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

MINUTES OF MEETING

Immunization Practices Advisory Committee
October 11 - 12, 1988
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207 at the Centers for Disease Control, Atlanta, Georgia, on October 11-12, 1988. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT
- Dr. Samuel L. Katz, Chairman
- Dr. Stanley Broadnax
- Dr. James D. Cherry
- Dr. Jeffrey P. Davis
- 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. John R. LaMontagne (NIH)
- Dr. Gerald Quinnan (FDA)

Liaison Representatives
- Dr. J. Michael Dixon (NACI)
- Dr. Edward A. Mortimer, Jr. (AMA)
- Dr. Michael R. Peterson (DoD)
- Dr. Stanley A. Plotkin (AAP)
- Dr. William Schaffner II (ACP)
- Dr. Ronald C. Van Buren (AAFP)

Executive Secretary
- Dr. Mary E. Guinan

HHS STAFF PRESENT

Navy Environmental Health Center
- CDR David Trump

CENTERS FOR DISEASE CONTROL

Office of the Director
- Ms. Verla Neslund

HHS STAFF PRESENT (continued)

CENTERS FOR DISEASE CONTROL

Center for Infectious Diseases
- Dr. Miriam Alter
- Dr. Karen Farizo
- Dr. Steve Hadler
- Dr. James M. Hughes
- Dr. Mark Kane
- Dr. Lisa Rosenblum
- Dr. Craig Shapiro
- Dr. Gary Schatz
- Dr. John Spika

Center for Prevention Services
- Dr. Edward Brink
- Dr. Robert Chen
- Dr. Steve Cochi
- Dr. Nancy Cox
- Dr. Rosamond Deward
- Dr. Paul Fine
- Dr. Maurice Harmon
- Dr. Alan R. Hinman
- Dr. Sonja Hutchins
- Dr. Lauri Markowitz
- Dr. Walter Orenstein
- Dr. Peter Patriarca
- Dr. Stephen Preblud
- Dr. Paul Stehr-Green
- Dr. Roland Sutter
- Dr. Walter W. Williams

National Vaccine Program Office
- Dr. Alan Hinman
- Dr. Yuth Nimit

Others Present

Dr. Jerry Boscia
Ms. Leslie Chapman
Dr. Pinya Cohen
Dr. William Darnall
Ms. Dawn Duperre
Dr. Bruce Dull
Dr. Caroline Dunn
Dr. David S. Fedson
Dr. Lance Gordon
Dr. Jill Hackell
Dr. Saul Krugman
Dr. Sharon Mates
Dr. David K. McCluitocle
Dr. Ellen McGuire
Dr. Steven Mento
Dr. Diane Mitrione
Dr. George Robertson
Dr. Catherine Sohn
Dr. Mason Stout
Dr. David West
Dr. Matthew A. Wikler

The meeting was opened at 8:30 a.m. on October 11 by Dr. Samuel L. Katz, Chairperson. Dr. Katz introduced Dr. Mary E. Guinan, Executive Secretary of Immunization Practices Advisory Committee (ACIP), replacing Dr. Jeffrey Koplan who has taken another position at CDC. Dr. Katz also introduced Drs. Mary Wilson and David Fraser, two new members on the ACIP.

Hepatitis B

Members from the Hepatitis Branch, Division of Viral Diseases, CID, led discussions about three issues concerning hepatitis B vaccine: the need for booster doses, alternative low-dose strategies for vaccination, and the impending licensure of a new recombinant DNA HB vaccine by Smith Kline RIT.

Dr Steve Hadler, Division of Viral Diseases, (DVD), Center for Infectious Diseases, (CID), CDC, Hepatitis Branch, discussed important issues for policy on HB vaccine booster doses. Studies of plasma-derived vaccine in adults reveal that about 33% of persons who respond to the initial series lose antibody by 5 years after vaccination, and that 50% lose antibody by 7 years. Loss of antibody in children who respond to vaccine is lower (about 15-20%) due to higher response to the primary series. Although risk of infection appears to increase as antibody levels become low or undetectable, the resultant infections do not cause detectable viremia or clinical illness. Worldwide experience on antibody decay and long-term protection is consistent and no examples of late clinical illness in vaccine responders have been reported to date. It was recognized that late infections do cause viral replication (as recognized by development of anti-HBc antibody), and in theory could result in transient infectivity to others or to viral integration into the host liver, with later induction of primary hepatocellular carcinoma (PHC). Nevertheless, this latter concern is not currently supported by available data, which do not show excess PHC risk in persons with transient HBV infection. Based on current information and estimated low cost-benefit of booster doses at current cost, it was concluded that current data do not support a need for a vaccine booster dose within 7 years after vaccination. Continued review of data on long-term protection and vaccine costs will be necessary before making a formal recommendation later this year.

The need for booster doses in infants of HBV carrier mothers was also discussed. Data from Dr. Cladd Stevens of the New York Blood Center shows no evidence of late infection during 5-year followup of 41 infants born to high risk HBV carrier mothers. Few other data are available at present; nevertheless, close attention must be given to this issue as infants and young children have the highest risk of developing chronic consequences of HBV infection.

Dr. Lisa Rosenblum discussed issues of low dose intradermal and intramuscular vaccination as a cost-saving measure. While initial studies showed a good response to intradermal vaccination with 0.1 the usual vaccine dose, larger studies have shown that as few as 81% of persons vaccinated by this route will develop adequate antibody response. This lower response would necessitate

postvaccination testing and revaccination of nonresponders and would reduce the cost savings from 90% to 15-70%. Various schedules for lower dose intramuscular vaccination have been tested but no single example provides adequate data to justify changing doses. Dr. Quinnan, FDA, pointed out that establishing a standard dose and schedule is the responsibility of FDA and that there is no precedent for ACIP adjusting dose schedules after vaccine licensure.

Dr. Jerry Boscia, Smith Kline & French Labs, presented clinical study data on the new recombinant vaccine produced by SK-RIT and currently under review at FDA. Two alternative dose schedules (doses at 0,1,6 months and at 0,1,2,12 months) are proposed for healthy persons, the latter being preferable in post-exposure settings and for travelers. It was noted that as more vaccines become available, and as recommended usage varies, that the ACIP recommendations will have to be made generic, noting "another vaccine has been licensed. Read the package insert for proper dose and schedule.'

Dr Hadler proposed that the Hepatitis Branch will prepare a draft revision statement on prevention of viral hepatitis for the next meeting, and that a final version will be presented at the final ACIP meeting next spring.

Update on Influenza Virus Strains and Molecular
Epidemiology of Influenza Virus Strains

Dr. Maurice Harmon, DVD, CID, distributed data on strains in various countries. A strain of influenza A(H3N2) which differed antigenically from strains circulating previously was the most frequently isolated type of the influenza virus during 1987-88. Influenza B, although much less frequently isolated than influenza A(H3N2), also differed antigenically from previously circulating strains of the influenza B virus. Dr. Nancy Cox also presented slides tracing the history of influenza A(H3N2) virus strains and changes in antigenic sites in strains.

Update on Mumps Vaccine
and Update of Mumps Epidemiology

The status of Mumps Vaccine and the changing epidemiology of mumps disease in the United States was given by Dr. Stephen Preblud, Center for Prevention Services (CPS), IM, and Dr. Paul Stehr-Green, CPS, IM. Two handouts were distributed to ACIP members preceding discussion and suggestions for a few changes in the current Mumps Recommendation. Since licensure of the live virus mumps vaccine in 1967, the U.S. has enjoyed great success in the control of mumps. By 1980, Measles-Mumps-Rubella (MMR) vaccine was recommended as the preferred vaccine for routine use in children.

In 1985, an all-time low of 2982 cases was reported, however, since 1986 a resurgence has been seen with 12,848 cases reported in 1987. This resurgence has been characterized by an increase in incidence in all age groups and a

shift in the age groups at highest risk to adolescents and young adults; this trend is exacerbated further in those states lacking comprehensive mumps immunization school laws.

Suggestions for the ACIP to consider were to take the existing statement and insert changes and paragraphs in the following: 1) Recommend enactment of comprehensive (i.e., K-12) laws for school immunization in all States; 2) Future policy emphasis should include enforcing existing laws requiring vaccination against mumps; 3) Emphasize the need for vaccinating adolescents and young adults, especially those in college, military and healthcare settings; and 4) Recommend more aggressive outbreak control.

DTP Vaccine

Dr. Edward Brink and Dr. Stephen Cochi, CPS, IM, briefly discussed some background epidemiology of pertussis surveillance in the U.S., 1980-1986, with these conclusions: 1) There was an apparent increase in the reported incidence of pertussis during 1982-86 in all age groups, particularly in adults; 2) Only 40% of children 7 months--4 years of age reported with pertussis received 3+ doses of DTP; and 3) The clinical efficacy of 3+ doses of DTP vaccine was high (90%).

Dr. Cochi presented data from 5 scientific studies: Lambert, (1965), Jenkinson, (1978); Jenkinson, (1988); Church, (1979); and Broome, (1981). Rationale for 5th dose at 4-6 year of age: A) Indirect evidence: comparative age distribution of reported pertussis in U.S. and in the U.K./Denmark which have only 3-dose schedules in infants; and B) Efficacy: (1) Clinical protection does not appear to decrease within 3-4 years of the last dose (MRC, Lambert, Jenkinson -1978). The results of long-term (greater than 3-4 years) clinical protection studies are not consistent (Lambert, Jenkinson - 1988, Broome, Church), but overall suggest waning immunity; (2) Assuming that waning immunity exists, the 4-6 year dose: a) directly protects children during a time of potential increase in risk of exposure at school entry; b) indirectly protect siblings by reducing the likelihood of transmission into the home.

Data were reviewed from an unpublished study by Dr. S. Long. One table compared pertussis agglutinin responses following a 3-dose and a 4-dose immunization schedule with the geometric mean antibody titers. A second table compared Pertussis Antitoxin responses following a 3-dose and a 4-dose immunization schedule with the geometric mean antibody titers. Impressive declines in these serological indicators occurred in the interval between the third and fourth DTP doses. Dr. Cochi also led a discussion of pertussis vaccine efficacy. The ACIP was asked if it would reconsider the timing of the 4- and 5-doses (the 4th dose justified in the past and reinforced at 18 months). The committee considered these data and voted to stay with current Recommendation of a 4 dose DTP primary schedule by 18 months of age and a booster dose of DTP at 4-6 years of age.

Dr. Brink presented the question "In a pertussis outbreak what is the age at which the first dose of DTP should be administered"? The AAP suggests the first doses at 2 weeks of age with administration of the next 2 doses at a 1 month interval. The ACIP reviewed data from the literature showing little difference in antibody response following 3 doses administered at various ages, including schedules that began as young as 2 weeks. However, in the absence of definitive data, it recommended no change in its current recommendation for primary immunization with DTP. The Committee pointed out that there is a range in age as well as in the interval between doses. In the outbreak setting, the youngest age and shortest interval should be used." Ms. Leslie Chapman, representing Dissatisfied Parents Together (DPT), said they will not support any movement of giving vaccine to young babies. Also, she stated that there is a need for clarity on what is an epidemic or what is an outbreak.

Mr. Ronald Teske, CPS, IM, briefly discussed Influenza Vaccine Cost-Effectiveness and Demonstration Projects. The first report on these demonstrations to test cost-effectiveness should be available in October 1990.

Measles Vaccine - Update

Dr. Lauri Markowitz, IM, CPS, CDC, gave a report of Edmonston-Zagreb (E-Z) Measles Vaccine Meeting held in Washington, DC. Data presented included preliminary results from the measles vaccine trial in infants in Mexico City and other trials. The E-Z Measles vaccine is not licensed in the U.S.

Pneumococcal Vaccine

Dr. Katz introduced the sub-committee on pneumococcal vaccine consisting of Drs. Caroline Hall, Marc LaForce, David Fedson, and John Spika. Dr. John Spika, Division of Bacterial Disease (DBD), CID, CDC, reviewed information from the last ACIP meeting in May, 1988, on pneumococcal bacteremia in Charleston County, South Carolina, where the overall rates were 2.3 times higher than in the previous study. Dr. Spika discussed an update on vaccine 6 or more years after immunization. The estimate of efficacy markedly declined although the number of isolates was very small. Data on reactions following revaccination were presented including an unpublished study by Merck. Revaccination with the 23-valent should be considered for persons who received the 14-valent vaccine who are at highest risk for fatal pneumococcal infection and persons shown to have rapid decline in pneumococcal antibody concentration. The Committee discussed the ACIP draft and concern was expressed about diabetes. The Committee voted to include diabetes mellitus in the list of chronic illnesses in adults at increased risk for pneumococcal disease. After thorough discussion of the ACIP Update, Dr. Katz suggested that the subcommittee review the update with the suggested changes and get something back within 4 weeks to Dr. John Spika.

Poliomyelitis Vaccines

Dr. Samuel Katz gave a report on the subcommittee of the Immunization Practices Advisory Committee (ACIP) which met at the University of Pennsylvania on August 25. This subcommittee was convened to review the report of the Institute of Medicine's (IOM) study "An Evaluation of

Poliomyelitis Vaccine Policy Options for 1988." Those in attendance were Drs. Mary Guinan, Steve Cochi, Jeff Davis, Marc LaForce, Stanley Plotkin and Samuel Katz. The subcommittee felt that ACIP should accept the report of the IOM and agreed with the two basic recommendations: 1) No change in the present policy at this time; 2) consideration of a combined schedule once E-IPV combined with DTP has been licensed. The subcommittee also felt it was important to generate studies which would answer a number of questions prior to the suggested changes. These would include an assessment of the circulation of wild virus in selected parts of this country; the levels of detectable antibody in young adults; the prevalence and levels of antibody in pre-school children, especially among those living in areas where immunization is not achieved early in life; studies of the current role of OPV vaccine virus circulation in the immunization of susceptible contacts; the duration of OPV shedding by HIV-infected infants; and whether HIV-infected infants respond to E-IPV. It was noted that some studies proposed and underway by McBean and colleagues at Johns Hopkins would begin to answer some of the unresolved issues. It was felt important to maintain close liaison with FDA and the pharmaceutical firms to keep abreast of any imminent availability of new vaccines and to provide stimulations for the development of new products.

Dr. Walter Orenstein, Division of Immunization (IM), Center for Prevention Services (CPS), CDC, reported on an outbreak of polio in Israel (he returned to the U.S. October 11, 1988) where he served as a member of a team of experts to advise the Israelis. They recommended vaccination of all people under the age of 40 in Israel with trivalent oral polio vaccine. Suspected wild polio viruses had been discovered in sewage in 8 of 15 Israeli subdistricts suggesting transmission may be widespread.

Dr. Stephen Cochi, distributed a draft "A New Epidemiologic and Laboratory Classification System for Paralytic Poliomyelitis Cases". An epidemiologic classification of paralytic poliomyelitis cases (ECPPC) has been in use in the United States since 1976. In 1985, this classification system was reviewed because of recent changes in the epidemiology of paralytic poliomyelitis and improved laboratory capability to definitively characterize poliovirus strains. An alternative classification system was devised, the epidemiologic and laboratory classification of paralytic polio cases (ELCPPC), that incorporated virus isolation and strain characterization with epidemiologic information.

Reported paralytic poliomyelitis cases for 1980-86 were classified by both the ECPPC and the ELCPPC classification systems. The new ELCPPC system classified 91% of the reported cases as vaccine-associated, while the ECPPC system classified only 73% of the reported cases as vaccine-associated. The greater descriptive accuracy of each category in the ELCPPC and the use of laboratory information provide more specific and useful information particularly concerning vaccine-associated disease. Enormous success in the control of paralytic poliomyelitis in the United States and other developed countries has generated interest in the eradication of the disease. Because of progress by the Expanded Programme on Immunization of the World Health Organization (WHO),

WHO adopted the goal of eradication of poliomyelitis by the year 2000. As countries achieve high polio vaccine coverage, surveillance for new cases becomes relatively more important. The proposed classification system may be useful in tracking and confirming the success of the initiative in individual countries.

Dr. Edward Brink briefly discussed a survey of State Immunization Project Managers concerning current and future implementation of the IOM study. The ACIP recommends that, (1) in the United States, polio immunization should continue to rely primarily on oral poliovirus vaccine (OPV), with selected use of enhanced-potency IPV as specified in the current Poliomyelitis Prevention Statement; and (2) after e-IPV combined with diphtheria-tetanus-pertussis (DTP) is licensed, consideration be given to a regimen of two or more doses of DTP-eIPV followed by OPV at 15-18 months of age and at the time of school entry.

National Vaccine Program

Dr. Alan Hinman, CPS, Coordinator for the National Vaccine Program (NVP) gave an update of activites of the NVP. The National Vaccine Advisory Committee for the NVP consists of 15 members and has met twice. One of the important activities of the Program is to monitor current vaccine research and development efforts and develop priorities to achieve national goals and describe an optimal use of resources to carry out these priorities. Implementation of the National Childhood Vaccine Injury Compensation Program has begun. The program can pay only 150 claims a year. Formation of the Advisory Commission on Childhood Vaccines has been advertised in the Federal Register.

Other ACIP Business

Concern was expressed with regard to editorial changes being made unilaterally on ACIP Statements submitted to the MMWR for publication. Dr. Mary Guinan will talk with Dr. Michael Gregg, Acting Director, Epidemiology Program Office, suggesting that any changes in submitted statements for publication in the MMWR be reviewed through the Office of the Director for approval. It was suggested that references be made for and included in these publications.

The next meeting was scheduled for February 21-22, 1989.

Dr. Guinan invited everyone to tour the new virology building.

With the thanks of the Chairman, the meeting was adjourned at 12:30 p.m.

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

Samuel L. Katz 13 Nov. 1988

Samuel L. Katz, M.D., Chairman Date