THE HISTOPATHOLOGY OF THE PARKINSONIAN SYNDROME FOLLOWING ENCEPHALITIS LETHARGICA.

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THIS sequel of encephalitis lethargica has attracted much attention on account of its great frequency. It was found in 70 out of 129 cases studied by Mme. Lévy (1). In the earlier pathological studies of the syndrome attention was focussed chiefly on the mid-brain; recent researches have proved that the changes in the nervous system are more widespread than were at first apparent.

In this case the areas examined in each hemisphere were: The frontal, precentral, post-central, temporal, calcarine and hippocampal, the corpus striatum, thalamus and hypothalamus. The whole of the mid-brain, pons and medulla were cut into blocks. The spinal cord was not removed. The stains used were toluidin blue, bleu de lyon, cresyl violet, iron-alum and eosin, and Scharlach R.

CLINICAL NOTES.

History.—In March, 1923, the patient, a weaver, had an attack of "influenza." There were periodic attacks of vomiting. She became very sleepy and was never out of bed. No squint was observed, but she lost the power of the right arm. Shortly afterwards a rigidity was observed which first appeared in the hands and arms, then the neck became very stiff. Increased salivation was observed. On admission here on September 8, 1925, she held herself absolutely stiff and had a vacant stare. She would gaze fixedly at one object for hours. She refused all food and had to be forcibly fed. She was unable to wash or dress herself. Perspiration was marked, the right side of the face perspiring more freely than the left. Drooling was constant. Her gait was staggering and uncertain.

Physical examination.—The head, ears, nose and throat presented no abnormalities. The lungs and abdomen were negative. There was a moderate degree of arterio-sclerosis. The pupils were unequal and irregular; the left reacted normally, the right only on accommodation. The consensual reaction was absent on the right side and sluggish on the left. The cilio-spinal reflex was negative.

Tendon reflexes were brisk on both sides, but more markedly so on the right, where there was both patellar and ankle clonus. The plantar response was extensor in type on the right side but doubtful on the left. The abdominal and epigastric reflexes were increased on the right side. Rombergism was present and Stellwag's sign was positive. There was coarse tremor of both hands, generalized rigidity of the biceps, and inability to flex the arms beyond a right angle.

Laboratory examination.—The urine showed a trace of albumen and a few pus and epithelial cells, but no other abnormalities. The Wassermann reaction was

negative in the blood and cerebro-spinal fluid. The cerebro-spinal fluid was clear, not under increased pressure, and showed sugar ·07%, cells 2·6, no globulin, and a colloidal gold curve of $0\frac{1}{0}$ 1100000.

Subsequent course.—She grew steadily and progressively worse. She became faulty in her habits and totally dependent. Swallowing became difficult. Distinct pulmonary symptoms developed, and broncho-pneumonia set in, followed by gangrene of both lungs. She died on November 4, 1926, three years and eight months after the onset of her illness.

Pathological Report.

External.—The brain showed no definite cortical atrophy. Beyond some thickening of the pia-arachnoid, no abnormalities were noted.

Microscopic examination.—Definite changes were found in the cortex. The cell changes were slight. They were shrunken in places, showed shadow formation, and there was evidence of chromatolysis. The changed cells were found amongst the normal cells in all the layers, but were most in evidence in the deeper layers of the frontal and temporal lobes. Mild satellitosis was observed in the deeper layers. There were, in many places, small perivascular infiltrations (lymphocytes and plasma-cells). These infiltrations were less marked in the parietal cortex. In the temporal lobes numerous amyloid bodies were scattered over the cortical and subcortical areas. There were no calcareous deposits in the cortex. There was a slight increase in the fat content.

Caudate nucleus.—The large ganglion cells of the caudate nucleus showed definite changes. Their bodies were pale, appearing as mere shadows in places. The nuclei were poor in chromatin and eccentric, and in a large number of cells no nucleus was visible. Similar changes were observed in the small cells. There was a slight increase of glia-cells and fibrils. The blood-vessels were prominent, and there was "cuffing" of some of the smaller vessels, with evidence of small hæmorrhages.

Thalamus and putamen.—The large ganglion cells of the optic thalamus were swollen in places, in others shrunken and irregular, and frequently in a state of chromatolysis. The small ganglion cells showed similar changes. The parenchyma was invaded with "gitter"-cells, which formed clumps in areas. There was evidence of excessive vascularization. The adventitial and endothelial cells of some blood-vessels were markedly hypertrophied. Small perivascular infiltrations (lymphocytes and plasma-cells) were visible here and there. Lipoids were present in large quantities in the vascular and perivascular spaces of the putamen.

Nucleus ruber.—The nerve-cells were greatly degenerated, especially in the area magnocellularis. Many of the cells had lost their shape, and were irregular in outline, while others showed shrinking

and shadow-formation. The nuclei were eccentric in many cases, pale and homogeneous in others, and in many cells they seemed to have disappeared. The parenchyma was invaded with cells, which appeared to be polyblasts. There was evidence of glia-cells invading many of the smaller cells; they were often seen in groups close to the cell body. Pigment was present in several of the perivascular spaces and there were some small diffuse hæmorrhages.

Substantia nigra.—Here the number of pigmented cells was greatly reduced. The cells in the zona compacta showed degeneration (shrinking, shadow formation, fragmentation, etc.), the nuclei in many cases being eccentric. Pigment was present in the perivascular spaces, and was also scattered throughout the section. There was evidence of infiltration of the blood-vessels by "gitter"-cells in places. Moderate quantities of lipoids were present.

The ganglion-cells in the globus pallidus were fairly well preserved. "gitter"-cells were numerous, often forming foci.

The gyrus rectus showed evidence of old hæmorrhages. Slight perivascular infiltrations were observed in the orbital gyrus.

In the cerebellum there was some vascular congestion with atrophy of the small cells in the granular layer. Purkinje's cells appeared normal. There was evidence of chronic cellular degeneration (shrinking, shadow formation, etc.) throughout the medulla and pons. The parenchyma was invaded with "gitter"-cells in many places. There was a slight increase of glia and fibrils. The blood-vessels were numerous, and often hyperæmic. There was "cuffing" of many of the small vessels.

Comment.

Parkinsonianism presents a well-marked clinical picture—a mask-like expressionless face, sialorrhœa, rigidity, perspiration and tremor, with retardation of the voluntary movements. The great variety of clinical forms found, the numerous symptoms and their variability from case to case, indicate that the lesion is a widely diffused one.

Here the conclusions are based on one case, and it hardly seems justifiable to generalize on the basis of a single observation.

Marked macroscopic changes were not in evidence.

The main characteristic of the histopathology was the evidence of the widespread distribution of the affection over different functioning areas of the central nervous system, though certain of these were more affected than others. The systematic examination of

the various parts showed that, though centred in the mid-brain, the disease affected all parts. Practically no region was quite normal. With the exception of the mid-brain, the lesions were scattered, the affected vessels and cells being found amongst others that appeared normal.

In the cerebral cortex the lesions were irregularly distributed, and no one region was more markedly affected than another.

A widespread and apparently independent degeneration of the nerve-cells was a notable feature. The cell changes were regressive. They were most marked in the basal parts of the brain, especially in the substantia nigra and the nucleus ruber. Cellular changes were also marked in the corpus striatum and thalamus, but the globus pallidus was only slightly affected. The trouble chiefly fell upon the mesencephalon, in the region of the crura and substantia nigra, extending towards the thalamus and the subthalamic regions, and so down to the pons and bulb, the lesions becoming less evident in the more distal areas.

The Parkinsonian syndrome is traceable to the corpus striatum and the structures in close proximity. In the corpus striatum we have a complex structure; the striate bodies are believed to comprise two chief systems—the neostriatum (caudate nucleus and putamen) and the palaeostriatum (globus pallidus). The striatum appears to have three main functions: The regulation of tonus, regulation of associated automatic movements, and the maintenance of muscular repose. The range of the functions may be appreciated when it is known that it represents "the highest motor control in these forms of life where there is no cortical function" (Wimmer) (2).

Souques (3) thinks of the centres involved as both motor and vasomotor. He believes that when the mesencephalon is but slightly involved and "reparable" in the course of the disease a Parkinsonian syndrome is produced; if the lesion is "irreparable" paralysis agitans results.

Tretiakoff (4) showed that in Parkinsonian states the substantia nigra is largely involved, and his findings have been corroborated by Bremer (5), Goldstein (6), Lucksch and Spatz (7) among others. Wimmer also found advanced changes in the substantia nigra and pallidum.

Hallevarden and Spatz (8) believe that the substantia nigra and globus pallidus are histologically and physiologically similar. In this case the substantia nigra was the one structure principally involved; though in some cases exhibiting marked Parkinsonian symptoms it has shown little change.

It is probable that lesions of the globus pallidus are responsible

for the increased muscular tone evident in the Parkinsonian syndrome, and that abnormal movements, such as tremor, are due to lesions of the putamen and caudate nucleus.

The changes in the nucleus ruber may be responsible for the rigidity. Weed (9) considers the mesencephalon, especially the nucleus ruber, of chief importance in the production of rigidity. Graham Brown (10) is of the same opinion. The nucleus ruber is believed to have a constant effect on the cells of the anterior horn, thus ensuring the control and distribution of tone. A lesion would thus produce loss of control, leaving the vestibular systems to act on the anterior horn-cells.

The Parkinsonian syndrome is thus probably the manifestation of deranged function of the basal nuclei of the cerebrum, the vestibular system and the mid-brain.

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