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COMBINED PROPHYLACTICS*

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The world literature on immunization is vast, and practitioners are confused by the wide range of prophylactics now available and by the contradictory advice of experts. Unfortunately, proposals which are immunologically ideal are not always considered administratively practical. In this paper I shall try to present the underlying principles of prophylactic immunization from birth onwards, but I wish to make it clear that my views and those of my colleagues do not coincide with official or even generally accepted opinion in either Great Britain or the U.S.A. Mention is made of the trend of official procedure in both these countries, but I have deliberately refrained from citing Canadian practice, except in one particular, because it will be discussed by other speakers. Combined prophylactics reduce the formidable list of inoculations hitherto advised, but such mixtures must be properly made and used so as to ensure that there is no material loss of antigenic efficiency.

I shall first review briefly inherited immunity against common infections, as this has an important influence on the time schedule of inoculations. (For an extended survey and references, see Parish (1951).)

Inherited Immunity

Diphtheria.—Many babies are immune at birth, since maternal immunity is transferred passively via the placenta. The amount of circulating antitoxin, which can be measured in the cord blood, varies within wide limits, but may be sufficient to interfere with active immunization. The rate of disappearance of this maternal antitoxin has also been measured (Barr *et al.*, 1949, 1950). Although babies have been given toxoid soon after birth, it is advisable to wait till the elimination of maternal antibody has proceeded for some months, when there is less likelihood of interference with the antigenicity of the prophylactic.

The general rule in other diseases besides diphtheria is that antibodies, when present in the maternal circulation, are transferred to the offspring and then gradually lost.

Tetanus.—In Great Britain babies are unlikely to have placentally transmitted tetanus antitoxin in their blood at birth, because few British mothers, except those who have served in the Forces, have been actively immunized, and, moreover, there is no natural immunity to tetanus. As in other infections when there is no reduction in responses by maternal antibody, active immunization is feasible during the early weeks of life.

Whooping-cough.—This is most dangerous in the first year, especially the first six months, and early active immunization is therefore extremely important. Although agglutinins and complement-fixing substances pass freely from mother to child via the placenta, evidence of the transfer of some immunity in the sense of lower susceptibility is less well established than in diphtheria, partly because protective antibodies are difficult to measure. Again, while the incidence of pertussis is lower in the early months of life, this is partly due to less risk from exposure to infection.

Tuberculosis.—Little or no immunity appears to be inherited, and the young child is accordingly readily infected. The timing of B.C.G. vaccination comes within the scope of this communication.

Smallpox.—The blood of the newborn baby has approximately the same content of specific antibody as that of its mother. Vaccination may fail to "take" in early life until some elimination has taken place.

Poliomyelitis.—Once again, the principle of antibody transfer and elimination applies. In this connexion one reason why combined immunization against whooping-cough, diphtheria, etc., has been advised in the first six months is that the chances of an associated poliomyelitis are lower during this period (see below).

Immunization in the First Six Months

Smallpox

In preparing a programme of inoculations, the first prophylactic to be considered is smallpox vaccine, although this has only a restricted use as a combined antigen. According to British opinion, primary vaccination against smallpox should ideally be carried out when alimentary equilibrium has been established, possibly during the third month or a little earlier, although the Ministry of Health (1952) considers that "probably the best age in a thriving infant is about 4 months." On account of the possible danger from certain complications of vaccinia, the date selected should also be about three weeks—a working compromise—before the start of a course of, say, diphtheria-tetanus-pertussis (or, triple) prophylactic. But when there is a special risk of smallpox, vaccination is done at once, even before the second month. Primary vaccination "at about the third month of age" is also recommended officially in the U.S.A. In certain parts of the world, where the available health services are limited, combined yellow fever and smallpox vaccination may be performed, although this method is not advised by the Ministry of Health. In French Equatorial Africa the Dakar mouse-

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brain yellow fever vaccine, mixed with smallpox vaccine, is often administered by scarification.

In the event of a first attempt at smallpox vaccination being unsuccessful, revaccination should probably be done after the close of the primary course of triple prophylactic, say, at the sixth or seventh month, when interference from maternal vaccinia antibody should be greatly reduced (Bousfield and Holt, 1954).

There are other circumstances in which primary smallpox vaccination might be carried out at a time other than the early months of life. Postponement is necessary in the event of severe eczema or other skin disease, constitutional disturbance, and contact with sufferers from skin lesions or other infections. All routine infant vaccinations and combined immunizations may be discontinued for a time by the local health office on account of the local prevalence of poliomyelitis. Further procedure in every case will depend on circumstances, and there can be no hard-and-fast rule about resumption.

I have gone into considerable detail over smallpox vaccination because, in the opinion of medical officers of the Ministry of Health, the deplorably low number of infant vaccinations in England and Wales must be increased quickly, and there must be no set-back from "accidents." It is therefore emphasized in Great Britain that, wherever possible, three weeks should separate a vaccination from all other inoculations (yellow fever vaccine, triple prophylactic, etc.) in order to reduce the possibility of untoward effects that might be ascribed to, or aggravated by, the administration of several antigens at the same time.

Whooping-cough, Diphtheria, Tetanus

Early protection against whooping-cough is of course much to be desired, and the present trend is to employ combined immunization right from the first injection, instead of giving consecutive courses of separate prophylactics—a much more troublesome procedure. In Great Britain clinical trials with mixed antigens are now in progress under the auspices of the Medical Research Council and the Department of Health for Scotland. Pending the results of these investigations, the commencement of a primary course of diphtheria-pertussis or diphtheria-tetanus-pertussis prophylactic may be advised at the third or fourth month (see also Parish *et al.*, 1954). In younger babies, interference with diphtheria immunization would be more likely to result from neutralization of some of the diphtheria toxoid in the prophylactic by maternally conferred antitoxin, and this would also upset the balance of the prophylactic (Barr, 1953). Triple prophylactic is preferred, as it ensures active protection against tetanus without additional inconvenience to either doctor or patient. Three doses may be given at intervals of four weeks.

The diphtheria-pertussis and diphtheria-tetanus-pertussis prophylactics now used in Great Britain do not contain alum, because there is some reason to suspect that the adsorbed type of combined prophylactic, with a pertussis constituent, may carry a somewhat greater risk of being followed by an associated poliomyelitis. Purified diphtheria and tetanus toxoids are preferred in the British preparations, formulae for which include the following:

Purified diphtheria toxoid ..	25 Lf	} in each ml.
<i>Haemophilus pertussis</i> ..	20,000 million	
or		
Purified diphtheria toxoid ..	25 Lf	} in each ml.
Purified tetanus toxoid ..	5 Lf	
<i>Haemophilus pertussis</i> ..	20,000 million	

In connexion with the general question of the administration of prophylactics to young babies, the first dose should

include a large amount of diphtheria toxoid, because the larger the dose the less the possible interference from maternal antitoxin and the better the response.

As already mentioned, health officers may advise the cessation of all immunization procedures during periods when poliomyelitis is prevalent. Secondly, whenever injections are given, the deep subcutaneous route of injection is often preferred to the intramuscular in order to reduce the risk of poliomyelitis. Other circumstances may of course arise which make it inadvisable to use a combined preparation: the ban may not extend to all the constituent antigens but only to the pertussis vaccine. The reason for this differentiation is that whooping-cough vaccination causes more trouble on the whole than diphtheria immunization. Accordingly, when there is a history of convulsions in the child or the family, or a severe reaction after a previous injection, it is sometimes decided to inoculate the infant with diphtheria prophylactic alone. Perhaps children with a recent history of respiratory or other infection, or of contact with such diseases, should also be excluded for a time from pertussis vaccination. These precautionary measures are directed against the development of the extremely rare cerebral "accident" or encephalopathy, manifested by convulsions and other serious nervous symptoms coming on within some hours of injection. (The aetiology of this sequela is obscure; certain cases could probably be ascribed to the accidental seepage of a particular antigen from the injection site into a venule.) However, while ailing babies should not be injected, postponement of the course may lead to children being overlooked indefinitely and running the risk of infection in later years—a risk much greater than that incurred from inoculation.

Sometimes, when whooping-cough vaccine is thought to be contraindicated, a diphtheria-tetanus prophylactic may be substituted. Even when this type of prophylactic contains alum, it probably does not carry a greater risk of associated poliomyelitis than diphtheria prophylactic A.P.T. (alum-precipitated toxoid) or P.T.A.P. (purified toxoid, aluminium phosphate). So far it is combined prophylactic containing pertussis vaccine in addition to alum which is in disfavour in Great Britain on account of associated poliomyelitis. Peach and Rhodes (1954) failed to show an association between recent inoculation and paralytic poliomyelitis in the cases admitted to the Hospital for Sick Children, Toronto, and they ascribe this failure to the use in Canada of an alum-free antigen, diphtheria fluid toxoid combined with pertussis vaccine and tetanus toxoid, which is given subcutaneously rather than intramuscularly. In contrast to the British and Canadian practices of avoiding alum in such mixtures, "an alum adjuvant pertussis vaccine mixed with diphtheria and generally tetanus toxoid . . . is commonly used in the United States for simultaneous immunization against all three diseases" (American Public Health Association, 1955).

Finally, a special plea is made for the active immunization of allergic children, for whom the emergency use of diphtheria or tetanus antitoxic serum would be very undesirable. In almost all cases toxoid preparations can be injected in early life without untoward effects, although it is prudent to try a small detector dose in the first instance. Many practitioners would select a combined diphtheria-tetanus prophylactic (adsorbed) for this work, instead of one containing pertussis vaccine in addition. If allergic children are to be inoculated against pertussis, rather more caution is advised, but the trouble involved seems to be justified, as immunization (if it can be achieved) is always preferable to infection.

Tuberculosis

B.C.G. vaccination may interfere with responses to other prophylactics, and it is undoubtedly a wise policy in our present state of knowledge to avoid the unnecessary use of B.C.G. In Great Britain the risk of children becoming infected with tuberculosis is very small in most areas, and mass B.C.G. vaccination is not required. The vaccine is rightly available, however, for the contacts of known cases

of tuberculosis. According to Heaf (1955), smallpox vaccination should be done first, separated by at least three weeks from B.C.G. vaccination. It is not known whether tuberculin allergy would develop fully if the first injection of diphtheria-tetanus-pertussis prophylactic were administered about three weeks after smallpox vaccination, as is often the case, and if B.C.G. were given at the same time.

A more serious matter is the risk of interference from repeated doses of B.C.G. The oral route is much used in South America, and Heaf (1955) states that it is high time it was tested in Great Britain. De Assis (1953) gives 100 mg. of B.C.G. orally during the first week of life, followed by similar doses at monthly intervals for three to six months. Sayé (1953) revaccinates contacts for six months with 100-150 mg. weekly, fortnightly, monthly, or every three months, according to the degree of exposure to infection. It is conceivable that this procedure might considerably weaken the responses to other antigens given towards the end of the period.

The Second Six Months

Many babies whose immunization programme has started early do not require any further injections in the second half-year. However, it is sometimes recommended that if the primary course of triple prophylactic is begun at the third month, a first boosting dose could with advantage be given about the first birthday; this dose should not be postponed too long, although in practice it is often deferred until the fifteenth month or later.

Notes on Official Policy in the U.S.A.

At this stage it might be useful to cite the procedure officially recommended for the first year or so of life (American Public Health Association, 1955):

"At 2 to 6 months of age two adequate doses of diphtheria alum toxoid alone or combined with tetanus toxoid, 4 to 8 weeks apart; or three doses of combined pertussis vaccine and diphtheria toxoid (with or without added tetanus toxoid) administered at 3- to 5-week intervals; or 3 doses of fluid toxoid. Whether with toxoid alone or combined, the basic course of inoculations must be reinforced by at least one recall or 'booster' dose within 3 to 12 months. Reinforcing doses are essential in pre-school life, desirable on entrance to school, and elective through school life and early adulthood. Where protection has been neglected in infancy, the program should be carried through as soon as the opportunity arises."

My colleague, Mr. A. T. Glenny, has discussed these American recommendations with me, and permits me to state his views. In the first sentence of the above quotation, "adequate" is the operative word. An "adequate" primary course should protect all except absolute immunological "freaks" for a year or so, but a reinforcing dose given about six to nine months—that is, not three months, which is rather soon—after the close of the primary course would carry the children on until school entrance at about 5 years. The sentence about further reinforcing doses "on entrance to school, and elective through school life and early adulthood" rather suggests that too many injections are being contemplated. Antitoxin tests carried out on a big scale would probably show that the pre-school injection would suffice until old age. If it does not, this might mean that the primary dose was not "adequate."

Notes on Official Policy in Great Britain

Many children are primarily immunized with pertussis vaccine between the second and fifth months, and with diphtheria P.T.A.P. or A.P.T. between the eighth month and the first birthday; the latter procedure is still the official recommendation of the Ministry of Health in respect of diphtheria immunization. Nevertheless, combined prophylactics are being used increasingly, and, after further experience has been gained, both in the laboratory and by means of field trials, are likely to be included in officially approved schemes.

There is some concern at the Ministry over any mass immunization schemes, which include the administrative task of ensuring that children primarily immunized in early

infancy receive early boosting in addition. The Ministry also wishes to avoid interference with smallpox vaccination, which should be carried out about the fourth month. It has therefore been suggested that combined immunization (diphtheria-pertussis) might be deferred to the end of the first year, and then be carried out on as large a scale as possible in order to give adequate protection during the years of maximum danger from diphtheria. This plan should have an indirect effect on the incidence of whooping-cough, as well as diphtheria, during the first year, because it reduces the incidence of both diseases among the older children who convey infection to their homes. The Ministry's suggestion has the administrative advantage of obviating all boosting doses in the intervening years before school entry.

As might perhaps be expected, these views, which differ widely from those held in the U.S.A., have not received universal acceptance in Great Britain, although it seems probable that practical considerations may lead to the adoption of a simplified procedure of this kind.

It is suggested as a compromise between opposing points of view that all infants might be "called up" at the age of 1 year as part of a national campaign, and that those who have already received a primary immunizing course at welfare clinics or elsewhere should be given a boosting injection only, whereas the others would receive three doses.

One of the advantages of making an early start with immunization is that many babies are more readily available during the early months of life at welfare clinics, which they are attending for other purposes. A primary course of combined prophylactic begun at 3 to 4 months might therefore be more convenient administratively than one begun at 6 months, which would be more effective immunologically. In a few babies ("failures") high passive titres at the earlier age would prevent the production of much circulating antibody, but these babies would develop sufficient potential immunity to enable good responses to follow the injection of a boosting dose given some six months later.

Age Period 1 to 5 Years

With modern whooping-cough vaccines injected as separate antigens or in mixtures there is little or no evidence of waning immunity two to three years after a primary course of three doses spaced by at least four weeks. Many babies who have had a first boosting injection around their first birthday or a little later probably do not receive another pertussis injection at all. Those who are not so protected should receive their first boosting dose (preferably of a triple prophylactic if this type of preparation was used for the primary course) at the earliest opportunity—certainly before entry to kindergarten or school. "About the age of 3 years" is sometimes advised as a suitable time for boosting: this is somewhat early for children who have already had a reinforcing dose, but very late for those who have not. In any event a reinforcing dose against diphtheria is given at the time of school entry (see below).

A boosting dose, either of the triple prophylactic or of the separate antigen, would also be needed on exposure to diphtheria or whooping-cough or after dirty cuts, unless a full primary course and a reinforcing dose have been given and the last injection has been less than, say, 18 months before. Yet another factor which should influence the decision would be the availability of the child's permanent record card of inoculations, simple in form and accurately kept; and here I would urge the practice of the safeguarding by parents of essential records, which must be readily accessible when required. A more detailed record for administrative purposes is quite rightly retained at the doctor's surgery or in the clinic—in an emergency conceivably hundreds of miles away. The advantage of some duplication of records is thus obvious.

School Age: 5 to 15 Years

The start of school life affords an opportunity for reviewing inoculation histories and making good any omissions. In this connexion there is at present considerable anxiety

in Great Britain over the comparative neglect of diphtheria immunization in the early years of life, notwithstanding the efforts of doctors and continued publicity. To give an example of the problem, the latest figures for London (L.C.C., 1953) show that the proportion of immunized children under 5 years of age had fallen to 51.5% in 1953—its lowest level since an intensive immunization campaign began; the need for an immunization drive in the schools is obvious.

When children have already received primary diphtheria immunization, 0.2 to 0.5 ml. of P.T.A.P. or A.P.T. is often given for boosting on school entry in Great Britain; as is shown below, diphtheria-tetanus prophylactic might be preferred. Further reinforcement may be given some four years later, and, in the case of P.T.A.P. or A.P.T., 0.2 ml. is recommended. If the milder prophylactic T.A.F. (toxoid antitoxin floccules) is selected, the dose for boosting should probably be 0.5 ml. At this point I should perhaps mention the Schick test, which is much less used than formerly, especially for children under 10 years of age. In older persons in Great Britain it has a subsidiary function as a detector of sensitivity to toxoid and thus replaces the Canadian Moloney test.

Whooping-cough immunization is not worth while for children in this age period; only 3% of the deaths from whooping-cough are in persons over 5 years of age. This means that combined prophylactics with a pertussis constituent are no longer required and diphtheria-tetanus-pertussis prophylactic, used in infancy, may sometimes be followed by a boosting dose of a combined diphtheria-tetanus prophylactic on school entry. (Whether an adsorbed prophylactic is necessary for reinforcing is debatable.)

When children have not received diphtheria or tetanus toxoid previously and have not had diphtheria, they may be given three doses of diphtheria-tetanus prophylactic (adsorbed) at intervals of four to six weeks as a primary course. Many more children are now presented for immunization against tetanus, especially in America, and this practice should be extended.

A warning is necessary when it is proposed to inject combined diphtheria-tetanus prophylactic into persons who already have some active immunity to diphtheria but not to tetanus. Children primarily immunized with diphtheria or diphtheria-pertussis prophylactic come into this category. On the basis of experimental work in animals, Barr and Llewellyn-Jones (1953b) and Barr (1953) have suggested that interference might lead to an unsatisfactory response to the tetanus component, unless the injection of the mixture is preceded by one dose of tetanus toxoid four weeks earlier. This variety of trouble with immune responses would be obviated by using triple prophylactic from the start of immunization in infancy.

It is impossible to generalize on the question of the number of boosting injections necessary for lifelong immunity: whatever the type of prophylactic employed, so much must depend upon whether the primary course is "adequate." In the case of diphtheria, two doses are generally advised in certain countries, although some children receive three, the usual interval being two to four years. To-day, titres of circulating antitoxin are not as a rule boosted naturally by subinfecting doses of toxigenic diphtheria bacilli to the same extent as they were between the world wars, and artificial boosting is all the more necessary. But, as repeatedly suggested in this paper, the main factor in successful immunization is that the primary course must be "adequate," after which even a single reinforcing injection may be all that is required.

In the case of tetanus, toxoid may be injected for boosting at intervals of five years; and it is also given increasingly, instead of antitoxin, to actively immunized persons who have received dirty cuts.

Other Combined Prophylactics for Children

These include T.A.B. (typhoid-paratyphoid vaccine), T.A.B. and cholera vaccine, and T.A.B.T. (typhoid-paratyphoid vaccine and tetanus toxoid). A special dilution

of the first has been used for children by the British Army authorities, and the introduction of a special preparation of the last is under consideration.

T.A.B. vaccination is not usually recommended officially for children under 1 year of age. Nevertheless, as reactions are generally slight in very young persons, there appears to be no adequate reason for not giving them any benefit that may result from immunization. Children of all ages may therefore be given T.A.B. vaccine (or T.A.B. and cholera vaccine) in appropriate doses when required for countries where the enteric fevers and cholera are prevalent.

Immunization of Adults

Combined Immunization in the Armed Forces

Concerted efforts have been necessary in many countries to reduce the number of inoculations required under Service conditions. In the British Army all recruits are Schick-tested and the positive reactors immunized with diphtheria A.P.T. In France, Canada, and elsewhere, diphtheria antigens are no longer used separately in the armed Forces: a combined T.A.B.T. with diphtheria prophylactic (T.A.B.T.D.) is employed. Such mixtures usually contain rather small amounts of diphtheria toxoid, but it is noteworthy that British opinion is cautious about the use of this type of preparation in countries where many adults may be completely non-immune.

In the U.S.A. Edsall *et al.* (1954) and others have shown that, as expected, very small doses of purified diphtheria toxoid in combined preparations often produce considerable increases in antitoxin values. But, as my colleague, Miss M. Barr, has pointed out to me, while such doses play a part in the maintenance of diphtheria immunity, they are probably much too small for primary immunization; and yet they may be large enough to interfere with the tetanus and T.A.B. responses in those already immune to diphtheria. In these circumstances, as mentioned above, injection of the mixture might have to be preceded by a single injection of tetanus toxoid or of T.A.B.T. four weeks earlier.

The composition of T.A.B.T.D. presents a problem of exceptional difficulty; on account of the wide variation in the immunity state of Service entrants, some form of compromise would have to be adopted to meet the needs of the majority. The present proposals for the use of T.A.B.T. in the British armed Forces are to give two doses spaced by six weeks, followed by a third dose about nine months later. No decision has yet been taken about the frequency of boosting doses.

When T.A.B. vaccine and tetanus toxoid are mixed, the vaccine sometimes enhances considerably the response to the toxoid. Unfortunately this is not a universal finding, since with some mixtures the response to the toxoid is reduced after addition to the vaccine (Barr and Llewellyn-Jones, 1953a). The second consideration—namely, the influence of the toxoid on the vaccine constituent of various mixtures—is unknown: it is hoped that the antigenicity of the vaccine for man is not depressed. British Army pathologists have noted that the Canadian armed Forces have used T.A.B.T. (phenolized) since the early years of the 1939–45 war, apparently with complete satisfaction.

B.C.G. vaccination has been given to troops at the same time as the second injection of T.A.B.T. The timing is administratively convenient, although it involves the risk of some depression of the response to the B.C.G. The effects are being observed carefully, so that the schemes may be modified if necessary.

Combined Immunization of Civilians (Travellers and Others)

T.A.B. vaccination is sometimes required for travellers and also for nursing and other contacts who have been or may be exposed to enteric infection. T.A.B.T. or possibly a mixed T.A.B. and cholera vaccine will sometimes be used.

Yellow fever vaccination is of considerable importance to persons travelling to or passing through many countries. Immunization is sometimes produced by scarification with

the Dakar modified yellow fever virus associated with smallpox vaccine (see also section on Immunization in the First Six Months).

Summary and Conclusions

The formidable list of inoculations now considered necessary for immunization is reduced by combined prophylactics. Procedures for different age groups from birth onwards are discussed.

In the early months of life maternal antibodies transferred via the placenta may be present in sufficient concentration to interfere with active immunization.

Vaccination against smallpox should probably be done in thriving infants about the third or fourth month, preferably three weeks before other immunization is begun. Although diphtheria-pertussis or diphtheria-tetanus-pertussis prophylactics are not yet officially sponsored by the Ministry of Health, these preparations are being used increasingly: three injections at four-weekly intervals are given *subcutaneously*. B.C.G. vaccination in infancy has also been advocated (for contacts), but should not be given less than three weeks after smallpox vaccination. It is not known whether repeated doses of B.C.G. vaccine would interfere with the responses to other antigens.

Allergic children can usually be immunized in early life without untoward effects, although it is prudent to begin with small detector doses.

The official attitude to immunizing procedures in the U.S.A. and Great Britain is discussed. Proposals which are immunologically desirable are not always administratively practicable. It is suggested as a working compromise that there should be a general "call-up" of children at 1 year of age: those who have already had their primary combined immunization could be given a boosting dose, while the others would receive three doses.

The number of boosting injections necessary for life-long immunity largely depends on whether the primary course is "adequate" to confer a high degree of protection to all but exceptional individuals for at least one year.

Combined diphtheria-tetanus toxoid used as a boosting dose for schoolchildren may produce considerable diphtheria antitoxin but very little tetanus antitoxin if the children have already been immunized against diphtheria only. Methods are suggested for obviating this type of interference.

Adult immunization with combined preparations such as T.A.B.T.D. sometimes presents a difficult problem on account of wide variations in the immunity state of individuals. Alternative procedures are discussed.

Before a procedure is taken into general use, research is always indicated on the extent and duration of antibody responses. This information is obtained by examining representative blood samples.

Owing to the variety of immunization procedures now in use and the need for essential information being readily available in an emergency, a record card of inoculations should be kept by parents. This record is not intended to replace the more detailed information retained by doctors or public health authorities. Haphazard and unrecorded immunizations are to be deprecated.

I wish to thank my colleagues, Colonel H. W. Mulligan, Mr. A. T. Glenny, F.R.S., and Miss M. Barr, for much helpful discussion and constructive criticism. I am also indebted to Dr. W. H. Bradley, Ministry of Health, for a number of valuable suggestions.

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IMMUNIZATION OF BABIES WITH DIPHTHERIA-TETANUS-PERTUSSIS PROPHYLACTIC

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Although immunization of babies with combined diphtheria-tetanus-pertussis prophylactics has been practised in the U.S.A. and Canada for some years, it is only recently that such preparations have been used in this country.

This paper gives the results of immunization trials in which two triple prophylactics were used. Preliminary results were shown by two of us at the Royal Society of Medicine (January, 1954), and by one of us at the British Paediatric Association meeting (April, 1954). Both preparations contained, per ml., 60 Lf of purified diphtheria toxoid, 12 Lf of purified tetanus toxoid, and 4×10^{10} *H. pertussis*: in one, the toxoids were adsorbed on to aluminium hydroxide, and in the other no mineral carrier was present. These prophylactics are referred to respectively as the "adsorbed" and the "fluid" preparation. The dose injected into babies was in all cases 0.5 ml. The objects of this work were to determine whether satisfactory immunity could be established in very young babies given the first of a course of three injections of adsorbed prophylactic at the age of a week, and to determine the optimum age at which to begin immunization with the fluid preparation. The question of age at the time of the first dose is of special importance when combined prophylactics are used. Many babies in this country are born with circulating passive diphtheria antitoxin acquired by maternal transmission. The titre of this antitoxin is high enough, in some babies, to neutralize and interfere with the action of a dose of diphtheria prophylactic if this is given at an early age.

Active immunization against tetanus, however, is still very rare, and babies seldom therefore acquire tetanus antitoxin from their mothers. In order to obtain satisfactory immunity to both diphtheria and tetanus, in the great majority of babies, immunization should be started