After the operation for mastoid. (a) When the temperature is raised the dura should not be opened, nor the brain explored by a needle. If this is done the patient will rarely, if ever, survive. With the subsidence of temperature there may be a complete disappearance of the signs of increased intracranial tension with recovery. (b) When the temperature is not raised and there is strong indication that an abscess is present, it is desirable to exercise patience and not to hurry to open the brain. Great harm is often done by inserting a needle into different parts of brain in order to try to discover where is the pus. Small abscesses are very difficult to locate when operating. In my experience patients with abscess of the brain only recover when an incision is made straight into the abscess with the first cut.

ACUTE ASEPTIC MENINGITIS

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Occasionally in acute cases of meningitis no bacteria can be found in the C.S.F. either by microscopical examination or by culture. This condition has been termed "acute aseptic meningitis." Much difficulty has arisen owing to the confused nomenclature of conditions coming under this definition. The term has been applied to the following:—

(a) Meningitic reactions (pleocytosis, increased protein) secondary to spinal anaesthesia with novocaine and other drugs, following intrathecal lipiodol injection and intrathecal therapeutic injection of horse serum, which augments meningeal permeability and produces a pleocytosis of perhaps 100 cells per cu. mm. These reactions are not of great clinical importance, and no further reference will be made to them.

(b) Hydrocephalus due to defective absorption of C.S.F. and not uncommonly seen as a late result of mastoiditis, otitis media, frontal sinusitis, etc. This is the so-called "otitic (or toxic) hydrocephalus" (Symonds 1931, 1937). It is due to thrombosis of the superior longitudinal sinus by extension from the lateral or other venous sinuses. Papilloedema is conspicuous, but headache and vomiting slight. The C.S.F. is under increased pressure, but shows no other changes. This condition, strictly speaking, is not a form of meningitis and again no further reference to it will be made here. Those interested may consult the papers of Symonds.

(c) Meningitis associated with a cranial focus of infection, e.g. mastoiditis, and in which the C.S.F. is sterile. This has also been styled "sympathetic meningitis." The majority of cells in the fluid are polymorphonuclears.

(d) Meningitis in which there is a marked lymphocytosis in the C.S.F. and from some cases in which a virus has been isolated. The prognosis is good. This syndrome has been described by different authors under the following names:—acute aseptic meningitis; acute benign meningitis; acute idiopathic meningitis; epidemic meningitis serosa; benign aseptic purulent meningitis; and benign lymphocytic (chorio-) meningitis.

The term "serous meningitis" possesses no meaning and should be discarded. It has been applied to all the above conditions in turn. The main distinction between the various forms of meningitis lies in the cellular reaction of the C.S.F. and on this the prognosis largely depends. It is simplest, therefore, to divide aseptic meningitis into acute aseptic purulent meningitis and acute aseptic lymphocytic (chorio-) meningitis, in which the cellular reactions of the meninges are mainly polymorphonuclear or mononuclear in type respectively.

ACUTE ASEPTIC PURULENT MENINGITIS

This is a syndrome characterised by the clinical signs of commencing meningitis and certain changes in the C.S.F. It is associated with otitis media, mastoiditis, extradural abscess, purulent sinusitis or brain abscess. Pathologically the condition is thought to be that of purulent

meningitis without demonstrable bacteria, but no actual studies have been made on uncomplicated cases.

The onset is indicated by the development of signs of meningitis during the course of one of the above diseases. There is nothing distinctive about the signs and symptoms. Spinal puncture reveals a fluid under increased pressure, usually cloudy or turbid and containing a variable number of cells, chiefly polymorphs. The protein is much increased, but bacteria are absent from smears and cultures. The patient may improve and recover within a short time or, on the other hand, the fluid may become thick and definitely purulent and bacteria may be found in smears. It is evident therefore that the condition represents merely a beginning of purulent meningitis, which may be averted if the patients' resistance is high. It may be questioned whether there is any advantage to be derived from the recognition of this syndrome.

The diagnosis depends on the existence of a purulent focus within the cranium, the signs of meningitis and the changes in the C.S.F. described. Prognosis was regarded as unfavourable, as in most cases purulent meningitis soon became established and not infrequently abscess of the brain may be associated. Nowadays, with sulphonamide therapy and prompt surgical treatment recovery frequently occurs. Treatment should consist of adequate sulphonamide administration, which may prevent the spread and development of the meningitic condition and, if the source of the infection is found, immediate operation should be undertaken. If focal signs are present the brain should be explored with a hollow needle, since an abscess is most likely.

ACUTE ASEPTIC LYMPHOCYTIC (CHORIO-) MENINGITIS

Before 1925 confusion was present in the description of various cases of meningitis, apart from syphilitic and tuberculous cases, in which the C.S.F. contained an increased number of mononuclear cells. At that time Wallgren clarified the situation by gathering a number of them into a symptom-complex of unknown aetiology, which he termed "acute aseptic meningitis." All these cases had an acute onset, fever and symptoms of meningeal irritation and recovered completely after a short illness. The C.S.F. was sterile on culture. Since that time three viruses, which gave rise to the clinical picture of acute lymphocytic meningitis, have been isolated.

Pathology.

Few cases have come to autopsy, but Viets and Shields (1937) found lymphocytic infiltration of the meninges with slight changes in the cortex in one fatal case.

Epidemiology and Aetiology.

The disease may occur in small epidemics and is often then considered to be poliomyelitis, parotitis and even zoster or mumps. Ford (1937) saw the disease in four of a family of five children. Sporadic cases may occur. The disease has been identified in America, France, Italy, Germany, Austria, Switzerland, Sweden, Denmark, Serbia and Japan as well as in this country. It is not uncommon. In some human cases of lymphocytic meningitis a virus can be demonstrated in the C.S.F. and it produces a meningitis if injected into mice, rats, guinea pigs and monkeys with fatal results. Of the three viruses so far isolated, the most commonly occurring is that of lymphocytic choriomeningitis, which has been found in America, Great Britain, France and Japan in both human beings and mice. The virus of swineherds' disease (*la maladie des porchers*) (Durand *et al.* 1936) also produces this picture, but is found only in neighbouring areas of France, Switzerland and Italy. Lastly, there is the virus of pseudo-lymphocytic choriomeningitis (MacCallum *et al.* 1939), which has been isolated in a few cases in this country. These three viruses provide only about one-third of the cases of acute lymphocytic meningitis. Occasionally a monocytic meningitis occurs in glandular fever, infective jaundice and the acute exanthemate. The remaining cases are as yet of unknown aetiology. Lymphocytic meningitis appears to be much more common in America than in any other country, possibly because it has been more extensively studied there. The virus was first isolated in 1934 in America by Armstrong and Lillie. The source of infection and portal of entry in man has not yet been settled. The weight of evidence indicates the grey mouse (*mus musculus*) as the reservoir of infection for the naturally occurring disease. The virus may be isolated from the viscera of mice, which show no outward signs of infection. Armstrong and his colleagues (1940) have found a much greater percentage of in-

fected and immune mice among those caught in the houses where human cases have occurred than among mice from houses where the illness has not been traced. Mice embryos may be infected *in utero* and they then may transmit the infection to their offspring and contacts by their nasal secretion. Their urine, faeces, saliva and semen also contain active virus. The virus may be present in the dust where infected mice have been. Dogs have also been shown to harbour the virus in their spleen and an inoculated dog transmits the infection to its cage-mate. If dogs in nature therefore do become infected with the virus they can readily transmit it. From personal experience of the disease it seems probable that dogs may transmit the disease to man. Three weeks before developing symptoms I took charge of a bull terrier, which slept in the same room. During my own illness the dog developed attacks of acute mania in which he rushed about biting all in sight. This necessitated his destruction. Farmer and Janeway (1942) also described a case in which a dog might have been the source of infection. There is no indication that cats are infected or carry the virus.

Thus there is an abundant source of virus in the excreta of animals to infect human beings by direct contact, contamination of food, inhalation of contaminated dust or the bites of insect vectors. The virus has been shown experimentally to infect unbroken skin of the guinea-pig, which suggests this is the portal of entry in those who handle infected mice without gloves. The virus does not seem to be transmitted from man to man. Although the precursory symptoms of infection often include upper respiratory disease there is little or no evidence of its spread in this manner. All attempts to transmit the disease from patient to patient by inoculation of nasal washings from the naturally occurring cases or from human cases produced by injection of infected mouse brain tissue have failed. The virus has been isolated only once from the nasopharynx of man and the patient never developed immune bodies so that proof that the virus was of human origin was lacking.

The virus of lymphocytic chorio-meningitis sometimes causes atypical pneumonia (Smadel *et al.* 1942) as broncho-pneumonia has been reported with several fatal infections from the virus. Further Reimann (1942) (*et al.*) report a case of atypical pneumonia, the serum of which strongly neutralised the virus of lymphocytic meningitis. In addition acute influenzal-like illnesses may follow infection with a virus, but no evidence of involvement of the nervous system can be found. In a few cases the virus has attacked the nervous system rather than the meninges producing an encephalomyelitis.

In America examination of sera has showed neutralising antibodies in 32 per cent of 58 cases diagnosed as aseptic meningitis, 28 per cent of 106 cases with recent influenzal-like illness with upper respiratory infection, but no signs of meningeal irritation, and 10 per cent of 1,000 individuals chosen at random, who gave no history of any involvement of the central nervous system. In this country the virus has been isolated much less frequently from human beings and neutralisation tests have shown a very small proportion of positives. The high percentage of positive sera from individuals showing no involvement of the central nervous system indicate that there is no single clinical picture which can be said to include all cases of infection with the virus.

Clinical Findings

There appears, therefore, to be several forms of the disease—meningeal, encephalomyelitis, pneumonic and influenzal-like types. In the non-meningeal type of the infection the acute illness lasts about a week. The symptoms begin with troublesome pains in the arms, shoulders and back and an accompanying temperature of about 99.5° F. There is loss of appetite, the lumbar pain increases and the fever lasts about 5–6 days. Weakness and prostration persist throughout the following week. A white blood count during the acute stages shows a marked leucopenia and the virus may be isolated from the blood. The serum may give strong protection against the virus six weeks after the illness. During the acute stages there may be a few physical signs in the chest and radiograms may reveal the shadows found in atypical pneumonia.

In the meningeal type of the disease no age group is exempt. Children are most frequently affected. The incubation period of lymphocytic choriomeningitis is presumably 1½–3 days as fever developed in this period following experimental inoculation of infected mouse brain into human beings. Certain indications may lead one to differentiate between a case due to the virus of lymphocytic choriomeningitis and one of acute lymphocytic meningitis of unknown origin. Thus in a group of 18 patients with lymphocytic meningitis of unknown cause only

three had a prodromal illness, whereas, in a group of 23 proved virus cases, 16 gave a history of an influenza-like precursory illness with malaise, generalised pains, headache, upper respiratory infection and fever, which lasted from one to three weeks before the onset of meningitis. During the prodromal period the fever ranges from 100–103° F. and usually shows two or three waves with a remission before the onset of the meningitis. The virus is present in the blood, usually from the onset of the fever to the onset of the meningitis. Although fever develops within three days of inoculation, symptoms do not appear until 5–10 days after exposure.

With the onset of meningeal symptoms whether in those cases due to known virus infection, or those from unknown cause, there is headache, chills, vomiting and the usual signs of meningeal irritation such as cervical rigidity, Kernig's sign and lumbar back-ache. Hyperaesthesia and dermatographism are always well marked. The former may be severe. In most cases there is no tendency to somnolence but on the contrary there is irritability, insomnia and intense restlessness. Occasionally there is drowsiness and disorientation however. The meningeal reaction is of varying severity and lasts 7–30 days, when it gradually recedes and is followed by recovery. Fever may be high, ranging from 102–103° F. It is continuous or remittent. The patient often seems to be alarmingly ill in spite of the benign nature of the disease. Drenching sweats during sleep occurred in my own illness. In young children there may be convulsions. Mild papilloedema or congestion of the optic nerve heads and occasional 6th nerve palsies are described. Nystagmus is mentioned by some writers, but as a rule the cranial nerves are spared. The lymph nodes may be enlarged. In some instances the throat is infected or inflamed. The fever usually ends by lysis. Sometimes it lasts no more than two or three days, whereas in others a slight evening temperature persists for 6–8 weeks. A peculiar metallic taste may persist in the mouth for 2–3 months.

Blood.

During the prodromal period there is a definite leucopenia with granulopenia and relative lympho- and mono-cytosis at first. With the onset of meningitis the blood counts are usually normal. The sedimentation rate is normal or slightly reduced.

C.S.F.

This is usually clear or slightly turbid. Rarely it is definitely cloudy and shows a fibrin clot on standing. The pressure is nearly always increased. The cell count varies from about 60–3,200 cells per cu. mm. with an average of 600–1,000 during the early meningeal phase. Of these 95–100 per cent are usually lymphocytes. According to some authors during the first few days leucocytes may predominate. It is usually stated that the cells are chiefly lymphocytes but in some cases they may be larger and resemble monocytes. The protein content may be normal, but it is commonly elevated to 50–200 mgms. per cent. Sugar and chloride content usually remains high, being either normal or nearly so, but in severe cases both may be reduced considerably. The tryptophane reaction, said to be specific for tuberculous meningitis, may be positive. The cellular reaction decreases to 10–15 cells per cu. mm. within 4–6 weeks of the onset of meningitis and may persist for some period after clinical recovery has occurred.

Detection of virus.

In virus cases the causative agent is present in the blood from the onset of fever to the onset of meningitis and may be occasionally detected in the first few days of the latter stage. It can be isolated from the C.S.F. during the first 7–10 days of meningitis, but is no longer detectable afterwards. A positive complement-fixation reaction with the blood commonly appears 3–4 weeks after the onset and disappears in 4–6 months. On the other hand demonstrable neutralising antibodies, which have been shown to be distinct from those giving complement-fixation do not usually appear until 6–8 weeks after the onset and persist for six months to five years.

Course and Sequelae

In most cases recovery is complete and sequelae are rare. A few cases have proved fatal. In one or two cases mental defect and epilepsy are said to have resulted. Occasionally personality changes, prolonged fatigue, headache, impairment of memory, mental depression, dizziness and strabismus have resulted from the disease.

Differential Diagnosis

The most likely disease to cause difficulty is tuberculous meningitis. Little difference may be noticed until the latter suddenly enters the terminal stage and is fatal. In the C.S.F. the web-like clot, which often forms on standing in tuberculous cases is sometimes helpful. The marked progressive reduction in the sugar and chloride content is not found in lymphocytic meningitis. The tryptophane reaction may be positive in both diseases. The percentage of lymphocytes in the C.S.F. rarely rises above 80 and the blood sedimentation rate is elevated in the tuberculous cases. The fact that the organisms cannot be demonstrated in the C.S.F. is of no significance, as it is rare to find them in tuberculous meningitis. The occurrence of other cases in the same neighbourhood favours a diagnosis of lymphocytic meningitis, and finally the favourable outcome of the latter disease clinches the diagnosis. Glandular fever is differentiated by the typical blood picture and the Paul-Bunnell reaction.

The disease may also be mistaken for non-paralytic cases of poliomyelitis, which gives an almost identical clinical picture. The diagnosis may remain in doubt after the most careful clinical study. Poliomyelitis more often occurs in the later summer months and there is said to be a rapid diminution in the number of cells in C.S.F. as the disease progresses.

If proof is desired of the virus aetiology of a case two courses may be followed. In the pre-meningitic phase inject 5–10 c.c.s. of blood intraperitoneally into a guinea pig and in the meningitic phase the same amount of C.S.F. Elevation of its rectal temperature to 104° F. probably indicates infection and the spleen and/or brain should be removed aseptically, placed in 50 per cent glycerine or saline and stored in the ice box until sent to a laboratory for identification. Serum taken in the acute stage and convalescent stages (5th–6th week) can be examined for immune bodies to lymphocytic choriomeningitis virus.

Treatment

Repeated lumbar puncture is recommended to reduce the intracranial pressure. The headache may be extreme and necessitate morphia injection. If the vomiting is persistent it is often due to alkalosis and the patient should be given frequent small amounts of milk or milk preparations to which glucose has been added. Sulphonamides are without effect and are contraindicated as they increase the severe nausea and vomiting. Otherwise treatment is restricted to proper nursing care.

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BOOK REVIEWS

ELECTROCARDIOGRAMS 2nd Edition

By WALLACE JONES and E. NOBLE CHAMBERLAIN.
 John Wright & Sons, Bristol. 1943. 5s.

We recommend every practitioner to read this excellent little book which, though primarily published for the medical student, is of general value in imparting a sound knowledge of cardiograms.

The only criticisms to be made are, firstly, the

picture of the electrocardiograph is, in our opinion superfluous, especially since more than one firm makes these machines, and they vary in each case; secondly, the illustrations Figs. 42 and 43 are not at all clear—there is no definite line of demarcation between the separate sets of pictures. We also feel that some of the illustrations suffer from too many superimposed letters; thirdly, no mention has been made of the other types of cardiogram available (granted the graph itself is the same, but the time marking, etc., may be different), and no reference has been made to the easy method of