DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
October 16-17, 1990
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Auditorium A at the Centers for Disease Control, Atlanta, Georgia, on October 16-17, 1990. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Samuel L. Katz, Chairman
Dr. Stanley E. Broadnax
Dr. James D. Cherry
Dr. David W. Fraser
Dr. Caroline B. Hall
Dr. Mary E. Wilson

Ex Officio Members

Dr. Carolyn Hardegree (FDA)
Dr. John R. LaMontagne (NIH)

Liaison Representatives

Dr. Kenneth Bart (NVP)
Dr. David Fedson (ACP)
Dr. Edward A. Mortimer, Jr. (AMA)
Dr. Stanley A. Plotkin (AAP)
Dr. William Schaffner, II (AHA)
Dr. Susan E. Tamblyn (NACI)
Dr. Ronald C. Van Buren (AAFP)

Acting Executive Secretary

Dr. Walter R. Dowdle

NAVY ENVIRONMENTAL HEALTH CENTER

CDR David Trump

HHS STAFF PRESENT

CENTERS FOR DISEASE CONTROL

Office of the General Counsel

Mr. Brian M. Willis

Epidemiology Program Office

Dr. Melinda Wharton

Center for Infectious Diseases

Dr. Claire Broome
Dr. James Hughes
Dr. Harold Margolis
Dr. Jay Wenger

CENTERS FOR DISEASE CONTROL (Cont'd)

Center for Prevention Services

Dr. Bill Atkinson
Dr. Roger Bernier
Dr. Robert Chen
Dr. Steve Cochi
Ms. Rosamond Dewart
Mr. Conrad Ferrara
Dr. Jacqueline Gindler
Dr. Stephen Hadler
Dr. Alan Hinman
Mr. Phil Horne
Dr. Sonja Hutchins
Dr. Ed Maes
Dr. Walter Orenstein
Dr. Peter Patriarca
Mr. Stephen Sepe
Dr. Peter Strebel
Dr. Roland Sutter
Dr. David West
Dr. Walter Williams

HEALTH RESOURCES AND SERVICES ADMIN.

Dr. Cynthia McCormick

OTHERS PRESENT

Nancy Berger
Jerome Boscia
Carlos J. Castillo
Jill Chamberlain
Dr. Pinya Cohen
Dr. Corry Dekker
M.F. Dye
Dr. James L. Gale
Dr. Jill Hackell
Dr. Carlos Hernandez
M.R. Hilleman
Dr. Gregory Istre
Cynsie Johnson
Patrick W. Kelley
David L. Klein
David M. Konys
Dr. Saul Krugman
Suzanne Laussucq
Dr. Charles U. Lowe
Sharon Mates
David K. McClintock

OTHERS PRESENT (Continued)

Ellen McGuire
Fabio Moheroaui
George Moonsammy
Dr. David Nalin
Peter Paradiso
Dr. Carlos Ramirez-Ronda
Cary Ruscus
Nancy Sabalusky
Jane V. Scott
Judith Shindman
A.L. Toliver
Dr. Joel Ward
Dr. Jo White
Mark Wolff
Walter Woods

IMMUNIZATION PRACTICES ADVISORY COMMITTEE
Meeting at
Auditorium A
Centers for Disease Control
Atlanta, Georgia
AGENDA

Tuesday, October 16

8:30 a.m.	Welcome and Opening Remarks	Drs. Sam Katz/Walter Dowdle/ William Roper
9:00 a.m.	DTP Study in Washington and Oregon	Dr. Jim Gale
9:30 a.m.	Update on Pertussis Symposia	Dr. Roger Bernier
9:45 a.m.	Discussion of DTP Statement	Dr. Steve Cochi
10:15 a.m.	BREAK	
10:45 a.m.	Discussion of DTP Statement (cont'd)	Dr. Katz/Committee Members
12:15 p.m.	LUNCH	
1:15 p.m.	Acellular Pertussis Vaccine Trials	Dr. Jill Hackell, Lederle-Praxis Dr. Carlton Meschievitz, Connaught Dr. John LaMontagne, NIAID
1:45 p.m.	Discussion	
2:00 p.m.	Vaccine Adverse Event Reporting System (VAERS)	Dr. Robert Chen
2:30 p.m.	Smallpox Vaccine to Health Care Workers	Dr. Bill Atkinson
2:45 p.m.	BREAK	
3:15 p.m.	Universal Immunization Against Hepatitis B - Has the Time Come?	Dr. Harold Margolis
4:00 p.m.	Pneumococcal Vaccination of Alaskan Natives and Other Residents	Dr. John Middaugh
4:30 p.m.	Measles Update	Dr. Bill Atkinson
5:00 p.m.	Immunization of Immunocompromised Individuals	Dr. Greg Istre
5:30 p.m.	ADJOURN	

Wednesday, October 17

8:00 a.m.	*Haemophilus influenzae* Update	Drs. Claire Broome/Jay Wenger
9:30 a.m.	Polio Update	Dr. Steve Cochi
10:30 a.m.	BREAK	
11:00 a.m.	National Vaccine Injury Compensation Program	Dr. Cynthia McCormick
11:30 a.m.	National Vaccine Program Update	Dr. Ken Bart
12:00 noon	ADJOURN	

The Immunization Practices Advisory Committee (ACIP) convened in Auditorium A of the Centers for Disease Control (CDC), Atlanta, Georgia, on October 16, 1990, at 8:35 a.m. Samuel Katz, M.D., Wilburt C. Davison Professor, Duke University Medical Center, presided as Chairperson.

In attendance were representatives of the pharmaceutical industry, media, academia, and interested groups, as well as members of local and national government agencies.

Welcome and Opening Remarks

Dr. Sam Katz, Chairman, opened the meeting by summarizing the responsibilities of the ACIP Committee, namely, that it (1) provides advice and guidance to the Secretary of the Department of Health and Human Services on all matters relating to immunization and the use of vaccine; (2) formulates recommendations used extensively by state, local and city governments and by the private sector; (3) maintains a continuous review of the state of the art in vaccine production and use in assessing the risks and benefits of immunization and in assessing alternative methods of disease control; and (4) issues statements used as the scientific policy basis of the National Immunization Program.

Dr. Katz introduced Walter Dowdle, Ph.D., Deputy Director, CDC, temporarily serving as Executive Secretary of the ACIP Committee. Mary Guinan, M.D., Ph.D., formerly Assistant Director for Science, has taken another CDC position. Dr. Katz introduced William Roper, M.D., M.P.H., Director, CDC, since March 1, 1990, and former Director of the Health Care Financing Administration (HCFA), the agency responsible for both Medicare and Medicaid.

Dr. Roper welcomed the group, asserting that he had a professional and personal interest in a question of overriding concern to the Committee, namely, how the nation can do a better job of delivering available vaccines to children in America. He noted that several of the priority areas that he hopes to focus on while he is CDC Director--strengthening the infrastructure for public health across the country; making prevention a practical reality in our health system; improving the health of children--touch upon this issue of delivering vaccine to children.

He said the current measles epidemics are a lesson in the difficulties of delivering currently available vaccines to children, particularly young, poor children in the inner city. But a recent survey suggests that an "astoundingly large portion" of children who are affected by measles are also members of families who are participants in other public programs, such as Aid to Families with Dependent Children and Medicaid.

He said that a series of demonstration projects looking at how the government can better integrate these programs with health services, particularly immunization programs, has been launched.

Dr. Roper said he believed the nation could successfully launch an effort to immunize 2- and 3-year-olds, just as in the late 1970s, the school-entry immunization drive had been successfully undertaken.

He added that he was cautiously optimistic that additional funds would be budgeted for the National Immunization Program because he felt the message had gotten across that our immunization coverage levels are "a national embarrassment" that "cannot be tolerated."

Dr. Katz asked all persons in attendance to introduce themselves and give their affiliations.

Dr. Katz announced that the 1991 meeting dates for the Committee are February 26-27 and June 4-5. The fall meeting dates have not yet been set; members will be contacted.

DTP Vaccine

Dr. Katz reminded the Committee that it was to issue a revised DTP statement. A subcommittee, headed by Dr. Ted Mortimer, worked to prepare the proposed new statement, which was distributed to Committee members at the June meeting. Two presentations of recent studies were chosen for this meeting because they were felt to bear on that revision.

SONIC: Dr. Jim Gale, Professor of Epidemiology, University of Washington, presented information on the Pilot Study of Neurologic Illness in Children (SONIC), the largest study to date of the association of acute neurologic illness with DTP vaccine in the United States. The study, conducted by researchers at the University of Washington in Seattle and at CDC, was a population-based case-control study in children aged 1 to 24 months in Washington and Oregon. An estimated 109,000 births per year occur in these states; and an estimated 368,878 DTP doses were given to children under surveillance during the study period.

The illnesses studied were acute encephalitis and encephalopathy, infantile spasms, nonfebrile seizures, complex febrile seizures (lasting approximately 15 minutes or more or accompanied by lateralizing symptoms or signs), and acute paralytic syndromes. The data show no evidence of significantly increased risk of severe acute neurological illness within 7, 14, or 28 days following DTP immunization. Risk estimates for some individual conditions were increased (encephalopathy, complex febrile seizures, or infantile spasms); another was decreased (nonfebrile seizures). However, 95% confidence intervals (CIs) always

included 1.0, indicating that the risk estimates different from 1.0 could have been due to chance. Nevertheless, the consistent elevation of estimated risk for some conditions, and the similarity of the odds ratio for NCES*-compatible cases (which were the more severe cases) with the NCES overall odds ratio, although not statistically significant, may be consistent with the NCES findings of an association between DTP and acute serious neurologic illness. (See 11-page handout, "Acute Neurologic Illness and DTP: Report of a Case-Control Study in Washington and Oregon.)

In his presentation, Dr. Gale repeatedly emphasized limited numbers of cases were involved.

Pertussis Symposium: Roger Bernier, Ph.D., M.P.H., Division of Immunization (IM), Center for Prevention Services (CPS), handed out selected abstracts of presentations from the Sixth International Pertussis Symposium held in September in Bethesda, at the National Institutes of Health (NIH). He briefly summarized new data from the 10-year follow-up study of NCES children. The followup study (by Dr. Madge et al) was designed to determine the current physical health, educational abilities, social behavior, and general development in the study children. This study tried to address some of the criticisms of the NCES, by following up controls and by using more recognized measures of adverse outcomes.

At followup, case-children, irrespective of vaccination status, were more likely than controls to have behavior problems, to perform less well in tests of educational attainment, to have convulsions, and to show evidence of neurological and/or physical problems. The relative risk (RR) of DTP immunization within 7 days before onset of neurological symptoms in previously normal children (excluding the infantile spasms) and in previously normal children who had died or who showed any evidence of later dysfunction, was statistically significant (5.5 RR). However, numbers were small and must be interpreted with caution.

Pertussis Multicenter Surveillance Project: Steven Wassilak, MD, IM, CPS, summarized a 2-year study on the efficacy of whole-cell pertussis vaccines conducted in Baltimore, Denver, and Milwaukee. By classifying illnesses as to severity, the researchers observed increasing vaccine efficacy (VE) similar to what was presented for Swedish data at the symposium, that is, increasingly higher

*The National Childhood Encephalopathy Study in the United Kingdom, which suggested that the overall risk estimate of serious acute neurologic illnesses within 7 days of DTP vaccination was 2.3 (95% CI) of 1.4, 3.9.

VE by increasing severity of illness. The U.S. data are more limited than the Swedish data, but they have fairly narrow confidence limits. VE estimates were up into the 90s, depending upon the types of definitions of severe illness.

Stephen Cochi, M.D., IM, CPS, reviewed proposed changes to the ACIP DTP Statement and the rationale for them. (See 5-page handout entitled "ACIP DTP Statement Revision Key Points-1.") Committee members discussed the suggested changes, using the handout and the draft of that statement, previously distributed to them.

Points 1 and 2 were passed as read. Point 3 was tabled until Dr. Ted Mortimer checks with the Michigan Department of Health to see if they will or will not distribute Pertussis Vaccine, Adsorbed. Point 4 was amended to indicate that the second dose of polio should not be given at an interval any shorter than 6 weeks after the first dose. Point 5 was passed but may have to be looked at again in light of whether Michigan is distributing Pertussis Vaccine, Adsorbed.

Considerable time was spent discussing the controversial conclusions #1 and #2 (Point 6 on handout). There was widespread agreement among Committee members to include a statement at the beginning of this section, giving the ACIP's conclusions and reassuring physicians that it is difficult to know the answers with certainty but that the risks of severe neurologic illness from DTP are exceedingly rare. Dr. Cochi was then directed to modify the two conclusions, incorporating the following points and criticisms. The wording of the first line of Conclusion #1 was contested because one "can't prove an absolute negative." The wording of the second sentence was considered unclear. The risk estimate for brain damage (1:330,000) is no longer considered accurate and lends an "air of precision" that can be misused by those who don't understand the uncertainties involved. A definition of serious acute neurologic illness is also needed.

Provided these modifications are made, the Committee voted to accept item #6, the new statement on DTP and serious acute neurologic illness. The unrevised statement reads as follows: (1) A causal relationship between DTP vaccine and brain damage has not been proven. If the vaccine does so, it must be exceedingly rare. (2) The risk estimates of 1:140,000 for serious acute neurologic illness and 1:330,000 for brain damage should no longer be used.

Point 7 was accepted. Point 8 was also accepted, but Dr. Katz suggested that it appear earlier in the paragraph. Point 9 was accepted. Point 10--to continue using an interval of 7 days for encephalopathy following DTP--was debated as to whether the interval should be shortened to 72 hours. No decision was reached, and the issue will be brought up for discussion again.

Point 11 was accepted, which consisted of a change in the current list of events occurring in temporal relationship to the administration of DTP and considered to be contraindications to further vaccination with DTP. Those events that will continue to be contra-indications are: "(1) an immediate anaphylactic reaction; (2) fever of 40.5 C (105 F) or greater within 48 hours; (3) collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours; and (4) encephalopathy, defined as an acute central nervous system disorder with severe alterations in consciousness, unresponsiveness, generalized or focal seizures, neurologic signs that persist more than a few hours and/or failure of recovery within 12 to 18 hours occurring within 7 days, even though causation by DTP cannot be established." Two additional events that were changed from contraindications to precautions, and the accompanying wording, were as follows: "Precautions: If any of the following events occurs in temporal relationship to receipt of DTP, whether to give subsequent doses of vaccine containing the pertussis component should be carefully considered. Although these events were considered absolute contraindications in previous recommendations, there may be circumstances, such as a high incidence of pertussis, that outweigh the possible risks involved, particularly in view of the fact that they are not recognized to produce permanent sequelae. (1) Persistent, inconsolable crying lasting three hours or more, occurring within 48 hours. (2) Convulsions with or without fever occurring within three days." Lastly, an unusual, high-pitched cry occurring within 48 hours was dropped from the list of contraindications or precautions.

Point 12 provoked some debate and Dr. Cochi said his group would work on it further. Committee members also agreed that item #13 needed further discussion. Item #14 was accepted. Dr. Cochi's group was asked to rewrite #15 to include a statement about when prophylaxis no longer provided substantial benefits.

Finally, Dr. Cochi said there were also some changes needed on the diphtheria and tetanus portions of the ACIP statement, but that these would be summarized and distributed to ACIP members.

Acellular Pertussis Vaccine Trials

Three presentations were given on the efficacy and safety of the new acellular pertussis vaccines. Dr. Jill Hackell of Lederle-Praxis reviewed the Japanese experience with whole-cell pertussis vaccines and then presented data from a recent U.S. randomized, double-blind, multi-center study designed to reveal the immunogenicity and safety of the Takeda acellular pertussis-component (APDT) vaccine product, for which Lederle-Praxis has just completed FDA product licensing application. She concluded that APDT, administered as a booster dose, is at least as immunogenic as DTP; filamentous hemagglutinin (FHA) responses are consistently higher in the APDT group. Immunogenicity rates are

approximately the same in U.S. and Japanese children. In terms of safety, over 6,500 doses have been given to more than 2600 U.S. children and infants. Safety data, collected by 20 U.S. study centers, indicate that the percentage of children with symptoms within 72 hours post-immunization is lower for APDT than for DTP. Another, double-blind randomized trial involving 10 centers again showed that the percentage of children with symptoms was always less with APDT.

Dr. Carlton Meschievitz, Connaught Laboratories, presented data on the Biken Acellular Pertussis Product. Since 1981, over 12 million doses have been used in Japan. It was evaluated in a Swedish efficacy trial, which began in 1986, and which demonstrated 92% efficacy at 42-months of follow-up (most of the follow-up came after the trial using different methods of case ascertainment). In addition, data from three large, multi-center U.S. trials of safety and immunogenicity of DTacP vaccine indicate that children and infants vaccinated with this product have significantly fewer reactions and significantly higher antibody levels.

Dr. David Klein, National Institute of Allergy and Infectious Diseases (NIAID), briefly explained NIAID's ongoing study, under the auspices of the National Vaccine Program, of the immunogenicity and safety of 13 different acellular vaccines from eight different manufacturers. The study will consider such issues as safety, what happens when more than 2 doses are administered, and examination of infants beginning at a lower age than in the Swedish trial. Thus far, 8 of the 13 vaccines have been looked at in infants; on the other hand, some products have never been tested in children at all. Dr. Klein said 120 children are needed in each study arm and that the vaccine efficacy trial will hopefully begin at the end of summer 1991. In addition, site visits are being conducted to four countries (Canada, United Kingdom, Sweden, and Italy) that are interested in having a vaccine trial to determine which country would be best suited for another phase-3 trial.

Discussion of these presentations followed. Dr. Stanley Plotkin, MD, liaison representative for the American Academy of Pediatrics (AAP), asked if the acellular vaccines shouldn't now be licensed at least for booster doses since data seem to be abundant that these vaccines are safe and efficacious. The AAP Red Book has taken this position now. A representative of the FDA said that applications have been filed with that agency by both Lederle and Connaught to license such vaccines for this purpose.

Dr. Bernier asked if the Committee agreed with Dr. Plotkin and, if so, whether the members thought a whole-cell vaccine needed to be included in the next trial. All participants, including

Dr. Plotkin, thought a whole-cell arm would still be desirable in the next round of efficacy trials.

Vaccine Adverse Event Reporting System (VAERS)

Robert Chen, M.D., IM, CPS, reported on the progress and the strengths and weaknesses of the Vaccine Adverse Event Reporting System (VAERS), a new streamlined reporting system (it combines CDC's and FDA's previous systems). VAERS is responsible for the collection and analysis of reports on all adverse events following receipt of any vaccine in the United States. A contract to assist in the collection of this information has been awarded to a contractor, ERC Biomedical Services, under CDC and FDA supervision. VAERS has a toll-free number (1-800-822-7967) and a new reporting form that has been pilot-tested. The system is expected to be fully operational, replacing the CDC and FDA systems, by November 1, 1990. Letters explaining the new system (see handout) together with a copy of the new form were mailed to physicians in relevant specialties about 2 weeks ago; in addition, announcements about the new system are forthcoming in the *MMWR* and *FDA Drug Bulletin*. In response to a question, Dr. Chen said that FDA is developing the process of how best to notify manufacturers about adverse reactions received via VAERS.

Smallpox Vaccine to Health Care Workers

William Atkinson, M.D., IM, CPS, addressed the issue of whether the current recommendations for smallpox (vaccinia) vaccine should be modified to add administration of vaccinia vaccine to clinical personnel not working directly with orthopox viruses in laboratory environments. This issue has been raised because of increasing numbers of inquiries and requests for the vaccine for investigators involved with human trials of a vaccinia-human immunodeficiency virus (HIV) recombinant virus. The consensus of an Interagency Group of the National Vaccine Advisory Committee convened to discuss this issue was that the current vaccinia vaccine recommendations are appropriate, but that health care workers who remove contaminated dressings directly from volunteers in clinical studies also should be vaccinated. It was felt that no other groups of health care workers would benefit from vaccinia vaccine. The Interagency Group also recommended that the ACIP consider adding health care workers who handle contaminated dressings to the ACIP "at risk" population, and recommend vaccinia vaccine for this group. (The consensus statement and a summary of the 1989 distribution of smallpox vaccine were attached to Dr. Atkinson's handout.)

In a followup question and discussion period, the group learned that 95% of requests for the vaccinia vaccine are now for vaccinia recombinant work, obviously reflecting fears that recombinant vaccinia virus may be much more dangerous. The ACIP concluded that these fears need to be addressed. Dr. Katz

suggested that the current (1985) ACIP Smallpox Statement be circulated among the Committee members with the proposed revision.

Universal Immunization Against Hepatitis.

Harold Margolis, M.D., Division of Viral Diseases (DVRD), Center for Infectious Diseases (CID), spoke on the strategy to eliminate hepatitis B from the United States through universal immunization. Phase one of the strategy was to prevent childhood infections, by focusing on prevention of perinatal transmission through universal screening of pregnant women for HBsAg, and on universal immunization of infants in populations with high endemicity of infection, such as Alaskan Natives, Pacific Islanders, and first-generation infants of foreign-born Asian mothers. Dr. Margolis said that Congress has appropriated $9.9 million to states through the immunization Grant Program, primarily directed at preventing perinatal transmission. Requests for additional funding have gone to Congress to address immunization of infants of Asian mothers.

The increasing incidence of hepatitis B in the last 8 years has been primarily in adults, but data show that high-risk group immunization of adults is not feasible. The prevailing conclusion is that either infants, preferably, or possibly adolescent immunization is the way to control this disease, though it may take 15-20 years to see the effects. Dr. Margolis presented preliminary data from a cost-benefit analysis of universal infant immunization for hepatitis B which showed the costs of such a strategy were significantly less than the cost of disease resulting from our current approach. After summarizing the impediments to and benefits of universal infant immunization, Dr. Margolis asked whether the Committee could make a recommendation for this action. Hawaii is moving toward universal immunization, and the AAP endorses the idea. Lack of an ACIP recommendation has been a problem, Dr. Margolis said, because it deters Congressional funding and policy implementation; many physicians also seem unaware that this vaccine can easily be integrated into the immunization schedule.

Members of the ACIP made it clear that the Committee is leaning toward a recommendation of universal infant immunization against hepatitis B, but that a major program of education and information concerning flexible dosage schedules are needed and studies on long-term efficacy must be continued.

Pneumococcal Vaccination of Alaskan Natives and other Residents

During a conference call, John Middaugh, M.D., State Epidemiologist of Alaska, discussed interpretations of the ACIP statement on pneumococcal vaccine as it applies to the unique

population and geography of that state. The questions and the Committee's suggestions are listed below:

1. Does the ACIP recommend revaccination for all Alaskan Natives who received the 14-valent vaccine or who received the 23-valent vaccine ≥6 years before? The ACIP "supports enthusiastically" what the Alaskan State Health Department decides is practical in its unique setting.

2. Does the ACIP advise vaccination of all Alaskan Natives ≥2 years old? The ACIP does support Alaska's aggressive approach with this population.

3. Does the ACIP advise vaccination of Alaskans other than Alaskan Natives, such as lifetime caucasian native Alaskans, who live in special environments or social settings similar to Alaskan natives? No, except in very remote areas because of access to health care.

4. Would ACIP endorse a State of Alaska proposed program to extend pneumococcal vaccination to all Alaskans regardless of race or ethnicity? If the state has the resources, as outlined in draft, this is certainly a scientifically responsible position.

David Fedson, M.D., liaison representative from the American College of Physicians, called for the ACIP's acknowledgement of the State of Alaska's role as a leader in immunization.

A discussion of HCFA's role in pneumococcal vaccination led to a related one on the need to look at Medicaid's lack of carrier reimbursement for pneumococcal vaccinations done at hospital discharge. Although there is a DOG waiver with regard to Medicare, the carriers don't seem to be aware of it. HCFA data suggest that only about 30%-35% of all the pneumococcal vaccine doses distributed are reimbursed. What's more, HCFA's level of reimbursement, according to another source, is clearly less than half the level determined to be cost-effective. Dr.Katz said that he would see that this barrier to implementation of pneumococcal vaccination be put on the agenda of the next meeting of the Public Policy Committee of the Infectious Diseases Society. Dr. Roper, who is the former director of HCFA, will be at that meeting.

Measles Update

Dr. William Atkinson reviewed the status of measles in the United States. As of October 6, 22,798 cases have been reported, representing a 73% increase over the total last year at that time. Twenty-three states have reported more than 100 cases; several states--California, Texas, and Illinois--have had more than 1,000 cases each. For the first time since CDC has been

able to collect accurate information on age starting in 1973, the proportion of cases in preschool children has exceeded the proportion in school-age children. Race data from 26 states suggest that rates of disease are highest among blacks and Hispanics. Only 22% of all cases this year had a history of being appropriately vaccinated. Thus far, 64 deaths have been reported and probably another 20 will be included; by contrast, there were 41-44 deaths for all of last year. Four of the fatal cases this year were known to be HIV-infected. Thirteen of these deaths have been among the Hmong population, indicating a 10% fatality rate for this disease in that population. Whereas last year, 71% of fatalities were in children <5 years of age, this year less than half have been so and 42% of all reported deaths have been in persons >20 years old.

Thus far this year, there have been 149 outbreaks (5 or more cases); two--the ones in Los Angeles and Dallas--each had over 1,000 cases. The Dallas outbreak now appears to be over; the Los Angeles epidemic, which has totaled 6,300 cases since 1987, is still ongoing, with 3,200 cases this year alone. There have been a number of interventions but none has had an obvious impact. New York City is also now having a significant outbreak (reports of at least 300 cases), Dr. Atkinson added.

Walt Orenstein, M.D., IM, CPS, spoke about the hypothesis that this upsurge in cases is a phenomenon of increasing exposure. For example, there is an apparent continent-wide problem with measles right now. Moreover, there is no evidence that the antigenic nature of the measles virus is changing or that levels of usage of immunization are declining. Dr. Orenstein also said that for 1991, almost all states, except Alaska and Florida, have a major voluntary or compulsory policy for a two-dose measles schedule. Dr. Orenstein also referred to the point mentioned in Dr. Roper's opening remarks, that 40%-91% of vaccine-eligible children are enrolled in public assistance programs, such as WIC, AFDC, food stamps, or Medicaid. This suggests vaccine delivery needs to be integrated with other federal programs. Finally, Dr. Orenstein noted that the National Vaccine Advisory Committee has taken on measles as one of its chief projects and is developing a "white paper" on measles control. The Committee has suggested that the major reason for the resurgence of measles is a failure of the vaccine delivery system. A major part of this white paper will be devoted to how to build the infrastructure for vaccine delivery.

Changes to the ACIP Adult Immunization statement on measles were proposed. There was considerable discussion about whether the date in the statement, "all adults born in 1957 or later who do not have a medical contraindication should receive one dose of measles vaccine unless they have a dated record of vaccination, etc." should be changed from *1957* to *1947*. It was learned that of measles cases documented between 1985-89, approximately 30% of

the cases occurring in persons born before 1957 were in health-care workers. It was therefore suggested that the statement be written to recommend that health care workers born before 1957 should be offered, or health care facilities should consider requiring them to receive, measles vaccine if such workers are believed to be susceptible.

Immunization of Immunocompromised Individuals

Gregory Istre, M.D., Oklahoma State Epidemiologist, asked whether the ACIP felt that a separate ACIP statement on immunization of immunocompromised individuals would be useful. The group decided it was, and Dr. Istre agreed to put together a small group to develop a short compilation of already existing statements (ACIP, Red Book, and package inserts), with one or two tables. Among the areas it will address are HIV/AIDS; congenital immuno-deficiency disorders; immunosuppression (cancer and chemotherapy) and steroids; organ transplants; and splenectomy.

***Haemophilus influenzae* Update**

Peter Paradiso, Ph.D., Praxis Biologics, updated the group on two large-scale studies of efficacy of a 3-dose regimen of HibTITER vaccine, conducted in Finland and in California. Efficacy in the Finnish study in which 53,000 infants received the vaccine was 89% with 1 dose; 95% with 2 doses; and 100% with 3 doses. Among the 22,125 children vaccinated with 3 doses in California, efficacy was 100%.

Mark Wolff, Ph.D., School of Hygiene and Public Health, Johns Hopkins University, spoke on the efficacy of a 2-dose regimen of Merck Sharp and Dohme's PedvaxHIB™ in a placebo controlled trial among Navajo Indians. Among cases vaccinated with 2 doses before 15 months of age, vaccine efficacy was 100%. No cases occurred in children between the first and second dose of vaccine, while eight cases occurred in the placebo group during this time period.

Joel Ward, M.D., UCLA Center for Vaccine Research, summarized the substantial differences in immunogenicity between these two vaccines.

Dr. Wenger then led a discussion of the list of 10 recommendations on pages 7-9 of the draft ACIP statement on Hib disease. It was suggested that a table summarizing recommendations 1-4 be included. The group voted to insert statements asserting that (1) the ACIP strongly supports use of Hib conjugate vaccination for infants attending day care facilities, and (2) concomitant administration of Hib vaccine with MMR is acceptable. It was also decided to amend item #9 to indicate that some immunodeficient older children who will not develop antibody titers after natural disease will respond to a

conjugate vaccine. A "permissive statement" to the effect that physicians who care for older individuals who may be immunocompromized may consider vaccination was also suggested. Item #8 will be amended to clarify that it is acceptable to give 3 doses in deltoid muscles.

It was then pointed out that Hib is the one vaccine-preventable disease for children in the United States that is not notifiable, although since 1986 many states have reported it voluntarily. Accordingly, the ACIP voted unanimously to endorse the idea of making this a reportable disease. Dr. Istre volunteered to carry this suggestion to the October 30 meeting of the Council of State and Territorial Epidemiologists.

Dr. Fedson reported that the Task Force for Adult Immunization of the American College of Physicians (ACP) was disbanded in April. Thirty-five letters protesting this action, including one from Dr. Mason, were sent to the ACP President. As a result, the issue will be mentioned and perhaps discussed at the next ACP meeting.

Polio Update

Four short briefings were presented on the epidemiology of polio in the United States, the status of the polio-eradication effort in the Americas, new molecular techniques for laboratory diagnosis of polio as well as the laboratory network in the Americas, and two studies of the efficacy of different sequential schedules of OPV and IPV.

Since 1975, Roland Sutter, M.D., IM, CPS, told the ACIP, an average of 11 cases a year of polio have been reported in the United States. There have been no cases traced to wild poliovirus since the last case in 1979. Fifty-six cases of these 100 vaccine-associated cases reported during 1975-1989 occurred in contacts of oral polio vaccine recipients and 44 cases in vaccine recipients. The calculated overall risk for acquiring polio from the first dose of oral polio vaccine is 1:710,000 doses distributed; the associated risk with subsequent doses is estimated to be 1:6.9 million doses.

Dr. Cochi said there has been great progress in the polio eradication effort in the Americas and that the disease will be close to eradication by the end of 1990. He said the main strategies accounting for PAHO's progress include strengthening routine vaccine delivery, supplementing routine vaccination efforts with national vaccination days in individual endemic countries; and mop-up operations, conducted under Rotary grants, whereby house-to-house vaccinations have been undertaken in high-risk areas. In 1990, a total of 28 confirmed cases have been reported, compared to 130 in 1989. There have been only four wild isolates from confirmed polio cases so far this year. The

recommendations from the most recent meeting of PAHO's Technical Advisory Group are to (1) continue to emphasize adequate and timely investigation of cases through collection of stool specimens (40% of confirmed cases in 1989 lacked stool specimens); (2) develop better diagnostic techniques; (3) submit and collate data for all discarded cases to the Regional office of PAHO; and (4) change the case definition to focus more on laboratory diagnosis as the basis for confirming cases. In 1990, the new case definition being employed is that a confirmed case requires wild poliovirus isolation.

Olen Kew, Ph.D., DVRD, CID, emphasized the importance of a collaborative network to monitor the molecular epidemiology of wild polioviruses. Molecular comparison of poliovirus isolates provides detailed epidemiologic data that are unobtainable by other means. Analysis of poliovirus isolates obtained from the laboratory network in the Americas and elsewhere has made it possible to map the geographic distribution of poliovirus genotypes (new term for strains). He said that wild poliovirus type 1 is now probably extinct in Mexico, and types 1 and 3 have probably been eradicated in Brazil.

Peter Patriarca, M.D., IM, CPS, discussed a study of four groups of children who received OPV alone, IPV alone, 1 dose of IPV followed by 2 doses of OPV, or 2 doses of IPV followed by 1 dose of OPV. The study suggests that local antibody responses are greatest with OPV, followed by OPV/IPV, and then IPV alone. However, the differences between the groups were "very minor." A second study of sequential schedules, conducted by Connaught and CDC, is ongoing in Baltimore. It is a very ambitious study, with 500 participants.

Dr. Katz asked members of the group if they would consider meeting for more than 1-1/2 days for future meetings. He said to please get back to him about this, as he really feels the ACIP needs more time to handle the items on the agenda satisfactorily.

National Vaccine Injury Compensation Program (NVICP)

Cynthia McCormick, M.D., reported on the status of the NVICP, which she said has undergone considerable change in concept and in practice since October 1988, when it began. Within 2 years, NVICP has changed from an administrative review program to a medically supported litigative program. As a court-based program, it is fundamentally adversarial, though various approaches have been tried to make the process more informal.

As it now functions, there is a medical review process that develops the Secretary's response to petitions and forms the basis for and supports the Department of Justice litigation. Expert witnesses come largely from academic centers, although some clinician practitioners are used. Most cases involve child

neurologists--a factor that may prove to be a limiting factor in future cases due to the tremendous volume of cases in comparison with the number of expert witnesses available.

Although the majority of cases filed in the first 1-1/2 years of the program were granted compensation by the court, now the defense (DHHS) is winning more than 80% of its cases. Of the 75% of cases contested, in fact, 83% have been won or dismissed. The 102 awards as of October 1990 have totaled $60 million; the average award for a disability is $1.2 million.

However, there is a tremendous backlog of cases and more than 3,000 cases will have to be heard in an 18-month period. It was hoped that NVICP would be granted an extension in the adjudication period, but there is no indication that significant relief will be granted in time. This may lead to inadequate airing of the issues.

A Senate bill was approved in both houses on October 12, 1990, to extend the October 1, 1990, statutory deadline for filing of new claims by 4 months and to give the court the authority to grant up to 6 months' extension of the now 420-day adjudication period, if needed. The bill has not yet been signed into law. Dr. McCormick said even this extension would try their resources; they had hoped for at least a 2-year extension.

In an attempt to deal with the tremendous case load, the court may be more willing to consolidate cases with the same issues into single hearings, such as tuberous sclerosis and infantile spasms, she said.

National Vaccine Program Update

Kenneth Bart, M.D., M.P.H., Director of the National Vaccine Program, OASH, updated the Committee on the National Vaccine Program, which he said is focusing on policy-program interface issues. Currently, first among these is measles. The National Vaccine Advisory Committee is preparing a position paper to give a careful, independent analysis of the causes for the reemergence of measles and problem of "failure to vaccinate," particularly among inner city minority and poor populations.

Dr. Bart also discussed two of the "Secretary's Initiatives" of interest to the ACIP. The first (Program Direction #4) concerns the possibility of Medicare and Medicaid reimbursement for immunization services. The second (Program Direction #8) refers to the need to improve access for children to immunization; immunization is to be used as an acute phase indicator of success for access to primary health care--rapid measurement can be made of changes in coverage, morbidity, and mortality.

Third, the program is studying how and by whom vaccine package inserts are used and what impact differences between recommendations made in package inserts, by the Red Book, and by the ACIP, have on providers.

Finally, Dr. Bart discussed the World Summit for Children held September 29-30, 1990. He said that it was the first time in history that so many Heads of State (70) had come together at all, much less for children. The world leaders issued a Declaration and Plan of Action for the Survival, Protection and Development of Children. Many of the items in this document concern immunization including the commitment to the global eradication of polio, the global elimination of neonatal tetanus and to substantial reduction in the morbidity and mortality due to measles by the year 2000. At the Summit, President Bush endorsed a Children's Vaccine Initiative to harness the biotechnology revolution to improve the available vaccines and develop new ones.

By way of background, Dr. Bart also said that in June, when UNICEF Director James Grant visited Secretary Louis Sullivan, M.D., to urge him to support the Summit, Mr. Grant invited the United States to undertake the development of a children's vaccine; that is, a single, heat stable vaccine delivered at birth to immunize against all the vaccine-preventable diseases. Children in many countries now must have as many as 14 contacts with the health care system to be fully immunized with currently recommended vaccines. With populations of some countries doubling over the next decade and resources dwindling, many public health experts feel that simplification of the immunization schedule by eliminating some, if not most, of these doses is required. Simplified immunization schedules also would do much to improve access in the United States to infants and children as well, and help to ensure a sustainable infrastructure to deliver vaccines.

Three meetings of experts were held in preparation for the Summit to discuss the concept of a children's vaccine, involving participation from academia and the public and private sectors from various countries. Basically, all three groups reached the same conclusion; namely, that the goal should be recast from the development of a single children's vaccine, which is beyond current science or technology's ability to produce, to the immediate launching of a long-term, multi-stage Children's Vaccine Initiative. This would move the world aggressively toward a children's vaccine while making substantial incremental progress.

<u>Summary of Agreed-upon Actions</u>

Following is a "reminder" listing of agreed-upon actions. For more details, see the related section of the minutes.

- Dr. Ted Mortimer agreed to check with the Michigan Department of Health to see whether or not it will distribute Pertussis Vaccine, Adsorbed.

- Dr. Steve Cochi will summarize changes needed on the diphtheria and tetanus portions of the DTP statement and distribute them to ACIP members.

- Dr. Katz suggested that the current (1985) ACIP Smallpox Statement be circulated among the Committee members with a proposed revision addressing the issue of health-care workers' apparent fear of recombinant vaccines. Dr. Bill Atkinson will follow up.

- Dr. Katz said that he would see that HCFA's low level of reimbursement for pneumococcal vaccination would be put on the agenda of the next meeting of the Public Policy Committee of the Infectious Diseases Society; Dr. Roper, former director of HCFA, will be at that meeting.

- Dr. Gregory Istre agreed to put together a small group to develop a short ACIP statement on the immunization of immunocompromised individuals.

- Dr. Istre volunteered to carry the ACIP's unanimous vote to endorse the idea of making *Haemophilus influenzae* a reportable disease to the October 30 meeting of the Council of State and Territorial Epidemiologists.

- Dr. Katz asked all members to consider meeting for 2 days instead of the current 1-1/2 and to let him know their decisions.

The meeting adjourned at approximately 12:15 p.m.

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

Samuel L. Katz

Samuel L. Katz, MD, Chairman
Date: 24 January 1991