DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA

SUMMARY MINUTES OF MEETING

January 15-16, 1975

The Immunization Practices Advisory Committee met in Atlanta, Georgia, January 15-16, 1975.

COMMITTEE MEMBERS PRESENT

Dr. David J. Sencer, Chairman
Dr. H. Bruce Dull, Executive Secretary
Dr. Elizabeth Barrett-Connor
Dr. Lonnie S. Burnett
Dr. William R. Elsea
Dr. Alexander D. Langmuir
Dr. Gilbert M. Schiff
Dr. Eleanor G. Shore

Ex Officio

Dr. Paul Parkman, Bureau of Biologics, FDA, DHEW

Liaison (American Academy of Pediatrics)

Dr. Samuel Katz

COMMITTEE MEMBERS ABSENT

Dr. E. Charlton Prather

ACIP CONSULTANTS PRESENT

Dr. Dieter Koch-Weser, Harvard Medical School
Dr. Gardner Middlebrook, University of Maryland School of Medicine
Dr. William H. Oatway, Jr., University of Southern California
Dr. Lee B. Reichman, New Jersey College of Medicine
Dr. John A. Sbarbaro, Denver Department of Health and Hospitals
Dr. David T. Smith, Duke Medical School
Dr. Donald Smith, University of Wisconsin

OTHERS PRESENT

Dr. Theodore Eickhoff, University of Colorado Medical Center
Mr. Jack Gertzog, Bureau of Biologics, FDA, DHEW
Ms. Frances Ogasawara, American Lung Association
Mr. Philip G. Rettig, Research Foundation
Dr. Morris Schaeffer, Bureau of Biologics, FDA, DHEW
Dr. Gene H. Stollerman, University of Tennessee

CDC STAFF

Office of the Center Director:	Dr. William H. Barker Mr. Don Berreth
Bureau of Epidemiology:	Dr. Philip S. Brachman Dr. Lawrence Corey Dr. Michael B. Gregg Dr. Michael Hattwick Dr. Charles H. Hoke, Jr.
Bureau of Laboratories:	Dr. Hugo David Dr. Walter Dowdle Dr. George Kubica Dr. Gary Noble
Bureau of State Services:	Mary Louise Atkinson Mr. Windell Bradford Dr. Lyle Conrad Dr. Phyllis Edwards Dr. Laurence Farer Dr. Vernon Houk Dr. Dixie Snider, Jr. Mr. Jerry Spyke Mr. Ferdinand Tedesco
Bureau of Training:	Dr. Winthrop N. Davey

The meeting was called to order at 8:30 a.m. by Dr. David J. Sencer, Director, Center for Disease Control, the Committee Chairman. Following introduction of Committee members, consultants, and guest participants, he described the objectives of reviewing BCG vaccines as a thorough assessment of their appropriate use in tuberculosis prevention in the United States. As general background for participants, he described the orientation of the ACIP and the audience to which it addresses its recommendations. He emphasized the ACIP's principal constituency as organized public health and not individual practitioners of medicine and encouraged the discussion on BCG to consider primarily the public health implications of vaccination.

Surveillance of Tuberculosis

Tuberculosis cases and deaths in the United States, reviewed by Dr. Edwards, have declined steadily since reporting began in the 19th century. Preliminary data for 1974 indicate that about 30,000 cases of disease and 3,600 deaths have occurred. Case and death rates per 100,000 population are generally about 50 percent lower than the corresponding rates ten years earlier (1964). Likewise, the rate of infection indicated by positive tuberculin skin tests has declined approximately 75 percent in the last ten years both for 6-year-olds entering school and adolescents. Prevalence of positive skin-tests among school enterers is now about 0.2 percent and among adolescents, about 0.7 percent. The infection rate among 6-year-olds is currently estimated at less than 0.03 percent per year.

The incidence of tuberculosis cases varies widely among different segments of the population in different localities. Cases occur twice as frequently in males as in females. Rates of disease increase sharply with age in all groups divided by race and sex. More than 80 percent of reported cases are in persons over 25 years of age and are typical post-primary pulmonary tuberculosis.

The risk of tuberculosis infection has regularly been observed to be greatest for those who have regular or occasional exposure to persons with sputum-positive pulmonary tuberculosis. Therefore, efforts to control tuberculosis in the United States have been early identification and treatment of cases and preventive therapy with isoniazid for infected persons who are at high risk of developing active disease. BCG has been used primarily in selected groups of persons who live or work where they have an unavoidable risk of exposure. It was emphasized that only the rate of new infections reflects whether tuberculosis transmission is actually occurring. This rate is undoubtedly the best indicator of the effectiveness of tuberculosis control and assessment of the need for preventive treatment or BCG vaccination.

BCG Vaccines

The Bacillus of Calmette and Guérin (BCG) was derived from a strain of Mycobacterium bovis attenuated by Calmette and Guérin through years of serial cultures at the Pasteur Institute, Lille. It was first administered to humans in 1921.

BCG vaccine is a generic designation in that there are many BCG vaccines available in the world today. All of them are derived from the original strain, but represent different numbers of passages in various bacteriologic media. They vary in reactivity, immunogenicity, and efficacy. Controlled trials of various liquid BCG vaccines were conducted prior to 1955 and showed protection ranging from 0 to 80 percent. All vaccines were prepared from different BCG strains, and a variety of dosages and routes of administration were employed. Valid assessment of the comparability of vaccines was, therefore, impossible.

BCG vaccines currently available in the United States differ from those used in the earlier field trials in that there have since been many culture passages of the bacilli and there have been modifications in methods of preparation and preservation. The efficacy of our current vaccines has not been demonstrated directly and must be inferred.

United States BCG vaccines are freeze-dried products containing live bacteria from historically identified strains of BCG. The strains demonstrate specified characteristics of safety and potency and are capable of inducing tuberculin sensitivity in guinea pigs and humans. (It was emphasized by Dr. Farer that the assumed relationship between skin sensitivity and immunity has not been proven.)

Complications from BCG vaccination have included severe or prolonged ulceration at the vaccination site, lymphadenitis, osteomyelitis, lupoid reactions, disseminated BCG infection, and death. Information on complications, most of it from other countries, reveals marked variation in the reported frequency of complications, largely depending on how thoroughly data have been sought. For example, the frequency of ulceration and lymphadenitis has been reported to range from 1 percent to 10 percent, depending on the vaccine, the dosage, and the age of vaccinees. Osteomyelitis reportedly has occurred in 0.1 per 100,000 vaccinees, although recent information from Europe indicates that the rate may be as high as 5 per 100,000 newborn vaccinees. Disseminated BCG infection and death are very rare, rates ranging from 0.008 to 0.1 per 100,000 vaccinees, and occur almost exclusively in immunoincompetent children.

Review Panel for Bacterial Vaccines and Toxoids with Standards of Potency - Special Report from the Bureau of Biologics

Dr. Morris Schaeffer, Director, Office of Efficacy Review, Bureau of Biologics, Food and Drug Administration, and Dr. Gene H. Stollerman, Bacterial Vaccines and Toxoids with Standards of Potency Review Panel Chairman,

described the status of reviews of currently licensed bacterial vaccines. They emphasized that the objective of review is to assess the safety, efficacy, and accurate labeling of each licensed product as a basis for product recommendations to the Commissioner, FDA.

Dr. Theodore Eickhoff, a member of the Review Panel for Bacterial Vaccines and Toxoids with Standards of Potency, summarized the Panel's consideration of BCG vaccines, pointing out limitations of available data, particularly on efficacy. He, like Drs. Schaeffer and Stollerman, looked forward to the results of current ACIP deliberations.

BCG Discussion and Draft Recommendation

Discussions which had accompanied the presentation of Tuberculosis Surveillance and a review of BCG Vaccines were continued throughout the afternoon with all Committee members, consultants, and guest participants taking active part. The discussion focused on drafting a recommendation on BCG Vaccines in the United States. In general, group consensus was a continuing but limited use of BCG vaccine in selected groups at particularly high risk of persistent and unavoidable exposure to infective tuberculosis. Discussion was directed toward designating and describing the groups at risk and the conditions under which BCG vaccines would be an optimal method of tuberculosis prevention and control. A drafting group was appointed by the Chairman to work beyond the adjournment of the day's meeting for purposes of preparing a summary of the Committee's deliberations. The group was comprised of: Dr. Lonnie S. Burnett; Dr. William R. Elsea; Dr. Kieter Koch-Weser; Dr. Alexander D. Langmuir; Dr. John Sbarbaro; and Dr. Eleanor Shore.

The morning of the second day of the conference, January 16, was devoted primarily to a review of a document prepared for consideration by the drafting group. A considerable number of suggestions and recommendations were made. Those representing consensus will be incorporated into a further draft recommendation and sent to Committee members and consultants for re-review.

The Chairman thanked the BCG Vaccines consultants for their contributions to the discussion and adjourned the BCG segment of the ACIP meeting at 12:30 p.m.

Reyes v. Wyeth Comment

Appellate decision for plaintiff in the litigation, Reyes v. Wyeth -- known to the ACIP in terms of its representing an alleged association of paralytic illness with polio vaccine given during an epidemic control program in south Texas -- was the subject of a 1974 petition to the Supreme Court for hearing. Recently, certiorari was denied. Implications of the decision, including direct warnings of consumers by the biologics producers, were felt by the ACIP potentially to constrain community immunization programs and vaccine acceptance. The group encouraged preparation of balanced benefit-risk

statements which might be endorsed by advisory groups making recommendations on immunization and which could serve as a basis for consumer information.

Influenza

Type A influenza has been occurring in epidemic form in parts of the South Atlantic and East South Central Divisions of the country since late 1974. Associated pneumonia and influenza mortality in early to mid-January began to reflect the presence of the epidemic. Data indicate gradual spread of the virus to other parts of the country.

The type A virus responsible for the outbreaks in the United States is related to A/Port Chalmers unlike type A viruses currently reported to be causing epidemic illness in other parts of the world. These viruses reportedly show a considerable drift from the A/Port Chalmers prototype.

Antiviral Drugs for Influenza

Among the numerous drugs tested in laboratories for anti-influenza effectiveness, amantadine hydrochloride has had the greatest study. Since an earlier review of amantadine by the ACIP, some additional data have accumulated which support evidence of moderate levels of protection against type A influenza. It was pointed out that the drug used in conjunction with influenza vaccine has shown the greatest protective efficacy. The Committee, on reviewing the data, particularly in terms of a public health utilization, reaffirmed its earlier position on influenza chemoprophylaxis issued in 1968 which did not recommend the drug as a public health measure for community control of influenza or a substitute for influenza vaccine immunoprophylaxis.

Other Business

The Committee briefly discussed the use of serogroup C meningococcal polysaccharide vaccine in epidemic control and recommended that this topic be a major agenda item at its next meeting selected as May 14-15, 1975. The meeting was adjourned at approximately 3:45 p.m.

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

for [signature] 2-3-75

Chairman Date