System Coordinator. This individual will then be sponsible for establishing the system in the Project ea and for coordinating its operation.

In establishing the system, the first task of the Sysm Coordinator should be to have Adverse Reaction Coordinators designated in each local health jurisdiction within the Project area. These could be individuals in county health departments or large public clinics. In addition, Adverse Reaction Coordinators should be designated in hospital emergency rooms wherever possible and representatives of the State and local medical societies and pediatric organizations should be invited to serve as liaison people to the system to promote the reporting of reactions from the private sector. (The establishment of these contacts can be delegated to the local coordinators.)

The designation of Adverse Reaction Coordinators will create a surveillance network which can be used to collect information about vaccine reactions and channel the reports to the points at which analysis can be carried out. These local Coordinators will have the specific responsibilities of implementing a reporting mechanism in their areas, of stimulating reporting by the public and local immunization providers, and of making sure that reports are submitted promptly and correctly to the Immunization Project Office. The System Coordinator in the Central Office may be the logical person to be responsible for monitoring all phases of the operation and for submitting reaction reports to the Center for Disease Control. Copies of the reports should be forwarded to the Regional Offices.

Establishment of a Reporting Mechanism

The next task of the System Coordinator is the establishment of a mechanism through which the public and immunization providers can easily report vaccine reactions. One possibility is the installation of a toll-free telephone which can be called without charge from anywhere within the Project area. Another possibility is the designation of local telephones in each health jurisdiction for receiving reaction reports. Both methods may be used conjointly.

The telephones should be attended during regular business hours by the designated Coordinator or other health professionnal. A supply of the form, "Report of Illness Following Vaccination" (Exhibit One),[8] should be kept near the telephone(s) so that reports can be documented on it directly. Consideration should be given to the use of tape recording units to handle calls made after hours.

Telephone communication should be the primary mechanism for receiving reaction reports in a Project Area. It may be supplemented, however, by a mechanism for receiving reports through the mail, primarily from immunization providers. This can be effected by supplying providers with the report form

[8] CDC's "Report of Illness Following Vaccination" form (Exhibit One) appears in this appendix as figure 3.7A.

THE VACCINE REACTION

"When it happens to you or your child, the risks are 100%"

Vol.1, No.4 *Published bi-monthly by the National Vaccine Information Center* Sept/Oct 1995

Barbara Loe Fisher, Editor

To The Reader: Since the beginning of September, I have been engaged in a remarkable dialogue with a scientist at the University of Southern California whose work I became aware of after reading an article published in the Riverside Press on August 28. Although the content for the September-October issue of *THE VACCINE REACTION* had already been scheduled, I came to the conclusion that this story was of such importance and potentially impacts upon so many individuals suffering from unexplained neurological, psychiatric and autoimmune disorder symptoms, that the entire issue should be devoted to covering it. I do not believe the significance of this research should be underestimated or minimized and, in the interest of public health and safety, expect that the Food and Drug Administration and Centers for Disease Control officials responsible for insuring the public health and safety will take their responsibilities seriously and act quickly to support continuation of this research to confirm or disprove these scientific findings. Failure to act now could jeopardize the health and well being of every baby born and every child and adult who may already be infected with an atypical cytopathic virus they contracted through exposure to contaminated vaccines or exposure to infected blood or body fluids. - ***The Editor***

DISCOVERY OF AN ATYPICAL VIRUS INFECTING HUMANS LINKED TO VIRAL VACCINES PRODUCED ON MONKEY TISSUES

In what could be one of the most important scientific discoveries of this decade, an award-winning pathologist and immunologist at the University of Southern California, W. John Martin, M.D., Ph.D., has discovered an atypical virus infecting both children and adults who are exhibiting neurological, psychiatric and autoimmune disorder symptoms with diagnoses including chronic fatigue syndrome, fibromyalgia, depression, schizophrenia, anxiety disorder, seizures, developmental delays, autism, lupus, multiple sclerosis, Alzheimer's, Parkinson's, unexplained encephalopathy and chronic vegetative states. Martin and his colleagues at USC's Infectious Diseases and Molecular Pathology Laboratories have been meticulously culturing out stealth viruses from patients for the past eight years and, in a stunning development earlier this year, successfully identified one of the viruses as being of African green monkey origin by using DNA sequence analysis. Kidney tissues from African green monkeys have been used to make the live oral polio vaccine (OPV) as well as other viral vaccines during the past three decades.

YOU CAN BE INFECTED AND NOT BE SICK - A distinctive feature of the virus Martin and his colleagues has characterized is that it belongs to a novel class of atypical cytopathic viruses (capable of causing pathologic changes in cells), which they refer to as

it into cats. In an article to be published in the December issue of Pathobiology, they report their remarkable findings of what happens to the cats after they have been infected with the virus.

THE MONEY HAS RUN OUT - A casualty of the budget cuts that are hitting California and other localities across the country, the minimal funding that has helped USC's Infectious Diseases and Molecular Pathology Lab conduct stealth virus research has now been exhausted. The Lab has been forced to drastically cut back on its research linking the proliferation of atypical neurologic, psychiatric and immune system disorders in children and adults to the detection of an atypical cytomegalovirus whose genetic code is almost identical to that of a virus that is commonly present in the kidney tissues of the African green monkey and could have, therefore, been inadvertently transmitted to humans during the production of the oral polio vaccine. Committed to continuing their research because they know their discovery has the potential to save lives, Martin and his seven colleagues have continued to work without pay for the past month in an effort to keep USC's lab open.

AN APPEAL TO THE FDA - Dr. Martin, who is professor of pathology and director of USC's Infectious Diseases and Molecular Pathology Lab, has received numerous awards, scholarships and fellowships during his 30-year career as a distinguished scientist at Harvard, University College in London, University of Sydney in Australia, NIH, Food and Drug Administration, and the National Cancer Institute. In June, Dr. Martin and S. Zaki Salahuddin, Ph.D., Li Chang Zeng, M.D., Khalid Ahmed, M.T., Jing G. Seward, M.D., John-Carl Olsen, Inderjit Singh Seehrai, M.D., and Mark Nowicki, Ph.D., applied to the FDA for a 6-month grant to:

1) Determine the prevalence of simian cytomegalovirus derived stealth viral infection in humans;

They are proposing a simple, quick and cost-effective way to do that by performing serological, polymerase chain reaction (PCR) and viral culture testing of blood and lymphocyte samples already stored in the National Heart, Lung and Blood Institute at NIH which were obtained during the federally funded Transfusion Safety Study (TSS) conducted in the 1980's. The University of Southern California acted as the prime contractor for the TSS, a study which was conducted because of the fear that blood products were contaminated with viruses, including HIV. The goal of the Transfusion Safety Study was to try to determine the prevalence of viral infections, including HIV, in well defined populations in the U.S..

In addition to the proposal to test the TSS samples for stealth virus infection, Martin has already obtained permission from the Los Angeles County - University of Southern California Medical Center's Institutional Review Board to test blood and fluid samples stored in their archives if funding can be obtained to do it. The scientists estimate that if they tested a total of 250 blood samples from both of these sources, it would be adequate to make an initial scientific determination of the scope of stealth virus presence in the U.S. population.

2) To screen monkey colonies used for the production of viral vaccines for the presence of stealth viruses.

Serious Reports by Criteria for Selected Vaccines

	Total Reports*	Total Serious**	Life-threatening	Hospitalized	Disabled	Died***
DTP	7321	1269	133	975	72	246
OPV	5832	1015	144	759	49	229
HIB Vaccine	5059	1027	121	781	36	225
Hepatitis B	4227	383	37	241	108	17
MMR	3502	434	50	372	43	26
Td	830	46	7	36	8	1
DT	268	27	6	21	2	3
Vaccines on VIT	10,969	1,710	193	1,332	162	278
Vaccines not on VIT	10,944	1,740	218	1,308	183	288
Total Database	17,221	2,625	301	1,935	316	360

* A report may contain more than one vaccine. These columns should not be added.

** More than one serious criterion may occur concurrently on one report.

*** This column represents the reports where death was selected in item 8 on the VAERS form, and does not represent a determination that death was the direct result of vaccine administration.

When reviewing and evaluating data from VAERS, it is important to note that for any reported event, no cause and effect relationship has been established. The event may have been related to an underlying disease or condition, to drugs being taken concurrently, or may have occurred by chance at the same time the vaccine was administered.

Accumulated reported events should not be used to calculate incidence or estimates of risk. They must be carefully interpreted as reporting rates and not occurrence or incidence rates.

Reports Stating That Only One Vaccine Was Administered November 1, 1990 - July 31, 1992

	Reports	Total Serious*	Life-threat	Hosp	Disabled	Died
DTP	853	72	11	50	15	3
OPV	15	9	2	6	3	1
HIB Vaccine	404	71	9	56	6	8
Hepatitis B	3507	229	27	138	76	9

* More than one criterion for serious may occur concurrently on one report; therefore, the columns of types of serious should not be added to obtain the total number of serious reports.

When reviewing and evaluating data from VAERS, it is important to note that for any reported event, no cause and effect relationship has been established. The event may have been related to an underlying disease or condition, to drugs being taken concurrently, or may have occurred by chance at the same time the vaccine was administered.

Accumulated reported events should not be used to calculate incidence or estimates of risk. They must be carefully interpreted as reporting rates and not occurrence or incidence rates.

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EMBARGOED: NOT FOR PUBLIC RELEASE BEFORE 6 P.M. EST WEDNESDAY, MARCH 2

NEW FINDINGS SUGGEST POSSIBLE LINK BETWEEN DPT VACCINE AND CERTAIN FORMS OF BRAIN DYSFUNCTION IN RARE CASES

WASHINGTON -- A 10-year follow-up on the children involved in a British study to investigate the relationship between diphtheria-pertussis-tetanus (DPT) vaccination and brain dysfunction led an Institute of Medicine (IOM) committee to conduct a new assessment. The committee concluded that the evidence is insufficient to indicate that DPT vaccination increases the number of children with chronic brain dysfunction because the dysfunction reported by the British researchers might be related to underlying brain or metabolic abnormalities.

Nevertheless the committee concluded that the evidence suggests -- but does not prove -- a possible link between DPT and chronic brain dysfunction, or death, in some of the children who experience a serious, acute neurologic illness within seven days of vaccination. The committee only can extend its conclusions to those acute and chronic brain dysfunctions as studied by the British researchers.

Both the IOM committee and British researchers emphasized that these data refer to rare occurrences and should not alarm parents. The number of cases of acute encephalopathy, or short-term brain damage, expected to result from DPT ranges from 0 to 10.5 per million immunizations. The subsequent risk of chronic brain dysfunction, or long-term brain damage, is smaller.

(MORE)

Limited copies of the report, *DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis*, are available from the Health Promotion and Disease Prevention Division, Institute of Medicine, at the letterhead address; tel. (202) 334-3935. Reporters may obtain copies from the Office of News and Public Information, also at the letterhead address (contacts listed above).

"As a pediatrician, I would not advise parents to forego DPT vaccinations for their children," said committee chair Richard B. Johnston Jr., adjunct professor of pediatrics at the Yale University School of Medicine, New Haven, Conn., and medical director at March of Dimes, White Plains, N.Y. "Diphtheria, pertussis, and tetanus are potentially serious diseases that pose real, proven threats to unvaccinated infants and children."

In 1991 IOM issued a report that found a causal link between DPT and acute encephalopathy. The evidence was insufficient at that time to indicate a causal relationship between DPT and long-term brain dysfunction. The appearance of a single, new report -- the 10-year follow-up to Britain's National Childhood Encephalopathy Study (NCES) -- prompted IOM to re-evaluate the possibility that DPT might cause long-term brain dysfunction.

The NCES, original results of which were published in 1981, is a case-control study of serious, acute neurologic illnesses in children in Great Britain and the only systematic study of long-term dysfunctions after vaccination with DPT.

Results of follow-up assessments of the NCES children were grouped into six areas of dysfunction -- neurological, behavioral, educational, motor, sensory, and the ability to care for one's self.

The IOM study was supported by funds coordinated by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health, Bethesda, Md.

The Institute of Medicine is a private, non-profit organization that provides health policy advice under a congressional charter granted to the National Academy of Sciences. A committee roster is attached.

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INSTITUTE OF MEDICINE
Division of Health Promotion and Disease Prevention

Committee to Study New Research on Vaccines

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Supplement

Pediatrics

AMERICAN ACADEMY OF PEDIATRICS ELK GROVE VILLAGE IL 60009-0927

in a randomized, double-blind fashion, and in this study the difference between the reaction rates following the extracted vaccine varied only slightly from the comparative whole-cell vaccines. The local reactions were less frequent with extracted vaccine, although the systemic reactions were not significantly different.[320]

In addition, there are no specific data concerning efficacy or frequency of uncommon temporally related severe neurologic events with this extracted vaccine. In terms of currently identified pertussis components, the extracted vaccine was not characterized or standardized and efforts to duplicate the vaccine suggested significant product variability.

Possible Components of Acellular Vaccines

Recent studies have significantly advanced our understanding of antigenic and other biologically active pertussis components.[12,32–34,37,38,40,44–46,48,55,56,60,75,76,123,135,138,166,261,322,323] Data regarding these *B pertussis* components and their role in the pathogenesis of infection and disease have been extensively reviewed earlier in this report (see "Antigenic and Biologically Active Factors," p 939; Table 1; and "Pathogenesis of *B pertussis* Infection, p 947). This information has afforded the theoretical potential for designing vaccines that contain only relevant protective antigens, free of extraneous materials.

Development of Acellular Vaccines in Japan

In Japan, pertussis component vaccines have been developed that mainly contain LPF and FHA.[126,235] Products of six manufacturers, using slightly varying processes, have been marketed. Component vaccines produced in Japan are of two types, B type containing approximately equal amounts of LPF and FHA and T type containing a preponderance of FHA, a lesser amount of LPF, and some agglutinogens. More than 30 million doses have been administered to children, largely T type. It is the T type that has had preliminary studies of toxicity and immunogenicity in the United States and the B type that was used in the recent Swedish efficacy trials. Acellular vaccines have been used for routine immunization starting at age 24 months in Japan since October 1981. The data concerning protection and side effects are derived from immunization of 2-year-old children and may or may not be applicable to immunization of young infants.

Transient Local and Systemic Reactions

In general, transient local and systemic reactions caused by acellular vaccines were less frequent and milder when compared with Japanese conventional whole-cell vaccines. A small number of children in the United States received a Japanese T-type component vaccine and similar mild reactions were observed.[247–249] However, in Japanese clinical studies several findings of special interest were noted. It was noted that local reactions appeared at a much later time after the first dose than following subsequent doses. In one study, the mean interval between immunization and local reaction was 7.9 days following the first dose and decreased to 2.6, 2.2, and 1.9 days following the second, third, and fourth doses.[235] The observation suggested delayed hypersensitivity to the initial dose and an accelerated response to repeat doses, although its significance is unclear. Also, in one study, the frequency of local erythema and induration on the first day after vaccination increased from 6% after the initial dose to 25%, 30%, and 41% with successive doses.[235] In a few cases, following booster doses there was marked erythema and swelling of the arm from the shoulder down to the elbow, some with appearance of blisters.[243] It should be noted that in Japan these adjuvant-containing vaccines are given by deep subcutaneous injection rather than by intramuscular injection, which is the usual method for DTP vaccines that contain an adjuvant.

Temporally Related Severe Events

Following a brief suspension of immunization in 1975 in Japan, immunization was reinstituted using the same whole-cell DTP vaccines starting at 24 months rather than at 3 months of age. Cases of presumed vaccine-associated reactions decreased (Tables 7 and 8). Several years later in 1981, the new acellular pertussis vaccines were substituted, but the practice of initiating immunization at 24 months of age was continued with the acellular vaccines.

In the 5 year period from 1970 through 1974, a period when standard whole-cell DTP immunization was started routinely at 3 to 5 months, there had been a total of 57 severe temporally related events and 37 deaths (9.5 severe reactions and 6.1 deaths per year) including presumed vaccine-associated encephalopathy and other CNS diseases, as determined by claims paid by the Japanese national compensation system. When whole-cell vaccines were initiated at 24 months of age, in the six years between 1975 and 1980, there were eight severe temporally related events (average 1.6 year) and three deaths. The whole-cell DTP vaccines used in the latter period were equivalent to those in prior use. Thus, the age of starting routine immunization appears to be a far

TABLE 7. Claims Paid by Vaccine Compensation System in Japan, 1970 through 1984*

Reactions	1970–January 1975		February 1975–August 1981		September 1981–1984	
	No. of Cases	No. of Deaths	No. of Cases	No. of Deaths	No. of Cases	No. of Deaths
With sequelae	57	37	8	3	5	2
Encephalopathy	29	21	2	1	0	0
Encephalitis	2	1	0	0	2	0
Acute infectious hemiplegia	2	0	1	0	1	0
Convulsions	8	1	3	1	1	1
Infantile spasm	2	0	0	0	0	0
Sudden death	11	11	0	0	0	0
Other	3	3	2	1	1	1
Without sequelae	82		34		14	
Mild encephalopathy	14		1		0	
Acute cerebellar ataxia	0		1		1	
Convulsions	4		0		0	
Febrile seizure	27		12		1	
Mild shock	8		3		1	
Exanthem	7		3		0	
Abscess	5		3		0	
Local reactions	8		7		11	
Others	9		4		0	

* From Noble et al.[238] Reproduced with permission.

more important determinant of temporally associated reactions than the switch from conventional whole-cell vaccines to acellular vaccines.

The conclusion can be drawn that either (1) DTP prepared with whole-cell *B pertussis* is less likely to cause neurologic disease when begun at 24 months or (2) the purported reactions in infants were in large part unrelated developmental events expected commonly in that age group but attributed to vaccine because they were time related. If the former is true, one cannot assess whether the new acellular pertussis vaccines used in the period from 1981 to 1984 are in fact different from whole-cell vaccines in their encephalopathic potential because they, too, were begun at 24 months of age. The rate of severe reactions does not differ significantly between the acellular and whole-cell vaccines when used at 24 months of age (Table 8). The decrease in severe reactions is slight, if any. The category "sudden death" is also instructive in that the entity disappeared following both whole-cell and acellular vaccines, when immunization was delayed until a child was 24 months of age.

It is clear that delaying the initial vaccination until a child is 24 months, regardless of the type of vaccine, reduces most of the temporally associated severe adverse events. Furthermore, analysis of cases with paid claims in the Japanese national compensation system indicates many of the putative cases to be related to other medical conditions.[243] There are no data at this time that allow prediction of the rate of temporally related severe events that could be expected if Japanese

TABLE 8. Adverse Reactions After Pertussis Immunization, Based on Claims Paid by Compensation System of Japan*

	1970–1974	1975–1980	1981–1984
Vaccine type	Whole cell	Whole cell	Acellular
Age at initiation (mo)	3–5	24	24
No. of doses of vaccine (millions)	25.1	19.8	20.4
No. of severe reactions (deaths) with sequelae	57 (37)	8 (3)	5 (2)
Incidence (deaths)/million doses	2.27 (1.47)	0.40 (0.15)	0.25 (0.10)
No. of mild reactions without sequelae	82	34	14
Incidence of mild reactions/million doses	3.27	1.72	0.69

* From Noble et al.[238] Reproduced with permission. Whole-cell vaccines were routinely administered to infants at 3 months of age until February 1975, when the recommended age was increased to 2 years. Use of whole-cell vaccines in this group continued until September 1981, when acellular vaccines were introduced for routine use in 2-year-old children. Vaccine distribution is based on calendar year, but adverse reaction data correspond to the vaccine type and strategy used.

TONY KNOWLES, GOVERNOR

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February 19, 1996

Honorable Lyda Green
Alaska State Senate
Room 423
State Capitol
Juneau, AK 99801-1182

Dear Senator Green:

Several questions arose during committee deliberation at the recent hearing on SB 185. Among these were:

1. What are the causes of death for the children under age 7 who die each year in Alaska?
2. How many of these deaths are from unknown causes?
3. Do other states or jurisdictions operate a monitoring program similar to what is called for in SB 185?
4. Does the State participate in the Vaccine Adverse Events Reporting System (VAERS)?
5. Are there currently protocols in place that deal with the issue of defective serums?
6. How many non-fatal adverse reactions to inoculations occur in Alaska each year?

The following responds directly to the questions raised and provides additional background information that may be useful to the committee in considering the issues and questions raised during that hearing.

- Over the ten year period 1985 - 1994 an average of 151 children aged seven and under died in Alaska each year. (The number of deaths in this age range has been declining steadily from 186 in 1985 to 113 in 1994.) During this period an average of 29 deaths annually were listed as resulting from SIDS and 3 deaths annually were from unknown causes.

- Our research could find no other state with a monitoring system similar to what is called for in SB 185.

- Alaska's Immunization Program, operated by the Division of Public Health, requires all providers participating in the state's Universal Vaccine Distribution System to report adverse events using Vaccine Adverse Events Reporting System (VAERS) reports.

- All deaths reported to the national Vaccine Adverse Events Reporting System are evaluated and additional information is sought by the Food and Drug Administration (FDA) which assesses vaccine risk before and after licensure.

- The number of adverse reactions associated with vaccine administration in Alaska are few, particularly when viewed in relation to the number of vaccine doses administered. The following tables present information on vaccine doses administered, number of adverse reactions reported, and detailed information on serious adverse reactions in Alaska during the past two years.

Vaccine Doses Administered to Alaska Children (0-9 years of age), 1994-95

Year	Total Doses Administered
1994	67,117
1995	49,216

Number of Reports to the Vaccine Adverse Event Reporting System (VAERS) for Children <age 7, Alaska, 1994-95

Year	Minor or Transient Reaction	Serious* or >1 month Duration
1994	20	3
1995	12	2

* Serious event = requires hospitalization or medical follow-up

Review of "Serious" Adverse Events

Year	Age of Child	Vaccines Received	Event	Outcome
1994	8 weeks	OPV Hib DTP	9 hours after vaccination - became limp and cyanotic; hospitalized for observation	Fully recovered
	2 months	OPV Hib DTP	6 hours after vaccination - continuous crying, 102° fever; observed overnight	Fully recovered
1995	18 months	OPV DTP	18.5 hours after vaccination - 1 seizure, fever > 100° ; not hospitalized	Fully recovered
	16 months	MMR DTP	9 days after vaccination - seizures for 2 hours; hospitalized	Fully recovered
	2 months	OPV Hib DTP	27 hours after vaccination - afebrile seizures, 5-6/day; hospitalized	Not resolved

Some background information on the VAERS may help the committee understand its strengths and limitations.

- The Vaccine Adverse Events Reporting System (VAERS) was created as part of the National Childhood Injury Act of 1986 and is one method of monitoring vaccine safety nationwide.

- Since 1990 VAERS report forms and information about VAERS have been mailed annually to all U.S. physicians who are likely to administer vaccines.

- Strengths of VAERS:
  - provides information on the number of adverse events reported nationwide,
  - permits collection and analyses of vaccine-specific and lot-specific information,
  - potentially identifies risk factors for adverse events that may be contraindications to additional doses,
  - **serves as a sentinel for the detection of either previously unreported vaccine adverse events or unusual increases in reported events.**

- Limitations of VAERS:
  - describes only the number of events reported, without placing in context of number of vaccines given,
  - cannot track the rate of similar events occurring in individuals who were not recently vaccinated,
  - cannot in itself establish causation.

- **A VAERS report does NOT mean that the vaccine caused the adverse event.**
  - The reporting system is "open" to all reports that an individual/provider wishes to make.
  - **The report indicates simply that an event was temporally associated with receipt of a vaccine -- NOT that the vaccine necessarily caused the event.**

In addition to specific questions arising at the recent hearing additional information to place the issue of general vaccine risk, and DTP vaccine risk particularly, in context with scientific knowledge about these risks might prove of value to the committee. The following provides a brief summary I hope will be of use to committee members.

- Infants, unfortunately die for many reasons such as infectious diseases, congenital defects and metabolic disorders which are unrelated to vaccination. However, chance alone dictates that infant deaths will occur from these, and other causes, following a vaccination. Almost all infants are vaccinated during the first year of life. Therefore, **any infant who develops a medical illness or dies is likely to have been vaccinated earlier in life.** Since vaccinations are usually administered three times during infancy (at ages 2, 4, and 6 months) there is an increased chance that any event, including illness or death, can occur within 24 hours of vaccination by coincidence alone.

- The vast majority of vaccine adverse events are minor and temporary, like a sore arm or mild fever. More serious adverse events occur rarely; some are so rare that risk cannot be accurately assessed. There are **so few deaths that could plausibly be attributed to vaccines that it is hard to assess the risk statistically.**

- The concept that DTP causes Sudden Infant Death Syndrome (SIDS) is a myth which developed because a moderate proportion of SIDS deaths occur in children who have recently been vaccinated with DTP. On the surface, this seems to point toward a causal connection. Nearness in time of two events is a common sense reason to examine the potential of a causal relationship. But it does not establish that the first event caused the second. If this logic were applied in a common sense way without scientific investigation **one might conclude that eating bread causes car crashes, since most drivers who crash their cars could probably be shown to have eaten bread within the past 24 hours.**

Because most SIDS deaths occur during the same range of ages when 3 shots of DTP are given, it is inevitable that DTP shots will precede a fair number of SIDS deaths simply by chance. In fact, a number of well-controlled studies have indicated that the SIDS deaths (within the study populations) would have occurred even if no vaccinations had been given. **In fact, in several of the studies children who had recently gotten a DTP shot were *less* likely to get SIDS.**

- **No deaths caused by anaphylaxis following DTP vaccination** have been reported to CDC since the inception of vaccine-adverse-events reporting began in 1978, a period during which more than 80 million doses of publicly purchased DTP vaccine were administered.

- All deaths reported to the national Vaccine Adverse Events Reporting System (VAERS) are evaluated and additional information is sought by the FDA. The deaths have been found to be related to a wide variety of causes. Most importantly, **no specific, clinical syndrome has been identified as would be expected if these deaths had the same cause, i.e., a vaccine reaction.** In consideration of this, a 1994 Institute of Medicine report indicated that the "vast majority of deaths reported to VAERS are temporally but not causally related to vaccination."

- Although no one can guarantee that the vaccines (or any medications) are totally without risk, it is important to look at both the risks and the benefits of vaccine use. **The risks of NOT being vaccinated are much greater than the risks associated with a vaccination.** If there were no vaccines, there would be many more cases of disease, and along with them, more serious side effects, including death.

- **A child is far more likely to be seriously injured by a vaccine preventable disease than by any vaccine.** While any serious injury or death caused by vaccines is too many, it is also clear that the benefits of vaccination greatly outweigh the slight risk, and that many, many more injuries and deaths would occur without them. The table below compares the risk from disease with the risk from the vaccines that protect against them. It illustrates the benefit we get from vaccinating our children.

- Even one serious adverse effect in a million doses of vaccine cannot be justified if there is no benefit from the vaccination. But an analysis of the benefit and risk of DTP immunization, for example, has shown that **without an immunization program there could be a 71-fold increase in cases of pertussis and a nearly 4-fold increase in deaths due to pertussis in the United States.**

Risk from Disease vs. Risk from Vaccines	
Disease	**Vaccines**
Measles Pneumonia = 1 in 20 Encephalitis = 1 in 2,000 Death = 1 in 3,000 **Mumps** Encephalitis = 1 in 300 **Rubella** Congenital Rubella Syndrome = 1 in 4	**MMR** Encephalitis or severe allergic reaction = 1 in 1,000,000
Diphtheria Death = 1 in 20 **Tetanus** Death = 3 in 100 **Pertussis** Pneumonia = 1 in 8 Encephalitis = 1 in 20 Death = 1 in 200	**DTP** Continuous crying, then full recovery = 1 in 100 Convulsions or shock, then full recovery = 1 in 1,750 Acute encephalopathy = 0-10.5 in 1,000,000 Death = None proven Information compiled by the Centers for Disease Control & Prevention (CDC, Atlanta)

- A **risk-benefit analysis** has been performed for the U.S. to compare the outcomes with or without a vaccination program using a hypothetical cohort of 1 million children from birth to 6 years of age who received and did not receive pertussis vaccination. Without a program, the estimated annual number of residual defects from encephalitis (both vaccine and disease induced) would decrease from 54 to 29 cases. However, **the estimated annual deaths from pertussis would increase more than 10-fold, from 44 to 457.**

- The **experiences of other countries** are also useful in evaluating the value of vaccination.

  In the mid-70s, the use of pertussis vaccine was greatly reduced in **Great Britain** because of fear about the vaccine. The effect was dramatic and immediate. A drop in pertussis vaccination in 1974 was followed by an epidemic of more than 100,000 cases of pertussis and **36 deaths** by 1978.

  In **Japan**, pertussis vaccination was used nationwide by 1950. By 1974, pertussis incidence had dropped from 100 cases to 1 case per 100,000 population. However, in the last half of the 1970s, vaccine utilization in Japan markedly decreased after two deaths occurred following pertussis immunization. A major epidemic of pertussis ensued, with an increase in incidence rate to 11.5 per 100,000 in 1977, and an **increase in the annual number of deaths from an average of less than 5 for the years 1970-1974 to an average of 32 during 1977-1979.**

I hope this information is useful to committee members in considering the value of activities proposed in SB 185. Department of Health and Social Services staff will gladly answer additional questions that may arise as members consider this bill.

Sincerely,

Karen Perdue
Commissioner