Chairman McGuinness: Ladies and gentlemen: it is presumptuous for one person to stand here and discuss alone immunization against a dozen diseases. Many of you know much more concerning many phases of the subject than your chairman. I therefore ask you all to help by free discussion in making this a round table in the true sense.

Diphtheria, Tetanus and Whooping Cough

I shall talk first about diphtheria, tetanus and whooping cough, and the use of single and then multiple antigens. Following this we will have a short period for discussion.

Diphtheria: Up to World War II it was generally assumed that most of the adult population of the United States was immune to diphtheria. Many studies since 1941 have shown this is no longer the case. Depending upon locality 25 to 50% of our adult population now is susceptible. Infants of susceptible mothers likewise are not immune, and there has been an increasing amount of diphtheria in infants under 6 months of age. This phenomenon, of course, is due to the steadily decreasing carrier rates. Immunity to diphtheria depends upon constant restimulation which now, in general, must be provided artificially. Immunity following active immunization cannot be counted on lasting more than 3 to 4 years.

Reactions to diphtheria toxoid have been one of the chief problems in diphtheria immunization, especially in older children and adults. Methods of purification developed by Pillemer and others in recent years have made available vastly superior toxoids which also contain considerably less alum than the pre-War products. One must remember, however, that some individuals are sensitive to toxoid itself, and such persons will react adversely to the material regardless of its freedom from impurities. Most infants and young children are not sensitive to diphtheria toxoid. Older children and adults should receive a Schick test and Schick test control prior to immunization in order to rule out those who definitely are sensitive to the material. Injections should be given deep subcutaneously or intramuscularly, otherwise the normally occurring allergenic cyst may break through the surface and result in a draining "abscess." Alum toxoids, either alum-precipitated or aluminum hydroxide-adsorbed, are far more antigenic than fluid toxoids, probably cause no more reaction, and therefore are


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the materials of choice. With respect to dosage, package instructions should be followed. In general, one immunizing dose is incorporated in 0.5 cc. of material. Two doses should be given at approximately one month intervals followed by a third dose 6 to 12 months later. Primary immunization should not be considered complete until the third dose has been given. If fluid toxoid is used 3 injections should be given in the initial series instead of 2. Schick testing is recommended prior to active immunization of older children and adults. If this is not possible the first dose should be 0.1 cc. of toxoid. Individuals reacting adversely to 0.1 cc. of toxoid should be given no further injections. If no reaction occurs following injection of 0.1 cc. of toxoid it probably is safe to proceed with 2 injections of 0.3 to 0.5 cc. each. Once an individual has received the basic series of injections (5 doses), 0.1 cc. of toxoid given every 3 to 4 years will maintain an adequate level of immunity. While I will discuss the problem later, there is ample evidence for starting diphtheria immunization early, say at about 2 months of age.

Pertussis: As 60% of the deaths from whooping cough occur in infants under 6 months of age, it obviously is desirable to immunize as early as life as feasible. Amples evidence is now available to show that most young infants do develop good antibody levels, particularly when the vaccine is mixed with alum or alum toxoids. It is recommended that there be intervals of 3 to 4 weeks between injections. Dr. Sauer being of the opinion the duration of immunity is longer than when injections are given at shorter intervals. Rapid protective levels can be attained by giving the vaccine at shorter intervals (one week) and one week intervals are recommended when pertussis is epidemic in a community. The matter of duration of immunity can be dealt with by giving booster injections. For many years there has been difference of opinion as to the relative merits of vaccines grown on medium containing sheep blood versus medium containing sheep blood. This argument has been settled by a recent ruling of the National Institute of Health which prohibits the use of human blood because of the potential danger of transmitting serum hepatitis. Selection of strains for antigenicity probably is the most important factor in vaccine production today. Dr. Emmett Holt, Jr., and his associates have been using unskilled organisms without adverse reaction and preliminary results indicate such vaccines may be much more antigenic than vaccines containing killed organisms. Of importance is the fact that some individuals inherently are unable to produce good antibody levels regardless of the amount of antigen injected. Dr. Pearl Kendrick and associates have shown a relatively high degree of immunity persists for about 4 years following active immunization against pertussis. On the basis of these studies, booster injections are recommended every 3 to 4 years. Previously immunized children should be given a single injection (15 to 20 billion organisms) following known exposure. Children not previously immunized should following exposure be given hyperimmune serum; preferably human serum in the lyophilized form or its gamma globulin fraction. Reactions to pertussis vaccine, particularly those of the encephalitic type, have been the cause of considerable concern. Infants with histories of convulsions and children with respiratory infections or in active stages of teething should not be immunized. A febrile reaction following an injection of pertussis vaccine should be cause for considerable caution in determining whether further injections should be given, and the amount of antigen injected. If there is any question it is better to err on the side of conservatism.

Tetanus: Tetanus toxoid is one of the best antigens available, and the youngest infants respond well with minimal reaction. Its effectiveness has been demonstrated beyond any doubt, and I feel every individual should be immunized against the hazard of this disease. Tetanus toxoids have been purified in the same manner as diphtheria toxoid. The alum-precipitated and aluminum hydroxide-adsorbed materials are antigenically superior to the fluid toxoids, and are recommended especially for primary immunization. Fluid toxoids give a slightly more rapid booster response. For primary immunization 0.5 cc. of toxoid should be injected twice at approximately one month intervals, 3 doses being necessary if fluid toxoid is used. Booster doses (0.5 cc.) should routinely be given at 3 year intervals. If an injury occurs when 4 years or more have elapsed since a booster dose, antitoxin (3000 units) should be given in addition to toxoid on the basis of the important studies of Dr. John Miller and his associates. In certain instances of massive wounding it may be advisable to give antitoxin as well as toxoid regardless of the time elapsed since the last booster, as the incubation period of tetanus in such cases occasionally may be as short as 24 hours.

Multiple Antigens: The value of the multiple antigens, particularly those containing diphtheria and tetanus toxoids with pertussis vaccine, is established beyond doubt. In addition to reducing the number of injections required for active immunization of infants, there is evidence resulting antibody
levels are superior to those obtained from injection of single antigens. Reactions in infants and young children are no more severe following injection of triple antigens than following injection of single antigens. Children over 4 years of age do appear to react more severely to the multiple antigens, however, and single antigens are recommended in children beyond that age. The antibody response is good in most infants after 2 months of age. Infants possessing maternal antibody against diphtheria may not respond as well to the initial series of injections, but they are temporarily immune anyhow, and will achieve good levels following injection of the first booster dose. The schedule recommended is three 0.5 cc. injections at monthly intervals starting at 2 to 3 months of age; a fourth dose at 12 to 18 months of age; and a booster dose at 3 to 4 years of age. This schedule will provide protection against diphtheria, tetanus and whooping cough from early infancy until school age.

DISCUSSION

**Question:** Should I give pertussis vaccine to a child with a history of convulsions?

**Chairman McGuinness:** As suggested before, a history of convulsive seizures should make one hesitant about attempting active immunization against pertussis. If a decision is reached to attempt immunization the initial dose of vaccine should be small, say 0.1 cc. saline vaccine. Subsequent doses should be increased cautiously on the basis of tolerance of preceding doses.

**Question:** Does this warning concerning convulsions apply equally to tetanus and diphtheria as it does to whooping cough?

**Chairman McGuinness:** No.

**Dr. M. W. Seymour, Columbus, Ohio:** Would you say something about the formation of subcutaneous nodules?

**Chairman McGuinness:** Nodules, or "allergenic cysts," as they sometimes are called, are a normal reaction to the local irritation set up by the antigen. In some individuals these cysts are larger than in others. Following injection of some of the older antigens, especially those containing large amounts of alum, these cystic reactions were larger and frequently drained through the skin surface. This is far less likely to occur following injection of the newer improved antigens; nonetheless, it is advisable to inject antigens deep subcutaneously or even intramuscularly.

**Question:** When a child who is not actively immunized against tetanus is given antitoxin following an injury, how soon after that antitoxin injection can you start active immunization?

**Chairman McGuinness:** Active immunization may be started immediately as long as the toxoid is not injected at the same site (or in the same syringe) as the antitoxin.

**Question:** What is the best site for injection of antigens?

**Chairman McGuinness:** I prefer the arm. Some individuals like to inject into the buttock, although I feel there is, at least theoretically, a greater chance for infection from injections given in the diaper area.

**Question:** What about the question of there being a possible relationship between poliomyelitis and antigen injections?

**Chairman McGuinness:** There have been recent reports by McClockey, Hill and MacCallum indicating that in Australia and in England there has been found evidence that when poliomyelitis has been preceded within several weeks by an antigen injection, paralysis has tended to be localized in the extremity where the injection was given. There is apparently no evidence to suggest that the antigen injections have increased susceptibility to poliomyelitis. I have seen no reports indicating that this phenomenon has been observed in the United States but I do know that in view of the British and Australian reports the National Foundation for Infantile Paralysis has the matter under extensive study in a number of areas.

**Dr. Nelles Silverthorne, Toronto, Canada:** To our knowledge, in the Dominion of Canada, and to those also in the United States who have had experience with an epidemic of poliomyelitis, and with all the inoculations which have been given, it would be a strange thing if one physician somewhere hadn't noticed the relationship before now. Certainly we have had no incidence in Canada. I am afraid we are a little old-fashioned concerning the use of alum-precipitated toxoids. We still use the fluid toxoid prepared by the Connaught Medical Research Laboratories for the following reasons: we have had no paralysis, and to my knowledge no outbreaks of whooping cough in private practice in those who have received booster doses. In my own experience in children up to 4 to 5 years of age, and up to 10, I have never seen a serious reaction on a booster dose at an age comparable to which you have been discussing.
Now one question: Is agglutination the only index of pertussis immunity?

Chairman McGuinness: No, I am sure it is not. It is a relatively simple test, however, and seems to correlate fairly well with actual clinical experience. With respect to encephalopathies following pertussis vaccine, many of the cases reported followed injection of saline (not alum) vaccine.

TYPHOID, SCARLET FEVER AND SMALLPOX

I shall speak but briefly concerning active immunization against these 3 diseases.

Typhoid immunization in children is generally limited to special situations or in particular parts of the country where the disease is endemic. One fourth to one half the adult dose of triple vaccine is recommended, depending upon the age of the child.

Scarlet fever immunization is recommended only for professional personnel—physicians and nurses—who are Dick test-positive and must work in communicable disease hospitals.

With regard to smallpox vaccination I should like to emphasize that the present calf lymph vaccines are very labile and deteriorate rapidly when not properly refrigerated. They also deteriorate with age. It is important to know that nonimmune individuals may develop a lesion with the appearance of an immune reaction following vaccination with deteriorated material. In any batch of vaccine points one should get a sufficient number of typical "takes" to establish the fact the material is of good potency.

Vaccination is recommended during the first year of life and should be repeated at 3 to 4 year intervals thereafter. Vaccination always should be carried out in the face of a possible contact or threatened epidemic.

DISCUSSION

Dr. James B. Stewart, East Cleveland, Ohio: What about intradermal vaccination?

Chairman McGuinness: Intradermal vaccination has been carried out using egg fluid vaccines. The immunity following vaccination with egg fluid materials has not proved to be as satisfactory as that obtained with calf lymph vaccine. I would not recommend the intradermal injection of calf lymph vaccine, as sufficient virus is introduced by the multiple pressure method, and severe reactions might follow the amount of virus one would introduce by intradermal injection.

Dr. Hoyne, when you fail to get a "take" following smallpox vaccination, how many further attempts do you make, and at what intervals?

Dr. Archibald L. Hoyne, Chicago: I believe that everyone who has not had smallpox should obtain at least one successful vaccination in a lifetime. Ordinarily, if there were no reaction I would repeat the vaccination yearly. In case of known exposure to smallpox, I would vaccinate every third day until there was some local evidence to reaction.

ROCKY MOUNTAIN SPOTTED FEVER

Chairman McGuinness: Vaccination is recommended only for those in or going into definitely endemic areas. The newer antibiotics are so effective in the treatment of this disease there seems to be little justification in the vaccination as it used to be carried out in any area where there were ticks.

MEASLES

The effectiveness of gamma globulin (immune serum globulin—human) in measles prophylaxis is established beyond doubt and is recommended following known exposure of susceptibles. Excepting under unusual circumstances, one should attempt to modify rather than afford complete protection.

GERMAN MEASLES

Children should be permitted, in fact encouraged, to get german measles. Because of the hazard to the young fetus we need some means of protecting women who become exposed to this disease during the first trimester of pregnancy. Convalescent serum has not given satisfactory results, and there is considerable question as to the usefulness of gamma globulin (immune serum globulin—human). Until more definite information is available, however, I would recommend two 6 to 8 cc. doses of gamma globulin at 5 to 7 day intervals for women exposed to the disease in early pregnancy. I believe that equally important is the removal of the pregnant women from the source of infection at the earliest possible moment.
INFLUENZA

Vaccination against influenza is not recommended for children except under special circumstances; e.g., a child with rheumatic fever in whom even a mild case of influenza would be considered hazardous.

MUMPS—ACTIVE IMMUNIZATION

Active immunization against mumps is indicated infrequently in children. The vaccine promises to be very useful for immunizing susceptible adults, although to date it would appear the immunity resulting from injection of mumps vaccine is relatively short—perhaps 6 months to a year. If following active immunization an individual is exposed frequently to the disease his immunity could be expected to be enhanced and prolonged through inapparent infection.

A useful adjunct in the field of mumps is the skin test for susceptibility which gives a positive tuberculin-like reaction in immune individuals. It is suggested that adults be skin-tested prior to being given vaccine as so many adults already are immune by virtue of previous inapparent infection.

MUMPS—PASSIVE IMMUNIZATION AND TREATMENT

Early results from use of convalescent serum in both passive immunization and treatment are inconclusive, except that in one well-controlled study in which the equivalent of 200 cc. convalescent serum was used in treatment, the incidence of orchitis in the treated group was 7% as compared with 28% in the controls. Serum from vaccinated donors (hyperimmune serum) is now under study in Philadelphia and preliminary results indicate this material may be of use both in passive immunization and treatment. Large doses of serum are necessary—50 cc. for passive immunization of exposed susceptibles and 200 cc. for treatment. Passive immunization and treatment generally are reserved for adult males.

WHOOPING COUGH—PASSIVE IMMUNIZATION AND TREATMENT

Hyperimmune serum, either in vacuum-dried form or in the form of its gamma globulin fraction, has been found useful both in passive immunization of exposed susceptibles and in treatment of the disease. The vacuum-dried form has the advantage of being safe for intravenous injection which is not the case with the gamma globulin fraction. There is evidence the newer antibiotics may be of some benefit in treatment, but it is felt that when the disease occurs in small infants the serum always should be given in addition to the antibiotics when the latter can be tolerated. Hyperimmune rabbit serum also is probably of some value, but the human products (which now are irradiated as a precaution against serum hepatitis) are to be preferred.
Round Table Discussion: IMMUNIZATION REVIEW
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