Neuropathology Simplified

A Guide for Clinicians and Neuroscientists

David A. Hilton
Aditya G. Shivane

Second Edition

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For Angela who has put up with my repeated absences whilst working on the book

—David A. Hilton

I dedicate this book to my parents.
And to Veena, Diya and Neel for their patience and endless support

—Aditya G. Shivane

Preface

Neuropathology is a highly specialised branch of histopathology and anatomical pathology which deals with the gross and microscopic examination of tissues of the nervous system thereby aiding the clinicians in the diagnosis and understanding of disease. Neuropathologists also examine skeletal muscle and peripheral nerve tissue removed as a part of evaluation in patients with neuromuscular conditions.

The field of neuropathology is quite vast and has witnessed immense growth in the last decade with ever-increasing research and rapid translation of basic science into clinical practice. It is not possible for a trainee or resident in clinical specialities like neurology, neurosurgery or psychiatry to receive all the training in neuropathology during their curricula nor can they keep up with the rapid advances in the scientific techniques and concepts. With the introduction of multidisciplinary team approach, there is much need for clinical residents or trainees to have a sound knowledge of basic neuropathology in order to better understand and keep pace with the recent advances in neurological disorders.

This book will aim to provide the reader with an up-to-date, practical and succinct overview of basic neuropathology. This book will certainly not replace the existing large reference textbooks in neuropathology, but will rather emphasise key concepts and basic principles including recent advances, genetics and classification, discuss important aspects of specific neuropathological disorders and also give practical hints on some aspects of neuropathology, including how to best use the neuropathology service and interpret the results of pathological tests.

The book is organised into fifteen chapters and follows a standard text disease groupings. The chapters are quick and easy to read, focusing on practically relevant information. We have tried to richly illustrate the book where possible with macro- and micro-photographs, diagrams and charts, thereby assisting the reader in recognising the morphology of various neuropathological conditions. The book also emphasises the clinico-pathologic correlations where necessary.

We sincerely hope that the readers of this book will achieve a sufficiently broad basic knowledge of neuropathology which will eventually help in their future clinical careers.

We welcome the readers to the second edition of *Neuropathology Simplified*. All chapters have been reviewed and updated where appropriate to take into account key developments in the field of neuropathology over the past 5 years. This has been particularly marked in the area of tumour pathology with the updated WHO

classification (2016) now taking into account tumour genetic alterations as a key diagnostic component of several tumour entities, which has led to the virtual disappearance of some entities such as mixed oligoastrocytomas. Increased general accessibility of advanced genetic testing in many countries has also led to an altered approach to the diagnosis of many neuromuscular disorders; however, biopsy remains valuable in many situations. One area where biopsy remains important is in the diagnosis of inflammatory muscle disease, but the classification of inflammatory muscle disease has evolved with a greater emphasis on serum autoantibodies and gradual disappearance of the generic term 'polymyositis'.

We hope that you find this new edition useful and would welcome any feedback.

Plymouth, UK
October 2020

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Normal Histology and Commonly Used Stains

1

The human nervous system can be broadly divided into two parts—the central and peripheral nervous system. The central nervous system (CNS) includes the brain and spinal cord. Both brain and spinal cord are surrounded by tough coverings called the meninges and are encased in a protective bony structure, the skull and the vertebral column respectively. The peripheral nervous system (PNS) includes the nerves (cranial, spinal and peripheral nerves), sensory ganglia (dorsal root ganglion) and autonomic ganglia (sympathetic and parasympathetic ganglia).

1.1 Cells of the Nervous System

The cells which make up the nervous system are the neurons and other supporting cells (glial cells) which include astrocytes, oligodendrocytes, Schwann cells, ependymal cells and microglia [1].

1.1.1 Neurons

A neuron is the basic functional unit of the nervous system. It is primarily responsible for collecting information, processing and then generating response. During development, they are derived from the neural tube and eventually migrate and populate different regions of the nervous system. A neuron is a post-mitotic cell and therefore cannot be replaced when damaged. It is also a highly metabolically active cell and requires continuous supply of nutrition for normal functioning. In an adult brain, neural stem cells have been identified within the subventricular zone of lateral ventricles, in the dentate gyrus of hippocampus and in the olfactory bulb.

The basic structure of a neuron include a cell body or *perikaryon*, many short processes or dendrites which receive information from other neurons and a single long process called 'axon' which transmits signals to other neurons. The dendrites and axons are collectively referred to as neurites. The cell body appears large in

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some types of neurons and contains a large nucleus with a prominent nucleolus. The cytoplasm of the neuron contains granular dark staining material rich in rough endoplasmic reticulum termed '*Nissl substance*' which is one of the important distinguishing features on microscopy (Figs. 1.1a and 1.2; Box 1.1). The region where axon begins is called an 'axon hillock' from where action potentials are generated.

The neurons come in various shapes and sizes. Neurons in some locations such as dentate gyrus and cerebellum appear small and rounded with no visible cytoplasm and are referred to as granular neurons. Neurons can be either multipolar (many dendrites, single axon. e.g. motor neurons), bipolar (single dendrite, single axon. e.g. sensory neurons in retina) or unipolar/pseudo-unipolar (single process which divides into central and peripheral axons, no dendrites. e.g. sensory neurons in dorsal root ganglia). The majority of neurons within the nervous system are multipolar (Fig. 1.1b).

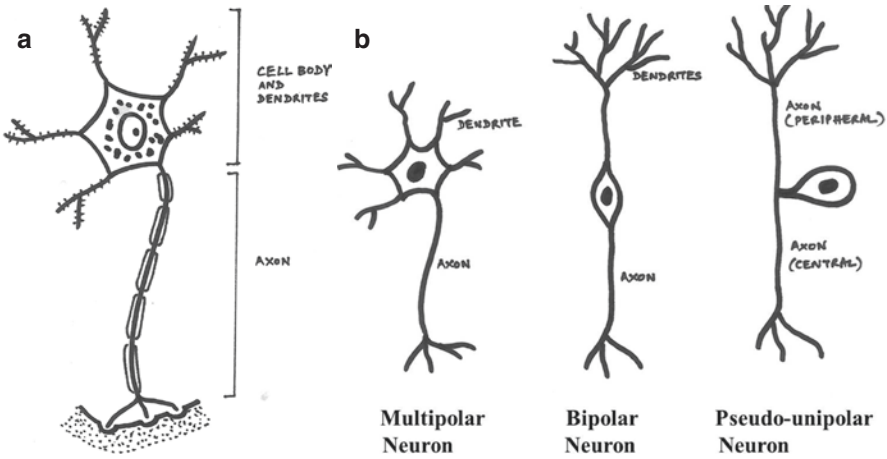

Fig. 1.1 (**a**) Diagram showing different parts of a neuron and, (**b**) the basic morphological subtypes of neurons

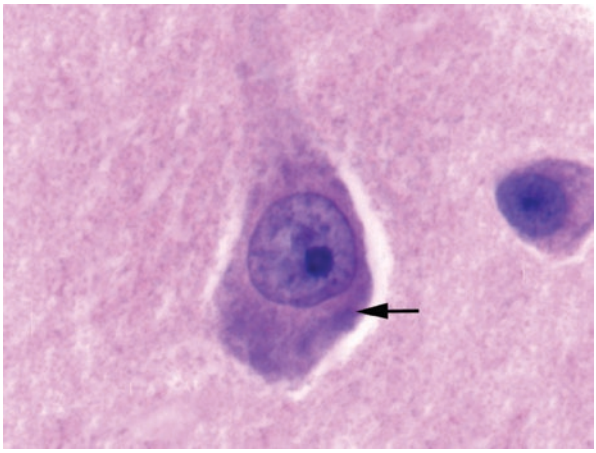

Fig.1.2 A cortical pyramidal neuron showing a large nucleus, prominent nucleolus and purplish granules (Nissl substance) in the cytoplasm (arrow). H&E stain

Box 1.1 How to Identify a Neuron
- Large cell and cell body
- Large nucleus
- Single prominent nucleolus
- Nissl substance (purplish granules on H&E)

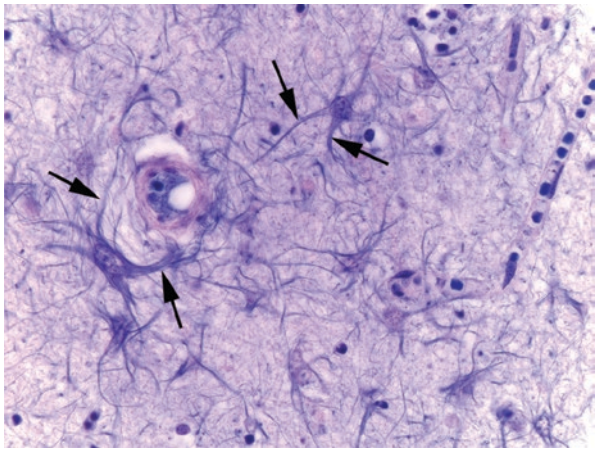

Fig. 1.3 Fibrous or fibrillary astrocytes with stellate cytoplasmic processes (arrows). PTAH stain

The cell bodies of neurons make up the bulk of grey matter and deep nuclei of the brain and spinal cord. Their axons run as bundles within the white matter. Occasional neurons can be seen within the white matter, especially in the temporal lobe. This should not be mistaken for a neuronal migration abnormality.

1.1.2 Astrocytes

Astrocytes are the most numerous of the glial cells and give structural and metabolic support to a neuron. Astrocytes are derived from radial glial cells during embryonic development. Astrocytes appear to have several complex roles in healthy tissue, some of which include—development of grey and white matter, regulation of blood flow, maintaining biochemical homeostasis, synapse function, and CNS metabolism [2]. The term 'astrocyte' means 'star cell' and refers to multiple radially arranged cytoplasmic processes which can be identified with a special stain such as phosphotungstic acid haematoxylin (PTAH) (Fig. 1.3 and Box 1.2). These processes abut on capillaries, neuron, axon, dendrites and pia mater (the innermost layer of meninges). The cytoplasmic processes contain characteristic filaments termed 'glial fibrillary acidic protein' or GFAP which can be demonstrated using immunohistochemistry. Astrocytes can be of two morphological subtypes—(1) fibrous or fibrillary astrocytes which have long processes rich in GFAP-positive filaments and are present in

Box 1.2 How to Identify an Astrocyte

- Medium-size cell
- Round or oval nucleus with pale vesicular chromatin
- Indistinct nucleolus
- 'Stellate' cell processes (seen with special stains such as PTAH; appear as pink background on H&E stain)

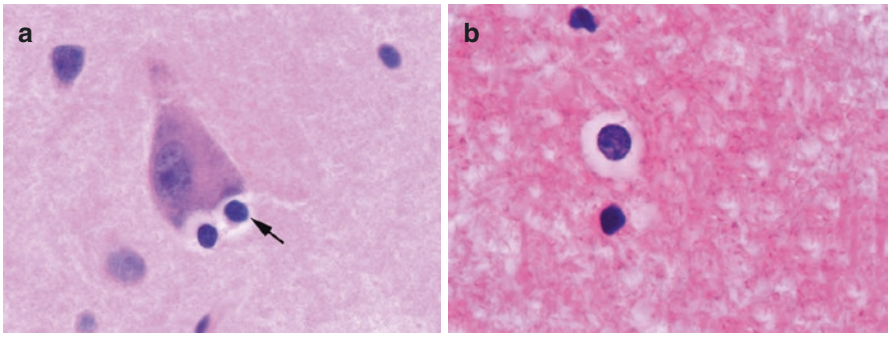

Fig.1.4 (**a**) Oligodendrocytes (arrow) clustered around a neuron (satellite cells) and, (**b**) a typical oligodendrocyte with round nucleus and perinuclear '*halo*' in white matter. H&E stain

the white matter and, (2) protoplasmic astrocytes with short processes and few GFAP-positive filaments and mainly confined to the grey matter.

The cell processes of astrocytes form the background fibrillary meshwork called as 'neuropil' (seen as pink background on the standard H&E stain).

1.1.3 Oligodendrocytes

Oligodendrocytes are the myelin producing cells within the CNS. Oligodendrocytes are presumed to be derived from a common progenitor cell which also gives rise to neurons and depend on various regulatory factors for their differentiation and migration. The process of myelination is complex and relies on neuronal and axonal signals [3]. Each oligodendrocyte forms myelin segments on multiple axons. They are mainly present within the white matter along bundles of axons which they myelinate. Within the grey matter they are often seen around the cell body of neurons as 'satellite cells' (Fig. 1.4a). Oligodendrocyte as the name implies, have fewer cytoplasmic processes compared to that of an astrocyte. These cell processes are not clearly visible on tissue sections. Therefore, these cells appear as naked dark round nuclei with perinuclear '*halo*' or '*fried egg*' appearance (Fig. 1.4b, Box 1.3). This cytoplasmic clearing is not evident in intraoperative frozen sections or tissue which

Box 1.3 How to Identify an Oligodendrocyte
- Small to medium-size cell
- Dark round nucleus
- Cytoplasmic clearing or perinuclear '*halo*' or '*fried egg*' appearance

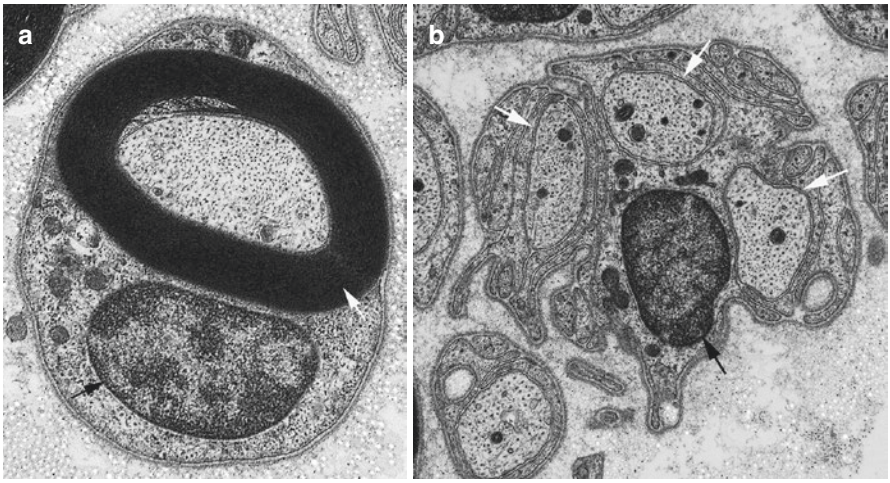

Fig.1.5 (**a**) Ultrastructure of a peripheral nerve showing a large myelinated axon (white arrow) surrounded by a Schwann cell (black arrow) and, (**b**) Schwann cell (black arrow) wrapping three unmyelinated axons (white arrows) also referred to as 'Remak cell'

is rapidly fixed in formalin and is considered an artefact of delayed fixation. However, this is a very helpful feature in recognising a cell as being oligodendroglial in origin within a glial neoplasm.

1.1.4 Schwann Cells

Schwann cells perform the function of electrically insulating axons of the peripheral nervous system. Unlike an oligodendrocyte, each Schwann cell myelinates only one axon. The cell processes of a Schwann cell wrap around an axon in multiple layers forming the myelin sheath (Fig. 1.5a). Large diameter axons are always myelinated whereas the small diameter axons can be myelinated or unmyelinated. Myelinated nerve fibers conduct electrical signals faster than unmyelinated fibers. Schwann cells also surround unmyelinated axons (Remak cell), with their cytoplasm wrapping around and isolating each axon from its neighbours (Fig. 1.5b). A Schwann cell also performs an important role in nerve regeneration after injury.

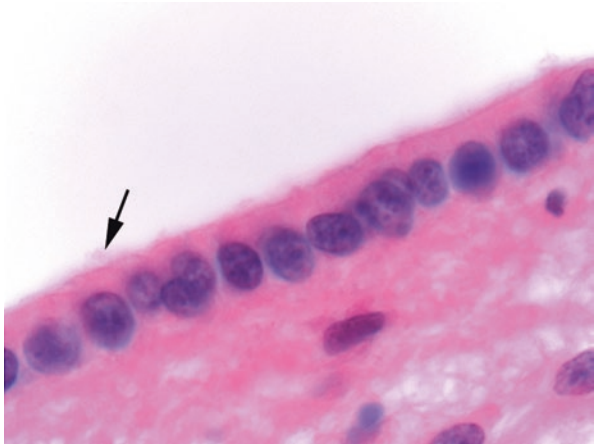

Fig. 1.6 A layer of cuboidal-low columnar ependymal cells with apical cilia/brush border (arrow). H&E stain

Box 1.4 How to Identify Ependyma

- A single layer of flattened or low cuboidal or columnar epithelium
- Uniform round to oval dark basal nucleus
- Apical cilia
- Moderate eosinophilic cytoplasm

1.1.5 Ependyma

The ependymal cells form the lining of the ventricular system (in the brain) and central canal (in the spinal cord). They are believed to arise from ventricular (germinal) zone cells or radial glial cells. The ependyma plays an important role during early stages of brain development and in mature brain by supporting and protecting the subventricular (germinal) zone cells and also possibly in the circulation of cerebrospinal fluid within the ventricular system [4]. They are composed of a single layer of flattened or low cuboidal to columnar cells with apical cilia (Fig. 1.6). They have round to oval dark basal nucleus (Box 1.4).

1.1.6 Microglia

Microglia are the resident cells of the immune system within the CNS. Therefore, in the strict sense they are not true glial cells but are derived from the bone marrow haematopoietic stem cells. They are now believed to have important role in synapse function and maintenance in a normal brain [5, 6]. They are small cells (in comparison to macroglia—astrocytes, oligodendrocytes, and ependyma) with oval to elongated nuclei and contain numerous cytoplasmic processes. They are generally inconspicuous in normal healthy brains on H&E stain, but on close scrutiny can be seen as elongated/oval ‘naked cigar-shaped immunohistochemistry’ (Fig. 1.7; Box 1.5). They

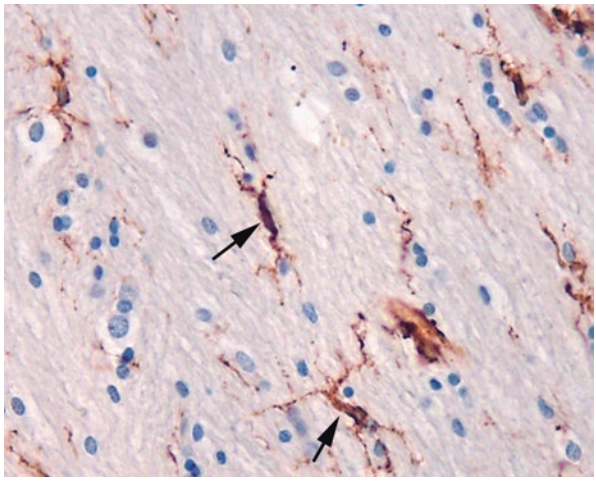

Fig. 1.7 Microglia or rod cell with elongated cytoplasmic processes. HLA-DR immunohistochemistry

Box 1.5 How to Identify Microglia

- Small cell
- Elongated or 'cigar-shaped' nucleus
- Numerous cytoplasmic processes (not visible on routine H&E stain; can be seen with specific immunostains such as HLA-DR and CD68)

become more prominent in response to disease or injury. They can also transform into macrophages and help clean up the cellular debris and microorganisms.

1.1.7 Supporting Tissues

The connective tissue which covers the brain and spinal cord is termed the 'meninges'. The dura mater (pachymeninges) forms the tough outermost layer, arachnoid mater the middle layer, and pia mater the innermost layer closely opposed to the brain surface. The arachnoid and pia mater are collectively termed 'leptomeninges'. The tissues of the nervous system are richly supplied with blood vessels.

1.2 General Architecture of the Nervous System

1.2.1 Grey and White Matter

The grey matter is composed of cell bodies of neurons, dendrites and supporting glial cells. The microscopic structure of grey matter varies between different brain regions. The majority of cerebral cortex (also referred to as '*isocortex or neocortex*' *or simply* '*cortex*') is made up of six distinct layers of neurons (Fig. 1.8a). The outer most layer

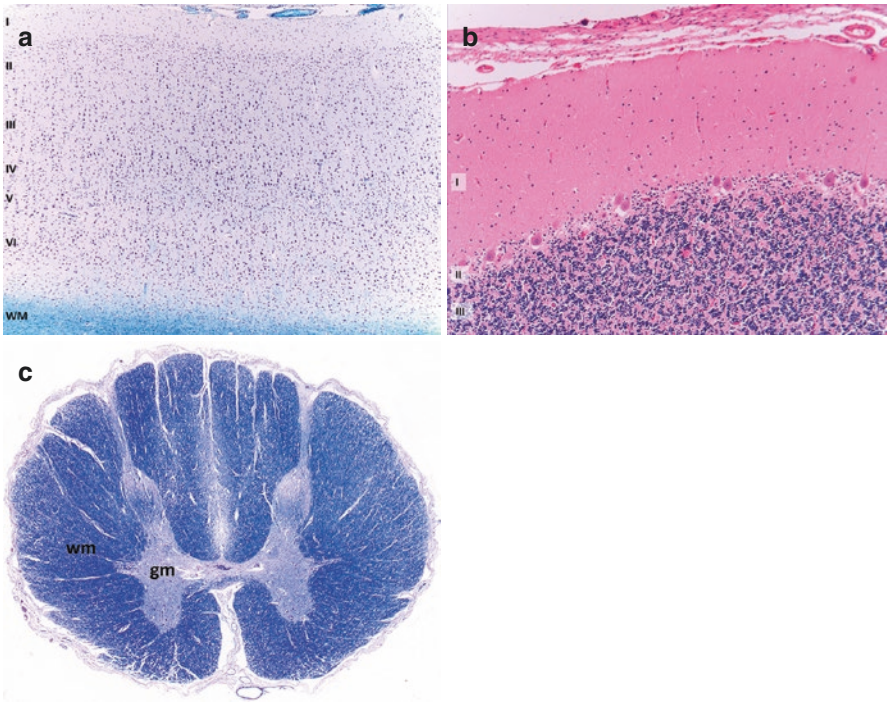

Fig. 1.8 (**a**) Six different layers of the cerebral cortex (LFB/CV stain), (**b**) three layers of the cerebellar cortex (H&E stain) and, (**c**) organisation of the spinal cord with grey matter on the inside and white matter on the outside (LFB/CV stain). *gm* grey matter, *wm* white matter

is the paucicellular molecular layer without any neurons. Small granular neurons and large pyramidal neurons alternate in layers 2 to 6. The hippocampus shows three layer architecture (also termed '*archicortex*'). The cerebellar cortex also has only three layers which include the outer molecular layer, middle Purkinje cell layer and inner granular cell layer (Fig. 1.8b). In the brain, the grey matter is outside and the white matter is inside, whereas in the spinal cord the grey matter is deep inside and covered all around by white matter (Fig. 1.8c). Collections of neuronal cell bodies can also be found deep within the cerebrum and these form the deep grey nuclei (like basal ganglia, thalamus, and dentate nucleus). The white matter is made up of bundles of myelinated axons. Bundles of myelinated axons which are responsible for similar function are termed as '*tracts*'. The midbrain, pons and medulla oblongata form the brainstem which contains the vital cardio-respiratory centres.

1.2.2 Peripheral Nerve

A nerve is a collection of axons (myelinated and unmyelinated) with other supporting cells including Schwann cells and fibroblasts. A peripheral nerve consists of three distinct compartments—the epineurium, perineurium and endoneurium. The

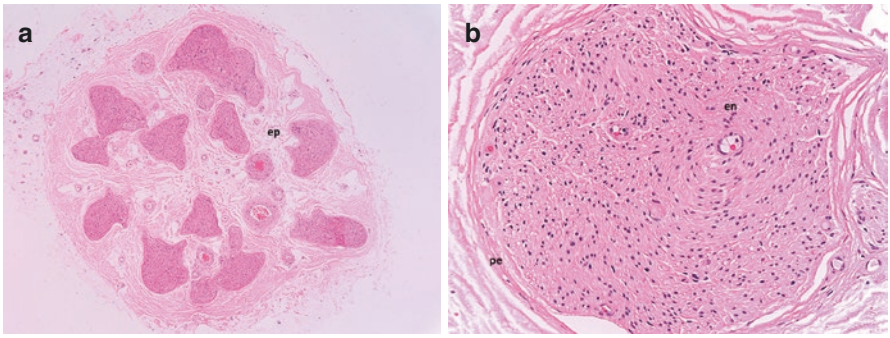

Fig. 1.9 Low (**a**) and high power (**b**) view of a normal peripheral nerve showing the three compartments—epineurium (ep), perineurium (pe) and the endoneurium (en). The endoneurium contains nerve fibers, Schwann cells, fibroblasts and blood vessels. H&E stain

epineurium is the outermost layer made up of fibroadipose connective tissue and also contains medium-sized blood vessels. The perineurium is the fibrous covering around a group of nerve fibers or axons and forms the nerve fascicle. The endoneurium is the innermost compartment containing individual myelinated (large or intermediate size) and unmyelinated (small) nerve fibers or axons along with Schwann cells and fibroblasts (Fig. 1.9a, b). (see Chap. 10 for more details).

1.2.3 Ganglia

A ganglion is a collection of neuronal cell bodies and their axons along with other supporting cells and lie outside the CNS (e.g. dorsal root ganglion of spinal nerves, ganglion of cranial nerves, sympathetic and parasympathetic ganglia). The dorsal root ganglia contain large pseudo unipolar neurons with their cell processes and surrounded by satellite cells (Fig. 1.10a, b). The autonomic ganglia contain smaller multipolar neurons.

1.2.4 Skeletal Muscle

Skeletal muscle is composed of compact fascicles of muscle fibres surrounded by the connective tissue, perimysium and epimysium. Each muscle fiber is polygonal or hexagonal in shape, has an outer cell membrane (sarcolemma) and inner cytoplasm (sarcoplasm). The nuclei are arranged at the periphery underneath the cell membrane (Fig. 1.11a, b). The sarcoplasm contains contractile proteins actin and myosin filaments. The connective tissue between each muscle fiber is scanty and is termed the endomysium. The perimysium is the connective tissue that surrounds groups of muscle fibers and forms a fascicle. Groups of fascicles are surrounded by epimysium. The muscle fibers are of two main types—type 1 (slow fibers) and type 2 (fast fibers) which can be recognised with histochemical stains (Fig. 1.11c). (see Chap. 9 for more details).

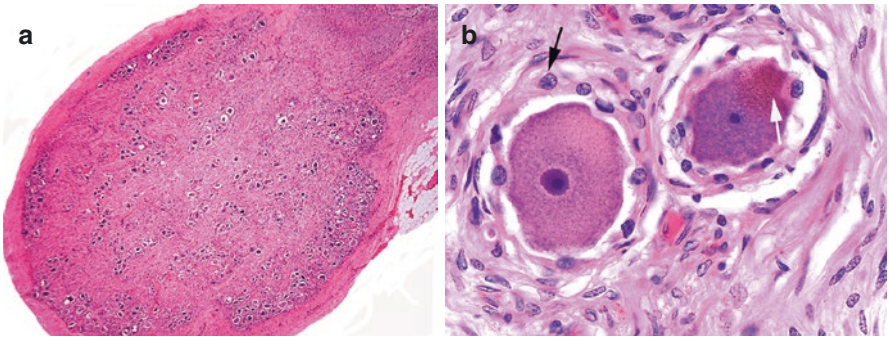

Fig. 1.10 Low (**a**) and high power (**b**) view of a dorsal root ganglion containing large neuronal cell bodies surrounded by satellite cells (black arrow). One of the neuron contains brown lipofuscin (ageing) pigment in the cytoplasm (white arrow). H&E stain

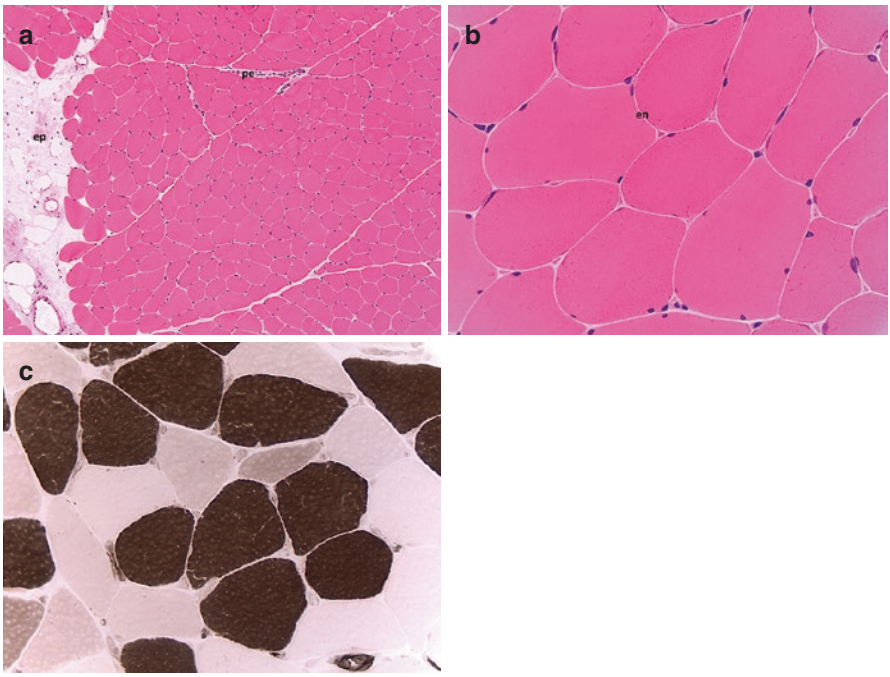

Fig. 1.11 (**a**, **b**) Low and high power microphotographs showing human skeletal muscle. The individual fibers are polygonal in shape with peripherally placed nuclei. H&E stain. (**c**) shows two fiber types, the dark type 1 fibers and pale type 2 fibers. ATPase pH 4.4. *ep* epimysium, *pe* perimysium, *en* endomysium

1.3 Commonly Used Stains in Neuropathology

1.3.1 Tinctorial Stains

A histopathologist or neuropathologist utilises several dyes to stain various tissue components thereby helping in the recognition and interpretation of abnormalities. The choice of stains used varies between different laboratories and also amongst pathologists. Table 1.1 lists some of the commonly used stains and their usefulness in diagnostic neuropathology.

Table 1.1 Tinctorial stains

Haematoxylin and Eosin (H&E)	Most commonly used stain in histopathology. Used for staining intra-operative smears, frozen sections, CSF cytospin preparations and formalin-fixed tissue. The haematoxylin stains nuclei blue and eosin stains the cytoplasm and cell processes pink. Most of the common pathologic features can be recognised using this stain
Toluidine blue	Rapid stain, used as an alternative to H&E stain, mainly for intraoperative smears. The nuclear details are better delineated with this stain. Also used to stain resin-embedded (semi-thin) sections of nerve and muscle for electron microscopy
May Grunwald Giemsa (MGG)	Commonly used stain to analyse cerebrospinal fluid (CSF) cytology specimens
Cresyl violet or cresyl fast violet (CV/CFV)	Mainly used to study the morphology and distribution of neurons. Cresyl violet stains the Nissl substance dark purple or blue
Bielschowsky	This is a silver stain used to demonstrate axons. Axons are stained black. The stain can be performed on both frozen and paraffin sections. Can also be used to demonstrate senile plaques and neurofibrillary tangles in neurodegenerative diseases
Palmgren	Also a silver stain, which demonstrates axons as well as cell bodies of neurons which are stained black
Luxol fast blue (LFB)	Stain used to demonstrate myelin within the CNS. Performed on formalin-fixed paraffin embedded tissue. Usually used in combination with Nissl stain (LFB/CV) or H&E (LFB/HE). Gives good contrast between grey and white matter and helps easy recognition of demyelinating lesions. Myelin is stained blue
Solochrome cyanin	Also a stain to demonstrate myelin; mainly used for peripheral nerves
Phosphotungstic acid haematoxylin (PTAH)	This demonstrates astrocytes and glial fibers. Before the advent of immunostains this stain was used as a glial lineage marker in brain tumours
Congo red	Stain used to demonstrate amyloid. Under polarised light amyloid shows apple-green birefringence
Gram	Stain used to demonstrate bacteria. Gram positive bacteria appear blue/black
Periodic acid-Schiff (PAS)	This is used to demonstrate fungal organisms, glycogen in muscle, mucin in adenocarcinoma (in combination with Alcian blue) and basement membrane. PAS positive structures appear magenta coloured
Grocott	This is a silver stain used to identify fungal organisms which appear black
Ziehl-Neelsen (ZN)	This is a stain for *Mycobacterium tuberculosis,* an acid-fast bacillus. Positive organisms appear as slender red rods. A modification of this stain demonstrates *Mycobacterium leprae* (Wade-Fite stain)

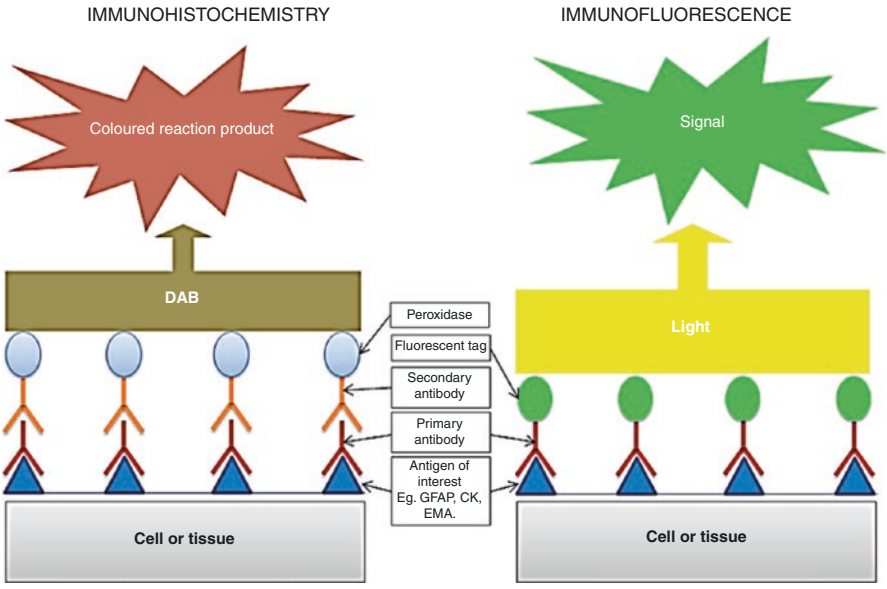

Fig. 1.12 Diagram showing the basic principles of immunohistochemistry (the peroxidise tagged to a secondary antibody binds to the antigen-antibody complex and converts DAB into a brown coloured reaction product) and immunofluorescence (a fluorophore tagged to a secondary antibody binds to the antigen-antibody complex and emits fluorescent signal under UV light) techniques. *DAB* di-amino benzidine, *GFAP* Glial fibrillary acidic protein, *CK* Cytokeratin, *EMA* Epithelial membrane antigen

1.3.2 Immunohistochemical Preparations

Immunohistochemistry is a technique of detecting tissue specific antigens by targeting them with specific antibodies. The resulting antigen-antibody interaction can be visualised in various ways. The commonly used detection method utilise antibody tagged with an enzyme called peroxidase (immunoperoxidase) which catalyses a colour producing reaction resulting in brown staining. Antibody tagged with a fluorophore (immunofluorescence) is also used widely in some laboratories (Fig. 1.12). Table 1.2 describes some of the most commonly used antibodies in diagnostic neuropathology. It should be noted that some antibodies act as surrogate markers for demonstrating genetic changes by specifically detecting the mutant form of the protein (e.g. IDH) or loss of expression (e.g. ATRX).

Table 1.2 Commonly used antibodies in diagnostic neuropathology

GFAP (Glial fibrillary acidic protein)	The intermediate filaments present in the cytoplasm of glial cells. This is widely used in identifying cells of glial lineage. It is strongly expressed in both reactive and neoplastic astrocytes and also variably in oligodendrocytes and ependyma
Synaptophysin	A major integral membrane protein of synaptic vesicles. This is a widely used marker of neuronal differentiation The staining is localised to cell membrane and cytoplasm
Neu N	A neuronal marker and is localised to the nucleus
NFP (Neurofilament protein)	A neuronal marker which is localised to cell bodies of neurons and their processes. It is particularly useful to detect native cell processes or axons within the tumours to distinguish infiltrative from non-infiltrative tumours
S-100	A protein expressed in cells derived from neural crest such as Schwann cells, glial cells and melanocytes. They are also expressed in chondrocytes, macrophages, adipocytes, myoepithelial cells, Langerhans cells, dendritic cells and keratinocytes
Mutant IDH-1 (Isocitrate dehydrogenase-1, R132H)	Detects mutant IDH-1 in glial tumour cells. A significant proportion of diffuse gliomas are IDH-1 positive
ATRX (α-thalassaemia-mental-retardation-syndrome-X-linked)	ATRX protein is strongly expressed in the nuclei of normal unmutated tissue. Loss of nuclear ATRX protein due to ATRX mutation feature prominently in diffuse astrocytomas
STAT6	Nuclear expression in solitary fibrous tumours/ haemangiopericytoma
SSTR2A (Somatostatin receptor 2A)	Used as a marker for meningioma
Pituitary panel of transcription factors and hormonal stains	**Pit-1** (mammo-somatotroph family), **T-Pit** (corticotroph family) and **SF-1** (Gonadotroph family) are transcription factors. Hormonal stains include—**GH** (growth hormone), **prolactin, ACTH** (adrenocorticotrophic hormone), **TSH** (thyrotroph secreting hormone), **FSH** (follicle stimulating hormone) and **LH** (luteinising hormone)
MIB-1 or Ki-67	Ki-67 is the antigen and MIB-1 is the antibody. This is the most commonly used marker for assessing proliferation. High grade malignant tumours have a large proportion of proliferating cells and a high labelling index (expressed as %) compared to low grade or benign tumours
EMA (Epithelial membrane antigen)	The secretory product of MUC 1 gene and is expressed in a wide range of secretory epithelia and also the meninges
Cam5.2, MNF116, AE1/ AE3, CK5/6, CK7, CK20 (Cytokeratins)	Intermediate cytoskeletal filaments present in the epithelial cells. They are useful in differentiating metastatic carcinomas from intrinsic brain tumours
Organ specific marker for tumours arising in	
TTF-1 (Thyroid transcription factor 1)	Lung and thyroid gland

(continued)

Table 1.2 (continued)

PSA (Prostate specific antigen) and PSAP (Prostate specific acid phosphatase)	Prostate gland origin
ORA (Oestrogen) and PGR (Progesterone) receptors	Breast origin
CD10, RCC, Pax8	Renal origin
CDX2	Colo-rectal origin
HMB-45, Melan-A	Markers of melanocytes and melanoma cells
LCA/CD45 (Leucocyte Common Antigen)	Generic marker for all leukocytes
CD3	T-lymphocyte marker
CD20	B-lymphocyte marker
CD68	Monocyte/macrophage-lineage marker
β-amyloid	This is the main component of most forms of CNS amyloid. It is widely used to detect amyloid in plaques and blood vessels in neurodegenerative diseases. Certain rare familial forms of amyloid disease can be negative with beta-amyloid
β-APP (β-amyloid precursor protein)	Expressed in axonal injury due to various causes
Antibodies used in classifying neurodegenerative diseases	**Tau** (Alzheimer's disease and other tauopathies), **α-synuclein** (Parkinson disease, Dementia with Lewy bodies, Multiple system atrophy), **TDP-43 and FUS** (Fronto-temporal dementia), **P62** (Fronto-temporal dementia and Inclusion body myositis), **Prion protein/12F10** (Creutzfeldt-Jakob disease)
Antibodies used in classifying muscular dystrophies	**Dystrophin** (Duchenne and Becker dystrophy); **Sarcoglycans, Dysferlin and Caveolin-3** (Limb-girdle dystrophy); **Emerin** (Emery-Dreifuss dystrophy); **Merosin** (Congenital muscular dystrophy); **Desmin and myotilin** (Myofibrillar myopathies)

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