DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
Atlanta, Georgia 30333

July 8, 1981

TO : Recipients of May 21-22 ACIP Minutes

FROM : Executive Secretary
Immunization Practices Advisory Committee (ACIP)

SUBJECT: Correction to Minutes

The minutes of the May 21-22, 1981, Immunization Practices Advisory Committee Meeting (ACIP), which were sent to you on July 1, contained an error regarding a possible association of Reye Syndrome and acetaminophen. Please substitute the attached Page 2 in which a correction has been made.

Thank you.

H. Bruce Dull, M.D.

Attachment

was reviewed with respect to influenza vaccine. Data are derived from public sector vaccination programs--for influenza vaccinations, a minor part of the total. Nonetheless the system can provide useful year-to-year comparisons. Between the 1979-80 and 1980-81 influenza seasons, the only years for which data were available, there were no statistical differences in the frequency of types of reactions. Most of the reports were of mild local side effects and fever.

Drs. Diane Rowley and Eugene Hurwitz described the surveillance and study of Reye Syndrome, an effort underway at CDC since 1973 in cooperation with State Health Departments. Using a standardized clinical and laboratory definition, considerable information has been obtained. In 1980, 548 cases were reported from 44 states, a large portion of them associated with influenza B, particularly during the 1979-80 influenza season. Cases varied in age from 3 months to 25 years (median 8 years). Fifty-one percent of them were female, and 91 percent were white. Case fatality was 22 percent, down 50 percent from earlier years. The lower case fatality was presumably the result of earlier identification of cases and improved therapy. Most of the mortality was among infants, particularly minority infants.

Besides an association with influenza B, the Reye Syndrome relationship with varicella was emphasized. The role of these two predisposing infections was exemplified in two outbreaks, one in Michigan in February 1980 where influenza B was occurring and one in Los Cruces, New Mexico, in February-March 1980 where varicella was associated.

A series of four case-control studies on an association between Reye Syndrome and salicylate usage was begun in the 1978-79 influenza season. Results of the four investigations clearly linked salicylate with an increased occurrence of Reye Syndrome. In three of them there was a statistically significant negative correlation with acetaminophen use. Plans are underway to assemble a panel of expert advisors within the coming months and to review these data and make recommendations.

Dr. Jonathan Kaplan reviewed CDC's surveillance of Guillain-Barré Syndrome which began in 1978 with the help of approximately 1800 neurologists who agreed to serve as sentinel reporters of the disease. The surveillance evolved from the original observation in 1976 of an association of GBS with influenza vaccination. Regular monitoring of any comparable relationship has become exceedingly important since then.

In essence, data collected on the occurrence of GBS during the three influenza seasons since active surveillance began show that there has been no clear association between influenza vaccine and GBS. It appears that the risk of GBS from vaccine, if any, is far lower in the groups for whom vaccine is recommended than are the risks from influenza itself. Surveillance is continuing further to substantiate this conclusion.

Dr. Wilfert led a general discussion on the information presented and guided the Committee's preparation of recommendations on influenza vaccine for 1981-82. In addition generally to updating the factual material in the ACIP statement distributed in 1980-81, it was recommended that the Committee explain the increased potency of vaccine for 1981-82 and develop a section on supplementary measures in preventing influenza including comments on amantadine hydrochloride, the anti-viral drug that can be useful in people

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Dr. Jonathan Kaplan reviewed CDC's surveillance of Guillain-Barré Syndrome which began in 1978 with the help of approximately 800 neurologists who agreed to serve as sentinel reporters of the disease. The surveillance evolved from the original observation in 1976 of an association of GBS with influenza vaccination. Regular monitoring of any comparable relationship has become exceedingly important since then.

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who need protection but have not been vaccinated. Several Committee members were charged with developing a draft statement on influenza vaccine to be discussed on the second day of the meeting.

Pneumococcal Polysaccharide Vaccine

Drs. Jeffrey Band and Walter Schlech summarized the surveillance of pneumococcal disease based on field and laboratory studies, epidemic investigations, and evaluation of the distribution of Streptococcus pneumoniae serotypes causing disease in the United States. They stressed that data on the precise occurrence of serious pneumococcal disease are not available and that projections come from limited surveys, research reports, and several community-based studies. Although widely variable in occurrence, four syndrome account for most of the pneumococcal disease in this country: in descending order of overall incidence, acute otitis media, pneumonia, bacteremia, and meningitis. Case fatality is precisely the reverse: meningitis, 32 percent; bacteremia, 20 percent; pneumonia, 5-7 percent; and otitis media, <0.1 percent.

Of particular importance with respect to recommending an effective pneumococcal vaccine is knowledge that persons with certain health problems are at increased risk of pneumococcal infections and/or a more severe illness. They include patients with sickle cell anemia, splenic dysfunction or splenectomy, multiple myeloma, cirrhosis, chronic renal failure, diabetes mellitus, congestive heart failure, and chronic pulmonary disease. Furthermore, persons with organ transplants who are receiving drugs for immunosuppression and patients with cerebrospinal fluid leakage complicating skull fracture or neurosurgical procedures are also at increased risk of pneumococcal diseases.

Drs. James Hill and John Robbins from the National Institute of Allergy and Infectious Diseases and the Bureau of Biologics, respectively, reviewed studies of pneumococcal vaccine in various populations and summarized recent reports on vaccine effectiveness. In general it was concluded from their remarks that healthy adults of all ages can respond to pneumococcal vaccine with a good rise in type specific antibody measured by radioimmunoassay. Lesser and quite variable responses are seen in patients with certain underlying chronic diseases or who are undergoing certain kinds of treatment. Despite this shortcoming, it appears that there is still sufficient antibody responsiveness to expect some degree of protection, against at least some vaccine strains.

Of recent interest has been detection of certain blood group antibodies in patients given some pneumococcal vaccine. It is not believed that the material stimulating these antibodies is inherent in the polysaccharide antigens but is more likely from the medium in which bacteria are grown in preparing the vaccine. Efforts are underway to overcome this problem.

It was emphasized that severe local reactions can occur after a second dose of pneumococcal vaccine in adults, an Arthus-type phenomenon. Although not known whether this characteristic will ultimately diminish with time, there should be no revaccination of adults within at least 5 years. In view of the fact that there is no characteristic "booster effect" on readministering pneumococcal polysaccharide antigens, using more than one dose must await additional evaluation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
January 20-21, 1982
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Auditorium A at the Centers for Disease Control in Atlanta, Georgia, on January 20-21, 1982. Those in attendance are listed below.

COMMITTEE MEMBERS PRESENT
Dr. Catherine M. Wilfert, Chairwoman
Dr. James Chin
Dr. John B. DeHoff
Dr. William M. Marine
Dr. Frederick L. Ruben
Dr. Jay P. Sanford

Ex-Officio Members
Dr. William S. Jordan, Jr. (NIH)
Dr. Harry Meyer, Jr. (BOB)

Liaison Representatives
Dr. J.M.S. Dixon (NACI)
Dr. Peter A. Flynn, Capt., USN (DOD)
Dr. Richard J. Jones (AMA)
Dr. Edward A. Mortimer, Jr. (AAP)

Acting Executive Secretary
Dr. J. Michael Lane

COMMITTEE MEMBERS ABSENT
Dr. Maxine Hayes
Dr. Stephen C. Schoenbaum

HHS STAFF PRESENT
BUREAU OF BIOLOGICS, FDA
Dr. Robert J. Gerety
Dr. Gerald Quinnan

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NIH
Dr. John LaMontague

CENTERS FOR DISEASE CONTROL
Office of the Director
Peggy Ruiz

Laboratory Improvement Program Office
Dr. Joyce Essien

Center for Infectious Diseases
Dr. Walter R. Dowdle
Dr. Donald Francis
Dr. Jonathan Kaplan
Dr. Karl Kappus
Dr. Alan P. Kendal
Dr. Gary Noble
Dr. Peter Patriarca
Dr. Diane Rowley
Dr. William G. Winkler

Center for Prevention Services
Dr. Robert W. Amler
Steve Barid
Dr. Kenneth Bart
Dr. Roger Bernier
Dr. Alan Bloch
Dr. D. P. Drotman
Dr. Alan Hinman
Dr. Walter Orenstein
Dr. Paul Wiesner

National Institute for Occupational Safety and Health
Dr. J. Donald Millar

The meeting was opened at 8:15 a.m. on January 20 by Dr. Michael Lane, Director of the Center for Prevention Services, Centers for Disease Control, also Acting Executive Secretary of the Immunization Practices Advisory Committee (ACIP).

Because Dr. Catherine Wilfert was delayed due to inclement weather, Dr. Lane assumed the Chair for the morning meeting.

Hepatitis B Vaccine

Dr. Donald Francis of the CDC Phoenix Hepatitis Laboratories presented a draft of an ACIP statement regarding inactivated hepatitis B vaccine. This draft was reviewed, and general issues were raised for clarification and expansion.

The Committee asked for the preparation of expanded background papers in five areas. These papers will be either included in a final ACIP statement or modified during the spring meeting to become a general supplement to that statement.

These five areas include (1) a further expansion of the exposition of the different high risk groups; (2) a detailed description of the available methods for screening, and the cost effectiveness of screening at different prevalences of hepatitis B infection; (3) a discussion of the problems posed both to institutions and individuals by identification of carriers of hepatitis B; (4) a general discussion of the ethical and legal aspects of screening and identification of carriers, particularly for hospitals and other groups of medical care workers; and (5) an introductory statement underlining the epidemiologic and philosophic differences between the hepatitis B statement and most of the usual ACIP vaccine recommendations.

The Committee was informed by representatives of Merck, Sharp and Dohme that vaccine would become commercially available in the fall of 1982.

The Committee was informed that the American Dental Association is having a meeting to discuss the problems posed to the dental profession by hepatitis B, and that a statement might be available from the ADA prior to the May meeting. A meeting of an ad hoc committee to further refine the definition of homosexually active males will be held in March, with recommendation about use of vaccine in these groups to be circulated to the ACIP prior to the May meeting.

Influenza Vaccine

The Immunization Practices Advisory Committee was joined by members of the Bureau of Biologics Advisory Panel. Dr. Theodore Eickhoff and Dr. Catherine Wilfert acted as co-chairpersons of the joint meeting to review the current status of influenza activity in the U.S. and the world, to review the current data on safety and efficacy of influenza vaccine, and to discuss a revised statement on influenza vaccine formulation and use.

THERS PRESENT

Dr. William H. Bancroft
Dr. A. Boudreautt
Frank Brandon
Robert Byrd
Colonel Alfred K. Cheng (USAF)
Dr. P. Cohen
Robert B. Couch
W. Creveling
Dr. H. Bruce Dull
Dr. Theodore Eickhoff
Dr. Herman M. Ellis
LTC. Frederick Erdtmann (USA)
Dr. Joanne E. Finley
Dr. Vincent Fulginiti
Dr. Alan Gray
Horst Hainz
John Chriss Hoffman
Dr. Saul Krugman
Dr. Arlene McLean
I. K. Mushahwav
June Osborn
Dr. Aubrey S. Outschoorn
Klaus Pressler
Dr. Robert Rietschel
G. G. Rigsby
Karlyn L. Shedlowski
Charles S. Taylor
Patricia E. Taylor
Walter E. Woods

The activity of influenza in the United States during the 1981-82 influenza season was reviewed by Dr. Karl Kappus of the Center for Infectious Diseases. This has been an unusually quiet year for influenza, both in terms of morbidity and in isolation of influenza strains. No major outbreaks of either influenza B or A have occurred during this influenza season.

The status of influenza in the world, and the characteristics of strains submitted to the World Health Organization Collaborating Influenza Center were reviewed by Dr. Alan Kendal of the Center for Infectious Diseases. There has been very little influenza activity in the northern hemisphere, and the strains circulating throughout most of Asia have remained similar to the strains of influenza A (H3N2) isolated during the last influenza season. The influenza A (H1N1) strains have also remained generally similar to A/England/333/80. The dominant influenza A (H3N2) strains have been generally similar to the prevalent A/Bangkok/1/19 and "intermediate" strains. In general, no major antigenic drift has been found in any of these strains although the identification of a proportion of isolates which resembled a minor variant A/Shanghai/31/80 was discussed.

Dr. Gerald Quinnan of the Bureau of Biologics reviewed vaccine immunogenicity and reactions. The current influenza vaccine continues to produce good elevations in antibody titers in individuals who have previously been sensitized to currently prevalent influenza A strains. Most local reactions have been in the expected range, and similar to those associated with previous influenza vaccines.

After a luncheon break, Dr. Jonathan Kaplan of the Center for Infectious Diseases reviewed the 1980-81 data on Guillain-Barre syndrome and its temporal association with influenza vaccination. Because of restrictions in funding, the network of neurologists reporting Guillain-Barre syndrome has not been actively contacted during the 1981-82 season, but reports continue to come in considerable numbers. The age distribution of the cases, the temporal distribution during the year, and the temporal period between influenza vaccination and onset of illness, plus the small number of cases (12 of some 359 reported cases) who have received influenza vaccine within 8 weeks prior to onset of illness cast doubt on the association of Guillain-Barre syndrome with influenza vaccine during the 1980-81 season. Comparing the attack rate in vaccinated and unvaccinated individuals, the relative risk of vaccinees getting Guillain-Barre syndrome is not significantly different from one. The Guillain-Barre data for the 1979-80 and the 1980-81 influenza seasons will be submitted for publication in the near future.

Dr. Peter Patriarca of the Center for Infectious Diseases presented material regarding the use of influenza vaccine in patients receiving anticoagulants. A case report in the New England Journal of Medicine had suggested that influenza may adversely influence the metabolism of anticoagulants and increase the risk of bleeding. These studies did not employ adequate controls. A small survey of patients in other clinical settings has failed to produce additional evidence that this problem is widespread.

Dr. Diane Rowley of the Center for Infectious Diseases reviewed the evidence of a temporal association of Reye syndrome cases and influenza A. There is agreement that influenza B outbreaks are commonly followed by increases in reported cases of Reye syndrome. Surveillance from the last two outbreaks of influenza A shows analogous, though smaller, increases in Reye syndrome cases with non-varicella prodrome. Evidence seems to be mounting that Reye syndrome may be associated with influenza A.

The Committee discussed the problem of recommending vaccine formulation for the coming influenza season. In the absence of substantial evidence of major shift or drift in virus strains, there seems to be little reason to change the current vaccine formulation. On the other hand, recent isolates that are increasingly A Shanghai/31/81-like raise the question of whether that virus should be used in making new vaccines. Recombinant strains are becoming available, and are being tested for their ability to produce high yield in the laboratory. The Committee agreed to defer decision about the best candidate influenza A (H3N2) strain for vaccine production until an additional month of the current influenza season had passed. This additional time may bring more information about currently prevalent strains, and permit further analysis of the ability of recombinant candidate strains to produce high yields of virus for vaccine production.

The draft ACIP statement for influenza vaccine use was presented and discussed. The recommendations for influenza vaccine, 1982-83, will be similar to that for 1981-82 with the following general differences.

First, the statement that Reye syndrome is associated with influenza in infants will be amended to include children and adolescents up to the age of 18.

Second, two doses of vaccine will only be recommended for previously unimmunized children less than 13 years old.

Third, heavy smoking will be added to the list of chronic problems in adults which predispose to lower respiratory tract infections, and thus are indications for influenza immunization in adults.

Fourth, influenza vaccination will be strongly recommended for all older persons, particularly those over age 65, because the risk of mortality in influenza outbreaks increases with age.

Fifth, the Committee will underscore the fact that no evidence exists currently to suggest that influenza vaccine carries any maternal or fetal risk, and thus it is safe to use during pregnancy.

Sixth, the statement will point out that active surveillance of Guillain-Barre syndrome since 1978 has not shown any association between current influenza vaccines and Guillain-Barre syndrome.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
October 15-16, 1980
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207 at the Center for Disease Control in Atlanta, Georgia, on October 15-16, 1980. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Catherine M. Wilfert, Chairwoman
Dr. James Chin
Dr. Suzanne E. Dandoy
Dr. John B. DeHoff
Dr. Maxine Hayes
Dr. William M. Marine
Dr. Frederick L. Ruben
Dr. Stephen Schoenbaum
Dr. Gary R. Smith

Ex-Officio Members
Dr. Harry Meyer, Jr. (BOB)

Liaison Representatives
Dr. J. M. S. Dixon (NACI)
Dr. Edward A. Mortimer (AAP)

Executive Secretary
Dr. J. Donald Millar

COMMITTEE MEMBERS ABSENT
Dr. Jay P. Sanford

Ex-Officio Members
Dr. William S. Jordan, Jr. (NIH)

Liaison Representatives
Dr. Asher J. Finkel (AMA)
Dr. Peter A. Flynn, Capt., USN (DOD)

HHS STAFF PRESENT

BUREAU OF BIOLOGICS, FDA
Ms. Barbara C. Meyer

CENTERS FOR DISEASE CONTROL
Office of Center Director
Mr. Donald A. Berreth
Dr. Walter R. Dowdle
Dr. William H. Foege
Mr. Gene W. Matthews
Ms. Peggy Ruiz

CENTERS FOR DISEASE CONTROL (cont'd)
Bureau of Epidemiology
Dr. Jeffrey D. Bard
Dr. Frank DeStefano
Ms. Julia S. Garner
Dr. George P. Schmid
Dr. Stephen B. Thacker

Bureau of Laboratories
Dr. Kenneth L. Herrmann
Dr. Alan P. Kendal
Dr. Stephen R. Preblud

Bureau of State Services
Dr. Roger Bernier
Dr. Alan Bloch
Dr. Steven Fite-Wassilak
Dr. Wayne L. Greaves
Dr. Alan Hinman
Dr. Timothy F. Nolan
Dr. Walter Orenstein
Dr. Peter Patriarca

OTHERS PRESENT
Dr. Claire Broome
Colonel Alfred K. Cheng (USAF)
LTC Frederick T. Erdtmann (USA)
Mr. John Chriss Hoffman
Mr. Geoffrey Kalish
Capt. R. L. Marlor (USN)
Ms. Karlyn L. Shedlowski
Mr. Charles S. Taylor

INTRODUCTION

The Fall meeting of the ACIP was opened by the new Chairwoman, Dr. Catherine Wilfert at 8:30 a.m., October 15, 1980. Dr. Wilfert introduced the two new members, Dr. Frederick L. Ruben, Associate Professor of Medicine, University of Pittsubrgh, and Dr. Stephen C. Schoenbaum, Assistant Professor of Medicine, Brigham and Women's Hospital, Harvard Medical School, and the new Committee Assistant, Mrs. Mary Ann Wilson.

Dr. Wilfert then called on Dr. Foege to brief the Committee on the plan for reorganizing CDC. Dr. Foege distributed an organography of the new structure incorporating six centers and three program offices. He noted that the basic proposal had been approved and that he anticipates six "tough" months would be required to implement the plan fully. He responded to questions from the Committee members.

Before leaving, Dr. Foege indicated that he had been approached by the Health Care Financing Administration concerning a proposal to reimburse for the cost of inoculating Medicare-eligible persons with pneumococcal vaccines. He asked the Committee for their recommendations as to his response. Dr. Wilfert indicated that the Committee would take up this issue later in the day and provide Dr. Foege with the results.

RUBELLA

Dr. Wilfert called on Dr. Alan Hinman to open discussions on a proposed revision of the statement on rubella vaccines. In discussion, questions were raised regarding greater emphasis on the vaccination of childbearing age females (especially in the face of outbreaks); the advisability of administering rubella vaccine again at an older age to assure immunization of those who had been missed as infants or the few who had an inadequate response to the first dose; the advisability of drawing bloods for serologic testing at the time of vaccination. Attention focused first on the latter issue. If drawn, such bloods could be tested later if it became evident that the vaccinated woman was pregnant within 3 months of vaccination. Detectable antibodies at the time of immunization would allay anxiety by documenting effective immunity. The Committee concluded that the advisability of drawing bloods depended on the situation. In school programs, drawing blood from all girls potentially capable of conception would be so formidable logistically as to result in cessation of school programs. On the other hand, in the context of a gynecologic practice, it might be feasible to encourage such testing for individual patients.

Dr. Greaves of the Immunization Division presented data on 59 females vaccinated with the RA27/3 strain of rubella virus vaccine during the first trimester of pregnancy. Forty-six were of unknown immune status at the time of vaccination, 8 were known to be susceptible, and 5 were immune. (Teenagers accounted for 59 percent of the cases.) All babies born to the 52 women who continued pregnancy to term were normal. There was no serologic evidence of infection in the babies nor was rubella virus isolated from any child. Seven

women terminated their pregnancies in the first trimester. Rubella virus could not be isolated from the single aborted specimen submitted to CDC. A question arose as to whether or not the new RA27/3 vaccine differed significantly from the HPV duck-embryo vaccine. Dr. Preblud indicated that the viremia with RA/23 persisted less time than was characteristic with the older vaccine.

There was discussion of the rapidly declining incidence of reported rubella. The total number of reported cases for the first 43 weeks of 1980 was 3,437 compared to 11,007 cases for the same period in 1979. However, the number of cases of congenital rubella syndrome reported to the national registry has not commensurately fallen. In 1979, a record annual low of 11,795 cases of rubella were reported; however, 58 cases of CRS have been reported thus far representing a reported incidence higher than all previous years except 1969 and 1970. The need was expressed for a clear definition of what is meant by the "congenital rubella syndrome" and that this definition be included in the rubella statement.

In recent months, outbreaks of rubella in schools with cases in teenagers and young adults continue to occur. Thus, there is the need to specifically address susceptible persons in these age groups. The risk of fetus infection incurred by vaccinating pregnant women remains as yet undetermined because it is too low to have been adequately measured. Dr. Smith asked, "Would it be good medical practice for women vaccinated during early trimester of pregnancy to be advised to have an abortion?" Committee members responded that available information on the risks should be given to the patient, and the option of abortion should be considered and discussed with the prospective vaccinee. The decision would ultimately have to be made by the patient after learning the facts and the unanswered questions. They also observed that the risk of abnormalities associated with immunization with rubella vaccine appeared to be lower than the "expected background" of malformations occurring among births to normal mothers in the United States. If one were to recommend that a vaccinated woman have an abortion to avoid the possibility of a malformed child, one would be in the ironic position of advising an interruption of pregnancy in the face of theoretical risks no greater than those accompanying ordinary pregnancy.

Discussion continued on the need for serologic testing of potentially pregnant women before vaccination. Some members felt that in a nonepidemic situation there is no reasonable alternative to serologically testing such women. An epidemic situation clearly posed extraordinary risks to the fetus and warranted consideration of other more expedient alternatives such as vaccination without prior serologic testing. A Committee member noted that once rubella immunization is made mandatory for potentially pregnant women, one must ask to what extent sero testing would assure a better choice. Other members noted that mandatory sero testing would in effect eliminate mass programs. At the present time it seems that potentially pregnant teenagers served by the public sector are far less likely to be immunized than those served by the private sector because health departments are unwilling to assume what they perceive to be legal liabilities for any problems that might ensue if the girl became pregnant after vaccination.

Dr. Hinman asked that the Committee not lose sight of the fact that there are still sizeable outbreaks of rubella in the country, that tragic cases of the congenital rubella syndrome continue to occur, and that we have the means to prevent

these tragedies. The means of prevention carries a small risk to the fetus, certain to be less than 4 percent (by the statistical parameters combining existing data for HPV77, Cendehill and RA 27/3 vaccines). We have not protected the most vulnerable population (potentially pregnant females) as yet, and we need to do so. The Committee members expressed agreement with his concise, accurate description of the situation, and urged that the statement on rubella contain such a straightforward, understandable description of the problem and the realities of dealing with it. Dr. Hinman was asked to write such a description into the next draft.

In commenting on the accumulating knowledge regarding the persistence of protection, it was noted by Dr. Hinman that of those subjects in long-term studies done by CDC who initially sero-converted, only 2 percent have lost detectable antibody after ten years. Added to those who failed to respond in the first place, less than 5 percent are without antibody at ten years.

Discussions then turned to the matter of revaccination for rubella. Dr. Orenstein summarized the four issues generally raised in this respect. 1) Is a second dose warranted in order to assure high levels of immunity in the population? 2) Do a significant number of primary vaccine failures warrant a second dose to more readily approach 100 percent coverage? 3) Does immunity wane with time? 4) What would be the most effective operational strategy in the event revaccination was accepted as advisable? For example, would one revaccinate at school entry, revaccinate people found "susceptible" when serologically screened for various reasons, revaccinate women of childbearing age, etc? After discussions noting the limited reduction of incidence in persons 15-19 years of age, and no reduction in the 20-29 year old age group, it appeared that the major failure in rubella control was a failure to get a dose of vaccine into a sufficient proportion of the susceptible population. Given limited resources, the best strategy seemed to be an increased emphasis on reaching persons who had never been vaccinated. There seemed to be little reason to urge a second dose of vaccine, and in fact, such a policy could aggravate the present situation by diverting resources and attention away from a goal of universal vaccination to one of a primary vaccination and subsequent revaccination. Dr. Mortimer indicated that the Redbook Committee had looked at this issue and were not as yet ready to propose any changes.

In review, it was noted that the revised statement needs: A definition of congenital rubella syndrome; a statement that any detectable antibody following immunization is an indication of immunity; a statement presenting the risks and effectiveness of rubella vaccine in pregnancy; a paragraph indicating that the Committee did not support "a second dose"; added information on serologic testing. Regarding the latter point, Dr. Schoenbaum expressed the opinion that Committee's real interest was in seeing the pool of susceptibles converted to immunes. In this regard, the risk of immunizing pregnant women is not large. We should recommend that the vaccine be given and that if providers are interested, they can bleed for subsequent testing but that this should not be mandatory. Dr. Schoenbaum agreed to prepare a draft for Dr. Hinman summarizing his opinion. A look at the rubella information sheet noted that it does not speak to serologic testing. Dr. Smith indicated that we should assure ourselves that the information statements include at least minimal data on such things as sero testing. Dr. Hinman indicated that he would prepare a subsequent draft and wished for comments on his draft within ten days.

Dr. Wilfert suggested that the statement be redrafted by Dr. Hinman to include the various concerns and issues that had been raised during the discussion. She asked Committee members to send to the Executive Secretary any further written comments on the current draft within ten days so that they could be incorporated into Dr. Hinman's next draft.

MEASLES ELIMINATION

Dr. Hinman provided a brief update of the status of measles elimination indicating that week 39 of this year resulted in the lowest number of reported measles cases ever recorded in the U.S. There were only 23 cases of which 16 were in one active chain of transmission that involved an outbreak in a private day school in Virginia started by an importation from England. The rest of the cases for that week are unlinked. There are an average of two importations of measles from abroad per week and these produced an average of one spread case each. The Committee drew attention to the significant numbers of cases for which no source can be found. Some of these represent diagnostic problems. Other Committee members wondered if subclinical cases of measles occurred and could be sources of transmission. Dr. Hinman indicated there was no evidence for this. The possible role of modified measles as a source of measles outbreaks was also raised, and Dr. Hinman reported that one such incident had been reported from Iowa. Dr. Dixon was asked if the Canadians were seeing measles imported from the U.S. He responded that Canada had "ample measles of our own" and few, if any, importations from the U.S. were identified.

Dr. Wilfert asked for comments from the military liaison representatives concerning measles in military recruits. Dr. Cheng reported that since measles and rubella immunizations had become routine in Air Force recruit camps, outbreaks of measles had been sharply reduced not only in recruit camps but also in all other installations to which recruits were sent. Dr. Hinman noted that the military had very greatly reduced measles transmission among its populations.

The Committee discussed whether or not the minimum age for measles vaccination should be reduced to 12 months as Dr. Marine had suggested in a letter previously circulated to the Committee. Dr. Orenstein was asked to report on any new information in this regard. He noted that the literature presented conflicting data and suggested that the existing minimum, 15 months, should be retained. One exception that might be considered is for children enrolled in day care centers. In such settings, it might be useful to reduce the minimum age to 12 months. Dr. Bernier reported that CDC had done a detailed epidemiologic review of outbreaks in day care centers which showed that these generally involved relatively small numbers of cases (15 to 20) among very young children, many less than 15 months. The attack rate had been as high as 77 percent in one center with young babies. A number of these outbreaks were in day care centers in proximity to military installations; the reduction of measles transmission in the military has reduced the risk of outbreaks in such day care centers. He noted that the Committee's previous recommendations indicated that in situations of "high risk", vaccination could be done as early as 6 months. He asked if the Committee would care to more explicitly define "high risk" in this regard. Did the Committee mean children in the same town? Same school? Same room?

recommended destroying or disposing of the remaining vaccine, two-thirds of which had been distributed to the periphery of the distribution system during the campaign in 1976. Committee members varied in their reaction to this, some indicating that they saw absolutely no conceivable possibility of using any of the swine flu vaccine in the future, while others found it quite plausible that in a situation of an outbreak of swine flu appearing elsewhere in the world and obviously spreading to the United States, the vaccine would prove very useful.

Dr. Dowdle reported that the Interagency Committee had also examined the matter of the appropriate dose of antigens contained in influenza vaccines and had recommended that whereas the initial 7 micrograms dose was appropriate for the first two years of immunizing a "virgin population", it now appeared prudent to recommend an increase in the dose of antigens in the vaccine to 16 micrograms which was felt not to risk a significant increase in reactogenicity. He indicated there would be further discussions of this at the Surgeon General's meeting in January. Committee members asked if there were investigations of intradermal use of influenza vaccine. Hearing a negative response, they suggested that such studies be seriously considered. They also requested that reports of the Interagency Influenza Work Group be sent to members of the ACIP.

Dr. Thacker brought the Committee up-to-date on the evaluation of new techniques for influenza mortality surveillance indicating that during this influenza season CDC would adopt a new method of analyzing mortality data employing the autoregressive integrated moving average. He provided handouts showing how application of this method had provided a much better fit to the previous mortality data than the modified Serfling-Sherman technique in previous use. There will be a two-part paper on this subject in the American Journal of Epidemiology in January 1981.

REPORTS ON MEETINGS

After lunch, Dr. Wilfert reported on her attendance at the International Symposium on Bacterial Vaccines. She indicated a considerable amount of new information on the mechanism of action of pneumococci; a growing understanding of the effects of the toxins of diphtheria and tetanus, and of the specifics of how antibodies interfere with these actions; a much clearer appreciation of these mechanisms is now possible permitting the future development of vaccines and other immunizing materials that might be much more specific than those we presently have. She indicated a live attenuated oral mutant typhoid cell vaccine is being tested in Mexico. Subcellular work on gonococci also offered the possibility of circumventing the heterogeneity which has frustrated vaccine development to date.

She also reported attending the Hepatitis B Symposium in which the results of the ongoing vaccine trials were presented. An outstanding feature was the presentation of Dr. Palmer Beasley's work in Taiwan relating hepatitis B surface antigen with cirrhosis and hepatic cancer among male Chinese. The vaccine appeared to be very efficacious and the results of the meeting were distinctly optimistic. Subsequent discussion revealed that the vaccine would cost about $20 to $25 per dose and would be administered in at least three doses. The vaccine is expected to be available in about two years, but there are concerns about the adequacy of supply even at that point. Data had also been presented indicating that HBIG given at birth is effective in preventing hepatitis B transmission to infants. Combining

this with vaccination might solve the problem of perinatal hepatitis. Apparently when mothers have the "e" antigen, there is a 95 percent probability that hepatitis will be transmitted to their infants and that 95 percent of the infants infected during parturition will become carriers. Problems with the availability of vaccine might yield eventually to recombinant DNA technology which would enable large scale production of vaccine.

SUMMARY OF ADVERSE EFFECTS FOLLOWING IMMUNIZATION

Dr. Hinman summarized the results of CDC's reaction surveillance program and noted that CDC has now learned of approximately 1400 events that have been reported following vaccination. A small number of these are reports from private sources. The purpose of the program is to detect previously undetected events following vaccination, to detect clusters of known reactions, and to refine estimates of the rates in order to permit a clear understanding of the risks of vaccination.

The Committee expressed the conviction that it was important to ascertain the "background rate" of events and to define those events which were related to immunizations rather than simply occurring after immunization. Dr. Hinman responded that the temporal distribution of events is being examined. There are no obvious differences between persons receiving immunization in the public sector as compared with the experience of persons being immunized in the private sector.

In the discussion, Committee members asked the status of a report of the Office of Technology Assessment on the liability and compensation issues regarding immunization. Dr. Hinman noted that the report was due to be completed shortly. A variety of options were being considered but a "no fault" insurance scheme for specific results seems to be most favored.

PNEUMOCOCCAL VACCINES

Discussion next turned to pneumococcal vaccines in order to reach a definitive response to Dr. Foege's charge. The Committee had received copies of two articles on the subject (one authored by Dr. Broome) and an editorial recently published in the New England Journal of Medicine. Dr. Broome made introductory remarks. The Committee concerned itself first with estimates of the efficacy of vaccine. Dr. Schoenbaum noted that in the studies by Broome and her co-workers, the confidence limits for the efficacy of vaccine were very wide so that real efficacy might have been anywhere on a scale which included "negative value" (the vaccine actually might have caused harm) at one pole up to the 79 percent asserted by the manufacturers. The width of these confidence limits made it extremely difficult to make judgments about the efficacy of vaccine. Dr. Ruben indicated that it would be helpful for the Committee to study the results of the NIH Contract Study in a population of patients served by Kaiser Permanente, with data evaluated by Dr. Robert Austrian.

Various members of the Committee agreed and requested that the pneumococcal vaccine statement be systematically reviewed at the next meeting of the ACIP, at which time the Committee be given the opportunity to review the unpublished Kaiser-Austrian data. They suggested that Dr. Austrian and representatives of the Office of Technology Assessment, who had published information on cost benefit analyses of the use of pneumococcal vaccines, might be invited to the meeting.

In developing a recommendation for Dr. Foege regarding his response to HCFA (regarding a proposal to reimburse for pneumococcal vaccines) the Committee dwelt primarily with two issues, one of technical nature and one related to public policy. The technical issue was the uncertain efficacy of pneumococcal vaccines. In order to recommend widespread use of the vaccine, the expected efficacy of it should be established and should be sufficient to justify recommending its use. The available literature was in considerable conflict on the point of efficacy. It appeared that data were not at hand to permit a reliable estimate of efficacy by the Committee.

The policy issue involved the desirability of encouraging HCFA to begin supporting some preventive measures. In this respect, the proposal to reimburse for inoculation with pneumococcal vaccines appeared to be a salutary change in the attitude of HCFA toward preventive services; several Committee members wanted to encourage this changed attitude so that other preventive measures might become eligible for financing by HCFA. To be sure, some Committee members felt that reimbursement was not the best way to encourage widespread use of a vaccine, citing experience that showed that public programs of vaccination offered much better prospects for widespread success. Nonetheless, to see HCFA endorsing any preventive measure would be welcomed by some Committee members. Influenza vaccine was viewed as a much better "first step" for HCFA to enter the prevention field in view of its clear benefits in preventing influenza among elderly persons for whom the vaccine was clearly indicated.

After discussions on these points, Chairwoman Wilfert asked each Committee member to vote by anonymous written ballot to indicate whether or not the Committee should recommend to Dr. Foege that he encourage HCFA to provide reimbursement for the use of pneumococcal vaccine among persons eligible for Medicare. The results of the poll were: unequivocally yes - 4; unequivocally no - 4; equivocal response - 2. These results were reported as such to Dr. Foege.

HEPATITIS

Chairwoman Wilfert solicited any additional comments or reconsiderations of the Committee's previous actions regarding the draft on hepatitis. Dr. Meyer indicated that while he had not been present at the last meeting (at which the hepatitis statement had been extensively discussed), he and others at the Bureau of Biologics felt there was evidence indicating a real difference between HBIG and HNIG in efficacy of prophylaxis of hepatitis B after acute exposures with HBIG being more effective; he wanted to be on record as so saying. In response, Committee members expressed satisfaction that their previous discussions had been sufficiently deliberate and thorough to warrant their conclusions; they saw no reason to reopen the issues at this meeting. Dr. Millar was asked to gather any last minute comments on the hepatitis draft and to proceed with preparing the statement for publication.

PLAGUE

Dr. Schmid introduced a revised plague statement. The revision is necessary in order to assure consistency between the package insert and the recommendations made by the Committee. In 1975, the manufacturer began to recommend that plague vaccine be administered in an initial dose of 1.0 ml followed by a second dose

of 0.2 ml a month or more later, followed by a third dose of 0.2 ml as a booster 3-6 months or more after the first dose. This represents a change from the previous package insert (and existing ACIP recommendations) which called for two 0.5 ml doses a month apart followed by an 0.2 ml dose six months after the first. The change in regimen reflects the accumulation of serologic data (largely from military use) indicating seroconversion in a large proportion of individuals after 1.0 ml initial dose, and awareness that subsequent doses of plague vaccine have been accompanied by considerable pain at the injection site in a large number of recipients. There seems to be less pain with the reduced dose. The Committee discussed the significance of serologic findings and Dr. Schmid indicated that, in general, titers of 1:128 was viewed as a significant response. Some individuals do not seem to seroconvert even after numerous injections. In response to the question regarding the number of persons being immunized, Dr. Erdtmann reported that the military routinely vaccinates groups that are placed on "readiness alert". The regimen used is a 2 dose regimen-- 1.0 ml is the initial dose, followed by 0.2 ml a month later. If the unit is actually deployed, each individual is given a third dose (booster dose) of 0.1 ml.

Civilians working in vector control activities also were thought to be major targets for vaccination, although Committee members were under the impression that many vector control workers do not actually take the vaccine because of its reputation for causing pain. In reviewing the draft, the Committee made several observations: The section on "Precautions and Contraindications" is actually a statement on side effects and should be so labeled; a paragraph should be added on measures other than immunization that could be taken to protect against plague; something should be said about what to do for persons who do not seroconvert. Dr. Wilfert requested that the Committee members send in their further comments on the draft and that these as well as comments made during the discussions be incorporated into a next draft revision to be reviewed by the Committee in due course.

PRIVATE VERSUS PUBLIC RECOMMENDATIONS

There followed a brief presentation by Drs. Smith and Marine on the subject of "Recommendations for Public Versus Private Sector." They had asked the Committee to discuss this issue because in considering proposed recommendations, the Committee increasingly must deal with the question of benefit to the individual as well as cost to the individual and/or society. The Committee's main charge is to make policy recommendations for immunization in public health programs. They feared the Committee might be unduly tempted to consider the cost aspect as the major policy determinant. They suggested the Committee always first determine which agent or dosage is most beneficial for the individual before considering any issues of costs. There should, of course, be the corollary objective of choosing the least costly agent or dosage when alternatives are of equal value. Moreover, the recipient of the vaccine should have enough information at hand to participate meaningfully in the decision.

In the discussion that followed, several opinions were stated by various members: the opportunity for information exchange may be better in private practice; on the contrary the potential advantages of the private practice setting are rarely used, and therefore "mythical"; cost is never incidental because in today's world, the costs of all medical care are increasingly borne by society through third party and governmental subsidies; when cost is a significant factor in a recommendation, the recommendation should acknowledge this "up front" and provide clear information

on benefits of the various alternatives; pneumococcal vaccine is a very poor example for discussions of benefit/costs comparison because its benefit, i.e. efficacy, has not been clearly established.

Committee members expressed pleasure at the opportunity to discuss issues of this nature and indicated a desire to address such issues in the future. They expressed the opinion, however, that there was no need for any specific actions in this regard.

THE ADVISABILITY OF A RECOMMENDATION FOR "IMMUNIZATION FOR YOUNG ADULTS AND ADULTS"

Dr. Wilfert introduced the subject by stating her own interest, and the interest of others, in having available a compendium of recommendations addressing young adults and adults. She indicated that most of the Committee's interest seemed to be focused on childhood immunization practices. The epidemiology of measles and rubella (with cases in young adults) as well as continuing concerns about the need for influenza immunization, suggested that a compendium addressing the immunization needs of young adults and adults would be of great value. Dr. Hinman agreed to formulate such a proposal for the Committee to review at a future date.

SMALLPOX VACCINE

Dr. Meyer indicated that despite the Committee's recommendations over the past several years for much more restrictive use of smallpox vaccine, the distribution of smallpox vaccine has not markedly changed. The Committee members heard the countries currently requiring smallpox vaccination of foreign travelers include Chad, Djibouti, Madagascar, and Kampuchea. Dr. Chin indicated that according to the International Conventions on such matters, letters could accompany travelers to such countries indicating a medical contraindication. One could not be sure how the traveler would be received, but in general it was felt the travelers were experiencing very few difficulties relating to smallpox vaccination. The Committee briefly discussed ways in which the distribution of smallpox vaccine might be legitimately constrained. One proposal included the distribution of the vaccine through U.S. Public Health Service clinics as was done previously with the Yellow Fever vaccine. Another idea was that State Health Departments be asked to distribute it as they are doing presently with the rabies vaccine. The States and CDC could collaboratively work out something for a more limited distribution.

Dr. Wilfert asked that the Executive Secretary contact the representatives of the Smallpox Eradication Program and ask that they prepare a proposal in collaboration with Dr. Meyer to attempt to limit the distribution of smallpox vaccine.

SUMMARY FOR THE DIRECTOR OF THE CENTERS FOR DISEASE CONTROL

Dr. Wilfert summarized the various issues of the discussions for Dr. Foege as follows:

Rubella: The Committee felt strongly that emphasis should be placed on reaching previously unvaccinated young adults; that we should expand the information made available to deliverers and vaccinees on the utility of serologic

testing; that the current statement include a definition of the congenital rubella syndrome; that the second dose of rubella vaccine was not routinely advisable.

Pneumococcal Vaccine: The Committee had been virtually evenly split as to what to recommend to HCFA regarding reimbursement for pneumococcal vaccines. The Committee did not feel ready at the moment to make any changes in its recommendations for the use of the pneumococcal vaccines. She encouraged additional efficacy studies of pneumococcal vaccines and indicated that the Committee wished to look at the paper by Austrian based on data from Kaiser Permanente.

Hepatitis: The Committee had confirmed its previous discussions on this subject; final comments were being received on the existing draft.

She then asked if other Committee members wished to make comments. Dr. Chin emphasized that there was great need to explore with HCFA the large issue of the financing of preventive services. It was very important that Medicare begin to support such services. However, pneumococcal vaccine "is not the white horse to ride" in entering the field of prevention; there are other preventive measures whose efficacy is much more firmly established and would have much greater benefits.

Dr. Foege indicated that the Committee's divergence of opinion would suggest to him that pneumococcal vaccine would probably not be the landmark service. He indicated that the pneumococcal vaccine proposal was part of a four component prevention package including activities pertaining to hypertension, influenza vaccination, and pap smears, as well as pneumococcal vaccines. After Dr. Foege made some further comments about the great success of the measles elimination program, the meeting was adjourned at approximately noon.

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

Catherine M. Wilfert 1/9/81

Catherine M. Wilfert, Chairwoman Date