DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
February 5-6, 1987
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207 at the Centers for Disease Control, Atlanta, Georgia, on February 5-6, 1987. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Samuel L. Katz, Chairman
Dr. Ellen S. Alkon
Dr. Jeffrey P. Davis
Dr. David S. Fedson
Dr. Anne A. Gershon
Dr. Edward A. Mortimer
Dr. H. Denman Scott

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

Liaison Representatives
Dr. Philip A. Brunell (AAP)
Dr. John Herbold (DoD)
Dr. J. M. S. Dixon (NACI)

Consultant
Dr. W. Paul Glezen

Executive Secretary
Dr. Jeffrey P. Koplan

COMMITTEE MEMBERS ABSENT

Mrs. Betty Bumpers
Dr. F. Marc LaForce

Liaison Members
Dr. Albert W. Pruitt (AMA)
Dr. William Schaffner II (ACP)

HHS STAFF PRESENT

FOOD AND DRUG ADMINISTRATION
Office of Biologics Research and Review
Dr. Gerald Quinnan
Dr. Carolyn Hardegree

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases
Dr. David L. Klein

CENTERS FOR DISEASE CONTROL
Office of the Director
Dr. Mary Guinan

Center for Infectious Diseases
Ms. Nancy Arden
Dr. Claire Broome
Dr. Mitchell Cohen
Dr. Nancy Cox
Dr. Martin Favero
Dr. Stephen Hadler
Dr. Maurice Harmon
Dr. Noreen Hynes
Dr. Mark Kane
Dr. Karl Kappus
Dr. Alan Kendal
Dr. Margaret Oxtoby
Dr. John Spika
Dr. Tom Torok
Ms. Harriet Walls

HHS STAFF PRESENT (continued)

CENTERS FOR DISEASE CONTROL (continued)

Center for Prevention Services

Mr. Steven Barid
Dr. Roger Bernier
Dr. Robin Biellik
Dr. Alan Bloch
Dr. Edward Brink
Dr. Steven Cochi
Ms. Debra Combs
Mr. Bill Doyle
Dr. Jaime Escolan
Ms. Jessica Gardom
Dr. Alan Hinman
Dr. J. Michael Lane
Dr. John Livengood
Dr. Lauri Markowitz
Mr. John Mullen
Mr. Dennis O'Mara
Dr. Ida Onorato
Dr. Walter Orenstein
Dr. Peter Patriarca
Dr. Stephen Preblud
Dr. Dixie Snider
Mr. Don Stenhouse
Dr. Walter Williams

Epidemiology Program Office

Dr. Robert Gunn

International Health Program Office

Dr. T. Stephen Jones

OTHERS PRESENT

Dr. Vincent Ahonkhai
Dr. Joseph Bawduniak
Dr. Steven Black
Dr. Scott Bolenbaugh
Dr. Queta Bond
Ms. Leslie Chapman
Dr. Pinya Cohen
Dr. Larry Cummins
Dr. Corry Dekker
CDR Mark Dembert, MC, USN
Mr. Ingram Douglas-Hall
Dr. Brian Gmerek
Dr. Alan Gray
Mr. John Chriss Hoffman
Dr. Jill Hackell
Dr. Garry Humphreys
Capt. Samuel C. Ingraham 3rd
Dr. Douglas Kelsey
Dr. Saul Krugman
Dr. Andre LaMotte
Dr. Ellen McGuire
Dr. Thomas Monahan
Dr. Marjorie Pollack
Dr. Al Reinhardt
Dr. Terry Rooney
Dr. B. A. Rubin
Ms. Karlyn Shedlowski
Dr. David Smith
Dr. Whaijen Soo
Dr. Cladd Stevens
Col. Ernest Takafuji
Dr. Michael Titus
Dr. Joe Trudelle
Dr. John Tudor
Dr. Ronald Vallancourt
Dr. Ralph Vosdingh
Dr. Allen Woodhour
Dr. Barbara Zajac

The winter meeting was opened by Dr. Katz at 8:30 a.m. on February 5, 1987. Dr. Katz introduced Dr. H. Denman Scott, new committee member, and Dr. W. Paul Glezen, Baylor College of Medicine, consultant. Dr. Katz announced that Dr. F. Marc LaForce, another new member, was absent. Dr. John Herbold represented Dr. Jarrett Clinton, Department of Defense, and Dr. Elaine Esber represented Dr. Paul D. Parkman, FDA. Dr. Koplan stated that the Supplementary Statement on the Pre-exposure Use of Human Diploid Cell Rabies Vaccine by the Intradermal Route recommendation was published in the December 12, 1986, MMWR.

Measles Prevention

Dr. Alan Hinman, Division of Immunization (IM), Center for Prevention Services (CPS), CDC, gave introductory comments on a draft revision of the Measles Prevention recommendation which had been mailed to the committee for review before the meeting. The draft, formulated by Drs. Brunell, Davis, and Mortimer in cooperation with the IM staff, includes current information about vaccine effectiveness, measles elimination efforts, an additional option for outbreak control (revaccination of persons initially vaccinated at 12-14 months of age), and new recommendations for international travel and medical personnel. Committee members were requested to send any additional comments on the draft to Dr. Koplan within 2 weeks.

Varicella Zoster

Dr. Stephen Preblud, IM, CPS, discussed the status of varicella zoster vaccine and clinical trials carried out by Dr. Anne Gershon. Dr. Barbara Zajac, Director of Clinical Research at Merck Sharp & Dohme Research Laboratories (MSD), gave an overview of MSD research efforts. They are optimistic about the newly formulated vaccine; however, it is premature to discuss the timing of application for licensure--probably not in 1987. New vaccination studies were not initiated in healthy individuals during the past 6 months. Followup continued on a subset of vaccinees for persistence of antibodies, breakthrough cases of varicella, incidence of zoster, and general safety. Dr. Gershon has continued immunization with research vaccine of children in remission with acute lymphocytic leukemia. Research and production groups at Merck have been evaluating the use of a research-like process for routine production of vaccine. The importance of PFU-to-antigen ratios in relation to the time of harvest has been evaluated, and vaccines are being produced with varying antigen levels. These formulations will be evaluated, hopefully in the spring, for tolerability and immunogenicity in clinical studies involving children with acute lymphocytic leukemia in remission for one year, healthy children, and healthy adults.

Influenza Prevention and Control

Dr. Alan Kendal, Division of Viral Diseases (DVD), Center for Infectious Diseases (CID), CDC, reviewed recent influenza A(H1N1) experiences and introduced a series of presentations as background information.

Dr. Thomas Torok, DVD, reviewed data from the WHO Collaborating Center for Influenza/Influenza Branch, DVD. This included age distribution of influenza isolates submitted by the WHO Collaborating Laboratories, United States, for the 1986-1987 season for types A(H1N1), A(H3N2), and B; percentages of deaths associated with pneumonia and influenza, and statistical values for expected and upper limits from 121 U.S. cities for 1981-1987; and data on an A/Taiwan/1/86-like influenza outbreak at the Key West Naval Base. There has been only one influenza outbreak in nursing homes this winter. Influenza A/Taiwan/86(H1N1)-like virus was isolated from two throat swabs obtained from ill residents of the home in January. The nursing home had offered the trivalent influenza vaccine to all residents and staff in November 1986; 50 (85%) residents and 14 (23%) of the 60 staff members had been vaccinated.

Dr. Maurice Harmon discussed hemagglutination-inhibition (HI) reactions of influenza A(H1N1) viruses for A/India 6263/80, A/Chile 1/83, A/Victoria 7/83, A/Taiwan 1/86, and A/Singapore 6/86; comparison of HI antibody titers for

A/Taiwan/86 and A/Chile/83 of students before and after receiving standard trivalent vaccine and after monovalent A/Taiwan vaccine booster given 2-3 months after the standard vaccine (data from Dr. Gorden Meiklejohn, University of Colorado Health Sciences Center); neutralization reaction patterns of influenza B viruses; neutralizing antibody response to trivalent 1986/87 influenza vaccine in 42 nursing home residents; HI reactions of influenza A(H3N2) viruses; frequency of identification of influenza variants from the 1985-86 season, WHO Collaborating Center for Influenza, CDC; and HI antibody response to trivalent 1986/87 influenza vaccine, influenza A(H3N2) viruses.

Ms. Nancy Arden discussed an updated draft recommendation for prevention and control of influenza. The draft includes the addition of statements about (1) updating influenza strains in vaccine for 1987-88, and (2) precautions for the use of amantadine hydrochloride (Symmetrel). She noted that the recommendation for prophylaxis has not changed. The committee was asked to review the draft overnight in preparation for a discussion the following day.

On day two, the committee continued reviewing the influenza draft update. Dr. Kendal stated that amantadine package insert issues will be handled in conjunction with the FDA. Several members stated they had been unable to obtain sufficient quantities of the new vaccine. The shortage was addressed in conjunction with the adult immunization initiative program. Dr. Fedson agreed to draft a paragraph on vaccine use surveillance to present to the committee at the spring meeting.

Dr. Katz asked the committee to mail any additional comments on the draft to Dr. Koplan within 2 weeks. Dr. Kendal will again revise the draft, and it will be mailed to the committee for final comments.

Dr. Kendal told the committee that an influenza education program organized by a private firm has published a manual, "Strategies for Clinical Practice," which is available to the practicing physician. The manual stresses that education in the areas of prevention, management, and control of influenza with safe and effective vaccines and medications can significantly reduce the burden of illness of influenza. Dr. Koplan will obtain copies of the manual and mail one to each member.

Dr. Kendal introduced Dr. Whaijen Soo, Hoffmann-La Roche, Inc., who gave an overview of an NDA (new drug application) filed with the FDA requesting approval to market rimantadine for the prophylaxis and therapy of influenza A virus. His clinical data included rimantadine efficacy, an NDA summary, rimantadine prophylaxis studies, summary of the study design, and prophylaxis studies on incidence of influenza A illness. After a lengthy discussion, Dr. Katz asked Drs. Fedson, Davis, and Glezen to work with Dr. Kendal and his staff on the development of provisional recommendations for use of rimantadine, so these would be available if FDA approval of the NDA was granted before next winter.

Smallpox Vaccine - Requests for Vaccine for Research Purposes

Dr. Mary Guinan, Acting Assistant Director for Science, CDC, told the committee that CDC has received a request from a research hospital in Miami, Florida, to supply smallpox vaccine for treatment of patients with melanoma. As the only source of smallpox vaccine for civilians, CDC provides smallpox vaccine to protect laboratory workers occupationally exposed to smallpox virus and other

closely related orthopox viruses. Dr. Guinan explained that this request has been reviewed by a CDC ad hoc committee which recommended that it be presented for review by the ACIP committee in an effort to determine (1) how CDC should respond to the request for smallpox vaccine for purposes not covered by the current ACIP recommendations, and (2) how to handle any future requests. The committee reviewed its current recommendations (MMWR Vol. 34/No. 23, June 14, 1985) and discussed the following revisions:

> The ACIP recommendation against the therapeutic use of smallpox vaccine does not apply to a research protocol conducted under an FDA-issued IND (Investigational New Drug). Protocols using smallpox vaccine for research purposes must include provisions for:
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> - adequate information to potential vaccinees on risks of smallpox vaccination
> - screening to exclude high-risk individuals
> - reduction of risk of spread to contacts
> - followup after vaccination
> - treatment of complications of smallpox vaccination.

Personal and Family History of Convulsions

Data presented at the previous meeting on the personal and family history of convulsions of persons reporting neurologic and non-neurologic adverse events following immunization with DTP and measles-containing vaccines were briefly reviewed by Dr. John Livengood, IM, CPS. At the previous meeting, Dr. Katz asked Drs. Gershon and Mortimer to work with the Division of Immunization and outside consultants to further consider the data presented and report back to the committee. The group met with Dr. Karin Nelson of the National Institutes of Health at CDC on January 5, 1987, to discuss the issue. A preliminary draft was formulated and mailed to the committee members for review prior to this meeting. The draft consisted of two sections: (1) Personal and Family History of Convulsions and Use of Measles Vaccine, and (2) Family History of Convulsions and DTP. Dr. Gershon led a discussion and asked for comments on the draft. Mrs. Leslie Chapman, representing the Ad Hoc Committee of Parents and Physicians for Safe Immunization and Dissatisfied Parents Together, suggested that the Important Information Statement form contain a description of signs and symptoms of convulsions which might occur. Dr. Katz thanked those who prepared the draft and asked the members to mail any additional comments to Dr. Koplan within 2 weeks. The DTP section will be published as a supplementary ACIP statement and the measles section will be incorporated into the pending revision of the Measles Prevention statement.

Pneumococcal Vaccine - Update

Dr. John Spika, Division of Bacterial Diseases (DBD), CID, briefly reviewed data from an article by Dr. Gail Bolan, and from Dr. Michael Simberkoff's trial results of pneumococcal vaccine among Veterans Administration (VA) patients in a VA cooperative study. Also, he discussed estimated efficacy of pneumococcal

vaccine. The committee considered the vaccine data to be inconclusive at present.

Haemophilus influenzae Type b Vaccine - Update

Dr. Claire Broome, DBD, CID, introduced a series of presentations on a polysaccharide vaccine for invasive (bacteremic) disease caused by H. influenzae type b (Hib). The vaccine was licensed in the United States in 1984. Dr. Lee Harrison, DBD, presented data on a case-control efficacy study of polysaccharide Hib vaccine from January 1-November 30, 1986, and a Finnish trial of clinical efficacy in 1974. Dr. Steven Black from Kaiser Permanente Health Plan, Oakland, California, gave preliminary data analysis of b-CAPSA 1 vaccine use in children 2-5 years of age at health plan centers, from June 1985-December 1986.

Bacillus Calmette and Guerin (BCG) Update

Dr. Dixie E. Snider, Jr., Division of Tuberculosis Control (DTC), CPS, gave an overview of surveillance of tuberculosis since 1969, and distributed copies of the current recommendation (dated June 1, 1979) and background material, on efficacy of infant BCG immunization, which had been mailed to the committee for review before the meeting. He introduced members of the DTC staff who discussed recent studies of the BCG vaccine and the present incidence of childhood tuberculosis in the United States. Ms. Debra Combs gave data on controlled community trials, with vaccine efficacy ranging from (-)56 percent to 80 percent. Recent case control and contact studies suggest that BCG vaccination in newborns and young children provides a significant level of protection against tuberculosis in childhood, especially against tuberculous meningitis, with efficacy as high as 95 percent. The protective effect of BCG against pulmonary tuberculosis is less certain, with vaccine efficacy ranging from 2 percent to 80 percent. The World Health Organization continues to recommend BCG immunization for all newborns or young children in high-risk countries or areas.

Dr. Alan Bloch's summary of the incidence of tuberculosis in children under 15 years of age revealed that minorities account for 80 percent of cases in this country. He reviewed data on the number of reported tuberculosis cases from 1962 to 1985 in the United States; cases by race/ethnicity in the United States during 1985; cases by country of origin; number of reported cases in non-Hispanic/White, Black, Asian, American, Indian, and Hispanic children in 1985; clinical characterics of children and diagnostic findings of reported tuberculosis cases in children; and tuberculosis death-to-case ratios during 1984 in the United States. The committee discussed sources for obtaining BCG vaccine in the United States. There are only two sources in this country (University of Illinois, and Eli Lilly/Connaught Laboratories, Ltd.). Although the current recommendation was made in 1979, the general consensus was that additional information is needed before a revision is made. Dr. Katz asked Dr. Snider to obtain additional background material and to propose changes to the current statement for presentation at the next meeting.

Poliomyelitis and Poliomyelitis Vaccines

Dr. Alan Hinman introduced the session by reviewing the six polio vaccine policy options discussed at the fall 1985 committee meeting.

Dr. Peter Patriarca, IM, CPS, gave the status of poliomyelitis in South America during 1986 and discussed strategies used. In 1986 there was a polio outbreak

in Brazil, where OPV was used exclusively, with more than 400 cases of type III. The efficacy of type III vaccine used in Brazil appeared to be low. Studies of the current type III vaccine as well as a more potent vaccine are underway. He also reviewed field and case-control studies on the efficacy of more potent IPV in Senegal in 1986. Dr. T. Stephen Jones, Jr., International Health Program Office, CDC, presented data on outbreaks in The Gambia. Dr. Roger Bernier, IM, CPS, reviewed a study on IPV and OPV carried out in Baltimore, Maryland, from 1980 to present. Dr. Edward Brink, IM, CPS, led a discussion on a draft, "More Potent Inactivated Poliomyelitis Vaccine," to supplement the current recommendation issued in 1982. The new draft provides information on the enhanced potency IPV, produced in human diploid cells, thought soon to become available in the United States (poliovirus vaccine inactivated; Connaught Laboratories, Ltd.).

Dr. Koplan reviewed the committee's past deliberations on polio as well as consideration for planning a symposium on poliomyelitis vaccines, under the auspices of the Institute of Medicine (IOM), National Academy of Sciences. The mission would be to clarify publicly the specific questions to be answered regarding policy for use of an improved vaccine in the United States. Dr. Queta Bond, IOM, stated that IOM is willing to provide a neutral forum and that Dr. Frederick Robbins, former President of IOM, would like to participate. The committee agreed that a meeting of this type would be a valuable step in reviewing the national vaccine policy in the United States, and asked that CDC work with IOM to set up such a meeting to provide further information to be used in considering U.S. polio vaccine policy at the autumn meeting of the committee. The consensus was that if a new IPV is approved before the next ACIP meeting, current recommendations would remain appropriate, merely substituting the new IPV for existing IPV.

Dr. Katz reported on a session he attended on oral polio vaccine issues during the FDA-sponsored Vaccine and Related Biologic Products Advisory Committee meeting, January 29-30, 1987, in Bethesda, Maryland.

Dr. Hinman stated that the Public Health Service Act has been amended to include the National Vaccine Program, established in the Department of Health and Human Services (HHS), to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines. The HHS Secretary (Otis R. Bowen, M.D.) has appointed the Assistant Secretary for Health (Robert E. Windom, M.D.) as Director of the Program.

Hepatitis B - Booster Doses and a New Hepatitis B Vaccine

Dr. Stephen Hadler, Division of Viral Diseases (DVD), CID, led a discussion of a revised draft update on hepatitis B prevention which had been mailed to the committee for review before the meeting. The draft provided an update on hepatitis B vaccine (HB) usage and its impact on disease incidence in the 5 years following licensure, recommendations for the use of a new HB produced in yeast by recombinant DNA technology, and an assessment of the need for HB booster doses in prior vaccine recipients. After a lengthy discussion, particularly on the need for HB vaccine booster doses, Dr. Katz requested the members to send specific comments on the draft within 2 weeks, and asked Dr. Hadler to prepare a revised statement to be circulated to the members for final comments, and then published.

Dr. Mark Kane, DVD, CID, distributed a draft update on prevention of perinatal hepatitis B virus (HBV) transmission and led a discussion on the strategy of screening women at high risk for HBsAg. The committee currently recommends that pregnant women in certain high-risk groups for HBV be screened for HBsAg during a prenatal visit and that infants of HBsAg positive mothers receive hepatitis B immune globulin (HBIG) and HB after birth. Several studies indicate that there are substantial problems in implementation of these recommendations, and Dr. Kane discussed the problem areas. Because of the complexity and lack of sensitivity of the current strategy of screening only women at high risk for HBsAg, Dr. Kane proposed that the committee consider a policy of universal screening of all pregnant women for HBsAg. He presented an analysis of the relative cost-effectiveness of several antenatal HBsAg screening strategies, and compared these to the cost-effectiveness of screening of all transfused blood for HBsAg, and that of antenatal or perinatal screening for other diseases. After a lengthy discussion, Dr. Katz proposed that Dr. Kane make his analysis available to the medical community (through publication) and requested that CDC discuss this proposal with the American Academy of Pediatrics and the American College of Obstetrics and Gynecology prior to the next meeting.

Other ACIP Business

Dr. Koplan announced that the Second National Adult Immunization Community Forum will be held April 27-28, 1987, in Atlanta, Georgia. Dr. Hinman distributed date-saver announcements of the 21st Immunization Conference to be held June 8-11, 1987, at the Fairmont Hotel in New Orleans, Louisiana. The Conference is sponsored by the Centers for Disease Control/Center for Prevention Services. Preregistration and hotel reservation forms will be available soon.

The next ACIP meeting was planned for Tuesday and Wednesday, June 23-24, 1987. Topics for discussion will include hepatitis B, BCG, poliomyelitis, varicella zoster, pneumococcal and Haemophilus influenzae b vaccines, as well as other items.

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

Samuel L. Katz 9 May 1987

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