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Medical Officers of Schools Association.

The
Diagnosis and Management of
Doubtful Cases of Diphtheria

BEING

AN ADDRESS

*Delivered before the Medical Officers of Schools Association on
November 26th, 1903.*

BY

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THE DIAGNOSIS AND MANAGEMENT OF DOUBTFUL CASES OF DIPHTHERIA.

MR. PRESIDENT AND GENTLEMEN,—Apart from its purely scientific aspect, the diagnosis of any infective illness possesses a special interest for the practitioner of medicine in view of the various measures of a preventive character which he may feel called upon to adopt. And to the members of this society who, in virtue of their office, are held responsible for the health of our large schools, each of which may be regarded as an aggregation of particularly susceptible subjects, the remark applies with special force. The medical officer to a large public school is so frequently called upon to decide as to the nature of doubtful cases of infectious illness, and the issues dependent upon his decision are in some instances so important, that he must necessarily have devoted a good deal of anxious thought and critical consideration to the elucidation of such questions. Fully realising this, I feel no small diffidence in addressing a society, most of the members of which, by reason of their special knowledge and experience, apart from their high scientific attainments, must rightly be regarded as experts, and I take this opportunity of expressing my appreciation of the honour you have done me in asking me to open this discussion. For the purpose of discussing the subject with which we are concerned this afternoon—viz., the diagnosis and management of doubtful cases of diphtheria—I would first direct your attention to the all-important question of diagnosis, and afterwards to the consideration of the measures of a preventive character, which have for their object the limitation of the spread of infection.

A well-developed attack of diphtheria in which definite membranous exudation is visible on the fauces is not likely either to escape recognition or to be mistaken for anything else. It is quite otherwise, however, in respect of those sore throats in which no exudation at all can be detected, or, at most, a little cheesy deposit on the site of the follicular crypts, or, perhaps, one or more small necrotic-looking areas on the surface of the tonsils. The real nature of such cases is often very difficult to determine on clinical evidence alone. The same thing is true

in respect to purely nasal diphtheria, which is very likely to escape detection altogether, especially when, as is usually the case, the patient presents but little if any indication of illness. It is to the purely nasal cases that I am referring. Instances in which the nasal cavities are involved, either by extension, or concurrently with the fauces, are, as is well known, characterised by more than average severity. These nasal cases are a distinct source of danger to the community by reason of the insidious character of the affection, and in many cases their existence has only been revealed after the lapse of a considerable period of time by their having infected other persons with severe and even fatal diphtheria. The havoc which may result from a single unrecognised case of nasal diphtheria in a school, institution, or ward in a children's hospital may be easily imagined, and need hardly be seen to be appreciated, and in any investigation into the source of an apparently sporadic outbreak of diphtheria, the importance of carefully examining the condition of the nasal cavities of those who have been in contact with the sick cannot well be over-estimated.

Although a considerable amount of assistance in the diagnosis of doubtful cases of diphtheria is usually to be derived from a careful consideration of the clinical appearances, it is hardly going too far to say that at the present day the nature of a doubtful attack is practically determined by the result of bacteriological examination. Now, without intending for a moment to minimise the immense importance of bacteriological examination in the hands of an expert observer, it cannot be denied that the insufficiency of our present knowledge on certain important points connected with the bacteriology of diphtheria, apart from a fallacy which is inseparable from the method itself, materially detracts from the complete reliability of the bacteriological test. I refer more particularly to the difficulty which is frequently experienced in the identification of the bacillus, owing to our uncertainty as to the limits of intranormal variation, both in respect to its form and virulence. The fact has long been recognised that in diphtheritic as in doubtful and even healthy throats, bacilli are not infrequently found, which, more or less, closely resemble the diphtheria bacillus, but which are innocuous when injected into animals. It has been customary to refer to such organisms collectively as "pseudo-diphtheria" bacilli, without regard to certain important differences which are now recognised as existing between them. The term has proved an unfortunate one, as tending to cause confusion and its use should certainly be restricted. Indeed, it would be better that the term "pseudo-diphtheria" were dropped altogether. The organism which has been most frequently referred

to under this name is the Hofmann bacillus, of which the special characters are now pretty generally known. It was originally described by Löffler in 1887 as not infrequently present in diphtheritic throats, and though, for this reason, it was frequently associated with the true bacillus, which it closely resembled, Löffler found it invariably innocuous to animals. In the following year Hofmann further extended the inquiry, and showed that the bacillus was even more often present in sore throats which were not diphtheritic, and, indeed, that it could by no means infrequently be recovered from the throats of perfectly healthy persons. He, like Löffler, found the bacillus devoid of virulence, and came to regard it as of a distinct species. This important observation of Hofmann, that the bacillus which bears his name is often present in normal throats, has been amply confirmed by a number of subsequent observers, notably by Roux and Yersin in France, and in this country by Cobbett and Graham-Smith in the course of certain admirably conducted investigations into outbreaks of diphtheria which occurred within recent years in Cambridge and Colchester, respectively.

The all-important question as to whether, under favourable conditions, the Hofmann bacillus is capable of developing into a true diphtheria bacillus, has been a fruitful source of experiment and discussion amongst bacteriologists for years. With but few exceptions, observers have confessed their inability to effect this conversion by artificial means. Richmond and Salter, it is true, claim to have succeeded by passing the organism through several generations of finches; Hewlett and Knight state that they were eventually successful in imparting virulence to what appeared to be a typical Hofmann bacillus by carrying it through a number of generations on different culture media, but in neither case were the experiments altogether convincing. more recently too, Lesieur claims to have brought about this result in three different ways: (1) by the introduction of the bacillus inclosed in collodion capsules into the peritoneum of rabbits; (2) by long-continued cultivation in peptone broth (in one case eight months being required); and (3) by simultaneous inoculation of the staphylococcus aureus. But the data on which Lesieur's claim is founded are wanting in completeness. If such transition be capable of taking place, however gradually, in the human subject, our views on the etiology of diphtheria, having regard to the frequent presence of the Hofmann bacillus in the normal throat, will have to be materially extended, and our measures of prevention re-considered. So far, however, whatever be the real possibilities in the laboratory, no evidence has been adduced that this ever does take place in nature, and

the balance of opinion is opposed to the Hofmann bacillus as a potential source of diphtheria.

Now the Hofmann bacillus, although, as I have stated, it is occasionally present in diphtheritic throats in association with the true bacillus, is readily distinguishable from the Klebs-Löffler organism by certain morphological, cultural, and biological features which are now well recognised. It would, therefore, seem permissible to speak of it as a "pseudo-bacillus"—if it be necessary to retain the term—and to assume that it is specifically distinct. In respect, however, to certain other bacilli which are frequently present in the throats or nasal passages of those who, without showing any obvious affection themselves, have been in close contact with the disease, the relation is by no means equally clear. I refer to those bacilli which are also commonly classed as "pseudo-diphtheritic," which, though quite indistinguishable from the true bacillus in their morphology, staining, and cultural reactions—especially the power of producing acid in glucose broth—are found to be devoid of any virulence when injected into guinea-pigs. Whether such organisms are attenuated diphtheria bacilli, capable of acquiring virulent properties under favourable conditions, or whether they are specifically distinct, has not yet been satisfactorily determined. The inadvisability, however, of applying the term "pseudo-diphtheritic" to an organism which simply differs from the genuine bacillus in respect to its virulence must, I think, be admitted, in view of our ignorance, not only as to the extent to which the virulence of that bacillus may vary, but also as to the factors which are responsible for it. The settlement of this question as to the relation which the one organism bears to the other must have an important bearing on the precautions which should be undertaken in the presence of an outbreak of the disease, and to this subject I propose to return again. From the point of view of diagnosis with which we are at present concerned, it appears to me to be most desirable that an organism having the characters above referred to should be classified as diphtheritic, and should the mucous surface from which the organisms have been derived present any, even the slightest, sign of inflammation, the case should be diagnosed as diphtheria, accordingly. Such, then, are the indications which appear to be derivable from a bacteriological examination in cases where bacilli bearing a distinct resemblance to the diphtheria organism are detected.

Now, what value should be attached to a negative result? I have little hesitation in saying, "Very little indeed," unless such result is confirmed by at least one, and, preferably, two subsequent examinations, if possible, on succeeding days. If the faucial secretion of diphtheria convalescents be carefully

examined daily during the third and fourth weeks of their attack, in more cases than not, the results will prove more or less contradictory. The bacillus may not be recoverable for a day or two, perhaps more, to reappear again on the day following, or it may be found continuously, except on some single occasion, when it may escape detection. Amongst the occupants of a diphtheria ward such vagaries are, no doubt, sometimes to be explained by actual re-infection by another patient, but the same thing, though, I believe, less frequently, may be observed in the case of persons who are treated in a room to themselves, in which case no such explanation is tenable. The fact cannot be ignored that a negative result simply means that the observer has failed to find the bacillus, not necessarily that the bacillus is not there. I can call to mind some half-dozen cases in which the clinical and post-mortem evidences were conclusive of diphtheria, yet repeated bacteriological examination by an expert observer—in three of these instances the examination was made by one whose experience in this particular field is probably unsurpassed in this country—entirely failed to reveal the presence of the diphtheria bacillus. Three of these patients subsequently developed paralysis, and two died from cardiac failure. These instances are, doubtless, very exceptional, but I simply mention them to emphasise an ever-present fallacy, the recognition of which is not by any means so general as it should be, if one may judge from the frequency with which a single unconfirmed negative result is accepted as sufficient to disprove the presence of diphtheria.

A failure to detect the bacillus, though present on the fauces, may result from an error at any one of three stages of the experiment. Bacilli may escape detection by the observer when making a microscopical examination, owing to their being but few in number in comparison with the other micro-organisms growing in the culture. Or, though present on the swab, they may fail to grow in the culture, owing to defective insemination, or by reason of their reproductive capacity being lowered, if not entirely annulled, as a result of previous antiseptic application to the throat, or, finally, they may escape attachment to the swab, in consequence of their being but sparsely distributed on the mucous surface of the fauces. The chances of failure are materially lessened by exercising great care in taking the swab, and by repeating the examination on one or more subsequent occasions. It is very desirable that an interval of at least two hours, and, preferably, more, should be allowed to elapse between the time of using any antiseptic application to the throat and the taking of the swab. This should be firmly pressed against the faucial surface at more points than one, especially

where any trace of exudation can be discerned, and the swab at the same time should be rotated between the finger and thumb so as to insure its whole circumference being impregnated with secretion. And the same precaution should be observed when rubbing the swab upon the surface of the culture medium.

The exercise of care in the impregnation of the swab is of particular importance in view of the valuable evidence which may often be derived from an immediate examination of a cover-slip preparation made directly from it when stained by Neisser's method. Having regard to the fact that such examination is within the reach of any practitioner who is equipped with a $\frac{1}{2}$ inch immersion lens and a slight familiarity with bacteriological technique, early information as to the positive nature of a diphtheritic throat may often be derived on the spot without having to wait the twenty-four hours or so which must usually elapse before the report on the result of cultivation can be received from the laboratory. Should the examination of the swab, however, prove negative the evidence is of little value, even less so than that yielded by a single negative culture, and the laboratory report must be awaited before coming to any decision as to the diagnosis. In any case, the examination of the swab, whether negative or positive, should be confirmed by subsequent cultivation. In the course of an investigation into the value of Neisser's stain on 100 consecutive cases admitted into the South-Western Fever Hospital certified as diphtheria, which I carried out some two years ago in conjunction with Dr. R. M. Beaton and Mr. W. C. C. Pakes, of Guy's Hospital, and which was subsequently recorded in the Transactions of the Pathological Society, the proportion of cases of proved diphtheria (both clinically and bacteriologically), in which the presence of diphtheria bacilli was revealed by a preliminary examination of material taken direct from the swab, and stained by Neisser's method was no less than 37 per cent.* Incidentally, I take the opportunity of recording my belief in the comparative value of Neisser's stain over all others in the diagnosis of diphtheria, a belief which is shared by many experienced bacteriologists both at home and abroad. Neisser in his original communication regarded the reaction as distinctive in young cultures grown at 35° C. Fraenkel, and more recently Lesieur, have stated their belief that, short of inoculation of animals, it is the most trustworthy test we possess. Dr. W. T. G. Pugh, of the North-Eastern Hospital, after an experience of three

* Dr. Leslie Easter states that in his experience the information yielded by immediate examination of the material on the swab stained by Neisser's method has corresponded with that subsequently derived from examination of the culture in no less than 93 per cent. of cases.

years, during which period it had been used as a routine confirmatory test, speaks most highly of its value. Bronstein found that in 135 out of 150 cases of proved diphtheria, the bacillus stained by Neisser's method was detected by direct examination of the swab, and the results obtained by Beaton, Pakes, and myself by this procedure I have already referred to. In our experience Neisser's method has proved, on the whole, more trustworthy than staining by Löffler's methylene blue, though, like all others, not invariably reliable. The appearance presented by the bacillus, moreover, when stained by Neisser's method is a very striking one, and on that account not likely to be mistaken by an observer of but little experience in bacteriological examination, a point of no small importance, if, as I suggest, an immediate microscopical examination be made from the swab.

The disabilities to which I have referred undoubtedly detract from the authority of the bacteriological test as commonly applied, and for this reason it should be regarded as of subsidiary value in cases where the clinical indications are at all distinctive. In cases, however, where the symptoms are anomalous or actually wanting, the test is of the highest importance; indeed, it may be said to furnish the only criterion available. I refer especially to that class of sore-throat in which little, if any, exudation can be seen, although the tonsils may be more or less enlarged, and the adjacent faucial structures obviously inflamed, and to those nasal affections in which nothing beyond a mucous discharge, attended, perhaps, with slight soreness of the external nares, can be detected. In the differentiation of follicular tonsillitis and faucial diphtheria some assistance can often be derived from the clinical aspect of the case, if attention be directed to the following particulars. In follicular tonsillitis, exudation, when present, occurs for the most part in spots, it is usually somewhat cheesy or friable in consistence, often limited in situation to the openings of the follicular crypts, and the spots but rarely coalesce into a definite pellicle. Even if they do, the exudation hardly ever spreads beyond the limits of the tonsil. It sometimes appears to encroach on the pharyngeal wall, but never, as far as I know, extends on to the palate. Actual extension of membrane on to the palate or uvula is almost distinctive of diphtheria. In follicular tonsillitis it is usual for both sides to be about equally involved, whereas, a diphtheritic affection is often more marked on one side than the other, and the same is true of the glandular enlargement which is apt to be more pronounced in diphtheria. The degree of pyrexia is likely to be greater in tonsillitis, and, indeed, it may be stated without fear of contradiction that the constitutional disturbance generally

is likely to be more severe in follicular tonsillitis than in a case of diphtheria sufficiently mild as to be mistaken for it. Rhinorrhœa is relatively uncommon in follicular tonsillitis, and the same may be said of albuminuria, which is a frequent symptom in diphtheria. The occurrence of hoarseness, stridor, or a croupy cough is very suggestive, while the advent of paralysis or cardiac disturbance at a later date is, of course, confirmatory of diphtheria. By a careful consideration of all the foregoing points a satisfactory diagnosis can often be arrived at. With respect to those cases in which no abnormality can be detected beyond the presence of a mucous rhinorrhœa, it is usually quite impossible to differentiate diphtheritic rhinitis from a simple nasal catarrh. Careful inspection of the anterior nasal fossæ through the external nares may reveal the presence of membrane, either on the septum or floor or the inferior turbinate, but in the majority of cases no exudation whatever is visible, even though the discharge may be teeming with diphtheria bacilli. The white appearance presented by a patch of Schneiderian mucus is a possible source of error, as it is very likely to be mistaken for an exudation, unless due care be exercised in the examination. Some degree of redness, and occasionally an impetiginous excoriation of the skin immediately within the nostrils may often be detected. This, when present, is strongly suggestive of diphtheria. It is dependent upon the irritant character of the discharge, a quality also shared by the rhinorrhœa, which so often follows scarlet fever in young children.

Having now referred to the chief evidences on which we have to rely in the diagnosis of doubtful cases of diphtheria, it remains to say a few words about the preventive measures which should be undertaken with the object of checking the spread of the disease. On becoming aware of a case of diphtheria among the members of a community living together in the close association which is incidental to school life, I think all must be agreed as to the advisability of immediately adopting the following precautions. (1) Isolate the patient. (2) Disinfect everything which he is likely to have worn, touched, or handled, and also the room in which he has been sleeping immediately before the attack. (3) Examine the throats and nasal passages of all persons with whom he has been in especially close contact, such examination, if possible (and in a school it always should be possible) to include a bacteriological examination. (4) Isolate, or at any rate exclude, all "contacts" who are found to harbour even doubtful diphtheria bacilli on their mucous membranes and all (even though a bacteriological examination proves negative) who present any suspicious appearance of the throat or nasal fossæ. (5) Search for any other possible source of infection besides a previous case

of diphtheria, not only as serving to explain the present attack but as a possible cause of fresh cases. (In this connection the possible agency of milk, drinking utensils, cats, wind instruments, &c., should be the subject of careful inquiry.) (6) Do everything which may possibly serve to lessen the infectivity of the patient, and thus shorten the period of necessary detention.

Now in school life the close and intimate association of the scholars during the hours alike of work, play, and sleep, and the special susceptibility to diphtheria incidental to their age are potent factors in favouring the spread of the disease. On the other hand, the fact of their living under disciplinary control, their supervisors being well educated and presumably intelligent persons, and the special facilities for isolation which are nowadays provided at most of the public and the higher class private schools should prove of material assistance in giving effect to the various measures to which I have referred. Although I hardly think there can be much room for difference of opinion as to the preventive measures which should be adopted at the outset there are several points which have an important bearing on the isolation of "contacts" and the length of detention and treatment of the patient which provide a legitimate field for discussion.

Let us first consider what bearing the presence in the throat and nose of diphtheria bacilli has upon the patient's capacity to infect other persons. Now, if the Klebs-Löffler bacillus be accepted as the causative agent in diphtheria it would seem but logical to regard every person harbouring these organisms in their mucous membranes as a potential source of diphtheria. It does not, however, necessarily follow that the conditions essential to successful infection are actually present. If they were diphtheria would be a good deal more common than it is, having regard to the frequency with which the diphtheria bacillus is present in the throat or nose of apparently healthy persons. I am using the term "diphtheria bacillus" in the wider sense which I have already referred to—*i.e.*, as including all bacilli which are indistinguishable from the Klebs-Löffler bacillus in respect to their form, staining, and cultural peculiarities, but the virulence of which has not been tested. The frequency with which diphtheria bacilli are to be found in normal throats is undoubtedly influenced, not only by the fact of whether or not they have been in contact with the disease, but also by the relative closeness which has characterised such contact. For instance, according to statistics which have been carefully compiled by Graham-Smith it is shown that, whereas bacilli were detected by Kober, Park, and Beebe, and by Denny in 2.7 per cent. of the throats of healthy persons who by careful inquiry were ascertained to have had no recent contact with diphtheria, the mean of the ex-

aminations made by different observers in connection with various outbreaks was, for the relatively close "contacts" in the household, 51 per cent. ; for the more distant "contacts" in institutions for the sick, 40 per cent. ; for poorer schools in which diphtheria was present, 24 per cent. ; and for the class of general "contacts," 12 per cent. In a large proportion of the cases included in these records the virulence of the bacilli was not tested, but in a good many it was, and of these the majority proved to be virulent ; yet very few of these persons developed an attack of diphtheria.

The very interesting question naturally follows, How is it that bacilli of proved virulence may often be found living in the human throat and yet their presence turns out to be quite innocuous to their host and only occasionally a source of infection to others with whom he comes into contact ? In the latter case it is not unreasonable to assume that the number of bacilli actually present in the throat would in large measure determine the chance of some being transmitted to others, whatever their ultimate fate when they get there. In the former case the question of access can hardly arise, since the bacilli are already in possession, and their reproductive capacity in a suitable medium and their virulence have already been proved by experiment. It would seem only fair to infer, therefore, that in these cases the failure of the bacilli to set up diphtheria in the person harbouring them is due to the absence of certain factors which are essential to the development of their full vital activity, while their failure to set up the disease in others would appear to be chiefly ascribable to their enfeebled reproductive capacity, as a direct result of which the likelihood of their spreading the disease would be relatively slight, since the number of bacilli available for transmission would remain proportionately small, however favourable to development the conditions might be in the throat of a chance recipient. In conformity with this view we come to recognise the existence of what might appropriately be termed a state of "active infectivity" in the host as opposed to the "potential infectivity" attaching to a person simply in virtue of his harbouring virulent bacilli in his mucous membranes. In the latter case, if one may be permitted a simile from another class of combatants, the bacilli might be said to be on "half pay," their fighting qualities, though latent, being none the less there, and available at any time for active service in circumstances calling for their employment.

For the purpose of forming an opinion as to when it is safe to allow an infected "contact" or a diphtheria convalescent again to mix with the community, it is highly important that the conditions which are capable of so modifying the vital activity of the bacillus as to influence the "infective capacity" of the

host should be clearly recognised. From a careful consideration of the evidences drawn from an experience extending over a good many years I am convinced that the most important factor is the presence of local inflammation, whether it be of the kind which in our ignorance we call simple or that definitely associated with the presence of pyogenic organisms.

The effect of inflammation in awakening the infective activity of the diphtheria bacillus is well illustrated by the recrudescence of the local lesion which may often be observed in the diphtheria convalescent as the result of an ordinary catarrh; and in the case of the infected "contact" by his developing definite diphtheria. The same thing may often be seen when scarlet fever occurs during convalescence from diphtheria, the tonsils once more becoming covered with exudation, to be followed in many cases by paralysis. So, too, when measles occurs concurrently with, or very shortly after, diphtheria. In these circumstances the condition before the days of antitoxin usually proved fatal by reason of the rapid and excessive formation of membrane in the air passages. If we admit the power of local inflammation to arouse to a state of active infectivity bacilli previously inactive, it necessarily follows that the increase in their numbers which it implies must materially augment a patient's infective capacity, and hence on theoretical grounds one comes to regard the presence of either faucial or nasal inflammation, however slight, as a sufficient reason for prolonging his detention. Confirmatory evidence of a practical character may be derived from consideration of the circumstances under which "return cases" usually arise, the common experience being that as the result of taking a cold shortly after returning home from the fever hospital a child is noticed to present evidence of nasal or faucial mucous relaxation, with the result that other members of the family are attacked with diphtheria. It is now some ten or twelve years since the late Sir Richard Thorne Thorne as a result of his wide experience in the investigation of outbreaks of the disease noted the fact that the appearance of genuine and widespread diphtheria was often preceded by the occurrence of anomalous cases of sore-throat, characterised by little virulence and of limited distribution. He recorded his belief in the occurrence, in connection with such outbreaks, of what he termed "a progressive increase of the property of infectiveness," a belief which is in accord with the explanation I have suggested.

Now as there can be no object in maintaining isolation after an individual has ceased to be a possible source of infection to others, it is important to ascertain whether any means exist by which the infective capacity of a person harbouring diphtheria bacilli can be destroyed or at any rate curtailed. This result

might be attained either by destroying the virulence of the bacilli or by reducing their number and consequent chance of dissemination. As a possible means to this end one naturally turns to antiseptics. That these agents, as their name implies, are capable of inhibiting, and, if used in sufficient strength, of altogether destroying, the reproductive capacity of micro-organisms growing under the artificial conditions of the laboratory is a well-proven fact and certainly justifies the inference that they would not be without some influence upon diphtheritic and other infective organisms, even when living under the altered conditions which characterise their existence in the human throat. This supposition is confirmed by actual observation. Not only do we usually notice that a fall of temperature almost immediately follows the adoption of efficient antiseptic irrigation of the throat in faucial diphtheria, quite apart from that produced by an injection of antitoxin, but in the slighter cases a microscopical examination of the swab taken on the day following the commencement of the treatment will commonly reveal a pronounced diminution in the number of bacteria in comparison with that observed on previous occasions. Moreover, the influence of antiseptic irrigation upon the reproductive capacity of the bacilli is frequently evidenced by their failure to grow in culture, should the swab have been taken within two or three hours after the antiseptic has been used, a fact which suggests the desirability of repeating the treatment at frequent intervals.

The power of antiseptic irrigation of the faucial or nasal passages to lower the virulence of the diphtheria bacillus, however, is more doubtful. Roux, amongst others, has shown that its attenuation can be brought about *in vitro* in various ways, amongst which the impregnation of the culture medium with a trace of an antiseptic is one of the most efficient. From these experiments we might argue that such might not improbably be effected in the human subject; but having regard to the fact that a partial reduction of virulence of the bacilli takes place in many cases normally during convalescence its occurrence, I believe, has never been satisfactorily established. Now out of the long and formidable list of antiseptics I prefer for irrigation of the fauces a solution of chlorine. Not the liquor chlori of the Pharmacopœia, but an acid solution of chlorate of potash containing free chlorine. The preparation is as old as the hills, but I know of nothing better or indeed so good. The solution I use is prepared by pouring five minims of strong hydrochloric acid on to nine grains of the powdered salt and shaking up with an ounce of water gradually added. This during the acute stage of the attack is used mixed with an equal bulk of hot or iced water every two to four hours according to the severity of the case and whether or not the

patient actively resists the treatment. During convalescence it may be used less frequently. For the nasal passages, in consequence of the somewhat irritant effect of the chlorine gas, I usually employ a solution of boric acid. An alternative to either of the above is a 0·5 per cent. solution of formalin, but its use is by no means pleasant. The value of chlorine solution has quite recently received confirmation from the results obtained by Dr. Mervyn H. Gordon in the course of an investigation into the comparative antiseptic effect of various solutions upon microorganisms present in the mouth. Some of the best known antiseptics were tested by Dr. Gordon and of these chlorine came out at the top of the list, a fact which was to me very satisfactory. Another agent which is capable of exerting no small influence in lessening the infective capacity of the diphtheria convalescent is free oxygenation. It acts beneficially both by its direct restorative effect on the system and by tending to render the tissues less favourable to the maintenance of bacterial existence.

On theoretical grounds we must admit the desirability of keeping apart from the community all persons so long as they harbour diphtheria bacilli, whether such have resulted from an attack of diphtheria or have been acquired simply by contact with the disease. Unfortunately, it is not always practicable to do so on account of the long persistence of the bacillus in some individuals. Although there are practical difficulties in the way of enforcing a rigid isolation for any great length of time in the case of some persons, particularly those who are bread-winners, the same objection could not be urged in respect to school attendance, and, whether a day pupil or a boarder, every scholar should be excluded from school until the throat and nose, as a result of three negative examinations, may be assumed to be free from diphtheria bacilli—that is to say, bacilli indistinguishable from the Klebs-Löffler organism in respect to their morphology, staining, and cultural reactions. The usually accepted view as to the relation of the Hofmann bacillus—viz., that it is a distinct organism and incapable of ever being converted into the Klebs-Löffler bacillus—I have already referred to. That the Hofmann bacillus, however, should play no part whatever in the development of diphtheria is perhaps not equally clear. The fact that certain observers have described outbreaks of apparently infective sore-throats in which the Hofmann bacillus alone was present and that in some of the cases fibrinous exudation *plus* Klebs-Löffler bacilli were also detected would appear to suggest that in certain circumstances the Hofmann bacillus may act as a predisposing factor in the development of the true disease. Dr. Joseph Priestley has recently described an outbreak of infective throat illness in a school in Lambeth characterised by tonsillar

exudation and pyrexia in which the typical Hofmann bacillus and no other was present in 38 out of the 43 attacks. The metropolitan branch of the Society of Medical Officers of Health, after careful consideration of the evidence, has lately affirmed its belief "that cases clinically resembling diphtheria but in which the Hofmann and not the Klebs-Löffler bacillus is found are infectious, and that consequently the usual precautionary measures of notification, isolation, and disinfection should be undertaken." Whether the Hofmann bacillus is competent to set up an infective membranous angina or not it would certainly be impracticable, in view of its comparative ubiquity, to make the simple fact of its presence in the throat or nose a test of the necessity for isolation. Roux and Yersin found it present in 44 per cent. of the children attending a school and in 27 per cent. of the patients in a hospital ward in which in neither instance diphtheria had occurred for many months previously. Cobbett detected it in the throats of 23 per cent. of a large number of healthy persons who had not been in contact with any known diphtheria, the proportions in well-to-do and poor persons being 4 per cent. and 25 per cent. respectively, while amongst 2,198 non-infected "contacts" examined by Cobbett and Graham-Smith the Hofmann bacillus was found in nearly 40 per cent.

The average length of time during which diphtheria bacilli are said to persist in the throat is variously estimated at from eight to twenty-four days after the disappearance of the exudation. The average period in a series of cases examined by myself was twenty days, but its duration in patients living in diphtheria wards might be assumed to be more protracted than in those treated in a room by themselves. In a fair number of cases bacilli are found to persist for six weeks, in a few more than eight weeks, and in exceptional instances bacilli may be detected as long as three months after the attack. The longest time on record is, I believe, 363 days. The presence of adenoids appears to be often responsible for undue persistence of the diphtheria bacillus, just as they are a frequent source of chronic nasal discharge. Great care should be taken that the naso-pharynx is free from bacilli before any operative measures are undertaken for their removal.

With the object of curtailing the period of potential infectivity of those harbouring diphtheria bacilli on their mucous membranes and of lessening the chance of their actually infecting others, I would strongly recommend the efficient flushing out of the fauces of all infected "contacts," three or four times a day with some reliable antiseptic solution, preferably chlorine, by means of an indiarubber ball syringe, and in the case of a person actually suffering from the disease the same procedure may with

advantage be instituted from the outset as a matter of treatment. No amount of gargling, spraying, or swabbing will be equally effective. In respect to the nasal passages an equally good result, unfortunately, cannot be obtained, since it is practically impossible to effectually reach their various diverticula. These, as might be expected, provide an excellent retreat for the bacillus. During the period of isolation as much time as possible should be spent in the open air, and out-of-door exercise should be encouraged. I should think that the instances where any real difficulty is likely to be encountered in carrying this out must be very uncommon, especially in good class schools, where some facilities for isolation are usually existent.

The injection with antitoxin of all "contacts" proved to be harbouring diphtheria bacilli has been recommended, but it is quite without effect in hastening the disappearance of the bacilli. In so far as it is competent to avert the danger of an attack, and so be a means of restricting the multiplication of organisms capable of spreading the disease, the injection of antitoxin is worthy of consideration. I am not prepared, however, to recommend its indiscriminate adoption as a prophylactic measure in the case of apparently healthy "contacts" living under skilled observation simply because diphtheria bacilli are present in their mucous membranes. In the case, however, of schools for very young children, particularly of the poorer class, there is a good deal to be said for the practice. Antitoxin should always be given, without exception, in the case of an infected "contact" who presents any indication, however slight, of either faucial, nasal, or laryngeal inflammation.