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In this postwar period of adjustment and expansion of public health activities to meet the needs of the future, we see a broadening of the conception of the field of public health taking place. Many activities, such as tuberculosis control, industrial hygiene, and maternal and child health are being expanded. Other activities, such as mental hygiene and cancer control are new in most states and under the stimulation of the Federal appropriations may be expected to take their places as parts of the state and local programs.

This is all good and proper but, lest in our enthusiasm for the new we neglect one of our old activities, it may be well to consider occasionally some phases of communicable disease control. It might be of interest to local health officers, particularly, to review briefly our immunization procedures. The speaker lays no claim to being an authority in the fields of immunology or epidemiology. My remarks will be made rather from the standpoint of a local health officer.

Although smallpox, diphtheria, and typhoid fever have been reduced over the years to only a small fraction of the levels of thirty years ago, we know that smallpox and diphtheria will break out again if immunization of the public is not maintained. During the war years immunization programs have been curtailed, due in part to shortages of health department personnel and to overworked private physicians, but also because of the shifting of population, the employment of mothers, school absenteeism, and similar factors. You are all familiar with the outbreak of Oriental smallpox that occurred last year on the Pacific Coast. You know also that diphtheria has increased in some sections of the United States in recent years. So let us review some pertinent facts regarding not only smallpox and diphtheria, but also pertussis, tetanus, scarlet fever, and typhoid fever immunizations.

**Smallpox**

The importance of maintaining adequate immunity of the population against smallpox is borne out by outbreaks, such as the one in Glasgow in 1942 which killed 24% of those infected, or the Hong Kong outbreak of 1938 in which 2,000 persons died, or the 1946 outbreak of Oriental smallpox in Seattle. Claims that present day smallpox is mild and, therefore, unimportant are wrong for it is well established that mild and severe forms may alternate in successive epidemics or coexist in the same
one. Finally, the relation between the incidence of smallpox and the extent and effectiveness of vaccination laws has been so conclusively shown that further elaboration is not necessary.

The shifting populations of the recent war years have provided a fertile soil for transmission of smallpox and have put current vaccination programs and methods to a vigorous test. Although several incipient epidemics of smallpox resulting from these conditions were readily checked by vaccination, the small number of failures reported may serve as a basis for critical consideration of the requirements that must be met to achieve successful vaccination. In any such consideration, it must again be emphasized that no immunization procedure is absolutely effective. The causes of vaccination failures can nevertheless, for the most part, be itemized as follows:

**Long interval since vaccination.**—The occurrence of smallpox in persons not vaccinated for many years merely points by contrast to the effectiveness of vaccination in persons also exposed, who having been vaccinated more recently, are found to be clearly protected.

**Use of impotent vaccine.**—Smallpox vaccine is a living virus when properly prepared, and successful vaccination depends on the ability of this virus to multiply in the tissues of the vaccinated person. Multiplication of the virus in the tissues may fail for many reasons, including: improperly prepared vaccines; improper storage of vaccine—it must be kept at temperatures below freezing for as much of the time as possible; use of outdated vaccine; and the use of less than the full contents of a capillary for each vaccination, as the virus-laden lymph tends to separate from the glycerin portion which is inactive.

**Faulty vaccination technique.**—A fully potent virus may fail to multiply in the vaccinated subject because of any one of various errors in technique. Thus, the presence of such antiseptics as alcohol, mercurochrome and iodine on the vaccination site destroys the virus as soon as it is applied and failure to achieve the right degree of penetration of the skin prevents the virus from obtaining a suitable site for multiplication.

**Incorrect interpretation of the results obtained from vaccination.**—A definite vesicle appearing at the site of vaccination is unmistakable evidence of a successful primary or accelerated reaction, but the small papule characteristic of an immune reaction is less specific and may be simulated by a traumatic reaction to the application of the needle. Furthermore, persons who have been previously vaccinated may exhibit a local allergic reaction to the antigenic substance in smallpox vaccine. A dead vaccine may thus induce a small papule, indistinguishable from an immune reaction except that it appears and disappears somewhat earlier. Thus the immune reaction should not be regarded as a successful result since it does not necessarily indicate immunity.

The only safe procedure is to repeatedly vaccinate persons showing this
reaction. Because of the frequent failures to obtain takes, some authorities recommended that two or more insertions be employed where maximum protection against smallpox is urgent. This is advisable whether or not the person has a history of previous vaccinations. Due to the small scars left by the multiple-pressure method, it is sometimes difficult to tell whether or not the person has had a previous vaccination.

There are, undoubtedly, differences in the protection afforded by vaccination due to differences in vitality of the virus employed, in the infectivity of the strain of smallpox encountered, and in individual response to the immunizing process. It is, therefore, wise to persist in vaccinating until a successful vaccination is achieved and to revaccinate at intervals of five to seven years and whenever there is probable exposure to smallpox.

As to the optimum age for vaccination, it is generally agreed that it should be done in the first year of life, preferably between three and six months of age.

At present nearly all vaccine used is prepared by inoculation on calves and other herbivora, but the virus can be cultivated in tissue media and in the chorioallantoic membrane of the chick embryo. Chick embryo vaccine, due to its cheaper production, may come into wide use if allergic reactions due to egg protein do not give difficulties.

Intracutaneous vaccinations have been tried with all three types of vaccines in the hope that immunity could be achieved without the necessity of producing a cutaneous vesicle, but results so far have been unsatisfactory.

Reactions to smallpox vaccination in a small percentage of cases are reported from time to time. Auto-inoculations and several types of rashes varying from local erythema to generalized vaccinia occur. Eczematous patients seem more prone to a generalized eruption and, therefore, should not be vaccinated unless exposure to smallpox is likely. Post-vaccinal encephalitis, which fortunately is very rare, is not accepted by all authorities as due to vaccination; that is, it may be due to other causes and only coincidental to vaccination. Post-vaccinal tetanus has almost been eliminated with the discontinuance of vaccination dressings and other factors responsible for this complication.

**Diphtheria**

There was a large epidemic of diphtheria in Europe with estimates of over a million cases for Europe, exclusive of Russia during the years 1943 and 1944. The rise occurred mostly in northern Europe where due to war conditions high levels of immunization were not maintained. In Great Britain, however, the immunization program was greatly expanded during the war years when children were being relocated in rural areas for protection against bombing. As a result, diphtheria continued to
decline in Great Britain, but in Norway and the Netherlands, where immunization was not prevalent, there was a tremendous rise in incidence.

In the United States as a whole there has been a rapid decline in diphtheria incidence from about 120,500 reported cases in 1924 to 14,150 in 1944 or from 106 cases per 100,000 population to about 10.7, in 1944. However, there was some slackening in the relative rates of decline after 1940, and some cities and geographic sections showed an increased incidence in 1944 and particularly 1945.

Is the increase due entirely to a falling off in immunizations of children? In California and elsewhere a definite increase in adult cases has been noted. This and other evidence suggest that extensive immunization of the population with the resultant reduction in diphtheria has been accompanied by a reduction in the carrier rate, hence in the frequency of naturally acquired stimuli to immunity and, in turn, a decrease in the general level of immunity in the population. Schick test surveys among young adults in England, Canada, and the United States have shown that 50–60% are susceptible to diphtheria in contrast to the incidence of 20–25% of positive reactions formerly reported in these age groups. Thus, a growing reservoir of adolescents and young adults susceptible to diphtheria appears to exist.

A parallel consequence of the reduced prevalence of diphtheria bacilli is that artificially induced primary immunity is likely to wane and disappear more rapidly than formerly. Hence, present control of diphtheria must be concerned, not only with immunization of a wider age group than previously, but also with the necessity of maintaining immunity once it has been established.

As to the choice of an immunizing agent, it has been well established that toxoid is a superior antigen to toxin-antitoxin. Furthermore, toxin-antitoxin may cause serum sickness. As to a choice between alum precipitated toxoid and fluid toxoid, both will give 95% Schick reversals within a few months after two doses of alum ppt. toxoid or three doses of fluid toxoid. Recent experience suggests that occasional or perhaps periodic reinforcing doses of toxoid are required to replace the stimulus no longer provided by diphtheria carriers. Such repeated doses increase the possibility of allergic reactions to constituents of the toxoid, and it appears true that alum precipitation markedly accentuates the capacity of toxoid to cause hypersensitiveness. There is particular danger of allergic reactions after long intervals. There is even some danger of a local reaction from second doses of alum ppt. toxoid. The choice between alum ppt. toxoid (2 doses) and fluid toxoid (3 doses) may depend upon such factors as geography, education, or administrative preference.

As to dosage and interval of time between doses, it is now well es-
established that fewer than 2 doses of alum ppt. toxoid or 3 of fluid toxoid are insufficient to produce an adequate sustained immunity. The interval between doses should be at least 3 weeks regardless of which agent is used.

The results obtained with toxoid vary with many factors, among the most important of which is the interval between immunization and follow-up. Fraser and Halpern have shown that 3 months after immunization with 3 doses of fluid toxoid a large number of previously selected children had over 0.02 units of antitoxin per cc. of serum, or more than 5 times the amount necessary for the production of a negative Schick test. A year later 3%, and 3 years later 8% of the group were Schick positive; whereas, 5 years later 34% had reverted to the Schick positive state and the average serum antitoxin titer was only 20% of the maximum obtained shortly after immunization. A more recent study indicates that among young adults the relapse rate may be as high as 20% in one year. Thus, the protection against diphtheria observed in any large group decreases in proportion to the interval since inoculation. Nevertheless, the clinical protection afforded by toxoid immunization is impressive. With few exceptions, the incidence of diphtheria among immunized persons averages about 10-15% of that among non-immunized controls. Also, the disease is milder in immunized persons.

For the immunization of adolescents and adults, toxin-antitoxin is still used by some because of the frequent reactions from routine dosage of toxoid. Such reactions, however, can largely be avoided by previous Schick testing and the performance of the Moloney test, using 0.1 cc. of diluted toxoid on the Schick positives. Nonreactors to the Moloney test may be given the regular dosage of toxoid. Reactors may be given toxoid cautiously in divided doses. Some authorities feel that such reactors have some immunity and that they will receive sufficient stimulus from the Schick and the Moloney test alone.

The importance of reimmunization at some time after the primary immunization is apparent. The dose required is often exceedingly small. The Schick test contains 1/1500 as much antigen as is in the same volume of toxoid yet it may have a booster effect. Booster doses of toxoid may raise the antitoxin titer to several thousand times the minimum necessary for protection. However, the method is not reliable for immediate protection following exposure to diphtheria since an adequate response may require a week or more. For routine maintenance of group immunity, however, it seems to be an advisable procedure in most areas of this country due to the low incidence of diphtheria.

The immunization of infants against diphtheria is done after 6 months of age due to the inherited passive immunity which persists for that length of time. But with the increasing number of non-immune
mothers, many infants are being born unprotected. This is a grave
danger since in infants diphtheria can be rapidly fatal. Efforts at ante-
natal immunization of Schick positive mothers so far have failed to meet
the problem due to the short duration of the transferred immunity in the
infant.

**Tetanus**

Tetanus has always been a serious menace to war casualties, but even
under the conditions of Western civilization in peace time, the possi-
bility of its occurrence must constantly be borne in mind. Adequate
cleaning and débridement of wounds remains the first defense against
tetanus. Treatment of wounds cannot be relied upon to prevent all
cases, however, for as many as 50% of cases may not be traceable to a
known injury, and many other cases follow neglect of such minor in-
fecions as those produced by a splinter. Since the tetanus bacillus is
found even in city streets, the possibility of infection with this organism
is ever present.

Until recent years reliance has been upon the prophylactic use of teta-
nus antitoxin. Occasional failures were noted following its use in World
War I, as well as in civilian use for many years. Thus, results from anti-
toxin are unreliable, the more so because tetanus infection may exhibit
a prolonged time lag between its introduction and its activation. More-
over, disadvantages of antitoxin are not limited to its undependability.
The wound may be slight, or even unnoticed, a person may be allergic, or
may have had serum before with resulting serum sickness.

Tetanus toxoid as an active immunizing agent obviates these objec-
tions. Its capacity to produce presumably protective serum antitoxin
levels in human beings is generally accepted.

**Number of doses required.**—One dose produces almost no detectable
immunity but prepares the subject to react effectively to subsequent
doses. Acceptable results are obtained by the administration of 3
doses of fluid toxoid or 2 doses of alum ppt. toxoid.

**Choice of interval between doses.**—For satisfactory results, successive
doses, at least 2 weeks apart, and preferably 4 weeks apart, are necessary.
Excellent results are achieved even with intervals as long as 2 years be-
tween doses of alum ppt. toxoid. The limit to such extended intervals
appears to be determined only by the period during which one can afford
to wait before obtaining adequate immunity.

**Choice of product.**—The principal advantages and disadvantages of
each form of tetanus toxoid are essentially the same as those pointed out
above for diphtheria toxoid. The use of alum ppt. toxoid by the U. S.
Navy and fluid toxoid by the U. S. Army during the war should provide
an unparalleled basis for comparison between the two.

**Response to primary immunization.**—Practically all workers have ob-
served marked variation in individual responses to primary immunization and have found occasional subjects in whom no detectable response appeared. In general, though, the antibody titer following primary immunization rises slowly to a maximum and then falls, at first rapidly, and later more slowly. Obviously, the interpretation of results depends considerably upon the interval chosen for the test. The interval between completion of immunity and the development of presumably protective antitoxin titer has been variously observed but significant levels occur within 2 weeks. The effective level; i.e., number of units of antitoxin in the blood, has not yet been established.

**Clinical evaluation.**—Massive clinical experience, although not correlated with serum antitoxin levels, has provided extensive statistical material for evaluating the efficacy of toxoid. Among over 10,000,000 soldiers in the U.S. Army in World War II, there were only 3 known cases of tetanus in soldiers who had the full course of immunization. The British had less perfect results but they omitted the booster dose after injury and relied on antitoxin.

On receiving a booster dose of toxoid, a previously immunized person exhibits a marked and rapid rise in serum titer. Hence, it has been generally advocated in this country that booster doses be given periodically to restore the immunity level, and also after injury to produce a maximal antitoxin level at the time of greatest danger of toxin absorption. The booster effect of injury is uncertain. So, until we have a satisfactory test for antitoxin level in the blood, the booster dose should be used following known injuries and to ward off the tetanus infections that can occur after unnoticed injuries. The efficacy of the booster dose does not appear to decrease as the interval between it and the primary immunization increases.

**Active-passive immunization.**—No clear-cut answer has yet been given to the dispute regarding combined active and passive immunization. For an injured unimmunized person exposed to tetanus, some claim both active and passive immunization should be given as is done in the Army. Others say the presence of antitoxin inhibits the effect of toxoid.

**Allergic reactions** have been reported occasionally with both fluid toxoid and alum ppt. toxoid but they have been few even in known allergic persons.

**Indications for immunization.**—The indications for the employment of tetanus toxoid have been well summarized as follows: in allergic persons or those with known sensitivity to horse serum; in farmers, hostlers, veterinarians, and others experiencing relatively frequent opportunity for contamination of wounds with tetanus spores; and by and large in children, among whom the incidence of infected wounds is high and many
unnoticed infections may result in tetanus. The combination of tetanus toxoid with diphtheria toxoid for immunization of children, therefore, appears wise not only in private practice, but also as an adjunct to diphtheria control programs.

The best type of schedule might well be adopted from that of the U. S. Army: primary immunization with 2 doses of alum ppt. toxoid or 3 of fluid toxoid at intervals of 1 month or longer, followed by at least 1 recall dose 6 to 12 months later and another recall dose after any injury of the sort that is known to involve the risk of tetanus infection. The available evidence suggests that active immunity is acquired within 2 weeks after the primary immunization is completed. The practice of administering prophylactic antitoxin routinely following accidents or injuries will have to be greatly modified in civilian practice. When such injuries occur to persons who are known to have been actively immunized, such as veterans of World War II, emergency prophylaxis should be obtained by administering a booster dose of toxoid.

**Pertussis**

Although infant deaths decreased 70% in the last 40 years, pertussis remains the most frequent cause of death among the acute contagious diseases of early childhood. Concentration of deaths in the first 2 years of life, especially under 6 months, is the same throughout the United States. In Massachusetts, 1924-'43, 58% of all deaths from pertussis occurred in the first year of life, and 84% in the first 2 years. Furthermore, in older children, the disease is frequently prolonged and debilitating. Hence, there is ample justification for control by immunization.

It is now possible to produce vaccines that in most studies reported protected a large majority of the persons immunized. The development of pertussis vaccine up through 1942 has been reviewed by Lapin, Felton, and Willard. With few exceptions the studies reviewed have demonstrated in large groups of children that the communicability rate of pertussis in persons vaccinated with seventy to one hundred twenty billion killed whole virulent pertussis bacilli is much less than the expected rate as determined by experience in unvaccinated children. Evaluation also shows that fewer severe cases occurred in the vaccinated.

Undoubtedly, there is considerable room for improvement in pertussis vaccines and vaccination. The protection rate, though it may be highly satisfactory from an epidemiological point of view, is not entirely so to the practicing pediatrician. The doses, 3–5 in number, have been large, and there has been a high incidence of local and generalized reactions. There is no proof, but the supposition is reasonable that the interval between doses can be increased from 2 to 4 weeks with better results.

Alum ppt. pertussis vaccine was introduced several years ago. Use
of aluminum hydroxide absorption has recently been reported and may prove to give fewer reactions.

Combination of pertussis and other vaccines was first suggested by Bordet ten years ago. We know that two antigens exert no mutual interference in animals or man as shown by antibody response. Kendrick and Sauer used alum ppt. combined pertussis vaccine and diphtheria toxoid and got protection against both. Various investigators have combined tetanus toxoid with the other two. Lapin and others now feel that best results (judged by laboratory tests and fewest reactions) are obtained by the administration of the pertussis vaccine alone and the combined toxoids as separate injections either concurrently or later; triple vaccines give many severe reactions and aluminum abscesses. The combined irritations of pertussis vaccine, alum, and toxoid tend to give a high incidence of local inflammatory reactions and abscesses. Hamilton and Knowf recently reported on a fluid triple preparation, giving excellent results and few reactions. However, Lapin and others prefer to give pertussis vaccine early, and combined diphtheria and tetanus toxoid later when a better response is probable.

Use of a booster dose is theoretically correct but not yet well tested. It does give a good antibody response and may protect when given immediately after exposure. On the other hand, a primary vaccination is probably of little value after exposure.

In young infants protection is less satisfactory in the first half of the first year (Sauer). Sako—on 4,000 infants less than 3 months of age reported the communicability rate in family exposures of only 19% in contrast to one of 92% in a control group. His results appear to justify immunization at an earlier age than is customary.

As to immunization of pregnant mothers (Cohn, Scadron, and Kendrick), antibody titers obtained in infants and mothers suggest that some immunity is induced by this method.

**Scarlet Fever**

There is general agreement that streptococcal toxin prepared, standardized and used according to the methods prescribed by the Dicks prevents the development of clinical scarlet fever in a great majority of persons exposed. It has abolished scarlet fever among nurses in communicable disease wards. Graham reports that follow-up Dick tests were negative in 86% of 50 private patients tested five to ten years after immunization and in 84% of thirty subjects 10 to 15 years after inoculation. Little reported 63 cases in 6,982 immunizations over 7 years, as compared to 915 cases in 8,063 unimmunized giving attack rates of 0.9 and 11.3, respectively.

Such an effective procedure would have been accepted long ago if it
did not have definite drawbacks. Foremost among these are the frequency and severity of the reactions produced by the dosage of the subcutaneous injections of toxin recommended by the Dicks, which are usually 650, 2,500, 10,000, 30,000, and 100,000 to 120,000 Skin Test Doses at weekly intervals. There is still, as Anderson stated, surprising unanimity of opinion regarding the severity of reactions to toxin injections, most observers mentioning severe reactions in as many as 10 or 15% of cases. Reactions include nausea, vomiting, fever, and a rash. It is difficult to justify the widespread use of a procedure that may cause reactions such as those described. Moreover, there is considerable doubt whether the scarlatinal rash is produced by only one antigenic type of toxin. Considering all factors, routine immunization is inadvisable until a more suitable antigen is found. Physicians, nurses, and ward attendants who may contact scarlet fever need immunization. Also, it is useful in military establishments or for civilians in areas where scarlet fever is widespread and severe. Many attempts have been made to find a better antigen, modifying the dose, and administration route, (intranasal, intracutaneous, oral). Attempts have been made to purify the crude toxin, and alum precipitation has been tried.

**Typhoid Fever**

Immunization against typhoid fever is not recommended today for the general population in most areas of the country. However, in some rural areas, particularly in southern states, insanitary conditions favorable to frequent occurrence of the disease still prevail. In such areas general typhoid vaccination programs are carried on. In times of floods and other disasters that endanger water supplies in any area, vaccination of the general public is warranted even though protection will be only partial. The same is true for family contacts of cases of typhoid fever. Immunization against typhoid fever affords a marked but not absolute degree of protection, as has been repeatedly shown in controlled studies. There are numerous reports of typhoid occurring in immunized persons, such cases often being atypical in nature.

Reactions to typhoid vaccination are often generalized and severe and constitute a serious objection to its use. A purified typhoid antigen free of the extraneous substances present in the whole bacteria, if produced, might aid in the elimination of reactions. The immunizing antigenic substance, a polysaccharid with immunizing potency several thousand times greater by weight, is effective and is less toxic. Its use awaits time to prove its preferability over the old time-tried vaccine.

The dosage of the ordinary vaccine is 0.5 cc., 1.0 cc., and 1.0 cc., at weekly intervals.

Immunity can be measured by agglutinin titre or by the mouse pro-
tection test. Re-immunization repeating the full dosage at 3-year intervals was formerly practiced. Now tests of immunity show that a single dose is sufficient using 0.5 cc. subcutaneously, or 0.1 cc. intradermally. For a high level of immunity, such booster doses are required annually but good results can be obtained from a single dose after a period of years.

Clinical evidence of the efficacy of the paratyphoid components in preventing para A & B fevers, however, has not been established on as sound a basis as has been done for typhoid vaccine.

EL PAPEL DE LAS INMUNIZACIONES EN EL PROGRAMA DE SALUBRIDAD (Sumario)

Describense a continuación los puntos más salientes en el control de las enfermedades transmisibles, tales como viruela, difteria, tos ferina, tétanos, fiebre escarlatina y tifoidea.

Los fracasos en la vacunación contra la viruela se atribuyen a (1) grandes intervalos entre vacunaciones, (2) uso de vacuna impotente, (3) técnica de vacunación defectuosa, (4) interpretación incorrecta de los resultados de la vacunación.

En la inmunización contra la difteria, menos de dos dosis del toxoide precipitado en alumbre o tres de toxoide fluido administradas a intervalos de por lo menos tres semanas, son insuficientes para obtener inmunidad sostenida. La reinyunización (dosis de sostenimiento) en fecha posterior, es importante. Debido a las posibles reacciones del toxoide, muchos prefieren la antitoxina-toxina para los adultos. La inmunización de los niños debe realizarse después que han cumplido seis meses de edad.

El toxoide tetánico ha reemplazado en gran parte a la antitoxina tetánica. Para obtener inmunidad efectiva se necesitan tres dosis de toxoide fluido a dos de toxoide precipitado en alumbre, a intervalos de 2 a 4 semanas entre dosis, recomendándose una inyección de sostenimiento administrada periódicamente o después de una herida.

La vacuna contra la tos ferina es efectiva, a pesar de que aún existe terreno para mejoramiento. Se necesitan de tres a cinco dosis y las reacciones son frecuentes, pero el empleo de la absorción con hidróxido de aluminio hace esperar reacciones menos frecuentes.

La toxina estreptocócica, adecuadamente preparada, crea una protección relativamente alta contra la fiebre escarlatina, pero las reacciones graves no son corrientes. No se recomienda la inmunización rutinaria hasta que se halle un antígeno más adecuado.

Al estudiar la fiebre tifoidea, el A. no recomienda la inmunización general de toda la población. Sin embargo, en zonas rurales, especialmente en el Sur y durante inundaciones y desastres, la inmunización está decididamente indicada. Se recomiendan tres dosis de la vacuna corriente de 0.5 cc., 1.0 cc., y 1.0 cc. a intervalos de una semana. Una dosis de sostenimiento de 0.5 cc., administrada anualmente, mantiene un alto grado de protección.