DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA

MINUTES OF MEETING

Immunization Practices Advisory Committee
January 21, 1980
Bethesda, Maryland

The Immunization Practices Advisory Committee (ACIP) met in Board Room 3D001 at the Uniformed Services University of the Health Sciences, School of Medicine, Bethesda, Maryland, on January 21, 1980. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Thomas M. Vernon, Jr., Chairman
Dr. James Chin
Dr. Suzanne E. Dandoy
Dr. John B. De Hoff
Dr. Maxine Hayes
Dr. Edwin D. Kilbourne
Dr. William M. Marine
Dr. Jay P. Sanford
Dr. Gary R. Smith
Dr. Catherine M. Wilfert

Ex-Officio Members

Dr. William S. Jordan, Jr.
Dr. Harry Meyer, Jr.

Liaison Representatives

Dr. J.M.S. Dixon (NACI)
Dr. Asher J. Finkel (AMA)
Dr. Peter A. Flynn, Capt. USN (DoD)
Dr. Edward A. Mortimer, Jr. (AAP)

Executive Secretary

Dr. J. Donald Millar

COMMITTEE MEMBERS ABSENT

(None)

HEW STAFF PRESENT

BUREAU OF BIOLOGICS, FDA

Dr. Bennett L. Elisberg
Dr. Edward A. Fitzgerald
Dr. Robert Gerety
Ms. Hope E. Hopps
Dr. Paul D. Parkman

CENTER FOR DISEASE CONTROL

Office of Center Director

Dr. William H. Foege, Director

Bureau of Epidemiology

Dr. Larry J. Anderson
Dr. Donald P. Francis
Dr. James E. Maynard
Dr. William D. Winkler

Bureau of State Services

Dr. Alan R. Hinman

OTHERS PRESENT

Dr. Pinya Cohen
Dr. Donald R. Hauler
Mr. John C. Hoffman
Dr. Saul Krugman
Dr. J. Anthony Morris
Dr. Eugene A. Rosenberger
Ms. Karlyn L. Shedlowski
Dr. Franklin H. Top, Jr.
Col. Charles F. Weiss

Chairman Vernon called to order, at 8:38 a.m., January 21, 1980, the winter meeting of the Immunization Practices Advisory Committee. He thanked Dr. Sanford and Ms. Howe for graciously serving as hosts for this meeting and commented on the excellent facilities of the Uniformed Services University of the Health Sciences. He welcomed Dr. Flynn, Capt. USN, liaison representative from the Department of Defense, and representatives of the 3 military services to the meeting, and invited their participation.

Rabies Prophylaxis

After introductions and brief announcements, Dr. Vernon called on the Committee and Drs. Winkler and Anderson to discuss the revised draft of the rabies statement. Dr. Meyer noted that the licensing of the human diploid cell rabies vaccine (HDCV) produced by Wyeth, Inc., did not appear as imminent as had been expected, because of some developments in the manufacturer's processes. Merieux Institute of France might market a similar vaccine in the United States in the near future, but probably not sooner than within the next month.

There was discussion on details in the draft which warranted amplification or clarification. The principal policy issue concerned the 5-dose regimen recommended in the statement, and the 6-dose regimen currently recommended by the World Health Organization. It was noted by Dr. Anderson that the United States has added significantly to the information available to WHO at the time of their recommendation for 6 doses. The original studies in Europe which had produced the data used to reach that recommendation had all been designed to test a 6-dose regimen. That regimen had proved highly successful, leading to its incorporation into the WHO recommendations. In the United States, 77 persons bitten by rabid animals have been treated with the 5-dose regimen without any treatment failures. In addition, some 250 persons have received the vaccine in the 5-dose regimen, and all developed antirabies antibodies. These findings significantly extend the findings of the European studies and indicate efficacy of the vaccine administered in a 5-dose regimen. This additional evidence of efficacy, the high cost of the vaccine, and the general desirability of limiting doses to as few as possible consistent with protection, all supported adoption of the 5-dose regimen.

Although the WHO recommendation for 6 doses resulted from the way in which the vaccine trials were originally designed, several Committee members felt that the precedent established by the WHO in recommending a 6-dose regimen was significant and could not be easily disregarded. They emphasized the need to consider the issue most carefully before recommending a 5-dose regimen, which would appear to users to be in conflict with the WHO recommendation.

Other Committee members felt that an ACIP recommendation of a 6-dose regimen, based primarily on perpetuating the precedent set by WHO, could result in a practically unalterable commitment to a 6-dose regimen "from now on," despite good evidence that the 5-dose regimen was adequate to confer protection. Indeed, if the appropriate studies were done, it might well be that 4 or even 3 doses would prove adequate for solid protection. Accepting a 6-dose regimen despite the additional evidence favorable to the 5-dose regimen would tend to inhibit further studies of fewer-dose regimens in the future.

Committee members noted that the current 5-dose recommendation calls for obtaining a blood sample after the fourth dose of vaccine, so that any person who had not developed antibody would be detected in sufficient time to add a sixth or even more doses to assure the development of antibody. Moreover, in use of the vaccine in the United States to date, there had been no instances in which persons had failed to develop antibodies.

Dr. Vernon asked Dr. Wilfert to draft language which would express the Committee's general agreement that the 5-dose regimen was considered adequate. In discussing the revision produced by Dr. Wilfert, the Committee members emphasized that the experience in the United States represented a significant extension of information concerning this vaccine, which appeared to warrant the 5-dose regimen. The ACIP recommendation should, in fact, spell out in some detail the evolution of data on the vaccine in Europe, and then subsequently in the United States, so the reader could clearly understand the rationale for selecting the 5-dose regimen.

Dr. Vernon asked that these, and other revisions recommended by the Committee, be incorporated by Drs. Winkler and Anderson into another draft to be completed and distributed to the membership for review within the next week, if possible.

Hepatitis Prophylaxis

Dr. Vernon then turned to the draft revised statement on hepatitis which had been sent to the members prior to the meeting. He suggested that participants focus on the issues raised by the draft so that the available time for discussion could assist in clarifying them. Drs. Francis, Krugman, and Maynard discussed some of the complexities of, and controversies about, the existing data on the use of immune serum globulin (ISG) and hepatitis B immune globulin (HBIG) in the prophylaxis of hepatitis B, and of non-A, non-B hepatitis. Dr. Jordan referred to a recent review paper by Seeff and Hoofnagle ("Immunoprophylaxis of Viral Hepatitis," Gastroenterology 77:161-182, 1979), in which the authors made recommendations at variance to the existing (and proposed revised) ACIP recommendations. He also noted several editorials in the same issue by hepatitis experts who varied in their reactions to the review. A brisk discussion ensued about the difficulties in interpreting previous studies of the prophylaxis of hepatitis B because many were done with ISG before this product was subjected to screening for hepatitis B surface antigen; also, there were apparently conflicting findings about the efficacy of HBIG in the prophylaxis of hepatitis B virus infections.

After lengthy discussion by participants, Dr. Vernon asked the group to specify, as explicitly as possible, the scientific questions which need to be resolved in order that the Committee might move forward on a revised recommendation. The following "issues" were consequently specified:

1. The need for standard nomenclature. The United States is the only major country using the term "immune serum globulin (ISG)." The term used elsewhere in the world, and recommended by WHO, is "human normal globulin (HNG)." The ACIP should facilitate the acceptance and use of this nomenclature in the United States.

2. Is there a role for ISG in the postexposure prophylaxis of hepatitis B? Is the evidence sufficiently convincing to enable the Committee to recommend HBIG over ISG for prophylaxis of hepatitis B in public health practice?

3. Is there a role for any immunoglobulin in the pre-exposure prophylaxis of hepatitis B? If so, what is the role, and when should the substance be used?

4. What should be the dose of immunoglobulin recommended for prophylaxis of hepatitis A?

5. Is there a role for ISG in prophylaxis of hepatitis B in infants born to mothers with hepatitis B infections? This issue must be addressed bearing in mind the 2 forms of transmission to which the infant may be subject: That from acute infection in the mother, and that from the chronic carrier state in the mother.

6. Attention must be paid to recommending appropriate amounts of immunoglobulin based on the titer of available materials and the quantity of the infecting dose. The notion that "if a little is good, a lot is better" should not be fostered; some intellectually more satisfying alternative should be presented.

7. It must be made clear that immunoglobulin is not a source of hepatitis infection.

Dr. Krugman emphasized the need to deal with these issues and produce recommendations, even in the absence of complete data; clinical situations requiring decisions about the use of these materials are occurring daily in practice. Physicians must have prudent guidance while we accumulate definitive data to clarify present confusion and rightly adjudicate existing controversies.

Several Committee members expressed the need to delve more deeply into the published literature before proceeding. Dr. Maynard offered to send to Committee persons a "packet" of major papers addressing various aspects of the problem. Dr. Millar promised to send out copies of the papers and editorials referred to by Drs. Jordan and Krugman to the Committee.

Dr. Vernon asked Dr. Millar to see to it that the issues specified were included in the minutes as a guide to further thought, discussion, and comment on the existing draft by Committee members.

Mumps Vaccine

Dr. Vernon asked Dr. Hinman to introduce discussion of the proposed mumps statement which, it was hoped, could be published soon. Dr. Hinman noted the changes that had been made in the draft and solicited further discussion. In response to a question by Dr. Mortimer about the availability of monovalent mumps vaccine, Dr. Hinman noted that monovalent mumps vaccine was available, as well as a rubella-mumps variation.

There being no other major changes, Dr. Hinman suggested that the Committee members take a final look at the revised draft "overnight" and provide any comments to him before leaving Washington; the mumps statement could then be published within the next week or two.

General Recommendations on Immunization

Dr. Hinman opened discussion on this proposed revision soliciting any "last-minute" comments by the Committee. There was some discussion about whether to mention bacterial vaccines in the section on pregnancy, because of the questions raised in this regard during discussion of rabies vaccines. Dr. Wilfert noted that in the absence of any known increased risks from bacterial vaccines during pregnancy, it would be inappropriate to raise unwarranted suspicions based on purely theoretical grounds. The use of Td antigens, for instance, was an important part of antenatal care, and could be crucially protective of life and health of both mother and newborn where need existed. The Committee would be doing the public a disservice to imply doubts that might inhibit this preventive practice. Dr. Sanford noted that for 20 years all patients coming into the obstetrical clinic of the Parkland Hospital, Dallas, Texas, were routinely immunized with Td antigens. Many infants were thereby spared life-threatening tetanus and diphtheria. Dr. Mortimer inquired as to the current epidemiology of tetanus; Dr. Hinman noted that only a few cases occur in children because of increased immunization activities.

Dr. Hinman again suggested that the Committee examine the existing draft "overnight" and provide him comments the next day. It was hoped that this recommendation could also be published within the next two weeks.

Smallpox

Dr. Millar briefly discussed the possible need for amending the existing recommendation for the use of smallpox vaccine. The WHO Global Commission on the Eradication of Smallpox had met in December, and had decreed the world free of smallpox; it seemed appropriate to consider the existing statement. Dr. Lane, Director of the Bureau of Smallpox Eradication, had suggested that the only civilian persons who should be vaccinated are those working with smallpox virus in laboratories. In the United States, this probably meant only people working in the CDC laboratory (which is anticipated to be the one U. S. laboratory approved by WHO to continue such work). Dr. Millar also noted that the military continues to recommend smallpox vaccination for active duty personnel, although they now recommend against vaccinating dependents. The Armed Forces Epidemiological Board intends to discuss smallpox vaccination at its upcoming meeting. It was stressed that the issue of vaccination of military personnel was different from that of civilians. Over 20 countries still require certificate of smallpox vaccination for international travel, although WHO has urged all countries to eliminate these requirements as soon as possible.

Dr. Wilfert suggested that concern must be given to workers with vaccinia, ectromelia, and other orthopox viruses; protection from variola virus was not the only issue for lab workers. Dr. Chin noted that effective January 1, 1980, Connaught Laboratories limited the availability of its smallpox vaccine, to distribution from one installation and use only for travelers to countries still requiring vaccination.

Dr. Meyer suggested that the Committee consider whether or not the State health departments might be designated the exclusive distributors of smallpox vaccine. Dr. Dixon indicated that in Canada, the distribution of smallpox vaccine had been limited to specific, well-defined points, and that a strong recommendation against the use of the vaccine for dermatologic and other purposes had gone out to practitioners. He noted that, as it had become more difficult to acquire the smallpox vaccine in Canada for these inappropriate purposes, other virus vaccines (such as polio) were being used. Dr. Dandoy suggested that the matter of appropriate distribution points for smallpox vaccine might be discussed with the State Health Officers and the State and Territorial Epidemiologists.

Dr. Vernon asked Dr. Millar to have Dr. Lane prepare a draft revision of the present statement on smallpox vaccine for consideration at the next meeting. Information on the current distribution and use of smallpox vaccine would also be appreciated by the Committee.

Summary

Dr. Foege arrived during the afternoon session. At approximately 3:30 p.m. Dr. Vernon began his Summary of the day's deliberations for the CDC Director.

Regarding rabies, Dr. Vernon noted that the major question was whether or not the data are adequate to justify the ACIP's recommending a regimen that differs from that recommended by the World Health Organization. While the additional data from the use of the vaccine in the United States seem adequate to justify recommending only 5 doses, the data necessary to produce a broad consensus are not available, and probably will not be for years. CDC may, in fact, have to assist WHO in carrying out any further studies necessary to reach a true international consensus on the point. He noted that the Merieux Institute of France may market its Human Diploid Cell Rabies Vaccine in the United States soon, and that Drs. Winkler and Anderson had been asked to make changes in the existing draft responding to points raised during the discussions.

Regarding hepatitis, Dr. Vernon reported that the Committee is continuing its discussion of a proposed revision. He noted great interest in, and difference of opinion about, the prophylaxis of hepatitis B. He defined the following issues as needing further attention: Nomenclature (ISG vs Human Normal Globulin); the role of ISG and HBIG in postexposure prophylaxis of hepatitis B; whether or not there is a role for immunoglobulin in the pre-exposure prophylaxis of hepatitis B; the role of ISG in the prophylaxis of neonatal hepatitis.

He also indicated that questions had been raised by the Committee about: Immunoglobulins as a potential source of hepatitis B virus; and the adequacy of levels of anti-A antibody in current ISG products. He noted that the Committee had been reassured on both the latter points by the day's discussions.

Dr. Foege responded that the long delay in proceeding with the CDC hepatitis B vaccine trials appeared to be over, and that the trials should proceed rapidly.

Dr. Vernon then reported that the revised recommendation on Mumps Vaccine, and the revised General Recommendations on Immunization, were to receive a "last look" by the Committee members and should be ready for publication shortly thereafter.* Dr. Vernon added that Dr. Millar had been asked to have the CDC Bureau of Smallpox Eradication prepare a revised draft of the statement on Smallpox Vaccine to be considered at the next meeting of the ACIP.

Dr. Foege then reported his recent discussions with Secretary Harris and Surgeon General Richmond about prospects for the continued availability of vaccines. He noted that pharmaceutical manufacturers continue to talk of "getting out of the vaccine business." His discussions with Secretary Harris and the Surgeon General included recommendations that: (1) An interagency group be established in the Public Health Service (analogous to the Interagency Influenza Work Group) to monitor developments regarding vaccine production; (2) Federal stockpiles of vital vaccines be established; (3) there be an increased Federal input into clinical vaccine trials, and (4) issues regarding liability, and compensation of victims of untoward effects of vaccines, be resolved.

He reported periodic "one-on-one" sessions with the Surgeon General, and noted that in these measles elimination has become a regular discussion item. The Surgeon General was most interested in this effort. 1979 was a "great year" in that, despite improved reporting of measles cases, there were only 13,500 cases reported, as opposed to a previous annual low of 22,500. Because of a large outbreak in Clayton County, Georgia, much of the measles currently occurring in the United States is "within walking distance of CDC." He was grateful that better surveillance and systematic investigation of outbreaks had led us to understand that "measles is not a mysterious disease." The current problems of measles transmission in the military and among refugee populations were correctable, and the agencies responsible were taking the appropriate actions. On the other hand, measles imported in travelers was not as easy to correct, nor was the problem of measles transmission in preschool day care centers; "finding the handle" to these problems was difficult.

He noted that the results of the large-scale WHO-sponsored BCG trial in India were receiving substantial publicity, including a recent comprehensive review by Dr. Larry Altman of the New York Times. Except for some on WHO's headquarters staff, observers consistently interpret the results as showing little effect of BCG in the prevention of tuberculosis.

The International Childhood Immunization Program ("Expanded Programme on Immunization") is about to "really take off." Excellent training had been done; there was a high degree of interest among donor countries; most important, the third world countries were viewing this program as crucially important to their developing health services.

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*They were approved and submitted to Morbidity and Mortality Weekly Report on February 4, 1980. The "General Recommendations on Immunization" are scheduled for publication on February 22, and the statement on "Mumps Vaccine" on February 29.

So, as previously stated, the ACIP's continuing leadership and wide-reaching impact make it one of "the truly dynamic committees at work in Government."

Concluding Remarks

Dr. Vernon then called for final remarks. Col. Weiss indicated that the military is finding itself in an awkward position viz-a-viz certain vaccines: The vaccine manufacturers are insisting that the military assume the "duty to warn" the vaccinee as a condition for buying the vaccine. On the other hand, for the military the "right to decline" is completely incompatible with the need for military preparedness. This dilemma most certainly will evantually affect the use of other prophylactic agents. The Department of Defense may require special legislation from the Congress authorizing the military to require specifically that military personnel be vaccinated. Col. Weiss also noted with pride that the Air Force was executing aggressive immunization activities against measles and rubella.

Dr. Vernon again thanked Dr. Sanford and Ms. Howe for their outstanding hospitality and adjourned the meeting at approximately 4:35 p.m. The next meeting is scheduled for May 5-6, 1980, at the Center for Disease Control, Atlanta, Georgia.

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

Thomas M. Vernon M.D 2 20 80

Thomas M. Vernon, Jr., Chairman Date