DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
June 5-6, 1990
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207 at the Centers for Disease Control, Atlanta, Georgia, on June 5-6, 1990. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Samuel L. Katz, Chairman
Dr. James D. Cherry
Dr. David W. Fraser
Dr. W. Paul Glezen
Dr. Caroline B. Hall
Dr. F. Marc LaForce
Dr. H. Denman Scott
Dr. Mary E. Wilson

Ex Officio Members

Dr. Carolyn Hardegree (FDA)
Dr. John R. LaMontagne (NIH)
Dr. Gerald Quinnan (FDA)

Liaison Representatives

Dr. Kenneth Bart (NVP)
Dr. David Fedson (ACP)
Dr. Edward A. Mortimer, Jr. (AMA)
Dr. Michael Peterson (DoD)
Dr. Stanley A. Plotkin (AAP)
Dr. William Schaffner, II (AHA)
Dr. Susan E. Tamblyn (NACI)
Dr. Ronald C. Van Buren (AAFP)

Executive Secretary

Dr. Mary E. Guinan

NAVY ENVIRONMENTAL HEALTH CENTER

CDR David Trump

HHS STAFF PRESENT

CENTERS FOR DISEASE CONTROL

Office of the General Counsel

Mr. Kevin M. Malone

CENTERS FOR DISEASE CONTROL

Employee Health Service Clinic

Dr. Naima Abd Elghany

Epidemiology Program Office

Dr. Melinda Wharton

Center for Infectious Diseases

Dr. James Hughes
Dr. Jay Wenger

Center for Prevention Services

Dr. Bill Atkinson
Dr. Roger Bernier
Dr. Robert Chen
Dr. Steve Cochi
Ms. Rosamond Dewart
Dr. Karen Farizo
Dr. Laura Fehrs
Mr. Conrad Ferrara
Dr. Alan Hinman
Dr. Sonja Hutchins
Mr. Dean Mason
Dr. Bernard Moriniere
Dr. Walter Orenstein
Dr. Peter Patriarca
Mr. George Seastrom
Mr. Bob Snyder
Dr. Mary Ann Sprauer
Dr. Raymond Strikas
Dr. Roland Sutter
Dr. Steven Wassilak
Dr. Walter Williams

Others Present

Wendy Arnold
Jill Chamberlin
Dr. Pinya Cohen
Dr. Corry Dekker
Dr. Maurice Harmon
Rose Mary B. Hoy
Cynsie Johnson
Mike King
Dr. David S. Krause
Dr. Saul Krugman
Dr. Raymond Kuehne
Barbara Kuter
Dace Madore
Mr. Charles Marwick
Steven Mento
Wayne Morges
Dr. David Nalin
Peter Paradiso
Hal Rathfon
Dr. Roselyn J. Rice
Nancy Sabalusky
Karlyn Shedlowski
Dr. Phyllis Stubbs
Agnes Thiellier
M. J. Winship
Dr. Rafal J. Wyszkowski

IMMUNIZATION PRACTICES ADVISORY COMMITTEE
Meeting at
Conference Room 207
Centers for Disease Control
Atlanta, Georgia

AGENDA

Tuesday, June 5

8:30 a.m.	Welcome and Opening Remarks	Dr. Sam Katz Dr. Mary Guinan
8:45 a.m.	Revision of DTP Statement	Dr. Ted Mortimer
9:45 a.m.	Measles Update	Dr. Bill Atkinson Dr. Walter Orenstein
10:30 a.m.	BREAK	
11:00 a.m.	Overview of Research Priorities and Activities in the Division of Immunization -Potential Rubella Vaccine Studies -Current Status of Polio Studies	Dr. Peter Patriarca
12:00 Noon	Current Prospects for EIPV and DTP-EIPV	Dr. Pinya Cohen
12:15 p.m.	LUNCH	
1:30 p.m.	Final Review - Rubella Statement	Dr. Laura Fehrs
3:00 p.m.	BREAK	
3:30 p.m.	Haemophilus influenzae type b	Dr. Jay Wenger
4:15 p.m.	Availability of Vaccinia Immune Globulin	Dr. Bill Atkinson
4:45 p.m.	ADJOURN	

Wednesday, June 6

8:30 a.m.	Final Review - Adult Immunization Statement	Dr. Ray Strikas
10:15 a.m.	BREAK	
10:45 a.m.	Perinatal Hepatitis B Grants	Mr. Dean Mason
11:00 a.m.	To Be Announced	
12:00 Noon	ADJOURN	

6/4/90

The meeting began with a welcome and opening remarks by Dr. Katz and Dr. Guinan. Dr. Walter Dowdle announced a program position change for Dr. Guinan and also expressed gratitude for the contributions of several outgoing members: Dr. Marc LaForce, Dr. Paul Glezen, and Dr. Denman Scott.

Dr. Ted Mortimer: Revision of the DTP Statement

Dr. Mortimer reviewed changes incorporated in the DTP statement with updated data. The changes that are of most interest were in regard to the changing concepts of postvaccination encephalopathy that reflect the questioning of whether the phenomenon is a direct and primary result of the vaccine and the revised section on the contraindications. The changes relating to the issue of postvaccination encephalopathy were brought about by recent new information, reanalysis of old information, and by the reviews of the issue by a number of organizations. These reviews have contributed to changing the interpretation of data upon which recommendations and contraindications have been based, including frequency of the event, whether the association is temporal or causal, and whether adverse events after the first dose presaged more severe adverse events following subsequent doses. While including a number of changes concerning contraindications, the statement also advises that a child with a neurological disorder deserves to be protected from diphtheria, tetanus, and pertussis. Health care providers need to consider carefully the child's history and ensure that the child's caretakers understand the pros and cons of immunization.

In addition to these changes, many references were changed. Data in Table 3 will be revised to be consistent with text.

There was a good deal of discussion concerning the groups who are investigating adverse events following pertussis and rubella immunizations and when these other groups would publish their reports. These groups include the American Academy of Pediatrics, the Institute of Medicine, and the Association of Child Neurologists. In addition, the British and Canadians are also reviewing policy statements. After much discussion about the ACIP statement and the pamphlets being prepared by the Division of Immunization under legislative mandate (vaccine information materials for parents and caregivers), the Committee decided to:

- recommend strongly that CDC delay completing the pamphlets until the other groups investigating this issue publish their reports so that the medical community would have a chance to consolidate opinion and present a unified message--even if this meant getting support at the PHS level to delay making the pamphlets available.
- devote at least one-half day at the next ACIP meeting to review current literature on the subject and investigate all views. Dr. Orenstein offered to send Committee members copies of relevant materials for their consideration before the meeting. Dr. Katz asked that members of the Committee who wanted to submit materials to be included in this review do this by September 1.

In response to one Committee member's question about the acellular vaccine under development, the representative from the Food and Drug Administration (FDA) reported that enrollment in clinical trials was going on and that efficacy studies may be underway by the end of the year.

Dr. William Atkinson and Dr. Walter Orenstein: Measles Update

Dr. Atkinson presented the summary data from 1989 and the available data to date in 1990, which show a substantial increase. (Provisional total for 1989 as of May 11, 1990 was 17,850.) These cases reflect a dramatic increase in the number of cases in all age groups and particularly among children <5 years of age. One-third of all cases in 1989 were unvaccinated, 40% of whom were children between 6 months and 4 years of age. Seventeen percent of those with measles had complications; 16% of this group were hospitalized one or more days. In 1989, deaths associated with measles numbered 41 in the United States and one from Puerto Rico. This was the greatest number since 1971 when 90 measles-associated deaths occurred. Of these 1989 deaths, 29 (71%) were children under age 5; only two of these children were known to be vaccinated and two had underlying medical conditions. Nine of the 10 adults who died were unvaccinated, and nine out of 10 were vaccine eligible. Three had underlying medical conditions. Outbreaks in 1989 numbered 248 with 45% occurring in preschool-age children and 32% in school-age children.

The situation in 1990 is not improving. Forty-two percent of cases this year are under 5 years of age, 28% are apparent vaccine failures, and 35% were unvaccinated, but eligible. There have been 35 reported deaths. CDC is aware of 90 current outbreaks in 25 states, the largest being in Dallas, Los Angeles, Chicago, and Milwaukee. Other outbreaks are occurring in Hispanic communities and in schools.

One committee member asked about available data on doubly vaccinated children and several from the Division of Immunization responded that the mechanism for collecting these data will be in place soon.

Dr. Orenstein reviewed the status of states which had requested and received state funds to implement the two-dose schedule as of May 1990. He also reviewed state policies concerning recommended ages for the two-dose schedule. In addition, Dr. Orenstein reported on the additional money appropriated for outbreak control ($12.0 million added to an original $9.9 million).

In describing a survey of immunization program managers from 63 projects (54 respondents), Dr. Orenstein reported that 96% reported that the supply of the vaccine was adequate, but one-half reported that children in one or more localities were not being adequately vaccinated because of problems with vaccine delivery. Of the 27 projects citing problems, insufficient staff (70%), insufficient clinic hours (56%), and inadequate locations (15%) were considered obstacles to immunization. Other barriers cited were that vaccination was not available on demand and that appointments were needed (93%); some required referral from a physician, while others required enrollment in a well-baby clinic.

Comments and questions by Committee members included discussion of the internal conflicts of delivering comprehensive care versus immunizing everyone, causes of the current outbreaks, decreasing funds at the state level for public health, research into the characteristics of strains of the virus, possible interface with other programs such as WIC and AFDC, and CDC's role in outbreak investigations.

Dr. Peter Patriarca: Overview of Research Priorities and Activities in the Division of Immunization

Dr. Patriarca reviewed Division resources, priorities, and current activities. Staff of the unit includes six medical epidemiologists who conduct both national and international activities. He stated that research activities and needs have been planned by using a Delphi survey of ACIP members (the results of which were distributed to Committee members during the meeting) and by determining long-term (e.g., evaluation of the two-dose schedule) and acute needs (e.g., research on arthralgia and the rubella vaccine).

A principal research priority now concerns measles issues, including evaluation of the two-dose schedule, age at initial vaccination, duration of immunization and vaccine failure, adverse events following first and second doses, improvements in laboratory diagnostics and the establishment of a measles laboratory at CDC, and other miscellaneous activities (e.g., evaluation of safety and immunogenicity for persons who are HIV-positive, and for the perinatal and adult populations).

Domestic research priorities include research in poliomyelitis, including:

- detection of wild virus circulation in the United States. This is not currently being done in the United States, although studies are being conducted (by CID) in Latin America.
- serosurveys in young adults
- serosurveys of inner-city preschoolers
- spread of OPV to susceptible contacts
- a sequential schedule of IPV and OPV to lower risk of vaccine-associated poliomyelitis

Research issues regarding pertussis include:

- additional trials of acellular vaccine
- the need for acellular vaccine in other age groups
- additional risk/benefit information that includes studies of adverse events following DTP vaccination and efficiency of routine surveillance
- the effect of erythromycin as prophylaxis and for which groups (e.g., household contacts)
- Laboratory studies (CID) on antigen detection and on serologic correlates of immunity

Other domestic research issues include:

- vaccine safety--neurologic events following DTP, detection of adverse events using linked databases, chronic arthropathy following rubella vaccination, and others
- efficacy of adult immunization--cost-effectiveness of influenza vaccine in the HMO setting, HCFA/Medicare demonstrations projects, cost-effectiveness of pneumococcal vaccine, and long-term persistence of antibody following MMR
- Others (e.g., collaborative efforts in varicella modelling)

Operational research issues include demonstration projects and "access" studies to determine reasons that cause the system to fail and how to coordinate with other social and public health services, special demonstration projects in high-risk areas, and evaluation studies.

International research projects concerning measles are addressing such issues as levels of antibody following EZ measles vaccine, safety of immunizing of HIV-infected persons (Kinshasa), comparative trials of EZ and AIK-C strains with DTP administered at 4 months of age, comparison of EZ vaccines from different manufacturers, evaluation of morbidity and mortality following widespread use of EZ vaccines in Kinshasa at 6 months of age, alternative routes of measles vaccine administration, and efficacy of Vitamin A in reducing measles mortality. Projects concerning polio (in conjunction with WHO) include vaccine trials on alternative formulations of OPV, EIPV, improved surveillance methods, detection of wild virus in the environment, and evaluation of mass vaccination campaigns.

Laura Fehrs is discussing the possibility with Walter Reed Army Hospital of doing a prospective cohort study of MMR among postpartum women at Army hospitals. Eligibles will be screened prenatally for rubella antigen and then followed after immunization to detect the incidence of arthritis or arthropathy, as well as the persistence of such symptoms.

During the discussion of the proposed research projects that would be done under contract, one Committee member asked about the process of letting the public and research community know about RFPs. Concern was expressed that many qualified researchers may not hear of requests. On the Committee's suggestion, Dr. Guinan promised to investigate the feasibility of CDC issuing a newsletter or utilizing some mechanism for more widespread distribution of research opportunities. In the interim, ACIP members will receive notices of research RFPs so that they are aware of these CDC activities.

Dr. Pinya Cohen (Connaught): Current Prospects for EIPV and DTP-EIPV

Dr. Cohen explained the reorganization of Connaught after its acquisition by Pasteur-Merieux that has occurred over the last three years. He then described the supply of EIPV as limited, but of sufficient quantity to cover limited use as cited in the current statement. Pasteur-Merieux believes its eIPV has fulfilled the requirements for licensure in the United States and hope that the FDA will license it soon. Future plans are to use the Pasteur vaccine as the primary vaccine and the Connaught as back-up as needed.

Dr. Laura Fehrs: Rubella Statement

Dr. Fehrs reviewed the changes in the rubella statement prompted by comments made by Committee members since the last meeting. These changes were in regard to the incidence of arthritis/arthralgia following vaccination with RA27/3 vaccine, the risk to the fetus following maternal rubella immunization, laboratory diagnosis of clinical infection and serologic evidence of rubella immunity, and risk of fetal infection following maternal rubella reinfection. After a review of the medical literature on the last topic, Dr. Fehrs discussed questions raised by reports of maternal rubella reinfection that include whether reinfection can occur in persons with prior adequate immunity, the risk of CRS after documented maternal reinfection, and whether the risk of CRS is associated with maternal level of immunity before exposure, presence or level of maternal IgM or IgA, and/or with neutralization activity. Current information suggests that reinfection can occur and that the risk of CRS following maternal reinfection is yet to be determined, but probably low. Concerning the third question, it is not yet clear from reports

what factors are associated with the risk of infection.

Although the issue of fetal infection caused by maternal reinfection is important, it probably is an infrequent concern because of the low incidence of rubella in the United States (about 400 cases per year, 40%-50% in children). Finally, Dr. Fehrs reviewed the limited techniques for estimating the risk for CRS following reinfection.

Based on this review the Committee made no change in the current statement on this issue.

Dr. Jay Wenger: Haemophilus influenzae type b

Dr. Wenger noted that although many studies showed substantial immunogenicity of Hib conjugate vaccines, efficacy has not yet been demonstrated (when given to infants at 2-6 months of age) in the United States.

Dace Madore, Ph.D., Steven Black, M.D., and Bruce Fireman reported on an efficacy study of the Praxis Hib conjugate vaccine conducted through the Kaiser-Permanente health plan in the Northern California area. The vaccine was administered at 2, 4, and 6 months of age (in conjunction with regular well-care visits). The process for case identification and the partially randomized clinical trial study design was explained. In 1988-89, no cases of Hib disease occurred among vaccinated children. Results from a case-control analysis of available data were also discussed.

Dr. William Atkinson: Availability of Vaccinia Immune Globulin

Currently, there is only one source of vaccinia immune globulin. The Department of Defense (DOD) has 800 vials and CDC is an indirect source with 229 vials. As of the date of this meeting, the entire U.S. supply will expire in 8 days. (CDC's supply came from DOD.) There are an additional 77 vials at CDC that have already expired. Dr. Atkinson described the process that began last January with DOD, FDA, CDC, and the manufacturers to extend the life of current VIG for another two years. Potency testing was completed showing that the serum met quality standards. Testing will continue every four months to assure potency. DOD has decided to appropriate funds to initiate manufacturing of additional VIG.

Dr. Ray Strikas: Adult Immunization Statement

Discussion at the beginning of this presentation centered on whether there was a need for an adult immunization statement because statements on individual disease categories existed in other statements and in the recently published Guide for Adult Immunization, 2nd Edition (American College of Physicians). Members of the Committee felt that it was important and useful to group recommendations for adults in one document, particularly to raise the consciousness of primary care physicians for the need for adult immunizations. Committee members suggested that it would be a good idea to send a notice to professional organizations that deal with adult health care and share this statement.

Dr. Strikas discussed the final changes to the adult immunization statement, which incorporates Committee members' comments from the last meeting. These discussions included:

- Notation of the variable response to immunization in immunocompromised patients and recommendation of antibody testing to determine antibody levels after vaccination, as well as immunoglobulin use upon exposure to infected persons, even for vaccinated immunocompromised persons.
- Skin testing of patients with histories of anaphylactoid reactions to tetanus toxoid. The recommendation for skin testing will remain as written.
- Cutoff date (1957) for measles and mumps immunization policies. (Discussion did not come to closure on this matter. Jim Cherry will draft a statement on this issue and circulate it among Committee members.)
- Assessment of polio vaccination status of adult immigrants, refugees, and foreign students as well as all adults 18-24 years of age. Although members thought this was ideal, it was logistically impossible. Assessing sewage workers' immune status for poliovirus and typhoid disease and their lack of increased risk for these diseases were also discussed.
- Influenza vaccination of pregnant women and HIV-infected persons.
- Risk of cholera for people receiving antacid therapy or who have had gastric or duodenal surgery. The committee decided not to include these risk groups in the statement.
- Addition of immunogenicity and reactogenicity data in the section on Haemophilus influenzae type b. (Committee members felt that data were insufficient at present to include a section on H. influenzae type b, but this could be considered when there is more information.)

After Dr. Strikas' presentation the Committee discussed a table that appeared in the recently published ACIP statement on influenza. The discussion centered on an ambiguous statement concerning the permissive age for the whole virus vaccine, especially in light of the lack of specific data to demonstrate risk of reactions. There was some discussion about who uses the table (manufacturers as package insert) and how to rectify the situation. Several Committee members were appointed to follow up on the issue.

Mr. Dean Mason: Perinatal Hepatitis B Grants

Mr. Mason described the proposal for elimination of perinatal HBV transmission that includes plans in the public sector to screen pregnant women for HBsAg positivity and to vaccinate and follow-up infants born to seropositive women to ensure their completion of a vaccine series. He also reported on funding for 1990 ($9.57 million) and which states have applied for grant funds. Funding will be appropriated according to need (projected number of HBsAg-positives in the population); merit; the extent to which the state supports the project, including screening, laboratory support, education, and the merit of the evaluation component.

The success of the program will depend on a number of factors including coalitions establishment, surveillance, recordkeeping, coordinated management of exposed infants, consumer and professional education, health-care provider training, and evaluation.

At the end of the meeting, Dr. Ken Bart from the National Vaccine Program was introduced, after which Dr. Bart talked about past successes and future plans for the advancement of prevention through immunization. He described several programs underway and mentioned that, in response to a charge to Dr. Sullivan to investigate safety of vaccines, a Task Force for Safer Vaccines had been established, to be led by NIH with the participation of FDA and CDC.

Dates for the next meeting were discussed (October 16 and 17) as well as possible dates for the next two meetings (February 26-27 and June 11-12).

The meeting was adjourned.

I hereby certify that, to the best of my knowledge, the foregoing summary of minutes is accurate and complete.

Samuel L. Katz

Samuel L. Katz, M.D., Chairman

Date: 28 August 1990