CERTAIN of the cerebral manifestations of infections such as delirium create but little interest, the experience of the ages having taught us that we can never correlate the delirium with the anatomical findings; certain others such as coma and convulsions, in adults at least, interest us in that they increase the gravity of the prognosis and upset our calculations for the autopsy table but little less often. For these reasons we find that it is with the more sharply localized manifestations or with manifestations more clearly psychic that the bystander most concerns himself.

An integral part of clinical medicine, the cerebral manifestations of infections have been frequently dealt with, and their causation ascribed to many conditions, such as the height of the fever, the presence in the blood of urea in increased amounts, or coincident nephritis or nephrosis. An observer of 60 years ago, C. H. Bastian, was convinced that plugging of cerebral vessels with thrombi explained all nervous symptoms. Murchison is clear, however, in his statement that "the severest nervous symptoms may be seen in cases whose brains showed little or nothing to a practiced eye," and the remarks of Stokes, the then celebrated student of the fevers of Dublin might well be remembered to-day—"Symptoms of inflammation of the brain do not necessarily indicate inflammation if the case is one of typhus, even such symptoms as inequality of pupils, strabismus, muscular rigidity, and perhaps opisthotonus may be present without inflammation."

To-day perhaps, our ability to detect conditions in the cerebro-spinal fluid has helped to explain some of the many cases with a meningeal syndrome, and the finer histology has given us the recognition of vascular and peri-vascular changes in such conditions as syphilis, encephalitis, and polio-myelitis, without evidence of gross changes. We are the further advanced by these improvements; nevertheless, the uncertainty of being able to demonstrate lesions to correspond to symptoms of cerebral involvement still exists; there is this comforting fact, however, in the consideration of many of the cerebral manifestations of general infections—the most severe symptom may be recovered from.

The common infections seen in a general hospital—the pneumonias, typhoid, influenza, septicemias, rheumatism, and erysipelas have a varied assortment of cerebral manifestations; meningitis, common to all, (especially to the pneumonias and to the septicemias), I am not considering, its very evident group of symptoms and the results of lumbar puncture usually dispel doubt. The appellation "meningism" well describes the condition we frequently see in the infections—active meningeal symptoms with clear spinal fluid under pressure and with increased cell count. This must be considered as meningeal irritation at least, though often only part of a general process of infection and very frequently recovered from. In cases ending fatally, singularly little may be found. In the respiratory infections, aside from delirium, the cerebral manifestations are few and the anatomical findings fewer. In no type of infection is the diagnosis of cerebritis or meningitis so often made, especially is this the case in children; the difficulty is in these cases to observe both the clinical course of the disease and the brain sections; amongst 120 cases actively delirious, I have recorded one with rigid neck, internal strabismus, and recovery; one with rigid neck, positive Kernig and Babinski sign, with recovery; one with rigid neck, the same positive signs, death, but no meningitis. Clear spinal fluids were found in all these cases.

Coma as an early cerebral manifestation of respiratory infections is unusual, and was a fatal sign in all of eleven cases beginning in this way; convulsions, early or late, were equally ominous, in adults. Four convulsive cases all died: one, with the typical signs an!
symptoms of meningitis in addition, showing, however, only the familiar oedema and congestion of the brain: no exudate, no organisms. A second showed flaccid paralysis of an arm and deviation of the eyes with his fatal convulsions, presenting a combination suggestive of some more localized pathological change. Psychic manifestations at onset, so pronounced that they separate themselves from the simple febrile delirium and the signs of the infection, are rare. Two instances of delusions of persecution were in my series, another was diagnosed as "dementia preeox developing in an epileptic." We are more familiar with the forms seen after crisis or lysis, "post critical delirium or psychosis." These are by no means uncommon and they are the more protracted if the case has had an alcoholic history. Ptosis, amblyopia, lethargy and nystagmus were unusual and transient manifestations occurring once each in a series of 350 cases: the two first would probably be considered as peripheral lesions.

There is no convincing pathology to offer; thrombosis, rare in pneumatic infections, is suggested in the case showing convulsions and monoplegia;—later case with rigidity of the left arm, paresis of the left side of face and semi-consciousness, went on to abscess formation in the lungs: there were thromboses of the peripheral veins in this case and thrombotic softening of part of the right cerebrum. No good instance of encephalitis (diffuse or focal), embolism, or haemorrhage, proven by autopsy, has occurred in my series; both encephalitis and haemorrhage are recorded, however, in respiratory epidemics such as have been seen of late.

The last hundred cases of typhoid in the Toronto General Hospital have shown singularly few cerebral manifestations apart from the early delirium, nor have I found specimens illustrating the thrombosis, meningitis or encephalitis which Osler considers the common anatomical changes in the cases with marked cerebral involvement. One case of deafness occurring early was considered a peripheral lesion, a neuritis, and was recovered from; it occurred coincident with a fatal laryngeal and pharyngeal paralysis; the direct cause of the paralyses in this latter case remained unproven in the absence of autopsy. Such conditions are referred to by the older writers and considered as analogous to the lesions of diphtheria. The following history illustrates one of the most severe cerebral manifestations of typhoid with a definite localization:—In the third week of a severe typhoid when the fever was subsiding, Mrs. A., 35 years of age, began to develop rigidity of her neck: her right arm and leg became rigid and she was quite unable to make more than a few incoherent sounds; after ten days of added delirium and weakness there was a gradual improvement and she went out recovered (save for some slight stiffness) and able to speak. Similar conditions are referred to more frequently in the course of typhus fever; they are considered as due to thrombosis, arterial or venous, and many good examples of this have been demonstrated. In the experience of some observers a focal encephalitis has seemed to be the cause. Not every case recovers as completely as did the one reported, for permanent rigidity and paralysis may remain. I have had no experience with the temporary aphasia reported in the typhoid infections of children.

No discussion of cerebral manifestations of typhoid is complete without a detail of the psychoses of this infection; their occurrence as an early delirium, as an aberration later in the fever, or as a condition in convalescence may be mentioned; they do not depend upon the severity of the attack. Dr. Rudolf allows me to describe an interesting case from his service:—Richard A., with a severe infection became fatuous, childish and tearful as his temperature fell; he was increasingly so in convalescence. A gall-bladder infection developed and later he relapsed: with the relapse active delirium for a few days, but as he cleared up he was seen to be free from his fatuity and quickly became normal. These psychoses are noted as usually being recovered from, though at times their course may be prolonged. Of unusual interest in the typhoid series was the development of typhoid in a case of chorea; the choreiform movements subsided as the disease progressed (case of Professor Rudolf).

It was expected that the influenza epidemic of 1919 would give us many instances of brain involvement; in this we were mistaken, for apart from the delirium of the severe and fatal cases, few nervous manifestations were seen. The supposed dependency of encephalitis upon preceding influenza was considered in this connection, and in the three hundred cases nervous signs and symptoms were regularly looked for.
In a few patients transient weaknesses of the eye muscles were observed, some pneumonies showed the meningeal irritation so often referred to, but real cerebral involvement was not a part of the last epidemic.

With the various septicaemias and with rheumatic fever are seen the best examples of real cerebral changes. The older descriptions of encephalitis, the forms distinct from the lethargic encephalitis, deal largely with lesions seen in the endocardial cases or in cases of acute sepsis; leaving aside the symptoms due to large emboli, we find many interesting histories.

A.—In one case paresis of legs, diplopia, ptosis, divergent squint and lethargy followed an active diverticulitis and abscess of the rectum, which in turn had seemed to follow upon an infected hand; weeks of unresponsiveness and childishness ensued and there were, in addition, remarkable spasms of the abdominal muscles—a persistent white cell count of 20,000—40,000, seem to indicate active infection. There was complete recovery.

B.—Two weeks of extreme restlessness with severe hyperaesthesia, confusion, then coma, with left facial weakness, was the history in a case with extensive endocarditis of mitral and aortic valves due to a staphylococcus aureus infection; multiple embolic abscesses were found in the brain sections.

C.—Headache, aphasia, and staggering gait preceded by some days the hemiplegia and unconsciousness in another case of mitral and aortic endocarditis with streptococcus haemolyticus infection: gross haemorrhages and pinpoint haemorrhages throughout the brain were the findings. These are the types of cases in which the extensive sub-arachnoid haemorrhages are prone to occur.

Coma, long recognized as a symptom of endocarditis, was only noted as late-occurring in the cases I have been able to review and to control with an autopsy record; mania of four weeks' duration preceded death in one case of the subacute form of bacterial endocarditis, and for months previous, this very powerful man had suffered from phobias of unusual sorts and would wander lost for days. Of the cases with distinct rheumatic history and endocarditis, and with careful post-mortem examinations, two may be detailed.

1.—A young woman with recurring attacks of acute rheumatism and a mitral valve lesion, became very irrational, had delusions and would wander from home. Two months after these mental features had been noted she had another attack of acute rheumatic fever, she was emotional, had active delusions, and after a few days became delirious and died. At autopsy, mitral endocarditis, oedema and congestion of the brain, with an area of softening posterior to the caudate nucleus were found.

2.—A woman of 33 with a history of repeated rheumatic attacks entered the hospital in a state of absolute coma. There were no paralyses; for two months she had been worrying, had been excitable and had had delusions; a loud systolic murmur was evident on examination; a rheumatic endocarditis, multiple petechial haemorrhages in the brain, and a haemorrhagic pachymeningitis was found. These cases showed nothing bacteriologically.

One may recognize from these details that cerebral manifestations of various sorts are to be looked for in many of the infections, their pathology is evidently very varied and their seriousness would seem to depend much more upon the nature of the infection than upon the symptomatology.

The following examples of the cerebral pathology in some infections, were prepared by Dr. E. L. Robinson, of the Pathological department, Toronto General Hospital.

PLATE 1.—From a case of general infection beginning with an anthrax pustule on the face. Signs of a general infection—fever, then absolute unconsciousness. Large sub-arachnoid hemorrhage over whole of cerebrum, myriads of punctate hemorrhages. (From a case in the service of Dr. H. A. Bruce).

PLATE 2.—Severe malarial infection. Patient in coma with fixed pupils; multiple emboli of parasites and pigment containing cells in the minute vessels of the brain. (Specimen lent by Prof. W. G. Macallum of Baltimore).

PLATE 3.—Case supposed to be an alcoholic; restless and irrational for weeks; marked hyperaesthesia, fatal coma; extensive endocarditis of mitral and aortic valve due to staphylococcus aureus infection; embolus of the left middle cerebral artery, sub-arachnoid hemorrhages, thrombus of right lateral sinus, multiple areas of minute pyemic encephalitis. (Service of Professor Duncan Graham).

PLATE 4.—Case of headache, aphasia, staggering gait for some days, then sudden hemiplegia of right side, unconsciousness: profuse mitral and aortic endocarditis, extensive sub-arachnoid hemorrhages, multiple minute hemorrhages in brain with no sign of reaction. (Service of Professor Duncan Graham).

PLATE 5.—Case of fever, weakness and paresis, and finally paralysis of all extremities and muscles, considered as encephalitis. At autopsy, endocarditis, multiple minute thrombi throughout brain. (Service of Professor Duncan Graham).