many people gall-stones cause no appreciable discomfort, or only such as can be relieved by medical treatment. But we have no medical means of dissolving or evacuating gall-stones; and although they sometimes pass spontaneously along the ducts, or escape through fistulae into the gastro-intestinal tract, they are very rarely completely evacuated in either of these ways.

The following are some of the serious consequences of delay before operating for the removal of gall-stones.

1. Suppuration, perforation, peritonitis, acute and chronic septicaemia, osteo-arthritis.
2. Jaundice and cholangitis, with risk of cholaemia and haemorrhage.
3. Cancer of the gall-bladder, which develops, according to Rolleston and others, in at least 5 per cent. of all cases of gall-stones. The danger of this complication is greater than that of operation.
4. Intestinal obstruction by gall-stones which have ulcerated into the bowel.
5. Pancreatitis.
6. Hepatic insufficiency.
7. Cardiac degeneration.

When possible, it is safer to wait for a quiet interval before operating, so as to allow thorough investigation and preparation of the patient. Fortunately, the acute symptoms, such as colic, jaundice, and fever, generally subside under careful medical treatment; for, unlike the appendix, the gall-bladder rarely perforates or sets up spreading peritonitis.

When signs of spreading peritonitis do develop, or an enlarged, tender gall-bladder can be felt, and symptoms such as vomiting, fever, and rigors do not abate, or signs of acute pancreatitis develop, an immediate operation is necessary. Similarly, when jaundice, associated with fever, fails to clear up under medical treatment, an early operation offers the best hope.

These emergency operations should be limited to simple drainage of the gall-bladder or common bile duct. Radical operations can be carried out later when the patient is better, the liver function is restored, and sepsis has subsided.

OPERATION.

Medical treatment having failed, operation for cholecystitis and gall-stones should be carried out before the disease has spread beyond the gall-bladder and cystic duct, so that the disease can be eradicated by cholecystectomy at a comparatively small risk. In later cases drainage of the gall-bladder or common bile duct may have to be established in order to save life. These delayed operations have a much higher mortality, and are more often followed by recurrence of symptoms, often demanding secondary operation.

REFERENCE.

- ¹ E. A. Graham and W. H. Cole: *Journ. Amer. Med. Assoc.*, 1924, 82, 613.

SOME RECENT ADVANCES IN THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE NERVOUS SYSTEM.*

BY

C. WORSTER-DROUGHT, M.A., M.D.CANTAB.,
M.R.C.P.LOND.,

PHYSICIAN TO THE METROPOLITAN HOSPITAL AND TO THE WEST END
HOSPITAL FOR NERVOUS DISEASES; CONSULTING NEUROLOGIST,
BETHLEM ROYAL HOSPITAL.

NEUROLOGY is a branch of medicine which I often have to defend, because I am told that, although it is a most interesting exercise in applied physiology, what treatment is possible in organic diseases of the nervous system? We maintain, however, that therapeutics in neurology compares very favourably with that of other organic medical diseases—of the heart, kidney, and liver, for instance. I propose, therefore, to review some of the more recent developments not only in the diagnosis of nervous system diseases, but also in their treatment.

One of the most important advances of recent years is the procedure known as "cisterna puncture"—that is, the insertion of a needle into the cisterna magna, that large

portion of the subarachnoid space which lies between the inferior surface of the cerebellum and the posterior aspect of the medulla. The puncture consists in penetrating the tissues between the occipital bone and the atlas vertebra, and withdrawing cerebro-spinal fluid. This may sound rather heroic, but is really quite as simple as lumbar puncture. The needle used should be graduated in centimetres, a depth of from 5 to 6 cm. being the maximum distance that the needle can be safely introduced in the adult before the medulla is reached. The surface point taken is the spine of the axis vertebra; the needle is inserted just above this and directed upwards at an angle of 30 degrees from the horizontal. After penetration of the skin it is advisable to remove the stylet from the needle before the latter is pushed onwards into the cisterna magna: then, as soon as the subarachnoid space is reached, a drop of cerebro-spinal fluid appears.

As regards the practical application of cisterna puncture, it may be mentioned that, apart from its use for the withdrawal of cerebro-spinal fluid for diagnostic purposes, it is of great value in the treatment of various forms of meningitis. In meningococcal and pneumococcal meningitis, for instance, the therapeutic serum can be introduced through the cisterna puncture needle and the serum thus brought into close contact with the site of maximum inflammation, which is invariably at the base of the brain. It thus replaces the older method of introducing the serum through a lumbar puncture needle. The puncture can also be used for injecting salvarsanized or mercurialized serum in the treatment of various forms of neurosyphilis. Further, it is of great value for the introduction of lipiodol in the localization of spinal cord tumours—a subject which I shall consider later.

A great deal may be learned from the pathological examination of the cerebro-spinal fluid. It is quite possible by this means to confirm a clinical diagnosis of compression of the spinal cord by tumour or abscess. In this condition the cerebro-spinal fluid shows fairly its characteristic reactions, which include a considerable increase in the amount of total protein present as compared with the normal of 0.02 to 0.04 per cent., but no increase in the normal number of cells (2 to 4 per cubic millimetre) and no alteration in the glucose and chlorides. This phenomenon has been termed "dissociation albumino-cytologique" by French physicians. Occasionally, in addition to the excess of protein, the cerebro-spinal fluid may be yellow in colour (xanthochromia) and may even coagulate spontaneously on standing; to this latter condition the term "Froin's syndrome" is applied, but the essential feature is the excess of protein with no increase in the number of cells. In addition to spinal cord tumour, dissociation albumino-cytologique may occur in cases of meningitis and certain forms of polyneuritis; and I have also seen it in cerebro-spinal arterio-sclerosis.

Another useful cerebro-spinal fluid test is Lange's colloidal gold reaction. The exact physio-chemical changes are complicated, but, briefly, the procedure consists of the application of the protective action of colloids on the precipitation of gold suspensions by sodium chloride to the protein in the cerebro-spinal fluid. Lange found that normal cerebro-spinal fluid, when diluted with 0.4 per cent. of sodium chloride, does not affect a solution of colloidal gold, whereas pathological fluid produces changes often characteristic for various diseases. Dilutions of cerebro-spinal fluid with salt solution, ranging from 1 in 10 to 1 in 5,120, are put up in a series of ten test tubes, each successive tube containing a higher dilution. A measured quantity of colloidal gold solution giving a purple coloration is added to each tube, and the series is examined after an interval of twenty-four hours for any colour changes that may have occurred. With normal cerebro-spinal fluid the purple colour is unchanged in each of the tubes. In abnormal reactions the colour changes range from blue to white in different tubes of the series. According to the resulting tints we can plot out a graph—the horizontal representing the series of tubes and the vertical the colour changes. Certain neurological conditions are indicated by typical curves. In general paralysis, for instance, we find what is known as a "paretic" curve. The first three or four tubes of the series undergo almost complete

* An address delivered to the City Division (Metropolitan Counties Branch) of the British Medical Association.

decolorization to white; from the fifth onwards gradual gradations occur until in the last few tubes no colour change takes place. Whereas the normal graph consists of merely a straight line along the base line, the "paretic" curve starts high on the vertical line, keeps straight on for a short distance, and then gradually falls to reach the base line; the curve therefore resembles one side of a tableland. This "paretic" curve is so characteristic of general paralysis that, personally, I hesitate in an untreated case to make a diagnosis of this condition in its absence. The cerebro-spinal fluid also yields a positive Wassermann reaction, but so do forms of neurosyphilis other than general paralysis.

In tubes dorsalis we usually find what is known as a "luecic" curve. The colour changes occur in the middle tubes of the series; the graph, therefore, rises from the base line and then gradually falls to the same level. In meningitis, and in some cases of cerebral tumour, the curve is often the reverse of the "paretic" curve, the maximum colour changes occurring in the last tubes of the series. The colloidal gold test is frequently of great assistance in the diagnosis of disseminated sclerosis. In this disease the cerebro-spinal fluid yields a negative Wassermann reaction, and there is little, if any, increase in the number of cells, while the protein shows only a very slight increase. The only really positive test, therefore, may be that of Lange. In acute forms of disseminated sclerosis, and particularly in those in which there is cerebral or cerebellar involvement, the colloidal gold curve is "paretic" in type, though the curve does not reach such a high level as that of general paralysis. In more chronic cases of disseminated sclerosis, and when the spinal cord is chiefly involved, the curve may be "luecic" in type. It is difficult to arrive at an exact estimate as to the percentage of cases of disseminated sclerosis giving a positive Lange reaction, since the actual clinical diagnosis is often uncertain. Our investigations at the West End Hospital for Nervous Diseases, however, show that in almost every case in which the clinical diagnosis is practically certain some change occurs in the colloidal gold curve. It is usually only in those cases in which the diagnosis is tentative, and therefore uncertain, that a completely negative result is found.

Following the examination of the cerebro-spinal fluid, we are able to confirm the diagnosis of obstruction in the spinal subarachnoid space—by a spinal cord tumour, for instance—and to localize its level accurately by the intrathecal injection of lipiodol and subsequent x-ray examination. Lipiodol is a heavy oily substance consisting of iodine in firm combination with oil of poppy; it is opaque to x rays, quite harmless, and very slowly excreted. Cisterna puncture is performed and 1 to 2 c.cm. of lipiodol injected. On reaching the subarachnoid space the lipiodol rapidly sinks down the spinal canal, and can be seen in the sacral region of a normal subject within half an hour. On the other hand, if the spinal canal is obstructed—for example, by a tumour—the lipiodol is held up at the level of the upper limit of the tumour. [Dr. Worster-Drought then exhibited x-ray films illustrating the value of lipiodol in the exact localization of spinal cord tumours. The first film showed the normal condition, the lipiodol being seen in the form of a tapering opacity, with its point downwards, at the upper end of the sacrum.]

In one case the diagnosis suggested an intramedullary spinal cord tumour; there was, however, no obstruction to lipiodol in the spinal canal, and subsequently the case proved to be one of syringomyelia with central pain.

In another case the lipiodol was held up at the level of the ninth thoracic vertebra, and subsequently an intramedullary tumour was removed from this situation.

A third case had been regarded as chronic sciatica, and the presence of a tumour was only suspected when the cerebro-spinal fluid, removed by lumbar puncture, was found to contain excess of protein but no increase in the number of cells. The lipiodol was seen to be held up, with a horizontal lower border opposite the body of the third lumbar vertebra, thus confirming a diagnosis of tumour of the cauda equina; an endothelioma was successfully removed by Mr. C. P. G. Wakeley.

A fourth case was remarkable. Clinically, the diagnosis was either syringomyelia or compression by tumour affecting the upper cervical region of the cord. On puncturing the cisterna magna no

flow of cerebro-spinal fluid occurred; it was obtained only after some difficulty, and 1 c.cm. of lipiodol was injected. In the x-ray film this lipiodol was seen not to have moved, but remained in the region of the foramen magnum. At operation a tumour was found actually compressing the lower part of the medulla.

During recent years much more attention has been paid to detail in radiography of the skull, and it is often possible to demonstrate the presence of a cerebral tumour. For instance, we sometimes find a general thinning of the bones of the skull due to increased intracranial tension. If the tumour is near the surface of the brain, as in the case of some meningiomas, we may see local erosion of the bone adjacent to the tumour. Also, the tumour itself may occasionally calcify—for example, glioma and tuberculoma—and so reveal its presence in the x-ray film. A further point is possible displacement of the pineal body. It has been shown that in about 60 per cent. of individuals the pineal body is calcified, and can be demonstrated on x-ray examination; its displacement to one side or the other may indicate the side on which the cerebral tumour lies.

A method recently introduced for the lateralization and possible localization of cerebral tumour is "air-ventriculography," in which the cerebro-spinal fluid in the cerebral ventricles is replaced by air. The lateral ventricle is punctured as follows. A point is taken about one inch above and one inch behind the external auditory meatus; with an ordinary bone drill a small hole is made in the bone, and a needle is inserted into the lateral ventricle, which lies at a depth of about two inches. Cerebro-spinal fluid flows as soon as the needle enters the ventricle. The fluid is gradually withdrawn and replaced by air by means of a special two-way tap joining the needle and a syringe. Care must be taken not to introduce more air than the amount of cerebro-spinal fluid withdrawn. Having completed the replacement on one side, the opposite ventricle is then dealt with. According to the changes in symmetry of the ventricles one can often lateralize the tumour, and sometimes localize it. Internal hydrocephalus is shown by symmetrical dilatation of both ventricles.

Another similar method of investigation known as encephalography consists in the introduction of air into the subarachnoid space through a needle inserted in the lumbar region. Personally, I do not favour this method, since it is easy to inject too much air, and the after-effects are often severe.

A further method is known as "ventricular estimation." The ventricles are punctured in the same manner as in air-ventriculography, and as much cerebro-spinal fluid as possible is withdrawn from each. The quantities of fluid from each ventricle are then carefully measured and compared. Normally, the amounts are approximately equal on the two sides; any pronounced difference indicates partial or complete obliteration of that ventricle yielding the smaller quantity of fluid, usually on the side on which the tumour is situated.

In hydrocephalus and in some cases of cerebral tumour the intraventricular injection of dyes may be of assistance. The substance phenolsulphonephthalein when injected is excreted in the urine, and an estimate is made of the quantity excreted in the first two hours following the injection. If this amount is small, some obstruction to the ventricular outflow is indicated.

I will now refer to a few of the conditions to which attention has been drawn during the past few years, and, first, to one which has been rescued from the heterogeneous group of epilepsies and is known as "pyknolepsy." This is a species of petit mal occurring in children; in it numerous attacks occur up to forty and even one hundred a day. It differs from ordinary epilepsy in that it is entirely resistant to treatment by bromides and luminal, and no intellectual deterioration occurs; also, it has the advantage that quite a good prognosis can be given, since the attacks entirely disappear in time. A second is "narcolepsy"—a condition in which I have for long taken a special interest. In the last few years many more cases have been reported, probably owing to the fact that attention has been drawn to the disease. The condition consists of two phases: (1) the narcoleptic attack, in which the patient falls asleep at any time and in any place; (2) the cataplectic attack, or cataplexy, which consists of a "crumpling-up"

—a sudden and general muscular hypotonia, occurring particularly when the patient laughs heartily or is emotionally disturbed. I am sure that if you bear the condition in mind you will meet with cases of this description. Treatment is very difficult, because we do not know the cause; a disturbance of the hypothalamic region of the brain—that part lying above the pituitary body—has been suggested. Having tried many forms of treatment, including bromides, thyroid and pituitary extracts, strychnine, and hyoscine, the only substance that seems of any help is caffeine given in full doses (caffeine 5 grains or caffeine citrate 10 grains) every four hours during the daytime.

Another disease of the nervous system described in recent years has been termed "Schilder's periaxial encephalitis." It is quite distinct from encephalitis lethargica, particularly as it affects only the white matter of the brain—hence the term periaxial—in contradistinction to encephalitis lethargica, which involves the grey matter. In its selection of the white matter Schilder's disease somewhat resembles disseminated sclerosis, but in this latter condition the sclerosis occurs only in patches, while in Schilder's encephalitis the degeneration of the white matter of the brain is diffuse. Gradually increasing blindness or deafness occurs, or insidious mental deterioration, according to the region of the brain affected; or gradual spastic paralysis, involving all four limbs owing to implication of the motor fibres; or we may see all the above symptoms occurring together.

A considerable amount of attention has recently been paid to head injuries, mainly on account of the work of Trotter, who has described a syndrome which is best termed "chronic cerebral contusion." This condition has undoubtedly in the past been confused with that of so-called traumatic neurasthenia. Sometimes even a comparatively slight head injury, which at the time causes a simple concussion or a localized trauma, may be followed by a characteristic group of symptoms. These include headache—usually paroxysmal—vertigo, insomnia, mental irritability, apprehension, and occasionally some impairment of memory. A feature of the headache is that it may not be experienced until the patient is up and about, and that it is made worse by changes in position such as stooping. This fact often helps to distinguish a contusion syndrome from a traumatic neurosis, since the headache complained of in the latter condition is usually constant, unvarying in intensity, and unaffected by changes in position. Further, in cerebral contusion a relatively slow pulse rate and a raised blood pressure may also be present. Another important point is that in every case of true concussion there is a period of retrograde amnesia preceding the accident—that is, the patient has no recollection of anything that occurred for the fifteen to twenty minutes preceding the head injury.

It must be borne in mind that most cases of cerebral contusion show no evidence whatever of fracture of the skull on clinical or x-ray examination. In head injuries the underlying soft structure (the brain) is far more likely to suffer than the hard bone, and it cannot be sufficiently emphasized that the brain may be very seriously damaged without any evidence of bone injury. In assessing the effects and possible consequences of head injuries far too much stress has been laid upon the radiographic appearance of the skull, and, if negative, the injury is often assumed to be slight, not only in legal but also in medical circles.

The pathology of chronic cerebral contusion is as follows. Quite apart from any laceration of the brain or compound fracture of the skull, the injury causes diffuse bruising, with serous exudation and petechial haemorrhages. The effect of such exudation is to cause an increase in the normal intracranial tension; on this the symptoms depend. This rise in intracranial tension can be confirmed by manometric reading of the cerebro-spinal fluid pressure taken through a lumbar puncture needle. One of the effects of increased intracranial tension is to embarrass the cerebral circulation by compressing the veins, which have a lower internal pressure than either the arteries or the capillaries. A localized cerebral contusion therefore becomes surrounded by an area of impaired circulation, which prevents absorption and removal of the exudate. A vicious circle is thus

formed which can only be broken by bringing about a lowering of the general intracranial tension. Such relief will allow the veins to dilate and the transudate to be absorbed. There are several methods of applying this treatment; probably the best and most direct is repeated lumbar puncture and the removal of the excess of cerebro-spinal fluid. Puncture may be performed every other day until the symptoms are relieved. Another method is the intravenous injection of hypertonic saline solution. The effect of the introduction of such a solution is to cause an active shrinkage of the brain by the absorption into the blood stream of its extravascular fluid contents and so lower the intracranial tension; 50 to 100 c.cm. of a 30 per cent. solution has been advised, but I prefer 50 to 75 c.cm. of a 15 per cent. solution. The effect of the injection is temporary, and it may have to be repeated at intervals of two or three days. An alternative method of cerebral dehydration is the oral administration of large amounts of magnesium sulphate; 3 ounces of a 50 per cent. solution is the dose given. The magnesium sulphate solution can also be given rectally (6 ounces of a 50 per cent. solution), or, if this is too irritating, 8 ounces of a 25 per cent. solution.

As one of the striking advances in treatment may be cited the malaria treatment of general paralysis. Provided cases are obtained in a sufficiently early stage, arrest and even improvement result in the majority of patients. I first used this method of treatment in 1923, and several of my patients treated that year are still progressing satisfactorily. The technique is comparatively simple, and there are two methods: the patient can either be injected with blood (2 c.cm.) from another patient while the latter has malaria, or he can be exposed to the bite of a malarial mosquito. Personally, I prefer the blood injection method. With the mosquito-induced method the malaria starts with a period of irregular pyrexia, and one is often uncertain when rigors actually begin; moreover, it is most exhausting for the patient and more difficult to control. The number of rigors allowed is usually ten to twelve—that is, if the patient develops a tertian ague. Often, however, he develops a quotidian form—that is, a rigor every day. In these circumstances one can seldom allow more than eight rigors. Following the cessation of malaria, the patient is given six injections of novarsenobillon at intervals of ten days, and apparently no further treatment is necessary, unless the patient relapses; in this case a second course is sometimes given. A remarkable fact is that malaria is the only treatment that has produced a negative Wassermann reaction in the blood and cerebro-spinal fluid in cases of general paralysis, but this does not occur until after the elapse of two or three years from the termination of the malarial treatment.

A great problem at present awaiting solution is the treatment of encephalitis lethargica. I think I have tried every form of treatment advocated, and have reached the conclusion that the best for acute and subacute cases is the intravenous injection of sodium salicylate, or sodium salicylate combined with glucose; 30 c.cm. of a 2.5 per cent. solution of sodium salicylate is given once or twice daily, and continued until the patient improves.

The chronic stage—and especially when accompanied by myoclonus or a Parkinsonian syndrome—is even more difficult to treat; some degree of relief only is possible. In most cases improvement can be maintained by giving hypodermic injections of hyoscine hydrobromide in gradually increasing doses—up to 1/50 grain three times daily. So frequent hypodermic medication, however, is difficult to arrange outside an institution, and it also becomes irksome for the patient. Unfortunately, the effect of hyoscine orally administered in no way compares with that when the drug is given hypodermically; it would indeed be a boon if some substance were forthcoming which when taken by the mouth gave an equally good result. Quite recently, at the post-encephalitis unit of the Metropolitan Asylums Board, we have tried a drug known as harmine, but after an extensive trial it did not give satisfaction—either by the mouth or injected—excepting in the possibility of its controlling the respiratory disorders that occasionally accompany chronic encephalitis. We are now obtaining more hopeful effects, however, with dried stramonium, but it is too early to report any definite results.