

THE DEVELOPMENT IN A COMMUNITY OF
INCREASED DIPHTHERIA IMMUNITY
ARTIFICIALLY ACQUIRED.

Thesis for the Degree of M.S.

presented by

James S. G. Burnett

M.B., Ch.B., D.P.H.

ProQuest Number: 13849842

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 13849842

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

The development in a community of increased
diphtheria immunity artificially acquired.

1. The historical aspect of diphtheria immunisation.
2. The development of the local scheme of diphtheria immunisation.
3. The scheme in its maturity.
4. The present extent of artificially acquired immunity.
5. The history of local diphtheria mortality and morbidity and the influence on them of artificially acquired immunity.
6. The future policy.

FOREWORD.

The following thesis is based on the results of a scheme of diphtheria immunisation introduced into the Urban District of Chadderton in November 1936.

The actual scheme of immunisation may be divided conveniently into three phases, the preliminary enquiry and preparation of data in support of the scheme carried out by a locum tenens in 1935 and 1936, the obtaining of official support and sanction, the launching of the preliminary propaganda and the initial inoculation of the first batch of some eighteen hundred acceptances carried out in the winter of 1936-37 by my predecessor with the aid of temporary assistance to enable the large numbers to be dealt with rapidly, and the subsequent expansion and development of the scheme since my advent as Medical Officer of Health of the Urban district in January 1938.

In the last five years, with the exception of an insignificant number of children inoculated by local private practitioners using prophylactic supplied free by the local authority, the complete work

has evolved and been developed by a team of four nurses and one clerk as part of the multifarious duties devolving upon them during the period of the world's greatest crisis and without the ungrudging co-operation and unselfish loyalty of these women it is difficult to see how the present satisfactory position could have been achieved.

Chapter One.

The historical aspect of diphtheria immunisation.

Although it was in 1913 that active immunisation of humans against diphtheria was first carried out by Von Behring and his co workers¹ and reported first at the Wiesbaden Congress for Internal Medicine in April of that year the underlying principles had been known and had been undergoing development in the preceding twenty years. A great stimulus was however developed as a consequence and the reports of the German workers were followed in 1914 by published accounts of work in America carried out by Park, Zingher and Serota and during the war years considerable development of the method took place in America as a result of Park and Zingher's experiments.

In this country a report² of the Ministry of Health issued at the end of 1921 recorded the results of work carried out at Bristol and elsewhere. The author of the report, Dr. S. M. Copeman, appeared to take a very conservative view of the practical utility of schick testing and immunising for he stated that,

"in the light of experience of the working of the Vaccination Acts in this country it is clear that, even if considered desirable, no attempt at a general immunisation of the infant population would be feasible."

Evidence that this view was not unsupported at headquarters is contained in a foreword to the report by Sir George Buchanan who wrote that,

"it would be premature to advise that in English communities general immunisation of persons susceptible to diphtheria should be attempted on the New York scale."

This view received official blessing by implication in the Ministry of Health Memo 68/Med.³ which advocated immunisation among hospital staffs and in semi-closed communities such as residential schools. Apparently the native caution of the Senior Medical Officer responsible for the section on General Health and Epidemiology at the Ministry was less well developed in some of his fellow countrymen practising public health in Edinburgh for in that city not only was testing and immunising of fever hospital nursing and domestic staffs commenced in 1922 but a scheme to cover the general child population of the city was launched in 1923.⁴

The successful results obtained by the immunisation of Schick

positive cases in closed and semi-closed communities and the early success of the Edinburgh scheme together with those in several cities abroad led to a veering of official opinion from that previously expressed so that in the Report⁵ of the Chief Medical Officer of the Ministry of Health for the year 1924 it was suggested that the time was,

"ripe for considering the question of the desirability or otherwise of making ~~this~~ method of protection against diphtheria more generally available to the child population of this country."

The necessity for securing the co-operation of education and welfare authorities was stressed also.

The weight of accumulated evidence was now sufficient and in the next Annual Report⁶ of the Chief Medical Officer immunisation of the child population against diphtheria was boldly advocated and a "one shot" method of administration was prognosticated. This advocacy has been increasingly maintained each year. Though official support and encouragement, through the medium of the Annual Report of the Chief Medical Officer of the Ministry of Health, was now clear cut pronounced schemes were slow in developing and at the end of 1926 the central department was

aware of 51 local authorities who were "using the method in any way" whilst in the 1927 Report it was stated that only 29 local authorities were offering facilities for immunisation.

The Annual Report for 1927⁷ gives a statement on the general aspect of active immunisation against diphtheria which is still remarkably up to date and is well worth quoting in part.

"Natural immunity depends on repeated exposure to small doses of infection, not in themselves sufficient to cause an attack of diphtheria but sufficient to stimulate the production of antibodies. Over 90% of children from six months of age to five years are susceptible to diphtheria, but with increasing age this susceptibility diminishes, particularly among those who live in towns. Most adults are immune. Individuals vary in their capacity to acquire and retain immunity, both natural and artificial. Once acquired it is never wholly lost. Its protective power may decline, but the person who has once been immune still retains a power of rapidly developing antitoxin which will stand him in good stead should he ever be exposed to a dose of infection sufficient to cause symptoms of diphtheria. Artificial immunisation therefore, even though it may not in itself be effective for the whole period of life, will at least safeguard most children during these early years when diphtheria is most to be feared. - - - - - Not only are most

young children susceptible to diphtheria, but they are more liable than older children to take the disease in a severe form. Most deaths occur under the age of five. Inoculation should therefore be done at as early an age as possible. Parents are inclined to wait until their children reach school age, but by doing so they leave the child unprotected during the most critical years of its life. Although it may be most convenient to inoculate children when they first enter school, local authorities should endeavour to reach the child at an earlier age. - - - - -

Owing to the few months which must elapse from the time of inoculation until the child is sufficiently protected to resist an attack of diphtheria, this type of inoculation has no IMMEDIATE effect in checking an epidemic. It is certainly during an epidemic that parents are most concerned for the safety of their children, but if they are inoculated then it should be clearly explained that the protection will not be complete for several months. Every effort should be made to encourage immunisation at a time when there is no immediate fear of the children being exposed to infection."

There is little in these observations recorded fifteen years ago that needs amendment in the light of present day knowledge.

A point of some administrative importance⁸ was made also in this report in so far as indication was given that where necessary local authorities and welfare authorities could seek sanction to incur necessary

expenditure under S.133 Public Health Act 1875 and S.1. Maternity and Child Welfare Act 1918 respectively.

A fairly considerable impetus was given to the formation of local schemes of diphtheria immunisation by the issue of a new memorandum,⁹ by the Ministry of Health, in 1932 that again advised, in restrained language the mass immunisation of children. These recommendations included the carrying out of a preliminary Schick test and Moloney test, inoculation with three subcutaneous injections, at fortnightly intervals, of formol toxoid or of toxoid-antitoxin floccules followed two to three months later by a further Schick test. These recommendations had the merit of attempting to provide a standard method of carrying out the work though the memorandum itself denies any such motive and states that it would be premature to specify a standard method of immunisation for universal adoption. Nevertheless the method suggested whilst scientifically sound was doomed to failure as a practical means of carrying out mass immunisation owing to the number of visits entailed. A system that required an average of six visits per child inevitably resulted in a high

percentage of failures to complete treatment and demanded greater numbers of staff than most local authorities could afford to employ on the work.

As an example of the lack of standard procedure at this time it can be pointed out that in 1933 immediately after the publication of Memo. 170/Med. I was inoculating probationer nurses with toxoid antitoxin floccules three subcutaneous injections at fortnightly intervals without Schick testing and that during the winter of 1934-35 the department launched a scheme of mass immunisation of children using the same material and the same technique with the addition of Schick tests carried out both before and after inoculation. In 1935 on transferring to the service of another local authority I found in operation a scheme that utilised the older toxin-antitoxin mixture three subcutaneous inoculations at fortnightly intervals being given without Schick testing and on taking up duties in January 1938 in my present appointment I discovered a recently introduced scheme of mass immunisation of children that made use of, without Schick testing, alum precipitated toxoid two intramuscular injections at fortnightly intervals being given to children of nine years and over and one intramuscular injection only of 0.5 c.c. alum precipitated

toxoid to children under nine years of age.

In point of fact at the time of publication of Memo.170/Med. field experiments were being carried out with the new alum precipitated toxoid and for a time some workers hoped that successful immunisation by one injection of this material might be a practical proposition. Park in America reported ¹⁰ successful results from this method and quoted a Schick negative rate of over 90% whilst Murphy ¹¹ with a small series of cases obtained a Schick negative rate of 93% and Haine ¹² with a larger series obtained 91%. More will be said in the next chapter concerning these attempts to find a satisfactory one shot method of immunising children in large numbers.

References.

1. Banus, M.G. International Journal of Public Health. 1921, 11, p.520.
2. Reports on Public Health and Medical Subjects. 1921, No.10.
3. Ministry of Health. Memorandum 68/Med., 1922, p.7.
4. Robertson, Wm. Proc. Roy. Soc. Med., 1925, Vol. 18, 7, p.41.
5. On the State of the Public Health. 1924, p.61.
6. On the State of the Public Health. 1925, p.50.

7. On the State of the Public Health. 1927, p.35.
8. On the State of the Public Health. 1927, p.38.
9. Ministry of Health. Memorandum 170/Med., 1932.
10. Walker, A.A. J.A.M.A., 1934, Vol. 103, 4, p.227.
11. Murphy, W.A. The Medical Officer. 1935, Vol. 53, p.177.
12. Haine, J.E. B.M.J., 1935, Vol. ii, p.896.

Chapter Two.

The development of the local scheme of diphtheria immunisation.

It was then in February 1936 in this atmosphere of doubt and uncertainty that a report on Diphtheria & Immunisation was submitted to the Urban District Council of Chadderton by the then Acting Medical Officer of Health. This report¹ after discussing general measures for the control of diphtheria including the use of antitoxin in immediate contacts goes on as follows,

"Mass Immunisation. - The above procedure must not be confused with the administration of "Toxin-Antitoxin" which is used to produce a more or less permanent immunity, or at any rate, one which is sufficient to last through the entire school life period. This is given in two or three doses at weekly or fortnightly intervals and is followed by a Schick (control) test from three to six months later, and causes the blood of the recipient to gradually build up its own antidote, but has the disadvantage that during the initial phase, there is a slightly increased susceptibility, and therefore it should not be used during epidemic prevalence. Further, it has been found that those immunised by this method may still become "carriers," and even, it is thought, to a greater degree than if no immunisation had been performed. It is obvious, therefore, from the point of view of "mass

immunisation," that is the Public Health aspect, that unless the whole, or a very large majority (not less than 70%) are thus protected, the incidence of Diphtheria amongst the remainder may not be lowered, but increased. Half measures, therefore, may even be detrimental. On the other hand "mass immunisation," if complete, is the most scientific, potent and economical method of eliminating the incidence of this deadly disease to an almost negligible degree, and is strongly favoured by the Ministry of Health.

In Chadderton this would involve the immunisation of about 4,500 children (ages 1 to 14 years) but only with consent of the parents, and the establishment of an immunity clinic. In some districts the latter is augmented by a fee - subsidised panel of local practitioners, supplied with a free issue of Toxin-Antitoxin, the cost of which per head would be 6/- and would be only a little more than the present cost involved per head by swab taking (5/- per head, less 10% discount).

The almost complete elimination of the heavy Isolation Hospital bills and other present expenses as wholesale swab-taking would, in the long run, considerably more than offset the expense of the immunisation. But it must be remembered that it all depends on the consent of all the parents, or at least 70% of them otherwise additional expense would be involved for nothing. General experience tends to show that this consent is seldom very easy to obtain in sufficient numbers.

In Oldham where an immunity clinic has been established about

3,000 children only have been immunised out of about 23,000; i.e., about 12%. In Manchester nearly 30%, Denton 25%, Sale 20%, Stretford 30% have been immunised, in Middleton and Royton, nil. There is a small difference between the Diphtheria rates of Oldham and Chadderton, in favour of the latter, and the populations are similar and adjacent. Diphtheria rate per 1,000 for 1935, Oldham 1.62 and Chadderton 1.35.

It is unlikely therefore that any greater numerical success would be obtained in Chadderton, unless exceptional measures were taken involving considerable intensive publicity propaganda.

The whole question is one that requires serious consideration for if general, or mass, immunisation is once commenced it could not easily be abandoned, and therefore under the circumstances we are of the opinion that it would be wiser to leave the matter over until the appointment of a permanent Medical Officer of Health."

In August of the same year another report was presented by the newly appointed Medical Officer of Health and after preliminary propaganda a scheme of immunisation was inaugurated in November 1936. This scheme followed largely the usual lines of propaganda for similar schemes. The Medical Officer of Health in his Annual Report² to the Council for 1936 states that,

"a lecture was given in the Town Hall by the Medical Officer on

the 10th November, partly dealing with this subject. A pamphlet explaining the procedure, etc. was issued to every school child, with a form of consent. The mothers at the Welfare Centres were also given a pamphlet. Short talks were given to the parents at school and at the Centres, on the subject, by the Medical Officer."

The decision as to the material to be used, the dosage and its spacing must be examined in the light of the prevailing circumstances.

As far back as 1921 the "Secondary Stimulus Phenomenon" had been demonstrated by Glenny & Sudmersen³ and subsequently Glenny⁴ and others had shown that precipitated toxoid possessed a higher antigemic efficiency than toxoid alone apparently due to the continuously stimulating effect of the only slowly absorbed relatively insoluble precipitate. This view led some to suppose that the ideal of one shot immunisation had been achieved. The method was tried out with enthusiasm in America⁵ after Park in 1934 had claimed with this method Schick immunity rates of 90 - 95%. Schick immunity rates of 100% were claimed in America two months after inoculation with alum precipitated toxoid and in this country Murphy⁶ reported a Schick immunity rate of 93% in 131 children tested

within five months of inoculation and Haine⁷ later in 1935 reported a Schick immunity rate of 91% in 794 children nine weeks or more after inoculation. It is important to note that Haine in his article implies that the population tested was in the main exposed to diphtheria infection. Saunders⁸ also obtained satisfactory results at Cork but implied⁹ that the "primary stimulus" of Glenny and Sudmersen had been provided by natural infection in the past and that in his case the one shot injection might represent the secondary stimulus. Other workers in this country failed to confirm the good results earlier announced and the method never received general approval. In fact there was a sharp conflict of opinion and open disapproval of the method was made by writers of authority.^{10,11,12,13}

The decision reached in Chadderton was a curious one. It was decided to use one shot inoculation, 0.5 c.c. A.P.T. (Burroughs Wellcome & Co.) in all children under the age of nine years and in the case of older children to substitute two injections 0.1 c.c. and 0.5 c.c. of the same material with a fortnight intervening between the injections. This procedure was based probably not on any doubts as to the antigenic

efficiency of alum precipitated toxoid used with the one shot method but rather on a fear of reaction in older children and represents a belief in the efficacy of one shot inoculation with, in the case of older children, the use of Chesney's¹⁴ small primary "detector" dose as a means of controlling reactions. Schick testing was not carried out at any stage and the inoculation which was originally given subcutaneously, was given later, on account of a few troublesome local reactions, by the intramuscular route. A part time medical practitioner was employed for two months and completed immunisation in about fifteen hundred cases the remainder being inoculated by the Medical Officer of Health.

In January 1938 when I assumed duties in Chadderton as Medical Officer of Health a total of 1,815 children, of whom 207 were under five years, had been inoculated through the medium of the scheme and of this total 973 had received a "one shot" inoculation. Alum precipitated toxoid had been made available free to practitioners in the area on request but this facility had not been utilised to an appreciable extent.

References.

1. A Report of M.O.H. Urban District of Chadderton, 1935, p.14.
2. Annual Report of the M.O.H. Urban District of Chadderton, 1936, p.83.
3. Glenney, A.T. and Sudmersen, H.J. Jour. of Hyg., 20, 1921, p.176.
4. Glenney, A.T. Buttle, G.A.H. and Stevens, M.F. Jour. of Path. and Bact.,
34, 1931, p.267.
5. Walker, A.A. J.A.M.A., 1934, 103, 4, p.227.
6. Murphy, W.A. Medical Officer, 1935, 53, p.177.
7. Haine, J.E., B.M.J., 1935, 11, p.896.
8. Saunders, J.C. Medical Officer, 1937, 57, p.39.
9. Saunders, J.C. Lancet, 1937, 1, p.1064.
10. Chesney, Geo. Medical Officer, 1937, 57, p.229.
11. Bousfield, G. Medical Officer, 1937, 57, p.15.
12. Maurice-Williams, Dear, and Stewart, Medical Officer, 1936, 56, p.45.
13. Bousfield, G. Medical Officer, 1938, 59, p.5.
14. Chesney, Geo. Medical Officer, 1934, 52, p.5.

Chapter Three.

The Scheme in its Maturity.

A review of the scheme at the beginning of 1938 showed that, for the time being it was moribund. No literature or propaganda had been before the public eye for some months, no inoculations had been performed for about six months and there had been no Medical Officer for more than three months. The initial impetus, which had been so satisfactory, had, of course, subsided in the Spring of 1937 following the inoculation of the great batch of "initial consents" but the resignation of the Medical Officer of Health prevented the next steps being taken so that the fine enthusiasm obtained at the opening of the campaign was dissipated and lost. It was apparent that since the school population at this date just topped the three thousand mark then rather more than 50% of the school population had completed inoculations¹ whilst with regard to the pre school groups, of whom there were rather more than two thousand, only a small fraction had been treated. Unfortunately more than half of the total number had undergone one shot inoculation.

The following decisions were, in consequence, taken.

The one shot method of inoculation would be abandoned immediately and be replaced by a two shot method to be used exclusively namely, 0.1 c.c. A.P.T. (B.W. & Co.) given subcutaneously followed after an interval of two weeks by 0.5 c.c. of the same material. This decision was subsequently amended in 1939 to provide a four week's interval in the light of Jones'² work and the initial inoculation was doubled in quantity as experience showed that with the smaller dose the loss of inoculum from leakage back along the needle track could be, on occasion, proportionately very large.

Those children who had previously received a single inoculation of 0.5 c.c. A.P.T. should not meantime be reinoculated or Schick tested. It was felt that since enthusiasm for diphtheria immunisation had to be created afresh any attempt to introduce reinoculation would be bad propaganda at this stage of development and in any case the necessary medical assistance was not available.

The main propaganda should be concentrated on two main groups,

namely the one year and five year age groups with, of course, supplementary efforts to attract older school children at school clinics and younger children at welfare clinics. It seemed essential that the good relations existing between young parents and welfare staffs in an area where over 80% of the infants born attended a welfare centre at least once before reaching the age of one year should be exploited to the full and that the basis of any reasonable scheme should be the saturation of the earliest age group each year. Again the value of the school environment was already well established and it was fairly certain that with the co-operation of infant teachers the immunity of the entrants group could be raised to about 60% fairly readily.

Until greater numbers had been inoculated Schick testing neither before nor after inoculation should be contemplated.

These decisions were made operative immediately except that it was not possible to put into effect an intensive propaganda effort and during 1938 only 141 children were inoculated of whom more than one third were new entrants to school. Preoccupation with civil defence

organisation during 1939 prevented the major scheme being launched but head teachers of infant schools were twice invited to distribute literature to the parents of their scholars. As a result, out of 267 children inoculated in 1939, 132 were between the ages of 5 and 7 years. In this year also the birthday letter principle was adopted and though it produced a positive response of rather less than 10% in its first year it laid the foundation of the new propaganda effort.

In the late Summer of 1940 the likelihood of large numbers of children being required to spend many hours in overcrowded conditions in air-raid shelters forced the issue to the surface once more and the much delayed campaign was launched. Infant head teachers co-operated at the beginning of the Autumn term by distributing leaflets and forms to all the children in their departments. A personal appeal was made to parents accompanying children at routine medical inspection and short talks were given at welfare centres. A greatly increased response was obtained from parents and whereas only 30 children had completed inoculation during the first six months of the year 71 were treated in

the third quarter and 226 in the last quarter of the year. The timing of this local campaign was extremely opportune since it was in full swing when the national propaganda campaign was inaugurated by Sir Wilson Jameson in November and in consequence received maximum benefit from it.

During the first six months of 1941 the immunisation team was fully occupied inoculating some 600 new cases. It was felt during this period that reinoculation of the children in the old "one shot" group could now safely be undertaken, and almost 100 of these were treated.

A review of the scheme at this time showed that a position was rapidly being reached where apart from a small core of intransigentists the main group left to be tackled was that comprising children not yet of school age and whose parents did not ordinarily make use of welfare services. This group was already being tackled through the general birthday letter scheme and by personal canvass by health visitors and it was now decided that systematic visiting of the homes of children known not to be immunised be carried out by health visitors. Details of inoculation were accordingly entered on the health visiting cards of

all children under five years known to be inoculated through the medium of the local authority's scheme and the health visitors arranged to make special visits to the homes of the remaining children. These visits were begun in the second half of 1941, and it is interesting to observe that during this period 191 children under five years were treated as against 115 children of school age. Whereas in 1936 out of 1,568 children inoculated only 136 were under five years of age in 1942 866 were inoculated of whom 486 were under five years of age. This, in point of fact was the first year in which the number of children inoculated during the year was greater in the under five years group than in the 5-14 age group.

During 1942 it was apparent that the number of children fully inoculated was now sufficiently large to justify the assumption that some modification of local diphtheria epidemiology might be taking place now or if not now then, at the present rate of inoculation, in the very near future.

Certain questions however first demanded an answer. What, for

example, was the natural Schick immunity rate for the children in the district ? What was the present Schick immunity condition of the thousand or so children inoculated six years earlier by the "one-shot" method ? What was the Schick reversion rate of those children undergoing "two-shot" inoculation ? To what extent had children been immunised artificially either by private practitioners or in other areas prior to removal into Chadderton ? If these questions could be answered satisfactorily then a clearer picture of the extent of immunisation, as opposed to inoculation would be obtained and its possible influence on the incidence of the disease might more clearly be seen.

It was decided therefore to offer a Schick test to all children under 15 years and it was hoped that in the process of carrying out this work sufficient data would be collected to provide an answer to each of these questions.

The material used was that supplied by Messrs. Burroughs Wellcome & Co., Ltd., the syringes were the B-D Yale Tuberculin type graduated to 1/100 c.c., and the needles were the Vim pattern, size No.20 supplied by

Messrs. Thackeray, Ltd. The test was, in the first instance, carried out in the orthodox manner except that the results were read at the end of the seventh day. The faintest reaction was read as positive unless its diameter was less than five millimetres. Apart from this qualification no attempt was made to measure reaction by size but positive reactions were divided into two groups marked + and ++ according to the intensity of reaction. It is fully appreciated that this quite arbitrary division is dependent on the examiners skill and memory of previous decisions as to where exactly will lie the dividing line but while recognising the limitations of the method for comparison with the findings of other workers ~~where~~ the results obtained seem sufficiently interesting to justify their retention. It should be made quite clear that all the readings were made by the one examiner and that he was unaware of the diphtheria immunity experience of the individual at the time of assessing the result of the Schick test. Some time after the work of Schick testing had begun it was decided to eliminate the control test except in those children who previously had had diphtheria and in those who

previously had been reinoculated. This decision was dictated by pressure of other work and the knowledge that any error in reading arising from this decision would be remote and that when it did occur it would be an error in the right direction from the point of view of the patient and his immunity state.⁴ Nearly 1,600 Schick tests were carried out, the results of which are summarised later in this paper.

The general position at the close of 1942 as regards diphtheria immunisation is shown in Table 1 of Appendix A.

Table 1 shows the number of children inoculated arranged in age groups at the time of inoculation and in the year in which inoculation was carried out. Those numbers grouped within the broken line rectangle represent the children who received one shot inoculation. It will be observed that by the end of 1942 certain inoculated children had grown out of the main age groups 0-14. Table 11 shows the number of inoculated children arranged according to the age group they occupy in 1942 expressed as a percentage of the estimated total number of children in the respective age groups. The figures given in column

three are not corrected beyond one year periods and the percentages given in column four in respect of the individual age groups are therefore approximate only.

References.

1. Annual Report of S.M.O. Chadderton Education Committee. 1937.
2. Jones, F.G. Amer. Jour. of Hyg., 1938, 28, p.359.
3. Bousfield, G. B.M.J., 1942, 1, p.449.
4. Wilson, G., and others. B.M.J. 1942, 1, p.315.

Chapter Four.

The present extent of artificially acquired immunity.

Some idea of the topographical features of the area must be given to permit a full appreciation of the administrative and epidemiological complexities that exist.

The administrative area of Chadderton covers some 3,015 acres representing that part of the administrative County lying between Manchester to the South West and Oldham to the North East. Historically it consists of a number of ancient hamlets with an industrial outgrowth after the middle of the nineteenth century along the northern and eastern boundaries from the adjacent cotton spinning town of Oldham and after the European war an urbanisation of the southern and eastern sections and to a much less extent the western portion following the building of two arterial highways. There is a considerable overlap of populations in industry and in schools, in churches and in places of entertainment and milk and other food distributing schemes bear no relation whatever to administrative boundaries. Furthermore as has been mentioned the

distribution of the population is very uneven so that the most densely populated parts of the area are on the periphery and as a result epidemiological problems almost always require joint action for their solution and control.

So far as diphtheria immunisation is concerned it has been a cardinal rule for a number of years that each health department shall endeavour to immunise as many children as possible irrespective of the place of domicile. Data are exchanged between the three departments at regular intervals in order to keep records up to date but in practice it has been found that so far as Chadderton is concerned the total of outward transfers practically equals the inward transfers. It has been found in practice, therefore, administratively easier to ignore the overlap and to use the figures of those actually inoculated in Chadderton for statistical purposes.

On the basis of the information given in Table 11 then 45.5% of the 0-4 years group and 73.2% of the 5-14 years group representing 62.1% of the 0-14 years group were successfully inoculated at the end of 1942.

The relative efficiency, or inefficiency, of the one shot inoculation method must now be taken into account. The results of Schick testing a sample of uninoculated children are shown first in Table 111.

Although the total numbers in the individual age groups are very small nevertheless the trend of the process of natural immunity is brought out. A natural Schick immunity rate of 29.4% over the whole group is a not unexpected result in the type of community already described and shows that while the child community has an appreciable diphtheria experience it in no way compares with the high herd immunity of the City of Cork where Saunders¹ found, among children under five years, Schick positive rates varying between 88.4 in 1932 and 66.6 in 1935. Bousfield² suggests that in several series he investigated, where the average ages of the subjects lay, in the different groups, between $5\frac{1}{2}$ and $7\frac{1}{2}$ years and the Schick negative rates between 15 and 20 per cent, the groups represented a fair average of herd immunity for the country at large. If this assumption is correct then the Chadderton average of 29% suggests, as

would be expected, an urban community with a fair degree of diphtheria experience. It compares with a Schick positive rate of 78.3% found by Wilson³ in Bucks., Wilts., Berks. & Oxfordshire and with Lewis'⁴ figure of 76.4% for Croydon.

If the degree of herd immunity in 1936 approximates to that of 1942 then one shot inoculation in the former year stood a fair chance of success. The results of Schick testing carried out in 1942 on 343 children inoculated by the one shot method are shown in Table IV.

The extent of immunity of this group is roughly twice that of the uninoculated group and if, as Bousfield⁵ suggests, the intensity of the reaction bears a relation to the amount of "specific protection" possessed by an individual then the individuals comprising the latter group possess in the main greater immunity than those of the former. This increased immunity, quantitative and qualitative, is insufficient to protect against diphtheria and practical illustration of this is available in the diphtheria experience of the area in 1938. Out of 58 cases of diphtheria notified during the year 14 cases had had one shot inoculation 1-2 years earlier.

It has been possible in the case of school children to estimate the expectancy of diphtheria in 1938 in the one shot inoculated children in the absence of inoculation by applying the attack rates applicable to uninoculated children after correction for age. The estimated cases that would have occurred among the two shot inoculation cases in similar circumstances also are compared in Table V with the actual number that occurred in the two groups.

It should be noted that whilst it is certain that none of the cases in the uninoculated groups, from which the attack rates were calculated, had previously been inoculated, nevertheless an unmeasured number, perhaps 5%, in the groups concerned had been inoculated previously otherwise than through the local authority's scheme. This would weight the attack rates and make them too low but does not invalidate the suggestion that while one shot inoculation had some influence in reducing the incidence of diphtheria in 1938 two shot inoculation was more than twice as effective in this respect.

Reinoculation was, as had already been said, offered to the one shot group and by the end of 1942, 233 children had been dealt with.

Schick tests were carried out on 44 of these not less than three months later and one Schick positive result was obtained. This case was again inoculated with 0.5 c.c. A.P.T. and three months after was Schick negative. It can be inferred then that of 973 children inoculated by the one shot method some 300 school children were, at the end of 1942, susceptible to diphtheria.

The efficiency of the two shot method of inoculation must now be investigated. Disquieting reports were heard early in 1942 of the relative impotency of certain brands of prophylactic and this matter, in consequence, required local investigation. Information was also needed concerning the Schick immunity state of children inoculated up to six years previously.

From the inception of the scheme alum precipitated toxoid, supplied by Messrs. Burroughs Wellcome & Co., Ltd., has been the prophylactic of choice but for a short period at the beginning of 1941 alum precipitated toxoid, the product of two other firms was supplied, under the Ministry scheme of free distribution, through the E.M.S. sector laboratory.

Table VI shows the results of Schick testing 345 children who had been inoculated during the period in question.

These extremely disappointing results led to an immediate investigation to determine whether a natural reversion to the Schick positive state had occurred throughout the two groups irrespective of the material used or whether the Schick positive state was related to any particular antigen.

Table VII shows the Schick test results given in Table VI analysed in relation to the antigen or antigens used. A.P.T. (B.W. & Co.) is represented by the symbol A and the other two prophylactics by the symbols B and C respectively. The symbols are shown grouped in pairs representing the first and second doses respectively. For simplicity of representation the time periods shown in Table VI are eliminated.

This analysis immediately exposed prophylactic C as defective in antigenic qualities. The first five combinations listed above were considered to represent inefficient immunisation and children inoculated with any of these combinations were offered reinoculation with 0.5 c.c.

A.P.T. (B.W. & Co.) 476 children had been inoculated with one or other of the above five combinations of prophylactic. After adjustment for a small number of reinoculations it can be inferred that some 96 children in this group were still susceptible to diphtheria.

Thirdly it had to be determined how effective, as measured by the Schick test, was the two shot method of inoculation after the lapse of several years. In Table VIII are shown the results of Schick tests carried out on 397 children one to six years after inoculation with 0.1 or 0.2 c.c. A.P.T., followed two to four weeks later by 0.5 c.c. after eliminating from the one and two years groups those children receiving an unsatisfactory combination of prophylactic as listed in the preceding paragraphs.

It is greatly to be regretted that the numbers of children falling in these groups are so small that they cannot possibly permit more than a cautious inference that with effective two shot inoculation with A.P.T. of reasonable antigenic potency there has been in this area a relatively slow relapse to the Schick positive state. It is estimated that of the

children remaining; i.e. under 15 years, in this group some 200 to 250 were susceptible to diphtheria at the end of 1942.

It is recognised that this assumption is in contradistinction to the experience of Wilson⁶ and his colleagues in the South and it was thought worth while to compare the carrier rate in certain schools in the area with that of 1938 when extensive swabbing took place in the schools. Unfortunately over zealous efforts to assist the paper salvage campaign had resulted in the destruction of the appropriate records and the idea had to be abandoned.

The hypothesis, therefore, that the endemic character of diphtheria in South East Lancashire though unable to produce a high natural immunity rate in this urbanised community has been, nevertheless, sufficient to prevent the rapid loss of artificially acquired immunity, though attractive, remains without proof of its validity.

In the light of the foregoing work the total figures shown in Table 11 may now be modified and an estimate arrived at of the total number of children treated under the Local Authority's scheme and at the

end of 1942, immune, in terms of the Schick test, to diphtheria.

Out of 3,478 children inoculated about 2,850 can be considered to be Schick immune.

Finally there is one other group that must be taken into account, that classified as children inoculated otherwise than through the scheme of the Local Authority. This is a heterogenous group as has been stated already and consists of children inoculated privately by medical practitioners, in hospital while convalescing from some other disease and in other parts of the country before coming to reside in Chadderton. It is considered that about 450 children come within this category and 181 of these were Schick tested during the routine work with the following result.

The results of Schick tests carried out on children
inoculated with undetermined prophylactics.

Positive.			Negative.	Grand total.	% age Positive.
+	++	Total.			
21	8	29	152	181	16.1

It would appear that about 72 of this group of 450 children are

susceptible to diphtheria.

The position may now be summed up by the statement that in Chadderton at the end of 1942 there was a total population under 15 years of approximately 5,600, of whom about 3,230 representing practically 58% of the whole were, in terms of the Schick test, possessed of satisfactory immunity, artificially acquired but aided by a natural immunity, whose rate in 1942 was of the order of nearly 30%.

References.

1. Saunders, J.C. Medical Officer, 1937, 57, p.39.
2. Bousfield, G. Medical Officer, 1938, 59, p.5.
3. Wilson, G., and others, B.M.J., 1942, 1, p.315.
4. Lewis, J.T. The Principles and Practice of Diphtheria Immunisation.
5. Bousfield, G. B.M.J., 1942, 1, p.449.
6. Wilson, G., and others, B.M.J., 1942, 1, p.315.

Chapter Five.

The history of local diphtheria mortality and morbidity and the influence on them of artificially acquired immunity.

An attempt has been made to review diphtheria mortality and morbidity in Chadderton over a period. Graph 1 shown in Appendix B compares the local diphtheria mortality with that of England and Wales since 1900.

Local records prior to 1914 are meagre and there is no specific information available concerning local outbreaks or individual cases in this period. Again the actual numbers involved locally are very small so that wide variations in the rate appear when the difference in actual deaths is but two or three. The later parts of the two curves are interesting in so far as the appreciable drop in mortality occurring after 1920 in the national curve is not apparent in the local curve which instead, shows a marked drop in mortality since 1939, that is after the immunisation scheme was well established and an even more remarkable absence of mortality for the four years 1929 to 1932 before the commencement of artificial immunisation.

Among the factors associated with the reduction in the national rate are the alteration, since the last war, of the ratio between children and adults so that the age groups at greatest risk are smaller relative to the total population and the reduction in risk of infection arising from diminution of overcrowding both in the smaller family and the smaller class at school. The total deaths occurring in the local population are too few probably to permit the effect of these factors to be apparent in the graph.

The two short periods of practically complete freedom from mortality however appear prominently in the graph and are apparently related to increase in herd immunity or a reduction in bacterial virulence or to both. They are best studied in association with the figures relating to morbidity.

Graph 11 shows the local diphtheria attack rate since 1900 and the corresponding national rate since 1911.

The Local Authority possesses no hospital of its own for the treatment of cases of infectious disease other than smallpox nor does it have any documentary agreement with a neighbouring authority for the

provision of bed accommodation. As a result, in times of epidemic, cases may be scattered over as many as eight different fever hospitals, though generally cases find their way into the two fever hospitals of Manchester or Oldham. This unsatisfactory position, I consider, has led in the past to some weakness of notification and accounts in some measure at least for the fact that whereas the local mortality rate tends oftener to be above than below the national rate the local morbidity rate on the other hand exceeds the national rate on four occasions only. It is certainly a fact that to-day appreciably more cases are sent into hospital for observation than was the case five years ago and it is noteworthy that in the main this practice is followed by the younger practitioners. It is the practice in this area to notify the Registrar General of corrections in diagnosis and in consequence the corrected figures for notifications of diphtheria in recent years may be taken as indicating the true extent of diphtheria occurring in the area. Since the beginning of 1941 errors in diagnosis corrected in hospital and subsequently notified to the Registrar General are equivalent to a rate

of 24.2%.

The marked divergence between the local and national rates since 1939 has its counterpart between 1930 and 1933 in morbidity as markedly as in mortality. There is then no direct evidence in this study of morbidity rates of diphtheria immunisation having a positive effect on the incidence of diphtheria.

It is of interest to note that Robinson & Marshall¹ demonstrated a marked rise in "gravis" infections admitted to Monsall Fever Hospital commencing towards the end of 1933 and coinciding with the increased morbidity and mortality in Chadderton. As has been stated earlier Monsall Fever Hospital is situated some two miles from the Chadderton boundary and admits cases from Manchester and the surrounding districts including Chadderton. There is some reason to believe that coincident with a waning level of herd immunity there was an increased prevalence of an organism of higher virulence.

Correspondingly in 1943 when despite a child inoculation rate of over 70% and a child Schick immunity of at least 60% diphtheria has

continued in endemic form and has occurred in inoculated subjects it is not surprising to find that "gravis" infections have been the rule.

Dr. J. T. C. Keddie has kindly supplied me with, hitherto unpublished, figures relating to diphtheria admissions to Westhulme Hospital, Oldham wherein it is shown that since January 1943 out of 184 admissions, 141 cases gave positive type findings of which 78% were "gravis," 5% intermedius and 17% mitis. It is certain that in Chadderton "gravis" infections have predominated during 1943 and that in the only outbreak known to involve more than one case a "gravis" type of organism was recovered from five out of seven persons involved.

It is to be remembered however that only one section of the population has been artificially immunised. Table LX shows the number of cases of diphtheria occurring since 1921 grouped according to age at the time of onset of disease, together with the percentage of cases occurring under the age of 15 years.

The number of cases under 15 years of age expressed as a ratio of the whole is demonstrated in graphic form in Graph lll and shows an

almost regular fall from 1938 to the end of 1942. Again however a roughly parallel picture is obtained in the pre-immunisation years 1931-34.

The explanation of these parallel phenomena would seem to lie in the diphtheria experience of the area in association with the artificial acquiring of immunity in the later period. The disease was rife in the area during 1927 and 1928 and was still rather above the average during 1929 and 1930. It is reasonable to suppose that by the end of this time a high degree of naturally acquired immunity existed in the child population and this factor together with a temporary reduction in virulence of the organism, suggested by the low national morbidity and mortality rates was responsible for the relative freedom from the disease during 1931-33. The increased number of cases in 1934 occurring coincidentally with an increase in "gravis" infections in the Manchester area has already been commented upon. In 1938 a sharp outbreak occurred in the last quarter of the year in which four of the principal schools taking nearly 45% of the school population were involved. If the number of cases occurring represents 10% of the number infected then

about 600 inhabitants, presumably mostly children, had their immunity boosted at this time. It is suggested that this naturally acquired immunity, together with the immunity artificially acquired during the past five years have been responsible for the maintenance of a relatively low incidence and an insignificant mortality. There is some reason to believe that it has caused a shift of incidence of disease to higher age groups whose level of circulating antitoxin is less high.

The incidence of disease amongst inoculated children has also been investigated. Table X shows the number of cases under fifteen years occurring each year since 1938 in relation to their inoculation experience.

In the case of the death occurring in the inoculated group it may be stated that the child died on the seventh day of illness two hours after admission to hospital and that death was certified as due to 1 (a) diphtheria (b) measles.

In addition to the tendency for cases to occur in later age groups therefore it would seem that as the number of children remaining uninoculated is becoming smaller and smaller the cases occurring are, as

would be expected, tending to concentrate in this group. This represents good evidence in support of the suggestion just made as to the effect of immunisation on the incidence of the disease, though the suggestion of Robinson & Marshall² that Schick immunity is not necessarily synonymous with freedom from disease in the presence of **virulent** strains appears to receive appreciable support in the occurrence during 1942-43 of diphtheria in eight satisfactorily inoculated cases with one death.

This study of diphtheria immunisation in Chadderton leads to the conclusion that in 1942 approximately 58% of the population under 15 years of age had been subjected to some form of diphtheria inoculation in the past and are now Schick immune, that fairly low diphtheria morbidity and mortality rates have prevailed in recent years and that while similar low rates have prevailed on other occasions in the past the present morbidity is tending to concentrate in the relatively small numbers of children remaining uninoculated and in uninoculated adults. The antitoxin level of immunity produced by present technique however apparently is not high enough or does not remain high enough to guarantee absolute immunity from

disease in the presence of virulent infection and from time to time an inoculated child may develop disease which is not necessarily mild in type, or alternatively anti bacterial immunity is also necessary and may be low against the invasive "gravis" organism.

References.

1. Robinson, D.T., and Marshall, F.N. Jour. Path. and Bact., 1934, XXXIX, p.551.
2. Robinson, and Marshall, Lancet, 1935, 2, p.441.

Chapter Six.

The future policy.

It is reasonable to believe, however, bearing in mind the conclusions just reached, that, in an administrative area whose boundaries bear no sensible relationship to modern population distributions, which has dense populations, more or less all around it and main arteries running through its heart and much of whose child population mixes freely and intimately with those of other areas in day schools, Sunday schools and cinemas, never through its own unaided efforts will it be possible to achieve complete immunity from diphtheria no matter how efficient is the application of the antigenic principle in prophylaxis. Nevertheless, with the passage of time, an increasing influence will be brought to bear on total incidence so that it will be reduced to a minimum and localised outbreaks among children entirely eliminated.

With the present prophylactic supplied from the sector laboratory, namely Burroughs Wellcome Alum Precipitated Toxoid given intramuscularly in doses of 0.2 c.c. and 0.5 c.c. with an interval of four weeks elapsing

between the doses a satisfactory Schick immunity can be established in nearly 100% of those inoculated.

About 600 more children, in addition to four fifths of the annual intake, require to be inoculated to achieve inoculation of approximately 80% of the population under 15 years. It is considered likely that this will not be achieved before the end of 1944, that is to say about 750 children will be inoculated in each of the next two years. The possibility of achieving inoculation much beyond a percentage of 80 is not very great because the final 20% includes all infants under 10 months, young children who have been ill from some unrelated disease and in whom inoculation has been deferred and those toddlers in their second year whose inoculation takes place only after the lapse of two or three months from their first birthday for one of many trifling but real causes.

Propaganda will continue to be directed principally at the parents of the pre-school child, particularly those who do not attend welfare centres and this can best be achieved by the conscientious health visitor during her periodic visits to the homes of children. Propaganda will

be directed also at the school entrant and the greatest assistance can be given here by head teachers. Two lines of propaganda are necessary at this stage, one to catch those children who have slipped through the meshes of the net of pre-school primary inoculation and one to foster the notion of one shot reinoculation to raise the waning level of immunity in those primarily inoculated three to four years earlier.

The suggestion that even Schick immunity is not necessarily proof against the production of disease by virulent organisms together with the apparent shift of incidence to the later age groups are indicative of the value of reinoculation of large numbers about the age of ten years.

In this area there is the ever present problem of the amount of time available to the complete team for the work of diphtheria immunisation and it must not be forgotten that it is only one of the multifarious duties devolving on the members of the team. It is already clear that in respect of the unimmunised child it is unnecessary to devote time to the performance of a pre-Schick test. Ideally a post-Schick test should be carried out in every case three months after completion of inoculation

and a certificate issued stating the details of inoculation and the results of Schick testing. Such a system would determine the odd 2% that has failed to be converted to the Schick negative state and so could be reinoculated immediately. Nevertheless it is not practicable here, from lack of staff, to attain this ideal.

Periodically also post-Schick testing should be carried out to test the efficiency of the prophylactic in use but as a consequence of the centralised system of supply of prophylactic now in use this need be carried out only in selected areas and at appropriate times.

Finally it is necessary to check personal technique from time to time and this can only be done within the area. It would be useful to carry out post-Schick testing in about 400 cases every two years or so.

It is believed that by such a procedure and with the technique and material described diphtheria as a public health problem will largely cease to exist and that at most the disease will evidence itself only in sporadic cases occurring scattered throughout the district and with no great tendency to affect chiefly the child population.

A P P E N D I X A .

S T A T I S T I C A L T A B L E S .

Table 1.

Total number of children successfully inoculated
through the medium of the Local Authority's Scheme.

<u>Age.</u>	<u>1936.</u>	<u>1937.</u>	<u>1938.</u>	<u>1939.</u>	<u>1940.</u>	<u>1941.</u>	<u>1942.</u>
- 1	6	9	-	1	6	29	91
1 -	38	26	29	70	85	163	182
2 -	36	10	17	20	26	76	65
3 -	29	12	4	12	21	82	70
4 -	27	14	9	15	20	70	78
5 -	152	71	50	60	73	117	94
6 -	143	26	8	47	43	75	66
7 -	164	26	8	25	16	57	33
8 -	168	16	6	6	12	69	40
9 -	173	13	7	1	6	43	37
10 -	155	3	3	1	3	35	40
11 -	168	5	-	2	8	41	29
12 -	158	9	-	3	2	28	23
13 -	141	7	-	2	5	19	16
14 -	10	-	-	1	1	3	2
15 +	-	-	-	1	-	-	-
Total	1,568	247	141	267	327	907	866

Table 11.

Total number of children under 15 years successfully inoculated through the medium of the Local Authority's Scheme.

Age group.	Approx. no. in age group.	Number inoculated.	Percentage inoculated.
- 1	450	91	20.2
1 -	450	211	46.9
2 -	450	234	52.0
3 -	450	232	51.5
4 -	450	256	56.9
	2,250	1,024	45.5
5 -	400	243	60.8
6 -	350	264	75.4
7 -	330	248	75.1
8 -	320	257	80.3
9 -	320	262	81.9
10 -	300	226	75.3
11 -	320	262	81.9
12 -	330	243	73.6
13 -	330	240	72.7
14 - 15	350	209	59.7
	3,350	2,454	73.2
Total	5,600	3,478	62.1

Table 111.

Results of Schick tests carried out on children
not previously inoculated with diphtheria prophylactic.

Age group.	Positive.			Negative.	Total tested.	Percentage Schick positive.
	+	++	Total			
3	0	1	1	0	1	100
4	2	12	14	0	14	100
5	13	22	35	7	42	83.3
6	7	14	21	8	29	72.4
7	6	17	23	12	35	65.7
8	9	20	29	18	47	61.7
9	16	30	46	13	59	78.0
10	15	24	39	19	58	67.2
11	11	26	37	13	50	74.0
12	11	14	25	11	36	69.4
13	11	10	21	18	39	53.8
14	2	3	5	4	9	55.5
Total	103	193	296	123	419	70.6

Table IV.

Results of Schick tests carried out on children inoculated with
0.5 c.c. A.P.T. (B.W.& Co.) 5-6 years previously.

Age group.	Positive.			Negative.	Total tested.	Percentage Schick positive.
	+	++	Total.			
6	0	0	0	3	3	0
7	4	2	6	6	12	50
8	10	2	12	9	21	57.1
9	13	3	16	18	34	47.0
10	16	3	19	31	50	38.0
11	29	6	35	49	84	45.2
12	17	4	21	47	68	30.9
13	18	8	26	35	61	42.6
14	3	1	4	6	10	40.0
Total	110	29	139	204	343	40.5

Table V.

Expectancy of diphtheria in 1938 among one shot and two shot children had they not been inoculated previously.

Inoculated children.					
One shot.			Two shot.		
Cases.		Percentage reduction.	Cases.		Percentage reduction.
Expected.	Actual.		Expected.	Actual.	
18	13	28	10	4	60

Table VI.

Results of Schick tests carried out on children previously inoculated with A.P.T. 0.2 c.c. & 0.5 c.c. with four weeks intervening.

Age group.	Period since completion of inoculation.											
	9 - 12 months.						1 - 2 years.					
	+	++	Total.	Neg.	Grand total.	% age Positive.	+	++	Total.	Neg.	Grand total.	% age Positive.
2	0	0	0	3	3	0	1	0	1	6	7	14.28
3	0	0	0	0	0	0	0	0	0	3	3	0
4	0	0	0	1	1	0	2	0	2	9	11	18.18
5	0	0	0	7	7	0	5	0	5	28	33	15.15
6	1	0	1	8	9	11.1	6	0	6	43	49	12.24
7	0	0	0	6	6	0	2	0	2	37	39	5.13
8	0	0	0	4	4	0	4	0	4	22	26	15.38
9	0	0	0	4	4	0	7	2	9	32	41	21.95
10	0	0	0	1	1	0	4	4	8	30	38	21.05
11	1	0	1	11	12	8.33	2	1	3	14	17	17.65
12	2	0	2	9	11	18.18	1	0	1	3	4	25.0
13	0	0	0	3	3	0	0	0	0	15	15	0
14	0	0	0	0	0	0	0	0	0	1	1	0
Total	4	0	4	57	61	6.56	34	7	41	243	284	14.49

Table VII.

Results of Schick tests carried out on certain inoculated children grouped according to the prophylactic used.

Prophylactic Combination.	Positive.			Negative.	Grand total.	% age Positive.
	+	++	Total.			
C and C.	14	5	19	41	60	31.66
C and B.	4	0	4	16	20	20.00
C and A.	1	1	2	20	22	9.09
B and C.	10	1	11	49	60	18.33
A and C.	1	0	1	13	14	7.14
B and A.	0	0	0	9	9	0.00
B and B.	0	0	0	2	2	0.00
A and B.	0	0	0	0	0	--
A and A.	8	0	8	150	158	5.09
Total	38	7	45	300	345	

Table VIII.

Results of Schick tests carried out on children previously inoculated with two injections of A.P.T. 0.1 or 0.2 c.c. and 0.5 c.c. with two to four weeks intervening.

Age group.	Period since completion of inoculation.											
	0 - 12 months.						1 - 2 years.					
	+	++	Total.	Neg.	Grand total.	% age Positive.	+	++	Total.	Neg.	Grand total.	% age Positive.
1	0	0	0	1	1	0	0	0	0	0	0	0
2	0	0	0	4	4	0	0	0	0	2	2	0
3	0	0	0	1	1	0	0	0	0	1	1	0
4	0	0	0	3	3	0	0	0	0	6	6	0
5	0	0	0	17	17	0	2	0	2	14	16	12.50
6	1	0	1	13	14	7.14	2	0	2	27	29	6.90
7	0	0	0	7	7	0	1	0	1	29	30	3.33
8	0	0	0	7	7	0	1	0	1	14	15	6.66
9	0	0	0	4	4	0	0	0	0	9	9	0
10	0	0	0	3	3	0	1	0	1	9	10	10.00
11	0	0	0	0	0	0	0	0	0	5	5	0
12	0	0	0	3	3	0	0	0	0	1	1	0
13	0	0	0	2	2	0	0	0	0	11	11	0
Total	1	0	1	65	66	1.51	7	0	7	128	135	5.18
	2 - 3 years.						3 - 4 years.					
	+	++	Total.	Neg.	Grand total.	% age Positive.	+	++	Total.	Neg.	Grand total.	% age Positive.
	+	++	Total.	Neg.	Grand total.	% age Positive.	+	++	Total.	Neg.	Grand total.	% age Positive.
4	0	0	0	2	2	0	0	0	0	3	3	0
5	0	0	0	4	4	0	1	0	1	16	17	5.9
6	1	0	1	3	4	25	0	0	0	4	4	0
7	1	0	1	7	8	12.5	0	0	0	3	3	0
8	0	0	0	19	19	0	0	0	0	24	24	0
9	0	0	0	13	13	0	1	0	1	30	31	3.2
10	1	0	1	13	14	7.1	1	0	1	4	5	20
11	0	0	0	1	1	0	0	0	0	8	8	0
12	1	0	1	0	1	100	0	0	0	3	3	0
13	1	0	1	0	1	100	0	0	0	2	2	0
Total	5	0	5	62	67	7.46	3	0	3	97	100	3.00
	4 - 5 years.						5 - 6 years.					
	+	++	Total.	Neg.	Grand total.	% age Positive.	+	++	Total.	Neg.	Grand total.	% age Positive.
	+	++	Total.	Neg.	Grand total.	% age Positive.	+	++	Total.	Neg.	Grand total.	% age Positive.
Total	1	0	1	8	9	11.11	2	1	3	17	20	15.00

Table LX.

Number of cases of diphtheria notified during the years
1921 to 1942 inclusive.

<u>YEAR.</u>	<u>0 -</u>	<u>5 -</u>	<u>10 -</u>	<u>% age of whole.</u>	<u>15 -</u>	<u>20 -</u>	<u>35 -</u>	<u>45 -</u>	<u>65 -</u>	<u>TOTAL.</u>
1921	8	7	5	91	0	2	0	0	0	22
1922	7	8	2	94	0	1	0	0	0	18
1923	5	4	3	100	0	0	0	0	0	12
1924	4	20	9	94	0	2	0	0	0	35
1925	5	4	5	88	1	0	0	0	1	16
1926	6	4	2	80	0	2	1	0	0	15
1927	16	31	13	94	2	2	0	0	0	64
1928	8	28	7	90	2	1	2	0	0	48
1929	7	13	3	92	0	1	1	0	0	25
1930	6	13	1	91	1	1	0	0	0	22
1931	2	1	0	60	0	1	1	0	0	5
1932	1	2	2	63	0	3	0	0	0	8
1933	1	2	3	100	0	0	0	0	0	6
1934	2	14	4	69	2	5	2	0	0	29
1935	7	18	12	97	1	0	0	0	0	38
1936	9	22	4	90	1	2	0	1	0	39
1937	4	7	1	92	1	0	0	0	0	13
1938	8	27	18	91	3	2	0	0	0	58
1939	2	9	3	74	3	2	0	0	0	19
1940	3	2	2	64	0	4	0	0	0	11
1941	1	2	4	88	0	1	0	0	0	8
1942	3	5	4	60	3	5	0	0	0	20
1943	1	6	3	53	4	4	0	1	0	19

Table X.

Inoculation experience of cases and deaths under 15 years since 1938.

Year.	Percentage of children inoculated.	Uninoculated children Cases.Deaths.		Inoculated children.						Total cases.
				L.A."One shot"		L.A."Two shot"		"Others"		
		Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	
1938	34	35	5	14	0	4	0	0	0	53
1939	36	10	1	4	0	0	0	0	0	14
1940	39	4	0	2	0	1	0	0	0	7
1941	55	6	0	0	0	0	0	1	0	7
1942	70	8	0	0	0	2	1	3	0	13
1943	76	6	1	2 ⁺	0	1	0	1	0	10

† One case reinoculated 1 dose 0.5 c.c. A.P.T. 1942.
One case reinoculated 1 dose 0.5 c.c. A.P.T. 1941.

A P P E N D I X B .

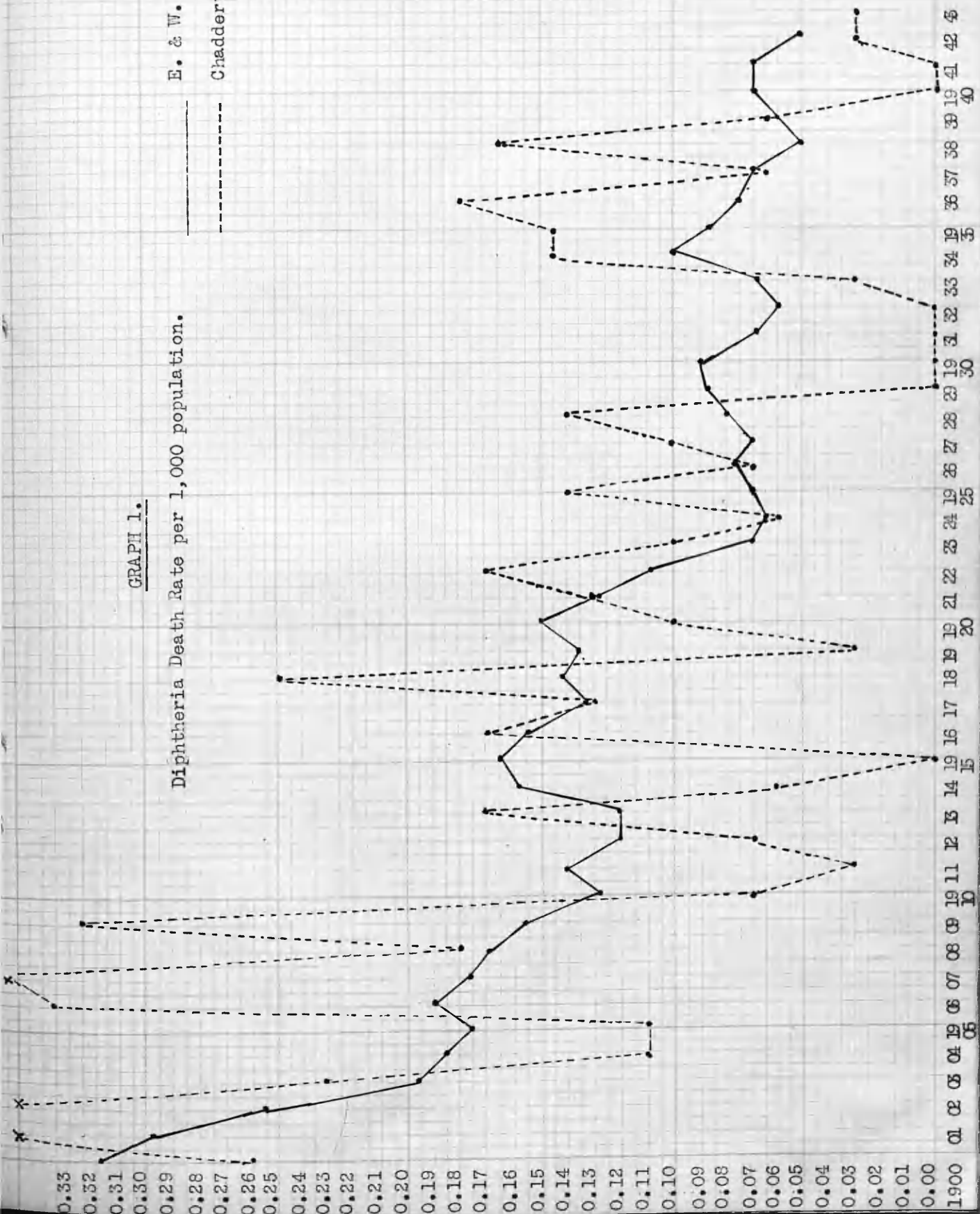
G R A P H S .

GRAPH 1.

Diphtheria Death Rate per 1,000 population.

E. & W.

Chadderton.

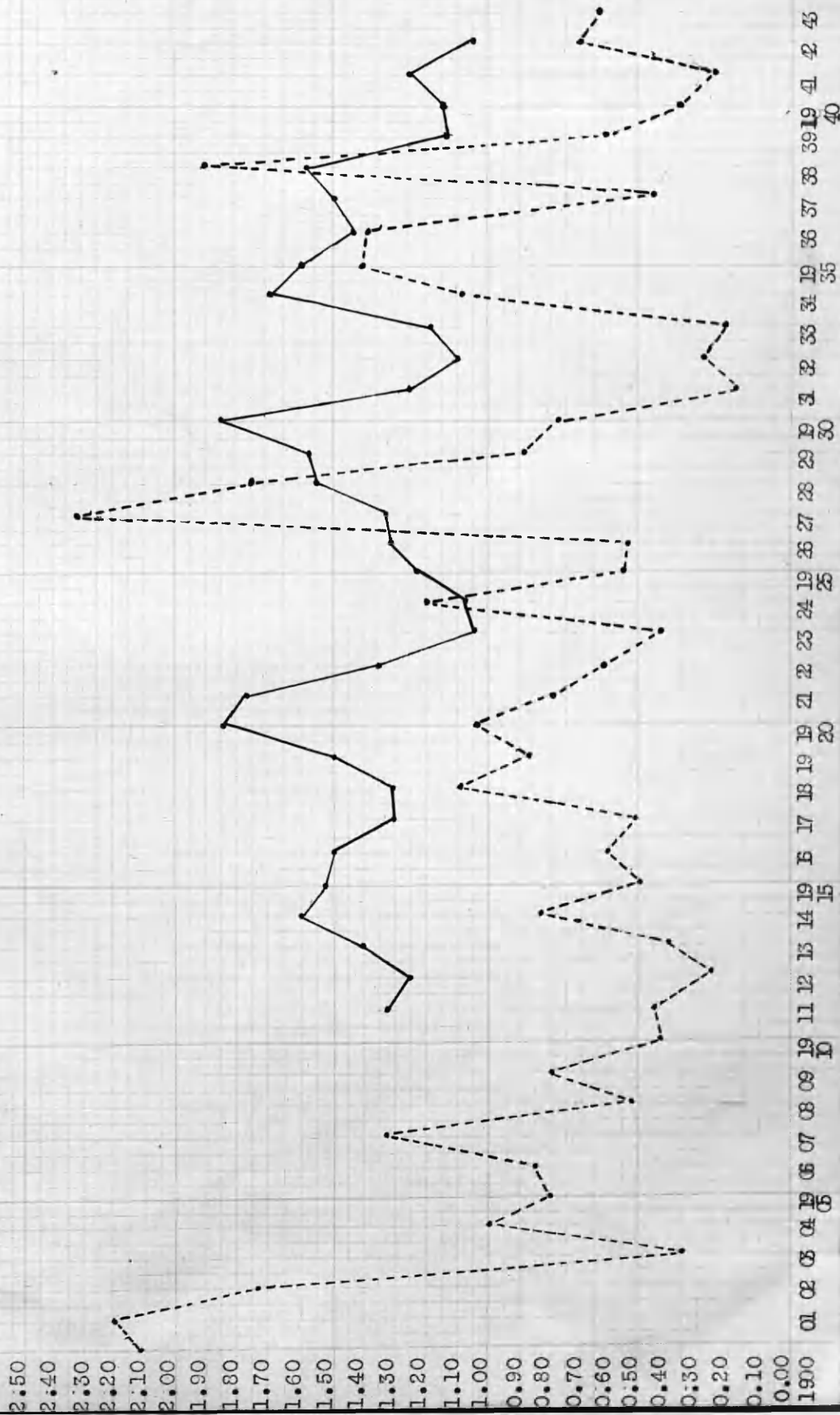


GRAPH 11.

Diphtheria attack rate per 1,000 population.

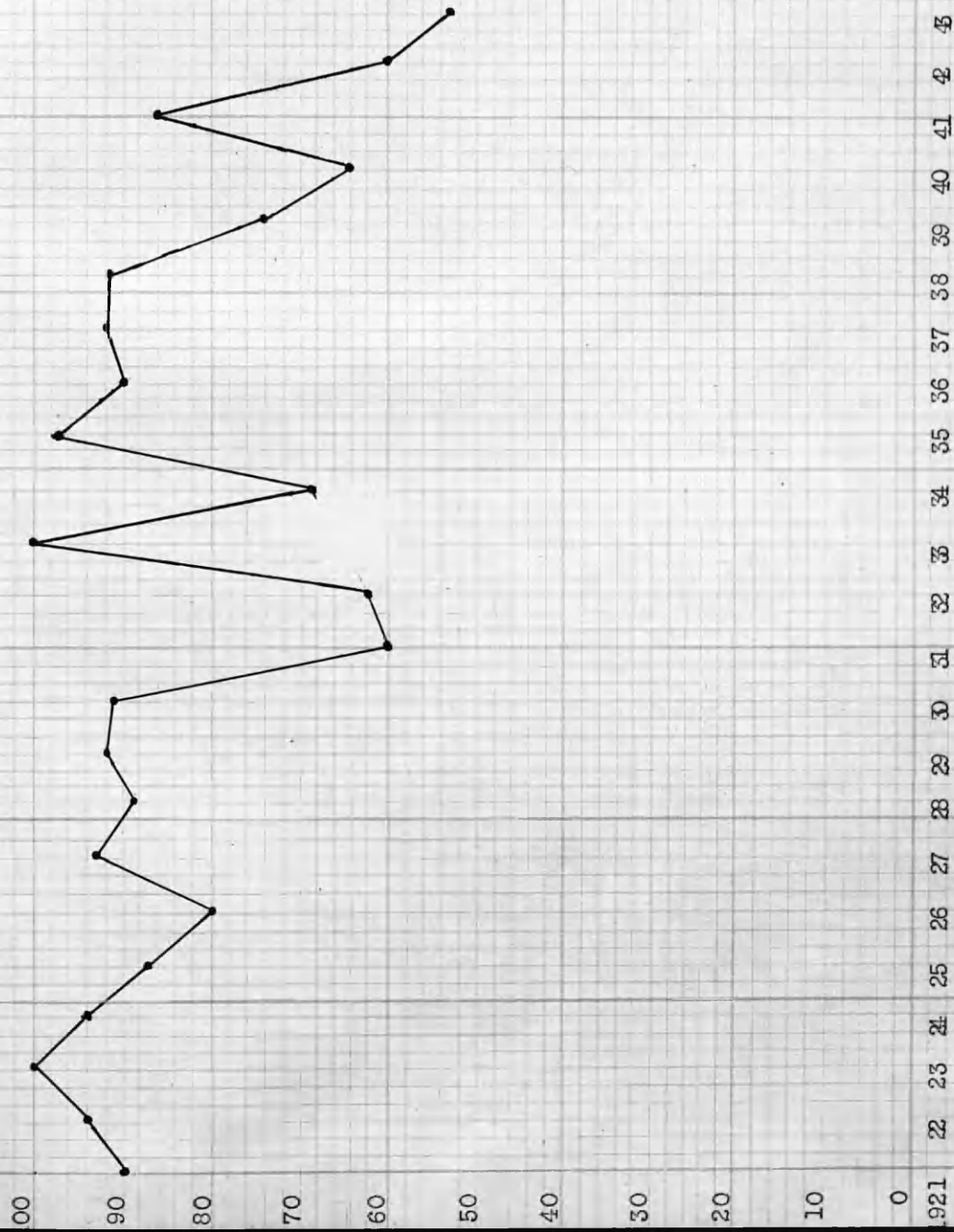
E. & W.

Chadderton.



GRAPH 111.

Ratio of cases under 15 years to total cases in each year since 1921.



A P P E N D I X C .

B I B L I O G R A P H Y .

Bibliography.

1. Annual Report of the M.O.H. U.D. of Chadderton. 1900 et seq.
2. Banus, M.G. Internat. Journ. of Pub. Health. 1921, 11, 4 & 5.
3. Control of the Common Fevers, 1942, McKinnon, Diphtheria Prevented.
4. Ibid. Harries, E.H.R., Diphtheria.
5. Dudley, S.E., May, P.M., and O'Flynn, J, A, Act.Immun. against Diph.,
M.R.C., 1934, No.195.
6. E.P.H.L.S. Mon. Bull., 1941, Dec., p.4.
Diph. infections in children inoculated with a single dose of A.P.T.
7. Ibid. 1942, April, p.1.
Reading of Schick tests after two, four & seven days.
8. Ibid. 1942, June.
Diphtheria in a Children's Home at Towyn.
9. Ibid. 1943, April, p.31.
Diphtheria Experience in the E.M.Pub.Health Lab.Serv. during 1941.
10. Fitzgerald, J.G., Fraser, D.T., McKinnon, N.E.Lancet, 1938, 1, p.391.
11. Forbes, J.G. The Prevention of Diphtheria. M.R.C., 1927, No.115.
12. Ibid. Diphtheria past & present, 1932.
13. Frost, W.H. Papers. Diphtheria: Infection and Immunity.
14. Ibid. Morbidity and Carrier Prevalence.
15. Glenny, A.T. and Sudmersen, H.J. Jour. of Hyg., 1921, 20, p.176.
16. Glenny, Butler, G.A.H. and Stevens, M.F. Jour. Path. and Bact., 1931,
34, p.267.

17. Jones, F.G. Amer. Jour. of Hyg., 1938, 28, p.359.
18. Ledingham, J.C.G. B.M.J., 1939, 11, p.841.
19. Lewis, J.T. The Princip. & Pract. of Diphth. Immun. 1942.
20. Ministry of Health. Memo. 68/Med. 1922.
21. Ibid. Memo.170/Med. 1933.
22. O'Brien, R.A. Lancet, 1929, 2, p.241.
23. On the State of the Public Health. 1920 et seq.
24. McKinnon, Ross, H.A., and Defries, R.D. Can. Pub. Health Jour., 1931,
22, p.217.
25. Picken, R.M.F. Lancet, 1937, 1, p.1445.
26. Reports on Public Health and Med. Subj. 1921, No.10.
27. Robinson, D.T., and Marshall, F.N. Jour. Path. and Bact., 1934, XXXIX,
p.551.
28. Robinson, and Marshall, Lancet, 1935, 2, p.441.
29. Ross and McKinnon. Can. Pub. Health. Jour., 1931, 22, p.333.
30. Russell, W.T. The Epidem. of Diphth. during the last forty years,
M.R.C., 1943, No.247.
31. Topley, W.W.C., & Wilson, G. The Principles of Bacteriology & Immunity.
32. Walker, A.A. J.A.M.A., 1934, Vol.103, 4, p.227.
33. Wilson, et al. B.M.J., 1942, I, p.315.