**First report of the Special Investigation Committee upon the Incidence of Phthisis in Relation to Occupations : the boot and shoe industry.**

Special Report Series No 1.

NATIONAL HEALTH INSURANCE.

# MEDICAL RESEARCH COMMITTEE.

## First Report of the Special Investigation Committee upon the Incidence of Phthisis in relation to Occupations.

## THE BOOT AND SHOE INDUSTRY.



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## First Report of the Special Investigation Committee upon the Incidence of Phthisis in relation to Occupations.

## THE BOOT AND SHOE INDUSTRY.

(*Approved for publication by the Medical Research Committee* 14*th October*, 1915.)

## Medical Research Committee.

(*National Health Insurance.*)

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## Special Investigation Committee upon the Incidence of Phthisis in relation to Occupations.

APPOINTED BY THE MEDICAL RESEARCH COMMITTEE.

*Terms of reference.*

To investigate and report upon the incidence of Phthisis in relation to particular occupations, and to prepare and suggest schemes for special research work in connexion therewith.

*Constitution of the Special Committee.*

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# First Report of the Special Investigation Committee upon the Incidence of Phthisis in relation to Occupations.

## I.—THE BOOT & SHOE INDUSTRY.

*To the* MEDICAL RESEARCH COMMITTEE.

### Introduction.

1. The Special Committee appointed on the 26th October, 1914, to investigate and report upon the incidence of phthisis in relation to particular occupations, beg leave to submit the following first report.

2. At an early stage in our consideration of the questions referred to us, we found that Dr. E. L. Collis, Medical Inspector in the Factory Department of the Home Office, acting in collaboration with one of his colleagues, Mr. W. F. E. Seymour, H.M. Inspector of Factories stationed at Leicester, had been conducting an inquiry, under instructions from the Chief Inspector of Factories, to ascertain whether tuberculosis was unduly prevalent in the Boot and Shoe Industry, and, if so, what measures, if any, should be recommended for its prevention. The Home Office courteously placed the information so acquired at our disposal, and our special attention was accordingly directed in the first instance to the special problems presented by the Boot and Shoe Industry. We are greatly indebted to the results of the Home Office inquiry; many of these, confirmed by our own observations, are incorporated within the report which is now laid before you.

### The Recent Development of the Boot and Shoe Industry.

3. In the last half century the boot and shoe industry has been completely revolutionised. Machinery for sewing or closing boot tops or uppers was first introduced about the years 1857–60; before that time practically the whole of a boot was made by hand in the cottage home, and the so-called factory was primarily a distributing and collecting centre. In a small measure this form of factory may still be found, but the invention and introduction of machines for dealing with the numerous processes through which a boot now passes in course of manufacture, have called into existence the modern

operative in place of the old-fashioned "cordwainer"* who, in his own home, seated on his stool, made a boot from start to finish by hand-sewing, cutting, and tooling. In a few old-fashioned factories some elderly men may still be found employed on special classes of work, making hand-sewn boots for which some demand persists, but this hand-work is only a relic of the past soon to be replaced altogether by the use of modern machinery. The manufacture of boots to-day comprises processes to be numbered by the hundred, for practically every one of which a special machine has been devised; a worker no longer makes a boot himself throughout, but is employed only in one, or at the most, two or three, of the processes carried out in his or her particular department.

*Topographical Distribution.*

4. At the Census of 1911, there were returned as employed in the boot, shoe, slipper, patten, and clog-making industries in England and Wales, 169,171 males and 44,523 females. When these figures are subdivided according to districts, they show that the industry is specially centred in certain places, such as Leicester, London, Northampton, Norwich, Kettering, Stafford, Bristol, Gloucester, and, for the manufacture of slippers, the neighbourhood of Rawtenstall. The numbers employed in the industry in the towns of Leicester and Northampton, taken in relation to the total population of these towns, show that these two towns must be regarded as the chief centres of the industry.

*Factory processes and hygienic conditions.*

5. The various processes concerned in the manufacture of boots and shoes are usually carried out in separate rooms or departments. Leather and linings for the upper parts after being cut into shape in the clicking room, are sewn together in the machining room. Thick sole and heel leather is shaped in the press room. The upper parts and soles are brought together in the making-up or lasting room. The final processes of scouring and polishing are carried out in the finishing room, and after these the completed article passes to the shoe room to be prepared for sale and packed.

6. The proportion of the personnel of a factory employed in each department calculated from information obtained from 80 factories, is as follows:—18 per cent. in clicking; 30 per cent. in machining; 10 per cent. in the press room; 20 per cent. in making-up; 17 per cent. in finishing; and 5 per cent. in the shoe room and warehouse.

7. *The clicking room.*—Work in this department is carried out by males, by whom the leather and material for the upper parts of a boot are cut into shape either by hand or by machine. At hand-cutting, the operator, known as a clicker, stands at a long bench or counter; on a cutting board resting on the bench he spreads a piece of leather and places a flat pattern or template on it; then, holding the pattern firmly in position with his left hand, with a sharp thin knife held in the right hand he cuts through the leather round the edges of the pattern.

* A cordwainer is a worker in cordewane or Cordovan leather, so called after Cordova, a town in Spain where leather was made in the Middle Ages.

The bench on which the work is done is of the same height for tall and short men alike, and although the men usually raise the cutting boards on blocks to suit themselves, clickers stoop at their work, and, as a class, are round shouldered, with poor chest development. The effect of clicking in impeding respiration is referred to on page 14.

At machine cutting, light power presses are used. A piece of leather is placed under a press with a knife-edged cutting tool of the required pattern placed on it, and then the press is brought into action by the operative. This process is more rapid than hand cutting, and is coming more and more into use. The cutting tools are, however, expensive, and unless a large number of boots are required of the same pattern, the rapidity of execution does not counter-balance the expense; the public fashion in boots changes so rapidly that the patterns of one season may be of no use for the next. Machine cutting does not cramp the respiration, as clicking with the knife does, and its introduction is therefore to be commended.

The art of clicking consists in cutting as many shapes as possible out of each piece of leather, and a miss-cut entails expense in wastage. For this reason good light is necessary, and the clicking room, on the top floor with ample window space, is the best lighted part of a factory.

The room is usually tidy, and the floor is only encumbered with scraps of leather from the day's work. These scraps have a commercial value, and are regularly swept up each day. Too often, however, this sweeping is done during working hours without any precautions to allay dust.

The air space, as measured by cubic capacity per person, always exceeds the minimum of 250 cubic feet, required by Sec. 3 of the Factory and Workshop Act, 1901, and was found in 100 factories of varying size to average some 800 to 900 cubic feet per head. In spite, however, of this large air space per person the air of a clicking room is often stagnant, due to the fact that, whatever means for ventilation, usually skylights or windows, are provided, the dread of being exposed to air currents or "draughts," which the clicker shares with other operatives employed in sedentary occupations, induces him to stop up every possible inlet.

Although a clicker stands at his work, the occupation of clicking must be classed as sedentary in that it entails no pronounced physical exertion; the clicker therefore is sensitive to cold, and adequate means, usually pipes heated by steam or hot water, are provided for warming the room. Such heating without good ventilation produces a condition likely to lead to lessened vigour and resistance to disease.

8. *The machining room.*—Work in this department is done by females, who deal with the materials cut into shape in the clicking room. Various processes of bevelling and "skiving"* the edges of leather, preparatory to folding and flattening, are carried out, and the materials are then stitched together and linings are attached, after which eyeletting and other processes follow.

Sewing machines and specially designed machines of similar size are used for these processes. Driven by mechanical power, they are

*The process of skiving consists in paring down leather from a thick centre to a thin edge.

usually arranged in two rows, one on either side of a long work bench, at which the operatives sit, each on a single seat, facing one another. The nature of the occupation is entirely sedentary.

For seamstress's work good light is necessary, and this department, which is often found sharing the top storey of the building with the clicking room, is usually well arranged in respect of daylight. Artificial illumination too is usually ample, but only in very few factories has attention been paid to the position of the individual lights, and too often they are so placed, between and slightly above the workers, as to throw direct light on to the eyes and eyelids. In a few factories lights concentrated on the work while leaving the worker's face shaded have been introduced, with a decrease of headache and fatigue for the workers, and an increase in efficiency and output for the employers. Although scraps of leather, linings, sewing thread and other materials accumulate in this department, floor cleaning is usually satisfactory; and, whatever may be the custom in other departments, sweeping is rarely done without previous damping to keep down dust. This must be ascribed to the influence of the women, accustomed at home to strew the floor with damp tea leaves before sweeping.

The air space, though exceeding the minimum standard of 250 cubic feet, is usually much less than that of the clicking room, and was found to average from 350 to 400 cubic feet. Although, therefore, no illegal overcrowding exists, a type of overcrowding, due to workers sitting close together, is found here which no measurement of cubic air space above the workers' head discloses, and this department usually appears more overcrowded than any other. As the workers generally face each other and are separated merely by the width of the table, the conditions favour the spread of possible infection by saliva spray. Ventilation is provided in the great majority of factories by skylights and windows under the control of the workers; heating on cold days is given by steam or hot-water pipes. Not infrequently the air of the room is stagnant and oppressive, but in the course of this inquiry we have noticed that girls are more amenable to the discipline of their forewomen than are men to their foremen. Intelligent forewomen frequently succeed with similar appliances in maintaining in a more crowded room a better condition of ventilation than that found in the clicking room. Nevertheless, what has been said above concerning the hostility to air currents shown by workers employed at a sedentary occupation applies to this department.

9. *The press room.*—Only men work in this department. Presses similar in design to those used in the clicking room, but stronger and of much greater weight, and with heavier cutting tools, are employed to cut thick leather for soles and heels into the required shapes. There is little hand-cutting, the men stand erect, and their work calls for considerable physical effort.

Owing to the weight of the presses this department is always on the basement floor, which, for some reason not easily understood, is often four or five feet beneath the ground level. This arrangement commonly makes the use of artificial light necessary, even at noon on a bright day.

Air space is always ample, and the atmosphere is seldom stagnant, though the facilities for ventilation in these semi-underground rooms are poorer than in the clicking and maching rooms. The more active work, however, and the greater physical effort involved, cause the men to welcome, or at least to disregard, currents of air.

10. *The making-up or lasting room.*—In this department the work is carried out by men. The uppers are moulded on to lasts by special machines, and attached to the inner soles. The boots are then placed in racks or frames mounted on castors, and pass from worker to worker through many subsequent processes, for the expeditious carrying out of which ingenious machines have been devised. Thus special machines are used for sewing the soles, for attaching the heels, for slugging, studding and nailing. Such machines, standing on their own bases, are from four to seven feet high and take up from 12 to 25 cubic feet of space. As a rule there are as many machines as men in a room. Much of the work entails physical effort; and although the old method of lasting at which an operator sat, leaning over his work, and pressing the last against his chest so that the sternum, or the ribs on one or other side became permanently depressed, has largely become obsolete, the operator, who now stands at his work, at some machines still presses his chest against the last.

The making-up room, which is usually situated on the ground or first floor, is generally provided with sufficient window space for lighting purposes; but, through lack of attention to window cleaning, the windows seldom admit the full complement of light, and the hours during which artificial illumination is used are unnecessarily prolonged for over six months of the year.

Cleanliness in this department varies greatly in different factories, and frequently receives too little attention. The floor is encumbered with racks and machines. Sweeping round and under these is difficult, and often carried out in a perfunctory manner, while preliminary damping to allay dust is the exception rather than the rule.

The air space in this department is difficult to calculate; the cubic capacity of the empty room is always ample, and even though the machines and the numerous racks occupy from 10 to 20 per cent. of the available air space, no illegal overcrowding was found. Each rack is about 5 feet high, 5 feet long and 1 foot deep, with 5 shelves, and stands 4 inches from the floor, and in a room where 30 men are at work there may be 70 of these racks; the heads and shoulders of the workers stand out above the racks like those of men in a field of corn. The racks not only take up air space, but also prevent free circulation of air, and so cause a certain degree of stagnation. This stagnation is accentuated by lack of ventilation; windows are depended upon for this purpose, but they are very rarely found open, even in summer.

In this room, as indeed is the rule throughout modern boot and shoe factories, heating is effected by steam or hot-water pipes. This method of heating, in the absence of proper ventilation, always seems to produce oppressive qualities in the atmosphere.

11. *The finishing room.*—Men only are employed in this department. Here the rough edges of the soles and heels are trimmed and

scoured on rapidly-revolving cutters and sand-papering wheels, the processes of padding, staining, and polishing are carried out on bobs and revolving brushes, and edge setting or burnishing is done by either machine or hand. The operator stands, and his work requires less physical effort than the processes of the making-up room.

Window space in this department is usually enough for lighting purposes, but the absence of window cleaning is more noticeable than elsewhere in the factory. Dust and *débris* are generated in the various processes, and, although adequate localised exhaust ventilation removes much from the room, the outlets from dust-settling chambers often discharge outside in close proximity to the windows, so that dust settles on these, rapidly soiling them and making them opaque.

The floor in this room particularly requires careful sweeping after previous damping, because here, more than in any other part of the factory, dust and *débris* accumulate, especially around the bases of the machines. Hoods and ducts are in every case fitted to the machines, and localised exhaust is induced by mechanical fans either incorporated in the body of the machine or acting on a main trunk with which the ducts are connected.

So far as ventilation is concerned, the volume of air extracted by the fans may be theoretically sufficient to keep the atmosphere fresh, but owing to inefficiency due to want of attention to detail in the construction and maintenance of the plant, a proper circulation is not always obtained. Moreover, the air is affected by numerous small gas jets used to heat the edge-setting or burnishing machines, at which the men work in such a position as to be likely to inhale continually the products of combustion.

12. *The shoe room.*—Here the finished boot is finally cleaned up, polished, and boxed. Those employed are nearly all women, who sit or move about at their work; the apartment is always light and clean, and the air space is ample. Ventilation, though better than in other departments, is not always good, partly owing to dislike of open windows and partly owing to piles of shoe boxes, whether in racks or not, impeding free circulation of air.

## The Prevalence of Phthisis in the Industry.

13. Among the trades which have a higher prevalence of phthisis than that found for the general population, that of Boot and Shoe makers must certainly be included. The evidence for this statement is derived from several sources. The Registrar-General has been in the habit, since 1890, of issuing a decennial supplement to his Annual Report in which the different occupational mortalities are discussed, the class of boot and shoe makers being specially considered. Further information has been obtained from the records of the National Union of Boot and Shoe Operatives, placed at our disposal by Mr. E. M. Poulton, Secretary of the Union, and from the deaths registers of the towns of Leicester and Northampton, to which the Medical Officers of Health have courteously given us access.

14. It cannot be said that the data are unimpeachable. Taking first the Reports of the Registrar-General, it is to be noted that he deals with a class termed "Shoe makers." In addition to boot and shoe makers, this includes patten and clog makers, slipper makers, and

also all dealers. As, however, the boot and shoe makers number 174,806 out of a total of 197,555, their mortality will so dominate that of the group that the figures for the whole group may be taken as approximately those of boot and shoe makers alone. Further, the numbers working at the trade are obtained from the Census, and the deaths from the death certifications. Since the two sets of data, namely, deaths and population have thus been obtained by different methods, the mortalities at each age can only be looked upon as approximate. Change of occupation is not uncommon, and a certain number of deaths really due to the unhealthy conditions of boot and shoe making may be registered under the heading of some other employment, in which workers unable to continue their ordinary tasks have sought some form of lighter work.

15. In the case of the records of the National Union of Boot and Shoe Operatives, data regarding deaths alone are available, and the evidence as to an excessive prevalence of phthisis must be looked for by considering the varying proportion which the deaths from that disease bear to the total deaths. This also applies to the evidence extracted from the deaths registers of the towns of Leicester and Northampton.

The statistics, as we have seen, fall into two groups, (*a*) those relating to population and deaths, and (*b*) those relating to deaths alone.

16. (*a*) A synopsis of the first is given in Table A. As a standard of comparison is necessary, in the first part of the table the death rates for all occupied males have been taken from the Reports of the Registrar-General. Three periods are considered, those around the Census for 1891, 1901 and 1911 respectively. The death rate is given for each age period, both from all causes and from phthisis alone. In the second part of the table similar information is given for the group called shoe makers. The comparison of these rates is of great interest. It shows that while there is little difference between the general health of shoe makers and that of all occupied males, the death rates from phthisis in the case of shoe makers are very much higher. In the Reports of the Registrar-General special notes are made on these tables, which may well be quoted. In the Report referring to the years 1890–92, Dr. Tatham remarks: "The comparative mortality figure is 920, and is accordingly but slightly lower than the standard for occupied males. The figures for diseases of the respiratory system and for accident are 18 and 63 per cent. respectively below the same standard; the mortality of these workers from alcoholism and from disease of the liver is also markedly low. The only numerically important causes of death are phthisis and cancer; the mortality from the former being 38 per cent. and from the latter 14 per cent. above that of occupied males.

Taking up the subject again in the Report referring to the years 1900–02, he says further: "Within the main working period of life the comparative mortality figure is 984, or within 2 per cent. of the average (which is taken as 1,000); the mortality from phthisis, however, is in excess by 45 per cent., but that from influenza and respiratory disease, as well as from alcoholism and liver disease, and Bright's disease, is considerably below the standard, and the mortality rom accident is little more than one-third of the average."

17. (*b*) The discussion of the data obtained from the National Union of Boot and Shoe Operatives and from the Medical Officers of Health of Leicester and Northampton is more difficult. Here there are no data as to the number of persons employed; deaths alone are given. If, however, the ratio of phthisis deaths at each age period to the total deaths is examined, both in the community as a whole and in recognisable and selected groups of the community, any notable excess of phthisis in a particular selected group will easily be revealed. The use of such data, however, demands caution, as the results must be expressed in percentages. A percentage difference may seem very large, though the actual difference it represents may be insignificant in reality. In the present case, for instance, the number of deaths recorded at most age groups is small, and consequently the probable error in the percentage expression is necessarily large. Further, when all ages are taken together, though the numbers are now larger, yet the age distribution in the two groups to be examined may be so different as to make the percentages of the totals meaningless. When large numbers, however, can be dealt with, the method is in general sound.

In Table B certain trades have been selected. The deaths from phthisis are shown on the left-hand side of the table in the figures as published by the Registrar-General, and a comparative table is placed beside it (to the right hand) showing that in general where the mortality of the trade from phthisis is high, the proportionate amount of phthisis to the total deaths in that trade is correspondingly high.

In Table B figures which are in excess of the standard set by occupied and retired males are printed in italics. Thirty-seven figures expressing death-rates per 1,000 are in excess, and in only two instances (printed in heavy type) are the parallel figures for proportionate mortality not also in excess, viz.:—the death-rates for cotton manufacture at age-period 55 to 64, and for wool, worsted, manufacture at age-period 65 and over. Forty-one figures expressing proportionate mortality are in excess, and in only six instances are the parallel figures not in excess; and in these six instances the excess over the standard is in every case too small, without other corroborative evidence, to justify any conclusion as to a probable excessive death-rate per 1,000.

In Table C a series of index numbers taken from the report of the Registrar-General is given for various diseases and for four classes of persons: first, all males; second, shoe makers; third, publicans and inn servants; and fourth, tin-miners. This table is given to show that phthisis is especially prevalent among shoe makers without any associated prevalence of lung diseases or alcoholism. It prevalence is therefore a special phenomenon. Where an influence such as an excessive indulgence in alcohol is present, not merely is there more phthisis, but practically all the chief diseases show a corresponding increase. With regard to tin-miners, where the inhalation of siliceous dust is a potent cause of lung disease, it is to be noted in contradistinction to shoe makers that the increase in the amount of phthisis is associated with a corresponding increase of all respiratory diseases.

The figures of Table D extend the comparisons shown in Table C, making use of the method of proportionate mortality. In the first part of the table the proportionate number of deaths from phthisis to the total number of deaths from all causes among males and females at six age periods is shown for England and Wales, for the period 1891 to 1900. Following these, similar figures are given for the Amalgamated Society of Engineers for the period 1902 to 1911. The first two proportions are based upon very large numbers, that for the Society of Engineers on sufficiently large numbers to make the ratios probable. In the second part of the table corresponding numbers are given for the National Union of Boot and Shoe Operatives and for the like operatives of the towns of Leicester and Northampton, the sexes being distinguished. The numbers here, with the exception of those of the National Union, are not large, but in every instance the tendency is towards a much higher percentage of deaths due to phthisis than that observed among the classes shown in the first part of the table. In the third part of the table the proportion of deaths from phthisis to the deaths from all causes is given for six age periods for the towns of Leicester and Northampton. It will be noted that the rate among the boot and shoe operatives is sufficiently high to influence the figures for the towns themselves.

The general high mortality of shoe makers from phthisis is thus fully illustrated. The question remains as to whether any special prevalence exists in any one branch of the trade. The figures which have been obtained relating to this are given in Table E. The numbers unfortunately are all comparatively small and distributed over six age periods. The method of examining these has been to make the assumption that at each age period the number of phthisis deaths should bear a constant proportion to the total number of deaths in each department of the trade, and then to calculate the theoretical number of phthisis deaths at each age and for each department. When these calculated deaths are summed up for all ages for each department and compared with the number actually found, it is seen that there is a considerable defect in the actual number of deaths among those employed in the division of the table termed "all other departments and not defined." It may be said that these suffer less from phthisis than the rest of the workers. The same process applied to the employees in the three main classes, namely, clicking, lasting, and finishing, shows a very slight excess of the actual number of deaths over the theoretical in the clicking department, and a similarly slight defect in the finishing department, but the differences are so small that no definite conclusion can be drawn.

19. There is one point, however, which must be borne in mind when any procedure is being considered with the view to diminishing the amount of phthisis. In every community, quite independently of occupations, a certain amount of phthisis is always present. All the modes by which this disease is maintained and its infection transmitted are not at the present time fully understood. The disease occurs among persons living in the best conditions, and not obviously exposed to special infection in workshops or elsewhere. So long as this amount of phthisis is present in the general community it can hardly be expected that any measures taken in any trade will result

in the reduction of phthisis in that trade to a level below that of the general amount present in the locality. If this be forgotten, the results of particular preventive measures may wrongly seem to be disappointing, and disappointment may lead to unfounded criticism of the measures or to their premature abandonment.

## Determining Factors of the High Phthisis Mortality in the Industry.

The causation of the special prevalence of pulmonary tuberculosis among boot and shoe operatives may be discussed under the following heads.

*Fatigue.*

20. While the operations of the workers in the different departments of the industry do not entail severe physical labour, they consist of a number of finely adjusted and rapid muscular movements which require the constant exercise of care and attention, and are frequently repeated. The nervous energy required is therefore considerable. The work of a clicker is accompanied by anxiety not to exceed the permissible amount of waste in cutting the leather—a costly material. The machines used in the trade probably require on the whole more guidance and control than the machines used, for example, in spinning or knitting; these occupations have a relatively low incidence for phthisis, though the atmospheric conditions of the spinning-mills and hosiery factories do not appear to us to differ notably from those of the shoe factories.

*Hereditary predisposition.*

21. The high percentage mortality from phthisis shown by boot and shoe operatives in every town in which the industry is carried on (see Table D), a mortality which is higher than that experienced in general by the township, appears to negative the supposition that this influence predominates.

*Poverty and consequent malnutrition.*

22. The earnings of boot and shoe operatives are certainly not less than those of operatives employed in other indoor trades in which a lower mortality from phthisis is found (see Table B); and no signs of malnutrition have been observed in an examination of nearly 700 boot and shoe operatives.

*Alcoholism.*

23. The Registrar-General's report does not support the contention that this powerful predisposing influence is predominant in the boot and shoe industry.

*Housing.*

24. There is no evidence that the housing of these operatives is worse than that of other operatives; on the contrary, Leicester and Northampton compare favourably with other industrial towns in this respect.

*Infection from materials used.*

25. Infection from leather manufactured from hides and skins of tuberculous animals, if it ever occur, must be very rare. The tubercle bacillus lives, not in the blood, but in ulcers or *foci* of necrosis, and an infected hide exhibits these ulcers when the hair is removed. Such ulcers destroy the "grain" of the skin, and the tanned hides would show holes where the ulcers had been, or, if the disease had not progressed so far, the destruction of the grain would prevent the leather from being "finished" in the approved manner. A tanner is careful to select hides as free from disease as possible, and for chrome leathers, which are almost always finished on the grain side, this selection is especially important. Even if the possibility of diseased skins being used is admitted, the tubercle bacillus probably cannot survive the modern processes of tanning.

*Overcrowding.*

26. The standard of space fixed by Sec. 3 of the Factory and Workshop Act, 1901, for every person employed in a factory or workshop is 250 cubic feet, and there is no clear evidence that this standard is not complied with in boot and shoe factories; but the exact air space is often difficult to estimate, owing to the number of movable frames used to convey the boots from worker to worker, and to the irregularly shaped machines present in the making-up and finishing departments. These industrial appliances always cause these departments to appear congested. In the clicking department, however, there is no congestion from manufacturing material, and the air space per individual, apart from any consideration of the actual content of the room when empty, always exceeds 250 cubic feet. Yet among the clickers the phthisis mortality is unduly high.

*Cramped position of the chest.*

27. The introduction of machinery has affected the posture of the workers considerably in the making-up department (lasters), and, to a less extent, in the finishing department. The laster used to sit at a bench and tuck the last into his chest; now although some lasting is still done in the old way, he usually stands at a machine. The available statistics appear to show that synchronously with this alteration in posture the phthisis mortality has fallen in this department, but as pointed out already the numerical data do not allow positive conclusions to be drawn. No such fall appears to have occurred in the finishing department. The posture of the clicker has not altered in recent years, and his mortality does not appear to have fallen. The clicker as he leans over his cutting board compresses his abdomen and lower ribs and interferes with diaphragmatic breathing, while at the same time the lift of the upper ribs is impeded because the shoulder girdle must be fixed to support the action of the arms when the pattern is held down and the leather cut; to-day the benches provided are of the same height for all operatives irrespective of stature, and the cutting boards, which are usually raised (but seldom sufficiently) by the men themselves, are flat. Although this question of cramped

position of the chest may be of importance among males, it does not seem to affect females in the closing department, who work at sewing machines. Yet the phthisis mortality among these workers is high (*see* Table D.).

*Sedentary indoor occupation.*

28. In this industry the work of machinists (females) is notably sedentary, while the clickers, even though they stand to their work, are bodily inactive; in other departments the workers move more from workplace to workplace, and their work calls for rather more muscular action, but still in the main the occupation is a sedentary one. The work generally is of such a character that it entails fine movements of the arm muscles with consequent fixation of the upper part of the thorax. With the exception of the pressmen the labour is not such as to occasion the movements of the lower limbs, deep breathing or movements of the body muscles, required to produce the efficient circulation, the full expansion of the lungs and the action of the abdominal organs, which encourage vigorous health. Reference to the phthisis mortality experienced in the various departments indicates a relation between the prevalence of phthisis and the extent to which the occupation is sedentary.

*The presence of an unusual number of sources of infection,* i.e., *infectious persons.*

29. In an industry in which a large number of individuals, often over 100, occupy the same room for 54 hours every week, and in which an infectious disease, in this case tuberculosis, is known to be prevalent, opportunities for transmission of the disease from the infectious to the healthy must occur more often than normally. One instance which came under notice will be sufficient to illustrate the danger—at a factory, in many ways in advance of the usual standard of hygiene found in the industry, a clicker, rather a careless man, developed phthisis, and was allowed to continue at work; before long, four other cases occurred among men working in his immediate vicinity. A possible means of transmission may be the use in common of tools and other appliances; we have found with the co-operation of Dr. James McIntosh that tubercle bacilli may be collected alive and virulent from templates intentionally infected in the laboratory one month before, and kept under the same conditions as they would be when stored in a factory. We may recall the evidence* establishing the fact that a consumptive person acts as a *carrier* of the disease, spreading infection by the sputum which he coughs up and sprays around him. Tubercle bacilli have been found on object glasses placed within twenty inches or so of coughing consumptives. Guinea-pigs have become infected when put to live in close proximity to two consumptives who lay in a small room with the window closed. In the summer, when the window was widely open, other guinea-pigs escaped infection. As the breathing volume of a man is at least one hundred times that of a guinea-pig, men must no less certainly breathe in the spray coughed out by a consumptive who works in his close

* *See* Appendix II.

proximity. When the soiled handkerchieves of consumptives, partly dried, are shaken close to cages of guinea-pigs, these animals become infected. Similarly the consumptive who shakes out his handkerchief, or spits on the floor, or contaminates his tools, patterns, etc., with the spray of his sputum, may spread infection to those near him. While infection is possible by the handling of contaminated tools, patterns, etc., or by the dust of dried sputum, the accumulated evidence shows that the danger of direct infection by spray coughed up is the greater. The spray does not travel far, and quickly falls to the ground; in agreement with this the experimental evidence shows that the danger is greatest within doors, when the proximity of the consumptive is less than one yard, and the windows are closed.

In the boot and shoe trade the clicker and the closer work almost within this dangerous proximity. The female machinists generally face each other on either side of a bench, and the opportunities for the spread of infection by coughing is obvious.

*Light.*

30. The influence of sunlight in destroying tubercle bacilli is generally recognised, and there can be little doubt that a maximum of light is advantageous both to health and for the carrying on of a skilled handicraft. In the clicking and closing departments the size of the windows and skylights commonly indicates the desirability of light, but the cleaning of the glass usually leaves much to be desired; and in the making-up, and especially in the finishing departments, the dirty condition of the windows often gives an impression of gloom, not dispelled by the artificial illumination frequently found in use on bright sunny days.

*Cleanliness.*

31. In the boot and shoe factory in every department the accumulation of *débris* from the materials used is inevitable, and this, unless it is frequently and efficiently removed, has ample opportunity of becoming infected with tubercle bacilli, so long as the objectionable practice of spitting on the floor is as frequent as it is to-day. These bacilli can remain alive for long periods in dust, and when disturbed can contaminate the atmosphere. This microbe-carrying function of dust must be carefully distinguished from the action of dust, *per se*, in predisposing the lung tissue to tuberculosis. The standard of cleanliness adopted has been found to vary considerably in different factories, and even in different departments of the same factory. In some the floors, after being damped by a disinfectant, are swept twice daily, in others the accumulation of days, or even of a week, are brushed up dry, with great generation of dust. Such dry sweeping of floors is an obvious source of danger.

*Imperfect ventilation.*

32. Throughout this enquiry the inadequacy of the ventilation provided has constantly been noted, though no definite evidence has been obtained that the presence or absence of carbon dioxide in the air bears a close relation to the point now under consideration.*

* Samples of air, taken from several factories, were analysed with special reference to this question.

Ventilation is imperfect when either (i) the air, no matter what its composition, is so still that the stimulating effect of moving air is absent; or (ii) air exhaled by one person can be inhaled by another, and this is probably the more important point in considering the danger from saliva spray infection. These two conditions are often present together, and the result may be expressed by the term "inadequate ventilation." With a few notable exceptions means for adequate ventilation have not been found in boot and shoe factories. Windows of adequate size, if clean, to admit light, but with too small a portion made to open, are the only means provided for ventilation; and, except on the warmest days, even the windows are very commonly closed by the workers, who complain if they are subjected to cool air currents. We feel confident that ready means are thus provided for the dissemination of an infectious disease such as phthisis, and that in inadequate ventilation is probably to be found the predominating influence upon which the prevalence of the disease in the boot and shoe industry depends.

## Summary of Conclusions.

33. The conclusions which have been reached may be summarised as follows:—

(i) Phthisis is specially prevalent among workers in the boot and shoe industry, as compared with the general population.

(ii) The individual worker is predisposed to infection by the sedentary nature of his employment, and possibly by the attitude he adopts at work.

(iii) The infection is probably

($a$) Increased by the number of infective workers, and

($b$) Favoured by want of light, the presence of infected dust, and inadequate ventilation in the work rooms.

## Recommendations.

34. The conclusions which have just been given point immediately to certain administrative measures likely to diminish the present unduly high incidence of phthisis among boot and shoe operatives. Such are, for instance, the improvement of lighting, floor cleaning and ventilation in the factories, and the introduction of periods of rest and exercise for the workers. Recommendations of administrative reforms, however, are not properly within the scope of the Committee.

It may be useful, nevertheless, if some account be given here of the chief physiological considerations which appear relevant to the questions raised, for these are based in part upon research work which has been done in the Applied Physiology Department under the Medical Research Committee, and they may serve to point the direction of further work in the future. Reference will be made also to the important question of the provision of suitable work for sanatorium patients drawn from boot and shoe factories, or from other places of work.

*Periods of rest and exercise.*

35. The deleterious effects of sedentary occupations can be counteracted by short periods of vigorous exercise in which body movements are made and by which deep breathing is induced. Such exercise is best taken in the forms of games or Swedish drills, and it has been suggested that opportunities should be given for the purpose by the provision of open-air exercise grounds, flat roofs, or courts upon factory premises, and by the institution of quarter-hour intervals at 11 a.m. and 4 p.m. The evidence we have obtained from a factory, where such play intervals have been instituted, shows that they are of economic as well as hygienic advantage. More and better work is done with, than without, such intervals. It is in our opinion contrary to physiological doctrine and to economic efficiency to keep girl machinists sitting at a bench for an unbroken four-hour spell.

*Ventilation.*

36. The erroneous conception that the ill-effects of close atmospheres are due to chemical changes in the atmosphere, and that exposure to cold is the cause of many ills, leads to much deterioration of the public health.

Physiological research has shown that it is the physical and not the chemical qualities of the atmosphere which in ordinary conditions most powerfully influence the health and vigour of the worker. Five-sixths of the energy output of man is spent in maintaining his body temperature ; the natural stimulus to a vigorous metabolism is exposure to the cooling effect of wind out of doors. Sedentary occupation in a warm atmosphere, in comparison with out-door work, determines a greater volume of blood to the skin, and less passes through the viscera; it diminishes the oxidation of food-stuffs, makes the breathing shallow, the circulation less vigorous. As less food is required, the appetite may become impaired, or more food may be eaten than is needed, with consequent digestive disturbances; in either case impoverished health results. The evidence gained from the study of the health of the new armies has shown the potent effects of open-air life. That drawn from results of open-air treatment of the wounded points in the same direction. The New York Commission on Ventilation has found that where men had the choice of doing work, 15 per cent. less work was accomplished at 75°, and 37 per cent. less at 86° than at 68°F. These figures show the economic importance of keeping factories adequately cool.

37. We have obtained evidence that the mucous membrane of the respiratory tract is swollen and congested on exposure to warm air, particularly when the feet are cooled by draughts on the floor. We have reason to believe that these changes lessen the resistance to infection by the organisms producing catarrh which are sprayed out into the factory air by the infected when they sneeze and cough. The change from over-warm rooms to cold outside air probably lessens the resistance to infection as a result of the sudden vascular constriction produced by the action of the cold on the swollen mucous membrane.

38. There is good reason then for keeping the factories adequately ventilated by fresh, pleasantly cool and gently moving air. Such ventilation cannot be secured by windows the opening of which is left

to the employees. We have seen, in one of the best factories, windows arranged so as to be fixed slightly open permanently, and notices posted ordering that all windows were to be thrown widely open in the dinner-hour. The permanent openings, however, were all closed by strips of material or paper, and the order was not carried out.

39. Importance should be attached to artificial ventilation arranged to give both impulsion at the eight-foot level and extraction at the roof. The heating mechanism should be separate from the ventilating mechanism, so that the air introduced is not heated. The extraction fan should be so arranged that fresh air can be impelled in hot weather. With the windows set open, a most efficient ventilation can then be established. The ordinary dry bulb thermometer only gives a measure of the loss of heat by convection in still air; it fails to give an indication of the cooling effect of moving air. The researches carried out with the Kata-thermometer* have shown that this instrument can be used to measure and secure an adequate rate of cooling. In the boot and shoe factories in this climate there is no need to consider the humidity of the atmosphere. The temperature and movement of the air and, to a minor degree, the radiant effect of the walls of the factory, are the chief factors to be observed. The Kata-thermometer can be calibrated so that it can be used to estimate these several factors, including humidity.

*The provision of employment for sanatorium patients.*

40. The advantages of sanatorium treatment are now generally recognised, and the State has organised a scheme for providing it. In practice, however, it is faced with two chief difficulties.

I. The patient frequently comes under treatment too late. Often this results from the patient being a wage earner with others dependent on him. Though consciously failing in health he may hesitate to seek medical advice, or even after he has ascertained the nature of his malady he may decline to surrender his livelihood by going into a sanatorium.

II. A patient who under sanatorium treatment has so far recovered as to be discharged, may return to work, but before he has settled down to the pace of the factory, working 54 hours a week, he may break down again.

41. These difficulties have been carefully considered, and in order to meet them we desire to advocate a modified form of sanatorium treatment. Briefly, the scheme is to establish, in connection with the ordinary form of sanatorium, a workplace for the manufacture of boots and shoes. Here consumptive operatives in an early stage of the disease, and convalescing patients, could carry on their trade under medical supervision for such hours as they are able, and earn wages in proportion. The value of work mentally and physically as an integral part of treatment is certain; and at present in sanatoria physical labour of a character unremunerative compared with the earning power possessed by skilled craftsmen is being invented. Such work often deteriorates the character of the young operative and turns him into a loafer.

* Report on Ventilation and the effect of Open Air and Wind on the Respiratory Metabolism, Prof. L. Hill. Local Government Board, 1914. Wyman and Sons, Ltd. Price 9*d*.

42. As health is re-established the working hours and earning capacity would be increased, until finally normal hours could be safely undertaken in many cases and factory employment resumed.

43. The conditions under which work would be done should preclude any possibility of the materials handled becoming sources of infection. Under ordinary factory conditions the materials handled by the clicker go to the closing room to be stitched together, and are later on dealt with in the making-up and in the finishing departments before they are issued to the public, and the possibility of infection exists at any stage. It would be among the more important advantages offered by the plan for a factory sanatorium if as a result of his stay an operative could be taught how to carry on his handicraft under hygienic conditions. The influence upon his fellow men of his acquired habits after his return to the factory might be considerable.

44. Employers of labour and representatives of the workmen who have been consulted have received the scheme favourably; and the steps necessary to its practical application have been discussed with them. But we do not consider that the administrative details involved fall within our scope as a committee for investigation.*

It may be said, however, that many circumstances seem to point to the Boot and Shoe Industry not only as one in which the evils of phthisis are conspicuous, but also as that for which the establishment of a sanatorium in which employment is provided is most easily practicable. The industry is not a scattered one, but is segregated in particular towns, and the nature of its technical processes raises no insuperable difficulties to their performance under sanatorium conditions.

45. Of the various centres of the industry, the district of Northampton has been suggested as being well placed at the present time for the initiation of such a scheme, and we have been informed that it has not yet completed its arrangements for the provision of sanatorium treatment. The past history of the Northampton Borough in matters of Hygiene and Public Health gives encouragement to a suggestion which is made for the inauguration of a pioneer movement there.

46. The latest returns of the M.O.H. for Northampton show that of the notifications of pulmonary tuberculosis in 1913, 48·4 per cent., making up 91 individuals, were engaged in the Boot and Shoe Industry. Roughly, it may be said that half the consumptives were boot and shoe workers. Now a fair proportion, if not all, of the remainder could possibly be given employment for such numbers of hours a day as they might be able to work in or about the sanatorium. Attached to the sanatorium proper there might be a farm, laundry, etc., which would reduce the maintenance cost, and also yield work for farm hands and laundresses, carpenters, painters and clerks, attendants, ward-maids, and so on, in such small numbers as are represented in the Northampton consumptives' list of those not

* It must be pointed out at the same time that the Committee have not regarded it as within their province to consider the questions connected with the payment of sickness benefit from the funds of Approved Societies to inmates of a sanatorium able to prosecute their trade or to earn wages for part-time work.

belonging to the Boot and Shoe Industry. Round the nucleus of the principal trade there could thus be gathered workers from most of the other occupations. To the question of compulsory suspension from employment of phthisical workers reference is made in Appendix III.

As to the amount of work and working space to be provided, it should be remembered that some of the patients would not be working at all in the early stages of the treatment, and that the others would be working for varying daily periods up to an approach to full time near the end of their cure. On the whole, it would probably be near the mark to take three hours daily per inmate as the average amount of labour to be expected. There were 91 notified cases in 1913 from the Boot and Shoe Industry, and if one-third be added for cases not notified, there would be about 120 cases in the Industry to be expected each year in Northampton. The provision of graded work for these at three to four hours daily each would correspond to the full-time work of about 50 operatives.

47. In the event of the practical adoption of such a scheme for modified sanatorium treatment as that just mentioned, the Committee would hope that they might be placed in a position to watch closely the development and progress of the new sanatorium, and to keep in touch with its results, both in regard to the health of individuals and in regard to the general health of the industry it would primarily affect. In connection with the proposed segregation and employment of phthisical workmen, problems needing special study may be expected to arise from time to time, and the Committee would desire to direct appropriate enquiry to them. If the modified sanatorium treatment, moreover, had its full result in removing the present exceptional possibilities of infection from the workshops, other possible subordinate contributing causes of the high prevalence of phthisis in the Boot and Shoe Industry might be unmasked, and should then be attacked in their turn by further investigation.

C. ADDISON.
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APPENDIX I.

# TABLE A.

Table showing mean Annual Death Rates per 1,000 of all occupied Males and of Boot, etc., Makers from all causes and from Phthsis in 1890–2, 1900–2 and in 1910–12 at successive age periods.

| OCCUPIED MALES. | Mean Annual Death Rates per 1000. | – | 20– | 25– | 35– | 45– | 55– | 65– | Total 15 yrs. & up. |
|---|---|---|---|---|---|---|---|---|---|
| 1890–2 ... ... ... ... ... | All Causes ... ... | 2·55 | 5·07 | 7·29 | 12·43 | 20·66 | 36·66 | 102·32 | 15·76 |
| | Phthisis ... ... | ·70 | 1·95 | 2·63 | 3·43 | 3·38 | 2·65 | 1·50 | 2·41 |
| 1900–2 ... ... ... ... ... | All Causes ... ... | 2·44 | 4·41 | 6·01 | 10·22 | 17·73 | 31·01 | 88·39 | 13·04 |
| | Phthisis ... ... | ·54 | 1·55 | 2·03 | 2·74 | 3·04 | 2·16 | 1·11 | 1·98 |
| 1910–12 ... ... ... ... ... | All Causes ... ... | 2·20 | 3·51 | 4·70 | 7·90 | 14·60 | 29·98 | 94·20 | 14·12 |
| | Phthisis ... ... | ·58 | 1·32 | 1·68 | 2·08 | 2·30 | 2·20 | 1·31 | 1·68 |
| BOOTMAKER (*i.e.*, Boot, Shoe Makers, Slipper Makers, Patten, Clog Makers. Boot, Shoe, Patten, Clog Dealers). | | | | | | | | | |
| 1890–2 ... ... ... ... ... | All Causes ... ... | 2·90 | 5·89 | 7·66 | 11·35 | 19·85 | 35·25 | 98·9 | 19·17 |
| | Phthisis ... ... | 1·08 | 2·73 | 4·00 | 4·42 | 4·86 | 3·14 | 1·55 | 3·31 |
| 1900–2 ... ... ... ... ... | All Causes ... ... | 2·64 | 5·14 | 6·33 | 9·8 | 17·38 | 29·2 | 83·1 | 15·7 |
| | Phthisis ... ... | 1·01 | 2·90 | 3·18 | 4·24 | 4·18 | 2·57 | 1·59 | 3·00 |
| 1910–12 ... ... ... ... ... | All Causes ... ... | 2·85 | 4·62 | 5·40 | 8·76 | 15·13 | 30·2 | 136·6 | 19·3 |
| | Phthisis ... ... | 1·20 | 2·20 | 2·98 | 3·32 | 3·55 | 2·86 | 2·60 | 2·76 |

# TABLE B.

Death-rates* from Phthisis, 1900–02, for certain classes of Males (England and Wales) distributed in Age-periods.

| Class. | Total number of deaths from Phthisis. | Death-rate per 1,000 living. | | | | | | | Proportionate mortality. | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Age-Periods. | | | | | | | | | | | | | |
| | | 15– | 20– | 25– | 35– | 45– | 55– | 65 and over. | 15– | 20– | 25– | 35– | 45– | 55– | 65 and over. |
| Occupied and Retired Males ... ... | 64,097 | 0·55 | 1·60 | 2·14 | 2·89 | 3·18 | 2·59 | 1·51 | 22·5 | 35·4 | 34·0 | 26·6 | 17·0 | 7·3 | 1·4 |
| Agriculturist (Agricultural Districts) ... | 1,341 | 0·36 | 1·09 | 1·10 | 1·02 | 1·16 | 0·88 | 0·81 | 19·3 | 33·2 | 29·5 | 19·1 | 12·6 | 4·9 | 1·0 |
| Ship-building ... ... ... ... | 388 | 0·51 | 1·23 | 1·53 | 2·04 | 2·11 | 1·59 | 0·70 | 20·8 | **37·5** | 31·3 | 23·2 | 14·2 | 5·2 | 0·8 |
| Commercial Clerk ... ... ... ... | 2,422 | *0·75* | *2·45* | *2·67* | *3·20* | 3·05 | 2·26 | 1·23 | *34·7* | *50·8* | *44·3* | *31·6* | **17·9** | 7·3 | **1·6** |
| Engine—Maker, Fitter ... ... ... | 1,963 | *0·60* | *1·74* | 1·87 | 2·36 | 2·74 | 2·58 | *1·61* | *25·4* | *40·2* | **6·9** | 26·6 | 16·3 | 7·1 | *1·6* |
| Printer ... ... ... ... ... | 946 | *1·03* | *3·44* | *3·65* | *5·13* | *4·34* | *3·68* | *1·87* | *32·2* | *56·8* | *55·1* | *47·4* | *23·4* | *10·8* | *2·0* |
| Cotton Manufacturer ... ... ... | 1,157 | *0·84* | *1·70* | 2·05 | *2·98* | *3·75* | **2·86** | *2·24* | *31·0* | *38·7* | **6·5** | *30·0* | *17·7* | 6·1 | *1·5* |
| Wool, Worsted—Manufacture ... ... | 474 | *0·69* | *2·38* | 1·81 | 2·26 | 2·89 | 2·35 | **1·88** | *31·4* | *46·7* | **34·5** | 24·5 | 16·0 | 5·7 | 1·3 |
| Tailor ... ... ... ... ... | 1,171 | *0·76* | *2·11* | *2·64* | *4·12* | *4·22* | *3·43* | *1·79* | *34·2* | *50·4* | *45·6* | *38·3* | *21·1* | *9·1* | *1·6* |
| Shoemaker ... ... ... ... ... | 1,886 | *1·04* | *2·95* | *3·27* | *4·41* | *4·40* | *3·21* | *2·15* | *38·8* | *56·8* | *49·4* | *44·5* | *24·0* | *9·4* | *2·0* |

* Calculated from Supplement to the Sixty-fifth Annual Report of the Registrar-General of Births, Deaths, and Marriages in England and Wales. Part II. 1908. Wyman & Sons Ltd. (Cd. 2619.) Price 1*s.* 10*d.*

# TABLE C.

Comparative Mortality from Certain Causes of Certain Classes of Males, aged 15 years and upwards, in England and Wales, 1900–1902.

| | Influenza. | Alcoholism and Liver Disease. | Cancer. | Phthisis. | Other Lung Diseases. | Circulatory Diseases. | Nervous Diseases. | Bright's Disease. | Accident. | Suicide. |
|---|---|---|---|---|---|---|---|---|---|---|
| Occupied and Retired Males | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Shoemakers ... ... | 67 | 77 | 103 | 145 | 84 | 100 | 101 | 86 | 38 | 100 |
| Publican, Inn Servants | 171 | 670 | 110 | 173 | 148 | 144 | 178 | 243 | 88 | 216 |
| Tin Miners ... ... | 104 | 28 | 101 | 436 | 419 | 105 | 84 | 143 | 92 | 32 |

# TABLE D.

Table showing the number of deaths from All Causes and from Phthisis at six Age-Periods for certain groups of Males and Females in England and Wales,
for certain Trades and for the towns of Leicester and Northampton,
with the proportionate Mortality from Phthisis.

| | | 20— | | | 25— | | | 35— | | | 45— | | | 55— | | | 65 and over. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Deaths. | | Per cent. | No. of Deaths. | | Per cent. | No. of Deaths. | | Per cent. | No. of Deaths. | | Per cent. | No. of Deaths. | | Per cent. | No. of Deaths. | | Per cent. |
| | | All Causes. | Phthisis. | | All Causes. | Phthisis. | | All Causes. | Phthisis. | | All Causes. | Phthisis. | | All Causes. | Phthisis. | | All Causes. | Phthisis. | |
| (1) Occupied and Retired Males (England & Wales) | 1891—1900 | 68,384 | 25,498 | 37·29 | 153,545 | 53,832 | 35·06 | 202,280 | 54,457 | 26·92 | 243,724 | 40,444 | 16·59 | 291,430 | 21,831 | 7·49 | 598,930 | 8,249 | ·14 |
| (2) Females (England & Wales) | 1891—1900 | 67,560 | 24,094 | 35·7 | 152,699 | 48,280 | 31·6 | 180,127 | 39,826 | 22·1 | 206,111 | 22,958 | 11·1 | 271,758 | 11,838 | 4·3 | 695,201 | 5,435 | 0·8 |
| (3) Amalgamated Soc. Engineers | 1902—11 | 381 | 115 | 30·2 | 1,274 | 447 | 35·1 | 1,334 | 286 | 21·4 | 1,759 | 198 | 11·2 | 2,515 | 144 | 5·7 | 3,869 | 44 | 1·1 |
| (4) National Union of Boot and Shoe Operatives, Males | 1st July, 1899, to 30th June, 1912 | 161 | 110 | 68·3 | 562 | 338 | 60·2 | 658 | 300 | 45·6 | 541 | 167 | 30·9 | 361 | 37 | 10·3 | 193 | 3 | 1·5 |
| (5) Leicester Operatives, Males ... ... | 1895—1900 & 1907—1912 | 113 | 60 | 53·1 | 255 | 155 | 60·8 | 244 | 105 | 43·0 | 219 | 51 | 23·2 | 197 | 21 | 10·7 | 233 | 10 | 4·3 |
| „ Females ... | | 47 | 20 | 42·5 | 46 | 27 | 58·7 | 26 | 10 | 38·5 | 10 | 2 | 20·0 | 9 | 1 | 11·1 | 9 | — | — |
| (6) Northampton Operatives, Males ... ... | 1901—1902 & 1908—1912 | 89 | 60 | 67·4 | 160 | 102 | 63·8 | 136 | 63 | 46·3 | 192 | 50 | 26·0 | 213 | 26 | 12·2 | 583 | 7 | 1·2 |
| „ Females ... | | 39 | 24 | 61·5 | 30 | 23 | 76·7 | 11 | 7 | 63·6 | 6 | 2 | 33·3 | 3 | — | — | 7 | 1 | 14·3 |
| (7) Leicester All Persons... ... ... | 1891—1900 | 809 | 330 | 40·8 | 1,690 | 622 | 36·8 | 2,132 | 576 | 27·0 | 2,417 | 315 | 13·0 | 2,954 | 163 | 5·5 | 6,243 | 47 | 0·8 |
| (8) Northampton All Persons ... ... | 1891—1900 | 386 | 161 | 41·7 | 858 | 329 | 38·4 | 973 | 263 | 27·0 | 1,166 | 162 | 13·9 | 1,512 | 106 | 7·0 | 3,232 | 32 | 1·0 |

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# APPENDIX II.

## THE PATHS OF INFECTION IN PULMONARY TUBERCULOSIS.

A general account of the state of knowledge with regard to the paths of infection in pulmonary tuberculosis may be found in the article by William Bulloch, M.D., F.R.S., in Allbutt's "System of Medicine," 1909, Volume V., page 299.

Heymann* found that the dust which was removed by a camel-hair brush from areas in contact with phthisical patients, infected guinea-pigs in ten cases out of 120. He and Ziesche† found that 30–40 per cent. of phthisical patients (65 were examined) sprayed out tubercle bacilli. It depended on the stage of the disease whether a patient sprayed out the bacilli or not, and the conclusion was reached that any phthisical patient might become a sprayer of tubercle bacilli at some time or other of his disease. The expulsion of infective droplets depends on the amount of viscosity of the sputum and the strength of the cough. As many as 430, 573 and 587 tubercle bacilli have been counted in one droplet.

Glass plates were exposed near phthisical patients for a certain time, and the presence of tubercle bacilli on the plates determined by microscopic means. Moeller‡ found the tubercle bacilli on the plates in 16 out of 30 cases. The infected droplets spread as far as one metre.

Findel,§ in an extensive series of experiments on 83 guinea-pigs, determined the number of tubercle bacilli which have to be inhaled to produce infection. Out of six animals which inhaled, as few as 20–40 bacilli, two manifested tuberculosis.

Chaussé‖ laid stress on the forcible nature of the air current which is required to drive off droplets from viscous sputum. He found only one out of 79 guinea-pigs was infected by being placed in a box into which phthisical patients coughed, and only two out of 107 guinea-pigs were infected when injected with the washings of Petri dishes over which phthisical patients had coughed.

Chaussé investigated 12 patients, and it is possible that he chose cases which were not sprayers. He kept guinea-pigs in a small ward (60 cubic metres in capacity) in which two phthisical patients slept. In the summer, when windows and doors were generally open, only one out of 14 was infected. In the winter, 29 out of 49 when the windows were closed at night. Only two out of 18 guinea-pigs were infected which were kept in the ward during the daytime, the patients having then left it, when the bed was shaken and made and the room cleaned. These experiments show the danger of continual close propinquity with phthisical patients with windows closed, and both methods of infection by dried sputum and by sputum droplets are proved to be possible.

Forty-three out of 73 guinea-pigs were infected when placed in a box in which the handkerchief of phthisical patients was agitated (24–48 hours after use). On the other hand, the agitation of pillow-cases infected none out of 78 guinea-pigs. It may, then, be concluded that infection is spread by sputum containing tubercle bacilli, whether as droplets coughed out or spat out partly dried and shaken from the handkerchief, or from sputum spat out, dried, and blown about in dust. The danger-zone for the spread of droplets is about a yard. Nurses and doctors escape infection in sanatoria because they generally do not come within or do not remain long within the danger zone, and because the ventilation is good. Close propinquity to phthisical patients and bad ventilation increase the danger of infection in factories. Repeated infection by daily propinquity is, of course, most dangerous.

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* Zeitschrift für Hygiene, 1899, xxx, 139 and 1901, xxxviii, 21.
† Zeitschrift für Hygiene, 1907, lvii, 50.
‡ Zeitschrift für Hygiene, 1899, xxxii, 205.
§ Zeitschrift für Hygiene, 1907, lvii, 104.
‖ Annales de l'Institut Pasteur, 1914, xxviii, 608, 720, 771.

# APPENDIX III.

## POWER TO SUSPEND FROM EMPLOYMENT INDIVIDUALS SUFFERING FROM PULMONARY TUBERCULOSIS IN AN INFECTIOUS STAGE.

Not everyone suffering from phthisis is in an infectious stage. When, however, the bacillus is present in the sputum, it is obviously undesirable that the patient should remain at work under ordinary factory conditions. The compulsory notification of phthisis provides a means for dealing with these cases, for information is thus obtained by the tuberculosis officers; but it still remains for these officers to be empowered to suspend from employment for such time as they remain dangerous to others those cases found to be infectious. Such power would be similar to that vested to-day in surgeons acting under the Regulations established, in pursuance of powers conferred by S. 79 Factory and Workshop Act, 1901, for certain industries, particularly those in which lead compounds are manipulated. In these industries the power is used in the interest of the individual to protect him from further danger; similar power reposed in tuberculosis officers would not only benefit the individual by withdrawing him from an unhealthy environment, but it would benefit his fellow workers by removing a potential source of infection. Action on these lines was advocated by the Departmental Committee on Tuberculosis when they recommended* "as an effective means of preventing the spread of the disease, the compulsory isolation of certain cases which are in a state of high infectivity, particularly in those instances where the patient's surroundings are such as to increase the risk of other persons becoming infected." Temporary inconvenience may result to individuals in whom the disease has not yet so affected their strength as to prevent them from earning wages, but the chances of ultimate recovery by early sanatorium treatment must outweigh this inconvenience; and it should be pointed out in connection with sections 40–47 above that if, by adoption of the scheme of notified sanatorium treatment already discussed, such workers could continue to exercise their handicraft and to earn wages, the inconvenience to them would be minimised.

* Final Report of the Departmental Committee on Tuberculosis, Vol. I, p. 8, § 15. H.M. Stationery Office, 1913. Price 2½*d.*

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## Report of the Special Advisory Committee upon Bacteriological Studies of Cerebro-spinal Fever during the Epidemic of 1915.

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# MEDICAL RESEARCH COMMITTEE.

## Report of the Special Advisory Committee upon Bacteriological Studies of Cerebro-spinal Fever during the Epidemic of 1915.

(*Approved for publication by the Medical Research Committee 13th January*, 1916.)

## Medical Research Committee.

(*National Health Insurance*).

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## Advisory Committee upon Studies of Cerebro-spinal Fever during the Epidemic of 1915.

With a view to the co-ordination of the results of scientific experience gained in different laboratories throughout the country during the epidemic of Cerebro-spinal Fever in the first eight months of 1915, both for their application in the administrative control of the disease upon the next occasion, and for the guidance of the directions of future research, the Medical Research Committee invited :

Professor F. W. ANDREWES, D.M., F.R.S. (Captain R.A.M.C. (T.) ).

Professor WILLIAM BULLOCH, M.D., F.R.S.

Professor R. T. HEWLETT, M.D., F.R.C.P.

to form an Advisory Committee, to consider and to report to the Medical Research Committee upon the published results of scientific work done in connexion with the epidemic and upon reports transmitted to the Committee by workers engaged in the study and control of the disease among the Military Forces.

(B45.) Wt. 52726—636. 1000. 2/16. Sir J. C. & S. Gp. 32.

# CONTENTS.

# GENERAL REPORT ON THE STUDIES OF CEREBRO-SPINAL FEVER transmitted to the Medical Research Committee from Cerebro-Spinal Fever Laboratories during the epidemic of 1915.

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## INTRODUCTION.

Twenty-four reports have been sent in from the central and provincial cerebro-spinal fever laboratories towards the establishment of which the Medical Research Committee gave assistance to the War Office in the Spring of 1915. Many of these reports are voluminous, and contain a mass of data requiring collation and analysis before conclusions can be deduced. This task was entrusted to us by the Medical Research Committee, and in fulfilling it our duty has been to study the several reports, compare the facts and figures given, and to add such criticism as seemed to us just and reasonable. We have then stated the conclusions, if any, which appear justified, and at the same time we have endeavoured to indicate the gaps in our knowledge of cerebro-spinal fever to which future research may profitably be directed. We have striven to fulfil the wishes of the Medical Research Committee that the results of the work which has been accomplished under their auspices may at once be made accessible to workers in general, and the advances in our knowledge of the disease clearly set forth, for guidance in future enquiries.

By permission of the Director-General, Army Medical Service, these reports from various sources, upon the bacteriological work done in connection with military cases, have been made available for the consideration of the Committee with a view to the present General Report and Summary.

In addition to a study of the twenty-four reports handed to the Committee, we have also taken into account certain published papers dealing with cerebro-spinal fever and its causal organism, which have appeared during the present year (1915), and where it seemed to us needful we have not hesitated to offer our criticisms.

By the courtesy of the Medical Officer to the Local Government Board, we have also been allowed access to the results of the work carried out by Dr. Eastwood and his colleagues in the Board's laboratories, and are privileged to allude to the data obtained there.

Cerebro-spinal fever and its control offer problems which involve bacteriology, medicine, epidemiology and administration. In this Report we have thought it best to restrict ourselves chiefly to bacteriological problems, and to those details of medicine and epidemiology with which bacteriology is principally concerned. We have regarded administrative matters as outside our province.

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The list of Reports furnished from the different centres of work,* and upon which this General Report is chiefly based, is as follows :—

| *Centre.* | *Reporter.* |
|---|---|
| 1. R.A.M. College, Millbank. | Major M. H. Gordon, with additional reports by Capt. T. Macaulay Hine and by Major Gordon and E. G. Murray. |
| 2. St. Mary's Hospital, London . . | Dr. Colebrook and Dr. Tanner. |
| 3. Cambridge . . | Capt. J. F. Gaskell with additional report by Lieut. Vines. |
| 4. Birmingham . . | Prof. Leith. |
| 5. Bristol . . . | Prof. Walker Hall, assisted by A. Renshaw, with additional reports by Dr. B. A. Peters and and Dr. O. A. Collins. |
| 6. Newcastle . . | Prof. H. J. Hutchens, D.S.O. |
| 7. Manchester . . | Prof. S. Delépine, with additional reports by Capt. A. Sellars and Capt. Tylecote. |
| 8. Sheffield . . . | Prof. H. R. Dean. |
| 9. Sheffield . . . | Major H. R. Drury. |
| 10. Leeds . . . | Major C. W. Vining. |
| 11. York . . . | Lieut. M. MacMahon. |
| 12. Nottingham . . | Lieut. Syer B. White. |
| 13. Norwich . . . | Dr. Claridge. |
| 14. Brighton . . . | Dr. G. Finlayson. |
| 15. Exeter . . . | Dr. R. V. Solly. |
| 16. Devonport . . | Dr. Warren Crowe, assisted by Dr. Donald and Dr. C. Shearer. |
| 17. Plymouth . . | Capt. Pethybridge. |
| 18. Falmouth . . | Capt. A. Gregor and Lieut. Lindsay. |
| 19. Canadian Contingent, Salisbury Plain . | Dr. Arkwright. |
| 20. Salisbury Plain area . | Lieut. J. M. Johnston.<br>Lieut. T. L. Llewellyn.<br>Lieut. J. M. Anderson.<br>Lieut. C. H. Treadgold.<br>Lieut. G. R. Bruce. |
| 21. Chester . . . | Capt. W. Allan. |
| 22. Netley, Royal Victoria Hospital . . | Major D. Embleton. |
| 23. Exeter district . . | Major L. E. A. Salmon. |
| 24. Woolwich. Royal Herbert Hospital . | Dr. James McIntosh and Lieut. W. E. Bullock. |

* A report from Cardiff by Capt. H. A. Schölberg was unfortunately received by us too late for inclusion.

In the following pages the Committee deals only with the bacteriological work gathered from the sources already mentioned. It has been thought desirable to report upon this now, without waiting for the results of the further work which is in progress.

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## Part I.

### The Biological Properties of the Meningococcus.

The evidence that cerebro-spinal meningitis is due to infection by the "*Diplococcus intracellularis meningitidis*," of Weichselbaum, commonly known as the "Meningococcus," is accepted as adequate by practically all bacteriologists. Nothing which is to be found in the series of reports which we have studied, or which has been published during the past year, appears to us to shake this evidence. Indeed, many of the new facts which have been established go far to remove some of the obscurities and difficulties which beset the subject.

We think it right, however, at the outset, to allude to certain papers which have recently been published suggesting that the meningococcus is only a form of a highly "pleomorphic" organism, perhaps a "late non-infective phase" of a microbe which may be a filter passer. In two papers published in the *British Medical Journal* (1915, Vol. I., pp. 541 and 715) Hort, Lakin, and Benians express this view, basing their opinions on growths obtained from the urine and cerebro-spinal fluid of cases of cerebro-spinal fever. The growths were found to be highly pleomorphic, and it is claimed that from one single colony no less than five different types of bacteria were recognized, some positive and some negative to Gram's stain: some were rods containing granules which were held to resemble the meningococcus. Shaw, also (*British Medical Journal*, 1915, I. 675), describes the existence of cocci, rods and clubs, in this connection. Donaldson (*Lancet*, 1915, I. 1333) while finding Gram-negative diplococci in every case of cerebro-spinal fever, also finds diphtheroid bacilli, and is disposed to regard this as "pleomorphism."

We find such views far from convincing, and they are at variance with the experience of the overwhelming majority of bacteriologists who have studied this disease. Pleomorphism or polymorphism is an ancient doctrine in bacteriology. It was developed especially by Hallier as the result of investigation of impure cultures and was the cause of great retardation of progress. The fixity of form among bacteria was established by Cohn and has been accepted by almost all bacteriologists as a result of

the study of pure cultures carried on through countless generations. In its true form, pleomorphism has not been demonstrated to exist. Variations in the size of bacteria may occur as a result of unsuitable media, and deformed individuals may make their appearance. These are "involution," but not pleomorphic, forms. The meningococcus has been grown without change of form in countless generations, and statements to the contrary are without doubt due to impure cultures. In most cases the so-called "pleomorphism" of the meningococcus is alleged as the result of methods beset with technical difficulties and peculiarly liable to lead to errors. No adequate evidence is brought forward that the aberrant forms found possessed the known biological properties of the meningococcus. In one of the reports which we have studied, Lieut. Treadgold (Salisbury Plain District) records observations in which he repeated certain of the experiments of Hort, Lakin and Benians, cultivating the Berkefeld filtrate of the cerebro-spinal fluid and urine from two cases of meningitis. In one of the two cases he obtained organisms resembling those found by Hort and his colleagues—beaded Gram-negative bacilli breaking down into coccoid granules. This case came to autopsy and proved to be one of pneumococcal meningitis. In the second case, which proved genuine cerebro-spinal fever, the results of the experiments were wholly negative. Treadgold rejects the positive results as due to secondary infections and, in our opinion, justly. The hypothesis of the "pleomorphism" of the meningococcus seems unwarranted by the statements which have been brought forward in its support.

### The Gram-negative Cocci of the Upper Respiratory Tract.

It may be of service here to recall the recognized species of Gram-negative cocci found in the nasopharynx, and to give their respective characters, since they are liable to be confounded with the meningococcus, and have, as a matter of fact, proved a source of confusion to some workers. Capt. Gaskell (Cambridge) has summarised them concisely and the following statements are taken from his report.

> *Micrococcus pharyngis siccus.*—Very common in the nasopharynx.* The colonies grow freely, are white and very adherent. On subculture these characters may quickly be lost, and the culture may then closely resemble that of the meningococcus. Grows freely at 23°C. Rapidly ferments glucose and saccharose (24 hours).
>
> *Micrococcus flavus I.*—Also very common in the nasopharynx. The colonies become yellow in colour, and on touching them they tend to slide about and can be picked up whole with the needle. Sometimes the consistence is stringy. Grows freely at 23°C. Ferments glucose and saccharose but usually takes two or three

* Other bacteriologists have not found M. Siccus common in the throat. Elser and Huntoon found it only twice, in their long series of observations.

days to do so, though change may be perceptible in glucose in 24 hours.

*Micrococcus flavus II.**—Rarely met with. More delicate in growth than the preceding. Colonies become yellow and are sticky and stringy, but easier to sub-cultivate than M. flavus I. Grows feebly at 23°C. in 48 hours. Ferments glucose and saccharose slowly: there is no distinct change under 3 or 4 days and the earliest change is often in saccharose.

*Micrococcus flavus III.*—Not very common. Colonies of a canary yellow colour, and of the consistency of paint like the meningococcus. Two forms are mentioned, one growing strongly at 23°C. in 24 hours, the other failing to grow at this temperature. Ferments glucose in 4 days, but not saccharose.

*Micrococcus catarrhalis.*—Only occasionally met with. Growth like paint, easily emulsified. Colonies white. Feeble growth at 23°C., soon failing. No sugars fermented: there may be a trace of acid in glucose on the third day, but by the fourth or fifth day both glucose and saccharose are alkaline.

*Meningococcus.*—Colonies whitish or with a very faint yellowish tinge. Their consistency is like paint, easily emulsified. Only very seldom is there slight growth at 23°C. Ferments glucose but not saccharose. With mannose† there is acidity in 3 or 4 days, but in 6 or 7 days the fluid is again alkaline—a reaction serving to differentiate the meningococcus from M. flavus III.

Capt. Gaskell summarises the fermentative reactions of these organisms in the following table, in which the sign + signifies acid production and the figure suffixed the day on which the reaction is first manifested.

| | Glucose | Saccharose | Mannose | Galactose | Inulin |
|---|---|---|---|---|---|
| M. pharyngis siccus | + $^{1}$ | + $^{1}$ | + $^{1}$ | — | — |
| M. flavus I. ... | + $^{1-2}$ | + $^{2}$ | + $^{3}$ | — | — |
| M. flavus II. ... | + $^{4}$ | + $^{4}$ | + $^{4}$ | — | — |
| M. flavus III. ... | + $^{3-4}$ | — alk. | + $^{3-4}$ | — | — |
| M. Catarrhalis ... | — alk. | — alk. | — | — | — |
| Meningococcus ... | + $^{4}$ | — alk. | + $^{3}$—$^{7}$ | — | — |

* It is not certain that Gaskell's Flavus II. is the same as this organism of other writers. Elser and Huntoon state that their Chromogenic II. corresponds to v. Lingelsheim's Diplococcus pharyngis flavus I.

† It must be noted that the reaction with mannose is still on its trial. Its value requires further testing.

## The Specificity of the Meningococcus.

Rejecting, as we have done above, the evidence on which a high degree of polymorphism has been claimed for this organism, it appears to us that the meningococcus is shown to be a good enough " species " in the natural history sense, as species go amongst bacteria. That is to say it can be adequately separated from other Gram-negative cocci by the exercise of reasonable care. By serological means it can be divided up, it is true, into certain immunological races or strains, as will be mentioned a little later, but this need not affect its specific entity. We are not disposed to assent to the axioms laid down by Dr. Warren Crowe (Devonport) in his report. He asserts, (1) " that no Gram-negative coccus isolated from the nasopharynx can be proved to be the meningococcus," and, (2) " that no Gram-negative organism, of a meningococcus-like appearance, and giving similar reactions on culture, can be regarded with certainty as incapable of producing meningitis." The degree of proof or certainty which is required and commonly accepted in bacteriological problems is necessarily of a different order from that demanded by the mathematician. But nearly all bacteriologists would agree that a given coccus from the nasopharynx *can* be identified as the meningococcus, or not the meningococcus, as the case may be, with a certainty comparable to that accepted in other bacteriological or biological questions, provided that those tests be employed which experience has shown to be satisfactory. No sufficient evidence is forthcoming that meningitis can be caused by Gram-negative cocci allied to, but not identical with the meningococcus, and we cannot perceive the force of Dr. Crowe's second dictum, for we should regard a meningococcus-like organism which gave *all* the cultural reactions of the meningococcus as certainly capable of producing meningitis. We venture to make these criticisms because, although we recognise that the difficult question of specificity amongst bacteria is one as to which we may eventually be compelled to reconsider our opinions, we do not consider it shown that any Gram-negative coccus from the pharynx, other than the meningococcus, is a potential source of epidemic meningitis. In the present state of our knowledge it would seem that the dangerous one *can* be picked out by suitable tests, and this is the whole crux of nasopharyngeal examination for meningococcus carriers, which will be confused and stultified if we accept any vaguer view without convincing evidence.

*Asserted differences between spinal and pharyngeal Meningococci.* Two reporters note certain points of difference between strains from the meninges and strains from the throat. Lieut. Vines (Cambridge) found that in a medium containing 1 per cent. each of peptone, starch and glucose, and tinted with litmus, the throat strains grew and formed acid while the lumbar puncture organisms did not. Again, Dr. Warren Crowe (Devonport) found that on a special blood medium which he used (to be mentioned later), the colonies of the spinal strains were usually milky instead

of transparent. When, however, such opalescent colonies were emulsified in saline and a post-nasal swab which had been in contact with the throat was dipped into the emulsion and plated out, the resulting colonies might be transparent, like nasal ones : the original appearance was regained on further subculture.

The explanation of these observations is not very clear. It is possible that a saprophytic life in the pharynx may enable the coccus to grow in a culture medium without serum, and that the presence of traces of nasal mucus may affect the character of the colonies (*see* Dr. Shearer's observations, below). It is not claimed that the differences found by Dr. Vines and Dr. Crowe are of specific value.

## The General Characters of the Meningococcus.

These are now well-known, and we need only recapitulate them briefly. It need hardly be said that they have been determined from the study of indisputable strains derived from the cerebro-spinal fluid. Certain points which are perhaps novel are brought out by different reporters and deserve mention, especially the careful observations of Lieut. Vines (Cambridge).

The *morphology* of the meningococcus is fairly constant, the only point to be noted being variation in size. Apart from the early occurrence of swollen involution forms, different strains seem to vary in their size. This is noted by Prof. Walker Hall (Bristol) : in three of his cases the cocci were very large, but became of normal size on subculture : in four other cases they were unusually small, with many involution forms. In the "large coccus" cases he states that recovery was rapid, while the "small coccus" strains were observed in more fulminant cases of the disease.

As regards *staining reactions*, one or two reporters comment on the occurrence of scattered Gram-positive cocci amongst the Gram-negative majority—a finding which probably depends upon the exact technique employed.

The *appearance of the colonies* is regarded by many of the reporters as so characteristic, that they place their chief reliance on this for the recognition of the organism. The colonies, must of course, be well separated, and some workers (Prof. Dean and Major Drury (Sheffield) take the trouble to replate doubtful colonies in order to ensure this. Stress is laid on the size, translucency and sharp definition of the colonies and on the development of a central granular area. The characteristic appearance of the colonies may not be reached till 48 hours have elapsed, and as it is not safe to defer subculture so long as this, many colonies have to be picked off on suspicion only. Where the colonies are numerous they tend to become confluent, but even then may give a distinctive picture.

*Growth at* 23°C. This test, put forward at first as of diagnostic value, has in the experience of most of the reporters proved an unreliable one. While most strains of the meningococcus fail to grow at 23°C., a certain proportion show some degree of growth,

though it is never profuse. Major Gordon (Millbank) found 3, out of 35 strains tested, to show growth on his "trypagar" medium in 48 hours; the other 32 not in 10 days. It would seem that this growth at low temperature is especially apt to occur on hæmoglobin-containing media. The test is regarded by many reporters as a useful confirmatory one, but devoid of absolute diagnostic value, and such use as it has is diminished by the fact that certain forms of Micrococcus flavus also refuse to grow at 23°C. Capt. Gaskell (Cambridge) makes some remarks under this heading. He asserts that constant subculture at 37°C. removes the power to grow at 23°C. in practically all Gram-negative cocci and concludes that the minimal temperature for growth is a variable factor amongst these organisms. He further adds the warning that failure to grow may be due to death, and advises removal of the culture from 23° to 37°C. on the third day, when growth ought to occur, and in the case of his true meningococci always did occur. Errors may also arise from variations in the temperature of the incubator, especially at night. Lieut. Compton, on the other hand, in a paper in the *R.A.M.C. Journal* (Nov. 1915) alleges that repeated subculture confers the power of growth at 23°C. upon meningococci which previously lacked it. His table of sugar reactions, however, makes it doubtful whether all his meningococci were the true organism.

*Fermentative reactions.*—There seems a fairly general consensus of opinion that the "sugar tests" are a valuable aid in the recognition of the meningococcus. The reactions have been found remarkably constant on the whole. The coccus forms acid from glucose and maltose, but not from galactose, lactose or saccharose. Mannose gives an initial acidity which soon fades. Capt. Gaskell (Cambridge) reports a strain of the genuine organism from the cerebro-spinal fluid which failed to ferment glucose at first, though after repeated subculture it developed the power to some extent. Major Gordon (Millbank) also met with three strains which failed to ferment glucose, and Lieut. Bullock (Woolwich) notes one such case. Gaskell further tested galactose thoroughly, using a specially purified sample prepared by Prof. F. G. Hopkins, and found it fermented by no Gram-negative coccus. Prof. Hutchens (Newcastle), however, states that the meningococcus gave acid with galactose as Gordon originally asserted. These discrepancies are probably due to the fact that galactose is a somewhat unstable sugar, and may undergo partial decomposition on heating, as was shown by Elser and Huntoon.

In view of the above facts, it would appear that the only routine sugars which need be used in the differentiation of the meningococcus are glucose and saccharose, and this seems to have been found sufficient by most of the reporters. To these mannose can be added in certain cases of doubt. It is, of course, necessary that the sugars should be pure and serum must be added to the culture medium. Capt. Gaskell remarks on the need for making subculture from those tubes which have given

a positive result to make sure that no streptococci are accidentally present. In case of failure on the part of an organism to ferment such a sugar as glucose, the culture should be examined to make sure it is not dead. We shall refer to the question of the best medium for the sugar reactions in considering the whole subject of media later.

The development of an acid reaction in liquid sugar media by the meningococcus is a slow one, and most observers agree that at least 3 or 4 days must be allowed. The amount of acid produced is never large. The nature of the process has been the subject of a very interesting research by Lieut. Vines (Cambridge). It was shown that when the organism was grown in the medium used for the sugar reactions, but with the sugars left out, a slightly alkaline reaction arose in a week or ten days. This is presumably due to proteolysis, but it is uncertain whether it is brought about by any extracellular enzyme. Side by side with this, when a suitable sugar is present, acid is formed by a sugar-splitting enzyme, which takes some little time for its elaboration. He obtained evidence of the presence of such an enzyme in the neutralised Berkefeld filtrate from a glucose culture: it was capable of giving rise to acid in a sterile glucose medium, in the presence of an antiseptic. Lieut. Vines holds that there is thus a balanced reaction between an alkali-producing proteolytic process and an acid-producing glycolytic one. In the ordinary glucose test for the meningococcus the acid formation gets the upper hand after the first few days. On this hypothesis, as Capt. Gaskell points out, some of the anomalies of the sugar reactions are explicable. Thus, it was shown that his aberrant strain of meningococcus which appeared unable to ferment glucose, was an exceptionally active alkali producer, as M. catarrhalis is. Even M. catarrhalis may show traces of acid formation in an early glucose culture.

Prof. Walker Hall (Bristol), notes that it is an advantage to warm the sugar media by putting them in the incubator for an hour before inoculation. In this way more rapid reactions are secured.

### *Other Biological Properties of the Meningococcus.*

One of the most serious difficulties encountered in the culture of the meningococcus is its tendency to die in a few days on solid media. According to Lieut. Vines (Cambridge) this is due to drying: the organism is singularly intolerant of this, indeed he found that actual desiccation kills it in 2 to 5 minutes. On the other hand he found it tolerant of light: all strains survived exposure to bright sunlight for half an hour, and some strains even for 7 hours. These facts have evident bearing on the vitality of the organism outside the body, and on certain details of technique in cultivations from the pharynx.

Lieut. Treadgold (Salisbury Plain district) carried out a number of observations on the vitality of the meningococcus. Isolated

colonies of the coccus were touched with dry, sterile West's swabs, which were then withdrawn into their sheath. Plates were inoculated from them at intervals, and it was found that no growth ever resulted after exposure to daylight and room temperature for 1 hour. If, however, the swabs had previously been moistened, growth occurred up to 2 hours, and, where daylight and desiccation were avoided, even longer. He also swabbed carriers in duplicate, using one swab at once, and keeping the other for testing vitality. It was found that when they were left on the laboratory bench they were nearly dry in 6 hours, and quite dry in 9. When cultures were made from them after 3, 6, 9 and 12 hours no meningococci ever grew, though various organisms, including other Gram-negative cocci, grew freely. When the duplicate swabs were kept in a dark cupboard, they were not completely dry even in 12 hours : from such swabs the meningococcus was sometimes grown, indeed in one instance he obtained a copious growth after 11 hours. He, therefore, recommends that if throat swabs cannot be plated at once they should be stored in an air-tight receptacle. These observations, so far as they touch the influence of light, seem opposed to the findings of Lieut. Vines, but it does not seem that Lieut. Treadgold tested the influence of light and desiccation separately.

*Agglutination as a Test for the Meningococcus.*

Some of the reporters have tried this mode of diagnosis. The best methods for its employment were determined some years ago, chiefly by the German workers. The macroscopic method is far preferable to the microscopic one, on account of the difficulty of preparing a microscopically homogeneous emulsion. It is necessary to allow a considerable time for agglutination—48 hours at least, at 37°C.—but better results are obtained at 55°C., at which temperature the readings may be taken after 24 hours, though some allow a longer time.

Most of those who have employed this test seem to have found it capricious and unreliable. The reason is probably to be sought in the important fact which we have next to consider, namely the existence of several races of the meningococcus differing in their immunological reactions.

## The Differentiation of Races of the Meningococcus.

Serological work with this organism has always offered problems difficult to solve. Those who wish to acquaint themselves with the subject will find it fully summarised and ably criticised by Dr. Eastwood, in his paper in the current number of the Medical Officer's Report to the Local Government Board. The methods which have been employed are (1) agglutination, (2) absorption of agglutinin, and (3) complement fixation.

It has been apparent almost from the first that serological differences may exist not only between strains of meningococci isolated from the meninges and those found in the pharynx, but

between different spinal strains themselves as well as amongst pharyngeal strains. Arkwright (1909, *Journ. of Hygiene*, Vol. IX., p. 104) was able to assert serological differences between some epidemic and some sporadic strains. Elser and Huntoon (*Journ. of Medical Research*, Vol. XX., 1909), found agglutinability a very unstable property of the meningococcus, many of their strains being apparently inagglutinable. The German observers endeavoured to prove that the strains found in the throats of non-contacts were "pseudo-meningococci," but they were unable to frame any definition of a pseudo-meningococcus which would not include some undoubted spinal strains. No serum has ever been produced which will certainly distinguish between the genuine organism and the so-called pseudo-meningococcus.

Dopter (1909, *C.R. Soc. de Biol.*) found in the throat meningococci which he at first thought were non-pathogenic and which differed in their serological reactions from his true meningococci: for these he introduced the term "parameningococcus." Later, however, he found these cocci in the meninges in true cerebro-spinal fever. His observations and those of his fellow workers tend to show the existence of at least two, and possibly more, strains of the organism in the disease.

The evidence which has so far accumulated suggests that comprised under the term meningococcus there are a number of races, differing in their immunological reactions, some apparently more virulent than others, but there is so far no justification for asserting any to be destitute of potential pathogenic powers. How sharply defined and stable these races may be we do not at present know.

The conception of "immunological races" within the limits of a single species is not a new one. Not to mention the organisms included in the Gärtner group of bacilli (B. enteritidis, B. suipestifer and B. paratyphosus B), we have a striking parallel to the state of affairs amongst the meningococci in recent work relating to the pneumococcus. Some five years ago, Neufeld and Händel showed that an immune serum against a given strain of pneumococcus was not effective against all strains. During the past few years a large amount of work has been done at the Rockefeller Institute on this subject, and it is ably summed up in Dr. Rufus Cole's Packard Lecture (1914). The cases of human pneumonia in New York are shown to be due to several strains of pneumococci, each with its own serum reactions, and yielding different rates of mortality. The serum prepared with one strain of pneumococcus does not protect against other strains, and the different "immunological races" of the coccus are separable by agglutination reactions. Methods have been devised for the rapid diagnosis of the particular race in any given case of pneumonia, and specific sera have been prepared against the two commonest and most important races of the coccus.

The conception of immunological races of the meningococcus seems to have been present in the mind of more than one of the present series of reporters. Thus Dr. Finlayson (Brighton)

considers that we have to deal with a "meningococcic group," as in dysentery or paratyphoid fever: a given serum had, he found, an agglutination titre which varies with different strains. Capt. Gaskell (Cambridge) tested three sera upon a number of strains of the coccus and got variable results. Dr. Warren-Crowe (Devonport) insists on the importance of testing the strain of meningococcus obtained from the meninges against the serum which it is proposed to employ for therapeutic purposes, to see whether it is agglutinable by this serum. He claims that none of his cases died where a homologous serum had a fair chance.

Major Gordon and his colleagues at Millbank have now worked out in detail the immunological characters of the strains of meningococcus concerned in the past epidemic. This was done by the method of "absorption of agglutinins," familiar enough in other fields of bacteriology.

The paper in which the work of Major Gordon and Mr. E. G. Murray is described has recently been published in the Journal of the Royal Army Medical Corps, and there is therefore no reason for relating it in detail here. We confine ourselves to a short statement of the methods employed and of the results obtained.

Standard emulsions were made by suspending the cocci in normal saline, sterilising at 65°C., diluting to 2000 million organisms per c.c., and adding 0·5 per cent. phenol. Such emulsions kept good for months in the ice-chamber and were used not only for all agglutination and absorption tests, but also for immunizing rabbits. Immune sera were prepared from young rabbits by an intensive method (1,000 million cocci intravenously, followed 48 hours later by 3 such doses at hourly intervals): a modification of this method has been shown by Capt. Hine to yield in 9 days a serum with a titre of 1 in 800.

The method of differentiating the strains lay not merely in the occurrence of agglutination, but in the anchoring and removal of the agglutinin when the serum was saturated with the coccus to be tested, adequate controls being introduced.

Thirty-two strains of meningococci obtained from the cerebro-spinal fluid of genuine cases in the recent epidemic were tested in the above fashion. A rabbit was immunized against one of the strains and its serum tested against the 32 strains and against the "parameningococcus" of Dopter. Nineteen strains were picked out by the serum, agglutinating and absorbing the agglutinin: these were classed as Type I. A rabbit was now immunized against one of the remaining strains, and its serum was found to pick out 8 of this residue, which were classed as Type II. The serum of this rabbit was unaffected by saturation with Type I. A third rabbit was now immunized against one of the remaining 6 cocci, and its serum again picked out 4 of them—Type III. Of the remaining 2 cocci, one,—Type IV., was unique: a rabbit was immunized against it, but none of the preceding 31 cocci absorbed the specific agglutinin from its serum. The other was Dopter's parameningococcus which thus appeared to be a strain different from any of the cocci concerned in the recent epidemic in this country.

Nine strains from the nasopharynx were then tested, all of them culturally indistinguishable from the meningococcus. Five of them were found identical with Type II. of the cerebro-spinal strains, and this was confirmed by immunising a rabbit with one of the five: the serum of this animal, tested against all the cerebro-spinal strains, picked out the 8 which belonged to Type II. No pharyngeal strain of the 9 tested (which all came from later stages of the epidemic) was identical with Type I., but subsequently a carrier of 6 months' duration, infected at an early period of the epidemic, was found to harbour Type I. in his throat.

In a more recent report, Major Gordon states that the examination has been extended to 63 strains of meningococcus from the spinal theca. Of these, 50 per cent. are found to belong to Type I., 30 per cent. to Type II., 16 per cent. to Type III. and 3 per cent. to Type IV., but there remain 10 strains which cannot be identified with any of the four types.

Dr. Fred Griffith, working in the Local Government Board Laboratories, has independently carried out a research on almost exactly the same lines as Major Gordon, and Dr. W. M. Scott, in the same laboratories, has employed similar methods in his work on the meningococcus. Their results are now being published in the Board's Reports, and having been permitted to see them in advance, we are able, with the authority of the Medical Officer to the Board, to state that they have found differences among meningococcal strains much the same as were found by Gordon. They do not, however, feel justified in asserting the existence of more than two principal types, and these are not sharply defined, for they find certain indeterminate and intermediate strains.

While this report was being written two further papers appeared on the subject of the classification of the races of meningococci, one by Capt. A. W. M. Ellis, of the Canadian Army Medical Corps, and one by Dr. J. A. Arkwright, the latter being a continuation of his previous work on the subject. These papers will be found in the *British Medical Journal*, 1915, Vol. II., pp. 881 and 885. Both observers base their results on agglutination only, and not on both agglutination and absorption of agglutinins, as Gordon and Griffith have done, and both arrive at a subdivision of the species into two main groups.

Ellis uses the macroscopic method, with undiluted monovalent rabbit sera, and carries out his technique at room temperature in capillary pipettes. He studied 46 strains of meningococci and found that they fell without exception into one of his two groups, and he refers Dopter's parameningococcus to his Type II. His strains came from various epidemic foci in England, and from the British forces in France. Amongst the English strains, Type I. was commoner than Type II.; in France the two were equally common; organisms of both types came from all of six epidemic foci. Three inagglutinable, or variably agglutinable, strains were found which were referred to Type II., because sera prepared from them agglutinated other cocci of Type II. In

the nasopharynx of carriers, Type II. was identified four times and Type I. once.

Arkwright employed the more ordinary technique, carrying out the agglutinations in small tubes at 37°C. He made a polyvalent rabbit serum, which agglutinated 30 out of 32 strains of the meningococcus, but not M. flavus unless the strain was auto-agglutinable; such a serum was therefore available for diagnosis. He also made 2 monovalent rabbit sera (A and B), for the differentiation of sub-races, and further employed the anti-meningococcal and anti-parameningococcal sera of the Pasteur Institute, both probably more or less polyvalent. The 35 strains which he tested came from various epidemic foci in England (including many from Salisbury Plain) and two from France. The differentiation into two main Types was not so sharp as in Ellis' results: his sera A and B placed 17 strains out of 35 in one group and 10 in another. The Pasteur Institute sera placed 15 in one group and 12 in another, the latter group being that best clumped by the anti-parameningococcal serum. The two groupings coincided in the main. Taking all these results together, he concludes that 30 out of the 35 strains could be assigned by his methods to one or the other group, while 5 could not: there was some evidence that 2 out of these 5 were intermediate between the 2 main groups. Of 3 pharyngeal strains tested, 2 fell clearly into one group, the other possibly into the second. The two groups were (1) mainly meningococci and (2) mainly parameningococci. Arkwright considers that there is no evidence that the two groups are permanently different stocks causing different types of disease, or are confined to different epidemiological outbreaks: severe and fatal cases may be due to either group. His recent work confirms that published in former years (1909 and 1912), in which he claimed that by agglutination and complement fixation tests he could divide both sporadic and epidemic strains of the meningococcus into somewhat overlapping groups, connected by intermediate strains, and that these groups could be further subdivided by the absorption of agglutinin test.

It is plain that at this stage of the researches we have just described there can be no pretence of finality. The separate "Types" of each individual worker will require comparison, and identification with one another. The precise limits of each observer's groups will probably be influenced in some measure by the chance of the particular strains which he happened to use in preparing the immune sera upon which he relies for identification. In any case it seems doubtful whether these immunological races will be found quite sharply separable. The races are defined by methods the relative values of which may still be disputed, and the differences brought out by these methods may be conjectured to depend upon slight changes in the atom-groupings of the bacterial protein determining its reaction with a particular antibody. We know very little as yet about the stability of such atom groupings and the extent to which they may undergo spontaneous variation.

Meanwhile it is satisfactory that the existence of these races or sub-species is clearly established, even if their number and precise limits cannot yet be affirmed with certainty. They probably cover the forms described as "parameningococci." It may be hoped that the terms "para-" and "pseudo-meningococcus" will in time be dropped.

Comparing the results of the different workers it seems clear that there are at least two principal "epidemic types," and possibly a number of rarer ones, within the limits of the species: these two types cover the great majority (some 80 per cent.) of the meningococci concerned in the recent epidemic in this country. We learn that Major Gordon has already identified both these types (I. and II.) in the cases which have begun to reappear during the present winter (December, 1915).

It must be observed, however, that the strains studied have been "epidemic strains," from the meninges. It is possible that the meningococci found in the posterior basic meningitis of infants in non-epidemic times will prove to belong to other types, and the same seems likely to be true of many of the meningococci found in carriers.

There is hope that the observations may bear immediate fruit in practical application, and this in more than one direction. In the first place it is proposed to supply from the Central Laboratory at Millbank monovalent rabbit sera which will agglutinate all the epidemic strains of meningococci commonly found, up to a dilution of 1 in 400. Should this series of homologous sera prove effective it will facilitate the recognition of the epidemic types of the meningococcus. In the second place it should afford the serum treatment of cerebro-spinal fever a better chance to prove its value than it has yet had in this country. For not only can a properly balanced polyvalent serum be prepared for general use, but by identification of the type of coccus in any given case the way is open for the use of a monovalent homologous serum of presumably greater potency. We learn from Major Gordon's report that such sera are already in preparation. It is possible, too, that the recognition of the type of meningococcus concerned may prove of assistance to the epidemiologist in tracing the progress of an epidemic and even suggesting the source of an infection.

Inasmuch as certain of the reporters have found the serum of a case of cerebro-spinal fever to agglutinate the homologous meningococcus, while having a variable effect upon other strains (Warren Crowe, Gaskell), it seems possible that by determining the agglutinating titre of the patient's serum upon standard suspensions of the different types sent out from the Central Laboratory, another method of recognising the type of coccus concerned may become available.

Before leaving the subject of agglutination, we may note a method put forward by Dr. Warren Crowe (Devonport) as simple

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*Nutrose-ascitic-agar* or "*nasgar*" was probably the most widely used of all media for the meningococcus, and its defects only became apparent when it was used on a large scale for throat swabs. Nearly every reporter has alluded to its unsatisfactory character for this purpose. The meningococcus will not invariably grow on it, and in any case vitality is short, so that the colonies are often dead in 48 hours. This was the medium at first sent out from the Central Laboratory at Millbank, but as nutrose and Witte's peptone became unprocurable, and it was difficult to obtain ascitic fluid in sufficient quantity, a "*war-nasgar*" was evolved, in which nutrose was replaced by a mixture of sodium caseinogenate and glycerophosphates, Witte's peptone by a standard peptone of Armour's, and ascitic fluid by normal horse serum. This medium proved little better than the original nasgar: some strains of meningococcus grew well on it, others did not.

The Millbank observers therefore conducted an elaborate series of experiments for defining the cultural requirements of the meningococcus, reported in detail by Major Gordon. Various proteins were added to agar, with and without glucose, and a further series of trials was made in which "water agar" (*i.e.*, a plain agar medium without broth) was used as the menstruum. The results showed that the most favourable results were obtained with serum albumin, hæmoglobin, fibrinogen or legumin, as the added proteins. Of these, legumin presented the advantages that it is cheap, easily prepared from common pea-flour, and sterilisable by heat without precipitation. As the result of the water-agar trials it appeared that Douglas' trypsin broth was a more favourable basis for making the agar basis than ordinary broth: it already contains so much sugar as to render the addition of glucose unnecessary. It was further determined that the most favourable reaction of the medium for the growth of the meningococcus was one exactly neutral to phenol-phthalein.

From these experiments there gradually emerged the medium at first termed "legumin agar" or "pea-flour agar," but which in its final form is known as "*Trypagar.*" This medium gave a higher proportion of positive results than others, and it is claimed that it best fulfils the requirements of an ideal routine medium in all respects save one, namely that the viability of the meningococcus upon it is short (some 48 hours only). The full details of the preparation of the medium have been published by Capt. Hine in the *Journal of the Royal Army Medical Corps*, and trypagar has become the standard medium which is sent out from the Millbank Laboratory. It is said to be improved by the addition of 2 per cent. of normal horse serum or, better, ascitic fluid, which somewhat increases the size of the meningococcal colonies and slightly prolongs their vitality. It is proposed to send out, with the medium, sufficient serum for this addition, when desired. Capt. Gaskell has used the legumin medium at Cambridge and speaks well of it. It now remains to be seen whether it will meet with general acceptance.

While we may hope that the problem of a routine culture medium has been thus solved, it must be noted that many of the reporters have evolved media of their own which they prefer to any which have been supplied from the central laboratory, and it is perhaps always true that an investigator obtains the best results from the medium with which he is in the habit of working. We must now notice these other media.

*Blood media.*—The effect of blood or hæmoglobin in promoting the growth of the meningococcus is well known. Major Gordon found that this effect was not diminished by heating, even to boiling point. It is probable that there is no better medium for the purpose than agar or nasgar smeared with a few drops of fresh human blood, and several of the reporters have used this in preference to all others. Prof. Walker Hall (Bristol), Prof. Dean and Major Drury (Sheffield), and Prof. Hutchens (Newcastle) have all chosen this medium for their work, and the first named asserts that until he used blood nasgar for his primary subcultures he got no reliable results. The Cambridge workers, Capt. Gaskell and Lieut. Vines, appear to have employed an agar medium mixed with rabbits' blood, though they have also used the Millbank media.

Dr. Warren Crowe has devised a blood medium of his own. It consists of 3 parts of defibrinated bullocks' blood and 1 part of Douglas' trypsin agar, 1 per cent. of glucose being added. The ingredients are mixed at 50°C., poured into tubes or plates and then sterilised on 3 successive days at a comparatively low temperature. The medium is dark brown, opaque, and glossy on the surface. There seems no doubt that the meningococcus grows well on it, but it would appear from the results which Dr. Crowe obtained by its use and to which allusion has already been made, that there is no small risk of confounding the meningococcus with allied organisms. Capt. Pethybridge (Plymouth), who also tried this medium, expresses a doubt as to whether all the organisms which passed as meningococci were truly that coccus. To most workers the opacity of the medium would prove a drawback.

*Serum media.*—Several of the reporters have preferred a medium in which some form of serum is added to agar, more or less after the fashion of Löffler's medium. Dr. Arkwright (Salisbury Plain) used serum agar; Dr. Claridge employed a 2·5 per cent. agar made with Lemco, adding 1 c.c. of fresh hydrocele fluid to each 5 c.c.; Drs. Colebrook and Tanner (St. Mary's Hospital) prefer Douglas' trypsin broth agar, to which 2 per cent. of ascitic or hydrocele fluid is added before use; Dr. McIntosh (Woolwich) uses a medium composed of 3 parts of 3 per cent. agar, neutral to phenol-phthalein, and 1 part of etherised serum, the ether being driven off before use; for cerebro-spinal fluid he uses a mixture of equal parts of the fluid which is to be cultivated and liquid agar.

All these media appear to have given satisfaction to those who have worked with them and to have proved better than nasgar: a drawback to most of them is that it is not always easy to pro-

cure a sufficiency of such ingredients as ascitic fluid and hydrocele fluid, especially of the latter, which seems a peculiarly valuable addition to agar media. In this respect Gordon's legumin should prove a good substitute for the animal proteins. It is noteworthy that those who have used Douglas' trypsin heart broth as the basis of their agar medium find it, as Gordon did, better than ordinary broth.

*Media for Prolonging the Life of the Meningococcus.*

None of the media so far considered satisfy one condition for an ideal medium: on the surface of all of them the coccus dies out in a few days, a circumstance which involves the trouble of very frequent subcultures in order to keep up the stock of any given strain. Lieut. Vines attributes this early death to drying and it seems certain that the viability of the organism is much more prolonged in liquid media. Major Gordon employs trypsin broth containing a little serum to keep up his stocks: in this he finds that the meningococcus lives for 3 weeks. Capt. Gaskell and Lieut. Vines find Vedder's starch medium equally good. It consists of beef broth containing 1 per cent. starch and 1·5 per cent. agar. Stab cultures in this medium (but not surface cultures)* were found to live from 2 to 3, or even 4 weeks.

*Media for the Sugar-reactions of the Meningococcus.*

There is a certain amount of dispute as to whether liquid or solid media are the better adapted for displaying sugar fermentations. The formation of acid is seen earlier on solid media, such as a serum agar tinted with litmus and containing 1 per cent. of the sugar, because there is less rapid diffusion. On the other hand, liquid media afford better opportunity for titrating the exact amount of acid formed. Judging by the reports before us the majority of the workers have preferred liquid media: of those who mention the point six express this preference, while only two seem to have chosen solid media. Of the liquid media used, the serum water of Hiss has given satisfaction, while others prefer veal broth with some added serum. Trypsin heart broth cannot, of course, be used unless its sugar is first fermented out. As an indicator most of the reporters have preferred litmus to neutral red.

**Special Circumstances affecting the Growth of the Meningococcus.**

There remain for notice some novel and important observations contained in certain of the reports, relating to adventitious circumstances which may facilitate or hinder the growth of the meningococcus in nasopharyngeal cultures.

(1) *The Influence of Nasal Mucus* on the growth of the meningococcus. Dr. C. Shearer (Devonport) has found the growth of this organism on artificial media very greatly increased in presence of a small trace of nasal secretion, and this even if the secretion has been sterilised at 60°C. or almost at boiling point. His method was to steep 10 used throat swabs all night in 50 c.c. water,

* Dr. Eastwood informs us that on egg medium, in sealed tubes, the viability of the meningococcus is prolonged for two or three months.

and then to squeeze out the swabs and sterilise the fluid by filtration or heat. The fluid can be stored and used as required. If half the surface of a culture plate is smeared with this fluid, partially dried, and then inoculated, much more vigorous growth of the meningococcus occurs on the treated than on the untreated half. This effect is much more marked with nasopharyngeal secretions than with oral saliva or Ringer's solution. Dr. Shearer found that, on legumin agar, growths can be obtained with much higher dilutions of the meningococcus when nasal secretion is used. These observations suggest that the mucus naturally present on a post-nasal swab on its withdrawal may influence the growth of the meningococcus on the culture medium, and it is possible that in catarrhal conditions the increased amount of mucus may still further facilitate its growth, so that, as Dr. Warren Crowe remarks, one might perhaps find a larger number of positive results in contacts suffering from catarrh than in those not so suffering, even though the true number of those harbouring the organism were equal in the two groups.

(2) *The Inhibitory Action of Saliva* on the growth of the meningococcus. This has been the subject of investigation by Dr. Gordon at Millbank. He found that normal saliva inhibits the growth of the meningococcus on a plate culture in proportion to the number of salivary streptococci which sprang up. The inhibition diminishes with dilution of the saliva. A broth suspension of some 1,000 million meningococci per c.c. is inhibited, as regards growth in subculture, by an equal volume of normal saliva. Nasal mucus has no such inhibitory power. By heating saliva to 55°C. for 30 minutes, or by centrifuging out all its bacteria, the inhibitory power is abolished. Broth cultures of saliva inhibit like saliva itself, losing this power on heating or on passage through a Berkefeld filter. Two strains of streptococci from saliva (longus and brevis) and one of a staphylococcus were separately tested : the staphylococcus was found to have no inhibitory power, but the streptococci possessed it, though in less potency than the mixed salivary culture. It is thus evident that saliva owes its inhibitory power upon the meningococcus to its contained streptococci : it is a case of bacterial antagonism similar to that about to be mentioned, between the pneumococcus and the meningococcus, worked out by Dr. Colebrook. Major Gordon's observations explain why, in examining contacts, it is the nasopharynx which must be swabbed, and why it is so necessary to avoid any contamination of the swab with the buccal secretions. We see why the saliva of carriers with abundant meningococci in the pharynx not only fails to yield that organism on culture, but inhibits its

growth just like the saliva of a normal person. It may well be that the saliva of carriers contains the virus to a greater extent than cultures would lead us to believe.

(3) *Bacterial Antagonism* between the Pneumococcus and the Meningococcus. Dr. Colebrook (St. Mary's Hospital) has recently published a paper (*Lancet*, 1915, Vol. II., p. 1136) in which he deals with this subject. He had found that when the meningococcus begins to disappear in a carrier it seems replaced by pneumococci or streptococci. On two occasions this disappearance appeared to be determined by the onset of an acute cold in the head. He therefore pursued the subject and found, in plate cultures in which streaks of the organisms were inoculated crossing each other, that there was a strong antagonism between pneumococci and streptococci on the one hand and the meningococcus on the other, the latter being prevented from growth where it came into contact with the former. This antagonism was found to extend to the other Gram-negative cocci of the upper respiratory tract (M. catarrhalis, M. flavus, &c.), but not to the gonococcus. It is a one-sided antagonism: the meningococcus exerts no injurious influence upon the growth of pneumococci or streptococci. By a number of elaborate experiments, Dr. Colebrook convinced himself that the effect was due to some inimical chemical substance elaborated by the pneumococcus during its active growth. There was no evidence that the pneumococcus deprived the medium of any substance necessary for the growth of the meningococcus. A culture of the pneumococcus in glucose ascitic broth, sterilised by heat or filtration, was found able to kill the meningococcus: 1 c.c. of such broth killed 40,000 meningococci in an hour. The effect is not due to acid formation, for it occurs with sugar-free media in which the pneumococcus forms no acid: the bactericidal agent is filterable and is destroyed by heating to 70° or 80°C.

From these observations it may be concluded that the presence of pneumococci or streptococci in the nasopharynx (and they are sometimes there in very large numbers) may mask the presence of the meningococcus in cultures. It is also possible that small numbers of the meningococcus may fail to establish themselves in a pharynx already tenanted by its antagonists, or may be destroyed on a later invasion by the pneumoccocus. Acting on this latter idea, Dr. Colebrook sprayed the nasopharynx of six chronic carriers of the meningococcus with living cultures of the pneumococcus, but the latter organism failed to establish itself there, and only this partial success was obtained, that in one of the six carriers the meningococcus almost disappeared for two days.

## Part II.

## THE BACTERIOLOGICAL DIAGNOSIS OF CEREBRO-SPINAL FEVER.

It is generally admitted that bacteriological examination is the only sure method of diagnosis in this disease. Many of the present series of reporters give lists of the conditions which have wrongly come under suspicion as cerebro-spinal fever. With these clinical errors, which have ranged from other forms of meningitis to influenza, rheumatism and acute alcoholism, and which in the course of an epidemic of cerebro-spinal fever are natural and unavoidable, we do not propose to concern ourselves here. The essential point to note is that they have practically all been cleared up by bacteriological examination. No case that we have found recorded in these reports, which appear quite candid, has been returned as cerebro-spinal fever by the bacteriologist and then proved to be something else, but in a certain minority of cases the bacteriologist has failed to confirm the diagnosis in genuine cases of the disease, for reasons which we shall presently consider. Almost unanimously the reporters have answered the question: "Is bacteriological examination of the cerebro-spinal fluid trustworthy?" in the affirmative.

There are two methods of examining the fluid withdrawn by lumbar puncture, namely microscopic examination and cultivation. As a rule both yield positive results, confirming each other, but either may succeed where the other fails: it is rare in competent hands for both to fail on repeated examination. Two reporters (Major Embleton and Capt. Gaskell) mention isolated cases in which examination of the cerebro-spinal fluid gave a negative result, but in which the diagnosis was later established by the finding of the meningococcus in the naso-pharynx.

*Microscopic examination* of the cerebro-spinal fluid. The mere finding of Gram-negative cocci in this fluid is held by many of the reporters sufficient for diagnosis (Capt. Gaskell, Lieut. Treadgold, Dr. Arkwright). This is probably a correct view since, with insignificant exceptions to which we shall refer directly, no Gram-negative coccus, other than the meningococcus, has been found in the cerebro-spinal fluid in this epidemic, though, as a pathological curiosity, we believe gonococcal meningitis has been described. Several reporters note the extreme sparseness of the meningococcus in the freshly withdrawn fluid, so that prolonged search may be required. The cocci are most commonly intracellular, but are sometimes almost entirely extracellular: Prof. Walker Hall states that he has found extracellular cocci more frequent in fatal cases. Dr. Arkwright asserts that the cocci may be more abundant after death than during life. Occasionally it has been found impossible to demonstrate the organism microscopically, though cultures have been successful. Many of the reporters note that this trouble may largely be overcome by incubating the withdrawn fluid at 37°C. for 24 hours—a device

which necessarily presupposes aseptic methods. Prof. Dean says that the cocci go on multiplying for 3 days in such incubated fluid. They are commonly abundant after 24 hours, and are now largely extracellular as well as intracellular.

Apart from the meningococcus, polymorphonuclear leucocytes are always found in the cerebro-spinal fluid during the active stages of the disease, as in other forms of septic meningitis. But several reporters note that in prolonged cases not only may the cocci disappear, but even the polymorphs, their place being taken by lymphocytes, so that the fluid may come to resemble that from a case of tuberculous meningitis. At this stage, therefore, the examination of the cerebro-spinal fluid may be misleading.

In the earlier stages the presence of polymorphs in the fluid is of importance in the diagnosis, when meningococci or other bacteria cannot be demonstrated. Capt. Gaskell remarks that their presence in a patient who recovers is almost certain evidence of cerebro-spinal fever, for no other form of purulent meningitis ends in recovery.

*Cultural examination* of the cerebro-spinal fluid. Many of the reporters record their own special methods for this procedure. Several take the precaution of making cultures both before and after incubation of the fluid, the latter being sometimes successful when the first fails. Hope of growth need not be abandoned till the culture has been incubated for 4 days. (Lieut. Vines.) Capt. Gaskell insists on the necessity for liberal inoculation of the culture medium. Dr. Claridge runs the fluid straight from the needle into the culture tubes. Prof. Walker Hall uses the centrifuge and sows the deposit on nasgar smeared with blood and glucose. Dr. Warren Crowe enriches the fluid by the addition of glucose, incubates for a day and sows the centrifugalised deposit on his blood medium. Dr. McIntosh and Lieut. Bullock mix 5 c.c. of the fluid with 5 c.c. of melted agar and pour into plates. All these methods seem to have given satisfactory results, and as a rule the diagnosis is easily made, though difficulties sometimes arise from no fault of the bacteriologist. The organism may be cultivated from the cadaver for the first 2 days after death. Prof. Leith (Birmingham) places the limit at 48 hours; Dr. Arkwright grew it once or twice 36 to 40 hours after death.

No Gram-negative coccus appears to have been grown from the spinal theca which had not the biological characters of the meningococcus, except in three cases mentioned by Capt. Sellars (Manchester) and one by Dr. McIntosh and Lieut. Bullock (Woolwich). Capt. Sellars reports that in 3 of his "negative" cases—*i.e.*, cases which proved not to be cerebro-spinal fever—organisms were obtained from the cerebro-spinal fluid which were like the meningococcus, but either grew at 23°C. or fermented saccharose. This statement appeared to us of such importance that we wrote to make further enquiries. Prof. Delépine, in reply to our queries, informs us that the 3 cases were civil ones

in which the material sent to the laboratory appeared to have been collected in an unsatisfactory manner, and that there was considerable reason for believing that these cocci may have been accidental contaminations: it is at least not sufficiently certain that they came from the cerebro-spinal fluid to make them an exception to the general statement laid down above. The case recorded by Dr. McIntosh and Lieut. Bullock was one of true cerebro-spinal fever: the first lumbar puncture yielded a pure culture of the meningococcus, the second a mixture of this organism with M. flavus, while later punctures again yielded the meningococcus alone.

Although the results of culture have been satisfactory in the majority of cases, in a not inconsiderable minority of cases of cerebro-spinal fever, clinically definite, culture was unsuccessful. Most of the reporters admit such negative results, and they sometimes amounted to 25 per cent. of the total cases examined. In a few cases cultures were negative even when the meningococcus had been found microscopically.

It is important to consider the reasons for such failures, which are usually no reflection upon the technique of the bacteriologist. They may depend upon extreme sparseness and lack of vitality of the cocci, or upon the fact that the cocci are not present in the spinal theca at the time of puncture. Amongst the reasons assigned for failure by different observers are the following:—

(1) In fulminant cases the coccus may not have had time to appear in the meninges, the patient dying within 24 hours from an overwhelming septicæmia. Cases of such septicæmia without obvious meningeal symptoms are not unknown. More than one instance of failure in the present reports seems due to the fulminant character of the case.

(2) It seems certain that, in the very earliest stages of ordinary attacks, the fluid withdrawn from the theca may be clear and sterile. In a case under the observation of one of us lumbar puncture was performed within 3 hours of the onset, and the fluid was in this condition becoming turbid and showing plenty of meningococci 24 hours later. Some of the reporters note that early punctures failed to yield growth while later ones were successful: Capt. Gaskell found this in some instances, and Prof. Walker Hall states that in 3 cases he did not succeed in growing the organism until the third puncture.

(3) Failure has occurred in cases recovering very quickly, in which presumably the meningeal infection was slight and soon overcome.

(4) Lieut. Vines states that failure may occur after anti-meningococcal serum has been introduced into the theca, even though the patient may apparently have derived no benefit from the injection.

(5) In the later stages of chronic cases the organism may have vanished from the theca. Very protracted cases fall into two groups. In one a smouldering infection persists in the meninges; Dr. Arkwright records two cases in which he recovered the meningococcus from the cerebro-spinal fluid on the 35th day and on the 75th day of the disease respectively. In the other the infection is overcome, but the patient lingers on, suffering from the after-effects of the meningeal inflammation—matting of the membranes and obstruction of the channels at the base of the brain, often leading to internal hydrocephalus. In these cases the fluid withdrawn from the spinal theca may be clear and sterile.

These reasons appear to us valid explanations of most of the instances of cultural failure recorded by the different reporters.

*The Presence of the Meningococcus in the Pharynx.*

The routine examination of the pharynx in cerebro-spinal fever does not seem to have been carried out with the same thoroughness as the examination of the cerebro-spinal fluid. Most of the reporters omit any reference to this matter, and some of those who mention it seem to do so rather as a side issue. Yet it is a point of considerable importance, and a fuller knowledge of the subject would be of much value in helping to determine the degree to which a case of the disease is a source of danger to those about him. It is one of the matters to which attention might profitably be directed in future work: there is need for an adequate body of data as to the presence of the organism in the pharynx at all stages of the active disease and during convalescence. Such information as can be gleaned from the reports is to the effect that the meningococcus has been much less commonly found during the attack than might have been expected. Prof. Walker Hall (Bristol) states that, although the meningococcus has been detected in the pharynx some time before the acute attack, by the time meningeal symptoms commence it is commonly absent. He was unable to detect it in 7 of his early cases (2nd to 7th day), but in 6 other cases it was present and persisted for from 19 to 41 days: in 19 further cases in which the onset was not well defined the organism was not found on the swabs after about 30 days. Dr. McIntosh and Lieut. Bullock (Woolwich) note that they failed to find the meningococcus in the pharynx in several of their acute cases (7th to 10th day), while out of 18 convalescents, 4 to 8 weeks from the onset, they found it in 3 only. Dr. Solly (Exeter) failed to find the organism in the pharynx in 4 definite cases and 1 doubtful one of cerebro-spinal fever. Prof. Delépine (Manchester) reports negative results in his small series of cases. Capt. Gaskell (Cambridge) and Major Embleton (Netley) each mention one case in which the organism was found in the pharynx. Dr. Arkwright did not examine the pharynx in acute cases, but of 7 convalescents (31

to 94 days from onset) he found it in one. In contrast to these figures, Dr. W. M. Scott, working in the Local Government Board Laboratories, informs us that he swabbed 19 cases of the acute disease and found the meningococcus in the pharynx in all but 3, persisting variably into convalescence. Some lost it in a week, others not for many weeks.

We may here recall the figures obtained by von Lingelsheim at Beuthen. From December 1904 to June 1905 he examined the pharynx in 635 cases of cerebro-spinal fever, and found the meningococcus present in 146 (22 per cent.), and in a later series of 163 cases he found it in 18 (11 per cent.). When he incubated the plates immediately he found it in 46 out of 49 cases. Bolduan and Goodwin found it in 18 out of 52 cases, and during the first week of the disease in 12 out of 22. Quenstedt found it in all cases in the pharynx, as did Herford during the first days of the disease.

It seems probable that systematic examination of the pharynx in the early stages of the disease would reveal the presence of the meningococcus more frequently than the figures of most of the reporters would suggest. At the same time it is clear that it is often missed during the acute stage, and fuller data concerning this matter are much to be desired. Arkwright assumes that all cases of cerebro-spinal fever are carriers for at least a short time before the attack.

*The Presence of the Meningococcus in the Blood.*

This is another subject upon which much fuller information is required. It seems to have been largely neglected during the recent outbreak for we find allusion to the subject in four of the reports only. Dr. Solly (Exeter) examined the blood in 5 cases, using 10 c.c. of blood for culture : in 4 cases the result was negative, but in one fulminating case he obtained the meningococcus. Major Drury (Sheffield) was once successful in cultivating the organism from the blood of a hæmorrhagic case. Lieut. Vines (Cambridge) states that he never recovered it from the blood. Dr. McIntosh and Lieut. Bullock (Woolwich) examined the blood in 8 cases, specially selected because they were fulminant ones or presented well-marked rashes : they employed 10 c.c. of blood in 50 c.c. broth, and in two of the cases the examination was repeated, yet they never got a positive result. They proved the suitability of the medium by afterwards inoculating it with the meningococcus.

It is well known that there is such a thing as acute meningococcal septicæmia, usually hæmorrhagic in character, and in all severe outbreaks of cerebro-spinal fever scattered cases of this nature may occur, running a rapidly fatal course. Considering the small number of blood cultures reported in the present investigation two positive results are perhaps as much as might have been expected. But there is a good reason for wishing a far more extensive series of observations on this point. It is not definitely decided how the meningococcus reaches the meninges

from the pharynx, which is assumed to be its primary seat in the body. The anatomical proximity between the pharynx and the base of the brain has led some to assume its direct transit by way of the ethmoid or some other route through the basis cranii. Others, and perhaps with more probability, have regarded the blood stream as the route by which the meninges are reached, but definite proof of this is still lacking. If we remember how our notions about the pathology of such diseases as typhoid fever and acute pneumonia have been altered as the result of thorough and systematic blood culture, it is not too much to hope that greater enterprise and pertinacity in the application of this method to cerebro-spinal fever might similarly clear up our doubts here.

*The Presence of the Meningococcus in the Urine.*

The statements made by Dr. Hort and his colleagues as to the presence of the coccus in the urine cannot be allowed, since no proof is furnished that the organisms cultivated were meningococci. A few of the reports with which we are here concerned mention this subject. Lieut. Vines and Dr. Solly both state that they failed in their attempts to cultivate the coccus from the urine. Dr. McIntosh and Lieut. Bullock examined catheter specimens of the urine in nine acute cases of cerebro-spinal fever, and failed to find the meningococcus. This is in accord with the accepted opinion that the organism is not excreted by the kidney. Nevertheless, in cases of extreme rarity, it may set up local complications in the urinary tract and appear in the urine. One such case is recorded by Lieut. MacMahon (York): A soldier suffering from a severe attack of cerebro-spinal fever developed purulent cystitis, with abundant meningococci in the urine. He died of general sepsis. In this connection we may recall the case of meningococcal spermato-cystitis recorded by Pick (*Berliner Klin. Wochenschr.*, 1907, XLIV., 947, 994). A boy of 18, suffering from cerebro-spinal fever, was found after death to have double empyema of the seminal vesicles, the bladder, testes and vasa deferentia being normal. The pus contained meningococci, and the organism was proved not to be the gonococcus by sugar reactions and agglutinations.

*The Presence of the Meningococcus in other Situations in Cerebro-spinal Fever.*

The only reporter who mentions this subject is Dr. Arkwright, and his findings are not very convincing, as he does not appear to have isolated and proved the meningococcus by culture. He refers to a case of purulent arthritis of the ankle-joint, in which organisms resembling the meningococcus were found microscopically, to a case with purulent pericarditis presenting similar microscopic appearances, and he examined pneumonic patches in the lungs, and also the bronchial secretions, without very definite results.

## Part III.

## MENINGOCOCCUS CARRIERS.

A very large part of the work of most of the reporters has lain in the routine examination of the pharynx of contacts with cases of cerebro-spinal fever.

### *Methods of Cultivation.*

Two reporters (Prof. Leith and Dr. Claridge) have preferred to make their cultures direct from the pharyngeal wall with a platinum wire. Dr. Arkwright used a swab on a bent wire, with the aid of a tongue depresser and a forehead lamp. But the great majority have been satisfied to use the form of swab in a curved protecting tube, introduced by Mr. C. E. West and known by his name. There is probably less risk of salivary contamination with this than with any other form of apparatus, and it demands much less experience and skill on the part of the operator than any form of naked wire or swab. Prof. Delépine has also devised an apparatus which has been used in the Manchester district and appears to be efficient.

The importance of immediate culture from the swab is emphasised by several reporters. An interval of an hour or two hours is probably the most that can be allowed to elapse, and even then precautions must be taken to prevent the swabs from becoming dry. Many have taken their plates to the scene of operations so as to inoculate them at once, and several have used travelling incubators for their transport to the laboratory, or such devices as a hot water bottle in a handbag. Lieut. Treadgold's observations on the vitality of the meningococcus on swabs illustrate the importance of care in this matter.

Plate cultures have been used by all the reporters except Dr. Claridge (Norwich), who has preferred sloped tubes : he states that these were so satisfactory that only once in 1,032 cultures did he have to plate out later. Thin sowing of the plate, in order to get the colonies well separated, has proved very necessary. Some have used two or three plates in succession to attain this. Prof. Walker Hall puts a drop of equal parts of blood and 1 per cent. glucose on the plate, touches the drop once with the swab, and then smears the surface. Lieut. Treadgold uses the condensation water on the plate in similar fashion. More than one reporter states that the plate should be moist when sown.

The examination of the plates should be carried out after 24 hours' incubation, especially if nasgar is used, lest the colonies be dead. The first subcultures have often presented difficulties from failure of growth. These have been overcome by subcultivating early and liberally, and using a medium of known value, such as blood nasgar or trypagar.

Some experienced reporters, such as Prof. Dean (Sheffield) and Prof. Hutchens (Newcastle), appear to have relied for diagnosis chiefly on the character of the colonies, but there is a universal impression that confirmatory tests are necessary.

Prof. Walker Hall (Bristol) distinguishes between rapid diagnosis for military purposes and confirmation for permanent record. A Gram-negative coccus with typical primary colonies, no growth at 23° C. and giving acid in glucose but not in saccharose, was returned as provisionally positive. The cultures were always re-examined and, if they bred true, were classed as permanent positives: he confesses that the second examination cut out a good many which had been provisionally returned as meningococci.

As an example of an adequate routine method of confirmation we may quote that of Capt. Gaskell (Cambridge). Having obtained an apparently pure subculture he proceeds as follows :—

(1) Sow in bulk, in glucose and saccharose broths.
Sow a slope culture and incubate at 23°C.
Make a starch agar stab-culture for stock.

(2) On the 2nd or 3rd day subcultivate the sugar broths to make sure they are pure.
If no growth has occurred at 23° C., transfer to 37°C. to make sure the organism is alive.

(3) If the sugar reactions are those of the meningococcus, or M. flavus III., sow a mannose broth tube for differentiation.

The only reporter who has discarded the confirmatory tests which others have found necessary is Dr. Warren Crowe (Devonport). He has relied entirely on his own method of observing agglutination, and, it would appear, not with the happiest results.

In the present series of reports agglutination has been little used as a confirmatory test, or tried and found too unreliable to be of service. Major Gordon now believes that the methods and special sera which have been introduced at the Millbank laboratories will in future form the most speedy and reliable confirmatory tests available. The sera which he hopes to be able to send out from the central laboratory should be of service for diagnosis by agglutination, so far as the principal epidemic types are concerned, but it is evident that the absorption method can only be used by specially skilled observers.

## The Results of Pharyngeal Examination.

In contrast to their experiences with the cerebro-spinal fluid, the great majority of the reporters complain of the unsatisfactory results of the methods for determining the presence of the meningococcus in the nasopharynx. Several of them had undergone a short course of training in the work at Millbank, but many, although well versed in ordinary bacteriological methods, had not previously had any wide experience in this particular form of investigation. The work is tedious and beset with pitfalls, while its results were often found ambiguous. Two of the reporters, indeed, express a doubt whether the swabbing of contacts is of sufficient value to be worth the trouble involved.

With the experience gained in the past epidemic and the improved methods now available, less should be heard in the future about ambiguous results. There can be no doubt that the bacteriological examination of the pharynx is well worth all the trouble involved : there is reason for believing that this is the best method available for determining the mode of spread of cerebro-spinal fever and the possibility of its control.

While we must allow a certain unavoidable margin of error in the gross results reported, we must also remember that most of the reporters are experienced bacteriologists who would quickly have adapted their methods to the novel work, so that the margin of error will probably not be a very large one. We will first tabulate the gross results of the work accomplished, where the figures given enable us to do so, and proceed next to analyse the data in accordance with the more detailed figures furnished by some of the reporters. We are dealing, be it remembered, with persons examined because they had been in contact, more or less close, with cases of cerebro-spinal fever, and at variable intervals after such contact.

**Table of the Gross Results of the Nasopharyngeal Examination of "Contacts." ***

| Reporter. | Station. | Total contacts examined. | No. of positives. | % of positives. |
|---|---|---|---|---|
| Crowe – – | Devonport – | ? | ? | 27–75 |
| Leith – – | Birmingham – | circa 50 | 3 | 6·0 |
| Hall – – | Bristol – – | 1,170 | 61 | 5·2 |
| Delépine – – | Manchester – | 113 | 1 | 0·8 |
| Gaskell – – | Cambridge – | 155 | 7 | 4·5 |
| Claridge – – | Norwich – – | 672 | 122 | 18·1 |
| Pethybridge – | Plymouth – | 24 | 3 | 13·0 |
| Finlayson– – | Brighton – | 1,443 | 60 | 4·2 |
| Solly – – | Exeter – – | 189 | 2 | 1·0 |
| Dean – – | Sheffield – – | ? | 0 | 0·0 |
| Gregor – – | Falmouth – | 293 | 9 | 3·0 |
| Vining – – | Leeds – – | 92 | 11 | 12·0 |
| Drury – – | Sheffield – – | 44 | 1 | 2·2 |
| White – – | Nottingham – | 45 | 9 | 20·0 |
| McMahon– – | York – – | 111 | 10 | 9·0 |
| Hutchens– – | Newcastle – | 626 | 58 | 9·2 |
| Arkwright – | Salisbury Plain | 349 | 4 | 1·1 |
| Do. – | Do. | 877 | 35 | 4·8 |
| Johnston – – | Do. | 1,143 | 136 | 11·9 |
| Embleton – | Netley – – | 1,148 | 86 | 7·5 |
| McIntosh and Bullock – | Woolwich – | 2,060 | 72 | 3·5 |
| | Total – | 10,604 | 690 | 6·5% average (excluding Devonport) |

* We are aware that these figures represent only a part of the work which has been accomplished in the examination of contacts during the past year, but they contain all the material present in the reports furnished to us.

A few of the reporters have not given their figures clearly, so that it has been a little difficult to draft the tabular statement, but we believe it to be nearly correct. It is seen that out of more than 10,000 contacts examined, the average number of meningococcus carriers found was almost exactly 6·5 per cent., if we exclude the abnormally high figures from Devonport. These we feel bound to exclude as doubtful in view of Major Gordon's report on the re-examination of Dr. Warren Crowe's contacts by Capt. Hine. The high percentage of positives recorded by Dr. Crowe appears attributable to the failure of his medium to distinguish sufficiently between the meningococcus and allied cocci, coupled with his abandonment of the usual confirmatory tests. Out of a large number of men segregated at Devonport as carriers, Capt. Hine, using the Millbank methods, could find the meningococcus in a small proportion only, and Major Gordon states that of the cultures of supposed meningococci sent to him by Dr. Crowe, none satisfied all the tests for that organism.

Apart from this, it is seen that the percentage of positive contacts found by different reporters varies from 20 to less than 1 per cent. The crude figures of the table have indeed not much value, save as a rough indication of the proportion of carriers to be found under widely varying conditions. No conclusions can be drawn from them as they stand, but fortunately many of the reporters have furnished further analyses of their figures which enable us to deal with them in more detail.

One probable cause of discrepancy between the figures of the different reporters lies in the fact that experience in the work must have been present in different degree. Another lies in differences of method. There can be no doubt that the culture medium employed affected the percentage of positive results. The only reporter who gives data in support of this is Prof. Walker Hall (Bristol) : his figures work out as follows :—

| Medium. | No. of examinations. | No. of final positives. | % of positives. |
|---|---|---|---|
| Veal nasgar... ... | 280 | 22 | 7·85 |
| War nasgar... ... | 316 | 28 | 8·86 |
| Blood war nasgar ... | 103 | 11 | 10 68 |

But besides these factors affecting the observer, there are others which relate to the contact. One is the time which elapsed between contact and swabbing. Many reporters note that the meningococcus frequently vanishes from the throat in a week or less : yet many of the cases have been swabbed 10 days or more after the last contact with a case of the disease. On the hypothesis that the carrier has derived his meningococci from the case of cerebro-spinal fever—a hypothesis which we shall discuss later on—this circumstance might seriously vitiate the results obtained. Thus it is possible that the low percentage of carriers found by Dr. Arkwright may in part depend upon the fact that some of his contacts were not examined till 3, 4 or even 12 days

after the last contact. The following figures, however, given by Dr. McIntosh and Lieut. Bullock (Woolwich), are of importance in this connection. They relate to 1,188 contacts of 41 cases of cerebro-spinal fever: the interval between the exposure to infection and the nasopharyngeal examination of the contact varied between 1 and 55 days. Sixty-five carriers were found and their distribution in relation to the interval after exposure was as follows, the days being reckoned from the date of onset of the case of cerebro-spinal fever with which the contacts had been in relation.

| Days. | No. of contacts. | No. of carriers. | Days. | No. of contacts. | No. of carriers. |
|---|---|---|---|---|---|
| 1 | 39 | 2 | 12 | 36 | 1 |
| 2 | 172 | 9 | 13 | 40 | 3 |
| 4 | 90 | 6 | 15 | 17 | 0 |
| 6 | 40 | 2 | 17 | 13 | 0 |
| 7 | 57 | 4 | 18 | 9 | 0 |
| 8 | 50 | 6 | 19 | 95 | 2 |
| 10 | 112 | 7 | 20 | 93 | 0 |
| 11 | 199 | 21 | 21 | 43 | 0 |
| | | | 55 | 83 | 2 |

If the figures are grouped in weeks we get the following results:—

| Week. | No. of contacts. | No. of carriers. | % of carriers. |
|---|---|---|---|
| 1st. | 398 | 23 | 5·9 |
| 2nd | 437 | 38 | 8·9 |
| 3rd | 270 | 2 | 0·7 |
| 8th (in part) | 83 | 2 | 2·4 |

Thus in the experience of these observers the proportion of positive contacts did not vary materially for the first two weeks after exposure, and then dropped very suddenly.

Again, the conditions of contact should greatly influence the results. Prof. Walker Hall urges that calculations of percentages should be made in relation to the circumstances under which the individual became a contact and not from general mass figures. Not a few of the reporters have recognised this principle, and record data from which useful conclusions may be drawn.

(*a*) *Conditions of Housing—i.e.*, whether the persons concerned were quartered in billets, huts, tents or hospitals. Hygienic conditions and intimacy of contact must vary considerably with this circumstance. Several reporters give relevant data.

Prof. Walker Hall (Bristol) gives the following figures:—

| Conditions of contact. | Floor space. | No. of Contacts. | No. of positives. | % of positives. |
|---|---|---|---|---|
| Billets | over 30 sq. ft. | 68 | 19 | 27·9 |
| Huts and barracks | 50 sq. ft | 315 | 27 | 8 5 |
| Hospitals | ? | 259 | 8 | 3·1 |

Major Vining (Leeds) states that :—

| | | |
|---|---|---|
| In a boarding-house | 16% | of the contacts were positive |
| In a roomy hut | 13·3 | ,, ,, |
| In a hospital | 6·4 | ,, ,, |

Prof. Hutchens (Newcastle) gives data from which the following figures may be obtained :—

| Conditions of contact. | No. of contacts. | No. of positives. | % of positives. |
|---|---|---|---|
| Billets ... | 131 | 22 | 17·8 |
| Huts ... | 191 | 26 | 13·6 |
| Under canvas ... | 149 | 4 | 2 7 |

(It must be noted that the cases under canvas were in May and June—a time when the general percentage of positive contacts was low.)

Lieut. Johnston (Salisbury Plain area) gives the following figures in relation to overcrowding :—

| Conditions of contact. | No. of contacts. | No. of positives. | % of positives. |
|---|---|---|---|
| Marked overcrowding | 406 | 81 | 19 9 |
| Moderate do. | 194 | 22 | 11·3 |
| No overcrowding ... | 542 | 33 | 6·0 |

The same observer adds the further figures :—

| Conditions of contact. | No. of contacts. | No. of positives. | % of positives. |
|---|---|---|---|
| Married quarters (same room) ... | 43 | 3 | 20·9 |
| Huts... ... ... | 453 | 89 | 19·6 |
| Barrack room ... | 16 | 2 | 12·5 |
| Store room ... ... | 13 | 1 | 7·6 |
| Married quarters (same house) ... | 44 | 2 | 4·7 |
| Guard room ... | 8 | 0 | 0·0 |
| Aylwin huts ... | 23 | 0 | 0·0 |

Lieut. Johnston is of opinion that, given overcrowding, the tendency is for the largest percentage of positive contacts to be found in large rooms, especially if used also for meals. He further gives examples of extremely high percentages of positive contacts in huts in which cases of cerebro-spinal fever had occurred (viz., 64, 38 and 30 per cent. respectively).

Lieut. MacMahon (York) gives data relating to the contacts of 3 cases, of which 1 only came from overcrowded and unhygienic surroundings. The contacts of this man gave 15·5 per cent. of positives: those of the other 2 were respectively 9% and 3·6per cent.

Capt. Allan (Chester) states that he found the number of positive contacts large in billets and small huts, once almost 20 per cent.

Major Embleton (Netley) states that where there was definite overcrowding the percentage of positive contacts was high.

(*b*) *Closeness of Contact* due to accidental circumstances, such as sleeping in adjacent beds, habits, &c. This factor is closely allied to the preceding, and several reporters give data bearing on its influence.

Dr. Finlayson (Brighton) records that 2 cases of cerebro-spinal fever occurred in a hut containing 360 men. He first swabbed 21 men who slept adjacent to the cases and found 6 carriers (28·5 per cent.). During the following week he swabbed the remaining 339 and found only 8 carriers (2·4 per cent.).

Lieut. Treadgold (Salisbury Plain) states that, out of a batch of 39 contacts, 32 slept in the same room with the case, and amongst these he found 21 carriers (66 per cent.). The remaining 7 were only occasional contacts, and of these only 2 were found positive, and these two were men who ate at the same table as the patient. Again, in another batch of 12 contacts, 3 slept in the same room as the patient, and 2 of them were found to be carriers : of the other 9 only one was a carrier.

Dr. Claridge (Norwich) suggests the influence of the sociability of the patient. The largest proportion of positive contacts he met with was in a group of 7 men billeted in a boarding house : they slept in separate rooms but were sociable at table. One developed cerebro-spinal fever, and, of the other 6, 5 proved to be carriers (83·3 per cent.). Again, he had 2 cases of the disease in barracks at Norwich : the first was a sociable man and yielded 20 per cent. of positive contacts ; the second was unsociable and gave only 5 per cent. Dr. Claridge thinks overcrowding, especially at meals, an important factor in the spread of the meningococcus. In hospitals he never found other patients carriers, but orderlies may be, especially those on night duty.

Major Embleton suggests that a case of cerebro-spinal fever with cough is more likely than another to give rise to positive contacts. Dr. Syer B. White also suggests, but on an admittedly small basis of evidence, that cases with catarrh may yield a larger proportion of positive contacts.

(*c*) *Absence of Segregation of Carriers.*—Dr. Warren Crowe (Devonport) points out the liability of positive contacts to infect the negatives if they are all herded together. In such circumstances he found the proportion of carriers to rise ; when the proved positives were kept apart this process ceased.

The reality of this danger is shown by the experience of Drs. Colebrook and Tanner (St. Mary's Hospital), where those who were carrying out investigations on a small group of carriers became themselves infected. The contact was here very close and no precautions were at first observed.

(*d*) *Period of the Epidemic.*—Two of the reporters note the influence of this factor on the proportion of positive contacts found. The proportion was much greater earlier in the epidemic

and became small towards its close. The figures must, however, be interpreted in conjunction with the time of year and the weather conditions.

The following figures are compiled from the data of Prof. Hutchens (Newcastle) :—

| Month. | No. of cases of C.S.F. | No. of contacts. | No. of positives. | % of positives. |
|---|---|---|---|---|
| March | 6 | 213 | 42 | 19·7 |
| May | 5 | 105 | 4 | 3·8 |
| June | 3 | 102 | 4 | 3·9 |

The experience of Lieut. Johnston in the Salisbury Plain area was much the same and is shown in the following table :—

| Month. | No. of cases of C.S.F. | No. of contacts. | No. of positives. | % of positives. |
|---|---|---|---|---|
| February | 16 | 246 | 33 | 13·4 |
| March | 12 | 318 | 77 | 24·2 |
| April | 9 | 304 | 22 | 10·7 |
| May | 9 | 207 | 4 | 1·9 |
| June | 6 | 168 | 0 | 0·0 |
| July | 0 | 0 | 0 | 0·0 |

Major Gordon confirms the decline in the percentage of positive contacts for the London area as the epidemic diminished.

The decline in the proportion of positive contacts as the epidemic waned in the summer months is capable of more than one interpretation.

(1) It might be argued that as the epidemic waned the individual cases diminished in virulence and infectivity. There are no facts to support such a thesis.

(2) It is probable that the more open-air life and freer ventilation of the summer months offered diminished opportunities for transference of the microbe, even though the cases retained their full infectivity.

(3) A still more probable explanation would lie in the supposition that a large proportion of the positive contacts found were not infected from the case of cerebro-spinal fever, but represented the proportion of carriers already present amongst the population where the case had arisen. This proportion would vary with the season of the year.

The detailed analysis of the figures given in the last few pages permits of certain conclusions, but we propose to defer the discussion of their significance till the close of this report, because they must be taken in conjunction with other data.

**The Results of Nasopharyngeal Examination in Non-Contacts**—(*i.e.*, in healthy persons not known to have been in contact with any case of cerebro-spinal fever). No statistics as to the number of carriers to be found amongst the contacts with cases of this disease can be properly interpreted unless we

know also the proportion of carriers among the population at large without reference to the local occurrence of cases of cerebro-spinal fever. Indeed, it may be asserted that, for a right understanding of the epidemiology of the disease, the most urgent need at the present time is a widespread "carrier census" as regards the meningococcus. We need to have such an investigation carried out amongst all sections of the population, in town and country, and for all months of the year, and for a non-epidemic as well as for an epidemic year. A comprehensive investigation of this kind would, we believe, go far to clear up the mystery of the incidence of cerebro-spinal fever.

Four of the present series of reports give figures dealing with this matter. Towards the close of the epidemic period, Prof. Hutchens began an investigation of the throats of men living in huts in the Newcastle barracks, where there had been 4 cases of cerebro-spinal fever earlier in the year. He examined 172 non-contacts and found 9 carriers (5·2 per cent.).

Dr. McIntosh and Lieut. Bullock examined 100 normal persons at Woolwich at a time when the epidemic was declining, and found 2 carriers amongst them.

Dr. Arkwright examined 48 selected non-contacts at Bulford Camp early in the year and found no carriers.

Prof. Delépine (Manchester) records the examination of 56 non-contacts: doubtful organisms were found in 4, but no certain meningococci.*

We are able to add certain figures for London. By permission of the Medical Officer to the Local Government Board, Dr. Eastwood has acquainted us with the results of his examination of the pharynx in 480 non-contacts at St. Bartholomew's Hospital. The subjects were out-patients in the Department for Diseases of the Ear and in-patients in the general wards of the Hospital: they were thus not normal healthy persons, and many of the aural patients in particular were not likely to have presented a normal pharynx, but none had been in known contact with any case of cerebro-spinal fever. 10·2 per cent. of those examined were found to harbour meningococci, or organisms to all tests culturally indistinguishable. Dr. Fred Griffith controlled these results by serological examination. This investigation was begun in spring when the epidemic was at its height and was continued throughout the summer (March 29th to July 22nd). The percentage of positives was highest in March and early April (20 per cent.), falling to 6, 7 and 9 per cent. later. Working in the same laboratory, Dr. Scott similarly examined 138 non-contacts from amongst the out-patients at Lambeth Infirmary—about half of them elderly persons—and found that 13·7 per cent. harboured the meningococcus, as proved by agglutination tests. Dr. Scott also examined the throats of 56 children in a rural school, but here he found only one doubtful carrier.

* Capt. Schölberg examined 1,000 non-contacts amongst the troops in S. Wales, at a time when there was little cerebro-spinal fever in the district, and failed to find a single carrier.

*The Number of Meningococci found in Carriers.*

Nearly all the reporters return their results as either positive or negative, without further comment. Prof. Hutchens (Newcastle), however, remarks on the small number of meningococci usually found on the positive plates, often only one or two colonies. Out of 58 carriers only 3 yielded practically pure cultures of the organism. The point is an important one, since the profuse carrier must be a greater danger to the community than one who only harbours the organism in small numbers. Drs. Colebrook and Tanner note that in the peculiarly intractable group of carriers with which they dealt at St. Mary's Hospital, 11 out of 12 yielded a profuse growth of the meningococcus. It would be interesting to know whether the number of meningococci in the pharynx has any influence upon the duration of the carrier condition, but we can gather nothing from the reports on this subject.

## The Duration of the Carrier Condition.

Some of the reporters make no statement as to how many negative examinations were required before a carrier was deemed free. Many have required at least two negative results before release, and there would seem to be need for this. Dr. Arkwright isolated 31 carriers at Bulford and re-examined them 3 times: only four were positive on re-examination, but they gave the following results :—

| | Original examination. | | | | | Re-examinations. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Jan. 19 | 21 | 27 | 28 | Feb. 6 | 11 | 12 | 13 | 14 | 17 | 18 |
| Case 1 | + | | | | + | | | | | + | − |
| ,, 2 | | + | | | − | | | − | | + | |
| ,, 3 | | | + | | | − | | | + | − | |
| ,, 4 | | | | + | | | − | | | + | − |

When meningococci become scanty in the pharynx a single examination may not suffice to detect them.

While it is right to segregate carriers from normal people, where possible, it is wrong to herd them together at close quarters, for their period of carrying is probably thus prolonged by reinfection from one another. Hence the value of open-air treatment for them. We have already alluded to Dr Warren Crowe's observations on this subject, and Drs. Colebrook and Tanner record that of 10 carriers treated by inoculation at St. Mary's Hospital, 5 gave negative swabs in a comparatively short time, but, living with other carriers, some of these became re-infected.

The actual experience obtained during the recent epidemic enables us to conclude that under favourable circumstances the period of carrying is usually a short one. In support of this we quote the following statements from the reports before us :—

Dr. Arkwright : most are free in 2 or 3 days. Prof. Hutchens : the great majority are free in a few days. Dr. White : all free in a week. Capt. Pethybridge : free in a few days. Capt. Gaskell : condition usually transient. Prof. Walker Hall : mostly

negative in 7 days. Dr. Claridge : mostly free in 10 days. Lieut. MacMahon : 9 cleared up in less than a week, 1 in a week, 3 in two weeks and 1 in three weeks.

Other reporters mention somewhat longer periods. Capt. Allan : generally free in a fortnight, but one took 3 months. Major Embleton : all cleared up in 5 weeks, most in 3 weeks, and many in 2 weeks or 1 week. Dr. McIntosh and Lieut. Bullock : average 2 to 3 weeks, many in one week, a few 6 weeks. Dr. Finlayson : all 60 carriers were negative by the 23rd day. Capt. Gregor : longest period 5 weeks. Major Vining : of 5 carriers 2 were detained 6 weeks and 3, 8 weeks. Prof. Hutchens records 7 cases in which the carrier period lasted from 19 to 55 days. Drs. Colebrook and Tanner, who dealt with an unusually obstinate group of carriers, say that the average duration was much longer than the 3 weeks of some observers. As the result of the observations on Salisbury Plain, Lieut. Johnston gives the following table of the observed periods of carrying, all the cases having the same mild antiseptic treatment :—

| Length of time positive. | No. of carriers. | Length of time positive. | No. of carriers. |
|---|---|---|---|
| 1– 5 days ... | 6 | 36–40 days ... | 7 |
| 6–10 „ ... | 24 | 41–45 „ ... | 0 |
| 11–15 „ ... | 24 | 46–50 „ ... | 11 |
| 16–20 „ ... | 20 | 51–55 „ ... | 4 |
| 21–25 „ ... | 15 | 56–60 „ ... | 1 |
| 26–30 „ ... | 13 | 61–65 „ ... | 1 |
| 31–35 „ ... | 8 | 66–70 „ ... | 2 |

It thus appears that while in most cases the pharynx speedily clears itself, there are not a few in whom the condition is more persistent, and some have suggested reasons for this. Prof. Walker Hall thinks pharyngitis a possible reason, though he notes persistence in carriers without pharyngitis. Capt. Gaskell believes that there is generally a local reason when the condition becomes chronic : he quotes 2 cases—enlarged tonsils and adenoids in one who carried for 1 month and chronic ear trouble in another who carried for 2 months. Dr. Claridge says that his persistent carriers were all of the " lymphatic " type, and thinks the meningococcus liable to persist longer in a pharynx with excess of lymphoid tissue.

## The Relation of Nasopharyngeal Catarrh to the Carrier Condition and to Cerebro-spinal Fever.

This was a matter to which the attention of the observers was especially called in the circular sent round by the Medical Research Committee, and nearly every report contains observations and opinions on the subject. Although we are dealing only with the carrier question in this section of our report, it will be convenient to summarise at the same time the relation of catarrh to cerebro-spinal fever, as a closely-related matter.

Only a few of the reporters conclude that there is any other than a chance relationship between the presence of the meningococcus in the pharynx and nasopharyngeal catarrh :—

Dr. Warren Crowe (Devonport) thinks that catarrh probably predisposes to the carrier condition because the excess of mucus favours the growth of the meningococcus.

Capt. Allan (Chester) thinks that catarrh predisposes to carrying because the two things almost invariably concur.

Major Salmon (Exeter) states that catarrh and sore-throat were present in the premonitory stages of all his 12 cases of cerebro-spinal fever.

Others are less confident in their statements :—

Major Embleton (Netley) merely relates that 3 out of 8 cases of cerebro-spinal fever had catarrh, as had many of his positive contacts.

Prof. Walker Hall (Bristol) was not content with the patients' statements, or with clinical appearances, but sought for pathological evidence by staining films from his swabs : where he found polymorphonuclear leucocytes and evidence of phagocytosis he assumed the presence of catarrh. He found this evidence of nasopharyngitis in 10 per cent. of his 1170 contacts, and of 61 carriers, 25 had catarrh and 36 had not. He considers that the evidence that catarrh is a predisposing condition is inconclusive, though in some cases the persistence of the carrier condition may be associated with catarrh.

Dr. Claridge (Norwich) states that about half his cases of cerebro-spinal fever gave a history of catarrh for some days before meningeal symptoms set in, but he does not decide whether this was an early symptom, a predisposing condition or a coincidence.

Capt. Gregor (Falmouth) mentions the coexistence of influenza, tonsillitis and bronchial catarrh with the cerebro-spinal fever epidemic. He thinks some of the cases diagnosed as influenza or sore throat may have been mild cases of cerebro-spinal fever, and that the prevalent catarrhs may have predisposed to cerebro-spinal fever. Lieut. Llewellyn (Salisbury Plain) says very much the same.

A larger number of the reporters could find no evidence of any connection between meningococcal infection and catarrh :—

Dr. Syer B. White (Nottingham) says that catarrh was not common amongst his contacts. He suggests, though on small evidence, that cases of cerebro-spinal fever with catarrh are more apt to have a sudden onset and to end fatally, than cases without catarrh.

Capt. Gaskell (Cambridge), thinks that catarrh does not predispose to cerebro-spinal fever. He saw no catarrhal stage, except one case with sore throat. No nasopharyngeal

catarrh was seen in carriers—the throats harbouring meningococci were all normal. Plenty of catarrhal throats were seen, but none showed the meningococcus. On the other hand he believes the presence of enlarged tonsils and adenoids is liable to render the carrier condition chronic.

Capt. Pethybridge (Plymouth) found no evidence that catarrh predisposed to, or was associated with, the carrier condition.

Dr. Finlayson (Brighton) found no evidence that catarrh played any part in cerebro-spinal fever. One carrier complained of a "stuffy" nasopharynx, but the rest were normal. Cases with enlarged tonsils were specially examined, but no carriers were found amongst them.

Major Vining (Leeds) found catarrh no commoner in carriers than in normal men.

Prof. Hutchens (Newcastle) concludes that there is no connection between catarrh and cerebro-spinal fever, except that the epidemic coincided with a period of the year when catarrh is prevalent.

Lieut. Bullock (Woolwich) says much the same. As practically everyone had catarrh at some time during the epidemic period, not much importance can be attached to its concurrence with cerebro-spinal fever.

Lieut. Johnston (Salisbury Plain) states that only one out of his 68 cases of cerebro-spinal fever gave a history of nasopharyngeal catarrh. He admits that the wet weather caused much catarrh and influenza, and these may have played a part in the dissemination of the meningococcus (by mouth-spray). Every contact on Salisbury Plain was asked about catarrh and examined for it. Of 1143 contacts, 62 had catarrh (5 per cent.). 10·3 per cent. of the positive contacts, and 4·7 per cent. of the negative contacts had catarrh. He concludes that as 90 per cent. had none, catarrh cannot have had much influence.

Lieut. Treadgold (Salisbury Plain) noted catarrh in a "fair proportion" of carriers. Only 45 contacts complained of sore throat and of these only 13, or less than 28 per cent. were found to be carriers. Judging by the presence of mucus on the swab he thinks that 27 per cent. of the contacts had catarrh, but only one third of these proved to be carriers. He concludes that there is no necessary connection between the presence of the meningococcus in the throat and pharyngitis: the organism behaves as a pure saprophyte in the carrier condition: sore throat and catarrh have little influence in encouraging the growth of the meningococcus, nor does he think they have influence in assisting the invasion of the blood stream.

The experience of Drs. Colebrook and Tanner at St. Mary's Hospital is instructive. Three medical men engaged in the treatment of carriers became themselves

infected. A watch was being kept on their throats and the date of the establishment of the carrier condition in them could be fixed to within a day or two: it was associated with no local catarrh or change in general health. The same observers have published the fact that in two chronic carriers the disappearance of the meningococcus from the throat seemed determined by the onset of an acute cold in the head.

We have deemed it right to quote all the individual opinions of the reporters on this subject, because they were a competent body of men specially asked to make observations on catarrh in its relation to carriers and cerebro-spinal fever, and with unrivalled opportunities for forming an opinion. It will have been seen that on the whole that opinion is adverse to any direct relation. While it cannot be denied, in face of some of the observations, that individual cases of cerebro-spinal fever may be ushered in by sore throat, the more usual relation between the disease and catarrh seems a fortuitous one dependent on the fact that catarrhs and cerebro-spinal fever have a similar seasonal prevalence: there is the same sort of relation as there is between catarrh and the price of coal. There seems, however, some reason for the belief that chronic catarrhal conditions of the nasopharynx may be associated with the persistence of the carrier condition. It may be added that more than one of the reporters suggests excessive smoking as a cause of much of the pharyngeal catarrh seen amongst the military population.

## The Treatment of the Carrier Condition.

Most of the reporters seem to have started with the impression that the meningococcus could be dislodged from the pharynx by local measures. Experience has undeceived the majority, and many now assert that local treatment is useless. In only one report, that of Capt. Gregor and Lieut. Lindsay (Falmouth) do we find it contended that local treatment is of great value: they employed argyrol and hydrogen peroxide (5 per cent. argyrol and 2 per cent. hydrogen peroxide) twice daily as a spray. Numerous antiseptics have been tried, those most widely used being potassium permanganate, silver preparations such as protargol, argentide and argyrol, and iodine, menthol and parolein spray. Capt. Gaskell found sprays and gargles useless, and got the best results with a nasal douche of permanganate three times a day: he thinks that this temporarily removes the meningococcus from the pharyngeal wall. Permanganate seems indeed to have been more widely used and to have given less dissatisfaction than any other local application.

Dr. Warren Crowe found that strong antiseptics did more harm than good, and advises only the mildest local measures. Dr. Claridge found all forms of treatment highly unsatisfactory,

while some did harm. One or two reporters assert that carriers with no treatment at all got well as quickly as those who were actively treated.

Four reports relate a trial of vaccine treatment, in no case with any beneficial result.

There is, however, one measure concerning which several reporters speak favourably, viz., the influence of an open-air life, or the provision of as much fresh air as possible. The influence of this is probably twofold: the general health and any local pharyngeal troubles are benefited, while the risk of reinfection from fellow carriers is materially lessened.

The general impression left on our minds by a perusal of the experience of the reporters is that local treatment by antiseptics is not of great value, though mild applications—*e.g.*, weak permanganate—help to cleanse the pharyngeal wall. But the tendency is for the normal pharynx to purge itself of the intruder unassisted, when the carrier is placed under healthy conditions and continuous reinfection is checked. The abnormal pharynx requires treatment, but this should be directed to whatever pathological condition is present rather than to a conscious attack upon the meningococcus.

This conclusion is perhaps emphasised by an important study of the treatment of carriers, contained in the report of Drs. Colebrook and Tanner. A group of 10 persistent carriers was interned in the research wards of the Medical Research Committee at St. Mary's Hospital for special study and the report shows that the investigation was a very elaborate and thorough one. Three lines of treatment were tried, (1) active immunisation by vaccine, (2) local application of antibacterial agents, (3) application of antagonistic bacteria.

*Immunisation.* The doses of vaccine employed ranged from 50 to 2,000 million subcutaneously and smaller doses up to 200 or 300 million intravenously. Subcutaneous doses below 1,000 million caused practically no general symptoms and only moderate local reactions: intravenous doses of over 100 million caused constitutional disturbance passing off in 12 hours. As the result of the treatment 5 of the 10 carriers gave negative swabs in a short time, but some later became reinfected. Upon the other 5 no effect was produced. The reporters point out that the carrier does not normally cure himself by becoming immune: he develops no immunity reactions, nor is it to be expected that he should, for the coccus is a pure saprophyte in his pharynx. Moreover, convalescent cases of cerebro-spinal fever may become persistent carriers despite the fact that they develop marked immunity reactions.

*Antiseptics.* A number of antiseptics were tested *in vitro* upon the meningococcus, in artificial films of nasal mucus. The most effective were 2 per cent. carbolic acid, and 5 per cent. watery suspension of argentide. Carriers

were therefore sprayed many times daily with 3 per cent. argentide, which was non-irritant and often rendered the pharynx temporarily free from the coccus: but in a few days the cocci reappeared and only in one case was this treatment permanently successful. The treatment seemed liable to extend the area of infection, meningococci appearing in the anterior nasal secretion. The reporters conclude that the meningococci cannot satisfactorily be reached by antiseptics: they are probably ensconced in more or less inaccessible regions. Other methods tried were ionisation by means of a pad of wool soaked in zinc sulphate, filling the nasopharynx, local applications of anti-meningococcal serum and the inhalation of water vapour at 55°C. All these were inefficacious.

*Antagonistic bacteria.* The experiments in which an attempt was made to oust the meningococci by applying cultures of the pneumococcus to the pharynx have been mentioned in the first part of this report. They were unsuccessful.

It must be conceded that if these carriers remained uncured it was not for lack of treatment. The failure of this Department of the Medical Research Committee to discover any reliable method of cure, after such varied and strenuous efforts, must convince us that it is not along the line of vigorous local treatment that we must look for success, and herein lies the very great value of Dr. Colebrook's and Dr. Tanner's work.

## Part IV.

## EPIDEMIOLOGY FROM THE BACTERIOLOGICAL POINT OF VIEW.

The full story of the epidemiology of the past epidemic will be dealt with, we presume, by someone who will have at his command the complete statistical data which are available. Here we propose to discuss the subject only from the bacteriological standpoint. We have to consider the data which are contained in the reports before us as to the mode of spread of cerebro-spinal fever and the conditions influencing that spread.

It must be assumed, as a working hypothesis, that the primary seat of infection is the nasopharynx, for no other is known. We remain completely in the dark as to the factor which determines the secondary invasion of the body, from this primary focus, which constitutes cerebro-spinal fever. Prof. Hutchens remarks that "the incidence of cerebro-spinal fever is consistent with a carrier distribution, but there is nothing to show what determines this incidence beyond individual susceptibility." Such a statement, while it doubtless expresses the present state of our knowledge, must rather be taken as a confession of our ignorance.

## The Mode of Transference of the Meningococcus.

The question is one of the transfer, from pharynx to pharynx, of an organism having little vitality and no power of growth outside the animal body, and is the same in principle as that involved in the spread of such diseases as influenza and common catarrhs. The transfer can evidently be accomplished by such contact as is involved in kissing or the use in common of feeding utensils. Short of this, the chief mode of transfer must be by droplet infection of the air by "mouth-spray"—a process now well known and effective at short range only. The only experimental study of this process in the case of the meningococcus is contained in the report by Dr. Colebrook and Dr. Tanner, working on behalf of the Medical Research Committee.

It was found that two observers who almost daily swabbed carriers without wearing masks, themselves gave positive swabs after 10 and 14 days respectively. It is worth noting that, under conditions of extreme liability to infection, so long a period should have elapsed before they became infected. The meningococcus was very seldom present in the anterior nasal secretion of the carriers, and only exceptionally in the saliva and then only in small numbers. The latter fact has already been considered in the first part of this report in discussing bacterial antagonism.

No meningococci grew on plates held directly under the nostrils of a carrier breathing heavily for several minutes. Explosive expiration, however, gave positive results: sneezing on to a plate gave many colonies, and 2 out of 5 carriers who coughed on to plates, held vertically about a foot away, gave one or more colonies. On 5 occasions plates were exposed in sitting and sleeping rooms used by a group of 7 carriers, on tables where they were writing, or at the head of a bed: only once were one or two colonies of meningococci found.

From these observations it was concluded that the organism is not easily dislodged from the nasopharynx, and that carriers would be little liable to convey infection if they always took the precaution of coughing and sneezing into a handkerchief, or into a piece of rag which could be burned. Observers who are engaged in swabbing contacts are advised to wear a simple mask over the mouth and nose.

In two other reports it is assumed that carriers are not infectious in the open-air—an assumption which all we know as to the distribution of bacteria by mouth-spray would render probable. Prof. Walker Hall (Bristol) argues that positive contacts may be kept at work with their fellows in the open-air so long as they are isolated for eating and sleeping. Lieut. Johnston (Salisbury Plain area) states that at Tidworth Camp only one case of cerebro-spinal fever occurred after the cases and contacts were isolated in buildings within barracks, although these buildings overlooked the busiest thoroughfare in the barracks, and passers by could converse with the men isolated. He therefore concludes that the disease is practically non-infectious in the open-air.

## Evidence as to the Infectivity of Cerebro-spinal Fever.

The absence of any serious danger of infection from sporadic cases of the disease, long familiar in children's hospitals as "posterior basic meningitis," may be regarded as well established. The experience of its epidemic form during the past year appears to show that the risk of direct infection from case to case is seldom great. In a sense this absence of infectivity is apparent rather than real, because only a very small proportion of those infected with the meningococcus develop cerebro-spinal fever.

While the direct spread of the fever, as such, is rare it is by no means unknown. The proportion of cases in which it occurs will be revealed when the full data of the epidemic are analysed, but a few instances are found scattered through the present series of reports. Even in some of these there may be a little doubt, since the presence of surrounding carriers is difficult to exclude. Major Salmon (Exeter) reports the case of a nurse who developed cerebro-spinal fever while nursing a soldier suffering from it: the interval was short—4 days only. Major Drury (Sheffield) states that the source of infection of one of his cases was traced to a man in the next bed at Woolwich. Major Vining (Leeds) relates that one of a group of 7 men billeted at a cobbler's house developed the disease, and that the cobbler's daughter got it a week later: here, however, both may have caught it from a common source. Lieut. Johnston found that in 2 cases on Salisbury Plain connection with a preceding case could be traced.

These few instances only throw into stronger relief the great mass of cases in which no relation could be traced with any pre-existing case. This was so in 66 out of 68 cases on Salisbury Plain, where also Lieut. Johnston affirms that not a single person in attendance on the cases suffered and not a single nurse or hospital orderly became even a positive contact, though they were often swabbed to ascertain if this were the case. Major Salmon states that, apart from the nurse mentioned above, no two of the Exeter cases could be connected. Of the 44 cases at Woolwich, Lieut. Bullock found no two apparently connected. In his report on the outbreak in the Navy in 1915, Surgeon-General H. D. Rolleston states that, out of 170 cases, some evidence of infection was traced in 59. He does not, however, say how much of this was direct and how much indirect infection.

It may be concluded from these facts that the direct source of infection in cerebro-spinal meningitis is usually to be sought, not in another case of the declared disease, but in the undeclared carrier. The conclusion is based on general considerations only, and in the nature of things it is not easy to find specific instances to support it. For when the case of meningitis is declared it is an open question whether the carrier found in connection with it has produced the case or has been produced by it. The most suggestive instances that we find in the present reports are two cases mentioned by Prof. Leith (Birmingham) in which two

soldiers, at home on furlough, were found to be carriers: attention was directed to them by the son of one and the daughter of the other developing cerebro-spinal fever.

## The Spread of Cerebro-spinal Fever by Military Movements.

Further evidence as to the conveyance of the disease by carriers is provided by its appearance in new localities in relation with the movements of troops or the migrations of individual soldiers on furlough. For reasons which we shall consider later, cerebro-spinal fever is specially apt to prevail amongst soldiers, and the movements of large bodies of troops which have been so perpetual of late in this country appear to have played an important part in the spread of the disease. It is, of course, the carriers and not cases of meningitis who migrate.

The reports from the Salisbury Plain area suggest, not indeed that the Canadians imported a new disease into this country, for we have always had it with us in sporadic form, but that they did introduce a virulent strain of meningococcus and were in some degree responsible for its spread. Cases had occurred amongst the Canadian troops even before they left Canada, and on the voyage over, so that there must have been carriers amongst them. Dr. Arkwright states that there had been 10 cases of cerebro-spinal fever amongst them before they arrived on Salisbury Plain: he isolated the meningococcus from 17 cases amongst the Canadians while he was there. Lieut. Johnston says that the first three cases of the disease on the plain were in Canadians, in October and November 1914, but that only in 18 per cent. of his other 65 cases could even probable association with Canadians be traced. Sixteen out of the twenty cases at Bulford Camp, however, occurred while Canadians were quartered in part of that Camp, and the troops mixed in canteens, picture shows, &c., which were usually overcrowded. At Tidworth Camp, where care was taken to prevent this mixing, only one case arose amongst the English troops while the Canadians were in barracks there.

Again, Major Salmon, speaking of the cases at Exeter, says that up to January the health of the troops at Topsham was good in spite of wet weather and some unavoidable overcrowding. Drafts of men from Hilsea were then brought into the district; the first three cases of cerebro-spinal fever were in men of the Hilsea drafts, and it was concluded that these drafts brought the disease into the Exeter district.

There is also a certain amount of evidence that soldiers were in part responsible for the spread of the disease amongst the civilian population. At Falmouth, says Capt. Gregor, all the civil cases were in the working class part of the town, all were in women, and in all there was direct contact with soldiers. Capt. Allan (Chester) states that his cases were mostly amongst the civilian hosts of billeted soldiers who were themselves well.

Capt. Gaskell (Cambridge) forms the opinion that there is a distinct connection between the giving of leave and the in-

cidence of cerebro-spinal fever. He thinks men were exposed to infection while away: some developed the disease while away, others shortly after their return. In 10 cases, he says, there had been no recent leave, and in 11 either recent leave or shifting from some other district. In 6 cases men had been on leave in districts where a good number of cases had occurred. In a group of 9 severe cases in April, 6 had had recent leave: in 5 the disease appeared within 2 days of return from leave.

The influence of the movements of individual men in determining incidence will clearly be most apparent in districts where the number of home-bred cases is small. The Cambridge experience was not everywhere noted, indeed Lieut. Johnston says that only 7 of the 68 cases on Salisbury Plain had been on leave.

We may conclude from all these facts that the spread of cerebro-spinal fever in the recent epidemic was mainly by carriers, and that military movements played a considerable part in the process.

## Other Conditions Affecting the Incidence of Cerebro-Spinal Fever.

Many of the reporters have endeavoured to answer the questions of the circular under this heading. The answers may be summarised as follows.

### *The Influence of Weather.*

Several reporters are indisposed to formulate any conclusion. Major Embleton (Netley), Prof. Hutchens (Newcastle), Dr. Claridge (Norwich), doubt the influence of weather, and Lieut. Bullock (Woolwich) regards it as a subordinate factor. Capt. Gaskell (Cambridge) thinks cases tended to occur during unsettled weather, early in the fall of the barometer, but he forms no definite conclusion.

Others dwell on the bad weather experienced during last winter and early spring. All over the country there was excessive rainfall with frequent storms. Lieut. Johnston thinks that on Salisbury Plain the weather assisted in the dissemination of the meningococcus by keeping men indoors with closed windows, and in the same way promoted the spread of influenza, catarrhs and sore throats. Several reporters, Capt. Gregor (Falmouth), Capt. Allan (Chester), Major Salmon (Exeter) note that the epidemic began to recede with the advent of fine weather. Major Salmon states that the epidemic seemed dying down in April as the weather got warmer, but that 4 further cases occurred in May during a sudden fortnight's spell of cold.

The conclusion would seem justified that cold and wet weather may have the indirect influence which Lieut. Johnston suggests —that of promoting the transference of the meningococcus, by favouring the aggregation of men at close quarters indoors and discouraging open windows. This, as we have previously remarked, is probably the chief factor in determining the seasonal incidence of cerebro-spinal fever.

Lieut. Compton, in a paper in the *Journal of the Royal Army Medical Corps* (November, 1915), gives curves of sunshine, temperature variations and atmospheric humidity in the Weymouth district during the epidemic period. He considers that the factors which apparently determine outbreaks of cerebro-spinal meningitis are sudden saturation of the air with moisture combined with equable conditions of temperature. He formulates a "cosmic" theory of infection presupposing a widely air-borne distribution of the meningococcus, a hypothesis to which all its biological properties are strongly opposed.

*The Influence of Overcrowding and Deficient Ventilation.*

The reporters are almost unanimous in declaring this to be an important factor in the spread of the disease, although a great many cases, perhaps more than half, occurred where there was no overcrowding. In Part III. of this report we have considered the influence of overcrowding in determining the proportion of carriers amongst the contacts examined. A similar influence is traced by most of the reporters upon the incidence of cerebro-spinal fever.

Lieut. Johnston states that in the 68 cases on Salisbury Plain there was overcrowding in 29 cases, and none in 39. But he points out that there may be overcrowding of an area, as well as of men's quarters, and that at Bulford Camp, where 20 cases occurred, both these conditions were present. Insufficient ventilation was often present—mainly the fault of the men themselves. In 10 cases the quarters were dirty, and in 6 meals were taken in the sleeping rooms—a practice much to be condemned.

Lieut. Bullock states that at Woolwich the disease did not always occur in the most overcrowded quarters, but sometimes it did and of this he quotes a striking example. Cambridge Cottages are small, badly lighted and badly ventilated buildings, which in time of peace accommodated 184 adults and 184 children. Last winter they held 864 men (on an average 700) and on certain days in February as many as 1,200–1,300 men slept there: 5 cases of cerebro-spinal fever occurred in the cottages during this period of maximum overcrowding.

Capt. Gaskell considers that overcrowding and lack of ventilation are powerful predisponents to the disease. In 11 of the Cambridge cases the cubic air space per man was 400 cubic feet or less: in 15 cases it was over 400 cubic feet. Out of 26 cases occurring in billets, only in 7 were the cubic space and ventilation adequate. In huts at Cherry Hinton, where a small outbreak occurred, the air space was 300 cubic feet, and the ventilation 2 square feet per man. Lieut.-Col. Sims Woodhead improved the ventilation by knocking out a board all round under the eaves of the huts and no more cases occurred.

It is well known, on the other hand, that in hospitals, where the air space and ventilation are good, cerebro-spinal fever very rarely spreads, indeed the case of the nurse at Exeter, already

mentioned, is the only case of the kind alluded to in these reports, while several of the reporters note the small proportion of carriers amongst nurses and hospital orderlies. Dr. Claridge never found other patients to be carriers.

The only reporters who found no overcrowding in the surroundings of their cases are Dr. Syer B. White (Nottingham), Prof. Hutchens (Newcastle), Capt. Allan (Chester) and Major Embleton (Netley), and these do not deny the probable influence of overcrowding. The manner in which overcrowding and deficient ventilation influence the spread of cerebro-spinal fever is obvious. It is by facilitating the transference of the meningococcus from pharynx to pharynx.

Further, it is probably this factor more than any other which renders the soldier more liable than the civilian to the disease. The recruit and the young soldier have not yet wholly passed the age of susceptibility, and the conditions of life in barracks and huts are such as to favour the spread of the meningococcus. When the number of young recruits is very large and military exigencies have led to considerable overcrowding, all the requisites for an epidemic of cerebro-spinal fever are at hand should the organism be introduced.

*The Influence of Fatigue.*

Seven of the reporters mention this subject, only to dismiss it as a factor of little or no importance. Capt. Gregor thinks fatigue may have lowered vitality in recruits from the class of shopkeepers and clerks, but not in those from the labouring classes, who stood it well. There appears no reason for believing that it predisposes to cerebro-spinal fever more than to any other bacterial infection.

*The Influence of Age.*

It is well known that the sporadic form of cerebro-spinal fever, as seen amongst the civil population, is mainly a disease of infancy and early childhood. It becomes rarer in adolescence and is uncommon in adults. Those of the reporters who mention civilian cases have much the same story to tell of the recent epidemic : the cases have mainly been in children.

Most of the data furnished refer, however, to the military population—ranging in age from 17 or 18 to 45 years, and chiefly near the lower limits of this age period. Susceptibility has not disappeared, though it may have lessened, and since the bulk of the soldiers were young recruits the age incidence of cerebro-spinal fever has been just what might have been foretold.

Nine of the reporters discuss this matter, and come to the general conclusion that the incidence was in proportion to the age of the military population. Lieut. Johnston says that on Salisbury Plain the maximum incidence was at 19 years : after 22 years it was low, and similar facts are stated by the other reporters. Cases in men over 30 were uncommon, though a few such are recorded, and only one or two cases are mentioned in men over 40.

### *The Influence of Length of Service.*

This question was one which it was almost superfluous to ask, since, as Lieut. Johnston points out, length of service must in this case be taken in relation to the seasonal prevalence of the disease. If war breaks out in August and young men are recruited in enormous numbers during the autumn, the seasonal maximum of the disease will catch them while they are recruits of only a few months' standing. Out of 51 cases on Salisbury Plain only 2 had been in the army before the war broke out. Capt. Gaskell, however, notes a difference in fatality: of the cases of less than 4 months' service, 6 died out of 9; of those recruited since the beginning of the war, but of more than 4 months' service, only 2 died out of 20. A much larger series of cases would be required before any conclusion can be deduced from these facts, which are not noted by any other of the reporters.

### *The Influence of Recent Illness.*

It might be supposed, *à priori*, that the lowering of general health caused by one acute infection would be apt to pave the way for another. We find recorded in these reports a few instances which may bear this interpretation. Dr. Syer White (Nottingham) mentions a case of cerebro-spinal fever occurring during convalescence from measles. Capt. Gregor (Falmouth) records two cases in soldiers, one of influenza the other of tonsillitis: both recovered sufficiently to go on duty, but in 24 and 36 hours respectively both went down with fulminant cerebro-spinal fever and both died within 36 hours. These cases are open to the criticism that the supposed influenza and tonsillitis may have been slight or larval cerebro-spinal fever, the fatal result being attributable to too early a return to duty.

The question of the relationship between cerebro-spinal fever and influenza, tonsillitis and catarrhs is discussed by more than one of the reporters. Capt. Gregor notes that during January, February and March all these diseases were very prevalent at Falmouth. He thinks it possible that some cases diagnosed as influenza and tonsillitis were really mild forms of cerebro-spinal fever, and Lieut. Llewellyn makes the same remark about cases on Salisbury Plain. It is probable that abortive cases of cerebro-spinal fever occur in which the signs of meningitis are ill-marked or absent, and which quickly recover; such cases would easily be passed over as influenza. There is further no reason for doubting that the debility following genuine attacks of influenza and tonsillitis may have predisposed to cerebro-spinal fever. There seems no further ground than this for assuming any relationship between the two groups of infections, and since in all these diseases the virus is one spreading from throat to throat, their epidemic concurrence during the climatic and housing conditions which prevailed amongst the troops last winter is readily explained.

Capt. Gaskell relates 3 cases at Cambridge, and Lieut. Llewellyn 2 on Salisbury Plain, in which cerebro-spinal fever followed inoculation against typhoid fever. The great majority of the troops underwent this inoculation, and it is therefore likely that the connection may have been a chance one : at the most, the transitory depression following inoculation may have been a predisposing cause. The same applies to 3 cases mentioned by Lieut. Llewellyn in which the disease followed vaccination against small-pox.

The relation of catarrh to cerebro-spinal fever has already been considered in discussing its relation to the carrier condition.

## The Incubation Period of Cerebro-spinal Fever.

In the case of most specific fevers, there is reason for believing that the virus begins its career as a pathogenic agent as soon as it gains access to the body. There is an interval during which it multiplies and spreads in the blood or tissues, and, finally, when it reaches a given concentration, the body proceeds to react against it by inflammation or fever or a rash. This quiescent period of incubation is in many fevers a very constant one, in point of time. But in cerebro-spinal fever it would seem that the case is very different. The meningococcus having gained access to the nasopharynx behaves, in the great majority of cases, as a pure saprophyte. After a period of " carrying " which commonly lasts a few days to a few weeks, the host rids himself of the intruder without having been any the worse for the invasion, though he may have passed on the organism to those in close contact with him. Only in a very small proportion of cases does the patient experience the secondary invasion of the body which goes by the name of cerebro-spinal fever. We have no data for deciding at what interval after the primary infection this may occur, but it is probably a very variable one. The most that we can do is to judge from certain individual cases how short the interval may sometimes be, and, from the supervention of the disease in known carriers, how long it may sometimes be.

With regard to the minimum period, the most convincing instance which we find in the reports is a case recorded by Capt. Gregor.. A man developed the disease within a few days of landing at Plymouth ; he had travelled from Australia, touching only at the Cape, and it appeared impossible that he should have been exposed to infection before reaching this country. Capt. Gregor puts the incubation period in this case at from 3 to 5 days. Dr. Claridge (Norwich) points out that there is much better opportunity for studying this question in rural districts where people mix less freely than in towns, and he gives a number of civil cases in the country illustrating incubation periods. He finds that it is usually 3 to 5 days, but may be 9 or 10. Lieut. Bullock (Woolwich) gives 3 cases pointing to a 4 days' incubation, and other reporters also mention cases suggesting a period of short duration.

On the other hand, we find cases reported suggesting an incubation period of from 9 to 18 days, and Prof. Walker Hall (Bristol) professes some scepticism concerning a short incubation : he quotes a series of cases from one house at intervals of 4 weeks.

There are really no adequate data for determining the maximum period which may elapse between the commencement of the carrier condition and the onset of cerebro-spinal fever. Judging from the reports before us, it seems very exceptional for the known carrier to develop the disease, indeed we find, out of 690 carrier cases reported, only 2 cases mentioned, one of which is doubtful. Lieut. Llewellyn (Salisbury Plain) states that a man slept in the same bed as a man who developed cerebro-spinal fever up to January 28th. When his throat was swabbed on February 12th he was found to be a carrier. On February 14th he developed a slight headache, which cleared up, and on February 20th cerebro-spinal fever declared itself. The facts suggest an incubation period of at least 23 days. Capt. Allan (Chester) relates the case of a contact declared free from meningococci at Cardiff, who developed cerebro-spinal fever 10 weeks later, but there is no proof that he was not reinfected. To these instances we can add a case under the personal observation of one of us in which, out of a batch of 6 men admitted to the 1st London General Hospital for various irrelevant affections, and who were known contacts with cerebro-spinal meningitis, 2 were found to harbour the meningococcus in the nasopharynx in considerable number. These two men were isolated and one of them developed a fatal attack of cerebro-spinal fever more than 3 weeks after admission. Surgeon-General Rolleston says that, of 170 Naval cases, 3 were in recognised carriers under treatment.

The foregoing considerations lead us to regard the disease as one which in the nature of things can have no definite incubation period such as we see in small-pox or measles. The systemic invasion may occur in as short a period as 3 or 4 days after the pharynx becomes infected, or may be delayed, certainly for 3 weeks and probably for longer.

## General Conclusions.

The facts and opinions which we have endeavoured, in the preceding pages, to summarise from the reports before us, appear to be in harmony with a hypothesis as to the spread of cerebro-spinal fever which has for some time been gaining favour with epidemiologists. The epidemic is not one of cerebro-spinal fever as such, but what may be termed a "saprophytic epidemic" of the meningococcus in the throats of the population at large, governed as to its local incidence by the opportunities afforded for transfer of the coccus from pharynx to pharynx. It is an epidemic prevailing in winter and early spring because climatic conditions bring people into closer contact indoors at that season : it dies out in summer for the converse reason. The

conditions of camp and barrack life render it pre-eminently liable to affect the military population. It probably prevails in towns to a much greater extent than in the country owing to the closer aggregation of the population. This meningococcal epidemic presents no objective or subjective features to attract attention, and is revealed only by systematic bacteriological observation.

Cerebro-spinal fever is an epiphenomenon of the epidemic. It is due to a secondary systemic invasion by the meningococcus from its saprophytic focus in the nasopharynx, occurring in sparse and isolated cases, which appear as a rule unconnected with each other. At present we do not know the conditions which determine the secondary invasion, nor have we the data for judging in what proportion of cases it takes place, though it seems a very small one. We know the number of cases of the declared disease, but not the total number of cases with pharyngeal infection. As regards these latter we can only form a crude guess from the proportion of so-called " positive contacts " detected.

The term " positive contact," in so far as it implies necessary infection of the carrier from the case of cerebro-spinal fever, which has led to its detection, is, perhaps, a misnomer. The proportion of positive contacts may, with equal justice, be regarded as an index of the percentage of carriers in the population amongst which the case of cerebro-spinal fever has arisen. It is just as likely that the carrier has infected the case of cerebro-spinal fever as that the latter has infected the carrier. Two considerations must be borne in mind, in forming a judgment. One is the observed prevalence of the meningococcus, perhaps exceptional and local, in the throats of non-contacts in London during the spring and early summer of last year, when Dr. Eastwood found 10 per cent. and Dr. Scott 13 per cent. of carriers amongst those examined. This has not indeed been found by observers elsewhere, but it is a fact of great significance. The other is that the proportion of positive contacts shows a seasonal variation corresponding to that of the disease, whereas there is little reason for supposing that cases of cerebro-spinal fever are less infective in the later than in the earlier stages of the epidemic. The case of meningitis should perhaps be regarded as a beacon which flares up as a warning of the prevalence of the carrier condition in the local population. It is not to be inferred that the disease does not cause carrier infection ; it certainly does so in a limited number of close contacts. It is only suggested that the bulk of the carriers found were probably carriers before the case of meningitis occurred.

The question is now, indeed, arising as to the relation between the meningococci found in the carrier, and especially in the non-contact, and those found in the actual disease. So long as the organism was regarded as a simple and indivisible species it was in the position of Peter Bell's primrose. But with the recognition of epidemic races of the coccus a new field of research opens out.

In the report of Drs. Colebrook and Tanner, three hypotheses are discussed as to the nature of carrier infection, with regard to the known fact that the great majority of carriers escape systemic infection. They point out that could an explanation be found for their escape, it might modify our policy as to the treatment of carriers.

The first hypothesis is that most carriers and normal persons possess an adequate natural immunity against the meningococcus : in other words the incidence of cerebro-spinal fever is determined solely by the susceptibility of the carrier. Against this hypothesis they urge that there is no evidence of such immunity in the blood of normal persons and carriers, though it can be detected readily enough in the blood of those suffering or convalescent from cerebro-spinal fever. The immunity reactions studied were agglutination, opsonin and bactericidal power, and only in one person who had not suffered from the disease did they find increased bactericidal power in the blood : in no case was opsonic power or agglutination increased. They point out that this is in contrast with what is found in the case of staphylococci, streptococci and B. tuberculosis, against which we have all had to defend ourselves from early years, while relatively few have encountered and survived attack by the meningococcus. Thus, they contend, the lack of a standing defence explains the overwhelming effect of the meningococcus when it does invade the blood and tissues.

The second hypothesis which they discuss is that the meningococcus found in the pharynx, notwithstanding its resemblance, is not the true cerebro-spinal organism, and has no affinity for the meninges. Against this view they urge the alleged circumstance that the organism is chiefly found in the pharynx of those who have been in contact with the disease. We say the " alleged circumstance," because the facts collected from the present series of reports show that sometimes, at least, the proportion of carriers from the population at large seems as great as amongst contacts. In any case figures must be taken in relation to the season of the year, density of population and circumstances of housing. This objection, therefore, loses some of its force. Dr. Colebrook and Dr. Tanner, however, come to the conclusion that most carrier strains are true meningococci.

The third hypothesis examined is that the pharyngeal coccus of the carrier, though a true meningococcus, is an attenuated strain incapable of determining a meningitis. It is true that there is no experimental demonstration of attenuation in carriers, but in favour of such lack of virulence are the facts that local symptoms are absent in the nasopharynx of the carrier, that he shows no immunising responses in the blood, and that he is not more susceptible than a normal person to large doses of vaccine. It may be that the mere fact of saprophytism is associated with loss of virulence : it may even be that the pharyngeal meningococci of a case of cerebro-spinal fever lack the virulence of the

organism from the blood and meninges. In this connection we may recall the parallel facts asserted by Rosenow as to the pneumococcus in pneumonia—the organisms from the blood possessing greater virulence and greater resistance to phagocytosis than those from the sputum.

Dr. Colebrook and Dr. Tanner do not come to any final conclusion with regard to these hypotheses, and necessarily so because the requisite data are lacking. It may be observed, however, that throughout their argument they make no allusion to the races of meningococci, which, though they have now been more closely defined for this epidemic, were clearly foreshadowed by Arkwright and others some years ago. And it is probably along these lines that we may hope for a solution of the problem.

The "types" defined by Major Gordon by means of the agglutinin absorption test were all from the meninges and had caused epidemic cerebro-spinal fever: that is to say, they are the "epidemic races" which were mainly concerned in the outbreak in England in 1914–15. But when Gordon applied his test to pharyngeal strains, he found that only a portion of them were to be included in his types; it is possible that the residue were non-epidemic and less harmful races. We may revert again to the parallel with the pneumococcus. The workers at the Rockefeller Institute determined 4 types of this organism, of which 3 were well defined and were found responsible for the great bulk of the epidemic pneumonia in New York. The 4th type consisted of a number of different strains apparently identical with the ordinary saprophytic pneumococci of the mouth: the relatively small proportion of cases of pneumonia due to this 4th group were mild in nature and of lower fatality than those due to the other 3 types.

It is at least possible that this parallel holds true for the meningococcus. We may conceive this organism to be essentially a saprophyte, though with potentialities of parasitism, divided up, as most bacterial species probably are, into a number, perhaps a large number, of races distinguished by their immunological reactions. At ordinary times, when cerebro-spinal fever is not epidemic, the saprophytic spread of these races is attended only by the development here and there of sporadic cases of declared disease in the most susceptible elements of the population—the posterior basic meningitis of infants. But from time to time, and hitherto very rarely in this country, individual races attain a greater virulence and their saprophytic spread is attended not only by a larger number of cases of meningitis, but by the attack of young adults, who in ordinary circumstances are immune. Such epidemic strains may be introduced into a community and lead to an outbreak of cerebro-spinal fever: there seems some ground for the belief that at least one out of the three principal strains concerned in last year's epidemic was introduced by the Canadian troops. In any given epidemic there will occur a saprophytic spread of the epidemic strains side by side with the domestic

and relatively harmless strains indigenous to the locality, so that there are carriers of either, indistinguishable except by serological means. Major Gordon suggests that only those carriers need be isolated who bear epidemic strains.

This conception of epidemic cerebro-spinal fever, already we believe held by many epidemiologists, must at present be regarded as a working hypothesis only. But it is one which may prove susceptible of demonstration by the laborious application of serological tests to strains of meningococci isolated from the pharynx. The task has already been begun, and is well worth carrying out on a comprehensive scale.

## Part V.

## SPECIFIC TREATMENT.

The reports which have been under our consideration contain a certain amount of clinical detail regarding cerebro-spinal fever. This we propose to refrain from discussing here, as it deals with nothing new. The specific treatment of the disease by serum and vaccines is, however, within our province, and we have to pass in review the generally unfavourable opinions expressed.

The average mortality of the cases which have been under the observation of the various reporters works out at a trifle under 50 per cent., though individual reporters record much higher and lower figures than this. Thus Capt. Pethybridge (Plymouth) had a mortality of 80 per cent. in his 5 cases, while Dr. Collins (Bath) had 7 cases with a mortality of only 14·3 per cent.

### Serum Treatment.

Sera from four different sources were used during the epidemic, two of American origin (Flexner's and Mulford's) and two of English make (Burroughs Wellcome & Co.'s and Lister Institute). In the great majority of cases the serum was given by the intrathecal route, and several of the reporters were unable to decide how much of the benefit which sometimes accrued was due to the serum and how much to the associated lumbar puncture.

A few of the reporters express opinions as to the relative values of the sera they employed. Prof. Walker Hall (Bristol) states that Flexner's serum seemed the best, then Mulford's, while that prepared by Burroughs Wellcome & Co. was the feeblest in its action. Lieut. Llewellyn (Salisbury Plain) says that Burroughs Wellcome & Co.'s serum was not very satisfactory, while Mulford's did good in some cases: several brands of Lister Institute serum, including one prepared from a local strain of the meningococcus, proved disappointing in bad cases. Lieut. Anderson (Salisbury Plain) records 10 cases treated with Lister Institute serum with a 50 per cent. mortality: 6 treated with Burroughs Wellcome & Co.'s serum with a 66·6 per cent. mortality, and 4 treated with Mulford's serum with a 75 per cent. mortality. Capt. Allan found Flexner's serum of service in early cases.

The impressions left on the minds of the different reporters may be summarised as follows. Dr. Warren Crowe (Devonport) maintains that the serum used should be tested as to its agglutinating power upon the meningococcus isolated from the case treated. He claims that no man died upon whom a really homologous serum had a fair chance, and he had a mortality of only 27·3 per cent. in his serum-treated cases.

Capt. Gaskell (Cambridge) places his reliance on lumbar puncture alone and considers that there is grave doubt as to the value of serum in addition. Dr. Claridge (Norwich) gave serum in two cases only, and says that it did no good. Capt. Pethybridge (Plymouth) used lumbar puncture and Mulford's serum, the combination giving better results than lumbar puncture alone. Capt. Gregor (Falmouth) states that intrathecal serum seemed of benefit, but cannot say how much was due to the lumbar puncture. He expresses himself in favour of large doses, 50 c.c. on each of three successive days, if more than this amount of cerebro-spinal fluid can be drawn off. In two severe cases of general infection he gave 10 to 20 c.c. of serum intravenously with benefit, and one of them recovered. Dr. Syer B. White (Nottingham) records recovery in a baby of 4 months after the injection of 5 c.c. of serum through the anterior fontanelle.

Prof. Hutchens (Newcastle) gave serum only once, and then unsuccessfully. Lieut. Llewellyn (Salisbury Plain) says that the results of serum were on the whole disappointing, though it did good in some cases. In 7 cases in which small doses were used the mortality was 71 per cent. : in 20 cases in which it was pushed the mortality was 65 per cent. Lieut. Anderson (Salisbury Plain) found the results of serum too variable for any conclusion. Major Embleton (Netley) has no evidence for or against serum, and Major Salmon (Exeter) thinks no special treatment of any use. Lieut. Bullock (Woolwich) is unable to determine whether serum did any good : no one brand seemed better than the rest.

It must be confessed that this summary of impressions is not very encouraging, for even those who speak in favour of serum have to confess a case mortality which somewhat belies their statements. Dr. Warren Crowe's figures are the only exception to this, and it may be noted that he is the only reporter who insists on the importance of a homologous serum.

Truly homologous sera, however, in the sense of monovalent ones prepared against the individual races of meningococcus, were not available during last year's epidemic, and, indeed, can scarcely be procured now. It may be hoped that when a supply of such sera is available Major Gordon's expectations will be fulfilled.* Until the type of coccus in individual cases is determined, and the homologous serum employed, it may justly be

* The polyvalent serum which has now been prepared at the Lister Institute from the epidemic strains isolated in last year's epidemic has already been employed in the treatment of a number of cases in the recrudescence of the epidemic (January, 1916), and apparently with considerable success.

said that the serum treatment of cerebro-spinal fever has not had its fairest chance. We can only suspend our judgment.

### The Administration of Human Serum.

Capt. Allan (Chester) states that in two of his cases of cerebro-spinal fever, serum from a patient who had recovered from an acute attack was given with almost dramatic results. The temperatures came down to normal and the symptoms largely abated within 24 hours. Capt. Gaskell (Cambridge) says that one of his cases was benefited by 5 c.c. of serum taken from the patient himself.

### Accidents of Serum Treatment.

Two remarkable cases are recorded in these reports in which anaphylactic shock is stated to have followed the introduction of serum into the spinal theca. Dr. Syer B. White (Nottingham) records the following case :—A soldier of 29 years, who had been ill for three weeks before admission to hospital, was found to have a mild attack of cerebro-spinal fever, confirmed by lumbar puncture. On July 23rd he received 25 c.c. of Burroughs Wellcome & Co.'s serum intrathecally, followed by a second dose of 50 c.c. on July 24th. On July 29th he was given a third dose of 25 c.c. by the same route : he became collapsed and unconscious and had delirium, sleeplessness and incontinence for a week. An ordinary attack of serum disease then set in, with an urticarial eruption and joint pains. After this he recovered.

A very similar experience occurred to Lieut. Bullock (Woolwich). The case was a severe one : lumbar puncture was performed eight times and serum was given five times : the brand of serum and the dosage are not stated. The last dose of serum produced shock almost at once, with laboured breathing and cyanosis, the patient becoming pulseless and collapsed. He also recovered.

Capt. Gregor (Falmouth) notes that during lumbar puncture late on in the disease patients are liable to transient collapse, but it is not clear that his cases are of the same order as the preceding.

### Vaccine Treatment.

It has already been seen that the carrier condition could not be cured by vaccines in the hands of Drs. Colebrook and Tanner, working for the Medical Research Committee. Dr. Warren Crowe also found vaccines of no effect upon carriers, and Lieut. Treadgold says the same.

Several of the reporters used vaccines in the treatment of cerebro-spinal fever, and with somewhat variable results. Dr. Warren Crowe (Devonport) employed an autogenous vaccine, which he prepared in a rapid and simple manner. The cerebro-spinal fluid, enriched with glucose (1 per cent.) was incubated for

24 hours, shaken up and lightly centrifuged: the upper part of the fluid was then found to contain 50 to 100 million cocci per c.c. It was sterilised at 70° C. for ten minutes, and then counted, 0·5 per cent. phenol being finally added. His dosage was very small, beginning at 1 million. He thinks that the treatment did some good, especially influencing the temperature.

Prof. Walker Hall (Bristol) employed vaccines in preference to serum. The vaccine used was made from 5 strains from the existing outbreak, and was a mixture of half sensitised and half unsensitised cocci. His dosage was 25, 50, 125, 250 and 500 million, at two days' intervals, and he states that the first marked effect was usually produced when the 125 million dose was reached. He does not seem very enthusiastic about the treatment, for he says that daily lumbar puncture appeared to furnish the more permanent results. His fellow reporters have no better story to tell. Dr. Peters used vaccine on two patients: in one it seemed to do good, in the other to determine the fatal issue. Dr. Collins says that vaccines seemed better than serum, but tended to cause headache.

Lieut. Llewellyn and Lieut. Treadgold (Salisbury Plain) used autogenous vaccines in two cases without effect, in doses of 5 to 250 million, while Lieut. Anderson could come to no conclusion as to the value of vaccine. Lieut. Bullock (Woolwich) states that he has no scientific evidence, but has a clinical impression that vaccines did no good. Capt. Allan (Chester) relates that he gave an autogenous vaccine in one case, in doses of 100 followed by 200 million, with excellent result, the patient recovering from an acute condition.

The general experience of vaccine treatment would thus seem to have been little more favourable than that of serum.

## The Prophylactic Use of Vaccine.

Two of the reports speak of this subject. At St. Mary's Hospital a dozen doctors exposed to infection from cases of cerebro-spinal fever or from contacts underwent prophylactic inoculation. The dose used was 150 million, given intravenously, which produced a short but sharp constitutional reaction. None developed the disease.

Lieut. Treadgold inoculated 79 carriers on Salisbury Plain, and no case of cerebro-spinal fever arose amongst them, though one case occurred amongst 49 carriers who were not inoculated. While it may be supposed probable that immunity may be conferred for awhile by this procedure, it cannot be said that much is proved by these small figures. The dosage used by Lieut. Treadgold was 50 million followed after a week by 100 million: no constitutional symptoms were produced, and the temperature never rose above 100° F. These doses, and probably larger ones, seem perfectly safe.

## Other Forms of Treatment.

The only drugs mentioned in the reports are hexamine and soamin. Dr. Peters used hexamine in five cases with no effect. Soamin was the chief form of treatment used by Prof. Hutchens, whose case mortality was 60 per cent. It was used also on Salisbury Plain, but apparently with little benefit, though Lieut. Llewellyn says it sometimes did good.

F. W. ANDREWES.

WILLIAM BULLOCH.

R. TANNER HEWLETT.