Current Status of Immunization Procedures

Tetanus, and Exotic Diseases of Military Importance *

ARTHUR P. LONG, Lt. Col. M.C., U.S.A., F.A.P.H.A.
Infectious Disease Control Branch, Office of the Surgeon General, Washington, D. C.

ACTIVE immunization against tetanus, advocated for use in human beings about twenty years ago, has now been widely accepted.[1] The experience with tetanus immunization in the British and American Armies has been quite completely summarized elsewhere.[2, 3] In reporting British experience, Boyd [2] concluded that the incidence of tetanus in African and European campaigns was negligible. He attributed this result largely to active immunization with tetanus toxoid, although it was the British practice to administer a prophylactic dose of antitoxin (3,000 International Units) as soon as possible after an injury rather than a stimulating dose of toxoid as was done for American troops.

In the United States Army but 12 cases of tetanus are known to have occurred during the period 1942 through 1945. Only one of these developed among the approximately one-half million troops reported to have been wounded. Of the 12 cases, 6 were in individuals with no active immunization, 2 in soldiers who had been basically immunized but had received no post-injury toxoid, and 4 in those whose records indicated that they had received the basic immunization plus the emergency stimulating dose at the time of injury. Five fatalities occurred, 2 of them among the 4 who had received the full course of toxoid. In the United States Navy, a total of 4 cases was verified, only 1 occurring in an individual receiving the prescribed toxoid prophylaxis.[4] Taking into consideration the number of individuals involved, the incidence of tetanus was essentially the same in the Army and Navy groups.

In the Japanese Army and Navy, where routine immunization was not practised, it was reported that from 1940 through 1944 tetanus occurred in about 10 per 100,000 wounded men, an incidence greatly in excess of that experienced in the American Army. A report from the unimmunized German Ground Forces in Normandy indicated more than 80 cases of tetanus, though none occurred among the immunized Luftwaffe personnel. During the Manila operation, over 400 cases and more than 300 deaths from tetanus in civilians were reported. Viewing this total experience, there can be no question that active immunization with toxoid is an effective means for the prevention of tetanus even under the severe conditions imposed by wounds and injuries incident to military operations.

The risk of tetanus in civilian populations under normal conditions is even more difficult to assay than that in military groups. There is no question, however, but that a certain risk does exist. The mortality rate from tetanus following injuries (including tetanus neona-

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torum) in the civil population of the United States was in the neighborhood of 0.7 per 100,000 for each of the three years 1936 through 1938. A breakdown of this incidence by age groups indicates that the period of childhood (up to age 15) holds the greatest hazard, and young adult life (age 25-34) the least. Tetanus neonatorum contributes heavily in the first year of life, the mortality rate for this period being 7.8 per 100,000. The next highest rate (1.2) was for the 5 to 14 year group. The special hazard to those subject to more than the usual risk of exposure to tetanus, such as farmers, horsemen and others whose activities increase the likelihood of injuries contaminated with tetanus spores is well recognized. For this group as well as for children, active immunization with tetanus toxoid would appear to be warranted, although the disease hardly represents a sufficient problem to require this procedure as a general public health practice.

The choice of immunizing agents lies essentially between fluid toxoid and the alum-precipitated preparation. The primary considerations in making this choice have been reviewed recently in some detail by Edsall.[5] Both types are highly effective as demonstrated by the results in the United States Army and Navy; the Army using fluid toxoid and the Navy, alum-precipitated toxoid. Three doses of the fluid type are required for the basic immunization while two of the alum-precipitated agent will suffice. Since the addition of alum to an antigen may act to increase its sensitizing properties as well as to enhance its antigenicity, the possibility of reactions of sensitivity to repeated doses of alum toxoid is to be considered. However, the new methods for processing toxoids reported by Pillemer and his coworkers,[6] may serve to minimize the likelihood of such reactions. In any event, it is extremely important that whichever type of toxoid is used be as free as possible of non-toxoid constituents which might produce undesirable reactions. On theoretical grounds at least, fluid toxoid, because of its more rapid absorption, would appear to be the agent of choice for the emergency or booster dose at time of injury. However, there is no indication that the alum-precipitated materiel is not effective for this purpose. Combined antigens, such as diphtheria and tetanus toxoid or this combination plus pertussis vaccine, are now available. The utilization of such combinations appears reasonable if adequate doses of the individual antigens can be provided without resulting in undue reactions, local or systemic. It is to be recalled, however, that protection from pertussis is required at an early age when an optimal response to diphtheria toxoid may not be obtained.[5] For the stimulating dose, tetanus toxoid alone, rather than in combination with other antigens, is preferred in order to minimize local and systemic reactions, particularly if stimulation is required in adolescent or adult life.

As indicated before, in using fluid toxoid, three doses of 1 ml. each, administered at intervals of 3 to 4 weeks, are required and with the alum-precipitated agent, two doses of ½ to 1 ml. 4 to 8 weeks apart. In United States military usage, this basic preparation was followed at the end of the first year by a single stimulating dose of 1 ml. During the first part of the war, another stimulating dose was administered to all Army personnel departing for a theater of operations unless such departure was within 6 months subsequent to a previous dose. For the last three years, however, no more toxoid has been given after the first stimulating injection unless indicated by the occurrence of a wound or other injury which might result in tetanus. No antitoxin is administered for prophylaxis unless some doubt is entertained as to previous active immunization.

It has been determined by blood-antitoxin-level determinations in soldiers * that this regime results in adequate protection after the initial series of toxoid injections and that for a period of at least 4 to 5 years after the single stimulating dose the circulating antitoxin level can be effectively raised within 1 week by the so-called emergency or booster dose. Findings in adults, who received fluid toxoid, are essentially the same as those of McBryde and Poston [7] in children following immunization with the alum-precipitated agent. These workers demonstrated satisfactory responses to booster doses 4 and 5 years after completion of the basic series. Further experience will be required to determine just how long this period of responsiveness will ultimately prove to be.

EPIDEMIC TYPHUS FEVER

The vaccine currently used for protection from epidemic typhus fever is a suspension of formalin-killed epidemic typhus rickettsiae and soluble antigen obtained by cultivation of the organisms in the yolk sac of fertile hens' eggs.[8] It is administered in 2 subcutaneous doses of 1 ml. each given with an interval of 7 to 10 days between doses. Additional stimulating doses of 1 ml. each are considered desirable every 4 to 6 months in the presence of the disease. At the present time, while there is no serious epidemic typhus situation in the world, this vaccination is considered desirable for those who are to travel or reside in east or southeast Europe, Asia, and Japan. Since epidemic typhus is known to occur in Mexico and certain sections of Central and South America, individuals traveling to these areas might also be well advised to be vaccinated against typhus if freedom from louse infestation cannot be assured. It is emphasized that epidemic typhus vaccines contain epidemic louse-borne typhus antigen only and hence cannot be expected to produce protection from the endemic or murine type of the disease. However, a vaccine for protection against this form of the disease is now available.

CHOLERA

It is now the general concensus that in areas where cholera is frequently encountered, vaccination with the best vaccine available should be practised in addition to the usual measures to prevent ingestion of the cholera vibrio. The vaccine obtainable in this country and currently used, when indicated, for military personnel, consists of a suspension of 8 billion phenol-killed cholera vibrios per ml. The organisms used are of the Inaba and Ogawa strains which are considered to be as fully virulent and antigenic as any obtainable at this time. Vaccination is accomplished by the subcutaneous administration of two doses of 0.5 and 1 ml. each with an interval of 7 to 10 days between injections. Subsequent stimulating doses of 1 ml. each are given at 4 to 6 months intervals in the presence of serious danger of infection. Experience in the American Army with this procedure added little to previous evaluations. The disease was present in epidemic or semi-epidemic proportions in a number of areas where troops were stationed, and only 13 cases occurred among them. These were in vaccinated personnel. No cases occurred among United States Forces in India although some were experienced in unvaccinated allied forces in the same area.

PLAGUE

The vaccine used is a suspension of 2 billion formalin-killed virulent plague bacilli per ml. The spacing and size of dosage, as well as the administration of

* The antitoxin titrations referred to were performed by Dr. M. V. Veldee and associates at the National Institute of Health, Bethesda, Md., and Dr. J. Howard Mueller, Department of Bacteriology and Immunology, Harvard Medical School.

stimulating injections, are the same as for cholera. No cases of plague were reported in American personnel during the recent war although troops were present in certain areas where the disease existed. It cannot be certain, however, that actual exposure occurred and since rat and flea abatement programs were emphasized, the relative effects of vaccination and of these procedures cannot be measured.

YELLOW FEVER

The effectiveness of yellow fever vaccination has been clearly demonstrated and needs no further elaboration here. The yellow fever vaccine most commonly used, and that employed for military personnel and others in this country who are to enter yellow fever zones, is a suspension of viable virus of the 17D strain obtained by chick embryo culture. Vaccine is administered subcutaneously as a single dose of 0.5 ml. of the indicated dilution of the desiccated material provided. The complication of homologous serum jaundice following the use of this material in the early part of the war was determined to have resulted from the small quantities of normal human serum added as a stabilizing agent.[9, 10] Since the deletion of human serum from yellow fever vaccine, this complication has entirely ceased to occur.

The duration of immunity to yellow fever following vaccination has been the subject of some concern particularly with respect to the quarantine requirements of certain foreign governments. This period is now generally accepted to be 4 years. However, data recently presented by Anderson and Gast-Galvis[11] indicate that immunity persists for as long as five years after vaccination. These authors conclude that neither children nor adults require revaccination at the expiration of the 5 year period following the initial injection of the 17D vaccine.

Yellow fever is today confined to certain sections of South America and Africa. These endemic areas have been defined in detail by the Expert Commission on Quarantine of UNRRA.[12] For purposes of fulfilment of foreign quarantine requirements, as well as for individual protection, individuals traveling to or through these areas should be vaccinated at least 10 days before departure from a non-endemic area. As stated above, for quarantine purposes such vaccination is now considered valid for 4 years.

JAPANESE ENCEPHALITIS

Vaccination against Japanese encephalitis is new and its value not yet clearly defined.[13] It was first employed in the United States Army in the Ryukyu Islands in the late summer of 1945. No conclusions as to its efficacy could be drawn since the epidemic had passed its peak at the time the vaccine was administered. Some three dozen cases did occur among American troops, 6 of which were said to have been in vaccinated individuals. Immunological studies indicated that the vaccinations performed during this period did not result in appreciable responses in neutralizing antibody titers. The lack of knowledge concerning the significance of such a response, however, did not warrant the acceptance of this finding as evidence of immunogenic failure of the vaccine. All troops in Japan and Okinawa were revaccinated before the encephalitis season the following year. No outbreak appeared in these areas but a few isolated cases occurred among unvaccinated troops in Korea.

The vaccine used during this past season has been that produced by Randall, Smadel, and others at the Army Medical Department Research and Graduate School[14] in the developing chick embryo and processed by drying from the frozen state. It is hoped that vaccine produced in this manner will

also be available for the ensuing season.

A proposed vaccination procedure involves the administration of three doses of 1 ml. each, the first two 1 week apart and the third approximately 30 days later.

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Courses in Laboratory Diagnosis of Parasitic Diseases

The U. S. Public Health Service in February completed the first of three refresher courses to be given during 1948 on the laboratory diagnosis of parasitic diseases by the Laboratory Division of the Communicable Disease Center in Atlanta. Two later courses will be given from July 12 to August 20, and October 11 to November 19.

This training is open to all grades of employed laboratory personnel. Although priority must be given to the laboratories of state and local public health departments, applicants from hospitals and private laboratories will be accepted if vacancies occur. There will be no tuition or laboratory fee, but travel and living expenses must be paid by the worker or his employer.

Applications should be made as early as possible since acceptance notifications are made approximately two months before the course begins. All inquiries should be addressed to R. F. Reider, Surgeon (R), Assistant Chief, Laboratory Division, Communicable Disease Center, 291 Peachtree Street, Atlanta, Ga.