SURGICAL ASPECTS OF MENINGITIS*

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There is general agreement that in the last 50 years adequate surgical treatment of infections of the middle ear and mastoid has greatly reduced the incidence of meningitis and other intracranial infections. This can be confirmed by comparing cases of the present day with those described by William MacEwen in his classic work, *Pyogenic Infective Diseases of the Brain and Spinal Cord*, published in 1893. Similarly, improved surgical cleansing and suture of open wounds of the head have effectively prevented many cases of meningitis. These facts are so well known that all that is necessary here is to remind ourselves what a valuable procedure it can be to release pus from the ear by prompt incision of the ear-drum or to spend time on careful treatment of the simple scalp wound.

Historical

Horsley (1890) seems to have been the first in modern times to operate for meningitis; a year before lumbar puncture was introduced he established continuous drainage of the cerebrospinal fluid (C.S.F.) through a laminectomy wound; and he also irrigated the subarachnoid space with weak bichloride of mercury. About the same time Mayo-Robson (1890) and others drained the lateral ventricles. These pioneer efforts were important for the development of neurosurgical technique, but did not save lives.

Surgical methods were employed for three main purposes: (1) the application of antiseptics and antisera; (2) drainage of C.S.F., continuous or intermittent; and (3) irrigation of the cerebrospinal pathways with "physiological" fluids. The only antibacterial substance whose use seems to have been attended by any success was Flexner's meningococcal antiserum. It was introduced into the lateral ventricles (Cushing and Sladen, 1908) and later, with more success, into the cisterna magna (Ayer, 1920): the advantage claimed for these routes over the usual lumbar route was that the serum might more easily spread to all parts of the cerebrospinal pathways, especially when there was a spinal block.

Dandy (1924) concluded that antiseptics were of no value for pyogenic meningitis, but wrote: "Despite past and present failures, one cannot but feel that the future treatment of septic meningitis may yet lie in antiseptics or sera. Though seemingly impossible from our present knowledge, the detection of a specific antiseptic or of a specific serum so accurately balanced as to be without injury to the naked nervous system seems no more unlikely than Flexner's remarkable antimeningococcal serum, or the recent brilliant discovery by Sicard that lipiodol could be injected into the subarachnoid space, cast a dense shadow, and still be harmless to the delicate host."

Continuous drainage from the cisterna magna or lumbar subarachnoid space was tried by a number of workers (Dandy, 1924; Spurling, 1928; Thompson, 1937), while a few favoured continuous ventricular drainage, particularly when hydrocephalus was developing (Hampson, 1935). The reasons advanced for drainage were: to provide exit for the inflammatory products; to reduce intracranial pressure; and to promote increased flow of C.S.F. and thus to dilute the toxins. Kubic (1928) advocated that during drainage large amounts of hypotonic fluids should be given by vein or subcutaneously, as well as water by mouth, to promote the flow of C.S.F.

Irrigation with Ringer's solution was tried—from lumbar region to cisterna magna (Murphy, 1907), from ventricles to the lumbar subarachnoid space (Day, 1913), and from cortical subarachnoid space to cisterna magna (Eagleton, 1921)—but without any clear evidence of benefit; though Hampson (1935) mentioned a case in which, after blocking at the foramen magnum by presumed tonsillar cone, the flow of C.S.F. was re-established by instilling fluid into the lumbar space under positive pressure while intracranial pressure was reduced by ventricular drainage.

In small groups of cases good results were reported after the use of one or more of these methods, and in meningococcal meningitis the results in larger series indicated a modest improvement on what had been obtained before (Ayer, 1920; Hampson, 1935; Tripoli, 1936). However, the "surgical" methods were not generally adopted, and their use in acute meningitis was largely abandoned as soon as sulphonamides showed their worth—an event which indicates that the subject of meningitis is dominated by bacteriological considerations and that surgical methods can play but a subsidiary part. Destroy the bacteria, and the inflammatory products and toxins can be looked after by the meninges without drainage of the C.S.F. or irrigation of its pathways.

Since the advent of penicillin in 1942 there has been a revival of surgical methods of treatment; for penicillin does not pass the blood-C.S.F. barrier in sufficient amount, and thus must be directly introduced. Surgical methods have also proved their worth in the application of streptomycin; though in the case of this drug it is difficult to understand why the intrathecal route should be necessary, as it clearly is, since good levels of streptomycin in the C.S.F. can be obtained by intramuscular administration alone.

Post-operative Meningitis.—The interests of the neurosurgeon in meningitis develop naturally from his concern to prevent meningitis after head wounds or "clean" operations such as removal of cerebral tumour. When the first cerebral glioma was removed by Godlee in 1884, "a slow

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infection of the wound occurred, and after four miserable weeks of disappointed hopes the patient died of meningitis" (Trotter, 1934). At one time in my practice one-quarter of the operative deaths were from intracranial infection, in particular from meningitis (Cairns, 1939b). The local application of penicillin before closure of the wound has reduced the incidence of infection in our major cerebral and spinal operations from 4.4 to 0.9% (Pennybacker *et al.*, 1947). This subject need not be considered in detail, but there are a few points of general application.

Pathology and Anatomy of Meningitis

I do not propose to describe the pathological anatomy of meningitis, but rather to touch upon some aspects of it which arise from surgical experience.

I. The Resistance of Brain Tissue to Infection

From our work on operative infections we concluded that the brain itself is relatively resistant to bacterial infection, whereas the large cerebrospinal pathways—the ventricles and basal cisterns—are much more prone to become infected.

1. Culture plates exposed in the operative field always yielded bacterial growth and showed that even with the most careful aseptic technique it is impossible to prevent bacterial contamination of the wound during long intracranial operations (Cairns, 1939b).

2. On occasions cocci have been seen in films and cultures of material aspirated from the bed of a cerebral tumour in the first days after operation, yet no sepsis has developed.

3. In the days before penicillin the incidence of infection after posterior fossa operations was 1 in 12, all of them cases of meningeal infection, whereas after operations on the cerebral hemispheres it was 1 in 30, and the majority of these were infections of the bone and scalp (Pennybacker *et al.*, 1947). In other words, most of our cases of intra-cranial infection have been cases in which there was a wide opening of the arachnoid cisterns or ventricles, though it is likely that just as many bacteria fell into the brain tissue as into the cerebrospinal spaces.

The relative resistance of the brain tissue, which may be due to the speed with which large numbers of microglial phagocytes gather at any injured part of the brain, may account for the remarkable freedom of the brain tissue from gross infection in many forms of non-surgical leptomeningitis. In pyogenic meningitis bacteria often get into the brain as well as into the leptomeninges; for example, in pneumococcal meningitis they can be seen at necropsy in the brain tissue itself beneath the pia-arachnoid and around the walls of the ventricles, yet in the cases which survive an early death abscess within the brain is an event of great rarity. Furthermore, drainage or excision of an abscess of the cerebral hemisphere is rarely followed by meningitis, although the brain must often be contaminated at the time of operation.

It is astonishing to see what a perfect intellectual recovery can often follow the most intense meningitis. In most bacterial infections of the leptomeninges it seems as though the brain looks after itself. Indeed, as regards subsequent brain function the complication most to be feared is arteritis of the penetrating vessels, with resultant cerebral infarction, rather than any purulent cerebritis (Cairns and Russell, 1946; Daniel, 1949).

II. "Saprophytic" Bacteria May Produce Meningitis

From our operative infections we have also learned that bacteria which are supposedly saprophytic to man may set up severe and even fatal meningitis and ventriculitis (Cowan, 1938); such organisms as *Micrococcus tetragenus*, *Diplococcus mucosus*, *achromobacter*, *Staphylococcus albus*, and

certain Gram-negative bacilli. In these infections the general symptoms may at first be slight, and so also is the cellular reaction in the C.S.F. But the meningitis is of an *adhesive* type: it blocks the cerebrospinal pathways and thus produces progressive hydrocephalus, perpetuating the lesion for which operation was undertaken in the first instance. This slow progressive post-operative meningitis has become less common since the introduction of antibiotics, a point confirming its bacterial origin, for some were wont to regard it as "aseptic meningitis."

The condition is important in adding to our understanding of certain cases of spontaneous progressive hydrocephalus of infective or probably infective origin (Dott and Levin, 1936). In these cases there is often no initial acute illness or obvious history of meningitis, and the case may masquerade as non-infective hydrocephalus. But in her important review of the pathology of hydrocephalus Dorothy Russell (1949) has shown that at least some of them are of bacterial origin.

III. The Influence of Raised Intracranial Pressure

In the acute stage of any form of meningitis intracranial pressure is raised. This rise of pressure is not usually an important cause of symptoms in the early stage—that is, before there has been time for adhesions to form—though it may become so later. In tuberculous meningitis we tried continuous drainage of the lateral ventricles in the acute stage in the hope of lessening the coma and other severe symptoms. There was no improvement; Dandy (1924) had the same experience on draining the cisterna magna in acute purulent meningitis.

In tuberculous meningitis we also found that withdrawal of the ventricular C.S.F. at its source was immediately followed by a very great rise of the protein content of the lumbar C.S.F. (from 100 to 4,000 mg. per 100 ml.) (Fig. 1) and an unusually early deposit of fibrin in the cisternae ambienae and interpeduncularis. Evidently, if C.S.F. is to be drained away in the acute stage of meningitis it should, if possible, be taken from the site of maximum inflammation and not from the ventricles. The diluting action of the newly formed ventricular fluid with its small protein content is probably useful in preventing deposition of fibrin and pus, with blockage of the cerebrospinal pathways. I must emphasize that these conclusions relate only to the acute stage: ventricular drainage may be of great value in the subacute and chronic stages of meningitis.

FIG. 1.—Two cases of tuberculous meningitis, showing rise of protein in lumbar C.S.F. following continuous drainage of lateral ventricle.

IV. Blockage of the Cerebrospinal Pathways

Any part of the cerebrospinal pathways may become blocked in meningitis, but this is not serious unless it affects the main bottlenecks and thus interferes with the onward flow of the bulk of the cerebrospinal fluid. The blockage may be due to fibrin and inspissated pus or to granulation

tissue in various stages of organization, and symptoms may arise during the stage of active infection or subsequently. In the latter case the stage of active infection may have been inconspicuous, or it may have occurred many years before the onset of symptoms of obstruction. Thus, Baker (1934) reported a remarkable case of death from hydrocephalus after three weeks' illness in a girl of 17

who had had meningococcal meningitis at the age of 18 months.

X-ray studies after air injection have enabled the site of obstruction to be determined with precision (e.g., Smith *et al.*, 1948, Figs. 5 and 6). Dyes have also been used, and we have found the use of antibiotics as trace substances convenient and helpful.

FIG. 2.—Sites of obstruction of cerebrospinal pathways. (1) Foramen of Monro; (2) aqueduct of Sylvius; (3) foramen of Magendie (and foramina of Luschka); (4) cisterna ambiens; (5) spinal subarachnoid space.

The main sites of obstruction are: (1) foramen of Monro, (2) aqueduct of Sylvius, (3) foramina of Magendie and Luschka, (4) cisterna ambiens, and (5) spinal canal. (Fig. 2.) It is possible also that obstruction as a result of meningitis might take place at the arachnoid granulations alongside the venous sinuses, but we have not obtained any convincing proof of that.

At the first three sites mentioned obstruction prevents the escape of C.S.F. from the ventricular system, with the result that there is little C.S.F. in the lumbar subarachnoid space, and the spinal pressure may fall. Dyes or antibiotics injected into the ventricles cannot be detected in the spinal C.S.F., and passage in the reverse direction is also blocked. These obstructions give rise to what Dandy (1918) called "obstructive hydrocephalus." On the other hand, if the obstruction is in the cisterna ambiens at the tentorial opening, C.S.F. escapes from the ventricular system and distends the infratentorial basal cisterns and distal subarachnoid space, but cannot reach the subarachnoid space over the cerebral hemispheres whence it is absorbed. There is then abundant fluid on lumbar puncture, and dyes or antibiotics injected into the ventricles pass freely into the spinal C.S.F. This condition Dandy termed "communicating hydrocephalus."

Obstruction of the spinal subarachnoid space does not interfere seriously with the circulation of the C.S.F. or cause rise of intracranial pressure, but it is important in preventing antibiotics administered by the lumbar route from reaching the cerebral subarachnoid spaces and ventricles. Spinal block can be easily studied in life, and thus provides us with an indication of the course of subarachnoid obstructions in general.

From daily lumbar puncture in our cases we have learned that the obstruction may be incomplete; that it may disappear within 24 hours or last several weeks or even longer; and that there is a strong tendency for it to disappear long before all the inflammatory granulation tissue has resolved.

V. Foraminal Herniations of Brain Substance

In the obstructions which produce rise of intracranial pressure a complicating factor is introduced by herniation of parts of the brain through foramina, such as the foramen magnum and the tentorial opening. These obstructions have been mainly studied in relation to intracranial tumours (Spatz and Stroescu, 1934; Vincent *et al.*, 1936; Jefferson, 1938; Cairns, 1939a), but the same factors may operate in meningitis (Hampson, 1935). When the lateral ventricles are dilated the hippocampal gyri tend to be displaced into the tentorial opening (Fig. 3) and thus may convert a partial obstruction of the cisterna ambiens into a complete one. When the foramina of Magendie and Luschka are obstructed the fourth ventricle dilates, with displacement downwards of the cerebellar tonsils through the foramen magnum (Fig. 4), thus perhaps converting a partial block into a complete one, or adding yet more compression upon

FIG. 3.—Downward herniation of temporal lobe through the tentorial opening.

FIG. 4.—Downward herniation of cerebellar tonsils through the foramen magnum.

FIG. 5a.—Upward herniation of cerebellar vermis through tentorial opening in a case of communicating hydrocephalus due to occlusion of the cisterna ambiens by tuberculous granulation tissue.

FIG. 5b.—Normal tentorial opening. For comparison.

the adjacent medulla oblongata; or the cerebellar vermis may be displaced upwards through the tentorial opening, adding obstruction of the subarachnoid bottleneck around the midbrain to the already existing obstruction at the exits of the fourth ventricle. This type of obstruction is also seen in communicating hydrocephalus from obstruction of the cisterna ambiens (Figs. 5a and 5b).

These additional obstructive factors may operate intermittently, with corresponding fluctuations in the clinical state of the patient. At an early stage the brain herniation can be relieved by one or more ventricular tapplings, and the patient may thus be tided over a dangerous period of obstruction. At a later stage the herniated brain may become impacted and then, though dangerous symptoms may be circumvented by continuous ventricular drainage, the patient usually dies from compression of the brain stem. Death is often quite sudden, the clinical events leading up to it being inconspicuous.

VI. Relapse

Relapse has long been recognized as a feature of meningococcal meningitis, and since other varieties of meningitis have been brought under control by sulphonamides and antibiotics they also have been shown to relapse. Thus it has been seen at Oxford in a high proportion of cases of pneumococcal meningitis (Smith *et al.*, 1946a), in meningitis due to *Pseudomonas pyocyanea* and other Gram-negative saprophytes (Lewin and Vollum, 1948), in tuberculous meningitis (Cairns and Taylor, 1949), and in influenzal meningitis (Neligan and Ounsted, 1949—personal communication).

Relapse or recurrence of meningitis may be due to infection from without, as in certain cases of chronic pneumococcal infection of the petrous bone and overlying dura, or to repeated infections through fractures involving the

paranasal sinuses with tearing of the overlying dura. More commonly it is due to recrudescence of an infective focus within the central nervous system. These foci are minute abscesses, or collections of fibrino-purulent material containing bacteria in the subarachnoid space (Smith *et al.*, 1946a, Fig. 3) or within the lateral ventricle (Fig. 6); or, in the case of

FIG. 6.—Fibrino-purulent clot containing Gram-positive cocci, in posterior horn of lateral ventricle in a case of pneumococcal meningitis after head injury. The patient was recovering from his first attack of meningitis, when he died of traumatic fat embolism.

tuberculous infection, fibrino-caseous material containing bacteria in the meninges or brain (Fig. 7).

The power of antibiotics to penetrate such non-vascular areas of infection is very limited, and the appropriate antibiotic must therefore be maintained in the C.S.F. until the fibrinous area has been completely absorbed, with release of all its bacteria, or until the lesion has become organized or enclosed in dense fibrous tissue, as may happen in tuberculous meningitis. This principle is important in the treatment of all cases of meningitis which are prone to relapse. In tuberculous meningitis, a disease which under treatment runs a very slow course, streptomycin must be maintained in the C.S.F. for many months.

FIG. 7.—Fibrino-caseous material containing numerous acid-fast bacilli in cisterna ambiens. From a case of tuberculous meningitis which was fatal on the 70th day of streptomycin treatment. (Diagram by Dr. Dawn Bosanquet.)

The Part of Surgical Operations in Meningitis

Operative procedures may be undertaken in connexion with meningitis for the following reasons: to prevent meningitis, to assist in rapid diagnosis of meningitis and of some of its complications, for the introduction of antibiotics, and to relieve or circumvent obstruction of the cerebrospinal pathways and the associated rise of intracranial pressure.

Prevention of Meningitis

The importance of prompt surgical treatment of scalp wounds and infected ears has already been mentioned. During the recent war, as a result of segregation and follow-up of Service patients with head injuries, we learned that meningitis was more common after head injury than we had formerly thought, and especially after fractures of the anterior fossa. Further evidence on this point was forthcoming when patients with pyogenic meningitis began to recover as a result of penicillin treatment. Five of our first 38 cases of pneumococcal meningitis followed head injury.

Case Report

A man aged 44 (No. 20301/43) was admitted in a confused but not comatose state to the Radcliffe Infirmary on Dec. 17, 1943, on the third day of an attack of pneumococcal meningitis. He was treated with penicillin intrathecally and intramuscularly and made a prompt recovery. By Dec. 27 he was lucid, and neurological testing showed severe hyposmia, which he said dated from a head injury due to a motor-cycle accident some seven years before. Inquiries revealed that at that time he had had a bruise on the left eye and temple with epistaxis, but no fracture had been seen in the radiographs, and there had been no leakage of C.S.F. from his nose.

The story suggested that his meningitis might have resulted from bacterial infection through an old fracture involving the paranasal sinuses. Radiographs taken after he had recovered from the meningitis showed no definite signs of an old fracture, but it was thought that there might be a deficiency in the posterior wall of the left frontal sinus. At operation on Feb. 15, 1944, the left side of the anterior fossa was explored intradurally through a frontal osteoplastic flap. No abnormality was found in the dura over the left frontal sinus, but further back, over the ethmoidal sinus region, there was a smooth-edged cleft (1 by 0.3 cm.) in the dura into which passed a diverticulum of arachnoid of the inferior surface of the left frontal lobe (Fig. 8). This was evidently the remains of a brain herniation through a dural tear and fracture at the time of the head injury seven years before, but all that it now contained was a leash of small blood vessels and some C.S.F. When the vessels had been divided and the sleeve of arachnoid had been detached from the bone it was possible to pass a probe down into the ethmoidal sinus. The cleft was closed with a graft of temporal fascia.

The patient made an uneventful recovery and returned to work in April, 1944. During the next five years, up to the time of his last report in February, 1949, he had remained well and at work, though suffering occasionally from headaches.

FIG. 8.—Dural tear and fracture into the left middle ethmoidal sinus. Repaired with graft of fascia lata.

I have seen meningitis develop at all stages between one day and 10 years after fractures of the anterior fossa involving the paranasal sinuses, with tearing of the overlying dura. Thus no one with an unclosed dural tear over a fractured ethmoid or frontal sinus can be regarded as safe from this risk. The meningitis, usually pneumococcal, may follow a cold in the head, but often it comes when the sinuses are not infected. In certain cases it is easy to predict the presence of a dural tear: cases with persistent cerebrospinal rhinorrhoea or with intracranial aerocele after head injury (Cairns, 1937), or cases like that just described in which there has already been one attack of meningitis. But there are other patients with anterior fossa fracture and loss of smell, but no rhinorrhoea or aerocele, who will get meningitis at some future time if a dural repair is not carried out. Much work was done on these cases during the war (Cairns, 1942; Calvert, 1942, 1947; Stewart and Botterell, 1947; Johnson and Dutt, 1947). Successful diagnosis depends largely on the radiographic evidence of fracture lines across the anterior fossa, and interpretation of these is still very difficult.

Fractures of the middle cranial fossa may establish a connexion between the middle ear and the subarachnoid space and thus give rise to meningitis, with or without escape of C.S.F. from the ear. In these injuries, other than those due to gunshot wounds, meningitis usually arises within the first few weeks if at all. In blunt injuries the path between ear and brain usually closes spontaneously. But after gunshot wounds operative dural repair may be necessary (Johnson and Dutt, 1947).

While on the subject of meningitis after head injury I must mention an uncommon complication which requires urgent surgical intervention. In a few cases the escape of C.S.F. from the nose may be so profuse that it is impossible to maintain an adequate level of penicillin in the C.S.F. by the usual intrathecal dosage. If meningitis has already begun in such a case it may be necessary to give penicillin by lumbar puncture twice or thrice daily in the usual doses and to operate to close the C.S.F. leak immediately the acute stage of the meningitis has been overcome.

Diagnosis of Meningitis

Ventricular estimation and ventriculography are sometimes important in diagnosis. Now that there is an effective treatment for most varieties of meningitis, early diagnosis has become a matter of great importance. The advice of Goodhart and Still (1913) on the diagnosis of tuberculous meningitis—to wait for the disease to declare itself—is no longer sound. Every hour of delay in applying the appropriate antibiotic intrathecally seriously diminishes the patient's chances of recovery. To arrive at the correct

diagnosis there is no need in most cases to employ operative methods; all that is required is lumbar puncture and bacteriological examination of the C.S.F., the whole procedure being carried through with all the sense of urgency that would be applied to the investigation and treatment of a patient with perforated duodenal ulcer. But in some cases the diagnosis cannot be quickly solved without the use of ventricular estimation or ventriculography.

For example, if the meningitis begins with focal symptoms and raised intracranial pressure, as it may occasionally do in both tuberculous and pyogenic meningitis, there may be need to exclude the presence of tuberculoma or brain abscess; for in the presence of a space-occupying lesion intrathecal injections of antibiotics may so alter the intracranial pressure as to precipitate catastrophic herniations of the brain. Streptococcal meningitis seems to be particularly dangerous in this respect, since it often coexists with a brain abscess whose symptoms are masked by the presence of meningitis (Smith *et al.*, 1946b); these cases must be distinguished from those in which meningitis and ventriculitis are the terminal events following rupture of a brain abscess into the ventricle.

There are also the cases in which the association of running ears with meningitis arouses suspicion that the meningitis is secondary to a brain abscess. There is yet another group of cases in which rapidly growing gliomas alongside the ventricles or basal cisterns may produce pleocytosis of the C.S.F., drowsiness, headache, and vomiting, and so simulate tuberculous meningitis. Red herrings are strewn across the path of clinical diagnosis in meningitis no less than in other diseases. By clinical methods, given time, they can be recognized for what they are; but time is not to spare.

The doubts and difficulties can be promptly solved by tapping the lateral ventricles. If both ventricles yield abundant C.S.F. it is safe to assume that there is no space-occupying lesion in the cerebral hemispheres (ventricular estimation): if the result of ventricular tap is equivocal there should be no hesitation in injecting air for ventriculography. We have used this method on many occasions in cases of acute meningitis and suspected meningitis and can report nothing but good from its use. It does not seem to upset the patient or aggravate the meningitis, whether tuberculous or pneumococcal. If there is no evidence of a space-occupying lesion the appropriate antibiotic can be promptly given by lumbar or ventricular route. And if a brain abscess is revealed, prompt evacuation or removal of the abscess combined with intrathecal chemotherapy may be life-saving.

Burr-holes for ventricular studies may on occasions disclose some unsuspected condition in the subdural space. In one case of very severe pneumococcal leptomeningitis burr-holes for the introduction of penicillin into the ventricles disclosed free pus in the subdural space, which was thereupon treated by local instillations of penicillin through an indwelling rubber catheter (Cairns and Russell, 1946, Case 5). In another case, of an infant with pneumococcal meningitis who could not retain penicillin in her C.S.F. for more than a few hours after lumbar injection of the usual amounts and thus could not get rid of her meningitis, burr-holes revealed a large subdural hydroma into which the subarachnoid penicillin was shown to be leaking (Smith *et al.*, 1946a, Case 8). After the subdural hydroma had been drained the arachnoid leak evidently closed, for the patient regained the power of retaining penicillin in her subarachnoid space and then her pneumococcal meningitis promptly subsided.

It was from this case that we learned that there is no barrier to the passage of penicillin from blood stream to subdural space, or in the reverse direction, as there is

between blood stream and C.S.F. The dura and subdural space behave like somatic tissues. This fact has since been repeatedly confirmed by studying the transmission of penicillin from the blood stream to subdural haematoma (Schiller *et al.*, 1948).

The cases which I have cited in this section are uncommon ones, and ventricular studies are not often needed in diagnosis of meningitis. But they may be required urgently in any case, and no hospital can regard itself as fully equipped to diagnose meningitis unless it has neurosurgical facilities readily available.

There is one further point: bacteriological diagnosis of the type of meningitis may sometimes be obtained from the ventricular fluid when repeated examination of the spinal fluid has failed. This applies especially in tuberculous meningitis, though in most forms of pyogenic meningitis also the organisms are abundant in the ventricular fluid.

Introduction of Antibiotics by Surgical Operation

(a) Into the Lateral Ventricles

In our first cases of pneumococcal meningitis to be treated with intrathecal penicillin, early in 1943, the ventricular route was used; but we soon found that penicillin injected into the lumbar subarachnoid space spread quickly into the ventricles "against the flow," and also into the cerebral subarachnoid space (Cairns *et al.*, 1944). Thereafter the lumbar route was used routinely, the ventricular route being reserved for those cases threatened with spinal block. The signs of impending block have already been described (Smith *et al.*, 1946a), and subsequent experience has strengthened our belief that, whenever there is suspicion that penicillin injected into the lumbar subarachnoid space is not spreading freely to all parts of the cerebrospinal pathways, frontal burr-holes should be made for tapping the anterior horns of the lateral ventricles. When the earlier impure preparations of penicillin were injected into the lateral ventricles they occasionally produced a reaction, but nothing of importance seems to attend the injection of the crystalline preparations in the usual dose (for adults, 10,000–20,000 units).

The *cisternal route* can be equally effective in cases of spinal block, but when there is severe head retraction or restlessness it may be difficult or dangerous; and we have observed a greater liability to severe reaction to antibiotics—stupor, pin-point pupils, incontinence of faeces—from cisternal than from ventricular injection.

In tuberculous meningitis the ventricular route for streptomycin has proved of great value in a small proportion of the cases, particularly in those in which the daily lumbar puncture becomes difficult. For a variety of reasons, which have been described elsewhere (Cairns and Taylor, 1949), we believe that, though they may not prove necessary, it is nevertheless an advantage to make frontal burr-holes at the beginning of streptomycin treatment in all cases of tuberculous meningitis.

These burr-holes are useful for other purposes than diagnosis and therapy: by ventricular estimation, supplemented at a later date by ventriculography, something can be learnt of the condition of the lateral ventricles in meningitis. At the beginning of pneumococcal meningitis the ventricles are smaller than normal, but within a few days they become slightly larger than normal. In tuberculous meningitis the ventricles are usually already dilated by the time there are signs of meningitis—a fact which suggests that the initial stages of this disease are relatively symptomless.

We learn from ventricular studies that there is always some progressive dilatation of the ventricles in meningitis, even in cases which show little or no sign of obstruction and no appreciable sign of brain damage.

(b) Into the Chiasmal and Adjacent Cisterns

In tuberculous meningitis the main deposit of granulation tissue is found at necropsy in the interpeduncular space, cisterna ambiens, cisterna chiasmaticus, and the adjacent sylvian fissures. These spaces are continuous with one another, and obstruction of the cisterna ambiens by fibrin or granulation tissue is likely to interfere with the spread of streptomycin, whether administered by the ventricular or by the lumbar route, to the more rostrally placed cisterns and to the sulci of the cerebral hemispheres. Therefore we have tried the effect of administering streptomycin direct into the chiasmal cistern through indwelling polythene tubes. Under local analgesia a small frontal flap is turned and the chiasmal region is exposed by lifting up the frontal lobe, and tubes are passed into the interpeduncular space and towards each sylvian fissure. Streptomycin solution (500 to 1,000 μ g. per ml.) is instilled through the tubes two to four times daily in amounts up to 6 ml. at a time for 10 days. Streptomycin levels in the fluid from the tubes at the end of six hours have usually ranged from 20 to 40 μ g. per ml.

We have used this method in seven patients, all but one of whom were infants or children. In one other case the tubes were inserted into the cisterna ambiens through a subtemporal approach, but very little fluid could be obtained from that cistern and the method seemed inferior to the chiasmal approach. Of the eight patients three made excellent recoveries and five died. In four of the patients, including one who recovered, the cisterns were already filled with organizing granulation tissue, and the tubes were probably of little use. The two best cases were those of an infant aged 20 months with intense infection and many positive films and cultures, and a boy of 9 years, both operated on about the eleventh day of symptoms, which was earlier than the others. In both cases abundant fluid escaped from the tubes in the intervals between streptomycin instillations.

The protein and cell content of the fluid from the interpeduncular region was always high, and in all except one case, in which there was a complicating spinal pachymeningitis, it was higher than that of the lumbar and ventricular fluids. For example, in one case, that of an infant of 8 months operated on on the fifteenth day of illness, samples of fluid obtained almost simultaneously showed:

	Protein (mg. per 100 ml.)	White Cells (per c.mm.)	Mycobacterium tuberculosis
Ventricular	40	62	—
Lumbar	130	98	++
Interpeduncular ..	1,000	175	++

It seems reasonable to conclude that from an early stage the most intense disease is in the interpeduncular and adjacent cisterns.

I have no evidence as yet that this method of administering streptomycin improves the recovery rate. If the cisterns are already solid with fibrin and granulation tissue it cannot be effective. On the other hand, if the cisterns are patent, streptomycin administered by the lumbar or ventricular routes should reach all parts and therefore there should be no need for interpeduncular application. Yet, since the protein content of the C.S.F. in the interpeduncular region is so high, continuous drainage of the fluid from that region for some days might be advantageous. This remains to be proved. From the experience to date we are satisfied that the method can be carried out without harm even in young infants who are seriously ill.

(c) Into the Subdural Space

In purulent pachymeningitis there is free pus in the subdural space and the condition is usually due to streptococcal infection, rarely β -haemolytic forms, and is secondary to spreading osteomyelitis of the skull following pansinusitis. The leptomeninges are often not infected until the terminal stages. Sometimes, however, the condition may accompany or follow leptomenigitis. The clinical picture is a sharply defined one, now modified, though not usually to an unrecognizable extent, by penicillin (Schiller *et al.*, 1948; Cairns and Schiller, 1948). Before the introduction of penicillin we treated 18 patients with this disease, and all died. Since early in 1943 ten cases have been treated with penicillin by the systemic, subdural, intraventricular, and subarachnoid routes, and seven recovered. In view of the fact that penicillin passes freely from the blood stream to the subdural space, it should theoretically be possible to treat this condition by the intramuscular route alone. But so far in practice it has proved necessary to instil penicillin solution into the subdural space at frequent intervals for several days through an indwelling catheter. One of the advantages of this method may be to prevent the formation of loculated subdural abscess, which is a common and dangerous complication.

Obstruction of C.S.F. Pathways with Rise of Intracranial Pressure, and their Treatment

There are two varieties of obstruction to consider: (i) obstruction by inspissated pus or granulation tissue which arises while the infection is still active, and (ii) obstruction by fibrous adhesions which comes on after the infection has subsided, sometimes years later. In addition the effects of these obstructions may be intensified by herniations of brain tissue, which have already been described. In general, treatment of obstructions in the purulent stage of meningitis should be by intermittent or continuous drainage of C.S.F., open operations being reserved for the cases which have reached the stage of fibrous adhesions and clear C.S.F.

It will be convenient to consider the obstructions according to site, but first some general remarks must be made on the question of diagnosis. In a case of acute meningitis which is not progressing favourably frontal burr-holes should be made. The onset of obstruction should be suspected from changes in the pressure and content of the ventricular and lumbar fluids. If pressures are rising and the lumbar fluid is still abundant, it is probable that there is blockage at the cisterna ambiens. If the lumbar fluid is scanty the hydrocephalus may be due to obstruction at the foramina of the fourth ventricle. Further information can be obtained from observing the spread of antibiotics. For example, if the fourth ventricle is obstructed an antibiotic injected into the lateral ventricle cannot be detected in the spinal fluid two to six hours later; or the test may be applied in the reverse direction. To be sure, the patient will already be having the appropriate antibiotic before the test is required, but with forethought doses can usually be so spaced that a satisfactory test situation is provided. If not, then a different antibiotic can be used as the test substance: for example, penicillin in tuberculous meningitis (Smith and Daniel, 1947).

In infants ventricular punctures can be made through the anterior fontanelle, which also serves as a useful guide to the state of intracranial pressure. In children the degree of separation of the cranial sutures as shown by radiographs is a reliable guide to the onset and course of hydrocephalus.

The onset of ventriculitis is apparent from the rise of protein, and usually also of cells, in the ventricular fluid.

The site of obstruction can be determined precisely only by ventriculography or encephalography. With skill in its manipulation a relatively small amount of air will suffice. In meningitis that is chronic from the start air studies should usually be made at an early stage of the investigations.

1. Foramen of Monro

Dott (1927) has described a case of unilateral hydrocephalus following fibrous obstruction of one foramen of Monro in an infant, due to an inflammatory process of infective origin, though there was no previous history of meningitis. The obstruction was successfully relieved by making a hole in the septum lucidum so that all fluid from both ventricles drained away through the healthy foramen of Monro of the opposite side.

There is another variety of obstruction of the lateral ventricle which we have observed after penetrating wounds of the body of the lateral ventricle (Cairns, *et al.*, 1947) and which Dorothy Russell (1949) has seen after haemorrhage at birth. A septum forms between the roof and floor of the ventricle, closing off a part of the ventricle which contains choroid plexus, with the result that there is progressive hydrocephalus of that part of the ventricle. I know of no evidence that it may follow meningitis, but it is possible that it might do so. It is important to recognize this condition, since it is easily cured by removing the choroid plexus in the obstructed part of the ventricle.

2. Aqueduct of Sylvius

If a patient with purulent ventricular fluid begins to deteriorate, with rise of ventricular pressure and increase of the protein content of the ventricular fluid, the probability of obstruction of the aqueduct of Sylvius by a plug of inspissated pus is considerable. The outlook is bad in such cases, and I cannot lay claim to any success. The treatment which we advocate in such a case is drainage of the C.S.F. from the ventricles in the hope that the purulent obstruction of the aqueduct of Sylvius will resolve: first, intermittent drainage by means of repeated ventricular taps; if that is not sufficient, as judged by the clinical condition of the patient and the ventricular pressure, then continuous ventricular drainage. Irrigation with Hartmann's solution (Sachs, 1942-3) might also be tried. I have heard it suggested that insufflation of air by the lumbar route might be attempted, to blow the plug of pus out of the aqueduct into the third ventricle, but this is probably more than most patients with this condition could stand.

Glial stricture of the aqueduct of Sylvius is not uncommon, but there is no evidence that it arises as a sequel of meningitis (Russell, 1949).

3. Foramina of Magendie and Luschka

Obstruction at the outlets of the fourth ventricle may arise as a sequel of acute infection, when it is usually meningococcal, or from chronic forms of bacterial infection, when the variety of infecting organism is often undetermined. The obstruction may take place during the purulent stage, from silting up of the foramina by inspissated pus and fibrin; or at a later stage, when the C.S.F. has already become clear, from organization of granulation tissue. The site of the obstruction can be determined by air injection.

It is easy to reopen the foramen of Magendie by open operation in these cases, but if possible the operation should be deferred until the C.S.F. has become clear, the patient being tidied over the acute stage by means of intermittent or continuous ventricular drainage. Operation at the stage of fibrous or glial adhesions is attended by the risk of recrudescence of the infection, and thus it should be accompanied by active chemotherapy.

If for any reason it seems inadvisable or impossible to deal direct with an obstruction in the fourth ventricle or in the aqueduct of Sylvius, an alternative pathway for the C.S.F. can be provided by ventriculo-cisternostomy, a procedure introduced by Torkildsen (1947). A catheter or polythene tube is passed into the posterior horn of the lateral ventricle and its other end is led into the cisterna magna. It is left *in situ*. This operation usually gives excellent results.

4. Cisterna Ambiens

Obstructions at the cisterna ambiens cannot be removed surgically. Alternative pathways for the C.S.F. can be provided by various routes, of which probably the most satisfactory is an opening of the anterior wall of the third ventricle (third ventriculostomy) so that fluid escaping from the third ventricle passes into the sylvian fissures, thence over the convolutions of the cerebral hemispheres to be absorbed. This operation is sometimes successful, but may fail for a variety of reasons—closure of the ventricular opening, escape of the C.S.F. into the subdural instead of into the subarachnoid space, or because entry to the sylvian and other cerebral fissures is still obstructed as a result of the previous meningitis.

With obstruction at the cisterna ambiens there is a great collection of C.S.F. in the posterior fossa and spinal subarachnoid cisterns. In the purulent stage of the disease repeated lumbar punctures with withdrawal of large amounts of fluid may tide some patients over from the stage of complete obstruction until the cisterna ambiens partly reopens itself.

5. Spinal Block

Spinal block does not usually produce symptoms, and its importance is that it interferes with the intrathecal administration of antibiotics. I have already indicated the alternative measures for continuing intrathecal therapy.

Risks and Advantages of Operations

The operative methods now used in meningitis carry little risk. Cases requiring major operations are infrequent, and by far the most common procedure is the fashioning of burr-holes for access to the ventricles. In our experience intermittent drainage of the ventricles is preferable to continuous drainage, which carries with it the risk of secondary infection, now lessened by the use of antibiotics, and in infants the risk of cerebrospinal fistula once the drainage tube is withdrawn. The use of air to localize obstruction in the subacute and chronic cases is followed by the risk of reactionary rise of intracranial pressure, which must be guarded against by intermittent or continuous ventricular drainage for a few days, if the obstruction is not immediately dealt with surgically. Another risk is recrudescence of acute infection following operative relief of obstruction in chronic meningitis, but this can be countered by appropriate chemotherapy. For the rest the risks of surgical intervention in meningitis are very small.

In acute meningitis operative methods may be useful in preventing sedimentation of pus. In the unobstructed case withdrawal of C.S.F. from the ventricle, the lumbar region, or any other part of the cerebrospinal pathways and injection of antibiotic must increase considerably the circulation of the C.S.F. and its mixture with the antibiotic, especially if fluid is aspirated and reinjected several times. This effect may be the explanation of the puzzling fact that intrathecal streptomycin treatment is necessary in tuberculous meningitis although a theoretically adequate level of streptomycin in the C.S.F. can be obtained by systemic administration alone.

The extra movement and attention which patients with meningitis receive when they have ventricular burr-holes may well be good for them, particularly if they are inert and comatose. There is considerable evidence that gravity acts unfavourably on the course of meningitis. In fatal pneumococcal or other forms of pyogenic meningitis a mass of gelatinous material is often found in the posterior horns of the lateral ventricles containing pus cells and bacteria which must for the time being be impermeable to penicillin and hence a possible focus of relapse. In fatal tuberculous meningitis it is almost invariable to find that exudate is more intense upon the dorsal than on the ventral surface of the spinal cord. The reasonable explanation of these phenomena is that they are caused by gravity; and it may

well be that the deposition will be prevented by frequent movement of the patient, and that restlessness is, within limits, a good thing for a patient with meningitis. I have been struck with the excellence of the results in patients with pneumococcal meningitis who are violently restless in the acute stage of the disease. The nursing of inert patients should therefore include frequent changes of position.

Conclusion

I have tried to indicate the surgeon's approach to the subject, based on anatomy and morbid anatomy, without defining any particular province which shall be his and his alone. The techniques employed in treatment and the sense of urgency which is required in any particular case come easily to the neurosurgeon by virtue of his training and his daily work, but they are not his exclusive province. The contribution which operative methods can at times make to the diagnosis and treatment of meningitis is considerable, but it must always remain subservient to the main problem, which is one of bacteriology and chemotherapy.

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In a recent issue of the *Journal of the American Medical Association* (April 30, 1949, p. 1284) there is a description of the United States Navy's scheme to set up bone banks in some of its hospitals. It is considered that the plan, which has been made possible by the improved methods of freezing and preserving bone, will assist hospitals in which bone grafting is undertaken. Frozen human bone has been preserved for as long as 308 days in an ordinary ice-cream cabinet, and then used successfully in bone-graft operations.