DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
October 6-7, 1986
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207 at the Centers for Disease Control, Atlanta, Georgia, on October 6-7, 1986. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Samuel L. Katz, Chairman
Dr. Ellen S. Alkon
Mrs. Betty F. Bumpers
Dr. Jeffrey P. Davis
Dr. David S. Fedson
Dr. Anne A. Gershon
Dr. Edward A. Mortimer

Ex Officio Members

Dr. William S. Jordan, Jr. (NIH)
Dr. Elaine Esber (FDA)

Liaison Representatives

Dr. William Schaffner II (AAP)
Dr. Philip A. Brunell (ACP)
Dr. John Herbold (DoD)
Dr. J. Michael Dixon (NACI)
Dr. Albert W. Pruitt (AMA)

Executive Secretary

Dr. Jeffrey P. Koplan

COMMITTEE MEMBERS ABSENT

None

HHS STAFF PRESENT

CENTERS FOR DISEASE CONTROL

Office of the Director

Ms. Gwen Strickland-Cid

HHS STAFF PRESENT (continued)

CENTERS FOR DISEASE CONTROL (continued)

Center for Infectious Diseases

Dr. Miriam Alter
Ms. Nancy Arden
Dr. Claire Broome
Dr. Carol Ciesielski
Dr. Bruce Gellin
Dr. Stephen Hadler
Dr. Lee Harrison
Dr. Noreen Hynes
Dr. Mark Kane
Dr. Alan Kendal
Dr. Karl Kappus
Dr. James E. Maynard
Dr. Frederic Shaw
Dr. R. B. Wainwright
Dr. Thomas Torok
Ms. Harriet Walls
Dr. Isaac Weisfuse

Center for Prevention Services

Dr. Roger Bernier
Dr. Robin Biellik
Dr. Edward Brink
Dr. Steven Cochi
Ms. Jessica Gardon
Dr. Alan Hinman
Dr. J. Michael Lane
Dr. John Livengood
Dr. Lauri Markowitz
Mr. John Mullen
Dr. Walter Orenstein
Dr. Peter Patriarca
Dr. Stephen Preblud
Dr. Susan Robertson
Dr. Walter Williams

Epidemiology Program Office

Dr. Jeffrey J. Sacks

OTHERS PRESENT

Dr. Salim Akrabawi
Dr. Steven Black
Mr. Gary Bridi
Dr. Alfred K. Cheng (USAF)
Dr. Pierre Claquin
Dr. Connie Cheng
Dr. Pinya Cohen
Dr. Corry Dekker
CDR Mark Dembert (MC USN)
Dr. John M. DeStefano
Dr. Bruce Dull
Dr. James Froeschle
Ms. Phyllis Freeman
Dr. Robert J. Gerety
Dr. W. Paul Glezen
Dr. Alan Gray
Dr. Brian Gurlich
Dr. Jill Hackell
Dr. Richard Hjorth
Mr. John Chris Hoffman
Dr. Garry Humphreys
Capt. Samuel C. Ingraham (USCG)
Dr. Victor Jegede
Dr. Saul Krugman
Dr. Andre LaMotte
Mr. Bruce R. Lesser
Dr. Michael Nestor
Dr. Marc A. Plattner
Ms. Carla Putnam
Dr. Al Reinhardt
Dr. Anthony Robbins
Dr. Terry Rooney
Dr. Cladd Stevens
Dr. Mason Stout
Dr. Joe Trudelle
Dr. John Tudor, Jr.
Dr. Ralph Vosdingh
Dr. Barbara A. Zajac

The fall meeting was opened by Dr. Katz at 8:30 a.m. on October 6, 1986. Dr. Katz introduced Dr. William Schaffner who replaced Dr. Theodore C. Eickhoff as the liaison representative from the American College of Physicians, and Dr. W. Paul Glezen, Baylor College of Medicine, attending as a consultant.

Dr. Koplan announced that although Rabies Prevention was not included on the agenda for the meeting, each member's packet of material contained a final draft of the supplementary recommendation on rhesus diploid cell rabies vaccine and the pre-exposure use of human diploid cell rabies vaccine by the intradermal route. He suggested that the Committee examine the draft "overnight" and give him last-minute comments the next day. The supplement is expected to be published by the end of October. The following recommendations have been published since the May 1986 meeting: Prevention and Control of Influenza (May 23); Monovalent Influenza A(H1N1) Vaccine for 1986-1987 (August 15); New Recommended Schedule for Active Immunization of Normal Infants and Children (September 19); Immunization of Children Infected with Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus (September 26).

Haemophilus influenzae

Dr. Claire Broome, Division of Bacterial Diseases (DBD), Center for Infectious Diseases (CID), CDC, introduced a series of presentations on Haemophilus influenzae type b (Hib). Dr. Steven Black, Kaiser Permanente, Oakland, California, presented data from post-marketing surveillance studies on safety and efficacy of Haemophilus b polysaccharide vaccine (b-CAPSA I vaccine)

manufactured by Praxis Biologics. The efficacy of the vaccine during the study period, June 1985 through June 1986, was 87%. This estimate is based on a preliminary analysis unadjusted for age or season. The studies were conducted by the Northern California Kaiser Permanente Health Plan in 22 medical centers, located from San Jose north to the Oregon border and east to the Nevada border. This population represents about 23% of all children in northern California and includes children from families in urban, suburban, and rural areas and all economic classes. As part of the general health care, children 2 to 5 years of age were recommended to receive the licensed b-CAPSA I vaccine; efficacy was estimated by comparing rates of disease in children who received the vaccine to the rate in those who had not been vaccinated. Dr. Bruce Gellin, DBD, reported that six of seven strains of Hib reported to CDC as resistant to ampicillin and chloramphenicol were found to be susceptible to chloramphenicol on testing at CDC. The consensus of the Committee was that the current recommendations remain appropriate for utilization of Hib vaccines and that continuing surveillance of prophylactic efficacy and of disease patterns should be maintained and reported regularly to ACIP.

Influenza Prevention and Control

Dr. Alan Kendal, Division of Viral Diseases (DVD), CID, gave an update on influenza activity and informed the Committee of a program being developed by a medical education company to improve the implementation of the Committee's recommendations for the prevention and control of influenza. Dr. Thomas Torok, DVD, discussed the availability of the monovalent influenza vaccine for protection against a newly emerged variant of influenza type A(H1N1). It is anticipated that the supplemental monovalent vaccine will be available in November 1986. Ms. Nancy Arden, DVD, discussed the use of amantadine in children and the need for further studies to determine the most appropriate pediatric dosage. Information about the availability of the supplemental monovalent vaccine and the occurrence of influenza will be made available to State health officials in the MMWR.

Measles

Dr. Alan Hinman, Division of Immunization (IM), Center for Prevention Services (CPS), discussed measles incidence so far this year, vaccine effectiveness, and measles elimination efforts in the United States. Dr. Lauri Markowitz, IM, reviewed surveillance data from the previous meeting; reported on measles cases from 1980 to date, age distribution and estimated incidence rates of measles during the first 26 weeks of 1985 and 1986 (3,921 measles cases reported through week 26 of 1986 exceeded the total number of reported cases in any year since 1980, when 11,564 cases were reported during the comparable period), age distribution and preventability of measles cases from 1984 to date, classification of measles cases from 1985 to date, measles outbreaks from 1985 to date (59 outbreaks in 1985, 90 to date in 1986), and summary of measles outbreaks with more than 100 cases in 1985. Incidence rates increased in all age groups in 1986, with the greatest increase in persons 10-14 years of age. The highest incidence rate is in preschoolers who account for almost 1/3 of all cases in 1986--due to two large outbreaks in New York City and New Jersey, most of whom were unvaccinated.

Dr. Walter Orenstein, IM, discussed a revised draft recommendation, "Measles Prevention," prepared by a subcommittee (Drs. Brunell, Davis, Mortimer) in

cooperation with the IM staff. The draft, mailed to the Committee members for review before the meeting, is quite long; but the subcommittee found it necessary to deal with several issues at considerable length. The draft updates the previous recommendation to include current information about vaccine effectiveness and measles elimination efforts. While there are no basic changes in approach, the draft includes an additional option for outbreak control (revaccination of persons initially vaccinated at 12-14 months of age), and new recommendations for international travel and for medical personnel. Members were asked to send any comments to IM, to be incorporated into another draft. Strategies for paring down this recommendation, and recommendations in general, were briefly discussed.

Risk Factors for Seizures Following Immunization

Following lunch, Dr. Hinman reviewed in detail the information he had mailed to Ms. Barbara Loe Fisher, Vice President of Dissatisfied Parents Together (DPT), on (1) the cooperation of CDC and FDA in monitoring adverse events following immunization and (2) the analysis of data on adverse events following DTP in siblings--data the DPT organization presented at the May 1986 ACIP meeting at CDC. Dr. Hinman also discussed contacts with the Division of Maternal and Child Health, National Institute of Child Health and Development, and the National Association of Medical Examiners relating to the definition and autopsy diagnosis of Sudden Infant Death Syndrome (SIDS).

Dr. John Livengood, IM, reviewed data from the first 4 years (1979-1982) of operation of the Monitoring System for Adverse Events Following Immunization (MSAEFI) and then updated this with MSAEFI data covering 7 years (1979-1985) of MSAEFI reports on personal and family history of seizures among persons reporting neurologic adverse events following immunization with DTP or measles-containing vaccines. Persons reporting neurologic events following DTP immunization are 6.6 times as likely as those with non-neurologic events to report a personal history of convulsions and 3.2 times as likely to report a history of convulsions in family members. Persons reporting febrile convulsions are 8.8 times as likely to have a prior history of convulsions and 4.1 times as likely to report a family history of convulsions. Persons reporting nonfebrile seizures were 7.8 times as likely to have a personal history and 3.9 times as likely to have a family history of convulsions.

For measles-containing vaccines, persons reporting neurologic events following immunization were 4.8 times as likely to have a personal history of convulsions than persons reporting non-neurologic events. Persons reporting febrile seizures were 5.8 times as likely to have a personal history of convulsions.

After a lengthy discussion, a subcommittee consisting of Drs. Gershon and Mortimer was appointed to consider these data further and report back to the Committee at the next meeting.

Hepatitis B - Booster Doses and a New Hepatitis B Vaccine

Drs. James Maynard and Stephen Hadler, Division of Viral Diseases (DVD), CID, discussed two issues regarding hepatitis B vaccine: recommendations for booster doses and the new recombinant DNA yeast-produced hepatitis B vaccine. Draft statements on these issues, intended as supplements to the current ACIP statement, "Recommendations for Protection Against Viral Hepatitis," had been prepared and mailed to the Committee before the meeting.

The Committee initially discussed the new genetically-engineered hepatitis B vaccine (Recombivax; Merck Sharp and Dohme) which was licensed by the FDA in July 1986. Dr. Barbara Zajac, Merck Sharp and Dohme Research Laboratories, presented an overview of production of this vaccine, of clinical trials with the recombinant vaccine, and comparison of the plasma-derived and recombinant vaccines. She noted excellent safety and comparable immunogenicity of the recombinant vaccine with the plasma-derived hepatitis B vaccine. Dr. Cladd Stevens, New York Blood Center, presented data showing over 90% efficacy of this vaccine, when given with hepatitis B immune globulin, in preventing perinatal hepatitis B transmission from HBsAg and HBeAg positive mothers to their newborn infants.

Dr. Hadler introduced a discussion of the need for hepatitis B vaccine booster doses, pointing out that available data indicate that protection against clinical or viremic HBV infections remains excellent for at least 5 years after vaccination. Studies show that for homosexual men and for hemodialysis staff who initially developed protective levels of antibody after vaccination, antibody declines below protective levels in 30-40% and becomes undetectable in 10-15% within 5 years. The large trials in homosexual men are becoming less useful for measuring waning immunologic memory because the men in the trials are changing their sexual behavior and becoming less at risk for acquisition of hepatitis B infection, and human immunodeficiency virus (HIV) infections may be changing their immunologic status. The Committee discussed whether a booster dose is currently necessary, and, if so, after how many years. Dr. Mortimer and others emphasized the need for additional data about the duration of immunity before establishing a fixed interval for providing booster doses, and stated that this was one of several reasons to monitor antibody response in recipients of vaccine. It was agreed that giving regular booster doses without serologic testing was the best strategy for vaccinees in general, but that the recommendations should allow hospitals to serologically assess response to vaccine, if preferred. Drs. Fedson, Schaffner, and others emphasized that the major need was to get unimmunized persons in high-risk groups immunized, this being more important than providing booster doses for the modest number of individuals immunized to date.

Dr. Robert Wainwright, Medical Epidemiologist from the CID/CDC Arctic Investigations Laboratory, Anchorage, Alaska, discussed antibody persistence in Alaskan Eskimos, noting better persistence of antibody in persons 0-19 years of age than in older adults. Dr. Hadler discussed considerations for booster strategy, including effectiveness, cost, simplicity/feasibility, acceptability, and programmatic aspects of different booster dose strategies. Dr. Saul Krugman gave data on booster doses of hepatitis B in children with thalassemia studied in Greece.

There was also considerable discussion about the best strategy for screening high risk women, or alternatively all pregnant women, for hepatitis B carrier state in order to prevent perinatal hepatitis B transmission.

Dr. Katz felt that the present hepatitis B vaccine recommendations should be updated and that the two draft statements should be incorporated into a single statement, in an effort to make recommendations readily accessible to health care workers. It was agreed that the CDC Hepatitis Branch should prepare a draft update statement on hepatitis B vaccine which would speak to the issues of: (1) the overall trends of use of hepatitis B vaccine to date, (2) evidence of safety and effectiveness of the recombinant DNA vaccine,

(3) the need for booster doses, (4) indications for testing for antibody status after vaccination, (5) safety of new and old vaccines, and (6) strategy for testing women and for vaccinating newborns.

Review of Pertussis Symposium

On day two, Dr. Hinman opened with a summary of the recent NIH-FDA-CDC sponsored Pertussis Symposium. This Symposium reviewed the requirements of licensure of improved pertussis vaccines, discussed the techniques for measuring potency of vaccines, reviewed the Japanese experience, including three household contact studies of the Takada vaccine, and presented the limited information available to date on vaccine safety coming from the Swedish trials. The Japanese experience is predominantly from immunization of 2-year olds, in whom the Takada vaccine seems safe and effective, but with modest information on children immunized as infants or 1-year olds. The Swedish trials involve children immunized at 6 months, but it will be late in 1987 before efficacy data are available. The Symposium also reviewed U.S. studies sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) of acellular pertussis vaccines and reviewed British plans for a trial comparing two or three different newer vaccines.

Dr. Mortimer emphasized that we still do not know which antigen elicits the protective antibodies. Dr. Hinman pointed out that the strategy of vaccination at age 2 allows considerable transmission in children under 2. Dr. Brunell noted that significant rare events are not measurable in the current trials, and postmarketing surveillance will be necessary to determine the rate of serious side effects. Dr. Katz pointed out that there is still considerable concern about the accuracy of pertussis diagnosis, and the adequacy of current serologic diagnostic techniques. Dr. Davis reviewed the Wisconsin experience briefly, which shows some optimism about current serologic markers as diagnostic techniques, and considerable efficacy of erythromycin in household contacts.

Dr. Katz asked Dr. Anthony Robbins, Boston University School of Public Health, to review the current status of legislative attempts to resolve the liability litigation situation, and there was a brief discussion about the pros and cons of current legislation.

DTP Follow-up

Dr. Hinman reviewed the attempts to analyze the clinical data presented by Dissatisfied Parents Together (DPT) at the May 1986 ACIP meeting. The Division of Immunization is pursuing ways to get additional clinical data on the families which DPT claims have had more than one child with a serious central nervous system sequelae to DTP immunization. Dr. Katz requested that a letter be sent to DPT about the status of attempts to investigate these cases further. OK - Hinman

Drs. Katz and Brunell reported attempts to approach pathologists and others regarding the criteria for diagnosis of Sudden Infant Death Syndrome (SIDS). This is still a diagnosis by exclusion, and quality control of the diagnosis is suboptimal. A forthcoming study by NICHD will reaffirm that there is no increased relative risk of SIDS in children after receiving DTP vaccine.

Mrs. Bumpers underscored the need to have medical guidelines for compensable events following vaccination. There was considerable discussion about the relationship between media, lawyers, and public health workers in explaining adverse sequelae of vaccines. IM will send copies of the current important information forms, used in publicly supported immunization programs to explain to parents about the risk and benefits of vaccines, to Committee members.

Other ACIP Business

The winter Committee meeting was scheduled for Tuesday and Wednesday, February 17-18, 1987.

> NOTE: This date has been changed to Thursday and Friday, February 5-6, 1987, because a meeting on influenza, sponsored by the World Health Organization, will be held February 16-18, 1987, in Geneva, Switzerland.

With the thanks of the Chairman, the meeting was adjourned shortly before noon.

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

Samuel L. Katz 23 Nov. 1986

Samuel L. Katz, M.D., Chairman — Date