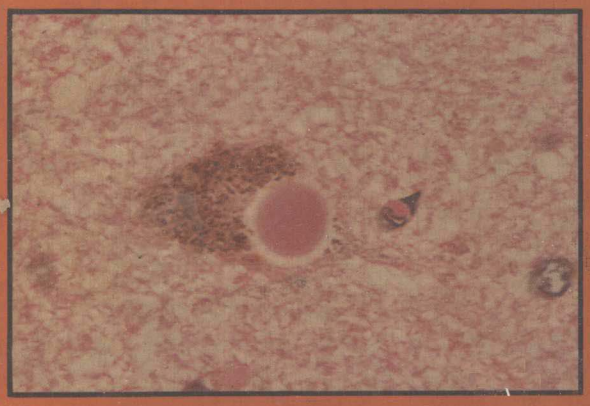
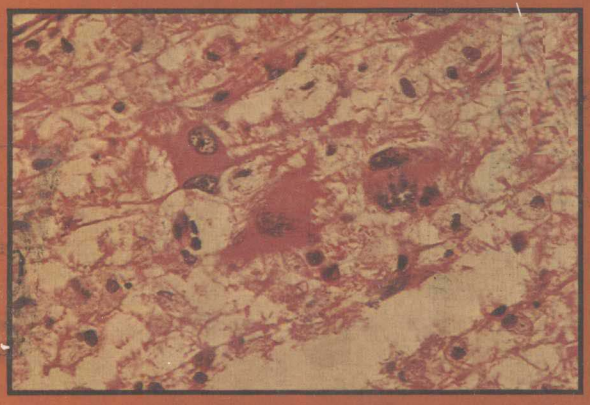
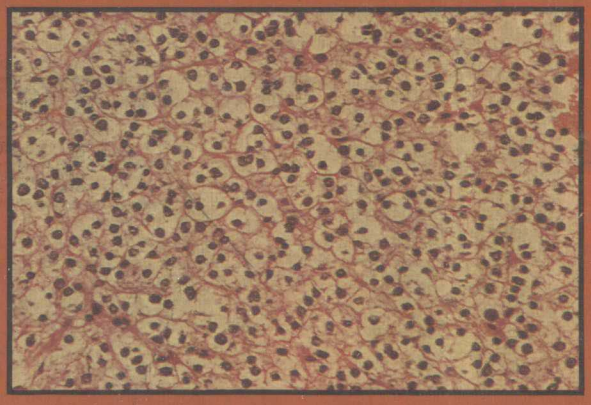
A Colour Atlas of Neuro-pathology

C. S. Treip







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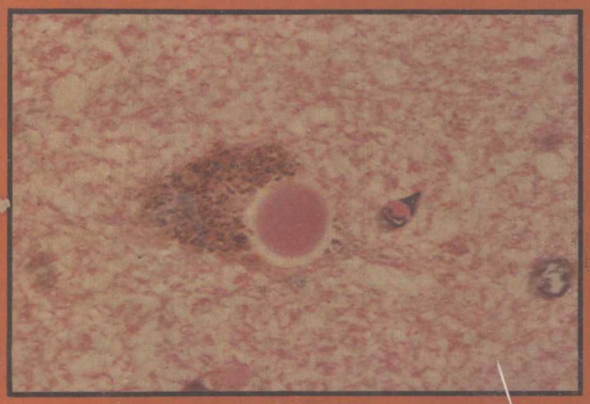

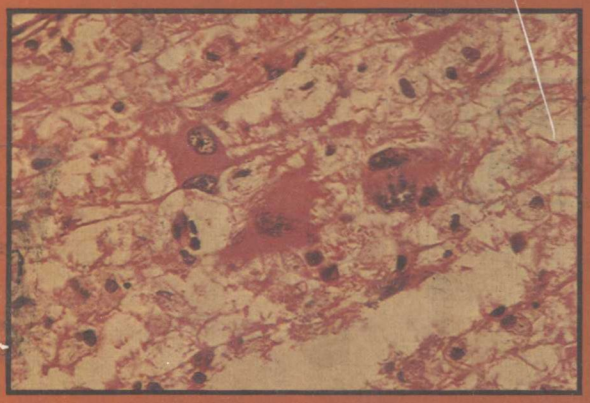
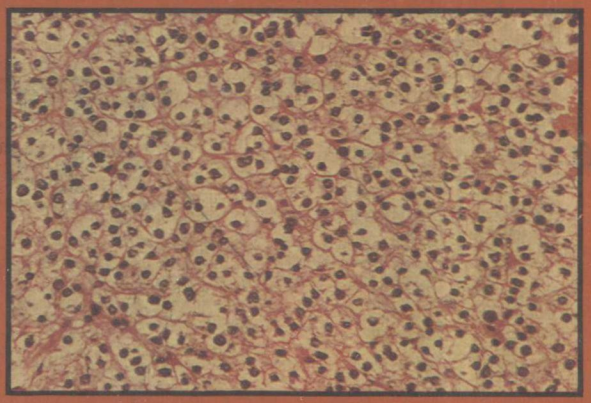

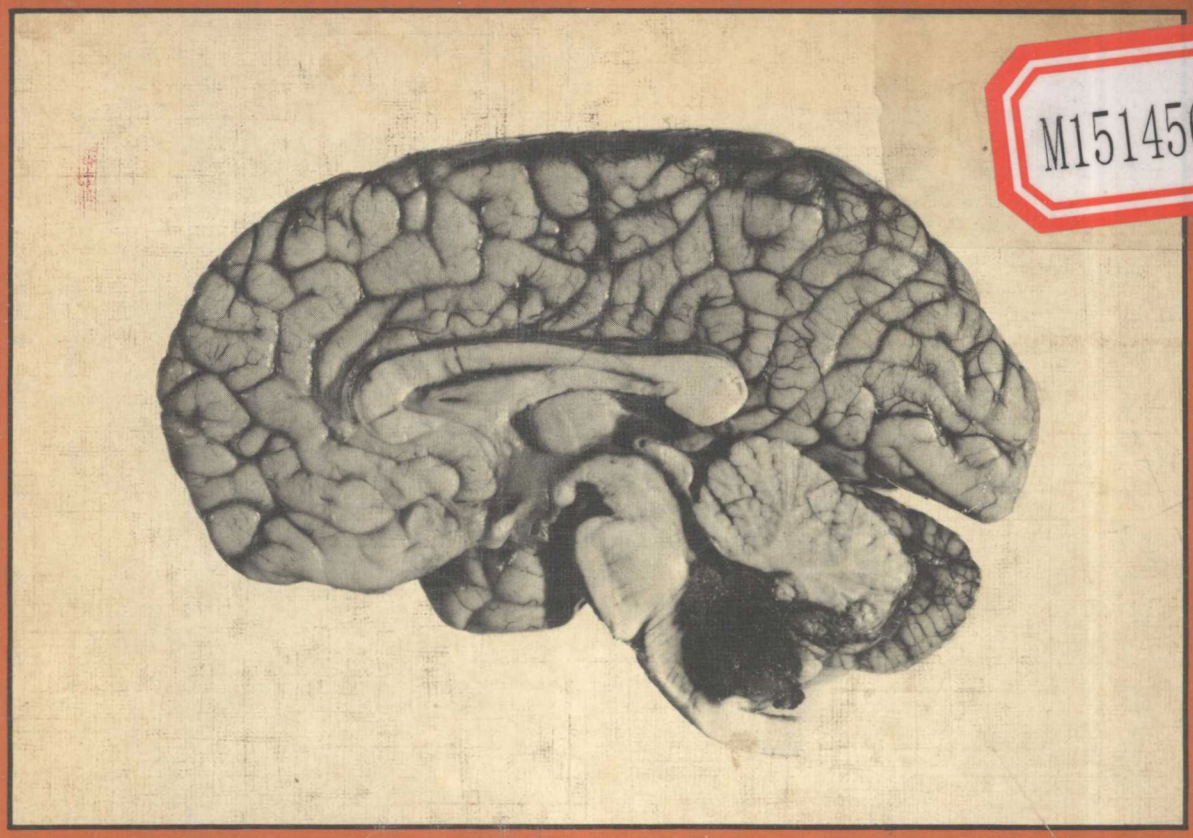

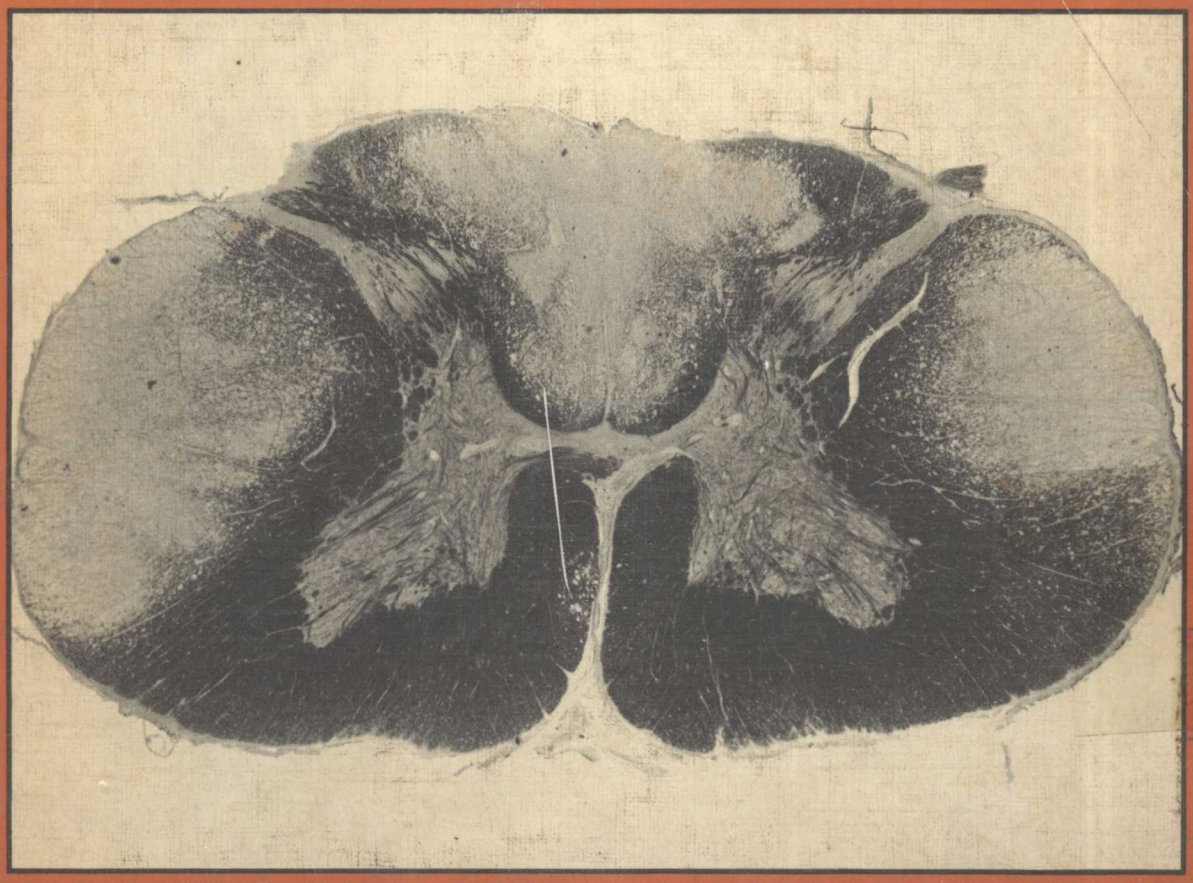

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TO MY FAMILY

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Introduction

The atlas is designed as an introductory manual of diagnostic neuropathology. With this practical aim in mind, it is addressed chiefly to pathologists in training and to senior medical students. It is hoped that it may also prove to be of use to those working in the field of clinical neurology, neurosurgery and psychiatry.

An outline is given in the first chapter of the basic histopathology of the nervous system. Those wishing to explore this important field more deeply are referred to the texts cited in the bibliography. An elementary knowledge of the anatomy and histology of the nervous system and of fundamental pathological processes is assumed. Emphasis must be laid on the careful macroscopic examination of the fixed brain and the spinal cord, entire or in coronal slices, for without experience of the naked-eye appearance of disease in the nervous system, the selection of suitable material for microscopy becomes haphazard and unrewarding. An attempt has therefore been made to illustrate in particular those diseases which have recognisable gross changes.

The references given in the bibliography are confined to text books, monographs, reviews and some papers in neuropathology that are of practical value. A short section on technical and other procedures is appended. In a book of this size some omissions cannot be avoided, but it is nevertheless hoped that most of the conditions commonly encountered by the neuropathologist have been included.

Chapter 1

Basic Histopathology of the Central Nervous System

The central nervous system (C.N.S.) comprises, apart from its mesenchymal elements (blood vessels and meninges), several cell types which are peculiarly its own, and though the reactions to injury of each of these special components may be limited, the combined patterns of response, sometimes the result of cellular interaction, are frequently complex.

The cells which make up central nervous tissue proper are the neuron and the glia (astrocytes, oligodendrocytes, ependymocytes, microglia).

Although the blood vessels, meninges and bony coverings of the nervous system are not neural elements, their reactions play an important part in neuropathology. Microglia, though of mesenchymal origin, is considered with the other constituents of central nervous tissue. The reactions of these essential elements in their varying proportions form the basis of neuropathology.

THE NEURON

Recent work with the electron microscope has vindicated the 'neuron doctrine' expounded by Ramón y Cajal in the nineteenth century. This doctrine stated that the nerve cells are discontinuous, discrete entities connecting with other neurons by synaptic contacts of their axons, and are not syncytial. Similarly, there is a bounding membrane between glial processes and those parts of the neuron with which they are in contact. The entire neuron consists of the cell body or perikaryon and its dendrites, the axonal fibre and its myelin sheath (if present, as some axons are unmyelinated), and the synaptic endings.

COMPONENTS OF THE NERVE CELL BODY (1)

Cell membrane. There is much variation of cell shape in different parts of the C.N.S.

Cytoplasm. The Nissl substance represents aggregates of granular endoplasmic reticulum associated with R.N.A., i.e. protein-forming ribosomes.

Nucleus. Usually central, often with prominent chromatin masses.

Nucleolus. Large and prominent.

The perikaryon can be demonstrated by staining with haematoxylin and eosin. The Nissl substance is better displayed by cresyl violet or toluidine blue. Dendrites and intracellular neurofibrils require silver impregnation.

The axon. The neuraxon is a hollow fibre which may show a good deal of variation in its diameter in longitudinal section. Special techniques, usually silver impregnation, are required to demonstrate axons. Unmyelinated axons are difficult to demonstrate even with silver impregnation and may require the use of frozen sections. The specialised axons of the neurons of the supraoptic and paraventricular nuclei of the hypothalamus, which carry neurosecretory material to the neurohypophysis, require the use of stains such as Gömöri's chrome alum haematoxylin for their effective demonstration.

The myelin sheath. The electron microscope has shown this to consist of a spirally wound sheath of complex lipid, each turn bounded by a thin lamella of cell membrane derived from Schwann cells in the peripheral nervous system and from oligodendrocytes in the central nervous system.

REACTIONS OF THE NEURON TO INJURY

Injury to neurons and their axons may result in reversible or irreversible changes.

Central chromatolysis. This change is also known as *axonal reaction,* as it is the response of nerve cells to transection of the axons. It develops in 48 hours, is maximal in 15–20 days, and may be followed by recovery if the transection is not too near the perikaryon. The essential changes are migration of Nissl substance from the centre to the periphery of the cell, from which it is normally absent (**2**); enlargement of the cell body and rounding off of the angles, by loss of dendrites, usually occurs. The changes are best seen in spinal neurons and in the

medulla. Trans-synaptic degeneration (as in the lateral geniculate body after retinal damage) may be seen. Cytoplasmic vacuolation often accompanies central chromatolysis (**3**). These changes can be inhibited experimentally by actinomycin D.

Hypertrophic degeneration. This change is peculiar to the neurons of the inferior olivary nucleus in the medulla, and results from damage to the fibres of the central tegmental tract in the midbrain, pons or medulla (p. 124). It may be associated with Purkinje cell and dentate degeneration. The change may be reversible or be followed by cell death. Enlargement of the neuron is accompanied by bizarre branching and tortuosity of the dendrites (**4**).

Ischaemic change. The commonest cause of neuronal damage is anoxia, to which, owing to their dependence on oxygen and high metabolic rate, neurons are very sensitive. It is probable that many of the toxic agents damaging nerve cells act through the oxidative pathways. Oxygen lack can arise as a result of territorial ischaemia or of generalised anoxia; in either case the neuronal changes are similar, though the histological pattern of neuronal damage may differ between different regions of the brain.

Early changes. There are loss of Nissl substance and the development of cytoplasmic eosinophilia and hyalinisation, shrinkage of the perikaryon and relative preservation of the nucleus (**5**). Under the electron microscope there is swelling and then disappearance of cytoplasmic organelles such as mitochondria, and clumping of nuclear chromatin. These changes are probably not reversible.

Late changes. The foregoing changes become more severe (**6**) and the nucleus disappears, leaving a ghost cell, which in its turn may disappear and leave an empty space. There may be a phagocytic reaction around individual dead cells – *neuronophagia* (**46, 75**).

Ferrugination. Dead neurons are sometimes not removed by phagocytosis; the dead cell body remains and becomes encrusted by iron salts – *ferrugination* (**7**). This change may be seen at the edge of an old infarct.

Intracellular depositions in neurons. *Lipofuscin* is a yellow pigment composed of fine granules of proteolipid. It occurs normally in neurons from the age of 8–9 years, increasing in amount with age, though variably (**8**). Sometimes its accumulation is pathological and destroys the cells, leading to dementia – a condition known as *ceroid lipofuscinosis* (p. 102).

Neurolipids may be sphingolipids (such as sphingomyelin) or glycolipids (gangliosides) and occur in abnormal amounts in the neuronal storage diseases or *neurolipidoses* (p. 101).

Mucopolysaccharides accumulate in abnormal amounts in neuronal storage diseases such as *Hurler's syndrome or gargoylism* (p. 105). Like the glycolipids, they may stain strongly with the periodic acid-Schiff stain (P.A.S.).

Neuronal inclusions. Inclusion bodies in nerve cells may be intracytoplasmic or intranuclear – occasionally intranucleolar. They may be divided into those associated with virus diseases of the nervous system and those that are not.

Viral inclusions. This type (Type A) is found in the *nucleus* of neurons and glial cells in cases of virus encephalitis such as herpes simplex encephalitis and subacute sclerosing panencephalitis (p. 44). They may have a clear halo or a thin rim of nuclear membrane or chromatin round them (**9**). *Intracytoplasmic* inclusions are found in rabies (*Negri bodies* – **10**). In both types the inclusions are usually well-defined and brightly acidophilic, and may represent degeneration rather than aggregations of virus.

Non-viral inclusions. Cytoplasmic bodies are found in the cells of the substantia nigra of the midbrain and locus coeruleus of the pons in patients suffering from idiopathic (non-viral) parkinsonism. They are known as *hyaline* or *Lewy bodies* and are of diagnostic significance. Characteristically they have an outer pale mauve zone and a brightly eosinophilic core when stained by haematoxylin and eosin (**11**).

Intracytoplasmic inclusions (Lafora bodies) resembling corpora amylacea (**30**) are found in the neurons of some patients with myoclonic epilepsy. The argyrophilic inclusions found in the neurons of patients with Pick's disease (p. 82) may be analogous to Lewy bodies.

Neurofibrillary change and senile plaques. *Neurofibrillary change* is seen in the neurons of the cerebral cortex, including the hippocampal cortex, of the basal ganglia and less frequently of the brain stem. It occurs chiefly in presenile dementia (Alzheimer's or Pick's disease) but is seen in other conditions such as senile dementia and occasionally encephalitis. The change can be produced experimentally by injection of alum phosphate into the brain. The perikaryon is often enlarged and distorted by the thickened, twisted or tangled neurofibrils within the cell (**12, 13**). The fibrils are best shown by silver stains; they also stain with Congo red (amyloid reaction). The degree of dementia is to some extent proportional to the number of abnormal cells, which may occur in groups, but are more often found singly.

Senile plaques are found inconstantly in the ageing brain and in the brains of patients with

presenile and senile dementia, in which they are frequently associated with neurofibrillary change. The plaques are from 30–100 microns across and consist of a central core and an outer, clear area containing many fine or coarse granules (**14**, **15**). Both core and granules are argyrophilic and the core is congophilic. The origin of senile plaques is still debated; they may be derived from dead neurons, glial cells, or condensations of the ground substance. They may be very numerous in presenile dementia, and are found in the cerebral cortex, hippocampus, cerebellum and basal ganglia.

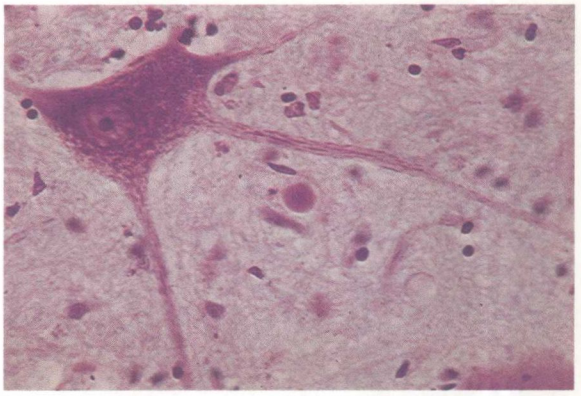
Axonal changes. Axons may be severed in traumatic injury, infarction or in leucodystrophy. Partial preservation of axons occurs in demyelination. Bulbous swellings known as *torpedoes* appear on the axons of Purkinje cells in some forms of cerebellar degeneration (**16**).

Retraction bulbs appear in white matter when axons are severed. They stain with eosin as round or ovoid, finely granular bodies, but are best seen with silver stains (**17**). Their frequent attachment to an axon suggests that they are globules of axoplasm exuded from the proximal cut end.

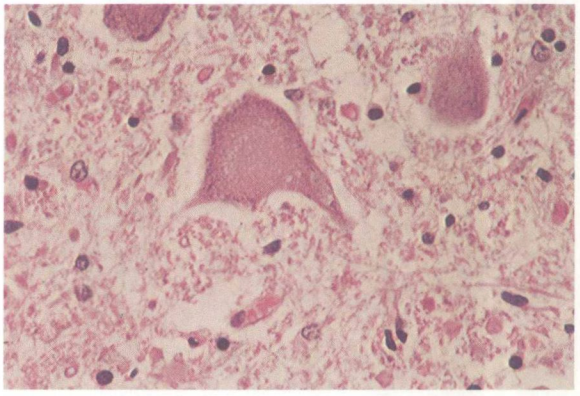
Changes in the myelin sheath. Damage to the myelin sheath may be primary (demyelination) or secondary to axonal or perikaryal damage (wallerian degeneration). The changes in demyelination are considered in Chapter 5. Secondary (wallerian) degeneration is more common. Wallerian degeneration was originally an experimental observation in the peripheral nervous system; the development of secondary degeneration in the central nervous system is less easily followed but the changes are essentially similar. Longitudinal sections of the pyramidal tracts or the spinal cord offer the best opportunities for study within the central nervous system.

Myelin breakdown begins in the distal part of the damaged or transected fibre 4–8 days after injury with the formation of ellipsoids and the appearance of lipid globules (**18**). Digestion chambers are formed and phagocytic cells (**43**), which are activated within 3 days of injury, remove the fat globules and migrate to blood vessels (**45**). The myelin sheath shows irregular vacuolation (**18**) and is completely disorganised at 7 days. At 10 days the lipid globules can be stained by Marchi's osmic acid technique (**19**). Cholesterol esters, not normally present in the central nervous tissue, are found at 15 days. At 4–6 weeks the lipid consists of phosphatides, cholesterol esters and neutral lipid (sudanophilic triglycerides, **20**). At 6 months degeneration of myelin is complete (when all lipid has disappeared) but often continues for several years in chronic disease. The axonal fibre breaks up distal to the lesion together with the myelin sheath, and is similarly phagocytosed. The perikarya of damaged fibres show a variable degree of axonal reaction (central chromatolysis), depending on the distance of the lesion from the cell body. Degeneration of synaptic contacts occurs within 4 days of an axonal lesion. Axonal regrowth and remyelination depends on the integrity of the perikaryon and of the Schwann cells or oligodendrocytes.

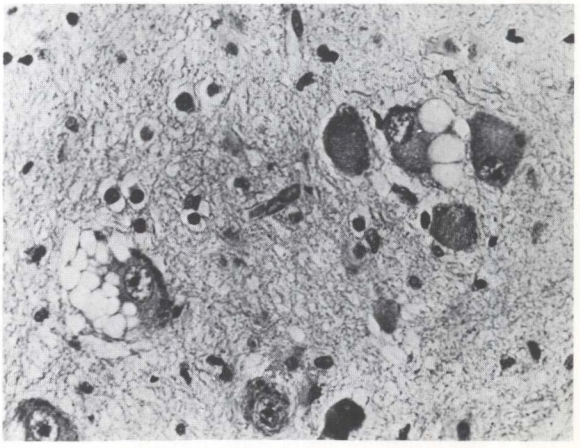
1. Normal spinal neuron. The nucleus is slightly eccentric, with partly aggregated peripheral chromatin. Nissl substance extends into the dendrites, with the exception of the axon hillock (top left). Two satellite oligodendroglial cells lie adjacent to the axonal hillock. *(Nissl × 250)*



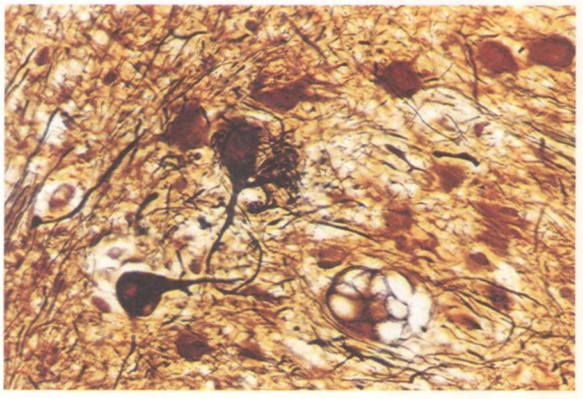
2. Central chromatolysis. The neuron shows peripheral displacement of the Nissl substance, fine vacuolation of the central cytoplasm and displacement of the nucleus into the base of a dendrite (bottom right). There is a rounding-off of the perikaryon. *(Haematoxylin and eosin – H.&E. – × 250)*



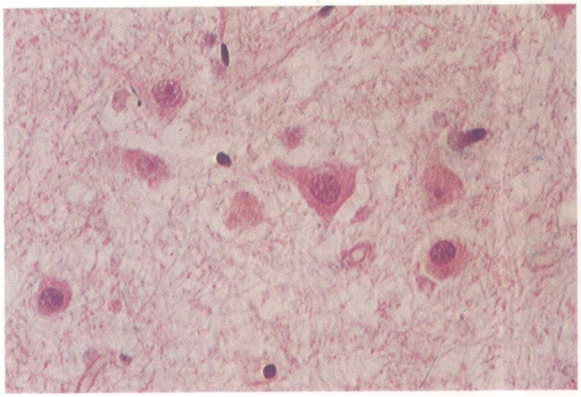
3. Central chromatolysis and vacuolation. There is severe cytoplasmic vacuolation of two neurons and central chromatolysis of several others. *(H.&E. × 200)*



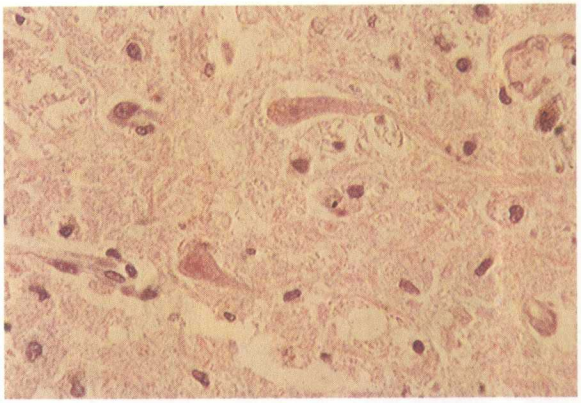
4. Hypertrophic degeneration of inferior olivary neurons. This change follows lesions of the central tegmental tract, which extends from the upper mid brain to the inferior olivary nuclei in the medulla. The cells are enlarged, distorted, sometimes vacuolated and show bizarre malformations of dendrites. *(Palmgren × 280)*



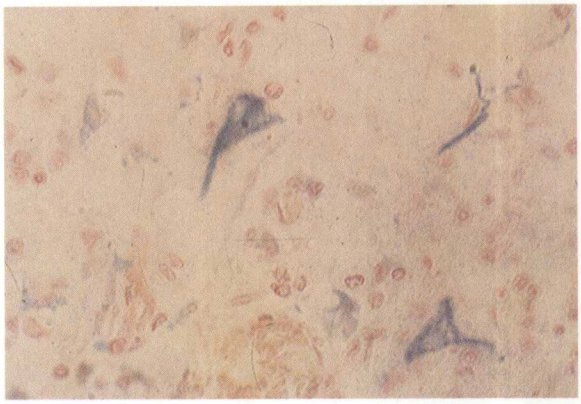
5. Ischaemic neurons. The cells are shrunken and have lost their Nissl substance and cytoplasmic basophilia. Nuclei are preserved, but nucleoli are indistinct. *(H.&E. × 280)*



6. Ischaemic neurons (later change). Cellular shrinkage is more pronounced than in **5** and the nuclei have almost disappeared. *(H.&E. × 280)*



7. Ferrugination of neurons. The cell bodies and dendrites of dead neurons are encrusted by fine granules of iron pigment, preserving the outline of the cell. *(Perls × 280)*



8. Lipofuscin. Two neurons contain aggregates of yellow-brown granules of lipofuscin, a proteolipid which appears in many neurons after the age of 8 years. *(H.&E. × 280)*