THE FULMINATING TYPE OF CEREBRO-SPINAL FEVER:

PATHOLOGY, AND CAUSE OF DEATH.

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CASES belonging to the fulminating type form one of the most distressing features of cerebro-spinal fever. An apparently healthy person is suddenly attacked, and dies within forty-eight hours from the onset of his illness.

In our series of cases during the epidemic of 1914-16 we noted a considerable number which may be classified under this heading. We have notes, including *post-mortem* records, of ten to twelve of these cases, and in addition clinical notes of several more which have belonged to this type.

All terminated fatally, and pathologically differed from the ordinary type in one essential feature, and it is principally to this that we wish to draw attention.

It has been recognized for some time that cases of intense meningococcal bacteraemia without any meningeal involvement may occur. While these cases are rare, it is not so uncommon to find others very similar in which the meningeal infection is very slight, and which apparently succumb to the general infection before the lesions of the meninges have time to develop fully. Our notes on one of these cases will sufficiently describe the class.

CASE I.

H., aged 21, became suddenly ill in the evening of April 9th, 1916, with headache, shivering and vomiting. On admission to hospital on the following day the patient looked ill; his face was pale and slightly cyanosed. He complained of slight headache and pain in the ankles. There was slight resistance on antero-posterior flexion of the neck; Kernig's sign was just present. Knee-jerks and the abdominal reflex were absent. *Tache cérébrale* was present, and there was a petechial rash on the trunk and limbs, with many large purpuric blotches. Cardiac dullness was increased to right side of sternum.

Blood Examination:

Total leucocytes	...	...	...	...	31,000
Differential count:					
Polymorphs	...	...	...	...	85 per cent.
Lymphocytes	...	...	...	...	5 "
Mononuclears	...	...	...	...	7 "
Myelocytes	...	...	...	...	3 "

Lumbar Puncture: 50 c.cm. perfectly clear fluid under pressure. No increase of cellular content; protein content not increased; no fibrin; reduced Fehling; 2 c.cm. spread on plate gave four colonies of meningococci; 1 c.cm. of blood in broth gave profuse growth.

The patient remained comfortable for some hours and did not complain of pain, but the pulse became more and more feeble, until it could not be felt at the wrist. The patient died suddenly. He remained conscious to the end; for some time before death no heart sounds could be heard and there was intense cyanosis.

A *post-mortem* examination showed the meninges to be congested. There was a slight amount of exudate about the optic chiasma and on the under surface of the cerebellum; faintly turbid fluid in the lateral ventricle, and extensive haemorrhage into the substance of the adrenal gland. There was also petechial haemorrhage under the pericardium, and into the intestinal mucous membrane, etc.

In the other type, after a similar abrupt onset, the patient becomes almost immediately unconscious. At first the signs of involvement of the meninges are present, but later they may be replaced by complete muscular flaccidity. A profuse purpuric rash appears, the breathing becomes stertorous, and the patient intensely cyanosed; cardiac dilatation commences, the heart becomes more and more feeble, and finally ceases to beat.

The cerebro-spinal fluid is extremely turbid, and is under considerable pressure. It contains many polymorphs and abundant meningococci, both intracellular and extracellular; fibrin is present, and it no longer reduces Fehling's solution. In most cases the meningococcus can be cultivated from the blood.

Blood Examination:

Polymorphs	...	...	...	...	74 per cent.
Mononuclears	...	...	...	...	8 "
Lymphocytes	...	...	...	...	18 "
Polynuclear count:					
I. 56 per cent.	...	...	...	...	83 per cent.
II. 27 "	...	...	...	...	
III. 14 per cent.	...	...	...	...	
IV. 3 "	...	...	...	...	17 per cent.
V. 0 "	...	...	...	...	

This shows the extent of the general infection. *Post-mortem* examination reveals extensive purulent infiltration of the cerebral and spinal meninges, and an increased quantity of cerebro spinal fluid, which is very turbid. There are haemorrhages into the adrenal glands, and petechial haemorrhages into other organs, as described in the first class, may be present.

These two classes are not sharply divided, and intermediate cases are met with.

Pathology.

Post-mortem examination also reveals two types of cases. In one the brain and cord are merely congested. The congestion may not be marked, there may be very little fluid in the lateral ventricles or cisternae, but this fluid is slightly turbid. This small amount, not more than normal, of turbid fluid is found chiefly in the lateral ventricles, and the cisterna chiasmatis, and may be the only macroscopic sign of involvement of the central nervous system. In the other there is extensive involvement of the pia arachnoid, giving the well known appearances.

There are, however, two conditions which have been invariably present in our series of cases of malignant cerebro-spinal fever, namely, a purpuric rash and a haemorrhagic state of the adrenals.

The rash is haemorrhagic, and varies from petechial spots to large areas of several square inches. There may be petechial haemorrhages on the epicardium and on the serous surface of the intestines. The adrenals are found to be dark-red, enlarged and friable. Their weight may be as much as 24 to 28 grams. Microscopically, the medullary substance is replaced by effused blood and very few chromaffin cells are to be seen. The reticular, fascicular, and glomerular zones show distended capillaries, and red blood corpuscles effused between the cortical cells. The cells are distorted by pressure, and many have lost their outline. The refractile granules are much diminished in number.

The occurrence of haemorrhage into the adrenal glands has been noted previously, but sufficient importance has not been attached to its frequency. The destruction, by haemorrhage, of the medulla of the adrenals would account for the curious clinical phenomena, diminution and later absence of blood pressure and muscular flaccidity.

The hypotension is, of course, directly due to the loss of epinephrin, the normal stimulus to the "myoneural function" of the sympathetic autonomic system. The muscular flaccidity, with loss of neck stiffness, Kernig's and Brudzinski's signs, and knee-jerk, is accounted for in the same manner, and would tend to confirm the view that epinephrin not only acts upon the plain muscle innervated by the sympathetic autonomic system, but also has a stimulating effect upon the tone of the skeletal muscles.

The presence of acute haemorrhagic adrenalitis, although not confined to cerebro spinal fever, is so common in that disease as to suggest a selective action by the meningococcus on the chromaffin cells, and the fact that the medulla is developed from the same neuroblastic masses as the sympathetic system affords further grounds for the theory.

But we have no proof that the haemorrhage and cell destruction commence in the medulla. The cortical cells and refractile granules share the same fate as the medullary cells, and it is quite possible that the cortex is the starting point. The lipoids of the cortex, thought to be specially related to the formation of myelin, may have initiated the pathological condition by their sudden withdrawal from the cortical cells, in response to the myelin degeneration taking place in the central nervous system.

Treatment.

The utilization of the knowledge of this tendency to haemorrhagic adrenalitis is important.

In the acute case, with rapidly falling blood pressure, adrenalin should be injected intravenously in such doses as will keep the arterioles sufficiently contracted to maintain the circulation, in the hope that either the chromaffin cells or the other parts of the chromaffin system will increase and take over the functions of the adrenals, or that the medullary cells will recover.