

THE HISTOLOGICAL CHANGES IN THE NERVOUS SYSTEM
OF DR BOX'S CASE OF PELLAGRA COMPARED WITH
CHANGES FOUND IN A CASE OF PELLAGRA DYING IN
THE ABASSIEH ASYLUM, CAIRO.

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METHOD EMPLOYED FOR PREPARATION OF SPECIMENS.

The brain, spinal cord, and a few of the posterior spinal ganglia and a small piece of the sciatic nerve were sent for examination. Portions of tissue obtained from various parts of the central nervous system were separately hardened and fixed in Muller's fluid for subsequent examination by the Marchi method for recent degeneration, and by the Weigert and Weigert Pal methods for fibre system degenerations. Other portions were hardened for a few days in 5 per cent. formalin, and transferred to alcohol in successive strengths for examination by Nissl method; some portions of the formol fixed tissues were subjected to the Bielschowsky method for demonstration of fibril changes in the cells.

The Muller hardened tissues were treated by the celloidon method before sections were cut by the Jung microtome.

The formol hardened specimens were embedded in paraffin and cut in the Cambridge rocking microtome. The sections were 10μ in thickness.

CHANGES OBSERVED IN THE FIBRES BY THE MARCHI METHOD.

Sciatic Nerve.—Recent scattered degenerated fibres were found in all the longitudinal and transverse sections of the sciatic nerve; not limited to any bundle of fibres, but general, though somewhat unequal in numbers in all. *Fig. 1* shews one of these bundles in transverse section; the black dots are the degenerated fibres. *Fig. 2*, a bundle in longitudinal section. Owing to the piece of nerve not having been pinned out on cork when placed in the hardening fluid before I received it the fibres are curled, consequently the sections have cut many of the fibres obliquely.

Cauda Equina.—The roots of the *cauda equina* shew similarly scattered degenerated fibres (*vide Fig. 3*).

Spinal Cord.—There is general diffuse and scattered degenerated

fibres throughout the white matter, more marked in the postero-lateral and posterior median columns than elsewhere.

CHANGES OBSERVED IN THE FIBRE SYSTEMS BY THE WEIGERT AND
WEIGERT PAL METHODS.

There is a slight general diffuse sclerosis throughout the white matter of the cord in all regions, but in certain regions there is a perceptible naked eye combined sclerosis affecting the direct cerebellar and Gower's tracts, Goll's column and the crossed pyramidal tracts. The ascending degenerations are very observable, as *Figs. 4 and 5* shew in the cervical region. This is to be expected, because in this region all the fibres belonging to these tracts have taken up a definite position, consequently disappearance of the fibre and replacement by neuroglia tissue is more obvious to the naked eye, but microscopic examination in any part of the cord shews the outfall of fibres in these systems and their replacement by neuroglia.

The descending degeneration in the crossed pyramidal tracts is obvious to the naked eye, but, aided by a hand lens, is very evident in the lower lumbar and sacral regions (*Fig. 6*). *Figs. 7 and 8*—Examination microscopically shews an outfall of fibre and replacement by glia tissue of the crossed pyramidal systems in any part of the course. The direct tract is much larger on one side than the other, and in the cervical region a well-marked outfall of fibres with sclerosis is observable with a low magnification. This is more obvious on the side where the direct tract is the larger. Some scattered sclerosis can be observed in the pyramids of the medulla.

CHANGES OBSERVED IN SECTIONS OF THE CEREBRUM, CEREBELLUM,
PONS, MEDULLA, SPINAL CORD AND SPINAL GANGLIA CUT BY THE
PARAFFIN METHOD, AND STAINED BY NISSL, POLYCHROME, GIEMSA,
LOGWOOD, EOSIN AND VAN GIESON METHODS.

It may at once be said that in none of the sections examined was there any evidence of meningeal or perivascular infiltration with lymphocytes or plasma cells or with polynuclear leucocytes. I mention this, firstly, because the terminal streptococcal infection had, therefore, not invaded the cerebro-spinal fluid, and could, therefore, as there was no inflammatory sign, account for the changes in the neurones. Moreover,

the absence of chronic meningo-encephalitis and myelitis, so characteristic of protozoal diseases, *e.g.*, malaria, in which the vessels may be filled with the organisms and yet no inflammatory perivascular and meningeal reaction is seen, so that it in no way disproves a protozoal origin of this disease; moreover, although all the changes are like those produced by a chronic toxæmia, yet the cause of that toxæmia has not been satisfactorily determined. Whether the two ulcers found in the intestines had any relation to a chronic toxic infection it is difficult to say. The combined sclerosis is not unlike that found in a pernicious anæmia which we know may be due to a streptococcal toxæmia.

By any one of the methods mentioned the following changes may be observed :—

All the posterior spinal ganglion cells shew in varying degrees a marked chromatolysis, swelling of the cell, disappearance of the Nissl granules, except at the periphery, and frequently eccentric position of the nucleus (*Fig. 9*). All the anterior horn cells and their homologues in the medulla and pons shew varying degrees of perinuclear chromatolysis; in some instances the cells are so markedly swollen, and the nucleus is so eccentric, that it appears as if the cell were dead. There was a marked chromatolysis of the cells of Clarke's column.

The Betz cells of the cortex shewed similar changes but not so marked (*Fig. 10*); likewise the cells of Purkinje; the pyramidal cells of the cerebral cortex did not appear to be markedly affected.

Wherever the nervous system was examined the cells which normally have a Nissl pattern seemed to shew a change in the nature of a disappearance of the granules partial or complete, without any evident changes in the vessels of an inflammatory nature to account for the same. Seeing that there is a combined sclerosis of the cord, obviously these changes could not be of quite recent origin, and, therefore, capable of being explained by the terminal generalisation in the blood of streptococci from the balanitis. Moreover, my experience tells me that the nerve-cell changes rather indicate a chronic toxæmia.

CHANGES OBSERVED IN THE CELLS BY BIELSCHOWSKY

FIBRIL METHOD.

The anterior horn cells and the cells of Purkinje, also the Betz cells, but to a less degree, shew in varying degrees, in different parts of

a section and in various regions examined, fibril changes similar in character. Some cells shew hardly any fibrils, others a few, others appear quite normal, as if they had been attacked in different degrees of intensity by the poison. This is not an unusual condition of things in chronic toxic conditions affecting the nervous system. *Fig. 11* shews the changes in the cells of Purkinje. *Fig. 12* shews a group of anterior horn cells.

Comparison of these changes in the cells of Dr. Box's case with those of a pellagrous patient who died at the Abassieh Asylum—for the notes and material of which I am indebted to Dr. PEARSON—shew that there is no essential difference. There is a combined sclerosis of the spinal cord more marked in the Egyptian case; there are the same changes in all the ganglion cells of the spinal cord and brain, and there are no signs of acute or chronic vascular or meningeal inflammatory changes. This case came from a district where the maize which the people had eaten was very bad. My assistant, Mr. MANN, has made a preliminary examination of this maize, and he finds that compared with sound maize there was a considerable diminution of phosphorised lipoids. It is possible that any impoverishment of diet, by which certain essential substances in the blood fall below the physiological minimum, may play a part in a degenerative process of the nervous system. Still, here we find these two cases of Dr. Box, in which diseased maize certainly could not have played any part in the production of degeneration of the nervous system, similar in histological details to those of a case which had come from a pellagrous district in Egypt, where unsound maize had been a staple article of diet. It seems that we must look for some other etiological factor as the essential cause of this disease, and we can but admire Dr. SAMBON's enthusiasm and energy in the endeavour to shew the protozoal origin of this disease by its epidemiology.

I wish to express my indebtedness to my assistant, Mr. CHARLES GEARY, for the photomicrographs and preparations.