DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

CENTER FOR DISEASE CONTROL
Atlanta, Georgia

SUMMARY MINUTES OF MEETING
Immunization Practices Advisory Committee
January 18-19, 1979

The Immunization Practices Advisory Committee (ACIP) met in Atlanta, Georgia, January 18-19, 1979. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT
Dr. E. Russell Alexander
Dr. Suzanne E. Dandoy
Dr. Edwin D. Kilbourne
Dr. Thomas M. Vernon, Jr. (Chairman)
Dr. Catherine M. Wilfert

Ex-officio
Dr. Harry Meyer, Jr.

COMMITTEE MEMBERS ABSENT
Dr. Maxine Hayes
Dr. Jay P. Sanford
Dr. Reuel A. Stallones

Ex-officio
Dr. William S. Jordan, Jr.

Liaison
Dr. Edward A. Mortimer
Dr. Asher J. Finkel
Dr. J. M. S. Dixon

CONSULTANTS
Dr. George W. Comstock
Johns Hopkins University
Dr. Kenneth R. Wilcox, Jr.
Michigan Dept. Public Health

CENTER FOR DISEASE CONTROL STAFF
Office of Center Director
Dr. William H. Foege, Director
Mr. Don Berreth

Bureau of Epidemiology
Dr. J. Lyle Conrad
Dr. David Fraser
Dr. Marjorie Pollack
Dr. Lawrence Schonberger
Dr. William Winkler

(CDC, continued)
Bureau of Health Education
Dr. Dorine J. Kramer

Bureau of Smallpox Eradication
Dr. Michael Lane, Director
Mr. Robert C. Hogan

Bureau of State Services
Dr. Donald Millar, Director
Mr. Roger Bernier
Dr. David Brandling-Bennett
Dr. Alan Hinman (Acting Executive Secretary, ACIP)
Dr. Kenneth E. Powell
Mr. John Seggerson
Dr. Mary Serdula
Dr. Dixie Snider
Mr. Jerry Spyke
Ms. Lisa Wohl

VISITORS
Dr. Alan Bernstein, Pharmaceutical Manufacturing Assn., Marietta, Pa.
Mr. J. Stanford Fisher, McGraw Hill News Bureau, Atlanta, Ga.
Dr. Geoffrey H. Kalish, Lederle Laboratories, Pearl River, N. Y.
Mr. L. William McIntosh, Merck, Sharp & Dohme, West Point, Pa.
Ms. Lee Motyka, Merieux Institute, North Miami, Fla.
Mr. Marc A. Plattner, Connaught Laboratories, Medford, N. J.
Mr. Douglas B. Reynolds, Connaught Laboratories, Swiftwater, Pa.
Mr. R. J. Saldarini, Lederle Laboratories, Pearl River, N. Y.
Mr. Charles S. Taylor, United Press International, Atlanta, Georgia

The meeting was called to order at 8:34 a.m. by Chairman Vernon. Following introductions, Dr. William Foege made some introductory comments, specifically thanking the ACIP members for the continued important service they are providing to the Public Health Service and to the American population. He stated that the role of the ACIP is of increased relevance lately because of the increased importance of objective technical recommendations in these days of increased public and political debate on vaccine issues. He also announced his hope that it would not be too long before an Assistant Director for Science would be named for the Center. This person will serve as Executive Secretary of the ACIP following the imminent retirement of Dr. Bruce Dull. Drs. Alexander and Wilcox mentioned the need for expanded Committee size and the need to include a representative of local health departments on the Committee.

At 8:56 discussion began on BCG. Following introductory comments by Dr. Dixie Snider, Dr. George Comstock described the collaborative field trial on BCG use which has been taking place in India. Planning for this trial began in 1964, and the Madras area was picked because of its high infection rate, absence of prior use of BCG vaccine, and high rate of sensitization with other mycobacteria. Field aspects of the study began in 1968 with a careful household census and skin testing of the population with 3 TU of PPD-S and 10 TU of Battey antigen. Following skin testing all members received one of three regimens: one-third got placebo, one-third received a standard dose of BCG (one-half of these received a Danish BCG and one-half a French BCG), and one-third got 1/10 of the dose of standard BCG (again, one-half Danish and one-half French). In total, more than 300,000 persons were involved, comprising 80-90% of the population in the area. Children in the study were periodically retested with skin tests, and every 2-1/2 years there was a complete X-ray survey. The study was carried out in double-blind fashion. In 1977 a committee of experts reviewed the data for the first 6-1/2 years of the study. The two major findings of this analysis were:

1. There was no evidence that BCG had any protective effect in the first 6-1/2 years, regardless of dosage level or vaccine type.

2. There was neither harm nor benefit from administering BCG vaccine to tuberculin reactors or to active cases of tuberculosis.

One rather unusual aspect of this study, which in some fashion complicates analysis of results, was that in spite of an annual infection rate of approximately 2% per year, virtually all of the cases of tuberculosis seen occurred in persons who were skin-test positive at the start of the trial. The significance of this is not entirely clear, and the possibility exists that further follow-up of the population will reveal some long-term protective effect, although the likelihood is felt to be low.

Dr. Comstock then gave a brief review of other BCG field trials which have indicated protective rates ranging from approximately 80% down to zero. One of the major conclusions Dr. Comstock draws from this is that there must be considerable variation between BCG vaccines and that the assertion that the BCG vaccines can be readily standardized is a considerable over-statement.

At 9:40 Dr. Snider took the floor again to guide discussion on the proposed revision of the BCG statement. It was stressed that none of the vaccines currently available in the United States have been shown to be effective in clinical trials in humans. Discussion then turned to specific items in the proposed statement, with some of the major discussion relating to the wording and location of comments on tuberculosis risk and prevention in health workers. Following a coffee break discussion continued on the proposed statement until lunch. It was agreed that a revised draft of the statement, taking into account the members' comments, would be mailed to members for review prior to final issuance. The Committee adjourned for lunch at 12:30 p.m. and reconvened at 1:20 p.m.

The afternoon session began with a summary of influenza surveillance data by Dr. Brandling-Bennett. Influenza activity in the current season first appeared in the western part of the United States and now has affected much of the country, most widely in the southeast and southwest. To date all influenza A isolates have been of the H1N1 strain; no H3N2 isolates have been recovered in the United States. As was the case in the last influenza season, H1N1 influenza has affected predominantly children and adolescents, with few isolates (and no outbreaks) reported in individuals over the age of 26. Two isolates of influenza B and one of influenza C have been reported, but no outbreaks due to these viruses have been reported. Outbreaks of influenza due to H1N1 virus have also been reported in Scotland, England, Jamaica, France, and Spain. Additionally, outbreaks and sporadic cases due to H3N2 influenza have been reported from Hungary, Bulgaria, and Israel.

Dr. Hinman then summarized activities in the Federally-supported influenza immunization program. Project grants have been awarded to 38 States and 10 large cities and territories. In total, 3.5 million doses of vaccine have been distributed, with vaccine distribution beginning in early October and not being completed (for the youth formulation split-virus product) until early December. Preliminary reports indicate that approximately 570,000 doses of vaccine were administered in public programs in the months of October and November. This total includes 170,000 doses of State-purchased vaccine in California as well as the Federally-purchased vaccine. The level of vaccine administration is somewhat lower than originally anticipated. Major reasons cited by project grantees in a survey carried out in late December included problems related to the lack of availability of funds until the first of October, the late delivery of vaccine, and problems associated with hiring individuals locally once funds became available. Another factor mentioned was the major emphasis being placed on the childhood immunization initiative and the precedence that this activity took over influenza immunization.

Dr. Hinman then brought up questions which have recently been raised about the risk status of the healthy elderly and other questions raised by the Office of Science and Technology Policy in the White House about the influenza immunization program. The relevance of these issues to the decisionmaking cycle for the coming influenza season was discussed. A meeting in early February is planned, to include members of the ACIP, the Bureau of Biologics Advisory Panel on Viral and Rickettsial Vaccines, consultants of the National Institute of Allergy and Infectious Diseases and other experts. This technical meeting will address the subjects of the degree of antigenic drift between this year's virus and last year's, recommended components for influenza vaccine for the coming year, and the need for clinical field trials. Additionally, the groups will also address issues of definition of high-risk individuals. It is then anticipated that a Secretary's Conference on Influenza will be held in March or April to discuss public policy on influenza and to provide a wider public forum for discussion of the risk status of different population groups.

Following introductory comments by Dr. Meyer on the subject of limiting factors in the production of influenza vaccine, Dr. Alan Bernstein then summarized the factors that influence the production of influenza vaccine. Dr. Bernstein, who works for Wyeth Laboratories, had been asked by the Pharmaceutical Manufacturers Association to speak for the industry. Additional comments were obtained from representatives of other manufacturers in the room. The extreme importance of timely decisionmaking on vaccine components and predictability of the size of the market were stressed. Early decision on vaccine components was felt to be the most important single factor in permitting the production of an adequate supply of vaccine.

Following the afternoon coffee break, Dr. David Fraser presented information obtained by Dr. Gregory Filice and himself in a study in Charleston, South Carolina, in which hospital records of all cases of pneumococcal bacteremia hospitalized in Charleston County were reviewed. This review indicated an overall incidence of pneumococcal bacteremia of approximately 8.5 per 100,000 per year, with the rate in blacks being nearly 6 times the rate in whites. Highest age-specific rates were seen in those under 2 years of age and those over 60, although there was more or less of a plateau (at least for blacks) in incidence rates above age 30. At all socioeconomic levels, the rates for blacks were approximately 6 times higher than for whites, and there was no real difference in incidence rates from one socioeconomic status group to another for blacks or for whites. Two-thirds of patients had pneumonia associated with their bacteremia.

Dr. Claire Broome then summarized current information on pneumococcal vaccines, including information on reactions to the vaccine. In pre-licensing trials, 3-4% of recipients had local pain and erythema, and about 1% had fever. Since licensure, pneumococcal polysaccharide vaccine has been administered to approximately 16,000 nursing home patients in the State of Massachusetts. Of these, about 5% had local soreness, 0.4% had temperatures $\geq$100°, and 0.2% had temperatures >102°. Essentially similar results have been found on preliminary analysis of data on some 10,000 nursing home patients in Ohio. In total,

approximately 1 million doses of pneumococcal polysaccharide vaccine are estimated to have been administered since licensure in this country. Two severe reactions possibly related to vaccination, both nonfatal, were described. In one of these the patient suffered severe bronchospasm approximately 30 seconds after vaccination; in the other, cardiorespiratory collapse occurred approximately 45 minutes after vaccination.

At least one attempt to study the clinical effectiveness of the vaccine in elderly populations has reportedly been thwarted by an opinion (of the review committee) that it was unethical to withhold vaccine from the control group.

In an attempt to determine the relative importance of different pneumococcal serotypes in the United States, a program to serotype all isolates from normally sterile sites has been undertaken in 40 hospitals in 24 States in cooperation with the National Nosocomial Infections Study. A total of approximately 420 isolates have been reported so far. Of these, 68% are of types represented in the vaccine, and an additional 10% are of related Danish groups, indicating that about 75% of the isolates are potentially of vaccine-preventable type. The meeting adjourned for the day at 4:30 p.m.

The meeting reconvened at 8:30 a.m. on January 19. Dr. Alan Hinman presented an update on the measles elimination program announced by Secretary Califano on October 4, 1978. Formal resolutions endorsing the program have been adopted by the U. S. Conference of City Health Officers, the National Association of County Health Officers, and the American College of Preventive Medicine. Additionally, the Executive Committee of the Association of State and Territorial Health Officers has endorsed the concept without formally passing a resolution. On December 7, 1978, several consultants were invited to the Center to discuss various aspects of the measles elimination program. In general they felt that the proposed goal was feasible and that the activities proposed were those most likely to lead to the elimination of indigenous measles in the United States.

The consultants had not felt that a routine second dose of measles vaccine (as recommended by Dr. Saul Krugman) was, at this point, necessary. However, several had felt that the need for a second dose should be continually reassessed as, even with exceedingly high levels of vaccination, the proportion of vaccine failures might possibly be large enough to sustain the transmission of measles. Discussion by members of the ACIP yielded essentially the same conclusion: it was possible that a second dose of measles vaccine might be needed to completely effect elimination of measles, but information currently available does not clearly indicate the need. A brief summary of the occurrence of measles in 1978 and during the beginning of the 1978-79 measles season was given, indicating that the reported incidence of measles in 1978 was more than 50% below the reported incidence in 1977, but that during the last 12 weeks of 1978 (beginning of the 1978-79 measles season) there had been an increase in reported cases.

At 9:30 a.m. Dr. Schonberger introduced Dr. Marjorie Pollack, who summarized the outbreak of poliomyelitis in the Netherlands in 1978. In total, 110 cases of polio (80 paralytic) were reported. There was 1 fatality. All reported cases were in members of religious groups which reject vaccination. They reside in many areas of the Netherlands. Of interest was the fact that members of these religious groups comprise less than 1/2 of the estimated susceptibles in the country. Nonetheless, no cases appeared in other unimmunized individuals in the Netherlands. Evidence was obtained that immunized schoolmates of members of these religious groups had substantial infection rates with poliovirus, although these were 50% lower than infection rates among the group's members.

There was then discussion about the degree of community protection or lack of it conferred by IPV and the problems of determining whether or not similar protection might be achieved in a country such as the United States, which is much larger than Netherlands and other western European countries, and also has a generally lower immunization acceptance rate.

Dr. Pollack then summarized the U. S. experience with polio from 1969 through 1977, and Dr. Melinda Moore gave a brief presentation on the cases so far reported for calendar year 1978. The polio surveillance unit received reports on 20 cases of paralytic polio in 1977, and 7 cases of paralytic polio have thus far been reported for 1978. The majority of these cases were associated with vaccine, primarily being classified as contact cases. An analysis of the number of cases of vaccine-associated polio and doses of OPV distributed for three 3-year periods (1969-1977) indicated an overall rate of 1 vaccine-associated case for every 3.12 million doses of OPV distributed with no statistically significant difference between the three periods. There then followed discussion about the need for more information about the effectiveness of the IPV currently available in the United States, and a specific suggestion was made that studies be carried out of combined IPV-OPV regimens such as are administered in some provinces of Canada. Questions continue to be raised about the interpretation of existing ACIP recommendations on polio vaccine, particularly with regard to immunization of adults. It was agreed the polio surveillance unit would propose revisions of the current recommendation to try to deal with these questions and that the proposed revisions would be mailed to the members well in advance of the next meeting.

At 11:25 a.m. Dr. Winkler made a brief presentation about rabies in the United States. He was followed by Dr. Larry Anderson, who spoke about the human origin vaccine presently being studied in the United States. The situation with animal rabies is that the fox continues as an important reservoir, particularly in central Appalachia; skunk rabies is primarily located in the Ohio and Mississippi River drainage patterns, and raccoon rabies is slowly spreading from its initial focus in Florida--it has now arrived in Georgia, South Carolina, and Alabama. It is anticipated that

raccoon rabies will continue to spread slowly in the United States. Bat rabies continues to be found throughout the country. There have been 9 cases of human rabies reported in the last 5 years. Four of these were imported, and 3 resulted from unusual circumstances (corneal transplant, laboratory accident). There has been no case of human rabies in the United States resulting from the bite of a rabid dog in more than 10 years.

A previously unrecognized problem has now been detected, and that is vaccine-induced rabies in animals, primarily dogs. Thirty cases have been reported in the past 2 years. Estimates of incidence range from approximately 0.1 to 2.0 cases per million vaccinations.

There are 2 major studies underway on the human origin vaccine presently being considered for licensure in the United States. One is through CDC: 772 people have been enrolled in the study, both pre- and post-exposure. Additionally, the manufacturer has enrolled approximately 2,500 individuals in studies; most represent pre-exposure immunization of veterinary students. No serious reactions to the vaccine have been discovered to date. About 50% of recipients have no reaction whatever. About 30% have a mild local reaction, and 15-20% demonstrate mild systemic reaction, primarily fever and headache. Of individuals receiving the 3-dose pre-exposure regimen (doses given day 0, 7, and 21 or 28), 100% develop antibodies. The titer is approximately 20 times higher than titers developed using duck embryo vaccine. There have been 63 persons bitten by proven rabid animals who received this vaccine in conjunction with human rabies immune globulin. None of them developed rabies. Post-exposure treatment regimen includes 5 doses at days 0, 3, 7, 14, and 28. A 90-day dose has also been discussed, but there is as yet no agreement as to its necessity. It is anticipated that licensure and availability of the vaccine is at least 9-12 months away because of problems in establishing a production facility. At about the time the vaccine is licensed there will be a need for ACIP to revise its statement, but there is no perceived need for revision at the present time.

Final discussion centered on the need to obtain data on effectiveness of combined IPV-OPV regimens and the need to obtain information about the effectiveness of the pneumococcal polysaccharide vaccine in protecting the elderly against pneumonia. The meeting adjourned at 12:16 on January 19, 1979.

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

Alan R. Hinman, MD 2/7/79

Acting Executive Secretary Date