wound. Trypsin will again come into account whenever, after the washing of the wound, leucocytes once more begin to emigrate, and phagocytose, and break down.

I see in the reduction of the antitryptic power of the lymph thus effected the prime cause of its corruption. Before attempting to obtain confirmation of this from crucial experiments, there was a set of findings to be cleared up. I had found in connexion with pus implantations made into serum that when this was heated to 60° C. for ten minutes one no longer obtained the same differential growth of streptococcus as with unheated serum, but obtained instead mixed cultures of streptococcus with sero-saprophytes, in particular staphylococcus and the wisp-like diphtheroid bacillus already made mention of. It seemed at first sight as if this could not possibly be related with a reduction in the antitryptic power of the serum, for it has, in view of the high quality of Opie's work on this question, been generally accepted from him that the antitryptic power of the serum is unaffected by exposure to heat until a temperature approaching the coagulation point of serum is reached. In reality, however, when this is reinvestigated quantitatively,* it emerges that the antitryptic power of the serum is reduced by one-third to one-half when we subject the serum to a temperature of 60° C. for ten minutes.

That difficulty having been removed out of the way of our hypothesis, we may proceed to take cognizance of the results of the crucial test experiments—experiments in which graduated additions of trypsin are made to serum as a preliminary to the implantation of sero-saprophytic microbes. The event of these experiments can be summed up in a sentence. When we add trypsin in quantities sufficient to reduce appreciably the antitryptic power but insufficient to give us any free trypsin, the serum is converted into an eminently favourable nutrient medium for sero-saprophytic microbes.

Our hypothesis is thus very strikingly confirmed. It will be necessary hereafter to follow it into all its consequences. For the present it will, however, suffice if we ponder on the following points. The antitryptic power of the blood would appear to be increased in every case of severe wound infection. We have perhaps here a defensive reaction of the organism directed against a possible invasion of the blood by sero-saprophytes. And we may perhaps look in this direction for an explanation of the non-specific benefit which has been observed to follow upon the inoculation of bacterial vaccines. It is clearly not impossible that the inoculation of a bacterial vaccine might contribute both to active and passive defence—to the active defence of the body against a particular microbe by calling forth a production of specific bacteriotropic substances, and to the general passive defence of the organism by calling forth a production of antitrypsin. And these two forms of immunizing response would not necessarily be linked together. The production of specific bacteriotropic substances would no doubt depend upon the quantum of bacterial antigen incorporated; while the production of antitrypsin might perhaps depend upon the breaking down of phagocytes and the liberation of their trypsin.

REFERENCE.

¹ *Technique of the Teat and the Capillary Glass Tube*, Constable, London.

* The quantitative method here employed was in essentials that described in my *Technique of the Teat and the Capillary Glass Tube*. It was varied only in the respect that the series of trypsin, serum, and calcified milk mixtures which are employed in that method were taken up, not into a many-stemmed pipette, but into a long, unmounted wide-bored capillary stem, which had, for the purpose of convenient filling in, been bent round at one end in the flame of a Bunsen into a siphoning curve.

(To be continued.)

A SCHEME, drawn up by Drs. William and Charles Mayo, of Rochester, Minnesota, for the establishment of a £200,000 foundation for medical research, has been submitted to the consideration of the University of Minnesota Board of Regents. It is proposed that the interest of the fund shall be used in research work to be carried out by medical graduates at Rochester.

The Minnesota State Medical Society intends to ask the State Legislature to set aside 10,000 acres of land to be used as a leper colony. According to the *New York Medical Journal*, about fifty persons in the State are known to be suffering from leprosy. It is also proposed to establish a branch hospital at the State Hospital for clinical purposes.

CEREBRO-SPINAL MENINGITIS :

DIAGNOSIS AND PROPHYLAXIS.

IS LUMBAR PUNCTURE JUSTIFIABLE?

BY

A. LUNDIE, M.B., CH.B. EDIN.,

BACTERIOLOGIST, ALDERSHOT COMMAND;

D. J. THOMAS, M.R.C.S., L.R.C.P., D.P.H. OXON.,

SPECIALIST SANITARY OFFICER, ALDERSHOT COMMAND;

AND

S. FLEMING, M.B., CH.M. EDIN., D.P.H. CANTAB.,

SPECIALIST SANITARY OFFICER, ALDERSHOT COMMAND;

LIEUTENANTS, R.A.M.C.

Nobody thinks of performing lumbar puncture on slight grounds. The indications for and against are carefully weighed. The operation is decided on the evidence obtained by a careful clinical examination of the case.

The indications for the operation are perfectly clear. An ingravescent headache, absolutely intolerable to the patient, is a very good reason for lumbar puncture at epidemic seasons. The concomitant symptoms may be diverse. There may be fever or no rise of temperature at all. The pulse may be accelerated, normal, or infrequent. There may be vomiting or no gastric disturbance at all. There may be a rash of one type or another, or the skin may be unaffected. There may be head retraction, or even flexion of the head. The knee-jerks may be normal, exaggerated, or unequal. Kernig's sign may or may not be present. The plantar reflex may be flexor or extensor. (The headache itself may be absent, and the symptoms present may be anomalous, and indicate delay.)

The cranial nerves ought to be examined systematically as far as possible, but it will be best first of all to study the patient's power of attention, before putting questions to him that he may answer at random. If his headache is really intolerable, it will often be observed that in spite of his being able to answer questions, the patient speedily lapses after each one into an apathetic state. He may, indeed, continue to mutter and groan, but he is not alert and alive to his critical condition. This condition contrasts most strikingly with the mental state prevailing in yellow fever. Here the patient is extremely alert. If he is of a certain mental calibre, he may clearly diagnose his own illness, and direct its treatment with the utmost non-chalance. He may fully realize his dreadful danger, and determine to do his level best to fight it out, or he may sink into a state of terror, and discuss the mortality of his disease with the attendant. He remains alert to almost the very end. On the contrary, in cerebro-spinal meningitis, there is early dulling of all the senses, and it is well worth while to stand at the bedside and make these observations, as they are of great diagnostic significance.

In testing the cranial nerves, it is best to adhere to the old system of beginning at the first and proceeding in the proper order. The sense of smell may be dulled or lost, optic neuritis should always be looked for. The movements of the eyeball should be tested. The other special senses should, if possible, be also tested. Hearing is commonly found to be defective, and if so, the deafness must not be mistaken for stupor. Hyperacusis has been observed.

A careful study of the nervous system will show the existence of some random process, and in each case there will be differences, proving that the lesion is not the same in every case, and that it is not possible to systematize the symptoms, so as to draw a classical picture of a typical case from nervous symptoms alone. Each case must be taken on its own merits. The acceleration or retardation of the pulse may indicate the point of greatest inflammation at the time the symptom is observed. The thermic phenomena are probably due to the same cause. It may be a matter of chance whether the thermic centre is involved in an inflammatory process or not. There probably is often a pan-encephalitis, rather than a meningitis; in one *post-mortem* examination the corpus callosum was across without being cut, simply owing to its own softened condition and the weight of the cerebral hemispheres. In another case there was a complete breaking down of the tissue forming the wall of the descending cornu of the lateral ventricle. There was no special reason why the other ventricle should not be similarly affected, unless the

one affected happened to have been shut off from communication with the other by inflammation at an early stage of the disease. The occasional phenomenon of many exaggerated reflexes is no doubt due to paralysis of higher controlling centres.

So striking are these random lesions of the nervous system that cases of pure throat affection have not been regarded as cases of the disease at all. The initial catarrh is so quickly got over that it is often ignored by the patient, or he imagines it to be his usual condition, due to smoking or to some other cause. But all the time toxin is being gradually absorbed, and at length it reaches the nervous system and depresses it, and thus the way is prepared for a general advance. Then, on the occurrence of any severe depression, a sudden change takes place, and the disease is then called fulminating. Why a fulmination takes place is not an easy matter to explain. Some cases develop all the serious aspects at once, and yet get well. The cerebro-spinal fluid at this stage is sometimes reduced so much that only a few drops can be got, but they usually contain pus cells and many organisms. A negative pressure has been alleged in these cases, but no air rushes into the cannula, while the few drops exude without suction. In these cases a reduction of the normal amount of fluid has taken place, and such cases are severe, and a second puncture gives an excess of fluid which is usually purulent.

Other cases give a clear fluid which is sterile. It contains no pus or formed matter at all on centrifugalization. But it has only once been found to be normal, in a chemical sense. Normal cerebro-spinal fluid contains dextrose 5 per cent., salts, and about 0.02 per cent. globulin. All these fluids contained an excess of albumin or albumose, and in the cases examined for sugar there was a loss of sugar, but never complete absence of it. Normal cerebro-spinal fluid is rendered pink by the addition of a 1 in 1,000 solution of potassium permanganate, and remains pink for at least five minutes, but in meningitis the clear fluid promptly becomes yellow. This is not due to reduction by glucose, but may be due to reduction of a glucose fermentation product, which must be the result of enzyme action, as there are no living organisms in the fluid.

The pathological process, then, seems to be this:

1. Local infection (that is, Stage 1).
2. General infection (that is, Stage 2). Toxic action on the nervous system, with excretion or escape of albumin into the cerebro-spinal fluid, transforming it into a culture medium for the invading organisms.
3. Breakdown of the defences of the meninges and general advance (that is, Stage 3). Occasionally the entrance of organisms to the cerebro-spinal fluid takes place early, accompanied by apparent absorption of fluid; but the general rule seems to be for an accumulation of sterile fluid first to take place, and then a breakdown of the defences, accelerated by the pressure of the fluid, and it therefore seems to be advisable to puncture early to prevent the occurrence of the final stage. The accidental escape of blood into the meninges would probably do good by supplying antibody where it is naturally deficient.

As regards the pain inflicted by puncture, it is quite tolerable when the operation is done skilfully, and in partially stuporose cases it seems to be totally ignored. In those cases in which the fluid happens to be clear and sterile, the relief of the headache is so marked that one patient made the observation that it was well worth suffering the pain of puncture to obtain the relief of headache which immediately followed it.

Sequelae of Puncture.—None have been observed yet. Sepsis, of course, should never occur, and in this Command Isolation Hospital it is unknown, although cases are sometimes punctured every day.

The Amount of Fluid to Remove.—As much as will come is a good rule. Three or four ounces can safely be removed. Early and frequent puncture has undoubtedly saved many lives, but this is encroaching on the question of treatment.

Number puncture in competent hands is always justifiable, and it gives the only criterion by which to diagnose the third stage of the disease. In fact, not a case yet notified in this Command has failed to present pus and meningococci in the cerebro-spinal fluid, and only such cases have been regarded in estimating the mortality. All sterile cases have been put in another category, awaiting a satisfactory nomenclature of the disease.

PROPHYLACTIC INOCULATION AGAINST TUBERCULOSIS.

By W. M. CROFTON, M.D.,

LECTURER IN SPECIAL PATHOLOGY, UNIVERSITY COLLEGE, DUBLIN;
PATHOLOGIST TO DR. STEEVENS'S HOSPITAL; VISITING
PHYSICIAN, ROYAL NATIONAL HOSPITAL FOR
CONSUMPTION, NEWCASTLE, CO. WICKLOW.

SINCE tuberculosis is, next to old age, the chief cause of death in these countries, there is no need to justify the assertion that some further measure or measures are necessary in dealing with the disease.

It is generally agreed that practically every one who has attained adult years has been infected by the microbe, and a large proportion show healed lesions *post mortem*. For instance, Hamburger and Monti investigated in Vienna the question on a large scale by means of skin and subcutaneous tuberculin reactions, and found that 95 per cent. of children who attained the age of 11 to 16 years were infected.

There are two ways in which a disease may be dealt with: (1) The microbe may be prevented from attaining access to the individual; (2) the individual may be rendered an unsuitable environment for the microbe to grow in.

Since under present conditions the infection is so universal, it would appear impossible to prevent the infection attaining access to the individual, although it is obvious that more might be done to prevent direct infection from the diseased, both human and bovine.

Taking Vienna again as an example, it is shown that while, as I have said, 95 per cent. get infected, only 15 per cent. develop tuberculous disease to a serious extent. That is, only in this percentage is the soil suitable for the continued growth of the bacillus. We must assume that in this proportion of the inhabitants (20 per cent.) the resistance to the disease is subnormal. If we could make the resistance of these to the disease equal to that of the 80 per cent., the problem would be solved, and the disease would occur only sporadically.

The development of the disease in the 15 per cent. may be due to:

- I. Bad hygienic surroundings.
- II. Lowered resistance due to infection with other microbes.
- III. Inherited low resistance.
- IV. Overcoming of a normal resistance by a virulent or continuous infection.

I. *Environment.*—The effect of bad environment is well illustrated by figures of tuberculosis mortality among the different classes in the Dublin registration area for 1912:

Professional and independent classes	... 0.41 per 1,000
Middle class	... 1.92 "
Artisans and small shopkeepers...	... 2.94 "
General service classes	... 3.16 "

We may take the middle class as having reasonable hygienic surroundings, and being people who are likely to die at home, so that good hygienic surroundings will not produce the desired result. Something further is necessary.

II. *Resistance Lowered by other Microbes.*—It is common knowledge that in children such infections as measles and whooping cough predispose to tuberculosis. More important, as far as pulmonary disease is concerned, are catarrhs of the respiratory tract brought about by the catarrhal microbes. The onset is constantly traced to acute or chronic catarrh, which is the primary infection, and not the tuberculosis. Frequently the ordinary methods of treatment entirely fail to cure the patient of these catarrhs. In my opinion it is seldom that tuberculosis of the lungs is not due to a mixed infection, and for successful treatment it is essential to deal specifically with the accompanying catarrhal microbes, as well as with the tubercle bacillus. It is, therefore, very important not to allow a catarrhal infection to become chronic. It is comparatively easy to clear off these infections with autogenous vaccines. However, while these catarrhal microbes are important help-meets of the tubercle bacillus, yet increasing the patient's resistance to them will not give the same guarantee against the disease as putting up the resistance to the tubercle bacillus itself.

III. *Inherited Low Resistance.*—I do not know whether the opinion that children of tuberculous persons inherit a