DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
October 14 and 15, 1981
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Auditorium A at the Centers for Disease Control in Atlanta, Georgia, on October 14 and 15, 1981. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Catherine M. Wilfert, Chairwoman
Dr. James Chin
Dr. John B. DeHoff
Dr. Frederick L. Ruben
Dr. Stephen C. Schoenbaum

Ex-Officio Members

Dr. William S. Jordan, Jr. (NIH)
Dr. Harry Meyer, Jr. (BOB)

Liaison Representatives

Dr. J. M. S. Dixon (NACI)
Dr. Richard J. Jones (AMA)
Dr. Edward A. Mortimer, Jr. (AAP)

Special Advisors

Dr. Joanne E. Finley
Dr. Gary R. Smith

Executive Secretary

Dr. H. Bruce Dull

COMMITTEE MEMBERS ABSENT

Dr. Maxine Hayes
Dr. William M. Marine
Dr. Jay P. Sanford

Liaison Members

Dr. Peter A. Flynn, Capt., USN (DOD)

HHS STAFF PRESENT

BUREAU OF BIOLOGICS, FDA

Dr. Robert Gerety

CENTERS FOR DISEASE CONTROL

Office of the Center Director

Donald Berreth
Dr. Donald Hopkins
Gene Matthews
Peggy Ruiz
Dr. Kathryn N. Shands

International Health Program Office

Diego Buriot
Billy G. Griggs
Dr. T. Stephen Jones

Center for Infectious Diseases

Dr. George Baer
Dr. J. V. Bennett
Dr. Kenneth Bernard
Dr. Adrian Chappell
Dr. W. R. Dowdle
Dr. Martin Favero
Dr. Donald Francis
Dr. Stephen Hadler
Dr. M. Kane
Dr. Alan Kendal
Dr. James Maynard
Dr. D. M. Morens
Dr. Gary Noble
Dr. Jack D. Poland
Dr. Lawrence B. Schoenberger
Edward Snow
Dr. William Winkler

Center for Prevention Services

Steven Barid
Dr. Kenneth Bart
Dr. Roger Bernier
Cheryl Blackmore
Dr. Alan Bloch
Dr. Stuart Brown

Center for Prevention Services (continued)
Dr. James Curran
Donald Eddins
Dr. Steven Fite-Wassilak
Dr. James T. Goodrich
Patrick Gould
Dr. Alan Hinman
Dr. Jonathan Kaplan
Dr. Olen Kew
Dr. Robert J. Kim-Farley
Mark Kramer
Dr. J. Michael Lane
Dr. Stephen Margolis
Joe H. Miller
Dr. Walter Orenstein
Dr. Gladys H. Reynolds
Dr. Sumner E. Thompson
W. L. Whittington
Akbar A. Zaida

OTHERS PRESENT
Norman Altman
Dr. William H. Bancroft
Bob Bartholomew
Dr. Byron S. Berlin
Bryan Brown
Colonel Alfred K. Cheng (USAF)
William A. Cliech
P. Cohen
W. F. Daly
Dr. Jules L. Dienstag
M. Downing
Dr. Theodore Eickhoff
LTC. Frederick Erdtmann (USA)
A. B. Fiskett
M. R. Hilleman
John Chriss Hoffman
Dr. Saul Krugman
Dr. Stanley M. Lemon
Dr. William B. Mahaffey (USN)
A. McLean
Katherine McRae
Joe Moore
R. D. Morr
Thomas M. Nylund
Paul M. O'Malley
Dr. David G. Ostrow
Dr. Aubrey S. Outschoorn
Dr. K. Starko
Cladd E. Stevens
Dale Stockbower
Stephen A. Szumski
Patricia E. Taylor
Timothy Williamson

Day One

The meeting was opened at 8:15 a.m. by Dr. Donald Hopkins, Assistant Director for International Health, Centers for Disease Control. In that the agenda for the morning's discussion involved hepatitis B and the developmental hepatitis B vaccine, Dr. Hopkins called attention to both the domestic and international involvement CDC has had with hepatitis investigations and surveillance. He also announced the appointment of Dr. J. Michael Lane, Director, Center for Prevention Services, as Executive Secretary of the ACIP, Dr. Lane's term to begin following the current meeting.

Dr. Catherine Wilfert assumed the Chair and called for a slight modification in the agenda to receive a special research report from Dr. James Maynard and his colleagues in the Hepatitis Laboratory Division of the Center for Infectious Diseases.

CDC Collaborative Trial of Hepatitis B Virus Vaccine

Dr. Maynard reviewed background and findings in a collaborative clinical trial of hepatitis B virus (HBV) vaccine prepared by Merck, Sharp, and Dohme and sponsored by the CDC Centers for Prevention Services and Infectious Diseases and carried out in five United States cities. Planning for the study began in January 1978, and it became operational in April 1980.

In brief summary, the trial was a double blind, placebo control, efficacy evaluation of Merck HBV vaccine, 20 micrograms. Vaccination was followed by only minimal side effects. Two doses of vaccine produced antibody in 80% of vaccine recipients. A booster dose 6 months after the first dose markedly increased the proportion of recipients who produced high antibody titers. The incidence of HBV events was markedly less in the vaccine recipients compared to the placebo recipients ($p=0.0004$). Between month 3 and 15 after receipt of the first dose, 44 more severe HBV events (hepatitis and/or hepatitis B surface antigen positive) occurred in the placebo group while only 9 occurred in the vaccine group. Eight of the 9 HBV events in the vaccinees occurred in hypo- or non-responders to the vaccine.

In commenting on the results, Dr. Maynard concluded that the vaccine appeared to be safe, showing essentially no side effects. Some discomfort at the injection site and low-grade fever were observed, but these, only rarely. The vaccine was immunogenic, approximately 80-85% of vaccinees developing antibody. And among those with antibody, there was essentially complete protection against hepatitis infection (97%). Furthermore, there was some evidence of modification of clinical illness when vaccine had been given early in the incubation period.

Discussion of the collaborative trial clarified several points. In particular, questions focused on the finding that approximately 15-20% of vaccinees did not produce measurable antibody. Some variation was noted among study sites.

With respect to the individual nonresponders, little is known at the present time, but additional evaluation is underway. It was reported by some participants that in other studies of HBV vaccine, nonresponders were known to be capable of producing antibody to other antigens and, that on revaccination, the majority did seroconvert.

Another issue discussed was the equivalency of the 20 microgram and other doses. Summary data were presented on the equivalency of 20 microgram and 40 microgram doses. It was noted that in young children even a 10 microgram dose was immunogenic.

Hepatitis B Virus Vaccine

The Committee returned to its prepared agenda on HBV and the HBV vaccine (expected soon to be licensed and to become available for distribution in mid-1982).

In reviewing the occurrence of hepatitis B in the United States, Dr. Donald Francis indicated that more than 200,000 persons are estimated to be infected with HBV each year, one quarter of them becoming jaundiced. More than 10,000 are hospitalized and, on average, 250 of them die with fulminant disease. Approximately 6% of hepatitis B cases become carriers, resulting currently in a pool of 400,000-800,000 persons.

Of the hepatitis B carriers, approximately 25% (100,000-200,000) develop chronic hepatitis which often progresses to cirrhosis. Furthermore there is an association of being a carrier and developing liver cancer. In general, it is estimated that each year in the United States 4,000 persons die from hepatitis B-related cirrhosis and more than 800 die from hepatitis B-related liver cancer.

With respect to potential patterns of vaccine use, attention was directed to the concept of target groups based on prevalence both of hepatitis B carrier status and hepatitis B antibody status. Among persons and groups at obvious risk of exposure are medical and laboratory workers exposed to human blood; hemodialysis patients; homosexually active males; users of illicit injectable drugs; and other persons and groups whose living, occupational, or recreational activities bring them into contact with HBV. There was considerable discussion of such categories in that they would become the basis of a recommended strategy for effectively using HBV vaccine. A draft statement will be circulated for comment prior to the next meeting.

Poliomyelitis

Following introductory comments by Dr. Alan Hinman, Dr. Jonathan Kaplan reviewed the status of poliomyelitis in the United States based on the "best available paralytic poliomyelitis case count" (BAPPCC), characteristics of which he described. Using a previously prepared tabulation, Dr. Kaplan traced the reported occurrence of poliomyelitis in the United States since 1979 and noted the steady decline from 22 cases (1979) to 8 (1980) to 6 (through October 1, 1981). Only in 1979 were there cases attributed to epidemic spread, the remaining ones being almost entirely related to receiving or having contact with a recipient of oral polio vaccine (OPV).

Dr. Olen Kew reported to the Committee on the laboratory technique of poliovirus oligonucleotide mapping. This procedure separates virus RNA fragments in a way which produces an identifiable "finger print", permitting remarkably reproducible strain characterization. The epidemiologic implications of the technology were of considerable interest.

Dr. Roger Bernier summarized newer developments in inactivated poliovirus vaccines (IPV), particularly the clinical field trials with high potency products developed in Europe. Results show a direct relationship between antigen mass and antibody response and a seroconversion rate after two doses of vaccine of 90-100%. Other vaccines with potency determined by D-antigen content are under development and are hoped to result in seroconversions of about 90% of vaccinees after one dose and 100% after two.

Dr. Robert Kim-Farley reported on the distribution of OPV and IPV in the United States since 1977. He pointed out that an average of approximately 24-25 million net doses of OPV were distributed annually in the last 5 years and that 40,000 and 29,000 net doses of IPV were distributed in 1979 and 1980 respectively.

The Committee reviewed a draft revised recommendation on poliomyelitis prevention and discussed at length the management of possibly exposed unimmunized or partially immunized parents and other household contacts of OPV recipients. Although alternative courses of action were considered, the Committee was eager that none should interfere with timely protection of infants and children.

Based on the discussion, an additionally revised draft will be prepared for distribution and final action by the Committee.

Plague Vaccine

Dr. Jack Poland reviewed with the Committee a draft revised version of its recommendation on plague vaccine. Primary emphasis in the revision was on clarification of dosage schedules and inclusion of additional data on side effects. Based on discussions, a subsequent draft will be prepared for final review by correspondence.

Day Two

Rabies Vaccine Reports

Dr. William Winkler introduced three reports on rabies vaccines: The first, presented by Dr. Kenneth Bernard, was a summary of antibody responses following pre-exposure immunization of humans with human diploid cell rabies vaccine (HDCV) administered by different routes. The objective of the comparisons was to investigate the equivalency of intradermal, subcutaneous, and intramuscular routes of vaccination. Data on more than 700 volunteers showed comparability of responses to a series of 2 or 3 (0.1 ml) intradermal and 3 (1.0 ml) intramuscular doses of HDCV. The Committee encouraged continued study of intradermal vaccination with HDCV and indicated an interest in considering it an alternative to intramuscular administration if additional experience continues to show comparable results.

Dr. George Baer presented tabular data on serologic responses to pre-exposure and post-exposure treatment with HDCV. All vaccinees (510/510) had protective antibody levels following pre-exposure treatment, and 99.9% (1299/1300) had protective antibody levels following post-exposure treatment. In view of these findings the Committee saw no reason to continue recommending routine serologic documentation of antibody responses when persons are properly vaccinated with HDCV. A brief supplementary statement on rabies vaccine and serologic testing was proposed for publication at an early date.

Dr. Byron Berlin, Deputy Laboratory Director, Michigan Department of Public Health, reviewed his Department's development and field testing of a rhesus monkey diploid rabies vaccine. This vaccine may eventually be proposed for use as an alternative to HDCV.

Adult Immunization

Dr. Hinman reported little success in developing a useful alternative presentation on adult immunization to that reviewed at the spring ACIP meeting. A more detailed version would require rewriting existing recommendations and create consistency problems whenever updates were undertaken. The Committee elected to reevaluate the earlier-proposed document which highlighted the need for vaccines in adult groups and pointed out important characteristics of vaccines in adults with respect to special needs and side effects. Dr. Hinman will prepare additional draft material for review at the next meeting.

Smallpox Vaccine

Dr. Stephen Jones and Mr. Billy Griggs reviewed a report requested by the Committee on the use of smallpox vaccine in United States civilians. The paper considered available evidence which might corroborate the vaccine's inappropriateness in patients with infections such as with herpes viruses. In his discussion, Dr. Jones demonstrated a considerable decline in the distributed doses of smallpox vaccine since 1972. In that year approximately 3.7 million doses entered the civilian market. In 1980, about 500,000 were distributed. Although the relationship between doses distributed and doses used is far from direct (e.g., multiple dose vials are involved in the count), the Committee remained concerned that only persons with potential exposure to vaccinia virus in laboratory and other settings should be receiving the vaccine. Discussion focused on ways to educate physicians and the public to the proper use of the vaccine and conceivably to ways to limit its distribution.

Other Business

The Committee was polled with respect to preferable dates for its winter meeting in January or February. Dates based on general preferences will be determined once personal calendars are reviewed.

of the statement and prepare guidelines which would be helpful to those evaluating exposures and choosing globulins.

Adult Immunization

Dr. Wayne Greaves presented an amalgamation of the sections of ACIP recommendations which deal with immunization of adults. This was in response to the Committee's recommendation that specific material on adult immunization be developed in order to focus attention on the need for continuing systematic immunization beyond childhood.

The Committee's discussion of the draft suggested that referral of readers to already existing recommendations would probably not be adequate. On the other hand, the Committee was concerned about attempting to reprint full information about all vaccines of value to adults, since doing so would pose editorial and publication difficulties with respect to the texts of other ACIP statements. It was recommended that in preparation for the next Committee meeting, alternative approaches to adult immunization recommendations be considered and that the matter be reexamined.

Day Two

Draft Statement Reviews

Much of the time available to the Committee was devoted to reviewing draft recommendations on influenza vaccine and pneumococcal polysaccharide vaccine and a revised section in the statement on immune globulin and hepatitis prophylaxis. Discussions and recommendations were extensive although mainly oriented toward clarification and organization. The staff was asked to compile and finally edit material to be examined by the Committee through correspondence and telephone communication before publication.

Measles Vaccine-Age Recommendations

Drs. Edward Mortimer and Walter Orenstein briefly reviewed some preliminary experimental evidence which suggests that the age of initial measles vaccination may influence the response rate on revaccination more than previously expected. The new data are from infants immunized at 6-10 months in which the youngest vaccinees had the least good responses to second vaccinations and failed thereafter to sustain antibody as measured by hemagglutination inhibition. Enhanced neutralization testing demonstrated the presence of antibody. Although not resolved, the question was posed as to the need to increase the minimum age for vaccination from 6 to 9 months during an epidemic control program. (Routine vaccination against measles is at a later age, but epidemic control has been a circumstance under which immunization of young infants has been recommended.) Additional discussion and more clinical evidence will help to resolve this matter.

Other Business

Fall Meeting

The Committee selected October 14 and 15 for its fall meeting. Items not covered at the spring session will be reintroduced. These include plague vaccine and current usage patterns of smallpox vaccine. In addition, routine reexamination and updating recommendations on statements for rabies and polio vaccines will be scheduled.

With the thanks of the Chairwoman the meeting was adjourned at 3:00 p.m.

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

Catherine M. Wilfert

Catherine M. Wilfert, Chairwoman — Nov. 5, 1981 Date