AN INVESTIGATION CONCERNING THE DISINFECTION OF MENINGOCOCCUS CARRIERS.

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THE PROBLEM OF THE CARRIER.

In the present as in past outbreaks of cerebro-spinal fever, where bacteriological investigations have been made, convincing evidence has been found that the main factor in the spread of this disease is the healthy carrier who harbours the meningococcus in his nasopharynx, whence it is liable to become detached when he sneezes, coughs, or possibly when he articulates loudly. In the acts mentioned droplets of secretion from the upper respiratory passages are liable to be sprayed out into the surrounding air, where they float for a short time, and may be inhaled by those in the immediate neighbourhood. In this, as in similar infections of the upper respiratory passages; however, successful transference of the disease is doubtless largely dependent upon dosage. Hence the extent to which the carrier himself is infected, his spraying capacity, the number of his friends, and the degree of bad ventilation or overcrowding obtaining in his immediate environment, have all an important influence in facilitating the successful passage of the meningococcus from one nasopharynx to another.

Though mostly free from symptoms, carriers of the meningococcus do not always escape. Careful observation of this matter during the present outbreak has shown that persons harbouring this micro-organism in their nasopharynx occasionally exhibit symptoms indicative of meningeal irritation, and, further, that sometimes carriers develop a definite attack of cerebro-spinal fever during isolation. The following instance is of interest from many points of view.

A case of cerebro-spinal fever occurred among soldiers billeted in a large dépôt. On proceeding to swab the segregated contacts, one of them was found to be absent, having been sent to hospital with a minor injury to his arm. As fifteen men from the same dépôt were also in this hospital at the time, all of them were swabbed. The only one of the sixteen found to be positive was the particular contact in question, who, it turned out subsequently, had slept next to the case for three nights immediately preceding the attack. This carrier was found to yield the same type of meningococcus from his nasopharynx—Type I—as was present in the cerebro-spinal fluid of the man who developed the disease. After isolation for six weeks, during which he was apparently quite well in spite of his nasopharyngeal infection, this carrier developed cerebro-spinal fever; the same type of meningococcus being now found in his cerebro-spinal fluid as had previously been found in his nasopharynx. After a severe attack of the disease this man recovered, but continued to carry Type I meningococcus in his nasopharynx for a further period of five weeks before he could be discharged to a convalescent home as free from infection. In addition to the case mentioned, four other carriers out of 185 under observation developed cerebro-spinal fever during isolation. This proportion is small; but it should not be forgotten that the constant presence of the meningococcus in the nasopharynx of the patient at the onset proves that every case of cerebro-spinal fever is an instance of a carrier developing this disease.

In all outbreaks of cerebro-spinal fever where bacteriological investigations have been made, carriers have been found greatly to outnumber the cases. From the evidence obtained by a careful bacteriological study of contacts in the present outbreak, however, it would seem that the extent of carriers of the true meningococcus has been somewhat over-estimated. By application of the agglutination test, based upon a study of meningococci isolated from the cerebro-spinal fluid of over 200 of the actual cases, and applied throughout in a strictly quantitative fashion with suitable controls, the number of persons who would otherwise be identified as carriers merely because

they harbour in their nasopharynx an organism resembling the meningococcus is reduced by as much as 30 to 40 per cent. But even with this precaution, the number of carriers considerably exceeds the number of cases. Thus from contacts of 16 cases 92 carriers were found in a recent outbreak.

Results of Previous Attempts to Free Carriers of the Meningococcus.

If the meningococcus were a highly resistant micro-organism, and survived equally long in every nasopharynx to which it obtained access, the task of checking the spread of this germ by isolating carriers of it would be a matter of great difficulty. Fortunately the majority of carriers become free of the meningococcus in a comparatively short space of time. There remain a few who become chronic carriers. These are the persons who undoubtedly constitute the source from which arise outbreaks of meningococcus infection culminating here and there in an apparently "sporadic" case of cerebro-spinal fever.

Some careful observations¹ on several chronic carriers made in the Therapeutic Inoculation Department of St. Mary's Hospital last year on behalf of the Medical Research Committee showed that vaccines were of little use in the treatment of carriers. Local treatment by means of heat or by zinc ions was equally unsuccessful. Further experiments carried out at the same time also indicated that the local application of disinfectants was unsuccessful, and if pushed too far might increase the period of carrying, thus doing more harm than good.

In contrast to this, in course of time if left alone many carriers are found to clear up by themselves. The rate at which they free themselves varies, in our experience, according to the degree to which they are infected—carriers whose nasopharyngeal secretion yields only a few colonies of the meningococcus becoming free, as a rule, more rapidly than those giving a copious growth of it. Dry warm weather with sunshine apparently has some beneficial influence in enabling carriers to become free, and cold damp sunless weather the opposite. How far this apparent influence of the weather is due to its effect on the secretion of the nasal mucus, or not, remains to be seen.

Grounds for Still Believing Successful Local Treatment by Disinfectant Possible.

Now the meningococcus is one of the least resistant of all pathogenic bacteria to disinfectants, and it is rapidly destroyed by some of the mildest of these bactericidal agents in concentrations easily tolerated by the mucous membrane of the nasopharynx. Theoretically, therefore, the meningococcus should be destroyed in the nasopharynx with ease if only it could be reached there by a suitable disinfectant. It was conceivable and even probable that the lack of success hitherto attending attempts to disinfect carriers might be due to restrictions imposed by the procedures followed. The means employed for applying disinfectants locally has consisted up to the present chiefly of hand sprays and douches. Some comparative observations made recently on carriers showed that when the carriers are not too heavily infected, distinct acceleration in clearing them of the meningococcus is to be obtained by causing them to sniff up vigorously 1 per cent. solution of chloramine, held in the palm of the hand, through the nose, expelling it through the mouth. This exercise was carried out twice daily and a permanganate gargle used as well.

On the other hand, carriers whose nasopharyngeal secretion gives a practically pure growth of the meningococcus often clear up extremely slowly if left alone, and are also as a class far more resistant to treatment. By local application of a disinfectant in the ordinary way the meningococcus is temporarily banished from their nasopharynx only to reappear there at the next examination. In other words, the meningococcus is not eliminated in these cases; it is merely reduced in numbers.

A probable explanation of this lack of success in the treatment of chronic carriers is either (1) that all the surface area of the nasopharyngeal mucous membrane carrying the meningococcus is not reached by the antiseptic, or (2) that the meningococcus lurks in the depth of this mucous membrane as well as on its surface. However

this may be, it is certain that the germ would readily be destroyed even by a comparatively feeble disinfectant, could the latter be got to it.

FIG. 1.—THE JET OF THE FALMOUTH ATOMIZER. No. 1 JET.

Parts of atomizer separated, showing construction.

A disinfectant in concentration sufficient to destroy the meningococcus without injury to the mucous membrane could conceivably be conveyed to the nasopharynx from without in one of the following ways:

1. In bulk, as in the douche, etc.
2. In droplet form, as by the ordinary hand spray or atomizer.
3. In the form of extremely fine droplets floating as a cloud, mist, or nebula, mixed with steam derived from an automatic spray actuated by high-pressure steam.
4. In the form of vapour, or of gas.

As methods (1) and (2) had already received considerable practical application, trial has been made of the procedure described under (3). A claim that successful results in the disinfection of meningococcus carriers had been obtained elsewhere^a by a similar method formed an additional incentive to this investigation.

OBJECTIVE OF PRESENT INVESTIGATION.

The primary object of the following experiments was to obtain a method whereby a suitable solution of disinfectant could be broken up into a fog of minute droplets and distributed in air so that it could be inhaled through the nostrils with ease, and in this way caused to impinge in a continuous series of fine showers upon as much as possible of the mucous membrane of the nasopharynx.

Such a method having been obtained, it was proposed to determine its practical value for the purpose of freeing chronic carriers of the meningococcus.

Preliminary Experiments.

The results of this preliminary investigation have been already recorded in the BRITISH MEDICAL JOURNAL for July 1st, 1916, but in order to preserve the sequence of events the following summary of the observations then described will be given.

As the matter was of some urgency, it was necessary to make a start without delay. A room of 1,050 cubic feet capacity was kindly put at our disposal by Surgeon-General Sir David Bruce, C.B., F.R.S., Commandant of the R.A.M. College, for the purpose of experiments. Through the courtesy of Dr. A. E. Thomas, M.O.H. of Finsbury, we obtained the loan of a Lingner spray. This machine was designed for disinfecting rooms with formaldehyde vapour mixed with steam. We found the Lingner spray very useful during the earlier stages of the investigation, but some of its shortcomings for the present purpose will be drawn attention to later.

In order to determine the bactericidal action of the air of the room when the spray was working it was necessary to have an index micro-organism. *Staphylococcus*

epidermidis was chosen for this purpose because it is far more resistant to disinfectants than the meningococcus, and is readily to be obtained by the simple expedient of rubbing a little broth on the skin of the hand and then distributing this skin washing over an agar slope.

The first disinfectant chosen for trial was chloramine-T, discovered by Dr. Dakin in a research carried out on behalf of the Medical Research Committee. Chloramine has the advantage of combining a comparatively high bactericidal value with low toxicity, and, in the strength used during the present experiments, does not coagulate albumin.

The first point determined was the bactericidal value of the air of the room when saturated with moisture derived from the apparatus charged with a known strength of chloramine. It was found that the spray itself immediately disinfected a staphylococcus plate when the concentration of chloramine used was 1.5 per cent. or over. With 2 per cent. of chloramine, plates sown with staphylococcus and exposed at a distance of 3 ft. from the apparatus were disinfected within five minutes.

The second point investigated was the extent to which the air of the room could be tolerated during these bactericidal tests. It was found that when 5 per cent. of chloramine was being sprayed the atmosphere was too pungent for comfort, but with 2 per cent. the atmosphere during the spring months could be tolerated easily for five minutes, and by some for twenty minutes or longer. The atmosphere during these tests became so dense that it was not possible to see across the room, but this steam-laden air, when inhaled through the nostrils, caused a not uncomfortable flow of secretion, and the chloramine impinging on the mucous membrane of the nasopharynx produced a pleasant tingling sensation.

Preliminary observations made on two carriers while 2 per cent. of chloramine was being sprayed showed that, provided they inhaled the spray-laden atmosphere vigorously through their nostrils, the meningococcus

FIG. 2.—THE JET OF THE FALMOUTH ATOMIZER. No. 2 JET.

Parts of atomizer separated, showing construction.

was temporarily destroyed in their nasopharyngeal secretion within five minutes. In one of these carriers the meningococcus reappeared; both were therefore submitted to further inhalations, after which the meningococcus could no longer be found in the nasopharyngeal

secretion of either of them. The method, therefore, appeared worthy of trial, not only on meningococcus carriers in general, but especially on the obstinate class of chronic carrier that had defied all methods of treatment previously essayed.

The following observations were undertaken at this point for the purpose of defining and improving the method.

1. Does the Bactericidal Action of the Air Vary Directly with the Amount of Moisture Derived by it from the Spray?

The preceding observations were not made until the air of the room had become saturated. The comparatively high wet bulb temperature of the air which this involved was found to be somewhat trying, especially in summer. A series of experiments, therefore, was undertaken in order to define the bactericidal value of the air of the room during the whole of the time that the spray was working when charged with 2 per cent. of chloramine. The dry and wet bulb temperatures were observed throughout. Stations were arranged at measured distances from the spray and relays of staphylococcus plates were exposed in these spots and changed every five minutes during the whole of the time that the spray was in action. As the result of these tests it was found to be quite unnecessary to wait until the air was saturated with water vapour. The bactericidal action of the air began with the spray and was more intense during the second interval of five minutes than either before or after. The bactericidal action was as a rule actually on the wane by the time that the air of the room reached the saturation point.

2. Does the Bactericidal Action of the Air Depend in any way upon Chemical Vapour or Volatile Product Derived from the Disinfectant in the Spray?

This question was settled by the two following experiments:

- A 2 per cent. solution of chloramine was boiled and plates sown with the staphylococcus exposed to the vapour. The staphylococcus was unaffected.
- A test was made in the inhaling-room, and in addition to the plates exposed in the ordinary position another set of plates was exposed in the same spots, but inverted. It

was found that whereas the former plates were disinfected as usual the latter were unaffected. Clearly, then, the bactericidal action of the air was entirely due to droplets of the chloramine solution derived from the spray.

3. How long does the Bactericidal Quality of the Air Continue when the Spray is Stopped?

Experiments showed that the bactericidal action of the air ceased within two minutes after the spray had stopped—further evidence, if such were needed, that the droplets from the spray are the sole factor in producing the bactericidal action.

FIG. 3.—FALMOUTH PORTABLE ATOMIZER, NO. 1.

SHORTCOMINGS OF THE LINGNER SPRAY.

While the points mentioned were being defined, the Lingner apparatus was in daily use for disinfecting carriers. During these observations attention was drawn to some defects of this apparatus for the present purpose. These faults may be described as follows:

- The Lingner apparatus gives out too much heat. A rise of 20 degrees or more in the air of the room when the apparatus was working was not uncommon. Such excess of heat is undesirable.
- The apparatus is not adaptable. Once charged and started it has to burn itself out. There is thus a tendency to waste disinfectant.
- At first the Lingner apparatus emitted a fine spray, but with continued use the droplets emitted by it were found to become coarser. Hence the spray became less effective for disinfecting the

nasopharynx of carriers than when first used.

NEW SPRAY.

By kind permission of the C.R.E., Falmouth, a spray which promises to be better suited for the present purpose has been specially designed and made for us by Second Lieutenant E. Gordon, R.E.(T.), who carried out a number of experiments before arriving at the present models. By means of this apparatus the disinfectant is broken up into a finer mist than was obtainable with the Lingner apparatus. As a result the present apparatus disinfects over a larger area of the room. It also economizes material; the disinfectant is under control, and every portion of it is broken up into fine droplets as it arrives at the nozzle. During the past two months the first of these sprays has been in continual use for disinfecting the nasopharynx of carriers.

The Falmouth Atomizer.

A portable apparatus was required that would atomize a disinfectant at the rate of 1 litre in twenty minutes over a space of 750 cubic feet. In order to accomplish this some motive agent had to be decided upon. Compressed air was first tried; a motor tyre foot pump, and a cylinder of compressed air being used in succession, with unsatisfactory results. Steam was then employed. A Wassmuth spray was tested with fair results; but was found to be unsuitable for the comparatively heavy rate of flow of disinfectant required. Various sprays and methods of feeding the disinfectant were then experimented with, the most satisfactory of all being a brass regulator to a gas jet, having a cup head into which the disinfectant is allowed to flow at the required rate, a jet of steam under pressure blowing the disinfectant

out into the air in fine droplets. In order to use the steam to the best advantage a cap was made to screw over the cup and slightly press on the disinfectant so as to ensure that the latter flows all round the jet of steam. A drawing of this No. 1 jet is attached (see Fig. 1, p. 674). Jet No. 2 is very similar, save that, in this case, when steam is passing through under pressure, the shape of the cap produces a strong suction which will pull up the disinfectant vertically from a point 18 in. below (Fig. 2). Owing to this suction, and to a certain amount of steam condensation, the spray from

No. 2 jet is somewhat coarser than that from jet No. 1.

Having arrived in this way at a more or less satisfactory spray, attention was next given to the provision of a portable plant. For the purpose of generating steam with suitable pressure, a 12 in. by 6 in. steel boiler was obtained with the necessary boiler fittings. This apparatus is shown in Fig. 3. The boiler is fired by a 3 in. primus burner connected by a horizontal pipe to its paraffin reservoir. The steam is generated and passes through a tap to the superheating coil, so arranged that it can be rotated over the exhaust boiler gases and thus heated. The advantage of this superheating is that the steam is rendered invisible, with the result that the visible particles sprayed from the jet are practically all composed of the disinfectant solution. The disinfectant gravitates to the jet from a bottle placed on the tank feeding water to the boiler. In practice, the pressure of steam is kept between 20 and 30 lb. on the gauge when this spray is in action; the heat necessary for maintenance of this pressure of steam being kept up by pumping on the paraffin in the reservoir.

The second form of portable atomizer shown has advantages over the former as regards lightness and simplicity, besides eliminating much of the heat given off by atomizer No. 1. The present apparatus consists of a 5 in. by 6 in. copper and brass boiler with four fire tubes (Fig. 4). This boiler is surrounded by sheet iron casing which keeps in most of the heat. Directly over the boiler there is a tray partially filled with water which absorbs most of the waste heat, and also serves as boiler-feed water, being connected to the boiler by a wheel valve. The boiler is heated by a pocket primus stove which can readily be slipped in and out from under the boiler. The boiler should always be left full, filling being accomplished by allowing the steam to die down and then opening both the wheel valve and tap. As soon as the water is seen to overflow from the tap, it is at the correct level for further

operation, and wheel valve and tap should be turned off. There is no steam valve on the top of this boiler, so that there is clear passage of steam to the jet, a safety valve being placed on the tube close to the jet. Either No. 1 or No. 2 jet can be used. With the former, when steam has risen, it is necessary to turn on the disinfectant. With No. 2 jet the bottle of disinfectant is placed on the boiler base, and, after the primus has been lighted, the plant is automatic.

With regard to regulating the flow of disinfectant, in atomizer No. 1 the liquid flows through an

extremely fine hole, which allows 1 litre to pass in twenty minutes. In No. 2 atomizer the air displacement is regulated.

A new revolving jet is being constructed with a view to getting better diffusion of the droplets. No. 2 atomizer will be used. By taking the steam off vertically from the boiler, considerable space will be saved.

DISINFECTANTS USED.

Experiments have been made with a considerable number of disinfectants, but the ones of which chief use has been made so far are chloramine 1 to 2 per cent., or zinc sulphate 1.2 per cent. Eusol was tried, but was found more irritating and less efficient for the present purpose than the substances named.

Procedure Followed.

The cubic capacity of the room in which the carriers have been subjected to treatment with the spray has been reduced, by means of a canvas ceiling, to 750 cubic feet.

FIG. 4.—FALMOUTH PORTABLE ATOMIZER, NO. 2. SECTION.

One litre of the solution of disinfectant is sprayed into this area in the course of fifteen to twenty minutes. The carriers remain in the room during the whole of that time, inhaling the air through their nostrils.

Results Obtained with Chloramine.

The concentration of chloramine in the solution sprayed was 1 per cent. or 1.5 per cent. in a few of the earlier trials, but in the majority of the tests the spray was charged with a 2 per cent. solution of chloramine.

The following tables show the results obtained with chronic carriers who represented the residue of 139 positive contacts of cerebro-spinal fever cases occurring between December, 1915, and May, 1916.

Degree of Infection.—The sign (+) signifies that the nasopharyngeal secretion of the carriers gave a few colonies only of the meningococcus, + a fair growth of colonies, ++ copious growth, and +++ a practically pure culture of that micro-organism.

The inhalations were carried out once daily, and on each occasion the carriers were in the inhaling room from fifteen to twenty minutes, during which time they vigorously inhaled the steam and spray-laden atmosphere through their nostrils.

TABLE I.—Showing Particulars of Chronic Carriers successfully freed of the Meningococcus by the Spray when charged with a 2 per Cent. Solution of Chloramine.

Name.	Degree of Infection.	Time previously under Treatment.	No. of Daily Inhalations required before Discharge.
N.	+++	17 weeks	10
B. 1	+++	14 ..	10
C. 1	+++	10 ..	9
C. 2	++	12 ..	6
K.	+++	6 ..	9
B. 2	++	0 ..	13
T.	+++	11 ..	6
S.	++	10 ..	4
B. 3	++	3 ..	9
B. 4	++	3 ..	9

With the exception of one man, all of the above were proved carriers of some standing. In each of them six successive negative swabs were obtained before discharge. Five of the cases were re-examined five or seven days after discharge, and found to be still negative.

On the other hand, three of the chronic carriers under treatment at the same time with the chloramine spray failed to clear up. Particulars of these are given in Table II.

TABLE II.—Chronic Carriers not freed by Chloramine.

Name.	Degree of Infection.	Time previously under Treatment.	No. of Inhalations of Chloramine Given.	Remarks.
S. 2	+++	16 weeks	16	Knocked up by chloramine.
L.	+++	14 weeks	14	Did not appear to inhale properly.
E.	+++	Contracted cerebro-spinal fever 9 months previously	15	Neurotic; did not inhale properly.

In addition to these thirteen men, another carrier was subjected to the chloramine spray. The carrier in question was an officer who was convalescent from cerebro-spinal fever which he had contracted two months before. At the beginning of treatment the plate from his nasopharynx gave a practically pure culture of the meningococcus. In contrast to the third of the carriers in the above table, he inhaled most vigorously while in the inhaling room. After seven daily inhalations he was found to have become free of the meningococcus, and was discharged.

Results Obtained with Zinc Sulphate.

With the advent of the warmer weather, and the consequent rise of the wet bulb temperature of the air of the

inhaling room, the chloramine spray became more trying. It was therefore decided to drop chloramine for the time being and to continue with solutions of zinc salts, which were found to be much better tolerated. The salt which has been principally used has been zinc sulphate, of which a 1.2 per cent. solution has been employed, as some preliminary experiments on carriers had proved that this was successful in freeing the nasopharynx of the meningococcus temporarily.

Since the majority of the chronic carriers had cleared up under the chloramine spray, only one known chronic carrier could be subjected to the zinc spray. His nasopharynx gave a copious growth of the meningococcus, and he had been carrying for four weeks before coming under this treatment. Although temporarily freed of the meningococcus by the zinc spray on many occasions, this carrier required no less than seventy inhalations before he could be discharged.

Table III contains particulars of cases which had recovered from an attack of cerebro-spinal fever, and were found to be still carrying the meningococcus in their nasopharynx; they were submitted to the zinc spray, with the results stated.

TABLE III.—Recovered Cases Treated with Zinc Sulphate Spray.

Name.	Degree of Infection.	Time from Onset of Cerebro-spinal Fever.	No. of Inhalations required before Discharge.
K.	(+)	6 months	9
R.	+	4 months	12
H.	++	15 weeks	30
D.	++	11 weeks	32
B.	++	10 weeks	44

Although strict comparison with the chloramine results was not possible, because the present men had undergone an attack of cerebro-spinal fever, and the former with one exception had not, these results with the zinc spray were greatly inferior to those that had been obtained with chloramine.

Newly discovered carriers of the meningococcus coming under treatment with the zinc spray during the summer may be divided into two classes according to the degree of their infection by the meningococcus.

TABLE IV.—Carriers Treated with Zinc Sulphate Spray.

Carriers Lightly Infected.			Carriers More Heavily Infected.		
Name.	Degree of Infection.	No. of Inhalations required before Discharge.	Name.	Degree of Infection.	No. of Inhalations required before Discharge.
G.	(+)	4	F. 1	++	42
C.	(+)	4	K.	++	38
B.	(+)	4	F. 2	++	37
T.	(+)	4	D. 1	++	18
S.	+	6	B.	++	27
Nurse G. ...	(+)	8	Nurse C. ...	++	31
R.	(+)	6	D. 2	+	17
B. 1	+	3	P.	+	12
W.	(+)	2	W.	++	8
C.	(+)	5	Mc.	+	8

It is seen that while the lightly infected carriers cleared up as a rule quite quickly, those more heavily infected by the meningococcus required a comparatively large number of inhalations of the zinc spray before they became free.

It is proposed to continue these experiments in an inhaling room so arranged that the boiler of the apparatus is outside, the steam being led into the room by means of a tube passing through a small window. The receptacle for the disinfectant can be either outside or inside the inhaling room, whichever is found to be most convenient for the attendant to regulate its flow to the jet. It is

proposed also to try other disinfectants, or combinations of disinfectants; and, as suggested by Colonel Reece, to compare the effects of the spray upon patients lying on their backs on the floor with the results obtained when they are sitting or standing; and also to see whether multiple inhalations are more successful than a single daily inhalation for the present purpose.

It should be added that during some recent experiments with a powerful experimental spray the use of 2 per cent. of chloramine produced a certain amount of bronchial irritation in two medical volunteers who underwent this treatment for catarrh. Although in no sense serious—both declared their catarrh benefited by the treatment—this effect is undesirable. No such bronchial irritation was observed when 1 per cent. of zinc sulphate was sprayed by the same apparatus. The result would appear to suggest that for disinfection of the nasopharynx of meningococcus carriers the finest possible spray is not essential, since the droplets of disinfectant, if very finely divided, penetrate further along the respiratory tract than is necessary, and reach the bronchi in some quantity. With a weaker solution of chloramine such irritant effect would doubtless be avoided, even in persons suffering, as these were, from a more or less acute form of catarrh at the time when they entered the inhaling room.

CONCLUSIONS.

These observations have led us to believe that, in the case of carriers of the meningococcus, prognosis with regard to the duration of their future period of carrying varies largely with the degree to which their nasopharyngeal secretion is infected by the meningococcus.

In our experience, the majority of carriers whose nasopharynx yields only a few colonies of the meningococcus clear up quickly. In the case of these persons good results follow local treatment either by direct application of a 1 per cent. solution of chloramine, or by subjecting them to inhalation of a steam spray charged with zinc sulphate.

On the other hand, carriers whose nasopharyngeal secretion yields a copious growth, or a practically pure culture of the meningococcus, are often far more difficult to cure. The results on these persons with zinc salts were disappointing, but they served to emphasize the success of those obtained with chloramine, which, though still somewhat few in number, are more than encouraging, and would appear to indicate that a large proportion of these chronic carriers can be definitely freed of the meningococcus by this form of treatment in a comparatively short space of time.

We would add that while these observations on meningococcus carriers were in progress, several cases of chronic nasal or post-nasal catarrh have been submitted to disinfectant treatment by the automatic steam spray. As in all of these persons improvement has resulted, we offer the suggestion that this method is worthy of trial on a large scale for the treatment of such cases.

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AN EXPERIMENTAL STUDY OF THE CULTURAL REQUIREMENTS OF THE MENINGOCOCCUS.

TOGETHER WITH A DESCRIPTION OF AN EASILY PREPARED
MEDIUM FOR THAT MICRO-ORGANISM.

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ONE of the functions of the Central Laboratory established at the Royal Army Medical College for dealing with outbreaks of cerebro-spinal fever is to supply district laboratories with medium for cultivation of the meningococcus. For this reason the following investigation was the first of

a series of researches carried out in the Central Laboratory during the outbreak of 1915.

Ordinary agar medium, which consists of about 2 per cent. of agar dissolved in meat broth with the addition of 1 per cent. of Witte's peptone and $\frac{1}{2}$ per cent. of salt, is generally recognized to require the addition of protein in some form before it becomes a satisfactory medium for the meningococcus. Animal protein in the shape of ascites fluid or blood gives good results when added to ordinary agar medium, but neither of these materials was employed for routine purposes in the present instance because ascites fluid was not procurable in large enough quantity and blood was found to have two disadvantages. First, it made the medium opaque, thus interfering with the differentiation of the meningococcus colonies, and secondly, in spite of all efforts to prevent it, the blood which we were able to obtain from the slaughterhouse was found to be contaminated. There remained horse serum, which we were able to get in quantity, but at considerable expense, and without a guarantee of its sterility.

Satisfactory results having been obtained previously with nasgar, and this medium having the great advantage that it can be sterilized by steam without losing its capacity of growing the meningococcus, it was decided to send out nasgar in the first place for routine purposes, using serum instead of ascites fluid for its manufacture.

Two difficulties, however, had to be met in making nasgar. In the first place, the supply of nutrose failed, necessitating recourse to a substance asserted to be identical with nutrose chemically—namely, a mixture of sodium caseinogenate with glycerophosphates. Secondly, the supply of Witte's peptone ceased. We therefore made nasgar with serum instead of ascites fluid, with artificial nutrose, and with Armour's standard peptone in place of Witte's. As regards reaction, the medium was rendered + 1.0 to phenolphthalein.

Nasgar made in this way was carefully tested and found to grow the meningococcus quite well in primary cultures from the cerebro-spinal fluid and also in subcultures. When swabs from the nasopharynx of contacts were plated out on it, a proportion of them grew colonies of cocci indistinguishable from the meningococcus. The medium also had the great advantage that it gave good differentiation of colonies of the meningococcus from those of other Gram-negative cocci of the nasopharynx, such as *M. flavus* and *M. catarrhalis*.

While a start was made with nasgar, an investigation was begun for the purpose of defining the conditions of growth of the meningococcus in artificial culture more thoroughly, with the special view of obtaining, if possible, a superior medium for routine purposes.

The chief requirements that a satisfactory routine solid medium for the meningococcus should meet may be summarized as follows:

1. It must grow the meningococcus with constancy in primary culture, as well as in subculture.
2. It must be transparent, so that colonies of the meningococcus developing upon it can readily be distinguished from those of other Gram-negative cocci.
3. It must be simple and easy to make, sterilize, and handle, and as far as possible free from materials of foreign origin.
4. When the supply of a large number of laboratories is in question, as in the present instance, it must be cheap.
5. The medium should be capable of maintaining the meningococcus alive for a considerable time, thus obviating the necessity of frequent subculture.

The research which has been made for the purpose of obtaining an improved medium has been carried out in three stages. In the first two experiments ordinary agar consisting of agar 2½, Witte's peptone 1, salt $\frac{1}{2}$, and meat broth to 100, was used as base.

In the succeeding experiments, where the value of individual substances for growing the meningococcus was under investigation, water agar, consisting of agar 2½, salt $\frac{1}{2}$, and water 100, was used as menstruum.

As a result of these observations a medium was arrived at that appeared to be full of promise. The third stage of the investigation, therefore, was to test the capacity of this medium to satisfy requirements in practice.

In the experiments now to be described, the sign — signifies that the meningococcus failed to grow; the sign (+) signifies a distinct but feeble growth; + a moderate growth; and ++ a good growth of this micro-organism.