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

MINUTES OF MEETING

Immunization Practices Advisory Committee
February 12-13, 1992
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACI met in Auditorium A at the Centers for Disease Control, Atlant Georgia, on February 12-13, 1992. Those in attendance are list below:

COMMITTEE MEMBERS PRESENT

Dr. Samuel L. Katz, Chairman
Dr. Katherine Edwards
Dr. Neal Halsey
Dr. Carlos E. Hernandez
Dr. Gregory R. Istre
Dr. Carlos Ramirez-Ronda
Dr. Rudolph Jackson
Dr. Mary E. Wilson

Ex Officio Members

Dr. Carolyn Hardegree (FDA)
Dr. John R. La Montagne (NIH)

Liaison Representatives

Dr. Pierce Gardner (ACP)
Dr. Caroline B. Hall (AAP)
Dr. Edward A. Mortimer, Jr. (AMA)
Dr. Georges Peter (AAP)
Dr. Michael Peterson (DoD)
Dr. William Schaffner, II (AHA)
Dr. Susan E. Tamblyn (NACI)
Dr. Ronald C. Van Buren (AAFP)

Executive Secretary

Dr. Claire V. Broome

NAVY ENVIRONMENTAL HEALTH CENTER

Capt. S. William Berg

ARMED FORCES EPIDEMIOLOGY BOARD

Capt. W.M. Parsons, MSC, USN

HHS STAFF PRESENT

Maj. Rob Lipnick, O

NATIONAL INSTITUTES F HEALTH

Dr. Regina Rabinovi

CENTERS FOR DISEASE ONTROL

Office of the Gener Counsel

Mr. Kevin M. Malone

Office of Health ar Safety

Dr. Naima Abd Elgha

Epidemiology Progra Office

Dr. Dan Fishbein
Dr. Melinda Wharto

Center for Infecti s Diseases

Dr. Miriam J. Alte
Ms. Inger Baker
Dr. Nancy Cox
Ms. Henrietta Hall
Dr. Harold Margoli
Mr. James Miller
Ms. Michele Pearso
Ms. Helen Regnery
Mr. Tom Toror
Dr. Ted Tsai

CENTERS FOR DISEASE CONTROL (Cont'd)
Center for Prevention Services

Dr. Robert Chen
Dr. Stephen Cochi
Dr. Susan Davis
Ms. Rosamond Dewart
Dr. Vance Dietz
Mr. Gary Euler
Ms. Judy Gantt
Dr. Jacqueline Gindler
Dr. Mark Grabowsky
Ms. Penima Haber
Dr. Stephen Hadler
Dr. Alan Hinman
Ms. Sonja Hutchins
Ms. Donna Jones
Dr. Charles LeBavor
Ms. Susan Lee
Mr. Arthur Manoharan
Dr. Lauri Markowitz
Ms. Anne Mellinger
Ms. Susan Mims
Dr. Bernard Moriniere
Dr. Walter Orenstein
Mr. Mark Papania
Dr. Peter Patriarca
Dr. Desiree Rodgers
Mr. Stephen Sepe
Dr. Raymond Strikas
Dr. Peter Strebel
Mr. Roland Sutter
Dr. Steve Wassilak
Mr. John Watson
Dr. David J. West
Dr. Walter Williams

OTHERS PRESENT

Mr. L. Barreto, Connaught Labs
Mr. Robert Byrd, Associated Press
Dr. Pinya Cohen, Connaught Labs
Mr. Corry Dekker, Uniron Corp.
Mr. Ingram Douglas-Hall, SmithKline Beecham Pharmaceut als
Dr. Geoffrey Evans
Dr. Lisa Ford, Lederle Praxis
Ms. Carol Frankel, Medeva International
Ms. Jana Froeschle, Connaught Laboratories
Ms. Rose Mary Hoy, Merck Vaccine Division
Dr. Clare Kahn, SmithKline Beecham
Dr. David Krause, SmithKline Beecham
Dr. Saul Krugman, New York University Medical Center
Mr. Toni Krzesowski, Parke-Davis
Ms. Lin Wenlii, AMVAX, Inc.
Ms. Anne Mather, Clayton, Georgia
Mr. Charles Marwick, Journal of the American Medical A ociation
Mr. Carlton Meschievitz, Connaught Labs
Mr. Frank McCarthy, Wyeth Ayerst Laboratories
Mr. David McClintock, Lederle-Praxis
Mr. Andrew Murdin, Connaught Labs Ltd.
Dr. David Nalin, Merck
Dr. Pearay L. Ogra, Child Health Center, Galveston
Mr. Peter Paradiso, Lederle Praxis
Mr. Stanley Plotkin, Pasteur-Merieux
Dr. Ciro de Quadros, Pan American Health Organization
Mr. Hal Rathfon, Smith Kline Beecham
Ms. Jane Scott, Lederle Laboratories
Mr. Irwin Shapiro, Tanabe USA
Dr. Judith Shindman, Connaught Laboratories, Ltd.
Mr. Howard R. Six, CLI
Mr. Dan Soland, CLI
Dr. Jo White, Merck Sharpe & Dohme Research Labs
Ms. Carolyn Weeks-Levy, Lederle Laboratories
Mr. Chris Zurawsky, Infectious Disease News, SLACK, I

IMMUNIZATION PRACTICES ADVISORY COMMITTEE MEET IG

CENTERS FOR DISEASE CONTROL
ATLANTA, GEORGIA
FEBRUARY 12-13, 1992
AUDITORIUM A

AGENDA

February 12, 1992

8:30 a.m.	Welcome and Opening Remarks	Dr. Sa uel Katz Dr. C ire Broome
8:45 a.m.	Acellular Pertussis Vaccines: Supplementary Draft ACIP Statement on Connaught/Biken DTaP Vaccine	Dr. S ve Wassilak
9:00 a.m.	Polio Eradiation and Measles Reduction in the Americas	Dr. C o de Quadros
10:00 a.m.	Japanese Encephalitis Vaccine	Dr. T F. Tsai
10:30 a.m.	BREAK	
11:00 a.m.	Hepatitis A	Dr. C ig Shapiro
12:00 p.m.	Immunization of the Immunocompromised	Dr. M k Grabowsky Dr. B Chen
12:45 p.m.	LUNCH	
1:45 p.m.	Meningococcal Disease in Canada	Dr. S an Tamblyn Dr. J Wenger
2:00 p.m.	Reevaluation of Polio Vaccine Policy	Dr. S ve Cochi Dr. B Chen Dr. V ce Dietz Dr. N l Halsey Dr. O n Kew Dr. P rey Ogra Dr. P er Strebel Dr. R and Sutter
2:45 p.m.	BREAK	
3:15 p.m.	Reevaluation of Polio Vaccine Policy (continued)	
4:45 p.m.	ACIP Statements: Purpose, Audiences, Length, and Format	Dr. R hard Goodman
5:30 p.m.	ADJOURN	

February 13, 1992

8:30 a.m.	Influenza Vaccine: Partial Strain Selection Information	Dr. Nancy ox
	Surveillance and Special Studies	Dr. Louisa hapman Dr. Joe Ke :
	Influenza Vaccine Supply and Distribution	Dr. Ray St kas
	Revision of ACIP Influenza Vaccine Recommendations	Dr. Louisa hapman Dr. Ali Kh
	False Positive Serologic Reactions for HIV, HTLVI and HCV After Influenza Vaccination	Dr. Joanna uffington Dr. Jay Ep ein
10:00 a.m.	BREAK	
10:30 a.m.	Report of the BCG Subcommittee	Dr. Pierce ardner Dr. Dixie ider Dr. Robin iebner
11:15 a.m.	Assessment of Immunization Levels in Preschool Children	Dr. Betty ll
11:40 a.m.	Vaccine Injury Compensation Program	Mr. Thomas . Balbier, Jr. Dr. Geoff rans
12:00 p.m.	Standards for Immunization Practice	Dr. Roger rnier
12:15 p.m.	National Vaccine Program Update	Dr. Ken Ba : CANCEL D
12:30 p.m.	ADJOURN	

2/6/92

Executive Summary

On February 12-13, 1992, the ACIP convened at the Ce :ers for Disease Control (CDC) to discuss the status of numerou: vaccine-preventable diseases and vaccine-related issues. Dr. S. uel Katz presided as Chairperson; Dr. Claire Broome was Executive ecretary of the ACIP Committee. Gloria Kovach, the new staff spec list for the ACIP, was introduced to the Committee.

Acellular pertussis vaccines were the first subject for d cussion. CDC's Dr. Steven Wassilak reported that the ACIP stateme on this subject was at the printers; that Connaught had resented information for licensure of their acellular pertussi vaccine product for the fourth and fifth doses on November 12; an that the Lederle product was licensed on December 17. The price s $15.56 per dose.

Dr. Ciro de Quadros, director of the Expanded Pro amme on Immunization for the Americas with the Pan Americ Health Organization (PAHO), updated the Committee on the polio e: dication effort in the Western Hemisphere. He explained PAHO's ystem of negative reporting of cases of acute flaccid paralys (AFP). Among 20,000 health units, 80% now report each week. If unit is not reporting at least one case of AFP per 100,000, this ndicates something is wrong with surveillance. Dr. Quadros also s ted that this surveillance indicates that Guillain-Barre syndrom (GBS) is much more common than once believed in children under 5 ars old.

Regarding the eradication effort, Mexico, Brazil, an Central America reported no cases in 1991. The dates of onset fo the last cases were April 16, 1991, for Colombia and September 5, 991, for Peru. Colombia has been the target of an intensi mop-up operation. One million households were visited withir a 2-week period twice last year. The Minister of Health is aunching another house-to-house campaign on February 17. And ano er major campaign, termed "the Last Inch," is about to be launche In Peru. Two million households will be visited from February 2 March 8. This house-to-house effort will be repeated in May. Chil en under 5 years of age will get another dose of oral poliovirus OPV).

PAHO has also just established surveillance for neonata tetanus. They've learned that, of 14 districts, only about 10% a at high risk for this disease.

Dr. de Quadros also updated the ACIP on the measles ini ative in the English-speaking Caribbean. Cuban led the way in att pting to eliminate the disease by vaccinating all children 1-15 years of age. The four to six cases still being reported each ear from Cuba are probably not really measles.

Subsequently, the Minsters of the Caribbean countries opted an

initiative to eliminate measles by 1995, using the Cuban trategy. In May, 1991, all the islands except Jamaica immunized ildren 9 months to 15 years regardless of previous vaccinatic status. Coverage was nearly 100%. In 1991, there were only three onfirmed cases of measles in the Caribbean; all were imported rom the United States. For 1992 thus far, only one case has been eported, also in a traveler from abroad.

As a result, an initiative to eliminate measles from t Central American countries by 1997 has been announced. Brazi is also launching a major campaign for measles elimination an will be immunizing all of its children from 1-14 years old. ıile and Argentina are also launching such projects.

As a result of all this interest, a meeting is being c vened on February 28 to review what's happening in the region egarding measles and to see what PAHO can do to coordinate effor .

Following Dr. de Quadros' presentation, Dr. Neal Halse reported that at a meeting on February 11 at PAHO headqu ters in Washington, D.C., new technical developments in measle antibody assays that will allow the diagnosis of laboratory onfirmed measles with a single blood test were announced. Dr William Bellini's laboratory, which has been instrumental in veloping this technology, has agreed to provide the training and the resources to put this technology into the Caribbean ar several other Latin American laboratories within the next couple months.

Japanese Encephalitis (JE) vaccine was discussed by CDC Dr. Ted Tsai. He reviewed experience from adverse events surve lance in Okinawa, Japan, begun after a mass immunization campai against JE. The campaign was launched after an outbreak of thre cases of JE occurred in active-duty Marine personnel on Okinawa st year.

CDC's Dr. Harold Margolis introduced a series of sp kers to discuss the performance of hepatitis A vaccines in variou stage of clinical trial and the epidemiology of this disease in e United States. Dr. David Nalin from Merck Sharp & Dohme present results of his company's experiences with the Merck inactivate vaccine. The vaccine has been well tolerated, with only expected m d, local and transient reactions. What's more, a two-dose regim yielded titers higher than those seen after immune serum globul (IG).

Dr. David Krause of SmithKline Beecham, presented dat on that company's candidate HM175-strain vaccine. First human t als were begun in 1988. To date, there have been 67 studi in 18 countries, involving 50,000 subjects. In terms o overall reactogenicity, about one-half of vaccinees report nc symptoms after the first dose. The most common general symptom malaise or fatigue. Clinical trials on several thousand adults r eal that the seroconversion rate is 96% one month after the firs dose and 100% after a second dose.

Dr. Charles Hoke from Walter Reed Army Institute of Research explained that soldiers are the heaviest consumers of IG in fact, Operation Desert Storm exhausted all IG supplies in e United States. He reported results of a field efficacy trial i Thailand of an inactivated hepatitis A vaccine. The SmithKline rain was used with approximately 20,000 5- to 14-year-old childr ; 20,000 received placebos. Thirty cases of hepatitis A occu ed. Of these, 29 occurred in children who had received the plac o, and 1 in a children who had received the vaccine.

CDC's Dr. Craig Shapiro said that with two apparer y safe, immunogenic, and efficacious vaccines available, the Uni d States may soon be facing whether to license a vaccine for u in this country. He said that ideally this decision should be ba d on the epidemiology of hepatitis A in this country. Historica y, there are periodic, nationwide epidemics of hepatitis A. here are significant geographic variations in the disease. As ptomatic infection predominates in infants and children, bu greater symptomatic disease and higher case-fatality rates occu in older adults. Racial/ethnicity data indicate that the diseas is least prevalent among Asians and highest among American Ind s. The most commonly reported risk factor for hepatitis A is ontact-- household or sexual--with an adult patient with hepatit .

CDC's Dr. Robert Chen presented a draft ACIP statement the use of vaccines and immune globulins in persons wit altered immunocompetence. He explained changes. The Committe voted to leave out the column entitled "Routine (Not Immunocompro sed)" in Table 2; to add a column on solid organ transplant rec ients to the same table; and to mention in the statement tha an ACIP statement on bone marrow transplantation is forthcoming

Dr. Susan Tamblyn from the Canadian surveillance program iscussed an outbreak of meningococcal disease in Canada. The pro rtion of cases attributed to Group C has increased from 26% of cas s in 1983 to 63% of isolates by 1990. A unique Group C clone, T 15, is being isolated from an increasing proportion of cas --three-quarters in 1991. This clone appears to be the clone that was mainly responsible for clusters of disease that were see in 1991.

Tremendous demand for vaccine was prompted by three eaths in teenagers in little over a week in Ottawa this past Decen er. Then in early January two more cases, one fatal, occurred Ottawa, prompting the decision to hold mass, publicly funded va inations in Ottawa and a number of other affected regions Canada. Vaccine uptakes were very high--over 90% in Prince Edwa Island. Very few adverse reactions have been reported. Th Ontario Ministry of Health's passive surveillance system receiv 200-250 reports for the 140,000 doses administered. These w e mostly local reactions.

CDC's Dr. Jay Wenger reported on the epidemiology of men gococcal

disease in Canada. He said it appears that partic .arly in children 10-19 years old, the rates of disease were in th range of 15-20/100,000--20 times normal. Given these data and the eport of meningococcal disease in a traveler to Ottawa, CDC issued . limited Travelers' Advisory about January 17 suggesting that chi ren 2-19 who were going to be in Canada for 3 days or longer shoul consider immunization. The clone causing disease in Canada is isolated throughout the United States.

Reevaluation of polio vaccine policy dominated the meetir for over 2 hours. Numerous speakers presented new informat: 1 to be considered in an evaluation of the ACIP polio vaccinati policy. CDC's Dr. Steve Cochi said that at least four options are ossible: 1) to continue primary reliance on OPV (the present p icy); 2) change to primary reliance on inactivated polio vaccine IPV); 3) change to a mixed schedule of IPV, followed by OPV; d 4) no stated preference. When an Institute of Medicine ommittee considered the issue 4 years ago, it endorsed optio #1, but proposed reconsidering the issue after additional da became available and after IPV was combined with DTP in a licensed product.

Presentations were made on the circulation of wild vi in the country; the levels of immunity to poliovirus in a lts and preschool children, especially those in inner cities; the xtent of OPV vaccine virus spread to contacts of recipients; and the mixtures of IPV and OPV that would yield maximum benefi

In reference to the last item, results of numerous st ies were presented. They confirm that schedules using OPV or eIP only, or sequential schedules with eIPV followed by OPV, are very ffective in inducing antibodies to all three poliovirus serotypes, esulting in seroprevalence levels of virtually 100% after two to t ee doses and high GMTs. One study suggested that at least two dos of eIPV are needed before OPV to protect against recipient vaccine-associated paralytic disease. OPV-immunized childrer also had better intestinal, but similar pharyngeal immunity com red with eIPV-immunized children. OPV is an excellent boosting a nt after eIPV; OPV given after three doses of eIPV induced a more ugmented humoral response than OPV given after three doses of V. And finally, incorporation of at least one dose of eIPV at th start of the immunization schedule tends to increase systemic a well as local antibody production.

Two meetings on prospects for new polio vaccines were sum rized by CDC's Dr. Olin Kew. One was a World Health Organizat on (WHO) meeting held in Geneva March 12-13, 1990. The other wa an FDA-sponsored international workshop on poliovirus attenua ion held December 9-10, 1991, in Bethesda. Dr. Kew said that a enuation involves a small number of substitution mutations; the liovirus genome is exceptionally plastic; and attenuation involves differential growth in intestinal but not neural cel . Also

discussed were new approaches for OPV safety testing such as Chumakov's molecular tests, cellular assays, and transg ic mice. Dr. Kew said that the bottom-line conclusions from bot meetings were that excellent progress has been made, but more n ds to be done, and that no one is going to depart radically from he Sabin strains.

The manufacturers of combined DTP/eIPV vaccines next resented data. Dr. Carleton Meschievitz from Connaught/Pasteur de nstrated a dual-chamber syringe design so that thimerosal, a prese ative in DTP, does not interfere with the poliovirus. The entr phase of Connaught's study of its vaccine is to be completed t s month; submission of data to the FDA is planned for October.

Peter Paradiso, Lederle/Praxis, explained its p orities, particularly the combination products. Their liquid rm of a DTP/HbOC combination vaccine, Tetramune™, has be fairly extensively studied as part of a three-dose, primary seri (nearly 7,000 infants have received this vaccine). A license a lication has been submitted to FDA. The safety profile is exce ent, and the immunogenicity is as good or better in the combined roduct.

Lederle has also combined its acellular pertussis vaccin with its HbOC combination vaccine for the 15-month dose. F mulation studies are completed; immunogenicity and safety studies ave been initiated. Lederle hopes to file for license by year-e .

Following the polio presentations, Dr. Katz asked the Co ittee to assimilate all the information they had received in the ntext of the following: a) the policy question--Should we co ider the reintroduction of IPV to precede OPV? b) Multivalent accines, which might combine *Hemophilus* b conjugate, hepatitis B, P, eIPV; and c) whether the expense, time and change in p icy are anachronistic in light of the move to eradicate polic within 8 years?

Dr. Richard Goodman, Editor of the *MMWR*, discussed th purpose, audiences, length, and format of ACIP statements. H primary concern was whether they are becoming too long and com ex to be usable and readable. CDC has undertaken a comprehensive aluation of the entire *MMWR* series, including a readership surve designed to characterize the audience and how it uses the publica on. The evaluation is slated to be completed in about 18 months

Several ACIP members and members of the audience comm ted that immunization divisions at the State level clearly eed the technical statements although 95% of their questions ar not that complicated; the detailed, "encyclopedic" knowledge is eded for the other 1%-5% of cases. Several people urged that the *MMWR* readership survey be sure to include State immunizations visions.

The Committee heard seven presentations on influenz vaccine. CDC's Dr. Nancy Cox said that the WHO strain selection m eting was not scheduled until the next week so she would be prese ing only partial information on the strains selection for t 1992-93 influenza vaccine. The FDA Vaccine Advisory Committee t at the end of January. Based on data from a variety of la oratories present at the meeting, it was decided that the current nfluenza A(H3N2) component (A/Beijing/353/89 virus) would rema in next year's vaccine. As for influenza A(HlNl), for the first me since 1986-87, a variant that is different from A/Taiwan/01/8 has been identified. As for B viruses, virus isolates characte zed thus far have been related to B/Panama.

Dr. Louisa Chapman said that the 1991-92 influenza seasc has been characterized by abrupt onset, the dominance of influen A(H3N2) among circulating subtypes, and widespread reports o dramatic outbreaks among school children, beginning in October, perseded by reports of outbreaks among adult populations beginni in mid-November. Excess mortality was first evidenced in late ecember.

CDC's Dr. Joseph Kent presented information from nu ing home outbreaks in New York, Ohio, and Connecticut. The inve igations raised the question of whether the ACIP statement shoulc ecommend that the optimal timing of influenza vaccination act ities be moved up substantially.

CDC's Dr. Raymond Strikas discussed CDC's findings about nfluenza vaccine supply and distribution, particularly during the last influenza season, prompted by widespread media repor of flu vaccine shortages. First, Federal, State and local vernment vaccine distribution accounts for less than 15% of th doses of influenza vaccine distributed. In 1991, manufacturers ha produced 32 million doses--a 12.7% increase over the amount p duced in 1990. A CDC survey of 55 immunization grant programs roughout the country was undertaken to determine the extent vaccine shortages during the 1990-91 influenza season. On De mber 14, seventeen programs needed vaccine, for a net need of abc 136,000 doses. However, eight programs had a surplus. Of the 0 States that did not purchase vaccine, 9 had some shortages. Wy h-Ayerst Laboratories bottled an additional 650,000 doses at were available in December. All of these doses of vaccine have now been sold.

Revision of ACIP Influenza Vaccine Recommendations fol wed this discussion. Dr. Chapman returned to lead the Committ through suggested changes to the ACIP flu statement. Most were latively minor, involving insertion of clarifying words or ph ses, all highlighted on a handout. One of these--involving whet r "child care facilities" should be spelled out as an exam e of an essential community service that might benefit from vac nation--caused considerable discussion. The Committee asked Dr. apman to draft a clear statement about the appropriateness of v cinating

staff of institutions to minimize disruption of major s vices.

A proposed substantive word change to the document egarding vaccinating persons with known hypersensitivity to egg or other components of the influenza vaccine (i.e., thimerosal) was then introduced. CDC's Dr. Ali Khan reported on his invest ation of these two areas. He said that only a minute amount o residual egg protein is in the influenza vaccine and that only r ely have these minute amounts been associated with anaphylaxis. Having a history of allergy to eggs, however, is an unreliable pr ictor of reactions to flu vaccine. Allergic individuals can e safely immunized if results of preliminary skin testing to nfluenza vaccines are negative. Even individuals who have positive intradermal skin testing to influenza vaccine may be su essfully vaccinated. A desensitization protocol has been develope that has allowed some researchers to vaccinate children with ysician-documented egg allergies and positive skin test But desensitization will not prevent anaphylaxis or other pe I and type IV mediated reactions. Reports of anaphylaxis after nfluenza vaccination have been infrequent: 1-5 reports per year, th 20-25 million doses of vaccine distributed a year.

Dr. Khan then summarized his investigation of thimerosal He said that it was apparent that a) exposure to vaccines ntaining thimerosal can lead to induction of hypersensitivity;) most patients who have positive patch tests or intradermal tests to thimerosal do not develop local reactions to imerosal administered as a component of vaccine; c) although v cination will be safe for the vast majority of people with ocula or skin-test sensitivity, thimerosal can cause severe, but reatable hypersensitivity.

Dr. Chapman then led a discussion about changes to the ACIP flu statement pertinent to Dr. Khan's report. The proposed a ition on thimerosal--basically as summarized above--was added, un anged.

Both CDC suggestions about egg hypersensitivity concer d adding phrases about consulting "a physician, preferably a clinical allergist or immunologist." In each instance, the ommittee decided to recommend only consultation with a physician Mention of undergoing appropriate skin testing was debated ex nsively. Consequently, Dr. Broome proposed that the subject of sk testing be added to the agenda for an upcoming ACIP meeting, si e it had generated so many questions. The Committee agreed.

Discussion then turned to remaining proposed changes i the ACIP influenza document. The first concerned target g ups for influenza and pneumococcal vaccination; members asked D Chapman to rewrite this section. Next, the Committee adopted th revision to propose that the optimal timing of influenza v cination activities be in the period October 15-November 15.

False-Positive Serologic Reactions for HIV, HTLV-1, and CV after Influenza Vaccination were reported on by CDC's D Joanna Buffington. In early December the FDA received rep ts from approximately 20 blood centers of 90 donors testing peatedly reactive to two or more of the ELISA screening tests for tibodies to HIV, HTLV-1 and hepatitis C virus. These did n confirm positive with more specific tests. Sixty of the 90 donor reported receiving the 91-92 influenza vaccine prior to their onation. Although there was and is no association between disease d either getting a flu shot or donating blood, the publicly perc ved risk of danger was a potential public health problem.

She gave the following results of a pilot study underta n by the American Red Cross: a) Initial investigation revealed multiple false seroreactivity at two centers, first occurring 1 April, 1991, the month they changed manufacturers for their anti-HBV screening kits; b) The incidence of multiple false activity increased dramatically in October and November, 1991, incident with peak flu vaccination season; c) Although flu v cination appeared to be significantly associated with this phenom on, many cases reported no vaccination history; and d) The fir ing that donors who were retested several weeks after testing pos ive were subsequently found to be negative, suggests that the re tion may be transient.

To determine the extent and timing of these reactions, su eillance forms have been sent to almost 200 blood centers in t e United States. A large case-control study involving approxi ately 15 centers is planned.

Dr. Pierce Gardner, liaison representative to the Comm tee from the American College of Physicians, reported that the B Working Group has a preliminary draft, and hopes to present a re final one at the June ACIP meeting.

Assessment of immunization levels in preschool children w next on the agenda. CDC's Dr. Betty Zell said that ana ysis of retrospective school immunization surveys reveals that a the vast majority of children get into the immunization syste prior to their second birthday, with the majority of these children receiving their first immunization prior to their firs birthday b) if these children could be kept in the immunizati system, coverage levels would increase considerably; c) an appare problem is the fourth DTP; OPV3 and DTP4 should be given togethe 23%-63% of children receive their OPV 3 before their first birt ay.

Dr. Geoff Evans, Deputy Director and Chief Medical Offi r of the Vaccine Injury Compensation Program since January, gave a presentation on that program. For pre-1988 cases, 4,095 etitions have been filed. There are 210 post-1988 petitions. total of 346 awards, totaling $200.2 million, have been made a of last week. But relatively few cases from the prospective p iod have

been adjudicated. Awards for death cases are fixed a $250,000 plus attorney fees. The average award for pre-1988 injur cases is $1 million. The program predicts a tremendous shortfa --$152.2 million. It will run out of money for the next fiscal y r in the next month or two. The law's original shutdown provisio -that if one of the portions of the program ran out of money, t program would stop within 6 months--has been repealed so that e n if the retrospective portion is without funding, the prospecti portion remains viable.

Eighty-five percent of cases are injuries; the rest are d ths. The program concedes about one-third of cases; the rest g to U.S. Claims Court. The program prevails in 40% of those ca es. The program is regularly denied its viewpoint with SIDS cas .

Because of the looming fiscal crisis with the program, r. Mason appointed a task force last summer with two functions: to come up with legislative proposals beginning with nonscientifi kinds of proposals; 2) to form a scientific subgroup. The legisla ve group made several propositions, some of which have been ad ted into law. The scientific subgroup, headed by Dr. Kenneth rt, made suggested revisions to the Aids to Interpretation, based rgely on an Institute of Medicine report issued last July. Those evisions were then presented to a specially formed subcommitt of the National Vaccine Advisory Committee (NVAC) and presente with its report in November. Those recommendations were then fo arded on to the Advisory Commission on Childhood Vaccines.

CDC's Dr. Roger Bernier gave a progress report of where e are in getting consensus for the publication of the new Sta ards for Immunization Practice. NVAC, in its review of the st dards in November, asked for two changes. Dr. Bernier is working resolve those issues before finalizing a draft. He is optimisti that the document will be finished in 30-60 days--before the ext NVAC meeting in April. The ACIP would then see the final rep t at the June meeting.

Dr. Bernier gave ACIP members a working draft. The o points brought out by NVAC are: 1) should package inserts be ntioned, not just ACIP and the Red Book, as sources of informatic 2) two new standards have been added (see pages 18-19 of handc).

There was considerable discussion about the third item nder the Contraindication Table (page 16 of handout). It was p nted out that "administration of multiple live virus vaccines (V & MMR) within 30 days of one another if not given on the same ay" is a theoretical risk, not a true contraindication. The A P didn't have quorum to vote, but the sense of those present wa that the ACIP did not want this policy guideline listed a a true contraindication, but as a footnote.

Dr. Broome summarized Dr. Kenneth Bart's prepared upd e on the

National Vaccine Program. The acellular pertussis effi cy trial will begin shortly in Sweden. The budget initiatives fo the next budget cycle have a continuing emphasis on infrastructu e repair for vaccine delivery, surveillance for adverse event: and an initiative to accelerate vaccine development for STDs a l TB and the Children's Vaccine Initiative. NVAC has cre ted new subcommittees to deal with policy and management bar .ers and adult immunization. The National Vaccine Program offic and CDC are working with the Health Care Financing Administration o review and make recommendations on Medicare and Medicaid regul: ions and guidelines as they relate to immunization coverage.

Dr. Broome reminded ACIP members that the dates of upcoming meetings are June 9-10 and October 21-22. The meeting ad urned at 12:22 p.m. A summary of requested follow-up actions appe s at the end of the minutes.

The ACIP convened in Auditorium A of the CDC, Atlanta, G rgia, on February 12, 1992, at 8:35 a.m. Samuel Katz, M.D., W burt C. Davison Professor, Duke University Medical Center, pr sided as Chairperson.

In attendance were representatives of the pharmaceutica industry media, academia, and interested groups, as well as m bers of national government agencies.

Welcome and Opening Remarks

Dr. Sam Katz, Chairman, opened the meeting by announcin that Dr. Mary Lou Clements and Dr. David Fraser would not be able o attend today's meeting. Dr. Katz then asked all persons in att dance to introduce themselves and to give their affiliations.

Dr. Katz then introduced Dr. Claire Broome, the Executive ecretary of the ACIP Committee. She introduced Gloria Kovach the new staff specialist for the ACIP.

Dr. Broome also reported that three ACIP statements ve been published since the October ACIP meeting, plus an ACIP eport on the first acellular DTP is at the printers. This re esents a substantial amount of committee work, for which Dr. Broo thanked members. She also reiterated that when members ha agenda suggestions or comments to make about a particular pic, to address them to the presenter, but to copy her office.

Dr. Katz noted that he has one complaint for the edito s of the *MMWR*, namely, that the subject of an ACIP statement ne ls to be listed as that in that publication's front-page table of ontents, not as a "Notice to Readers," which can easily be mis d. Dr. Broome said that this criticism had been formally disc sed with the *MMWR* editors and would be acted upon.

Acellular Pertussis Vaccines: Supplementary Draft ACIP tatement on Connaught/Biken DTP Vaccine

Dr. Steve Wassilak, Division of Immunization (IM), Natio l Center for Prevention Services (NCPS), reported that the d ft ACIP statement on acellular pertussis vaccine (DTaP) is at the rinters. At the October meeting, there had been one unresolve concern, namely, whether this vaccine should be given at all as ne first three doses in children who were 2 years of age or old . There were dissenting opinions about this issue. Shortly a er that meeting, the American Association of Pediatrics (AAP) Co ittee on Infectious Diseases met, debate continued, and cons sus was reached. The conclusion was that DTaP should be recomm ded only for use as the fourth and fifth doses, regardless of a ch d's age. Dr. Katz agreed that CDC was then cleared to publish the atement. This statement, provided to Committee members, is what as been sent to the printers. Also provided is a draft ACIP upda to fill

in the holes about the fine points of the Connaught vacc e's use. Dr. Wassilak asked that any comments about the fine poi s of use of this vaccine be submitted within 2 weeks.

On November 12, Connaught presented information for li nsure of their product for the fourth and fifth doses. When Conna ht would obtain licensure is not certain. It could be any time thin the next several months; CDC expects it before the next meet g. This ACIP update would be published in the weekly *MMWR* upc product licensure. The Lederle product was licensed on Decembe 17; the *MMWR* announcement was published on December 20. The pri for the acellular DTP product was $15.56 dose in the private sec r, which includes $4.56 F.E.T.

Dr. Katz asked Dr. Wassilak if there were any differe es being proposed in the update. Dr. Wassilak said no, but pointe out that Connaught, as opposed to Lederle, has data for use at 15 nths and 16 months of age. Nevertheless, the recommendations tha came out of the ACIP in October for the other product, including e range, will also apply for this product.

Polio Eradication and Measles Reduction in the Americas

Next, Dr. Ciro de Quadros, Regional Advisor for the Pa American Health Organization's (PAHO) Expanded Programme on Im nization (EIP), updated the Committee on the polio eradication eff t in the Western Hemisphere. Although the EPI was begin in 19 , it was not launched in the Region of the Americas until 1977, at which time vaccine coverage was very low. By 1984, polio inc ence had reached the lowest historical level, <0.1/100,000. About 1 out of the 48 countries had achieved this level of control. How er, many countries with high populations didn't have these low tes, and active surveillance was not in place. At this time, PAH began to think in terms of eradicating polio in the Americas. I 1985, an initiative to eradicate this disease from the Western misphere was proposed and approved by the Directing Council of P O.

The major concerns to accomplish this were the necessary olitical and social will, vaccine efficacy and stability, and sur illance. Strategies to accomplish this were establishing an i eragency coordinating committee and a Technical Advisor Group, decentralization of resources, and publication of a HO Field Guide for Eradication. Specific vaccination strategie included routine delivery of oral poliovirus vaccine (OPV through established health services; application of National V cination Days with OPV (two per year); and mop-up operations i areas of risk.

Countries were classified as to whether they were poli infected (indigenous cases reported within the previous 3 years) r polio-free. The latter group was divided into high risk (i.e vaccine coverage in children <1 year old is below 80% in any ge olitical

unit within the previous 3 years) or low risk. Case d initions were also refined and included suspected cases (acute aralytic illness in an individual under age 15), probable (susp ted case with acute flaccid paralysis [AFP] with 10 weeks to r classify based on analysis of laboratory specimens and follow-u clinical exam) and confirmed (wild poliovirus isolate o vaccine associated).

A system of negative reporting of cases of AFP was a begun. Among 20,000 health units, 80% now report on time each ek. This very efficient system never existed before and can be ised for cholera surveillance as well. If a unit is not reportin at least 1 case of AFP per 100,000, this is a "red light" that so thing is wrong with the surveillance, since that has been determ ed to be the background rate of AFP. (Note: Dr de Quadros said th it used to be believed that Guillain-Barre syndrome [GBS] was ot very common in children under 5. Their surveillance system ndicates that GBS--which accounts for 60%-65% of the AFP cases--is uch more common than believed.) Another indicator for surveilla e is the proportion of AFP cases for which stool samples are sub tted for analysis. Some 80% of AFP cases have stool samples subm ted, Dr. de Quadros said. Finally, virologists meet every 8 nths to review problems with surveillance.

In terms of the status of the eradication effort thus f , Dr. de Quadros said that, by 1990, there were a total of only co irmed 24 cases of polio in the Americas. In 1991, Mexico, B il, and Central America reported no cases. The dates of onset fo the last cases were April 16, 1991, for Colombia and September 5, 991, for Peru.

Colombia has been the target of an intensive mop-up opera on. One million households were visited within a 2-week period ice last year. It was so successful that on February 17, the M ister of Health is launching another house-to-house visit. An a major campaign, termed "the Last Inch," is about to be launche in Peru, site of the last known polio case. Last week the gov ment of Peru announced a plan of action to visit and vaccinate t million households (two-thirds of the area) from February 29-Marc 8. This house-to-house immunization effort will be repeated in May. Children under 5 years of age will get another dose of V.

He said that the initial major concerns about the polio e dication effort--about political and social will, vaccine effi cy, and surveillance--have been removed. Some $112 million as been donated by a variety of external agencies, illustratin hat the political will exists to solve this problem. Finall Dr. de Quadros reiterated the general criteria for the certif ation of eradication: no confirmed cases in 3 years; no wild viru isolated from the environment or AFP cases; program evaluation. (Dr. de Quadros also urged Canada and the United States to star hinking about environmental sampling.) Coverage in the Americ is now

about 80% for all the EPI vaccines.

Neonatal Tetanus Surveillance

PAHO has also just established surveillance for neonatal tetanus. Of 14 districts, only about 10% are at high risk for neonatal tetanus.

Measles Reduction in the Americas

Next, Dr. de Quadros updated the Committee on the measles initiative in the English-speaking Caribbean. Vaccine was introduced into the region in 1982, and very high coverage was obtained within a very few years. Cuba led the way in attempting to eliminate the disease, by vaccinating all children 1-14 years of age. The 4-6 cases still being reported each year from that country are probably not really measles, Dr. de Quadros said.

Subsequently, the Ministers of the Caribbean countries adopted an initiative to eliminate measles by 1995, using the Cuban strategy. In May, 1991, termed Measles Elimination Month, all the islands except Jamaica immunized children 9 months to 15 years regardless of previous vaccination status. Coverage achieved was "incredible"--nearly 100%. In 1991, there were only three confirmed cases of measles in the Caribbean; all were imported from the United States. For 1992 so far, only one case has been reported, also in a traveler from abroad.

As a result, an initiative to eliminate measles from the Central American countries by 1997 has been announced. Brazil is also launching a major campaign for measles elimination, and will be immunizing all of its children from 1-14 years old (some million children). Chile and Argentina are also launching such projects. As a result of all of this interest in measles elimination, a meeting is being convened on February 28 to review what's happening in the region regarding measles and to see what PAHO could do to coordinate efforts.

Dr. De Quadros reported in his summation that a major concern is whether to include in the measles surveillance system all rash and fever illnesses or only those that meet the case definition, so that the system is not flooded with too much information. Another concern is whether paired sera should be used--which are extremely difficult to obtain in developing countries.

After Dr. de Quadros' talk, Dr. Halsey reported that at a meeting on February 11 at PAHO headquarters in Washington, D.C. it was reported that there are new technical developments in measles antibody assays that will allow the diagnosis of lab-confirmed measles with a single blood test. Dr. William Pellini's laboratory, which has been instrumental in developing this technology, has agreed to provide the training and the resources to

put this technology into the Caribbean and several ot r Latin American laboratories within the next couple of months. Careful evaluations will be performed to determine how reliable is test is. (Predictions are 90%, if the specimen is provided thin 15 days.)

Subsequent Committee discussion indicated that the best eans of mobilizing private physicians to the measles eliminatior campaign in the Caribbean are the media. The fact that no legal stacles exist in South America to mount such universal campaigns as also pointed out as a critical factor in their success. Co ern was raised about repeatedly immunizing with MMR. Dr. de Qua os said 1.8 million susceptibles have accumulated since the last mpaign. The campaigns would not need to be repeated if the Western Hemisphere would be vaccinated and a high level of overage maintained. Dr. Walter Orenstein, IM, said that measles ctivity in the United States is down 95% from reports at this me last year, and that CDC is only aware of one major current out eak, in Corpus Christi, Texas. He said that $46 million has been located during FY 1992 for infrastructure and service delivery. C is now eliciting comprehensive plans from immunization programs t oughout the country.

Japanese Encephalitis Vaccine

Dr. Ted F. Tsai, Division of VectorBorne Infectious iseases (DVBD), National Center for Infectious Disease (NCID), eviewed experience from adverse events surveillance in Okinaw Japan, begun after a mass immunization campaign against apanese encephalitis (JE). The campaign was launched after an ou reak of three cases of JE occurred in active-duty Marine per nnel on Okinawa last year. Although there were no deaths, t se were relatively severe cases: one patient remains in a semi-v getative state, and another has significant psychomotor retardati . After this outbreak, the U.S. Navy promulgated a mass imm ization campaign of 9,000 active-duty personnel (predominantly Ma nes) and 2,000 dependents.

Surveillance revealed 30 cases of urticaria and/or a gioedema following JE vaccine, and a case-control study of these allergic reactions was performed. About half of the reactions occurred after the first dose of the vaccine. There are differenc between first- and second-dose reactions: a) the interval between immunization and the onset of symptoms was 12-24 hours a first-dose reactors versus 4-6 days in second-dose reactors b) age differences c) possibly more first-dose reactions in non-Caucasians. A past history of drug or hymenoptera allerg or other urticarial reactions was associated with a threefold grea er risk. However, a past history of asthma, allergic rhinitis, atopic dermatitis without history of urticarial reactions c ried no increased risk. The rate of reactions appears to have be a higher among dependents, one-half of whom were children.

One death temporally associated with JE vaccine was rep ced in a 21-year-old man who previously had a history of unexpla ed rash, chronic diarrhea, and oral yeast infection. (Tests for IDS were negative.) Anaphylaxis was a possibility. He was four dead 60 hours after receipt of his first dose of JE. He had als received the third dose of plague vaccine the day he was found dea Autopsy did not determine any specific cause of death. Serum ryptase, which is sometimes markedly elevated with anaphylaxis, wa reported to be undetectable.

In response to questions from the Committee, Dr. Tsai aid that about 10% of sudden deaths in men of this age have no tectable etiology. Dr. Berg, from the Navy Environmental Healt Center, said that there are at least two cases of unexplained de hs every year in service personnel. Dr. Tsai also clarified that here may be no specific findings on autopsy for death by an nylaxis. Walter Reed is going to review the autopsy data, but it may take several months.

There was extended discussion about the adverse reac ons and interpretations of this death and the advice about JE v cination that should be given to travelers. Finally, Dr. Ka halted discussion saying the Committee was not ready to come to ny final decision on an ACIP statement on this vaccine--especiall since it isn't even licensed yet in this country. He asked Dr Tsai to point out other areas the Committee members needed to ow about for them to study for homework. Dr. Tsai said the other eas were primarily editorial changes. Dr. Katz asked that any no proposed on handouts be written up and mailed to Committee mem s. The deadline for returning comments was mid-March. Dr. ix from Connaught Laboratories offered to submit the produ insert submitted to the FDA; Dr. Katz said that would be xtremely helpful.

This discussion also brought out the suggestion that i ormation for travelers about the use of vaccines that are not li nsed for use in this country might be an appropriate *MMWR* articl

Hepatitis A

Dr. Harold Margolis, Division of Viral and Rickettsia Diseases (DVRD), NCID, reported that hepatitis A--with over 31 00 cases reported in 1990 in the United States--is a signific t public health problem. He introduced a series of speakers to d cuss the performance of vaccines in various stages of clinical tri . and the epidemiology of hepatitis A in the United States.

First to speak was Dr. David Nalin, Director of Clinical esearch, Merck Sharp & Dohme Research Laboratories, who presented sults of his company's experience with the Merck inactivated h atitis A vaccine. Phase-1 and -2 studies have been conducted a ng 1,265 adults and 774 children. In the Monroe, New York, p tective-

efficacy, randomized, double-blind study, 50 adults and 569 children were enrolled. In a total of 2,658 individuals v ccinated to date with this vaccine, Merck has had no seriou adverse reactions. The vaccine has been well tolerated, with onl expected mild, local and transient reactions. A two-dose regime yielded titers higher than those seen after immune serum globul (IG).

In the Monroe trial, seronegative participants received either a placebo or 25 ng of hepatitis A vaccine. There were 2 clinical cases of hepatitis A, most occurring in persons rece ing the placebo. Of those occurring in persons who received he atitis A vaccine, none occurred 2 weeks after receipt of vaccine. Merck is planning flexibility of schedules for the booster do s to be compatible with other vaccines and existing regimens.

Dr. David Krause, Director, Medical & Scientific ervices, SmithKline Beecham Pharmaceuticals, next presented dat on that company's candidate HM175-strain hepatitis A vaccine. I antigen content in an adult dose is 720 Elisa units, wh n gives seroconversion rates of 100% after one dose. First hu n trials were begun in 1988. To date, there have been 67 stud s in 18 countries, involving 50,000 subjects. In terms o overall reactogenicity, about one-half of vaccinees report nc symptoms after the first dose. The most common general symptom malaise or fatigue. Soreness at the injection site is the mc common local symptom. Reactogenicity rates compare favorably v ch those for hepatitis B vaccine. Clinical trials on several thous d adults reveal that the seroconversion rate is 96% one month fter the first dose and 100% after a second dose. There are vi ually no nonresponders. The evidence that this vaccine is prot ctive is very strong: a) antibody quality, b) the antibody tite produced by two doses is approximately 5-10 times higher than tha produced by IG, c) animal studies at the NIH, revealed that ccinated chimps were totally protected, and d) field trials, whi are now under way. Several questions remain to be answered a out this vaccine: a) the long-term duration of immunity provid ; b) the effect of simultaneous administration with other ediatric vaccines; and c) and the efficacy in a postexposure setting. Studies are planned or ongoing to answer all of these q stions.

Dr. Charles Hoke, Walter Reed Army Institute of Research, xplained that since World War II soldiers have been the heaviest onsumers of IG to protect them against hepatitis A. In fact, peration Desert Storm exhausted all IG supplies in the United Stat . Thus, there's a lot of interest in the hepatitis A vacci in the military. Dr. Hoke reported results of a field efficac trial in Thailand of an inactivated hepatitis A vaccine among Thai hildren, conducted by Dr. Bruce Innis, with the Armed Force Research Institute for Medical Sciences. The SmithKline HM-1 -derived strain was used in this study; it was administered at 0 1 month, and 12 months, but efficacy data are based on just t o doses. Approximately 20,000 5- to 14-year-old children receive vaccine;

20,000, placebos. The case definition used was an illness compatible with viral hepatitis severe enough to cause ab nteeism from school and elevated antibody. Among 5,000 illnesses at were evaluated, 30 cases of hepatitis A occurred. Of these, 29 ccurred in children who had received placebo (145/100,000) and 1 ccurred in a child who had received the vaccine (5/100,000; effica ', 97%). In the ensuing discussion period, Dr. Hoke said that with an earlier vaccine made at Walter Reed and first given to ople in 1986, people were successfully vaccinated with four dc es or a total of 8 ng of antigen. That amount is extremely immu genic--that's less than 1/5,000 of the antigen in the hepatitis B accine.

Next, Dr. Craig Shapiro, DVRD, NCID, summarized the epidem ology of hepatitis A in this country. With two apparent safe, immunogenic, and efficacious vaccines available--one already commercially available in Europe--the United States may soon be faced with making decisions on how to use hepatitis A v cine in this country. Ideally, these decisions should be base on the epidemiology of hepatitis A in this country, said. Historically, there are periodic, nationwide epidemics of patitis A. There are significant geographic variations in the isease, with the West having the highest rates, and the South and st, the lowest. Asymptomatic infection predominates in inf its and children, but greater symptomatic disease and higher case atality rates occur in older adults. Racial/ethnicity data indi te that the group with the lowest rates of disease are Asians, fc owed by whites, blacks, and finally, American Indians, who hav a rate about 10-fold higher than average. The most commonly repc ed risk factor for hepatitis A is contact--household or sexua -with a patient with hepatitis A. Other risk factors are drug se, day care (either among children or employees--this category ccounts for about 10% of cases), international travel, and being e posed as part of a water or foodborne outbreak. For about 40% of eported cases, no risk factor is identifiable. About 38% of th general population in the United States are seropositive for anti odies to the virus, based on testing of sera from the National H lth and Nutrition Examination Survey II.

To translate these epidemiologic data into strategies fc vaccine use, public health officials and policy-makers need to de ide what they want to accomplish with this vaccine, such as prot tion of specific groups as opposed to general vaccination. For example, some of the more accessible risk groups, such as inte national travelers, don't really account for a large percentage of epatitis A cases. Also, do we want to think in terms of er dicating hepatitis A infection, since the virus only has a single erotype, and there's no significant animal reservoir? Finally several issues are still unresolved: long-term protection; ef cacy in postexposure mode; combined vaccines; cost-efficacy (ta; and feasibility of delivery.

In the ensuing discussion, Dr. Shapiro was asked about economic

impact data. He said this area was being studied. In a lts, of whom 12% are hospitalized, the impact can be significant n terms of direct and indirect costs. Committee members emphas ed that the percentage of hepatitis A cases linked to day car may be greater than is reflected by surveillance data, that pa nts may get the disease from asymptomatic day-care children, and hat the link to the day care may not be recognized.

It was also learned during the discussion that the Merck patitis A vaccine will be submitted for licensure in Europe withi a year. The Product License Application should be filed within th next 12 months. Dr. Hoke said SmithKline also expects to file in ıe third quarter of this year.

Immunization of the Immunocompromised

Drs. Mark Grabowsky and Robert Chen, IM, NCPS, presente a draft ACIP statement on the use of vaccines and immune glo lins in persons with altered immunocompetence for discussio by the Committee. The principal changes in this ver on are reorganization of sections and some minor changes in cont ıt. For example:

--the introduction was so written that a practicing inician can read it and then refer directly to the acc ıpanying tables.
--Immunocompromised persons have been divided i ɔ three groups in this draft: severely immunocompromised, ı due to HIV infection; persons with HIV infection; and per ons with conditions which cause limited immune deficit (e.g., asplenia, renal failure) that may require use o special vaccines but which do not contraindicate use of any p ticular vaccine.
--Section III now includes a discussion and table c the use of immune globulins, as requested by the Committee.

Dr. Katz then asked if there were any questions or comme s on the new draft. The following suggestions were made:

--relook at page 3, which appears to be ternally inconsistent.
--The section on page 6 on BCG may need refinem t. Dr. Grabowsky said they were waiting to do that unti the BCG Working Group met.
--on page 9, first paragraph, 2nd sentence, change ounseled accordingly" to "that they are not protected against epatitis B"; in next paragraph, last sentence, reconsider phrasing since it may imply persons should be tested for *N. meningitidis* and such testing is not available.
--in the definition section, further clarify what 'use, if indicated" means on tables.
--on Table 2, leave out column "Routi (Not

Immunocompromised)." This was agreed upon by vo of the committee.
--clarify whether you're talking about previously no mmunized persons or not (Dr. Nalin's point)
--make sure the terms introduced on page 1 are co istently adhered to (for example, it isn't readily clear to t reader, on page 5, in the OPV section, which categories the subjects who are "immunodeficient" and "immunosuppressed" fa l into.
--distinguish further between adults and children.
--add a column on solid organ transplant recipients (who are about to become immunocompromised) to Table 2 and p haps add to definitions on page 1.
--on page 5, under MMR, clarify whether a .5 mL- .25-mL dose of IG is to be administered to symptomatic HIV atients; also, change the last sentence to "There is clearly ecreased immunogenicity if vaccination is given less than th e months after IG administration."
--on page 10, review role of tetanus antitoxin, w ch is a horse serum product, and the implication that e "same dosages and schedules" are needed for immunocompro ised and immunocompetent persons. The last point enerated considerable discussion. Dr. Grabowsky pointed out hat this section was from an existing ACIP statement and tha CDC had avoided making new recommendations in this c pilation statement.
--The statement should at least give recognition at some other prestigious groups (PAHO, WHO) may disagree th CDC's statements for use of some vaccines (e.g., OPV) and y employ other strategies for other countries. This sugge ion was generally agreed upon by Committee members.

May is targeted for the final draft of this ACIP stateme . There was discussion about whether it should be held up til the Committee has heard from Dr. Donnenberg about bo marrow transplantation (after which a new set of ACIP recom ndations would be published regarding that subject). The consen s of the group was to mention in this ACIP statement that a b e marrow special issue is forthcoming. There was agreement tha the bone marrow transplant statement would be reviewed at the ne meeting and published separately.

Meningococcal Disease in Canada

Dr. Susan Tamblyn from the Canadian surveillance program iscussed meningococcal disease in Canada. In recent years the umber of cases of this disease has increased, though rates hav remained low. However, the proportion attributed to Group C has ncreased dramatically: from 26% of cases in 1983 to 63% of i lates by 1990. A unique Group C clone, ET 15, is being isolate from an increasing proportion of cases--three-quarters in 1991. is clone caused several outbreaks in Ontario in 1989 in s ool-aged children, and it appears to be the clone that is mainly r ponsible

for the clusters of disease that were seen in 1991.

In a 2-day period in early December, Ottawa had four case occur in teenagers; two died. Within a week, a teenager at a nea y school died of group C disease. Chemoprophylaxis was ex nded to everybody at the two affected schools, followed school vaccination. Tremendous media coverage attended thes events, which in turn created demand for vaccine in aff ted and nonaffected areas. Then in early January, two more ses, one fatal, occurred in Ottawa. This prompted the decisic to hold mass, publicly funded vaccinations in Ottawa and in a umber of affected regions in Quebec. This campaign was coord ated by provincial epidemiologists and local authorities, with co ultation provided by the LCDC, the Canadian equivalent of CDC. Ottawa, Quebec, Prince Edward Island, and British Columbia ld such vaccinations for varying age-groups.

There was not enough vaccine available; Connaught quick brought in more from Swiftwater. The Canadian Bureau of Biolog s sought additional sources in Europe through SmithKline and Merieux. Program delivery went very smoothly. Vaccine uptakes ere very high--over 90% in Prince Edward Island, for example. Very few adverse reactions have been reported. The Ontario Mi stry of Health's passive surveillance system received 200-250 r orts for the 140,000 doses administered (<.2%). These were mo ly local reactions.

Dr. Jay Wenger, Division of Bacterial Diseases (DB , NCID, discussed the epidemiology of meningococcal disease in nada and the United States. He said it appeared that during e recent outbreaks in Canada, particularly in children 10-19 ars, the rates of disease were in the range of 15-20/100,000, which is twenty times normal. Given these data, and the port of meningococcal disease in a traveler to Ottawa, CDC issued limited travelers' advisory on January 17 that suggested that chi ldren 2-19 who were going to be in Canada for 3 days or longer shoul consider immunization. Although there was some concern abou vaccine supply, since a large amount of vaccine had been shipped Canada, Connaught and the FDA helped solve this problem. Dr. We er added that the clone causing disease in Canada has been identif d in the United States. Several studies to evaluate risk of men gococcal disease are under way among children and college-age st ents.

Reevaluation of Polio Vaccine Policy

For 2-plus hours, speakers presented new informati to be considered in a re-evaluation of the ACIP polio vaccinati policy.

Points for Committee Consideration

Dr. Steve Cochi, IM, said that in 1988 the Institute o Medicine (IOM) conducted a review of polio vaccination policy in e United

States. The IOM Committee had examined four option 1) to continue primary reliance on OPV (the present policy); 2)) change to primary reliance on IPV; 3) to change to a mixed sc dule of IPV, followed by OPV; and 4) to state no preference. The IOM Committee endorsed option #1, but voted to reconsider afte IPV was combined with DTP in a licensed product. The ACIP sub quently endorsed these conclusions. In addition, the IOM propose several research questions in 1988: 1) Is wild virus circulati in the country? 2) What are the levels of immunity in adults? 3) What are the levels of immunity in preschool children, especia y those in inner cities? 4) To what extent in the United States t lay does OPV vaccine virus spread to contacts of recipients? and 5) What mixtures in schedules of IPV and OPV would yield the maximum benefit?

Question #1: Is wild poliovirus circulating in the Unite States? Dr. Cochi said that epidemiological evidence from st dies of imported cases (recent immigrants or travelers) indicates iat only two cases occurred from 1985-1991, with the most recent ich case occurring in 1986. Particularly with the polio control fort in the Americas, imported cases are less and less of a thre to the United States.

Question #2: What are the levels of immunity to poli irus in adults?

Dr. Cochi said that there have been two studies of im nity in young adults. One, of Army recruits, was published in MA last fall. It showed that 97.5% were seropositive for type 99.3%, for type 2; and 87.3%, for type 3. The second stu was a Massachusetts serosurvey, performed in 1982 in sixth-, te h-, and twelfth-grade students. At a screening titer of 2, the seroprevalence to types 1 and 2 was 100%, and 99.9%, to pe 3.

Question #3: What are the levels of immunity to poli irus in preschool children, especially those in inner citi ? Two presentations addressed this question. Dr. Vance Dietz, M, CDC, summarized OPV coverage data from nine retrospective imr ization coverage surveys of school children in nine cities in 19 . These provided information on the immunization status of appi ximately 800 current kindergartners and first-graders when the were 12 months and 24 months of age. Coverage levels at 12 mont s of age were <90% in all nine cities for OPV2 and OPV3. At 24 nths of age, coverage levels for OPV3 were <90% in all nine cit s. With the exception of Cleveland and St. Louis, levels for OPV are also <90%. Even for children 5 years of age, only two cities-- leveland and El Paso--had OPV3 coverage rates of 90% or above.

Next, Dr. Chen presented polio seroprevalence data from t studies of inner-city preschoolers in Detroit and Houston. The f st study showed that among both vaccinated and unvaccinated chi iren the data for both sites were very similar, revealing modera ely high

seroprevalence that is generally higher for poliovirus t… e 2 than type 1, which in turn is greater than for type 3. The se… nd study involved small numbers of nonimmunized children who were …ound to have very low seroprevalence rates (usually <50%). T… s study again showed that type 2 seroprevalence was dominant, pr… ably due to contact spread from OPV vaccine. However, the stud… suggests that contact spread from OPV alone does not result in …ry high titers in this inner-city population.

Question #5: What mixtures of IPV and OPV would yield t… maximum benefit? Four studies have been published on this sub… t since the 1988 review.[1-4] Dr. Roland Sutter summarized the majo… findings of these studies.

Study #1 (McBean et al.[1]): A total of 1,111 children …ges 8-13 weeks in Baltimore City and County, and Prince Georg… County, Maryland, were randomly assigned to three vaccinati… groups between November 1980 and July 1983. Group A received t… e doses of eIPV produced by Institute Merieux; Group B rec… ved the standard OPV produced by Lederle; and Group C rece… ed eIPV produced by Connaught. Vaccines were administered at 2, …, and 18 months of age, and blood was collected at 2, 4, 6, 1… and 20 months of age and tested at the FDA for neutralizing a…tibodies against the three poliovirus serotypes. After two dose… of eIPV, virtually 100% of children had detectable antibodies to …l three poliovirus serotypes, a rate 7%-8% higher than after tw… doses of OPV. A third dose of eIPV after a 14-month interval rais… GMTs to all three serotypes to significantly higher levels than …ter OPV. The most important finding of this study was that at …ast two doses of eIPV are probably needed before OPV to protec… against recipient vaccine-associated paralytic polio.

Study #2 (Onorato, et al.)[2]: This study examined t… mucosal immunity induced by three doses of either eIPV or OPV. … total of 143 eIPV and 117 OPV recipients were enrolled; these … included children from the previous study and from well-child c…inics in Baltimore and Prince George's County. The most …mportant confirmatory finding of this study was that OPV-immunize… children had better intestinal, but similar pharyngeal immunity … compared with eIPV-immunized children. However, intestinal immun… y is not an all-or-nothing phenomenon. Onorato et al. showed …lso that resistance to excretion is dependent on challenge virus …sage for both the OPV and eIPV groups. Intestinal immunity indu… d by OPV can also be overcome by a sufficient dose of challenge …rus. In addition, excretion of poliovirus was highly correlat… with a serologic response. However, the excretion rates in t… pharynx were similar in the OPV and eIPV groups, suggesting that …aryngeal immunity was similar in the groups.

Study #3 (Modlin et al.)[3]: This study examined t… humoral immune response to a challenge dose of monovalent ty… 1 OPV.

Children ages 19 to 52 months from a public and a priva e health clinic in Maryland, as well as from study #1, were enro ed; they had a history of either three doses of eIPV or three dos s of OPV administered at 2, 4, and 18 months and a challenge dose of monovalent P1 OPV between 19 and 52 months of age. he most important finding of this study was that OPV given af r three doses of eIPV resulted in a more augmented humoral response compared to OPV given after three doses of OPV.

Study #4 (Faden et al.)[4]: This study was the first t directly compare two different sequential schedules of eIPV follo d by OPV with schedules using eIPV or OPV alone. Small numbers o children (16-53 in each group) were assigned to four groups: OP PV-OPV; IPV-IPV-IPV; IPV-OPV-OPV; or IPV-IPV-OPV. All schedules resulted in high seroprevalence rates after two doses of either (V, eIPV, or EIPV followed by OPV. The GMTs were highest in the e PV-eIPV-OPV group, particularly poliovirus type 2. The mucosal immunity was highest in the group that received only OPV, and low t in the group that received eIPV only. However, the excretion ates of poliovirus 1 month after receipt of the third dose of vac ne at 13 months of age were not significantly different in the st y group. The most important finding of this study was that incorp ation of at least one dose of eIPV at the start of the im nization schedules tends to increase systemic as well as local antibody production.

Ogra Study: Dr. Pearay Ogra, senior author of e Faden study, next summarized another recently published stud of his.[5] His data and observations from previous studies suggest at "wild (virulent) virus or development of reversion during repl ation of OPV in the gut may provide a more potent stimulus for in ction of mucosal immune response than attenuated parent strai of the vaccine viruses."[5] In addition, preceding receipt of eIP may lead to increased excretion of revertants.

Denmark Data: Following Dr. Ogra's presentation, Dr. Katz said the ACIP was examining this subject in an attempt to educe 6-10 vaccine-associated cases of polio each year. Pointin out that Denmark has had a combined schedule since 1968 (three dos of IPV, followed by three doses of OPV), he asked Dr. Sutter to mment on that country's vaccine-associated cases. Dr. Sutter aid that since 1968 there have been only two cases of vaccine- sociated polio in contacts, not recipients. Thus, the risk of vaccine-associated illness in Denmark is roughly one-half of t in the United States.

Halsey Study of Sequential eIPV-OPV Schedules: Dr. chi then introduced Dr. Halsey to present information from an addi onal, in progress study that looks at three different sequentia eIPV-OPV schedules and compares them with the standard OPV sch dule and standard IPV schedules alone. Neutralizing antibody sponses,

development of nasopharyngeal antibodies at 15 months o age, and response to challenge with OPV at 18 months of age are un r study. Boosts in antibody are being seen in all groups; the lar st boost upon challenge with OPV at 18 months occurred primari in the children who had received only one previous dose of V or no previous OPV at that time. Dr. Halsey said more data hould be available from this study in 1-1/2 years.

Question #4: To what extent in the United States toda has OPV vaccine virus spread to contacts of recipients? Next, r. Peter Strebel, NCPS, reported on the recent epidemiology of pol myelitis in the United Sates. He said poliomyelitis caused by ld virus has been virtually nonexistent since 1980; vaccine-associ ed cases are now the predominant form of this disease in this country. Since the introduction of OPV in 1961, the incidence o vaccine-associated paralytic polio has remained stable, at appro mately 1 dose per 2.5 million doses. Since 1980, 80 vaccine-associ ed cases were reported (8 per year), no indigenous cases, and imported cases. Of the vaccine-associated, 30 were OPV recipient 32 were contacts, 4 were classified as community-acquired, and 1 occurred in immunologically abnormal persons. In terms of v cination history, 87% of recipient cases occurred after receipt of he first dose of OPV. Of contact cases, 66% were unvaccinated. e groups at elevated risk of vaccine-associated illness are infa s; adult contacts who are inadequately vaccinated; and immun ogically abnormal individuals, predominantly children wit immune deficiencies of the humoral system.

Dr. Strebel also discussed the potential impact of a quential eIPV-OPV schedule on the occurrence of vaccine-associa d polio.. He said that the rationale for use of eIPV varies accordi g to case category. The high immunogenicity of eIPV should prote against recipient vaccine-associated polio. Moreover, eIPV dec ases the duration and intensity of polio virus shedding after chal enge with OPV, and hence should reduce the transmissibility of vac ne virus to contacts. For immunologically abnormal infants, some otection against vaccine-associated disease should result from delay in the scheduled administration of the first dose of OPV to 5 months. This delay would increase the likelihood of letecting immunodeficiency problems, which are a contraindication OPV use. In short, if a schedule of two doses of eIPV followed OPV for the third and fourth doses were instituted, and all the ecipient vaccine-associated cases (related to the administrati n of the first and second dose of OPV), but only half of the cor ct cases and half of the immunologically abnormal cases were pr ented by such a strategy, the reduction in vaccine-associated ill ess would be approximately 70%.

Potential New Polio Vaccines

Next, Dr. Cochi said that any discussion of polio v cination policy must include prospects for new polio vaccines that are

safer, less prone to reversion, and more immunogenic.

Meetings: In the last 1-1/2 years, two meet gs have addressed new oral polio vaccines. One was a WHO meeti g on new polio vaccines held in Geneva on March 12-13, 1990. The ther, an FDA-sponsored international workshop on poliovirus attenu ion held December 9-10, 1991, in Bethesda.

Dr. Olen Kew, DVRD, NCID, then summarized these meetings. Although enhanced immunogenicity is on everybody's "wish list," ıe noted that the problem may well be that humans just do not re: ɔnd well to type 3 antigen. Greater genetic stability and improved thermostability are also desired. The following are ıggested questions for further research: 1) What is a mec nism of attenuation at the cellular level (neural cells vs. testinal cells?) 2) What are the physiologic blocks in neural lls? 3) How does the mouse model, which does have a lot of a antages, compare with the monkey neurovirulence test and human testinal infection? 4) If such vaccine strains were available, ɔw would seed stocks be prepared? How would they be manufactured 5) What would be the possible clinical trials of new OPV strain:

Many of these issues were discussed at the USFDA wc shop in Bethesda. Conclusions were: 1) attenuation involve a small number of substitution mutations; 2) the poliovirus nome is exceptionally plastic; and 3) attenuation involves di erential growth in intestinal but not neural cells. Also discusse were new approaches for OPV safety testing, such as Chumakov's olecular tests, cellular assays, and transgenic mice. Dr. Kew said the bottom-line conclusions from both meetings were that xcellent progress has been made, but more needs to be done, and t t no one is going to depart radically from the Sabin strain. In r ponse to a question, Dr. Kew said that he's not aware that anyone nows how to enhance immunogenicity by genetic engineering, he most challenging of the desired properties on the wish list.

Manufacturers' Product Updates: Dr. Cochi then intr luced the last piece of the puzzle in the polio vaccine upda --status reports from the manufacturers of combined DTP/eIPV vacc ıes. Dr. Carleton Meschievitz from Connaught/Pasteur demonstrate a dual-chamber syringe design so that thimerosal, a preservati in DTP, does not interfere with the polio virus. Connaught's stu design, built around 414 subjects: 207 of whom were randomized receive the DPT/eIPV combination at 2 and 4 months of age; 207 of hom were randomized to receive DTP and eIPV at two separate sites At 15 to 20 months of age, each of the groups will be randomized receive either eIPV or OPV. The entry phrase is to be comp ted this month. Submission of data to the FDA is planned for Oct ɔer. Dr. Meschievitz also summarized the Danish history with thi schedule (already discussed, in which only two cases of vaccine- sociated polio have been reported since 1968) and Prince Edward Is ınd's 25-year experience with IPV/OPV. (With 50,000 children vacc ıated, no

cases of polio have been reported.)

Next, Dr. Peter Paradiso, Lederle/Praxis, updated that ompany's priorities, particularly the combination products. In he past several years, it has focused on currently recommended oducts, acellular DTP, *Hemophilus influenzae* b conjugate (HbOC), id eIPV. Such a combined product is several years away. Lederl is also looking at inactivation of the Sabin strains--i.e., maki a Salk vaccine from Sabin strains. Lederle's liquid form of a TP/HbOC combination vaccine, Tetramune™, has been fairly ex ensively studied as part of a three-dose, primary series (nea y 7,000 infants have received this vaccine); a license applicatio as been submitted to FDA. The safety profile is excellent, and the immunogenicity is as good or better in the combined proc t.

Lederle has also combined its acellular pertussis vaccin with its HbOC combination vaccine for boosters at 15 months. Fo mulation studies are complete; immunogenicity and safety studies ve been initiated. Lederle hopes to file for license by year nd. Dr. Paradiso also said that Lederle is working to reduce vaccine-associated cases with studies of Pfizer strain sequences

Further Points for Committee Discussion

Dr. Cochi then re-addressed the Committee, asking them t consider the following points for discussion: 1) Have the esearch questions raised by the Institute of Medicine been a equately addressed? 2) Are there issues other than those rais l by the Institute that still need to be addressed? 3) If D -IPV is licensed, is the ACIP prepared to consider a change to a s quential IPV/OPV schedule?

Dr. Katz thanked Dr. Cochi and the presenters for prep cing the information on this subject for the Committee. Then Dr. tz asked the Committee to assimilate all the information they rec ved this afternoon, in the context of 1) the policy question-- ould we consider the reintroduction of IPV to precede OPV? 2) m tivalent vaccines, which might combine <u>H. flu</u> b conjugate, hepatit B, DTP, eIPV; and 3) whether the expense, time and change in po cy would be anachronistic in light of the move to eradicate pol myelitis within 8 years?

A Committee member asked if there were any studies looki at wild virus in sewage. Dr. Kew responded that there is no env onmental sampling going on in the United States, but that if you now what to look for, we now have the techniques to detect wild rus at 1 part per million.

<u>ACIP Statements</u>

Next, Dr. Richard Goodman, Editor of the *MMWR*, disc sed the

purpose, audiences, length, and format of ACIP stateme s. His primary concern was whether they are becoming too long ar complex to be usable and readable. Supplements were introduced .n 1965; originally approximately two per year were published; by)89, 25% of space in the weekly issue was being taken up by ACIP s ıtements and other recommendations, so these became supplementary, ıder the name "Recommendations and Reports." The primary audienc for the MMWR series (circ. 51,500) are public health practiti ers and health-care professionals.

He illustrated the growing length of ACIP statements by sl ving the average page length of measles, hepatitis and mumps stat ıents in 1972 and 1989:

Statement	1972	1989
measles	3 pages	17 pages
hepatitis	4 pages	26 pages
mumps	2 pages	9 pages

Acknowledging the valid reasons for the increasingly echnical nature of the report (e.g., more immunizing agents, ıcreased knowledge about risks and adverse effects, more cc)licated schedules, change in audience), Dr. Goodman asked the Cor ittee to consider the impact such length was having on usability. He said that some of the ACIP statements could now be des ibed as monographs.

Dr. Goodman asked whether longer statements should be ac)mpanied by a brief set of recommendations and a table to illustı :e them. He urged the Committee to consider if the statements are the appropriate format to reach the intended audience.

In response to a question, Dr. Goodman said that CDC has ı dertaken a comprehensive evaluation of the entire MMWR series, ir luding a readership survey designed to characterize the audience d how it uses the publication. The evaluation is slated to be cor leted in about 18 months.

In an ensuing discussion, several people commented t t State immunization divisions resoundingly make clear that they ıeed the technical statements. This is true despite the fact th : 95% of their questions are not that complicated; the etailed, "encyclopedia" knowledge is needed for perhaps only 1%-5% f cases, but when it's needed, it's really needed. Several pec .e urged that the *MMWR* readership survey be sure to inclı e State immunization divisions.

Dr. Georges Peter, liaison with the American Academy of] diatrics (AAP), was asked if the Red Book, which has also been ç)wing in length, has faced this question. He acknowledged that i' ıas been a concern, but one readily addressed because the reasor for the increased length are so apparent. He said occasionally a review

will say the Red Book is too long, but he has never hac ı reader say this.

One Committee member said that one state health c)artment synopsizes the statements for the public health nurses because there's a real need for a concise statements for this g)up, who work with most cases. It was also suggested that a conc se table be published in the *MMWR* coincident with a separate, deta led ACIP statement.

The meeting was adjourned for the day at 5:40 p.m. It ı :onvened on February 13 at 8:05 a.m.

Influenza Vaccine

The Committee heard seven presentations on influenza vac(ne. Dr. Nancy Cox, the new Chief of CDC's Influenza Branch, old the Committee that Nancy Arden had rejoined the Influenza P)gram as Chief of the Epidemiology Section.

Strain Selection Information

Dr. Cox informed the Committee that the WHO strain :lection meeting was not scheduled until the next week so she ould be presenting only partial information on the strains select for the 1992-93 influenza vaccine. The FDA Vaccine Advisory Comr :tee met at the end of January. Based on data from a va iety of laboratories present at that meeting, it was decided hat the current influenza A(H3N2) component (A/Beijing/353/89 vi s) would remain in next year's vaccine. For the first time since .986-87, an influenza A(H1N1) variant that's different from A/Tai an/01/86 has been identified. Thus far, about one-third of virus isolates are antigenically similar to this new variant, A/Tex s/36/91. Influenza B activity has been minimal in the West t s year; however, major outbreaks have occurred in schools in Chi , Japan, and Korea. Virus isolates characterized thus far have be related to B/Panama/45/90, the current influenza B vaccine compc ent.

Surveillance in the Current Influenza Season

Dr. Louisa Chapman, DVRD, NCID, said that the 1991-92 nfluenza season has been characterized by abrupt onset, the dom ance of influenza A(H3N2) among circulating subtypes, and v lespread reports of dramatic outbreaks among school children, beg ning in October, superseded by reports of outbreaks among adult pc ılations beginning in mid-November. Excess mortality was first e .dent in late December. Over 99% of the 5,181 viruses reported b the WHO Collaborating and HCFA Surveillance Laboratories combine between October 1, 1991, and Feb. 1, 1992, have been influenza Of the 2,739 influenza A isolates subtyped, 83% have been H3N2.

Nursing Home Outbreaks

Dr. Joseph Kent, DVRD, NCID, presented information f m three nursing home outbreaks (in New York, Ohio, and Co ecticut) investigated by public health officials. Dr. Kent emph ized the early appearances of these outbreaks. The New York i luenza A (H3N2) outbreak occurred from December 9, 1991, to Ja ıary 10, 1992, among 337 nursing home residents. Fifty-two of 5 (18%) vaccinated residents met the case definition for illne , as did 13/42 (31%) unvaccinated residents. The calculated bes estimate for VE was 43% for preventing clinical illness an 45% for preventing pneumonia.

The Connecticut nursing home outbreak was also caused l A(H3N2) and occurred between December 7-January 5. Ninete of 60 vaccinated residents and 15/34 unvaccinated ones met he case definition. The VE for preventing clinical illness was 8%.

The Ohio outbreak, from November 10-December 2, was ıe first influenza outbreak in an adult population reported to C for the season. The outbreak was also due to influenza A(H3N and was characterized by the CDC laboratories as A/Beijing. For -five of 335 residents met the case definition, for an attack rate f 13.4%. Ninety-three percent of residents were vaccinated Nove er 13-15 during a vaccination campaign--too late to prevent the utbreak. The staff, on the other hand, had been vaccinated earli , during the first week of November. Based on a nonrandom sample f 24% of the 660 employees, 58% reported having been vaccinated Illness that met a case definition occurred in 6/89 vaccinated taff and 14/67 unvaccinated staff, giving an estimated VE for eventing illness among healthy adults of 68%. Although this nu ing home had complied with ACIP recommendations and had a very hi rate of immunizations, this outbreak began prior to their im nization program.

Dr. Kent then presented data indicating that in three o the last four seasons when influenza A(H3N2) predominated, the p umonia & influenza mortality curve has exceeded the epidemic th shold in late December or early January, reflecting significant i luenza A activity among the elderly by early to mid December.

Vaccine Supply and Distribution

Dr. Raymond Strikas, NCPS, then presented a brief dis ssion of CDC's findings about influenza vaccine supply and distrib ion over the past 6 years, and a more detailed discussed of th subject during the last influenza season, prompted by widesp ad media reports of flu vaccine shortages in the 1991-92 season.

Overall, influenza vaccine distribution to U.S. civ ians is accomplished by private enterprise. From 1985-1989, Federal, State, and local government vaccine distribution accounte for less than 15% of the doses distributed. This is markedly diff ent from other vaccines: 40% to 55% of polio, DTP, and MMR va ines are

purchased with public funds.

This year, very early onset of flu-related illness amo school children, school closings in some states, and warnings of creased influenza activity all served to increase demand for the accine. Manufacturers had produced 32 million doses of the vaccine n 1991, a 12.7% increase over the amount produced from 1990, a d a 33% increase over the amount used in 1990. (Manufacturers say hat 25% of doses are returned after most influenza seasons; DC data indicate returns range from 8.4% to 15%.)

A CDC survey of 55 grant immunization programs throu out the country was undertaken to determine the extent of vaccine ortages during the 1990-91 season. Of these programs, 25 had rchased vaccines with State funds this past year. At the tin of the survey, December 14, seventeen programs needed vaccine, r a net need of about 136,000 doses. Eight programs had a surplu Of the 30 States that did not purchase vaccine, 9 had some s rtages. Wyeth-Ayerst laboratories bottled an additional 650,000 oses of influenza vaccine that were available in December. All f these doses of vaccine have now been sold.

CDC plans to continue to work with vaccine manufacturers) assess possible problems in distribution, perhaps through u of an electronic bulletin board.

Revision of ACIP Influenza Vaccine Recommendations

Dr. Louisa Chapman returned to lead the Committee through ggested changes to the ACIP flu statement. Most were relative minor, involving insertion of clarifying words or phrases, all hi lighted on a handout. One of these--involving insertion of the h d-faced phrase into the following sentence, caused considerable di ussion:

> Persons who provide essential community services and students or other persons in institutional settings (e.g., schools, colleges **and child care facilities**) may be consi red for vaccination to minimize disruption of routine a ivities during outbreaks.

Dr. Halsey proposed that the Committee accept Dr. Carol Hall's recommendation to make a clear statement about the taff of institutions, since Committee members all agreed the are an appropriate group to be vaccinated to minimize disruptio of major services. (It was emphasized that this, together with imm ization of the elderly and others at high risk of influenza, was he goal of the influenza control program.) Dr. Chapman was asked rewrite this phrase.

Dr. Chapman then introduced for discussion a proposed su stantive wording change to the document regarding vaccinating pe ons with known hypersensitivity to eggs or other components of the influenza

Since an estimated 18 million people in the United ates use contact lenses, a not insignificant number may consider emselves allergic to thimerosal, and therefore ineligible for v cination with a vaccine containing it. In one study, 10/46 hospital employees who were potential recipients of hepatiti vaccine reported ocular sensitivity to thimerosal-containi ocular solutions; the sensitivity resolved after they swit ed to a solution not containing this compound. All nine f those individuals who consented to vaccination were su essfully vaccinated.

A literature review suggests that hypersensitivity re tions to vaccines containing thimerosal are rare. Dr. Khan co d locate only four reports of patients who had systemic reacti s to it. There have been approximately a dozen case reports and tters to the editor describing individual patients who have been r orted to have had hypersensitivity reactions to the thimerosal co onent of hepatitis B vaccine, and similar reports of local reacti s to DTP and dT. No reported local reactions to influenza vaccin ion have been attributed to thimerosal hypersensitivity. The pre lence of cell-mediated contact dermatitis due to thimerosal varies rom 1.3% to 16.3% in select populations. Only a small percentag of those individuals who demonstrate skin sensitivity to thimero l have a history of clinically significant reactions.

In summary, Dr. Khan said that it was apparent that a) e osure to vaccines containing thimerosal can lead to indu tion of hypersensitivity; b) most patients who have positive p ch tests or intradermal tests to thimerosal do not develop hypers sitivity reactions to thimerosal administered as a component of v cine; c) although vaccination will be safe for the vast majority f people with ocular or skin-test sensitivity, rarely thimerosal an cause severe, but treatable hypersensitivity reactions.

Dr. Chapman then led a discussion about changes to th ACIP flu statement pertinent to Dr. Khan's report. The proposed a lition on thimerosal was added, with minor changes. Based on ommittee discussion and FDA comments, it reads as follows:

> The potential exists for hypersensitivity reactic s to any vaccine component. Although exposure to vaccines ntaining thimerosal can lead to induction of hypersensiti ty, most patients do not develop reactions to thimerosal ad nistered as a component of vaccines, even when patch or i radermal tests for thimerosal indicate hypersensitivity. W n it has been reported, hypersensitivity to thimerosal ha usually consisted of local delayed type hypersensitivity r ctions.

Dr. Khan's references were handed out; the Committee wa asked to review them soon and let Dr. Chapman know if they disa ee about their inclusion in the document.

Both CDC suggestions about egg hypersensitivity concer ed adding phrases about consulting "a physician, preferably clinical allergist or immunologist." In each instance, the Committee decided to recommend only consultation with a physician Mention of undergoing appropriate skin testing was debated exten vely. Dr. Nalin suggested that the document mention that if a p rson with sensitivity is to receive vaccine, the physician shou l have on hand the wherewithal to treat shock. (This is the curre standard of medical care in the community regarding *all* vaccines, nd is not unique to influenza vaccine.) Dr. Chapman was aske to pull together proposed alternative wordings and to circulate them next week among the Committee, so comments can be returned pidly for May publication of the document. Dr. Peters also ged that amantadine be mentioned as an alternative to vaccine persons with a history of hypersensitivity to the vacci or its components.

Dr. Nalin said package inserts have changed regardi adverse reactions and reassurance should be given. Dr. Chapman agreed to rewrite this paragraph and circulate it within the Comm ttee.

However, Dr. Broome proposed that the subject of hyper nsitivity to vaccine components be added to the agenda for an upc ning ACIP meeting, since it had generated so many questions. The Committee agreed to put it on the agenda.

Discussion then turned to remaining proposed chang in the document. The first concerned target groups for inf luenza and pneumococcal vaccination, with the following bold-faced dition so that the ACIP does not falsely assure that there's need to consider additional vaccination with pneumococcal vacc e:

> The target group for influenza and pneumococcal ccination overlap considerably. Both vaccines can be given the same time at different sites without increasing sid effects. However influenza vaccine must be given each yea **whereas pneumococcal vaccine is generally given only once o all but those at highest risk of fatal pneumococcal disea (refs.)**

Next, the Committee discussed the following proposed bstantial change to the statement: that the optimal timing of influenza vaccination activities be in the period October 15-No mber 15. Although there was lengthy discussion about what dates should be recommended, and whether the somewhat lengthy reasonin should be included, it was finally decided leave it as propo d in the handout with minor modifications.

At mid-morning break, Dr. Broome was asked about the st us of the report on GBS. She said CDC is working hard to cc plete the report, complete with an outside review as requested b the ACIP, and hopes to present a final review at the June ACIP m ting.

that it was necessary.

Before the next presentation, Dr. Broome said she ould get together a "to do" list for the committee because there vas quite a bit of homework to do. She reminded members t t it is appropriate to send comments to the different programs, th a copy to her.

Assessment of Immunization levels in Preschool Childrer

Dr. Betty Zell, IM, CDC, said that analysis of retrospect ve school immunization surveys reveals that a) the vast majority c children get into the immunization system prior to their second birthday, with the majority of these children receiving th r first immunization prior to their first birthday b) if thes children could be kept in the immunization system, coverage le ls would increase considerably; c) an apparent problem is the f rth DTP; OPV3 and DTP4 should be given together; 23%-63% of child n receive their OPV 3 before their first birthday.

Vaccine Injury Compensation Program

Dr. Geoff Evans, Deputy Director and Chief Medical Offic of this program since January, gave this presentation. Mr. homas E. Balbier, Jr., was not able to attend. As background, r. Evans explained that the program consists of two port ns: a retrospective portion, for cases in which the vaccine as given prior to October 1, 1988; and a prospective portion, or shots given on or after that date. For pre-1988 cases, 4,095 petitions have been filed. There are 210 post-1988 petitions. A t al of 346 awards, totaling $200.2 million, have been made as of st week. But relatively few cases from the prospective period ave been adjudicated. Awards for death cases are fixed at $25 000 plus attorney fees. The average award for pre-1988 injury c es is $1 million. The program predicts a tremendous shortfa --$152.2 million. It will run out of money for the next fiscal y r in the next month or two. The law's original shutdown provisic --that if one of the portions of the program ran out of money, t program would stop within 6 months--has been repealed so that e n if the retrospective portion is without funding, the prospecti portion remains viable.

Eighty-five percent of cases are injuries; the rest are c aths. The program concedes about one-third of cases; the rest to U.S. Claims Court. The program is successful in 40% of th e cases. The program is regularly denied its viewpoint with SIDS ases.

Because of the looming fiscal crisis with the program, r. Mason appointed a task force last summer with two functions: to come up with legislative proposals beginning with nonscientif kinds of proposals; 2) to form a scientific subgroup. The legisla ive group made several propositions, some of which have been ad ted into

circulate it among the Committee members.

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

Samuel L. Katz, MD, Chairperson
Date: 11 May 1992