MENINGOENCEPHALITIS: A DIAGNOSTIC SURVEY

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There are two complementary approaches to diagnosis. By the first we seek to recognise and identify in our patient a condition which we have seen before, or of which we have read a vivid and memorable description. Mongolism, achondroplasia and Graves' disease are examples of conditions recognisable at a glance. As our clinical experience grows and our reading extends we are better able to identify less overt disease states. To assist this collation our text-books of medicine have become descriptive catalogues portraying typical "diseases," such as tuberculous meningitis, epidemic encephalitis, typhoid fever. The aim of diagnosis has in the past been largely to match the patient's illness with one of these described pictures of disease and to label it accordingly.

But our clinical studies soon teach us that the vast majority of patients, especially in the early stages of their illness, do not present consistent or uniform patterns of disease, and that the attempt to fit them into text-book portraits is both forced and unreal. Accurate and satisfying diagnosis of disease demands a different method.

This second approach to diagnosis proceeds from a deeper understanding of disease. It emphasises that the manifestations of disease depend on (a) *disturbance of function* resulting from local *structural change* (the "seat of disease") due to (b) *causes*, which may or may not be known (1). Thus the patient's presenting symptoms and signs should be so grouped that they point to the site of disease, to functional disturbances (which often indicate the likely site of disease), and to the cause or causes of disease. The advantages of this method, especially in the less obvious case will, it is hoped, be manifest in this introductory paper. It is the more natural approach in that it proceeds directly from the patient's symptoms and signs to the "seats and causes" of disease; it employs the inductive method of science; it forms the basis of a rational therapy; and it reveals those limitations in our diagnosis which are too often masked by a label.

General Principles

Infections of the central nervous system produce symptoms which vary according to (i) the tissue dominantly affected, (ii) the nature of the infective agent and (iii) the duration of its activity. It is convenient for descriptive purposes to classify the resulting symptoms as due to:—

1. *Meningitis.*
2. *Encephalitis, myelitis, or both.*
3. *Vascular lesions*, e.g. endarteritis which may lead to thrombosis (as in syphilis); thrombophlebitis in typhoid fever; and embolism in infective endocarditis leading to mycotic aneurysm.
4. "*Tumour*" formation with the signs of an expanding lesion—e.g. abscess, gumma, tuberculoma, parasitic cysts; internal hydrocephalus and circumscribed serous meningitis resulting from infection belong to this group.

That these should not be looked upon as sharply defined "diseases" or "entities" is generally recognised in tuberculous and syphilitic infections of the nervous system, but we must not overlook the fact that in all other infections of the nervous system the same principle holds. The patient's symptoms may well be mainly referable to one of these groups; but in him or other patients there will be found evidence of the infective agent having produced changes in other sites. For example, in meningococcal infections the meningitic signs may swamp the neurological picture, but occasionally the dominant clinical and pathological signs are those of encephalitis; in acute anterior poliomyelitis it is customary to encounter at the outset a meningitic picture followed in a day or two by the paralysis which indicates infection of the spinal cord itself.

THE CLINICAL PICTURE OF MENINGOENCEPHALITIS

It is not proposed to discuss the symptoms attributable to pachymeningitis or those associated with clear-cut vascular lesions or "tumour" formation. Our discussion will be confined to the clinical picture of meningoencephalitis, though this may be accompanied in any type of infection by "vascular" or "tumour" signs.

All forms of meningoencephalitis may present symptoms and signs belonging in varying proportions to one or more of four groups; these result from (1) *meningeal irritation*, (2) *increased intracranial tension*, (3) *disturbance of function of the central nervous system*, and (4) *their causative factors*.

Meningeal irritation occurs not only from infections of the meninges—*meningitis*—but also from the presence in the subarachnoid space of *blood, neoplastic or leukaemic or lymphadenomatous cells, therapeutic sera, spinal anaesthetics or the contents of parasitic cysts*. Hence its signs are common to all these causative factors which must be considered in the differential diagnosis of meningitis. The characteristic signs of meningeal irritation are **pain, hyperaesthesia, and muscular rigidity**. The *pain* is usually intense and felt in the occipital, temporal and frontal areas; it often radiates down the back of the neck; it is aggravated by attempted movement of the head and neck, especially flexion, and by factors raising intracranial pressure. The site, intensity, and character of these symptoms will vary greatly, but are easily interpreted in the light of the mechanism of their production (2). The *pain* and *hyperaesthesia* result from irritation of the meningeal nerves and of the intrathecal parts of the cranial and spinal nerves; the *rigidity* arises from a *meningeal-motor reflex*. *These symptoms are exactly analogous to the pain, hyperaesthesia, and rigidity of peritonitis and their mechanism is identical*. Hence in localised forms of meningitis, localised pain, hyperaesthesia and rigidity may be found. But the free communications of the subarachnoid fluid spaces allow in most acute infections a rapid spread throughout the whole cerebro-spinal axis, and thus pain and hyperaesthesia at first localised to the head and neck, with rigidity of the retrocollic muscles, quickly become general and produce the classical picture of meningitis. The spreading spinal meningeal irritation gives pains in the back and limbs and opisthotonus. In the more chronic forms the symptoms may be more focal, and in infections of the cord, e.g. at the onset of poliomyelitis, they may be first evident only in the back and lower limbs. The signs associated with the names of Kernig, Brudzinski, Bikeles, and others, are elicited by manoeuvres which increase by stretching the irritability of the inflamed meninges and the nerves which traverse them. The meningeal inflammation may excite not only sensory nerves, giving pain and hyperaesthesia, but also motor nerves giving muscle spasm, for example, a spastic strabismus; or it may paralyse nerves, both motor and sensory, with resulting paresis or anaesthesia. The "cry" of meningeal irritation is the wail of a practically comatose child in response to pain. The clinical picture will be determined by the site and extent, the intensity, and the rapidity of development of the meningeal irritation.

Increased intracranial tension in meningoencephalitis unaccompanied by an inflammatory "tumour" results from two changes—(1) the increased formation of cerebro-spinal fluid (modified in composition) due to the meningeal inflammation, and (2) the inflammatory swelling of the brain in encephalitis due to hyperaemia, oedema, and possibly haemorrhage. That the former is the predominating cause is shown by the more severe signs which accompany the higher cerebro-spinal fluid pressure findings in meningitis. The signs of increased intracranial tension common to whatever be its causes (and these include new growths, injuries, etc.) are **headache**—which is diffuse and aggravated by coughing, sneezing, stooping, straining, and all factors which normally raise intracranial pressure; **vomiting**—often "projectile" or "explosive," though occasionally accompanied by nausea; **slowing of the pulse rate; slow and often irregular respiration** (Biot or Cheyne-Stokes type); and **disturbances of consciousness**. The more rapid the rise in intracranial tension the more marked are these signs likely to be; yet another instance of the general principle that the *severity of the clinical manifestations of a pathological lesion is proportional to the rate of its development*. It is, of course, true that these signs arise from disturbance of brain function, but it is through their recurring association that we are led to suspect a raised intracranial pressure. If the rise in pressure is prolonged for weeks or months impaired venous return may lead to oedema of the optic disc (papilloedema), though this should lead us to suspect that the infection may have given rise to "tumour" formation; this is often due to hydrocephalus or a localised serocystic meningitis. Some varieties

of meningoencephalitis may involve the optic disc directly—a true “optic neuritis”—with ophthalmoscopic appearances similar to those seen in papilloedema. It is worth noting that papilloedema is rarely seen in epidemic encephalitis; when it appears in a patient thought to be suffering from this infection the diagnosis should be reconsidered.

Disturbance of function of the central nervous system.—The symptomatology attributable to this is co-extensive with the functions of the brain and spinal cord. Over-activity (“irritation”) or under-activity (“paralysis”) of any part—large or small—of the central nervous system may accompany *encephalomyelitis*. Acute widespread encephalitis may produce, in addition to the signs of its presence in a circumscribed area (so-called *focal* signs), temporary ablation of practically all neural function as evidenced by coma, generalised flaccidity, etc.; so-called “cerebral shock.” Signs may result from the unleashed activity of lower cerebral centres freed from the control of those higher centres which have been damaged by disease (“release phenomena”), for example, spasticity, parkinsonism. And finally, the clinical picture may include signs of the uncontrolled and inco-ordinated discharge of neuronal energy from toxic or vascular causes resulting in oxygen deprivation. These may be paroxysmal or continuous. Convulsions and transient convulsive movements are examples of the former, and it is probable that epidemic hiccough and the myoclonus accompanying some forms of encephalitis are examples of the latter.

The symptomatology of encephalomyelitis is thus practically limitless. General and focal, irritative and paralytic, “release” and “discharge” symptoms, may all occur with varying intensities, and in varying proportions, whatever be its cause.

The Causes of Meningoencephalitis

Thus far we have considered the signs which lead us to recognise (a) meningeal irritation, (b) increased intracranial tension, and (c) disturbance of function in the central nervous system. How do we determine that the *cause* of these is an infection, and how is the infective agent identified?

There are as many causes of meningoencephalitis as there are known pathogenic organisms. Some are common; meningococci are responsible for over 30 per cent of all cases of meningitis, and tuberculosis accounts for another 30 per cent; streptococci, pneumococci and influenzal organisms cause many of the remaining cases. Syphilitic meningoencephalitis in its varied forms is very frequently encountered. The devastation wrought by epidemics of poliomyelitis and encephalitis lethargica is well known, though the latter in its acute form has now happily almost disappeared.

It was earlier stated that no organism evokes an exclusively meningitic or encephalitic reaction. But some, e.g. meningococci, usually produce a dominantly meningitic picture. Others, e.g. encephalitic viruses, give almost wholly the signs of encephalitis or myelitis. In a few instances, the dominance of the meningitic or encephalomyelitic picture fluctuates as the illness progresses, e.g. in polioencephalitis, signs of meningitis may precede by some days those of encephalitis, whilst in a cerebral abscess the encephalitic evidence may rapidly give way to that of meningitis if the abscess ruptures into the subarachnoid space or ventricles. In tuberculous and syphilitic infections meningitic and encephalitic lesions are often concurrent, though in syphilis, meningitis is apt to occur at an earlier stage of the infection, and the various manifestations of encephalitis later. With these observations in mind the following comprehensive table of the causes of meningoencephalitis may help in recognising the cause in the more obscure case:—

A. Encephalomyelitis. 1. *SUPPURATIVE*—caused by bacterial infections from—

- a. *Direct spread* from fractures of the skull, especially basal; penetrating wounds; infections of nasal air sinuses or mastoid cells; osteomyelitis of skull or vertebrae.
- b. *Pyæmia* and *septicaemia*. (Meningitis in some degree almost invariably accompanies and may precede suppurative encephalitis.)

2. *NON-SUPPURATIVE*—due to—

- a. *Established virus infections*: polioencephalomyelitis, infective polyneuritis, encephalitis (including encephalitis

lethargica, St. Louis encephalitis, Australian X disease which is due to the same virus as louping ill, Japanese encephalitis, equine encephalomyelitis, rabies, herpes zoster, smallpox, chickenpox, vaccinia.

- b. *Associated with infectious diseases of unknown etiology*—mumps, measles, Sydenham's chorea, whooping-cough, influenza (? virus). (Not all the nervous complications of the exanthems are due to meningoencephalitis; vascular accidents—thrombosis, embolism, and haemorrhages, and "serous" meningitis may be the cause.)
- c. *Spirochaetes*:—*Treponema pallidum*.
- d. *Protozoa*: malaria, trypanosomiasis, toxoplasma.
- e. *Parasitic worms*: cysticercus, echinococcus, trichinella.
- f. *Rickettsia*: *R. prowazeki* (typhus), *dermacentoxenus rickettsi* (tick-bite fever).

B. Meningitis.

- 1. (*PACHYMENINGITIS*)—not considered in this paper except in so far as it may spread and produce the signs of leptomeningitis.

2. LEPTOMENINGITIS—

- a. *Cocci*: Meningo-, strepto-, pneumo-, staphylo-, gono-.
- b. *Bacilli*:—*B. tuberculosis*, *B. proteus*, *B. typhosus*, *B. coli*, *B. influenzae*, *B. anthracis*, Friedlander's bacillus, *Br. melitensis*, *Bact. tularensis*.
- c. *Spirochaetes*: *Treponema pallidum*, *leptospira ictero-haemorrhagicae*.
- d. *Streptothrices*: *Actinomyces*.
- e. *Protozoa*: Malaria.
- f. *Fungi*: *Torula*, *coccidioides*, *monilia*, *aspergillus*.
- g. *Viruses*: Polioencephalomyelitis, acute infective polyneuritis, benign lymphocytic meningitis, mumps, infective mononucleosis (glandular fever).
(Experimental infections with pronounced meningeal involvement have been produced with the viruses of psittacosis, herpes febrilis, and yellow fever.)

From the diagnostic standpoint it must be remembered that the demyelinating diseases, disseminated sclerosis and neuromyelitis optica (Devic's disease), present the clinical picture of a disseminated encephalomyelitis.

DIAGNOSIS

The recognition of the cause follows from *clinical signs and changes in the cerebro-spinal fluid*. In meningitis the former are suggestive, the latter often diagnostic; in encephalomyelitis the clinical picture is often more helpful than the examination of the cerebro-spinal fluid.

The *presence of an infection* may be suggested by the *general signs of toxæmia*—pyrexia, hot skin, dry furred tongue, etc. Owing to the increased intracranial pressure there may be no associated rise in the pulse rate. This relative bradycardia and the accompanying headache may lead at the onset of a typhoid infection to the suspicion of meningitis and vice versa; even pneumonia, in which in the first few days a pulse rate lower than might be expected from the pyrexia is commonly found, may be mistaken for the onset of meningitis. Pneumonia also may be the mistaken diagnosis in poliomyelitis. Several years ago I saw a woman who had been ill for forty-eight hours; she was cyanosed and breathing rapidly; her temperature was 103° and pulse rate 84; she had very severe headache with slight neck rigidity. Her doctor suspected pneumonia with possible complicating meningitis, but examination revealed that the cause of her cyanosis and tachypnoea was paralysis of her respiratory muscles due to poliomyelitis; the headache and rigidity were the signs of the meningitic phase, and the cerebro-spinal fluid was typical.

The more acute the infection, whether of meninges or brain, the more marked are the general signs of toxæmia; the vascularity and large absorptive area of the meninges explains why in meningitis these signs are more evident than in encephalitis. Indeed, in encephalitis, even suppurative, general signs of an infection may be absent, a fact of vital significance which must not be overlooked in the diagnosis of **cerebral abscess** (a localised suppurative encephalitis). The possibility of infection is then raised by the previous history, associated signs, and the *time curve* of the onset of disease.

Lesions, which appear suddenly, or develop their maximal signs within twenty-four hours, are rarely caused by infections; they are commonly vascular in origin, due to embolism, hæmorrhage or thrombosis. The signs of meningeal irritation due to **subarachnoid hæmorrhage** appear with dramatic suddenness. The patient is seized in the midst of apparent health with agonising pains in the head, which, owing to the rapid diffusion of blood in the subarachnoid space, spread rapidly down the back; within a few minutes or, in the case of a slow leak, an hour or two, there is marked neck and back rigidity or "cerebral shock," and the cerebro-spinal fluid is blood-stained. But an acute infection can develop so rapidly that the victim is gravely ill within twenty-four hours of the onset of symptoms; these, however, continue to advance for a few days if death does not supervene, or if the infection is not overcome by specific therapy. Less acute and chronic infections may take several days or even weeks to reach their height. Very chronic infections, e.g. syphilis, degenerations and neoplasms, unless complicated by vascular lesions and disturbances of the flow of cerebro-spinal fluid, slowly advance over a period of months or years. Thus, apart from the general signs of an infection, the rapid development of symptoms and signs over a period varying from twenty-four hours in very acute, to 3-4 weeks in subacute, disease of the nervous system, followed by gradual retrogression of symptoms, is suggestive of an infection or a toxæmia of non-infective origin.

The cause of the infection may be sought on clinical grounds by considering the following points:

1. **The prevalence of an epidemic.** In the presence of a known epidemic, e.g. of meningococcal fever or poliomyelitis, the most bizarre and protean manifestations may be readily recognised; in sporadic cases these would be diagnosed only with difficulty. But it must not be forgotten that during an epidemic of one disease, other infective and non-infective lesions can occur. I well recall the frequency with which victims of tuberculous meningitis, cerebral thrombosis, and even intracranial tumours were mistakenly diagnosed as suffering from epidemic encephalitis during the pandemics of that infection over twenty years ago.

2. **The maximum site of the lesion.**

(a) *Is the symptomatology dominantly meningitic or encephalitic?* As we have seen above, some infections more commonly give symptoms attributable to one or other; some to both.

(b) *Which area of the meninges, brain or cord, is affected?* The causes of disease have "sites of predilection." Thus epidemic encephalitis tends to affect especially the mid-brain, hypothalamus and striatal regions; hence the classical ocular palsies, disturbances of sleep rhythm, choreo-athetoid movements, and parkinsonism. Polioencephalitis and poliomyelitis damage the motor cells of the cortex and cranial motor nerve nuclei, and the motor cells of the anterior horns of the spinal cord, hence the evidences of upper and/or lower motor neuron changes. Meningococcal and tuberculous meningitis are most marked at the base of the brain, giving the well-marked neck rigidity, occipital and retronuchal pain, especially in meningococcal infection in infants (posterior basic meningitis). Pneumococcal meningitis is often at its onset most marked over the vertex of the brain; hence though headache may be excruciating, neck rigidity and the accompanying signs (of the Kernig type) may be absent. We should then ascertain as far as is clinically possible the predominant *site* of the lesion, for it, too, is a piece of evidence which may be useful in determining the cause.

3. **The significance of other etiological factors.**

(a) *Age.* This is not a striking lead, though some infections show a well-marked age incidence, e.g. over 50 per cent of all cases of tuberculous meningitis occur between the ages of six months and four years; but this infection may occur at any age. Poliomyelitis is pre-eminently a disease of childhood, over 70 per cent of its victims being under four years old.

(b) Neither *sex* nor *heredity* appears to play a significant role in determining infections of the nervous system except perhaps for the greater frequency of chorea in girls.

(c) *Previous history.* This is of great importance. A history of tuberculous glands in the neck of a child followed in a few months by signs of leptomeningitis is clearly a relevant association. The frequency of tuberculous infection following whooping-cough or measles in infancy must be remembered. The history of an aural discharge, of nasal operation, of head injury, of a previous syphilitic infection, or of an exanthem may be quoted from many which offer a guide to the cause of an existing infection of the nervous system.

(d) *Accompanying signs.* The presence of acute mastoiditis and nasal air-cell infections, of active phthisis, of spinal caries, of empyema and bronchiectases or lung abscess, of cerebro-spinal rhinorrhoea—these and any other pertinent signs of a primary infection should be looked for and correctly assessed in the presence of meningoencephalitis. Especially important are somatic signs produced by the infective agent responsible for the nerve lesion; thus the rashes of meningococcal septicaemia, purpuric and erythematous (of the nodosum type), and accompanying arthritis are valuable clues; so also is the onset of encephalitic signs during the efflorescence of an ophthalmic herpes. Knowledge of the general signs produced by any infective agent in the body is indispensable for accurate clinical diagnosis, and the value of such accessory tests as blood examinations, including agglutinations, Mantoux reactions, etc., in testing provisional diagnoses must be remembered.

(e) *The course of the illness.* Many infections of the nervous system will be suspected from their typical courses. The evolution of poliomyelitis has above been noted and is fairly constant. We may recognise the usual march of tuberculous meningitis progressing inevitably to its fatal termination, or the patient with epidemic encephalitis making an apparent recovery and then, after an interval of months or years, passing into the phase of progressive parkinsonism. (The student should tabulate in detail under the above headings the clinical manifestations of the common infections of the nervous system.)

It will be clear from this brief discussion that these considerations enable the experienced clinician to present in most cases a reasoned opinion on the probable cause of an infection of the nervous system, but no diagnosis is completed until the results of examination of the cerebro-spinal fluid are considered.

4. The cerebro-spinal fluid.

There is a widespread tendency to regard examination of the cerebro-spinal fluid as so certain and accurate a method of diagnosis in nervous disease as to render nugatory a detailed clinical examination. This view is groundless and dangerous. It is admittedly true that in many infections, especially those that are dominantly meningitic, the cerebro-spinal fluid reveals the cause directly, but in others, especially where the brain and cord are primarily involved, the additional evidence it offers serves only to confirm clinical suspicions, and thus allows more accurate inference of the probable causative factors.

General principles must again be stressed. Leptomeningitis of all types is associated with damage to the walls of the meningeal capillaries and the vessels of the choroid plexus which form the barriers between blood and cerebro-spinal fluid. This inflammatory damage results in:—

(a) An increased formation of cerebro-spinal fluid; thus the *pressure increases* usually well above the high normal limit of 150–200 mm. of water.

(b) An outpouring into the subarachnoid space of inflammatory cells—*pleocytosis*. Normally an occasional lymphocyte (not more than 1 or 2 per c.mm.) is found in the cerebro-spinal fluid; several thousand leucocytes per c.mm. may be found in acute meningitis. The cells must reach a few hundred per c.mm. before causing “shimmering” or turbidity of the fluid so that a crystal clear fluid does not exclude meningitis or meningeal reactions accompanying encephalitis; indeed in tuberculous or syphilitic meningitis, and the meningeal reactions of poliomyelitis, herpes zoster, polyneuritis, etc., a clear fluid is usual. The type of cell depends on the acuteness of the inflammation rather than its cause. A polymorphonuclear pleocytosis is the common finding in meningococcal and other acute coccal infections, whilst in the less acute tuberculous and syphilitic infections a lymphocytosis is usually found. But in acute tuberculous meningitis I have found 90 per cent polymorphonuclears in the cerebro-spinal fluid, and in chronic meningococcal infections over 90 per cent lymphocytes. If a

cerebral abscess is suspected, the finding of even a few polymorphonuclears amongst the scanty cells of the cerebro-spinal fluid is valuable confirmatory evidence. A few red blood cells are seen in the more acute forms of meningoencephalitis. In chronic syphilitic disease, plasma cells are present. In the rare parasitic infections, eosinophils may be found.

(c) Changes in the *chemical composition* of the cerebro-spinal fluid due to the increased permeability of the barrier between blood and cerebro-spinal fluid. These are presented in the following table:—

	NORMAL		MENINGITIS
	Blood plasma	Cerebro-spinal fluid	Cerebro-spinal fluid
GROUP I— (Substances normally present in greater quantity in the plasma than in the fluid)	Protein, 6-7 per cent Inorg. P. 2-4 mg. per cent Uric acid, 2-4 mg. per cent Cholesterol, 150 mg. per cent Calcium, 10 mg. per cent Sulphates, 4 mg. per cent Glucose, 100 mg. per cent	Trace 1.25-2 mg. per cent Trace Trace 5-6 mg. per cent 1 mg. per cent 50-80 mg. per cent	Increase Increase Increase Increase Increase in early stage; decreased later
GROUP II— (Substances normally present in greater quantity in the fluid than in the plasma)	Chlorine, 560-620 mg. per cent (as NaCl) Magnesium 2-3 mg. per cent	752-750 mg. per cent 3-4 mg. per cent	Decrease Decrease
GROUP III— (Substances which either naturally or after injection are present in the plasma, but normally do not pass into the fluid in any but the most minute traces)	Fibrinogen Iodides Salicylates Nitrates Sod. fluorescein (uranin) Agglutinins (meningococcal) Bile pigments Organic arsenic Sulphonamides, etc.	All these have been shown to pass into the cerebro-spinal fluid in meningitis.	

All these changes can be summarised in the general law—in meningitis the chemical composition of the cerebro-spinal fluid approaches that of the blood plasma (3). Glucose may appear to be an exception to this rule because it tends gradually to diminish in meningitis. It must be remembered, however, that glucose is an assimilable foodstuff utilised by the organismal cause of the infection, by the inflammatory cells in the fluid, and by the inflamed cells of the choroid plexus and meninges; hence as the glucose falls lactic acid begins to appear in the cerebro-spinal fluid. The degree of chemical change in the meningitic fluid will depend upon the intensity, extent and duration of the infection.

Especially noteworthy in the clear cerebro-spinal fluid in tuberculous meningitis is the "feathery" or "gossamer" clot of fibrin which appears on standing and the marked lowering of glucose and chlorides. A finding of less than 600 mgm. of NaCl per cent in a clear fluid is practically diagnostic of tuberculous meningitis; this is in part due to the coincident fall in the blood chlorides which occurs in generalised tuberculosis. When the meningitic phase of the illness is short-lived, as in benign lymphocytic meningitis, poliomyelitis, herpes zoster, and toxic polyneuritis, although there is a slight protein and cellular increase, there is no significant change in the chlorides or glucose. The normal glucose and chloride content of the fluid in encephalitis lethargica is one of the most valuable differentiating points from the fluid in tuberculous meningitis.

It should be noted that only when there is free communication between the various parts

of the cerebral and spinal subarachnoid spaces is the fluid obtained by lumbar puncture an accurate index of the intracranial inflammatory reaction. Adhesions may shut off the cerebral from the spinal spaces, parts of the cerebral or spinal spaces from others, e.g. the basal cistern may be isolated, the ventricles from the subarachnoid spaces, and so forth. These will clearly modify the composition of the cerebro-spinal fluid, and cisternal or ventricular tappings may be necessary before the findings can be adequately interpreted.

(d) Special tests may reveal the *cause* of the infection—

- (i) Staining the cellular deposit or the "feathery" clot (in tuberculous meningitis) for organisms; cultures; guinea-pig inoculation. The inhibitory effect of sulphonamide therapy on the growth of certain organisms, especially coccal, from the fluid should be remembered in assessing the significance of negative findings on culture.
- (ii) Wassermann reaction—for syphilis.
- (iii) Colloidal gold, benzoin, and other tests may reveal inflammatory change; they suggest a possible cause only in conjunction with other findings—a fact frequently overlooked. The same form of curve may be found, for example, in neurosyphilis, disseminated sclerosis, epidemic encephalitis and other lesions, such as neoplasms in which increased protein is found in the cerebro-spinal fluid.

The term "**meningismus**" is applied to a transient condition of meningeal irritation, occurring during the course of a general infection, with a rise in the cerebro-spinal fluid pressure, and a very slight pleocytosis; no organisms are found, and the chemistry of the fluid is unchanged. The essential pathology of **encephalitis** is neuronal necrosis of all types and degrees of intensity, a cellular reaction around the damaged cells, and a distension of the Virchow-Robin spaces with leucocytes (so-called "perivascular cuffing"). The meningeal reaction is usually mild in uncomplicated encephalitis, hence the cerebro-spinal fluid changes are relatively slight. The pressure will be increased by the swelling and congestion of the brain, there will be a slight increase in protein (usually globulin), a moderate pleocytosis (rarely more than 100 cells per c.mm.), and changes in the colloidal reactions; the chemistry of the fluid—glucose, chlorides, etc.—is not significantly altered. Although a positive Wassermann reaction or the presence of trypanosomes may reveal the cause, in most cases of encephalitis examination of the cerebro-spinal fluid simply confirms the clinical suspicions and throws no further light on the cause.

Thus in meningoencephalitis the cerebro-spinal fluid changes reflect mainly the meningeal component.

The foregoing survey aims at applying the general principles of diagnosis to the special problem of meningoencephalitis. It starts with the patient, and endeavours to show how, from the signs and symptoms he presents, we are led to infer the presence of meningoencephalitis and to search for its cause. It should help us, moreover, to recognise the limitations imposed on diagnosis by the available evidence.

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