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MINUTES, MEETING NO. 5, ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES - FEBRUARY 17-18, 1966

I. The Advisory Committee on Immunization Practices met at the Communicable Disease Center on February 17-18, 1966. Those in attendance were:

a. Committee

Dr. David J. Sencer, Chairman
Dr. H. Bruce Dull, Acting Secretary
Dr. Ernest A. Ager
Dr. Gordon C. Brown
Dr. Alice Chenoweth (for Dr. Lesser)
Dr. Geoffrey Edsall
Dr. David T. Karzon
Dr. Theodore A. Montgomery
Dr. Roderick Murray
Dr. Paul F. Wehrle

b. Invited Participant

Dr. Louis Jacobs, Division of Foreign Quarantine, Public Health Service, Silver Spring, Maryland

c. Consultant

Dr. Saul Krugman, Professor and Chairman, Department of Pediatrics, New York University School of Medicine, New York, New York

d. CDC Staff - Participants and Discussants

Immunization Activities: Dr. F. R. Freckleton

Laboratory Branch:
Dr. U. Pentti Kokko
Dr. James O. Mason
Dr. Bernard Fields
Dr. Brian E. Henderson
Dr. Roslyn Q. Robinson
Dr. Telford Work

Epidemiology Branch:
Dr. Alexander D. Langmuir
Dr. Ronald F. Johnson
Dr. Philip R. Nader
Dr. Beryl Rosenstein
Dr. Robert J. Warren

II. Measles Vaccine Discussion

In general review and updating the previous A.C.I.P. statement on measles vaccine, detailed consideration of various aspects of vaccine administration, community acceptance and general programs, reactions, complications, and the duration of protective antibodies ensued.

In a current surveillance statement, it was noted that, to date, some 13,000 doses of live attenuated measles virus vaccines have been distributed (6 million in 1965). An estimated 10 million susceptibles between the ages of one and four largely in the middle and upper socioeconomic groups have been immunized. The Bureau of the Census estimate is that approximately 25% of children under age 10 have received measles vaccine.

It was generally felt that the full impact of vaccine on the number of measles cases reported will be muted by the fact that the same pediatric practices now utilizing the vaccine have also previously been the poorest reporting.

Deterrents including the variably high costs of vaccine, general cooperation in community programs, and inconveniences of combined vaccine-globulin are among items related to the "sluggish" approaches in some areas to plans for measles eradication. Dr. Paul Wehrle reported preliminary data from a recent survey of 410 pediatricians in the Los Angeles area where 46 replies received in eight days netted evidence that more than 42,000 doses of measles vaccine had been administered up until the survey.

With respect to the serological accessment either of responses of vaccine effectiveness, considerable attention was paid to correlation of the variably sensitive laboratory procedures. Dr. Saul Krugman presented data on the better correlation of the seemingly highly sensitive Norrby procedure with neutralizing antibody titers but not necessarily with the regular serological tests.

Comprehensive review of the prime age for live measles vaccination demonstrated that the previously accepted 12 month suggestion was still most generally useful, although a permissive attitude toward administrations beginning at 9 months was felt perhaps to allow flexibility in community and health clinic programs.

A series of nine cases of neurological disorders conceivably associated to measles vaccine in 1965 were reviewed. Less than six of them were considered as being even possibly associated, and in some of these, major questions involved the very brief intervals between vaccination and response. None was felt to have been clearly related to vaccination.

Preliminary observations of local Arthus-type reactions at the site of live measles vaccine infection in some children previously given inactivated vaccine were reviewed. Although the suspect reactions of this sort were relatively few, the interval between the killed and live vaccine is generally greater than six months.

Discussion of State-wide and community-wide programs was introduced by a description of the Rhode Island measles vaccine project recently completed (Dr. Beryl Rosenstein) and review of measles epidemic control employing live virus vaccine (Dr. Philip Nader).

Much of the foregoing discussion and a large number of other areas of interest have been incorporated into a draft of the original A.C.I.P. measles vaccine recommendations by a subcommittee which met during the evening. (Drs. Karzon, Montgomery and Murray, with Dr. Warren acting as staff member.) (See Appendix)

III. 17D Yellow Fever Vaccine Associated Encephalitis Fatality

The details of clinical, laboratory and general epidemiological findings surrounding a recent fatal childhood case of encephalitis associated with the administration of 17D yellow fever vaccine were presented by Drs. Philip Nader and Bernard Fields. Comprehensive review of the case is being prepared for publication by all contributing to the investigation. No Committee action was indicated.

IV. Immune Globulin in the Control of Transfusion-Associated Hepatitis

Results from currently available investigations on the risk attending transfusion and on the lack of uniformity of findings in attempts to show protection of transfusion-associated hepatitis by immune globulin were discussed at length. Evidence was felt to be clearly insufficient for making any recommendations other than that supplies of immune globulin not be used for this purpose routinely. A subcommittee (Drs. Edsall, Wehrle, with Drs. Mosley and Johnson acting as staff members) was appointed

by the Chairman to prepare a draft of such a statement for Committee approval. (See Appendix)

V. On the second morning of the meeting, careful review and alteration of drafts of statements and recommendations prepared by subcommittees during the previous evening, was followed by discussion of agenda items for consideration for the next meeting:

1) Smallpox vaccination in the U.S.

2) Influenza review and vaccine recommendations.

3) Typhoid vaccination schedules.

4) Immune globulin prophylaxis of rubella.

5) Botulinus antitoxin.

VI. The regular spring meeting of the A.C.I.P. was tentatively scheduled for Monday and Tuesday, May 16-17 in Atlanta. The Committee Secretary will prepare the agenda as discussed and distribute related materials prior to the meeting.

VII. With the thanks of the Chairman, the Committee adjourned at 1:00 P.M., February 18, 1966.

H. Bruce Dull, M.D.

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MEASLES VACCINES - STATUS AND RECOMMENDATIONS FOR USE

Prepared by the Public Health Service
Advisory Committee on Immunization Practices

Highly effective, safe vaccines are available for eliminating measles in the United States. Virtually all children will at some time have clinically evident measles unless protected by vaccine. Measles is often a severe disease and is of particular concern because of frequent complications including broncho-pneumonia, middle ear infection and encephalitis. Moreover, the encephalitis which follows measles approximately once per 1,000 cases often results in permanent brain damage and subsequent mental retardation. An average of one measles death occurs in every 10,000 cases.

All susceptible children by virtue of not having had natural measles or measles vaccine should be immunized. Programs directed toward vaccinating children at about one year of age should be established by all communities. Also of particular importance is the immunization of susceptible children entering nursery school, kindergarten and elementary school, since they are often responsible for transmission of measles to other children in the community.

A. Live Attenuated Measles Virus Vaccines (Edmonston and Schwarz Strains)

Live attenuated measles virus vaccines prepared from the Edmonston strain or Schwarz (further attenuated) strain are available for use in the United States. The Edmonston strain is propagated in either chick embryo or canine kidney cell cultures and may be given alone or simultaneously with Measles Immune Globulin according to manufacturers' directions. The Schwarz strain is prepared only in chick embryo cell

culture and is suitable for administration without Measles Immune Globulin. The live attenuated measles virus vaccines produce a mild or inapparent, non-communicable infection. Fifteen percent of those receiving either Edmonston strain with Measles Immune Globulin, or Schwarz strain, may experience fever of 103°F. (rectal) or greater, beginning about the sixth day and lasting no longer than five days. Edmonston strain alone may have about twice the frequency of such responses. However, the great majority of reports indicate that even children with high fever experience relatively little discomfort or minimal toxicity and reactions often go unnoticed by the parents.

An antibody response develops in virtually all susceptible children given live attenuated measles virus vaccines. The level and persistence of antibody induced by Edmonston strain administered alone is similar to that seen following regular measles. Antibody titers attained following Edmonston strain with Measles Immune Globulin or following Schwarz strain are slightly lower. However, with all three vaccine schedules, protection against naturally occurring measles appears to be long lasting.

On the basis of experience with more than 10 million doses administered in the United States, live attenuated measles virus vaccine appears to be one of the safest immunizing agents in use. To date, serious reactions associated with the live attenuated measles virus vaccines have been very rare. In some few instances, febrile convulsions without known sequelae, have been recorded.

B. Inactivated Measles Virus Vaccines

Inactivated vaccines derived from Edmonston strain measles virus and prepared in either chick embryo or monkey kidney cell cultures are available. These vaccines are administered in a three dose schedule at monthly intervals with subsequent boosters. Reactions are not more frequent than after administration of diphtheria and tetanus toxoids.

Following the primary immunization with inactivated measles virus vaccines, the protection achieved has been satisfactory for the first few months, but has been shown to decline rapidly thereafter. In view of the greater efficacy and the safety of live attenuated measles virus vaccines, inactivated vaccines are not recommended except in those instances where the use of live vaccines is contraindicated.

Combined schedules employing inactivated vaccines followed by live vaccines have been used (see Table). However, there are not sufficient advantages to recommend the use of these schedules; and, furthermore, there have been preliminary observations of untoward local tissue reactions when live attenuated measles virus vaccines have been administered to individuals previously immunized with inactivated measles vaccines.

C. Recommendations for Vaccine Use.

1) Age

Vaccine is indicated primarily for children who have not had measles. For maximum efficacy, live attenuated measles virus vaccines should be administered to those at least 12 months of age. However, they may be given to infants 9-12 months of age with the realization that there may be a slight reduction in efficacy, particularly if Measles Immune Globulin

is administered with the vaccine. Vaccination of adults at the present time is rarely necessary because most individuals are serologically immune by age 15. Limited data indicate that in the adult, reactions to vaccine are no more common than in children.

2) High Risk Groups

Immunization against measles is particularly important for children with chronic illnesses such as heart disease, cystic fibrosis, and chronic pulmonary diseases and, indeed, for any individual prone to serious complications following natural measles.

3) Prevention of Natural Measles Following Exposure

If administered up to and including the day of exposure to natural measles, live attenuated measles virus vaccines are usually effective in preventing disease. Limited studies reported to date indicate, however, that there is no protection conferred by the vaccines when given at longer intervals following exposure.

D. Community Immunization Programs

1) Ongoing Programs

Universal immunization as part of good health care should be accomplished through routine and intensive programs conducted in physicians' offices and public health clinics. Programs aimed at immunizing children at about one year of age should be established by all communities. In addition, susceptible children entering nursery school, kindergarten and elementary school should receive vaccine because of their particular role in community spread of natural measles.

2) Community-wide Mass Programs

Mass immunization programs may be useful to supplement the ongoing administration of live attenuated measles virus vaccine in communities or segments of communities in which the proportion of individuals so protected is known to be low. However, the following points should be considered in a community-wide mass immunization program:

a. The active cooperation of nearly all physicians as well as official health agencies normally concerned with the care of children is important.

b. Since live attenuated measles virus vaccines are administered parenterally, an adequate number of medical and nursing personnel are required.

c. Despite the acknowledged high incidence of measles and its frequent, serious complications, substantial effort may be required to achieve complete community support.

d. Since measles vaccine is contraindicated in some children, preliminary screening to identify such individuals is desirable in mass measles immunization programs.

e. Although a number of children may have febrile reactions following live attenuated measles virus vaccine, experience in community-wide campaigns and in private medical practice indicates that only a small fraction of these reactions require medical attention.

3) Control of Measles Epidemics

Measles surveillance can pinpoint potential outbreaks in ample time to institute effective control. Several studies have shown that measles epidemics can be curtailed or halted by vaccination of selected groups of children in a community, particularly the susceptibles in nursery school, kindergarten and the first two or three grades of elementary school. However, once measles is widely disseminated in a community, it may be necessary to immunize susceptible children of all ages in order to alter the course of an epidemic.

E. Immunization Schedules

Recommended immunization schedules are shown in the accompanying Table.

F. Precautions in the Use of Live Attenuated Measles Virus Vaccines.

1) Severe febrile illnesses.

Vaccination should be postponed.

2) Tuberculosis

Exacerbations of tuberculosis by natural measles infection have been noted, and by analogy might theoretically accompany infection with live attenuated measles viruses. (An observed basis of similarity between the natural and attenuated viruses is their ability to suppress tuberculin skin test positivity.) Therefore, individuals with active tuberculosis should be under treatment when live attenuated measles virus vaccines are given.

Although tuberculin skin testing prior to age one year is desirable as part of ideal health care for individual patients, it should not be a routine prerequisite in community measles immunization programs. For children included in these programs, the risk from natural measles often far outweighs the theoretical hazards of possible exacerbation of undiagnosed tuberculosis.

3) Recent immune globulin administration.

Following the administration of more than 0.01 ml/pound of immune globulin, immunization should be deferred from six weeks to three months depending on the relative dosage administered, since the persistence of measles antibody in the globulin may interfere with response to the vaccine.

4) Marked hypersensitivity to vaccine components.

Measles vaccines produced in chick embryo cell cultures should not be given to children sensitive to egg protein as indicated by their inability to eat eggs or egg products. Similarly, vaccines produced in canine cell cultures should not be administered to children highly sensitive to dog hair or dog dander.

5) Concurrent use of live attenuated measles virus vaccines with other live virus vaccines.

Theoretical possibilities of superimposed reactions and suppressed antibody responses have led to general

acceptance of the desirability of not administering more than one live antigen at a time when they can efficiently be given separately. Ideally, primary oral poliomyelitis immunization should be completed prior to the time indicated for measles vaccine and the two antigens separated by at least one month. Since smallpox and measles vaccines may each produce febrile reactions, similarly, there is merit in administering them at different times. When combined administration is elected for reasons of patient inaccessibility or threat of concimitant exposures, current information from field investigations would suggest that results comparable to those following separate administration can be anticipated.

G. Contraindications to Use of Live Attenuated Measles Virus Vaccines. If measles immunization is indicated for persons with diagnoses listed in the following three groups, inactivated measles vaccine should be used.

1) Leukemia, lymphomas and other generalized malignancies. Although there are no reports of unusual complications of vaccine administration in children with severe underlying diseases other than leukemia, it is conceivable on theoretical grounds that in such individuals, potentiation of the attenuated measles virus infection might occur.

2) Altered resistance from therapy with agents such as steroids, alkylating drugs, antimetabolites, and irradiation.

3) Pregnancy

Purely on speculative grounds, there is reluctance to risk fetal damage which might theoretically be related to attenuated measles virus infection.

H. Continued Surveillance

Intensive surveillance of measles and its complications is needed to appraise the effectiveness of national immunization programs. Such surveillance activities can delineate failures to achieve adequate levels of protection and the definition of groups in which epidemic control programs should be instituted.

Although more than 10 million doses of measles vaccine have been administered in the United States, continuous and careful review of adverse reactions is of utmost importance. All serious reactions should be carefully evaluated and reported in detail to local and State health officials. The Communicable Disease Center should maintain close surveillance of all such experiences.

IMMUNIZATION SCHEDULES FOR MEASLES VACCINES

SCHEDULE	TYPE OF VACCINE	AGE	DOSES* AND ADMINISTRATION	COMMENTS
1	Live attenuated measles virus vaccine (Edmonston Strain)	12** Months and Older	1	Although the live attenuated measles virus vaccine may be administered safely with or without Measles Immune Globulin, many physicians will wish to give the two simultaneously because of the lessened frequency of clinical reactions.
2	Live attenuated measles virus vaccine (Edmonston Strain) plus Measles Immune Globulin	12** Months and Older	1 plus Measles Immune Globulin (.01 ml per lb. at different site with different syringe)	
3	Live "further attenuated" measles virus vaccine (Schwarz Strain)	12** Months and Older	1	Clinical reactions approximate those observed in schedule 2; Measles Immune Globulin is not recommended with this vaccine.
4	Inactivated Vaccine	Any Age	3 (monthly intervals) plus a booster dose at one year	In view of the rapid fall-off in antibody and evidence of decreasing immunity following a primary immunization series, use of this vaccine is not recommended except for special groups in which live attenuated measles virus vaccine is contraindicated.

IMMUNIZATION SCHEDULES FOR MEASLES VACCINES

SCHEDULE	TYPE OF VACCINE	AGE	DOSES* AND ADMINISTRATION	COMMENTS
5	Inactivated vaccine followed by live attenuated measles virus vaccine	12 Months and Older	1 dose inactivated vaccine followed in 1 to 3 months by 1 dose live attenuated measles virus vaccine	The preceding administration of inactivated vaccine serves to reduce the frequency and severity of clinical reactions following live attenuated measles virus vaccine administration. Local tissue reactions have been noted in some instances.
		Under 12 Months	3 dose inactivated vaccine at monthly intervals followed by 1 dose live attenuated measles virus vaccine at 12 months or older.	

*Manufacturers' directions regarding volume of dose should be followed.
**May be given to infants between 9 months and 1 year with the expectation of slightly decreased efficacy especially if administered simultaneously with Measles Immune Globulin.

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PREVENTION OF TRANSFUSION-ASSOCIATED HEPATITIS

Prepared by the Public Health Service
Advisory Committee on Immunization Practices

At the meeting of February 18, 1966, the Public Health Service Advisory Committee on Immunization Practices adopted the following statement regarding the current status of methodology in the prevention of transfusion-associated hepatitis:

The risk of viral hepatitis following blood transfusion represents a serious and continuing problem. A number of reports indicate that the incidence of clinical hepatitis is greater among recipients of blood obtained from certain categories of donors. The risk also becomes greater as the number of transfusions increases. In addition, the case-fatality rate of transfusion-associated hepatitis increases with advancing age.

Evidence has been advanced both for and against the effectiveness of immune globulin in the prophylaxis of transfusion-associated hepatitis. Although the administration of immune globulin in a dose of 10 ml at the time of the transfusion and again one month later has been reported by some investigators to be effective in reducing the number of cases, evidence of the efficacy of this procedure is lacking in other carefully conducted trials. In view of these uncertainties, existing data do not provide a basis for allocating supplies of immune globulin for its routine administration to recipients of blood transfusions.

Several methods for lowering the incidence of transfusion-associated hepatitis are available. More attention should be directed toward enforcement of adequate standards of donor quality, development of central registries for the identification of known or suspect carriers, and encouraging the practice of using blood and potentially icterogenic blood products only when necessary.