An Address

ON

THE POSSIBLE FUNCTIONS OF THE CEREBRO-SPINAL FLUID.

DELIVERED BEFORE THE NEUROLOGICAL SECTION OF THE ROYAL SOCIETY OF MEDICINE.

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So much has within recent years been written about the cerebro-spinal fluid that I must apologize for my want of originality in selecting that subject for this address. But however hackneyed the subject, we are still far from possessing complete knowledge as to the functions and significance of the fluid. From the pathological as well as from the physiological point of view, we at least know that this remarkable fluid is one of the greatest importance, and its careful examination in many diseases has yielded results of inestimable value. During the last few years it is a subject at which I have myself worked, and I have been fortunate in securing as my collaborator such a skilful and accurate experimenter as my colleague Professor W. E. Dixon, F.R.S.

One cannot work at any subject for any length of time without speculating beyond actually observed data. It is the safest rule to keep ideas of this nature to oneself, but there are some occasions when it is permissible to speak rather more freely; this is one of them. I happen to be the unworthy occupant of a presidential chair, and for an hour or less I shall be free from contradiction and criticism, so I propose to inflict upon you during that time some speculations, and have only safeguarded myself in the title of this address by alluding to the functions of the fluid as possible rather than probable. As my colleague Dixon is away on war service, I have had no opportunity of discussing the matter with him, so that if I say anything that is wildly improbable he, at any rate, is free from responsibility.

May I, after this preface, proceed next to another chapter, which is also of a prefatory character, and state as shortly as I can the present state of our knowledge regarding the characters, composition and fate of the fluid? The fluid, as you know, is, under normal conditions, as clear as water and of low specific gravity; it contains in solution inorganic salts similar to those in the blood plasma, a trace of coagulable protein, and a certain amount of a reducing substance—which has now been definitely proved to be glucose; it is practically free from formed elements. Under various abnormal conditions the protein matter may be largely increased, or other substances than the usual ones may be added to it, such as cholesterol and choline (or a choline-like substance). It may further have added to it various kinds of cellular structures, the differentiation between which is a valuable aid in diagnosis, and in other cases parasites of different sorts may be found. The fluid is primarily formed by the secreting cells which are so prominently found covering the choroid plexuses in the cerebral ventricles, so that this structure may be appropriately designated, as Mott first suggested, the choroid gland. The fluid is normally present at a certain pressure, and this pressure is not the result of arterial pressure passively transmitted to the fluid. The cerebro-spinal pressure, it is true, may be affected by changes in the arterial and venous pressures, but it is not dependent on them; and it may and often does vary quite independently of these. The true cerebro-spinal pressure is the result of the secretory pressure of the choroid epithelium cells. In other words, the cranio-spinal contents cannot any longer be regarded as a fixed quantity without the power of expanding or contracting in volume.

The rate of flow and the pressure of the fluid can be readily investigated in animals by placing a cannula in the subcerebellar cisterna and connecting it with the necessary apparatus. It is then found that there are three groups of substances which promote the flow and increase the pressure independently of those which affect it secondarily by

altering the blood pressure. The first group consists of excess of carbon dioxide (or lack of oxygen) in the blood, as in asphyxia, and drugs which interfere with respiration. The second group is that of the volatile anaesthetics, which may act by interfering with the respiration or by altering the physical conditions of secretion. The third group is specific, and consists of an extract of the choroid gland, or of the brain. The former is the more powerful. The chemical nature of the hormone in this extract is uncertain, but it is probably some product of nervous metabolism which, arising in the brain, passes to the choroid plexuses, accumulates there, and stimulates the secreting cells to activity; it cannot be discovered in the normal secretion, but in cases of general paralysis and brain softening—conditions in which catabolic processes are excessive—it can be recognized (by physiological tests) in the fluid itself. The choroid plexuses are abundantly provided with nerves, but there is no evidence that these are secretory in nature; indeed the evidence derived from experiments with atropine and similar alkaloids points in the opposite direction. The hormone, whatever its nature, acts probably not on nerves, but on the secreting cells directly.

There is no doubt that this fluid is being continually formed, and the next question is, What becomes of it? Large quantities of a neutral fluid, such as physiological saline solution, disappear within a few minutes when introduced into the cranio-vertebral cavity, and the course taken by such fluids, and presumably also of the normal cerebro-spinal fluid, can be traced by adding some substance which can be easily recognized by its colour, or by chemical tests, or by its physiological action. Using such methods it has been demonstrated that the exit is by the blood stream and not by the lymph channels of the nerves, which was formerly thought to be the case by a number of French observers.

If such substances are readily diffusible the speed with which they appear in the blood is very remarkable, especially if they are introduced into the subcerebellar region. An injection, for instance, of adrenaline, nicotine, or atropine produces typical physiological actions within a few seconds, in fact, almost as rapidly as if the injection had been made into the venous circulation direct.

On the other hand, substances which are not readily diffusible (such as commercial peptone) do not produce their characteristic effects when they are introduced into the cerebro-spinal fluid, so that one of the older theories, that actual valved orifices exist leading into the large veins at the base of the brain, must be abandoned.

The diffusion process is most rapid in the subcerebellar district, but is extremely slow in the spinal, especially the lower spinal region.* It probably occurs into the venous sinuses by the microscopic arachnoid villi described by Weed. There is also a possibility that, in addition to this, transference may occur through the thin walls of the blood vessels within the central nervous system, for, as Mott has pointed out, contact of these vessels with the cerebro-spinal fluid is maintained throughout their extent by the perivascular spaces which are continuous with the subarachnoid cavity. Diffusion in the opposite direction from blood to cerebro-spinal fluid does not occur except in an almost negligible degree in the case of a few drugs, such as alcohol and urethane.

But, in addition to this, there is another and minor communication between the fluid and the other parts of the body. Dixon and I found that dyes added to the fluid travel along the course of certain cranial nerves, and this is especially true for the olfactory nerve. This is not the case for the spinal nerves; no dye can be detected in their sheaths outside the spinal canal, and no dye is discernible in the lymph of the thoracic duct. I have spoken of this cranial (olfactory) outlet as a minor one, but clinical experience has shown that it is not a negligible one. For this loophole affords an opportunity for the entry of infective agents, as Flexner has shown in the causation of infective poliomyelitis.

Such, then, is a brief and, I fear, imperfect summary of the present state of our knowledge, and I propose now to pass to the main object of my address, which is to discuss the meaning and functions of the fluid we are dealing with.

* This is tacitly accepted by those who produce spinal anaesthesia by the injection intrathecally of substances of the cocaine group, for they recognize the danger of absorption if the drug reaches the medullary region.

In the first place, it can hardly be doubted that the presence of fluid within and around the structures of the central nervous system fulfils certain mechanical functions of support and pressure. That, however, does not explain why ordinary lymph would not do just as well, as it does in the majority of other organs. The relationships, however, of the brain and cord within a closed cavity are peculiar, and it may be that ordinary lymph is here insufficient to maintain a more or less constant pressure. For the pressure of ordinary lymph is wholly dependent on blood pressure; here, in addition, we have an independent pressure—namely, the secretory pressure of the choroidal secreting cells, and it is therefore quite possible that this may come into play in maintaining, equalizing, and adjusting those pressure relationships which are most advantageous for the well-being and function of the brain and cord. It is further quite possible that the ameliorative effects not infrequently noticed as a result of withdrawal of the cerebro-spinal fluid by lumbar puncture may be due to the relief of cerebral pressure. But such considerations offer no explanation of the peculiar composition of the fluid. Its characteristic chemical composition must have a deeper meaning.

It is very common to speak of the cerebro-spinal fluid as the lymph of the brain. Let us now examine this phrase more fully, and see if it has any scientific accuracy.

In the first place, we must be quite clear as to what lymph is, and what it does. It is a fluid which exudes through the thin walls of the blood capillaries. Whether lymph formation depends solely on physical conditions (filtration and osmosis), or whether in addition we have as a factor a secretory activity of the vascular lining membrane, is an interesting physiological problem which need not concern us now. The leakage fluid resembles blood plasma in its composition, except that it is comparatively poor in protein material, the diffusion of which through membranes is so difficult. This lymph, when formed, acts as the intermediary or middleman between the blood and the tissue elements, conveying to the latter, on the one hand, the oxygen and nutritive substances they need; and, on the other hand, it is into the lymph primarily that the tissues pour the waste products of their activity, and thus these are started on their journey to the organs of excretion (lungs, kidneys, etc.). The very essence of a lymph is that it should be in free communication, except for an intervening membrane, with the blood stream, and that this membrane should be equally permeable to water and other substances in both directions. The arrangement of the perivascular and perineuronal spaces, filled as they are with cerebro-spinal fluid, certainly resembles that of a lymphatic system, and therefore it is not surprising that the idea has caught on that cerebro-spinal fluid plays in the central nervous system the rôle of lymph. The peripheral nerves have a true lymphatic system analogous to that found in other organs, but anatomists are far from unanimous on the question whether the central nervous system possesses real lymphatic channels apart from the system of intercommunicating spaces occupied by cerebro-spinal fluid. The mere difficulty of discovering true lymph vessels does not indeed finally negative their existence, but until they are satisfactorily demonstrated we may provisionally assume that they are absent. If, then, cerebro-spinal fluid is the only fluid which actually comes into contact with the tissue elements of the brain and cord it necessarily follows that it must play the part played by lymph in other districts of the body; it must be, for example, the intermediary medium which is traversed by the oxygen on its way from blood to the tissue elements; and oxygen we know is essential for the continuance of nervous life and energy. Furthermore, it must be the vehicle by which other nutriment reaches the cells and fibres of nervous tissue. The next point is, Have we any evidence that the products of nerve catabolism pass into the fluid from the tissue elements as they do into ordinary lymph? If it were only possible to analyse and compare the composition of the fluid before it enters the perineuronal spaces, and after it leaves them, it would be possible to answer this question authoritatively, but in the absence of such proof one can only argue from probabilities. Seeing that the fluid is the only one available for the purpose, an affirmative answer seems inevitable, and this is supported by the fact that cerebro-spinal fluid is rich at any rate in one waste product—namely, carbon dioxide.

The expression "lymph of the brain" is therefore so far justifiable. But we have absolutely no proof that the cerebro-spinal fluid is in part an exudation from the blood, and it is in the origin of the fluid that the analogy between lymph and cerebro-spinal fluid breaks down. Whatever views we may hold as to whether a secretory factor comes into play in the production of ordinary lymph (and, at the best, such a factor can only be an insignificant one), we can have no hesitation in proclaiming that cerebro-spinal fluid is a true secretion arising in a definite glandular structure. Such a fluid must obviously be the best one for maintaining normal life in the nerve cells, and the whole living membrane of the spaces in which it resides appears to co-operate with the choroid gland in maintaining its constancy of composition, and to militate against the escape into it of substances from the blood stream, such as drugs or poisons, which would be foreign to the fluid or harmful to the delicate and sensitive structure which it bathes.

We have seen that the essential feature of a true lymph is the free interchange between it and the blood in both directions. This essential character is lacking in the cerebro-spinal fluid; in all probability the lining membrane of the cerebro-spinal spaces is permeable to substances passing from it into the blood, but it appears to be impermeable (except for oxygen) in the direction from the blood to the fluid. The nutritive materials the fluid contains appear to be formed in the choroid gland, and not to be merely exuded from the blood stream; otherwise one cannot explain why the protein it contains is not similar to that in the blood or in exudations (lymph) formed from the blood.

If, as Weed has suggested, cerebro-spinal fluid is partly formed as ordinary lymph is by exudation from the blood in the perivascular spaces, it is difficult to understand why readily diffusible drugs and poisons do not escape readily into the cerebro-spinal fluid as they do into ordinary lymph. The difficulty is quite intelligible when we regard the choroidal epithelium as a stalwart barrier of cells which keeps back these materials, and only allows its own normal secretion to escape. This useful work would be undermined and frustrated if the general lining were easily permeable to foreign substance.

Camus found that barium chloride, which is a very active poison to the central nervous system, will kill a rabbit of 2 kg. weight when $\frac{1}{10}$ mg. is introduced into the subarachnoid space, whereas the lethal dose is one thousand times greater when this salt is given subcutaneously. It is well known that anaphylaxis can be produced by smaller doses of proteins administered into the brain than when given elsewhere. The use of salvarsan in locomotor ataxy and similar post-syphilitic affections via the cerebro-spinal fluid has been abandoned, as it is fatal not only to the syphilitic organisms, but also to the patient. It is further known that salvarsan and its homologues are of little or no use in tabes and general paralysis when it is given by the ordinary channels, for in these later manifestations of syphilis the baneful spirochaete has got into a harbour of refuge (which we may speak of as extravascular) beyond the reach of the poison. The stalwart epithelial layer lets none escape, and does not realize how much both doctor and patient would rejoice if it could be made to understand that in this instance at least it did not form such an effective barrier.

May I add, in way of parenthesis, how very desirable it is that chemists and pharmacologists should apply themselves to the solving of this difficulty? The future treatment of tabes and allied conditions should aim at the discovery of some blander arsenic compound which could be introduced straight into the cerebro-spinal fluid and kill the syphilitic organism in its lair without at the same time slaying the host who harbours it.

Is not the very simplicity of the normal fluid suggestive? I remember when I was a student that normal or physiological saline solution was regarded as a physiological fad, for surgeons continued to use sponges—usually dirty ones at that time—soaked in water during operations. What a change has now come over the spirit of their dream! They have realized that water, even clean water, is a protoplasmic poison, and that osmosis is a real force and not a negligible phenomenon. I remember at about the same date witnessing, and in a humble measure assisting, Dr. Sydney Ringer in his epoch-making work on the effects of saline mixtures on living structures. The attitude of

the profession generally in those days was a tolerant one—just the sort of attitude adopted by a grandfather indulgently watching his descendants playing with their toys. But who has not heard of Ringer's solution to-day? Who can write a paper on almost any physiological or pathological subject without mentioning it or alluding to the part it has played in his investigations?

Ringer's fluid is the ideal physiological salt solution; its saline constituents are present in the same proportion as they occur in the natural body fluids, and in that way the normal osmotic pressure is maintained when living structures are bathed in it. Ringer's original solution resembled frog's blood in its saline composition, but since then several modifications have been introduced. The most important of these is the one we owe to Locke, who has altered the proportion of the various salts (increasing, for example, the amount of sodium chloride from 0.6 to 0.9 per cent.), so that the fluid may be employed with success on the living tissues of the mammal. Locke has also added a small proportion of the sugar glucose, and when in use it is kept saturated with oxygen. It is well known that in such a fluid living structures can be preserved in a living condition for hours, or even days and weeks. Locke's most striking results have been obtained with the mammalian heart; this can be kept beating for prolonged periods after its complete isolation from the body if it is perfused with the oxygenated fluid. The salts supply the normal stimulus to the cardiac fibres and maintain their physical integrity; the sugar acts as a source of energy and is consumed as activity continues.

Ringer's fluid, so compounded in the laboratory, is somewhat more than thirty years old. But in reality it is as old as the hills, or rather as man himself. Just as the Venus of Milo existed potentially from past ages in the block of marble from which it was ultimately hewn, so does Ringer's fluid exist in the blood and lymph, although its simple composition is obscured there by admixture with the blood proteins and corpuscles.

Here may I introduce another parenthesis and allude to another physiological puzzle, and that is the significance of the large amount of protein in the blood plasma and lymph? The meaning and use of the blood corpuscles we understand, or at least we think we do, but the meaning of so large a quantity of protein in the blood fluid and the part it plays in nutrition is still hidden from us. The amount of protein necessary for the repair of the tissues is not great, and the modern doctrine of maintenance and growth is that the tissues help themselves, not from proteins directly, but from the various amino-acids which are the result of protein cleavage. The great protein store may be another instance of the prodigality of Nature in providing a large margin for conditions of weakness and stress. However this may be, the presence of protein is not necessary, or it may even be harmful when it is added to Ringer's or Locke's solutions in experiments with perfused organs.

But to resume the thread of our argument. Thanks to Ringer some thirty years ago, physiologists were provided with a suitable fluid for experimental work, but the choroidal epithelium knew the secret of extracting it from the blood for untold ages before Ringer was born. For what, after all, is cerebro-spinal fluid but Locke's modification of Ringer's fluid?

The view I have been led to take is—the nervous mechanism being so sensitive, so easily influenced by anything unusual—that therefore the neurons must be bathed in an ideal physiological saline solution to maintain their osmotic equilibrium; the trace of protein it contains is probably quite sufficient for nutritive processes, and is no doubt the kind of protein particularly suited to repair the small amount of wear and tear which is the result of nervous action. The sugar, just as in Locke's solution, would serve for a supply of energy. The choroidal epithelium, in its wise choice of a suitable circumambient medium for the neurons, is really exercising a protective function. In order to keep out harmful proteins (toxins and the like), the comparatively harmless ones are kept back also, almost completely; all share the same process of exclusion. This protective action applies in addition to the majority of soluble drugs; this, as we have seen, may operate so as to be detrimental in diseased conditions. But we can hardly expect discrimination on the part of the epithelial secreting cells. The non-access of metallic and other poisons to the nervous elements is such a *sine*

qua non for their health, that during those periods when such substances are given for the relief of disease, or the slaughtering of parasites, the choroidal cells are unable to change their habits and so do not allow the drugs to get through.

Such, I believe then, is the real significance of the simple composition of this remarkable secretion. But I must allude, in conclusion, to some other possible additional functions which the fluid may exercise.

The late Dr. Gaskell approached the question from the embryological and developmental point of view; he held that the neural tube represents an ancestral digestive canal, and those who adopt Gaskell's hypothesis might conceivably argue that the cerebro-spinal fluid is the representative of a primitive digestive juice, and is secreted by an organ which was formerly a digestive gland. However interesting such speculations may be, one can hardly suppose that any one could seriously urge that the cerebro-spinal fluid retains any such functions to-day.

Dendy is one of many comparative anatomists who have not accepted Gaskell's views, and he has suggested that the important function fulfilled by the choroid plexuses is that of an intracerebral gill, and is concerned in respiration. The structure of the plexuses is certainly gill-like, but it is always unwise to argue from mere anatomical resemblances. Mott, who analysed the gases of cerebro-spinal fluid, found the quantity of carbon dioxide there very high (about 60 per cent.), and there is, therefore, something to be said in favour of the respiration hypothesis. It is quite possible that the choroidal epithelium may allow the escape of, or even actively excrete, this catabolic product, and it is unnecessary to point out how severe a poison any undue accumulation of carbon dioxide is in the central nervous system. Coupled with this fact is another I have previously mentioned—namely, that carbon dioxide is one of the most potent means of promoting a flow of the fluid. Just as urea is the best diuretic and bile the best cholagogue, so carbon dioxide is one of the most powerful cerebral lymphagogues.

One further point and I have done. The ependyma is lined by ciliated epithelium. Some doubt exists, I believe, as to whether the cilia are functionally active. But if we admit they are, the question arises—In what direction do they act? This is a question which is hardly susceptible of actual observation in man or the higher animals, but in the Amnocaetes, which Professor Dendy has so largely used in his investigation, he has brought forward evidence which shows that the movement is in a forward direction. I know it is not always wise to draw conclusions from such lowly animals and apply them without reserve to the higher ones. There are certain cases where such deductions are quite impossible; for instance, in some of the humble fishes the central canal of the spinal cord does not terminate blindly at its posterior extremity, but opens out by an orifice into the surrounding tissues.

In this case one can only speculate, and the rapidity of absorption of the fluid in the forward regions in comparison with that in the spinal district appears to favour Dendy's surmise, and the cilia, if they are active, would no doubt further the flow of fluid from the cord region to the large veins at the base of the brain, where it so readily leaves the subarachnoid space by entering the venous blood stream.

There are doubtless other problems in connexion with the cerebro-spinal fluid that demand solution, but my task for this evening is over. My main object has been to present the thesis in which I feel there is, at any rate, some truth—namely, to regard the cerebro-spinal fluid as the perfect physiological medium, more perfect doubtless than the artificial fluids we can make in the laboratory, but in its essential features closely resembling those associated with the names of Ringer and Locke.

I think already I have said finally, or in conclusion, more than once, but will you pardon me if, like the proverbial writer of sermons, I say it a third time, and this is really my concluding sentence? These are days of specialization, but however necessary specialization in medical science may be it has its attendant evils. Particularly regrettable is the divorce between those who pursue their investigations by the bedside and those who work in the laboratory. Neurology specially is a branch of our science in which an attempt should be made to bring about a closer *rapprochement* between the two sets of workers.

Speaking personally, I have derived inestimable benefit from meeting with and hearing here the clinical side of the subject. Those responsible for the management of this section of the Royal Society of Medicine have realized this, and in having elected this year a president who is a laboratory person they have shown that they see the value of the *entente* I have alluded to; and I can only trust that my year of office may not be detrimental to those who form the larger contingent in the Neurological Section—namely, those who pursue more specially the study of disease by the bedside.

INCIDENCE AND TREATMENT OF ENTAMOEBA HISTOLYTICA INFECTION AT WALTON HOSPITAL.

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(Report to the Medical Research Committee.)

SINCE the beginning of March, 1916, I have made a number of protozoological examinations of the stools of military patients in the New Zealand 2nd General Hospital, Walton-on-Thames. These examinations were made, in the first place, in order to detect carriers of *Entamoeba histolytica*. Detected carriers were then, whenever possible, treated; and during and after treatment I examined their stools at frequent intervals in order to ascertain the results. All the results so obtained, as far as they have any interest, are embodied in this report. It deals with the first 200 men examined at Walton, and five others sent there for treatment—205 cases in all. Upon these I have made more than 800 examinations.

Although I alone have been responsible for the examinations, on which the results here recorded are based, the investigation was only made possible by the cordial co-operation of the hospital staff. To Lieutenant-Colonel Myers, N.Z.A.M.C., now A.D.M.S. to the New Zealand Expeditionary Force, and to Lieutenant-Colonel Mill, N.Z.A.M.C., his successor in command at the Walton Hospital, I am indebted for permission to publish the results, and for the helpful interest they have taken in the work throughout. To Lieutenant Matthews, N.Z.A.M.C., who was directly in charge of the treatment of the cases, I owe the clinical details which he has kindly allowed me to include. The co-operation of Miss F. M. Durham, while acting as assistant pathologist to the hospital, alone made it possible for me to make the examinations at a distance. Miss Durham also most kindly undertook to extract from case sheets, and by personal questioning of patients, such details of clinical history as I am able to give. The work of examining the specimens has all been done at the Wellcome Bureau of Scientific Research. To Dr. A. C. Stevenson and other members of the staff I owe my best thanks for their hospitality and for much kind assistance in various ways. The investigation has been carried on by aid of a grant from the Medical Research Committee. Dr. H. H. Dale, of their staff, suggested the trial of emetine bismuthous iodide (Du Mez), of which the successful results are here recorded, and has shown constant interest in this phase of the investigation. To all I gratefully acknowledge my obligations.

The Protozoological Findings.

Examination of the stools of patients at Walton has given the following results:

Number of men infected with —		
<i>Entamoeba histolytica</i> ...	22	11%
<i>Entamoeba coli</i> ...	84	40.9%
<i>Giardia</i> (= <i>Lamblia</i>) <i>intestinalis</i> ...	40	19.5%
<i>Chilomastix</i> (= <i>Tetramitus</i>) <i>nasalis</i> ...	16	7.8%
<i>Trichomonas hominis</i> ...	5	2.4%
<i>Isospora</i> sp. ...	1	0.48%

It must be explained that the number of cases at Walton infected with *E. histolytica* has been much higher than that given above, because for some time past carriers have been sent there for treatment. These men, of whom there have been altogether about a dozen, were detected as carriers in another series of examinations undertaken by

Dr. A. C. Stevenson and myself. Their inclusion in the present series would therefore give a disproportionate value for the percentage of infection with *E. histolytica*. But as 5 of these imported cases have now been treated—forming part of the series of treatments here recorded—I have included them as supernumeraries, and left them out of account in calculating the percentage of men infected with *E. histolytica*. There are thus 27 cases (22 belonging to Walton, with 5 supernumeraries) of *E. histolytica* infection dealt with in this report. The 22 cases were found in the routine examinations of 200 men, and the percentage infected is therefore 11. In considering the infections with other protozoa, however, I have included the infections found in the 5 supernumeraries; so that these infections are calculated from 205 men.

It should be emphasized that the figures given denote the minimal number of men infected. It is not possible to be certain that a man does not harbour any given protozoon unless he has been examined repeatedly. One or two examinations are not sufficient. It is not only possible, but even probable, that of the 178 men here included as uninfected with *E. histolytica*, some at least are really infected, for 29 of these have been examined only once, and 65 only twice. The rest have been examined three or more times. If it had been possible to examine all these cases many times, it is almost certain that all the percentages would have been much higher.

Incidence of Infection with *E. histolytica* in Men of Different Classes.

All the men examined are New Zealanders who had served, as far as I can ascertain, in Egypt and Gallipoli before coming to England. They have thus all passed from a non-endemic into an endemic, and back again into a non-endemic centre of amoebic dysentery. I have therefore examined whenever possible not only those who entered Walton for dysentery, but also those entering for gunshot wounds and other complaints, since all appear to have been similarly exposed to infection with *E. histolytica*.

Of the 200 Walton men examined, 130 entered hospital for dysentery, enteric, or other intestinal ailments, or for debility following these; whereas 70 were in hospital for wounds or complaints other than intestinal. Of the 22 men infected with *E. histolytica*, 11 belong to the first category, and 11 to the second. Among the intestinal cases 90 entered for dysentery (or debility following) or persistent diarrhoea. Of these, 9 were found infected with *E. histolytica*. There were thus 13 infections among the 110 non-dysenteric patients (including among these many cases of intestinal disorder). These facts may be better appreciated as percentages, as follows:

Percentages of Cases Infected with <i>E. histolytica</i> .			
Intestinal cases ...	...	...	8.2 per cent.
Dysenteric cases ...	...	...	10.0 "
Non-dysenteric cases ...	...	...	11.8 "
Non-intestinal cases ...	...	...	15.7 "

The facts speak for themselves. They clearly show the importance of examining all men, not merely the dysenterics or suspected dysenterics, returning to England from a centre of amoebic infection. Obviously the number of men examined has been small, but it can hardly be regarded as insignificant. On the other hand, exact significance cannot be attached to the percentages, as the probable error in these is large.

I have ascertained that most of the men infected with *E. histolytica* (27 cases) have histories of dysentery, or acute diarrhoea, contracted at some time during their sojourn in the Mediterranean area. At least 2, however, and probably 4, have no such history, and have therefore been regarded as contact carriers—not convalescent carriers like the others. Reliable information on this subject is almost impossible to obtain in many cases, the testimony of the men themselves being all there is to go upon. With this reservation the character of the infection in the 27 cases studied may be stated as follows:

Ordinary convalescent carriers ...	22 cases
Contact carriers ...	4 "
Acute dysentery ...	1 case

All these cases were treated at Walton except one (No. 11), who was sent elsewhere to be treated for syphilis, and whom I have been unable to follow. Case No. 11 received special treatments which will be noted separately later.