

Section of Epidemiology and State Medicine

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DISCUSSION ON THE USE AND ABUSE OF THE SWAB IN COMBATING DIPHTHERIA

Dr. H. J. Parish: It should be unnecessary to debate this subject. Diphtheria is preventable, and, if immunization by modern methods was universal and timely, the use and abuse of the swab would not be a major topic for discussion as it is to-day. But we are not living in Utopia, and it is fitting that clinicians, public health administrators, and bacteriologists should have an opportunity of stating their special difficulties and problems. The existence of a remarkable diversity of opinion and practice on the subject of diphtheria diagnosis was revealed some eighteen months ago in a lengthy correspondence in the *British Medical Journal*.

Inquiry into the reasons for deaths from diphtheria suggests that, in many instances, the relatives of the patient are at fault in delaying to seek medical advice, while doctors frequently have the patient under observation for several days before administering antitoxin. Carey (1919) investigated 1,000 deaths from diphtheria in Massachusetts; 27% of the patients had been ill for more than seven days before the medical attendant was summoned. Fifty-six deaths from diphtheria were reviewed in the *Weekly Bulletin* of the City of New York Department of Health, February 5, 1927; 82% of the patients were not seen by a doctor until they had been ill for from one to five days; in 52% the practitioner delayed the administration of antitoxin for a further one to fourteen days. In the Annual Report for 1929 of the Medical Officer of Health for Birmingham, Dr. E. H. R. Harries analysed particulars of 69 cases of diphtheria which ended fatally; 38% of the patients had been ill for more than four days before the medical practitioner was called in. The doctor, moreover, was frequently at fault; 35% of the patients had been swabbed before admission, yet only 7% had been given antitoxin—surely an instance of the misuse of the swab!

The discussion on the swab falls under three main headings, viz.: (a) The information the swab can give to those in clinical and administrative charge of the patient; (b) the ideal technique to be used in the examination of the swab in the laboratory; and (c) the application of this special technique to diagnostic, administrative, and research purposes.

(a) AID TO THE DIAGNOSIS OF CASES

It must be clearly recognized in the first place that the responsibility for the diagnosis of diphtheria rests entirely with the clinician. The detection in the laboratory of organisms morphologically resembling the diphtheria bacillus does not prove the disease to be diphtheria, nor does their absence necessarily exclude that condition. The swab is, or should be, only of confirmatory value in the diagnosis of typical cases; in other cases where the presumption is on the whole against clinical diphtheria, it attains a more important rôle and helps the clinician to make up his mind as to the nature of the disease. Good technique is, of course, essential both at the bedside and in the laboratory. *The taking of a swab is a manipulation of major importance and must not be delegated to a student or junior nurse.* A

tongue depressor is necessary, and it is important to have efficient lighting so as to obtain a good view of the fauces. An antiseptic gargle should not have been used for several hours before the taking of the swab. If there is only a small nidus of infection, the practitioner must be careful to rub the actual lesion, and to avoid heavy contamination with saliva. When he wants help with a difficult case, he must afford adequate data to the bacteriologist, who, for his part, should avoid unnecessary delay in furnishing his report. In many laboratories this will involve an improvement of the present organization, and admittedly the cost of the examination will be higher. The actual bacteriological methods to be employed will be discussed later in this paper.

Is antitoxin to be given at the earliest possible moment to every patient from whom we take a swab? This is debatable, but exceptions should be infrequent to the golden rule of our student days, viz. to inject antitoxin whenever we swab a suspicious throat. Many lives are still being lost through failure to give serum early enough. Of two evils, a serum rash is preferable to a fatal issue, and the practitioner who withholds serum until the laboratory report is forthcoming may incur a grave responsibility.

(b) ADMINISTRATIVE VALUE

(i) *Notification of cases.*—The swab should be regarded as of greater value to the clinician and the Medical Officer of Health as an administrative measure than as an aid to diagnosis. Notification of doubtful cases should be deferred until the results of the examination of the swab are known. If the report is negative, another swab should be taken, and if this also is negative, the patient may safely—so far as risk of diphtheria is concerned—be nursed at home, even in contact with many Schick-positive children. If he has already been admitted to hospital, the authorities may await a second negative report and then discharge him, thereby effecting considerable saving of expense. He may, of course, have Vincent's angina, streptococcal sore throat, or even infective mononucleosis, and require further treatment in hospital.

I have been surprised at the extent to which the diagnosis of patients admitted to hospital as cases of diphtheria has to be revised on further investigation. Caiger and O'Brien (1924) reported that the diagnosis could not be confirmed in 41% of 529 patients admitted as cases of diphtheria to the South Western Hospital, London. In the Annual Report for 1929 of the Medical Officer of Health for Birmingham, Dr. E. H. R. Harries stated that the revision of diagnosis was necessary in 706 (83.6%) of 2,099 cases admitted, and in the Report for 1934, his successor, Dr. J. McGarrity, could find no clinical evidence of the disease in 585 (87.7%) of 1,551 patients admitted. In 1933 and 1934 in Cork, Dr. J. Saunders reported that revision of diagnosis was necessary in 204 (47.9%) of 426 cases notified as diphtheria.

It is unfortunate that patients cannot be sent into hospital merely for observation, but have to be definitely *notified as cases* of the disease. The relatives of a patient discharged with a revised diagnosis within a short period of admission to a fever hospital as a case of diphtheria have just cause for complaint, and may criticize adversely the diagnostic capabilities of the practitioner responsible for the notification. On the other hand, the error in diagnosis may not be disclosed by the hospital authorities, which is equally unsatisfactory to the patient, and introduces a fallacy into the statistics of the incidence of diphtheria. It will cause no surprise to the psychologist that the practitioner should tend to overlook the next atypical case of diphtheria which occurs in his practice, or, at least, may not inject antitoxin until a positive bacteriological report gives the necessary assurance to himself and the patient's friends.

An "observation certificate" which would suffice for the removal of a patient from his surroundings and his admission to hospital, would obviate much administrative waste and the rebuff the practitioner experiences when his diagnosis is

revised. A further extension of the admirable policy of the London County Council, in providing cubicles for the isolation of patients would be requisite to make the scheme practicable. In the long run I think there would be considerable saving of money.

A minor problem of notification arises in connexion with very transient true diphtheria in persons who are nearly immune. As these cases are for the most part rapidly self-curative, the membrane on the throat observed by the practitioner responsible for notification may have cleared completely before the patient's admission to hospital. Obviously no blame is to be attached to the practitioner, although his diagnosis of diphtheria may be revised by the hospital staff, who regard the illness as tonsillitis in a carrier of virulent organisms and may even discharge the patient within a week of admission.

(ii) *Examination of contacts and carriers.*—It is often necessary to swab contacts in order to acquire early information about the spread of infection. The nose should be swabbed as well as the throat, since in very many instances a nasal swab will give a positive result when a throat swab will not.

In many outbreaks it is the profuse carrier or ambulatory case which constitutes the real menace. In transient carriers the bacilli are probably often sparse, and while we may assume that these individuals serve a useful purpose by helping in the immunization of the general population, they may at times give rise to a fatal infection in a person with low immunity or resistance. In considering the isolation and treatment of carriers we must be guided by the presence of abnormalities in the nose and throat, the numbers of organisms grown on culture, and the period over which a swab may have been positive, remembering that the sparse carrier to-day may be the profuse and therefore dangerous one to-morrow.

Another problem for discussion is the disposal of the convalescent or spontaneous carrier who does not "clear" after a long period of detention and treatment in a fever hospital. The introduction of tellurite media into laboratory practice has increased the number of positive bacteriological reports, and imposes additional responsibility on the clinician who has to interpret them.

Carriers may develop sore throats from causes other than diphtheria, and I need hardly remind my listeners of the Schick test which will often help in the differential diagnosis of true diphtheria and tonsillitis in a carrier of virulent K.L.B. Nor need I emphasize the supreme importance of tests for virulence in convalescents and carriers, in whom non-virulent forms of the diphtheria bacillus occur frequently.

(c) AID TO RESEARCH

Recent lines of research in which the swab is invaluable include the occurrence of diphtheria in Schick-negative reactors, the invasiveness of *C. diphtheria* "gravis," the investigation of carrier rates, the effect of artificial immunization on the carrier rate, and the origin of natural antitoxin.

Certain strains of *C. diphtheria* "gravis" appear to be more invasive than the epidemic strains met with a few years ago, and are responsible for the majority of cases of diphtheria occurring in Schick-negative reactors. Dudley, May, and O'Flynn (1934) and Parish and Wright (1935) have reported the occurrence of small outbreaks of diphtheria due to strains of this type in immunized populations. These were administratively a nuisance, but would have had more serious consequences in the absence of immunization. It is suggested that the degree of protection indicated by a negative Schick reading may occasionally be inadequate to prevent infection by special virulent strains, and that the aim of the practitioner should be to confer as high a degree of protection as possible in the subjects immunized. But this is another question, and is outside the scope of this discussion.

With the increasing prevalence of the "gravis" organism in various parts of England, there has been an increase not only in the number of cases reported in

Schick-negative reactors, but also, occasionally, in the number of carriers associated with those cases. Admittedly, in the past, estimates of the number of carriers of diphtheria bacilli in any population have fallen short of the actual numbers. Parish and Wright (1935) have reported two outbreaks associated with a virulent carrier rate of 40%, and Seager (1935), working with Professor Hedley Wright in Liverpool, found that 63% of the patients in a scarlet fever ward were carriers of virulent K.L.B. But even more surprising was his observation that some of the patients were Schick-positive reactors, which upsets the oft-repeated dictum that carriers, other than the most transitory, must be Schick-negative. This recalls too, the work of Dudley, May and O'Flynn (1934) who found five Schick-positive reactors who were harbouring virulent bacilli without symptoms of sore throat. We ourselves have recently observed a patient of Dr. Byers of the Bromley and Beckenham Isolation Hospital, who showed no signs of infection, but harboured virulent organisms (numerous at first, but later scanty) in his throat for several weeks; throughout the period of investigation there was no detectable antitoxin in his serum. Clearly there is some other factor in immunity against diphtheria besides circulating antitoxin.

The effect of artificial immunization on the carrier rate will probably be discussed by subsequent speakers. If the carrier rate is high in an immunized population, is this to be ascribed to the immunization *per se* or to the introduction of a more virulent and invasive strain? Of one thing there can be no doubt, viz. that mass immunization of a community reduces the incidence of diphtheria to a negligible quantity.

A final word with regard to the origin of natural antitoxin in locations where clinical diphtheria is rare or absent. Work in India and elsewhere, and amongst the Eskimos, suggests that a specific stimulus is at work, and that persons become Schick-negative as a result of carrier conditions and latent specific infections. Similarly there is little doubt that the natural antitoxin of horses is also specific in origin.

LABORATORY METHODS

It is necessary to consider in what respect some of the older methods of investigation have been found wanting, and what refinements of technique have been introduced of recent years or are undergoing trial now.

The clinician should realize that the newer knowledge has complicated the work of the bacteriologist. Some laboratory workers now believe that it is no longer sufficient to rely solely on Loeffler's serum for the cultivation of the diphtheria bacillus, because (1) more positive results have been obtained with a tellurite medium, as Allison (1930), McLeod and other workers in this country, and Clauberg (1934) and his colleagues in Germany have pointed out, and (2) the polar staining of many "gravis" and "intermediate" strains may be absent on *primary* culture on Loeffler, so that the organisms resemble harmless diphtheroids. This may be the explanation of some of the not infrequent negative reports from the bacteriologist in undoubted clinical diphtheria, which suggest that some modification of laboratory technique is desirable. I have also observed a dry swab, which had not been moistened in condensation water in the culture tube or in saline, being rubbed over old Loeffler medium which had dried and could not have had growth-promoting properties. The unsatisfactory results which are inevitable with dry media can be obviated by the use of McCartney's screw-capped bottles

Tellurite media should be included in the practice of every bacteriologist, for the following reasons: (1) Tellurite media give from 10 to 25% more positive results than Loeffler's serum; (2) they inhibit more or less completely other organisms, so that colonies of *C. diphtheriæ* can readily be "picked off" for biochemical and virulence tests; (3) on tellurite media, colonies of *C. diphtheriæ* are easily differentiated from those of *C. hofmanni*; (4) on McLeod's medium, "gravis,"

"intermediate" and "mitis" strains of *C. diphtheriæ* give characteristic types of colony.

Tellurite media tend to shorten the diphtheria bacillus so as to make microscopic recognition difficult—a disadvantage which need not be a deterrent to their use. Loeffler's serum should always be used in conjunction with tellurite media.

It is suggested that some such procedure as the following should be adopted in the laboratory:—

(1) Examination of direct smear, mainly to exclude Vincent's angina. (This practice should be universal as Vincent's angina is by no means rare.)

(2) *Either* inoculation of Loeffler serum and McLeod's chocolate tellurite medium (Anderson, Happold, McLeod and Thomson, 1931) in plate or McCartney screw-capped bottle. (Unfortunately McLeod's medium has the disadvantage of being rather difficult to prepare in the small laboratory.)

Or inoculation of Loeffler serum; preliminary report after eighteen hours; whether microscopically positive or negative, the overnight growth to be heavily subcultured on to Horgan and Marshall's tellurite medium (Horgan and Marshall, 1932, O'Meara and Parish, 1933, Parish, 1934) in plate or screw-capped bottle. (Horgan and Marshall's medium is easy to prepare.)

(3) Colonies "picked off" the tellurite medium for fermentation tests (including starch), and virulence tests. (In many areas virulence tests of cultures of the prevailing "gravis" and "intermediate" types appear to be unnecessary, since over 99% of strains belonging to these types are virulent, *see table*.)

(4) Final report.

VIRULENCE TESTS IN RELATION TO TYPE

| | "Gravis" | | "Intermediate" | | "Mitis" | |
|--|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|
| | No. of strains tested | Per cent. virulent | No. of strains tested | Per cent. virulent | No. of strains tested | Per cent. virulent |
| Robinson and Marshall (1934), Manchester | 97 | 96.9 | 118 | 94.1 | 96 | 80 |
| Parish and O'Meara, London | 366 | 99.5 | 116 | 99.1 | 67 | 86.6 |
| | "Barred" | | | | | |
| Mair, London * | 1,214 | 99.7 | 1,702 | 99.9 | 2,158 | 87.5 |

* I am indebted to Dr. Mair for permission to quote his data, which he communicated at the January Meeting of the Pathological Society of Great Britain and Ireland. The "barred" forms described by Mair correspond closely to the "intermediate" type of the Leeds workers, and his "mitis" type includes all other strains which do not ferment starch. Twenty-four per cent. of the strains examined by Dr. Mair were of "gravis" type, 33.5% "barred," and 42.5% "mitis."

The serum-treated swab (Folger-Solé).—The serum-treated swab was originally used by Folger in 1902, and has recently been redescribed by Solé (1934), Brahdý and his collaborators (1934 and 1935) and myself (Parish, 1935). It improves the rapidity and reliability of diagnosis, and therefore merits careful consideration. A small bottle of normal serum without antiseptic is supplied with the ordinary cotton-wool swab. When required for use, the swab is dipped into the serum, heated over a flame until steam just begins to rise, and then rubbed carefully on the lesion. It is incubated for four hours—in an emergency in the practitioner's waistcoat pocket. The bacilli multiply in the "culture" on the swab, and can be readily detected in smears stained by Albert's method. On transfer to Loeffler or Horgan and Marshall's medium, rapid growth ensues so that sufficient K.L.B. for virulence test may often be present in a sixteen-hour culture. The new method contrasts very favourably with the old, in which Loeffler slopes inoculated direct from an untreated swab usually show a much smaller percentage of diphtheria bacilli when examined overnight.

Brahdý and his colleagues claim to be able to furnish accurate reports in over 80% of cases of clinical diphtheria within two hours of receipt of the swab in the laboratory and in 95% within four hours, in comparison with only 83% accuracy within eighteen hours by the classical Loeffler method.

APPLICATION OF A COMPLETE LABORATORY TECHNIQUE

Value in administration and research.—The value of the swab in administration and research is very high, and for this purpose we must have the largest possible number of isolations. But although full use should be made of modern bacteriological methods, common sense must be used in their application to practical medicine. To give but one example, a special difficulty may conceivably arise in dealing with persistent carriers—are they to be released from strict isolation before they are bacteriologically negative? This step should only be taken after a thorough overhaul of their upper respiratory passages by a competent specialist to exclude a dangerous nidus of infection.

Aid to the diagnosis of cases.—The Folger-Solé swab method deserves the special attention of those who have to send swabs through the post over long distances. In a recent paper Helen Kelsey (1934) found that untreated swabs yielded 97·4% of positive cultures after a delay of twenty-four hours before inoculation on Loeffler's serum, 91·8% after forty-eight hours' delay, and only 48·7% after ninety-six hours' delay, results which cannot be regarded as satisfactory. Kelsey has advocated the use of inoculated, but unincubated, tubes of media for transit through the post. A similar procedure has been used for some years in U.S.A. It is suggested that serum-treated swabs would be equally satisfactory.

Unfortunately, modern refinements add considerably to the cost of the laboratory investigation. Although a complete bacteriological examination involving the use of tellurite media is superfluous in the majority of typical clinical cases, there have been cases of genuine diphtheria which have yielded negative cultures because of the limitations of the Loeffler's serum technique; better methods are obviously desirable for the cultivation of the organisms from those cases, and they are available.

It may also be objected that the more general use of tellurite media will lead to the notification of many bacteriological non-clinical cases, in other words, that while Loeffler may give rise to too few positives, by the use of modern methods we tend to get too many. But surely the bacteriologist is not fulfilling his function unless he uses the very best means known to him for detecting diphtheria bacilli even if they are present only in very small numbers. Of course, if he experiences special difficulties in isolation he should say so in his report.

Thus, we are brought once again to the only safe rule, viz. that swabbing must not be employed as a primary or chief means of diagnosis. Diphtheria is a disease and not a bacteriological finding; it is necessary to differentiate between clinical diphtheria and the presence of diphtheria bacilli in the throat. Close collaboration between physician and bacteriologist is essential—much closer than is often the case at present. Every large fever hospital should have its own bacteriological laboratory. The physician must remember that the onus for early diagnosis and treatment rests with himself; he should have some knowledge of the methods used by his bacteriological colleague, and not express surprise or contempt for laboratory procedure if an early negative report is revised subsequently. It is, moreover, the function of the clinician to endeavour to interpret the laboratory findings.

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Dr. C. O. Stallybrass: My contribution is meant to represent the views of the Public Health Department and of the hospital administrator.

The subject seems to divide itself naturally into the consideration of the value of the swab: (a) In the diagnosis of diphtheria before admission; (b) in the diagnosis and administration in the isolation hospital; (c) in the search for carriers and missed cases. It is, of course, assumed that the use of the swab is supplementary to, and not in substitution for, methods of artificial immunization.

THE SWAB BEFORE ADMISSION TO HOSPITAL

To what extent is the swab used outside the isolation hospital in the diagnosis of diphtheria? Is its use valuable, injurious, or neutral? Two years ago with a view to obtaining an answer to these and certain other questions a questionnaire was filled up in respect of about 200 consecutive cases admitted to Liverpool hospitals as diphtheria; of these 175 were regarded as diphtheria in hospital. Disregarding the clinically negative cases which comprised about 12% of the total, the following figures apply:—

| | (1) | (2) | (3) | (4) | (5) | (6) | (7) |
|-----------------------|--------------|-------------|--|---|--------------------------------------|---------------------|---|
| | No. of cases | Average age | Average period elapsed before sending for doctor | Average delay from time first seen by doctor to time of first dose of serum | Average first dose of serum in units | Case mortality rate | No. of cases in which swab was taken before admission |
| Total cases | 175 | 10 years | 36 hours | 16.1 hours | 17,000 | 8% | 21 133 = 15.3% |
| Fatal cases | 14 | 5 years | 65 hours | 35.4 hours | 40,500 | — | 1 |
| Cases swabbed outside | 21 | 14 years | 26 hours | 19.7 hours | 14,000 | 4.8% | 21 |
| | 133 | | | | | | |

The question as to whether a swab was taken outside was not asked at the first, but was an afterthought, and the replies relate to only 133 of the 175 cases. A swab was taken before admission in 15% of cases of diphtheria admitted to hospital.

From the above table it will be observed that: (a) The average age of fatal cases was, as might have been anticipated, only half that of the total; on the other hand, the average age of cases swabbed was higher than the average of all cases; swabs were much more frequently taken from adults than from children; (b) the average delay in sending for the doctor was much greater in fatal cases than in other cases; this high average is largely due to the inclusion in the average of three cases in which delays of 192, 148, and 107 hours occurred respectively before sending for the doctor; in one of these a further delay of sixty-five hours occurred between the doctor being sent for and the patient being sent into hospital; no swab was taken in this case. (c) In fatal cases the delay between sending for the doctor and the administration of the first dose of serum was double that of the average. We cannot exempt this lapse of time from having some contributory influence on the fatal course of the disease. On the other hand, the difference of 3.6 hours between the swabbed cases and the average of the whole series had little influence upon the mortality as, in the case of the one child who was swabbed and who died (a child aged 3½ years), a delay of fifty hours was extended by only another ten hours before admission to hospital was arranged. (d) The condition of the patient—as judged by the dosage of serum administered on admission—was much graver in the

fatal cases, and definitely lighter in the cases swabbed outside. (e) The case mortality rate of the patients swabbed outside was little more than half the average of the series, i.e. 4·8 and 8·0% respectively. The definitely high case mortality of the whole series was associated with the prevalence of a *gravis* type of organism and is not watered down by any inclusion of diphtheria carriers without clinical symptoms.

Considering the factors which led to death, the fourteen fatal cases of the series may be tabulated thus:—

FOURTEEN FATAL CASES

| | |
|---|--------------------------------------|
| Thought by parents to be mumps | 2 cases (3 and 6 years old) |
| Parents' delay (over 48 hours ill) | 5 ,, (3½, 4, 5, 5, and 10 years old) |
| Doctors' delay (over 24 hours) | 2 ,, (2 and 6 years old) |
| Parents' and doctors' delay | 1 case (3½ years) |
| Parents' history probably incorrect as judged by condition on admission | 1 ,, (5½ years) |
| Hæmorrhagic | 1 ,, (3 years) |
| and doctor's delay | 1 ,, (6 years) |
| Rapidly became severe | 1 ,, (5 years) |

In only one fatal case—that of a child, aged 10—did death result from laryngeal diphtheria, and in this case there was definite delay by the parents, as one hundred and forty-eight hours of illness elapsed before they sent for medical aid.

If this series is typical—and I believe it is—we must conclude that the main factors in the causation of these deaths were (a) prevalence of a severe type of infection, (b) failure either on the part of parents (9 cases) or of doctor (3 cases) to realize the gravity of the infection in young children, (c) that time spent in taking a swab did not contribute to the fatal issue. In fact, it may be stated that, if all concerned had been as alert to the urgent need for correct diagnosis in these young children as the doctors were in relation to the diagnosis in adults and adolescents—i.e. those over 15 years of age, of whom 7 out of 15 (nearly half) were swabbed and admitted to hospital—the mortality would have been very definitely diminished. The urgent need for an early and correct diagnosis, or alternatively of an adequate dose of serum, in children under 7 years of age suffering from sore throat or enlarged glands, stands out prominently from this investigation.

In the series of 21 patients swabbed outside the fever hospital, it may be said that four swabs were taken in general or children's hospitals and two by doctors on the public health or hospitals staffs.

So much for the use of the swab outside the hospital in the case of faucial or laryngeal diphtheria. The use of the swab is to be urged in all cases where doctors are in doubt, and at least for all children under 7 years of age; the patient should simultaneously be given the benefit of the doubt, and either serum should be administered or the child should be admitted to hospital as a suspect. One point in the series of persons swabbed is significant, namely that only one of them was a nasal case. I cannot believe that 1 in 133 represents the prevalence of nasal diphtheria; my own experience points to a much greater prevalence, and if all cases of purulent nasal discharge were swabbed, I would prophesy that a much higher proportion of nasal cases would be admitted. It would appear that nasal cases of diphtheria are much more infectious than faucial cases.

Concerning the value of the swab outside the hospital, I think it may be asserted that if a positive swab does not necessarily mean diphtheria, even when a virulence test is positive, a negative swab even less establishes that it is *not* diphtheria. I remember being called to see a prominent citizen whose practitioner was puzzled by two negative swabs in what he otherwise regarded as a clear case of diphtheria. The solution was that the patient was using a strong antiseptic gargle and the swabs were sterile. Here, all that was necessary was to make a decision between diphtheria and Vincent's angina, and examination of a stained film was quite conclusive.

For the distinction between diphtheria and Vincent's angina the use of the swab is invaluable. If every swab sent to the laboratory for examination for diphtheria were also examined for Vincent's angina it is probable that a considerable number of the negative swabs that occur in what is regarded clinically as diphtheria would be found to be from cases of Vincent's angina. The two diseases may coincide, and every direct examination of a swab microscopically should be followed up by culture.

THE SWAB IN THE ISOLATION HOSPITAL

Let us now turn to the use of the swab in the hospital. Here I believe that the position has been radically changed by the differentiation of the strains of diphtheria bacillus into *gravis*, *intermedius* and *mitis* types. I desire to express my acknowledgments to Dr. Robinson of Manchester, and especially to Professor Hedley Wright of Liverpool, in this association.

The practice in regard to diphtheria in the Liverpool hospitals is as follows: As soon as a patient notified as having diphtheria is admitted to an isolation hospital he is seen by the resident medical officer, who decides whether the case is to be regarded clinically as diphtheria or some other infectious disease, or whether, on the other hand, the diagnosis is doubtful or negative. If in the first category he is sent to a general ward, if in the second he is admitted to a bed-isolation ward or a cubicle. A swab is at once taken and a Schick test is carried out, followed, if necessary, by a dose of serum after an interval of four to six hours. The cultures, if positive, are tested for virulence, a negative culture will be followed up by a second culture a few days later. If typing is carried out I believe that the virulence test may be omitted in all except *mitis* strains. The following figures obtained from Wright demonstrate this point:—

Of 145 *gravis* strains only 1 was non-virulent.

Of 116 *intermedius* strains only 4 were non-virulent.

Of 121 *mitis* strains 43 were non-virulent.

A later group of 110 *mitis* strains showed that 57, or just over half, were non-virulent.

We can now treat the patient according to the findings:—

(a) *Clinically negative; bacteriologically negative; Schick-negative.* Discharge from hospital if clinical condition warrants this. The stay in hospital of these patients is reduced to seven to ten days. I have never known a return case in this group. Most of the cases bed-isolated fall into this group.

(b) *Clinically negative; bacteriologically negative; Schick-positive.* If no serum has been given the Schick test can be repeated after ten to fourteen days. If still positive, the patient may be discharged and referred to the immunization clinic. If the Schick test becomes negative the case is probably diphtheria. Such cases are, however, infrequent.

(c) *Clinically negative; bacteriologically positive; Schick-negative.* This is a diphtheria carrier and may be treated as such.

(d) *Clinically negative; bacteriologically positive; Schick-positive.* This is a mild case of diphtheria and illustrates the difficulty of diagnosis. These are patients who are in process of natural immunization, and they are discovered not infrequently in ward outbreaks of diphtheria in children's wards.

This procedure greatly reduces the length of stay of these patients in hospital. It should be adopted in all cases who have been inoculated against diphtheria, and in these cases the virulence test should invariably be carried out.

We have now to consider the effect of the typing of strains upon isolation hospital procedure. And I would here like to interpolate the findings in Liverpool where the severity of diphtheria has been a prominent feature for a considerable number of years. A severe outbreak occurred at the end of the Great War and the fatality rate rose to 17.5% in 1918. A fresh outbreak occurred in 1930 and still continues. Sir Arthur Newsholme surveyed a similar occurrence in Lancashire in

the eighties of last century. I drew attention to this rise of virulence in 1923. Last year the results of a preliminary survey by Robinson pointed to the prevalence of a high proportion of gravis types in Liverpool comparable to those obtained in Leeds, Hull, and other Northern Cities. Professor Hedley Wright informs me of 1,200 consecutive swabs—not individual patients—taken in nine months of 1935, the results were; 34·8% gravis; 34·5% intermedius; and 30·7% mitis.

A further survey of 108 consecutive admissions into Fazakerley Hospital gives 37·2% gravis (with two deaths) 45·8% intermedius (with three deaths) and 17·0% mitis (with no deaths).

A series of patients have been followed through their stay in hospital. It has been found, most significantly, that the type not infrequently changes during the course of their stay. I give two illustrative cases, for which I am again indebted to Professor Wright:—

| CASE A.857. | | | | | |
|------------------------|-----------|----------------------|---|--|------------------------|
| October 18 | Negative | | | | |
| " 29 | | | | | |
| November 5 | N + T - | Mitis (non-virulent) | | | |
| " 11 | N + T - | " | " | | |
| " 16 | N + T - | " | " | | |
| " 25 | T + | " | " | | + intermedius |
| | N + | " | " | | + intermedius + gravis |
| December 2 | N + | " | " | | + intermedius |
| | T + | " | " | | |
| December 9, 11, and 16 | Negative | | | | |
| CASE S.666. | | | | | |
| October 5 | Admission | T + N - | | | Intermedius |
| " 16 | Negative | | | | |
| " 28 | N + T - | Intermedius | | | |
| November 11 | N + T - | " | | | |
| " 18 | N + T - | " | | | |
| " 25 | N + T - | " | | | |
| December 2 | N + T - | " | | | |
| " 17 | N + T - | " | | | + virulent mitis |
| January 1 | N + T - | Mitis (virulent) | | | |
| | | N = nasal swab. | | | T = throat swab. |

In view of these findings, which point clearly to the occurrence of cross-infection with other types of corynebacterium as not infrequent, we may have to revise our ideas of hospital administration. Are all cases to be given the benefit of bed isolation until they have been typed, and then only admitted into a ward restricted to their particular strain? Or are all cases to be treated on bed-isolation methods throughout their stay? Such methods might somewhat shorten the average length of stay in hospital but not very much; the length of stay in hospital is much more dependent upon the severity of the disease and the fear of the late onset of paralysis than upon bacteriological findings. Those happy individuals, if there be such, who have had only to deal with mitis diphtheria and not with gravis and intermedius epidemics, have still much to learn about this disease.

THE DISCOVERY OF CARRIERS AND MISSED CASES

The third function of the swab in combating diphtheria is in the discovery of carriers and of missed cases either in hospital, in an institution, or in the world at large.

When a case of diphtheria occurs in a children's ward a sort of standstill order is at once put into operation. The procedure adopted in Liverpool is embodied in a circular memorandum.

As soon as the results of the swabs from nose and throat and of the Schick test are known it is possible to separate the children into four categories:—

(a) *Schick-positive, swab-positive.* These are candidates for diphtheria and should be isolated and receive a dose of serum.

(b) *Schick-negative, swab-positive.* These are carriers and should be isolated pending the result of the virulence test.

(c) *Schick-positive, swab-negative.* These patients should remain in the ward and immunization should be begun as soon as permission can be obtained.

(d) *Schick-negative, swab-negative.* These patients also remain in the ward but require no further action.

Having separated those with positive swabs from those with negative swabs, the standstill order may be relaxed. Dr. Parish has already referred to the outbreak of diphtheria in a scarlet fever ward reported by Seager where, probably as the result of a nasal case having been missed, no less than 63% of the other children were found to be carriers of virulent bacilli. The use of the swab in these circumstances is the mainstay in combating diphtheria and restoring the ward to its normal function.

When an outbreak occurs in an institution a somewhat similar mode of procedure may be followed. Opinions may differ as to the value of the administration of serum to the Schick-positive, swab-positive class. Many would proceed to active immunization forthwith. If this type of community has once become thoroughly infected it may be a most difficult matter to eliminate all carriers, especially if one has to do with a hospital with sufficiently prolonged stay to retain the more or less chronic carrier, but with a constant influx of newcomers, who have to be immunized after admission. Such hospitals become a nightmare to the administrator who goes about with swabs in his pocket for long periods. Nevertheless with active immunization the carrier rate will fall. I might instance a children's sanatorium with 200 beds. During the last four years swabs have been taken as follows:—

| | | | |
|-------|------------------------|-------|------------------------|
| 1932. | 133 swabs, 13 positive | 1934. | 395 swabs, 46 positive |
| 1933. | 471 „ 69 „ | 1935. | 265 „ 2 „ |

Active immunization was begun in August 1933. The average duration of stay is about seven months. Many of the swabs were duplicates or repeated positive results from the same individual. Most of the children were swabbed on admission. Typing was not carried out.

Of course, this search for carriers in institutions such as orphanages, cottage homes, residential schools—the semi-isolated communities—by the taking of swabs, is only an adjunct to active immunization. Some thirty such communities have been immunized in Liverpool and if all new entrants are immunized, as is generally the case, the combined contribution of the institutions to the city's diphtheria register becomes negligible.

In elementary schools I was engaged in the examination of contacts for a period of ten or twelve years, and I still believe this to be a useful activity. If 100% of children could be immunized the taking of swabs could no doubt be omitted; but as the percentage of acceptances varies from 20 to 50 as a rule, it appears to be advantageous to swab contacts in a class or school where diphtheria is occurring. In particular, all children who have nasal discharge, sores about the face, or a recent history of sore throat should be examined. The position is similar to that of the dead rat and the trapped rat in relation to plague; one is much more likely to find plague bacilli in rats that have died a natural death than in those that still take an interest in their food. No doubt the discovery of carriers or ambulatory cases of this type is not going to prevent their fellows ever getting in touch with the corynebacterium, but it does seem desirable to reduce the volume of infection so as to give the process of natural or artificial immunization a reasonable chance.

A few years ago I visited the Blegdams Hospital in Copenhagen and was informed of Professor Bu's findings of corynebacterium in facial sores. Returning to Liverpool I suggested to the school doctors and the skin specialists that they should take swabs at random from cases of "impetigo" and "eczema" of the face. We were promptly rewarded by a plentiful crop of cases of nasal diphtheria. In one such case reported from a minor ailments' clinic, I visited the home and found two other similar cases in pre-school children. Now at the children's skin hospital at Belmont Road Institution it is the routine to swab all such cases on admission. But still diphtheria creeps in and the only solution appears to be to treat all such cases by isolation methods. Even persistent swabbing has its limitations.

I cannot speak from first-hand experience of the value of swabs taken from contacts of diphtheria in the home, and must leave it to others to speak on this point.

This paper refers mainly to the *use* of the diphtheria swab. It appears to me that its abuse lies mainly in allowing the bacteriological finding to warp one's judgment so as to err either on the side of declaring a clinical case of diphtheria to be something else; or alternatively of declaring a mere carrier of diphtheria to be a case. This conclusion, however, still leaves open the question as to what are the criteria of a clinical case of diphtheria.

APPENDIX

CITY OF LIVERPOOL

Steps to be taken on the Occurrence of a Case of Diphtheria in a Ward

- (1) The patient should be isolated as soon as possible.
- (2) All children in the same ward should be put to bed for forty-eight hours. Swabs from their throats and from the nose or ears if discharge is apparent should be taken and submitted for examination. A very careful watch for nasal diphtheria should be kept.
For the information of the bacteriologist, a distinction should be made between throat swabs on the one hand, and nasal swabs, ear swabs, or skin swabs on the other hand, because of the presence of diphtheroids in the latter. At the same time it is desirable to ask for a virulence test to be carried out where a positive result has been reached.
- (3) It can be assumed that a positive report signifies a carrier needing isolation pending a virulence report subsequently. Avirulent carriers can be released from isolation at once.
- (4) While they are in bed, all contacts should be inspected four times in each twenty-four hours, and their temperatures should be taken every four hours. This is particularly important when a prophylactic dose of diphtheria antitoxic serum has not been given.
- (5) If it be decided to give a prophylactic dose of antitoxic serum, 1,000 units should be given intramuscularly. It is not necessary to take this course when the contact supervision is adequate, and it has the objection that serum sensitiveness may result.
- (6) All cups, forks, spoons, and plates used by the children in the ward should be boiled or otherwise sterilized after each meal. Such sterilization should continue for one week after the removal of the last case or carrier.
- (7) In the case of contact children who will be under institutional treatment for a sufficient length of time, active immunization against diphtheria should be considered. Inoculation for the active immunization of contacts can be commenced within three days of the removal of the case or carrier. When prophylactic serum has been given, however, active immunization should be postponed for three weeks until the effect of passive immunity has passed.
- (8) In hospital wards to which cases are admitted for periods averaging over a month the question of active immunization of the patients should be taken into consideration.

Public Health Department,
Municipal Annexe,
Liverpool,

10th March, 1932.

W. M. FRAZER,
Medical Officer of Health.

Dr. J. D. Rolleston: I have been asked to deal particularly with the clinical aspects of the question. I am fully in accord with the remarks of previous speakers, not only with regard to collaboration between the physician and bacteriologist, but also as to the onus of the diagnosis resting primarily on the clinician. This is a point of extreme practical importance and is constantly emphasized *viva voce*, as well as in textbooks and periodical literature by bacteriologists and clinicians alike, but nevertheless it still only too frequently happens that delay occurs in giving a patient antitoxin or sending him to a fever hospital because the report on the throat swab has not been received or is negative. It is an important fact that a malignant form of diphtheria may simulate quinsy or mumps, and it is just in these cases that the swab may be negative, owing to the bacilli being deeply situated between the necrotic layers of the mucous membrane and the submucosa, and only become positive when the membrane begins to separate (Friedemann). The mistaken

diagnosis of quinsy leads not only to an error of omission in withholding antitoxin but also to one of commission in incising the inflamed throat and thereby considerably aggravating the condition. Of 43 cases of malignant diphtheria reported by Gordon and Young which had undergone incision of the peritonsillar tissue, owing to the condition having been mistaken for quinsy 25 died, a mortality of 58%, as compared with one of 3.4% among cases of equal severity in which no incision had been made. Such errors, which lead to fatal results in a large proportion of cases, are especially liable to be made by recently qualified hospital residents, but may also be committed by general practitioners of some years' standing.

Dr. Parish has raised the question as to whether antitoxin should be given in every case in which it is thought necessary to take a swab, as was suggested by the late Dr. Claude Ker many years ago. There is much to be said in favour of such a procedure, but certain exceptions may be made: (1) Generally speaking it is much safer to wait for the bacteriological report in the case of adults than it is in that of children, in whom, as a rule, the disease runs a more rapid and severe course. On the least suspicion of a severe attack, however, antitoxin should be given at once irrespective of the patient's age; (2) a discrete deposit on the tonsils without any involvement of the uvula, soft palate, or pharynx when the sore throat has been in existence some days does not require immediate injection of antitoxin. Although the angina in such cases may be due to diphtheria, the disease is of such a mild type that the bacteriological report may be safely awaited; (3) in cases of suspected diphtheria in which the disease is purely nasal, ocular, aural, or cutaneous, and tends to assume a mild and rather chronic course, it is not necessary to give antitoxin before the bacteriological report is received. The usual practice in such cases is to give a small dose of antitoxin if organisms morphologically resembling diphtheria bacilli are found, but a further examination should be made to determine their virulence which is usually not done in the case of faucial diphtheria.

A few words may now be said about the value of direct smear and cultures respectively. The direct smear has only a limited value. The proportion of positive results in cases which cultures subsequently show to be diphtheria varies considerably with different observers, ranging from 25%, according to Sims Woodhead and Friedemann, to the "vast majority of cases" found by Schamberg and Kolmer. A negative result is of course quite inconclusive. In their recent monograph on diphtheria, Lereboullet and Joannon go so far as to say that the direct film should be given up altogether as being unreliable. This, however, is too strong a statement, as the direct film is of value in the diagnosis of Vincent's angina, and also, as Marfan has pointed out, in showing the predominance of certain organisms such as streptococci, staphylococci and pneumococci which may be the only cause of the angina or of an infection associated with diphtheria. The presence of the rather uncommon condition known as pharyngomycosis or keratosis pharyngis, can also be detected by examination of direct smears. The employment of the direct film should be strictly limited to cases of acute faucial diphtheria owing to the likelihood of fallacies in nasal and other localizations of diphtheria, while in the case of carriers it is futile. ("Medical Research Council Monograph.")

Cultures: There is at present a much greater tendency than formerly not to send patients to hospital with the certificate of diphtheria until a positive culture has been obtained. On behalf of this practice it may be urged that the patient is not compelled to leave his home unnecessarily and that notification and disinfection need not be carried out in vain. Moreover, the practitioner does not wish to be taunted by the patient or his friends for having made an erroneous diagnosis. Presumably, however, when circumstances do not permit constant observation and care, the family doctor will safeguard himself by showing that though the diagnosis is not certain, the removal of the patient is the wisest course to be taken.

On the other hand, as I have already pointed out, the disadvantages of waiting for a report before making at least a provisional diagnosis and injecting antitoxin or

sending the patient to a fever hospital, considerably outweigh the advantages. I need not dwell on the danger of relying on a single negative culture if the clinical features indicate diphtheria, as this has already been done by Dr. Parish, but the folly of such action does not seem to be realized by some practitioners. I will merely repeat that a negative result may be due to struggling of the child, taking the swab too soon after food or application of an antiseptic or inexperience of the examiner. In cases in which the first examination of a culture is negative, it is advisable, especially if the clinical appearances are those of diphtheria, not only to take another culture, but also to re-examine the first after a further incubation of twenty-four hours. The value of this procedure is proved by the fact that of 549 cultures which were negative when first examined by Marshall and Guthrie, 52 (9.47%) were positive on examination after a fresh incubation of twenty-four hours. More recently G. H. Burnell and D. L. Barlow found that nearly 30% of their positive results were obtained at the second examination only.

It is in extrafacial localizations of diphtheria, that cultures of the lesions are most valuable and indeed indispensable for determining their nature, as in such cases diphtheria often does not present its usual appearance but may adopt various disguises. Subjects of clandestine diphtheria like clandestine prostitutes are of considerable epidemiological importance, as both owing to their innocent appearance may widely spread disease before their true nature is recognized. In the course of isolated nasal diphtheria, which only in the minority of cases assumes a membranous form, not only must a culture be taken to establish the diagnosis, but the virulence of the organism morphologically resembling *C. diphtheriæ* must be tested. The same remark applies to suspected diphtheria of the conjunctiva and middle ear. In the dermatological field, diphtheria, like syphilis, is a great imitator, and may simulate various banal skin lesions, such as eczema, herpes and different forms of suppuration. During the War a large number of wounds, especially in Germany, as shown by Anschütz and Kisskalt and in the Egyptian Expeditionary Force by Walshe, were found to be infected by diphtheria bacilli, and in many cases typical diphtheritic paralysis resulted. The commonest form of skin lesion, however, in my experience, is the whitlow, which though due to *C. diphtheriæ* in no way differs on naked-eye examination from that due to ordinary pyogenic organisms. It is, therefore, advisable in cases of whitlow which do not readily yield to treatment to have an examination made for diphtheria bacilli, and not infrequently a positive result will be obtained, and a rapid cure ensue after injection of antitoxin in cases which have hitherto proved refractory to ordinary treatment. Twenty years ago I recorded a remarkable example of this kind in a boy with multiple whitlows which had been in existence for two and a half months but which completely healed within a week after a positive swab had shown their true nature, and a small dose of antitoxin had been injected.

The question arises whether all sore throats or at least those in which there is any deposit—the *angines blanches* of the French—need be cultivated. In the following conditions I think cultures are usually unnecessary:—

(1) *Scarlet fever in the eruptive stage.*—While diphtheria is not uncommon, though most frequently in a purely nasal form, in convalescence from scarlet fever, and scarlet fever occasionally attacks diphtheria convalescents, the co-existence of the two diseases in the acute stage is in my experience very rare. I, therefore, do not think it necessary to swab every scarlet-fever throat in the acute stage in which there is some deposit on the tonsils, as I find is generally done by medical officers when they first take up fever work. In nearly all such cases throat cultures show numerous colonies of hæmolytic streptococci, and if any organisms resembling *C. diphtheriæ* are present they are usually found to be non-virulent.

(2) *Tonsillectomy.*—One of the most frequent forms of surgical scarlet fever is that which follows tonsillectomy. In such cases as well as those in which this operation has been performed without scarlet fever subsequently developing, the

appearance of the throat may at first sight resemble diphtheria, but close inspection will show that the membrane present is strictly limited to the cut surface. It is only in exceptional cases that diphtheria supervenes and unless the membrane shows a tendency to spread beyond the cut surface a swab is necessary.

(3) *Syphilis*.—In syphilitic sore throat due to the presence of a primary chancre or mucous patches a swab for *C. diphtheriæ* is usually unnecessary, but may sometimes be required, owing to the occasional co-existence of diphtheria in syphilis.

As regards abuses of the swab, I take the opportunity of saying, in my capacity of medical superintendent of a fever hospital, that wholesale cultivation of the noses and throats of the inmates of a school, hospital, or other institution, and treating as cases of diphtheria those who show organisms morphologically resembling *C. diphtheriæ*, without a virulence test, is a flagrant example of such abuse. In many instances such cases which further examination prove to be negative merely serve to fill up the accommodation of a fever hospital which is needed for more suitable patients.

In view of the well-known intermittency of the carrier state I am very sceptical as to the scientific value of terminal swabbing before the patient is discharged from hospital. The usual two negative swabs of the nose and throat that are the rule in many hospitals, are no guarantee that the patient is free from infection, although the great majority lose the bacilli long before they are ready to leave hospital. Moreover, it has been repeatedly shown, as I have pointed out elsewhere (1929), that the return case rate is no higher in those hospitals which have given up the practice of swabbing patients before discharge, than in those in which it is observed. The practice, however, of terminal swabbing possesses a certain forensic value, as its observance shows that certain precautions were taken before the patient was discharged and so prevents vexatious legal actions.

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Dr. Guy Bousfield said that in many poorer-class districts medical men were unwilling to give antitoxin injections to their patients unless they had a positive swab report. The reason for this given by some doctors was that they were anxious to avoid the reputation of being "the doctor who gives a painful injection into the abdomen" to every patient with a sore throat. In actual practice very few men in poorer districts gave any antitoxin themselves to diphtheria cases. The one desire was to get the patient into hospital. Therefore although the elaborate methods suggested by Dr. Parish were undoubtedly of value in institutional and research work, it was doubtful whether they would be helpful to the bacteriologist who was attempting to assist the practitioner in primary diagnosis. The unavoidable delay involved by these methods might be a danger to the patient who was unlikely to receive any antitoxin until a report was issued. It was probably better to do one's best with a direct examination and Loeffler's serum culture, warning the practitioner that any really suspicious case should be treated as diphtheria in defiance of a negative bacteriological report.

Turning to the utility of the methods in the "carrier" problem: It was probable that most profuse carriers would be identified by successful positive cultures on Loeffler slopes. The only thing remaining for consideration was the "sparse" carrier. While the tellurite media would undoubtedly show many more positives in these cases, it was not quite clear whether it was desirable to identify and segregate all such sparse carriers. The primary stimulus on which the establishment of herd

immunity depended was undoubtedly due to the presence of such sparse carriers among the population, especially in large towns. One must seriously consider the danger of upsetting the natural processes leading to such a partial herd immunity, in which experience of diphtheria bacilli was a great factor. In a very large number of Schick tests performed during the last ten years or so, he (Dr. Bousfield) had the distinct impression that the persons giving Schick-positive readings were *less positive* as regards the intensity of reaction than they were a few years ago, although the percentage of Schick-negative persons did not seem to have been increased. The suggestion was that the average child was getting some experience of diphtheria which would stand it in good stead if actually attacked by the disease; the natural processes were working well, without excessive outbreaks of diphtheria, and it was doubtful whether the more thorough identification of carriers might not be harmful to the public. If this attempt were successful, herd immunity might vanish.

Dr. E. Ashworth Underwood said that he wished to register a mild protest against the continued inclusion in textbooks of the late Dr. Claude Ker's dictum referred to by Dr. Rolleston, that whenever the practitioner found it necessary to take a swab, he ought also to give antitoxin, without waiting for the result. Ker was a supreme physician in the field of infectious diseases, and it must be assumed that when he found it necessary to take a swab in order to establish the diagnosis he had already weighed up in his own mind all the other conditions which might come into the differential diagnosis and that, having excluded these, he still felt that the condition was sufficiently like diphtheria to warrant the taking of a swab and consequently the giving of antitoxin. When this dictum was applied to practitioners who were not so experienced in the diagnosis of infectious diseases as were Ker and other superintendents of fever hospitals, it was natural to think that the clinical diagnosis had not been dealt with so thoroughly, so that swabs were taken in many cases in which the specialist in infectious diseases might have made a provisional diagnosis without their aid. As a result antitoxin was given to many patients unnecessarily. He (the speaker) had worked out some figures for an area with which he was connected. In a period of a year, out of 1,297 throat swabs submitted for examination, just under 7% were positive, and of 105 nasal swabs about 12% were positive. These figures surely suggested some abuse of the practice of swabbing, and if Ker's dictum had been strictly adhered to in these cases a great number of children and adults would have received antitoxin unnecessarily. One speaker had suggested that doubtful cases should be removed to hospital, but he (Dr. Underwood) would point out that in certain areas there were administrative difficulties which prevented the adoption of this course. He himself was definitely of opinion that fever hospitals should be used for diagnosis as well as for treatment. In every case of definite throat symptoms and signs, when a careful examination had not excluded diphtheria, there should be facilities for removal to a fever hospital for observation.

Dr. R. A. O'Brien said he would suggest that Dr. Underwood might consider meeting the needs of the practitioners who took over 1,200 swabs, of which only 7% were positive, by instituting a laboratory diagnostic service, using the Folger-Solé serum swab. Brahdý, with this method, had given a "positive" verdict in 95% of cases of diphtheria within four hours of receiving the serum swab. In this way perhaps Dr. Underwood could show that it was not necessary to wait until the next day for a laboratory report.

He would further point out that McLeod had noted in Leeds that if all cases having a "gravis" infection were put into one ward, the type of bacillus remained true throughout the whole course of the child's stay in hospital; there was no mixing of types—in other words, in the ordinary hospital it looked as if a great deal of cross-infection with different types of diphtheria went on in the ordinary ward, in the same way as, according to Griffith's suggestion, the super-position of different types of streptococci occurred in children in a scarlet-fever ward.