NERVOUS TISSUE

Plate 143. Histogenesis of Nervous Tissue

The entire nervous tissue develops from the ectoderm (see Plate 1). Initially, it is a simple columnar epithelium (Figs. a, A), beneath which the notochord is located (Figs. a—e, Ch). The notochord induces the formation of the medullary or neural plate (Fig. b1), the wall of which becomes a thick pseudostratified epithelium as a result of mitotic divisions (Fig. B). Subsequently, the neural plate deepens, forming the neural groove (Fig. c1). The cells of the neural crest (Fig. e2) temporarily appear at the two lateral folds, and the epithelium of the neural groove continues to thicken through high mitotic activity (Fig. C).

At a somewhat later stage, the neural folds fuse and give rise to the medullary or neural tube (Fig. d). Simultaneously, the neural crest cells separate from the folds and form a continuous plate (Fig. d1) under the surface ectoderm (Fig. d2). After the neural tube has formed, the neuroepithelial cells continue to divide (Fig. D) and the wall of the tube becomes even thicker. This pseudostratified epithelium is termed neuroepithelium. Once the neural tube is formed (Fig. e), a new type of cell differentiates from the neuroepithelial cells, the so-called primitive nerve cells or neuroblasts, whose number soon increases as a result of vigorous division. They form an easily recognizable mantle zone (Figs. e1, E1).

When the short genesis of the neuroblasts is over, primitive support cells, glioblasts, develop from the neuroepithelial cells and also migrate into the mantle zone. Neurons, i.e., the definitive nerve cells complete with processes, can only differentiate from neuroblasts. Glial cells develop by differentiation of the dividing glioblasts. The mantle zone subsequently becomes the gray matter of the spinal cord. The processes of the neuroblasts form a marginal zone (Figs. e2, E2), from which the white matter of the spinal cord originates.

Only one layer (formerly termed the matrix) of cuboidal cells with basal processes, ependymoblasts (Fig. e3, E3), persists from the neuroectoderm, and these cells differentiate into the ependymal cells that line the central canal (Fig. e4) and cerebral ventricles. The cells of this layer – called epithelium – also serve as a primordium for the development of other components of the central nervous system (see Plate 144). At the stage of the neural tube, the neural crest (Fig. e5) is divided into rounded segments, which supply various types of cell (see Plate 144). (See embryology texts for further information.)

Magnifications: Figs. A–E, × 1,000

REFERENCES
Plate 144. Cells Originating from the Neural Tube and Neural Crest

This plate gives a general view of the cells that derive from the neural crest (A), mantle (B), and epithelium (C).

A. From the neural crest develop:
1. Neuroblasts, i.e., nerve cells of the spinal ganglia
2. Glioblasts of the peripheral glia, from which develop the satellite cells (2a) of the spinal ganglia cells and Schwann's cells (2b)
3. Sympathoblasts, which develop into both nerve cells of the sympathetic ganglia (3a) and medulloblasts, i.e., the chromaffin cells of the adrenal medulla (3b) and part of the paraganglia
4. Melanoblasts, i.e., melanocytes (4a)
5. Microglia cells and part of the mesenchyme in the head region ("mesectoderm")
6. C cells of the thyroid and possibly other endocrine cells of the amine precursor uptake and decarboxylation (APUD) system
7. Cells of the leptomeninges.

B. From the mantle zone of the neural tube develop:
8. Glioblasts, i.e., glia cells of the central nervous system: protoplasmic (8a) and fibrillar (8b) astrocytes and oligodendrocytes (8c)
9. Neuroblasts, i.e., nerve cells (9a) of the central nervous system and some sensory cells (9b).

C. From the epithelium develop:
10. Ependymoblasts, i.e., ependymocytes (10a) and so-called ependymal differentiations
11. Epithelial cells of the choroid plexus
12. Pituicytes, i.e., cells of the neurohypophysis
13. Pinealocytes, i.e., cells of the pineal body

Although there is still some debate with respect to some of these details (see embryology texts for further information), this summary indicates the pluripotentiality of the neural tube and crest.

REFERENCES
Millhouse EO (1972) Light and electron microscopic studies of the ventricular wall. Z Zellforsch 149:149-174
Plate 145. General Distribution of Nervous Tissue.
Central and Peripheral Nervous Systems

The central nervous system consists of the cerebrum (1) with brain stem, cerebellum (2), and spinal cord (3). Spinal ganglia (4), peripheral nerves (5), efferent and afferent nerve endings (6), and autonomic ganglia (7) form the peripheral nervous system. (See anatomy texts for further information.)

REFERENCES
Yamadori T, Yagihashi S (1975) A scanning and transmission electron microscopic observation of the fourth ventricular floor in the mouse. Arch Histol Jpn 37:415-432
Plate 146. Simplified Scheme of the Relationship Between Neurons and Glia Cells in the Central and Peripheral Nervous Systems (Modified from Rhodin 1974)

The rectangle depicts cells of the central nervous system (CNS); the structures outside this rectangle belong to the peripheral nervous system. The direction of nervous impulses is indicated by arrows. The nervous system is made up of nerve cells (1) and glia cells. Each nerve cell has a body, the soma or perikaryon, and usually several processes. In the cell body is found the nucleus (2), surrounded by cytoplasm, here termed neuropil. A nerve cell basically has only one cell-process, the axon (3), and several cell-processes, the dendrites (4). A nerve cell with its processes constitutes a structural and functional unit termed a neuron. At certain sites, termed synapses (5), neurons come into contact with one another. In this manner, neuronal switching circuits develop, which are essential for the function of the nervous system. Since the nervous tissue is very highly differentiated it possesses its own mechanically supporting tissue, the neuroglia, or glia for short. The glia cells are located between the blood capillaries (6) and neurons and constitute an extremely important cell system involved in the metabolism of the neurons. In the gray matter of the CNS, protoplasmic astrocytes (7) are situated between the neurons and capillaries. With their processes (7a), these astrocytes delimit the CNS from the peripheral nervous system (PNS) and from adjacent tissues. In the white matter, the nerve fibers are supported by fibrous astrocytes (8). Axons in the region of the CNS are surrounded by a myelin sheath, produced by oligoden-
Plate 147. Glia of the Central Nervous System. Ependymal Cells

The neuroglia performs several important functions in the nervous system. In addition to its role in mechanical support, isolation, and metabolism of nerve cells, it is involved in synthesis of the myelin sheaths, phagocytosis, and scar formation. The neuroglia is classified as follows:

A. Glia of the central nervous system
1. Ependymal cells or ependymocytes
2. Astrocytes (macroglia)
3. Oligodendrocytes
4. Microglia (Hortega cells or mesoglia)
5. Epithelial cells of the choroid plexus
(see Plate 12)

B. Glia of the peripheral nervous system
1. Schwann's cells
2. Amphiocytes (mantle or satellite cells)

The ependyma forms a layer of simple cuboidal or columnar cells which lines the cavities of the brain and spinal cord. In the embryo, a branching process, the ependymal fiber (Fig. A1), grows from the base of the ependyma. This fiber usually recedes (Fig. A2) in adults. Thus, e.g., in the mature organism, the posterior median septum (Fig. A3) of the spinal cord develops from the interwoven ependymal fibers. In all fetal ependymal cells, the free surface still bears cilia (Fig. A4).

Differentiated ependymal cells have a round, basally or centrally located nucleus (Fig. B1) with a nucleolus. Mitochondria are somewhat more numerous in the basal half of the cell than in the supranuclear cytoplasm. The Golgi apparatus consists of only a few flattened cisternae and vacuoles. The profiles of rough endoplasmic reticulum are short and narrow. Large numbers of free ribosomes and a few smooth vesicles, lysosomes, residual bodies, and microfilaments are found scattered in the cell body.

The majority of differentiated ependymal cells bear microvilli and bundles of cilia (Fig. B2) on the free surface. Many ependymocytes have processes (Fig. B3) which lead from the basal pole, extend between the subependymal cells, and come into contact with the blood capillaries (Fig. B4). Ependymal cells with such processes are termed tanycytes.

It has recently been discovered that the surface of various ependymal regions is covered with a network of long cytoplasmic extensions. Further studies have shown these structures to be largely supraependymal unmyelinated axons with expanded mitochondria-rich areas (Fig. B5). They form synapselike junctions (Fig. B6) with the ependymal cells. In addition to the axons, nerve cells (Fig. B7), from which these axons presumably derive, are found on the ependymal surface. The function of these nerve cells still remains to be clarified; they are possibly a type of receptor.

One or more cell-poor subependymal glia cell layers (Fig. B8), with predominantly horizontal glia cell processes (Fig. B9), are located beneath the ependymal cells. This zone of undifferentiated glia elements is important in adults in the regeneration of glia cells.

Between the ependymal cells, which contact one another by means of terminal bars, are interposed cilia-bearing processes of cerebrospinal fluid-contacting neurons (Fig. B10), the precise function of which has not been identified (possibly osmoreceptors). (See Plates 170, 171 in Krstic 1979.)

Magnification: Fig. B, × 7,000

REFERENCES
NERVOUS TISSUE

Sections from different parts of the central nervous system – cerebrum (Fig. A1), spinal cord (Fig. A2), and cerebellum (Fig. A3) – are shown in Figs. B–D as they appear under the light microscope after routine staining. In each section, a rectangular inset marks the gray matter, and a circular inset the white. The structures in the rectangular insets are summarized in Fig. E.

Proto-plasmic astrocytes (Fig. E1), following Golgi staining, appear as stellate cells which contact both nerve cells (Fig. E2) and blood capillaries (Fig. E3) with their processes. The connections formed between astrocytes lead to the formation of a glial supporting framework with neurons located in the interstices. The astrocyte processes that are attached to capillaries terminate in footlike expansions, termed perivascular feet, which cover most of the capillary surface. Thus, a membrana limitans gliar perivascularis develops, which in the central nervous system replaces the connective tissue envelope and is involved in the formation of the blood-brain barrier. Other astrocyte processes give rise to the membrana limitans gliar superficialis at the outer surface of the central nervous system (see Plate 153).

The circular insets in Figs. B–D display an enlargement of a fibrous astrocyte (Fig. F1) within Fig. E. Since these cells occur in the white matter, their processes follow, i.e., are largely parallel to, the nerve fibers (Fig. F2).

The smaller cells adjacent to the nerve cells (Fig. E2) and between the nerve fibers are oligodendrocytes (Figs. E4, F3).

A further, special form of astrocyte (Fig. G1) is found in the cerebellum. These cells have winglike (velate) extensions and appear in the region of the cerebellar glomeruli (Fig. G2) of the granular layer (see Plate 152).

Magnifications: Fig. B, ×20; Fig. D, ×10, Figs. E, F, ×400; Fig. G, ×700

REFERENCES

Phillips DE (1973) An electron microscopic study of macroglia and microglia in the lateral funiculus of the developing spinal cord in the fetal monkey. Z. Zellforsch 140:145–167
This plate provides a clearer impression of the relationship between a nerve cell (1) and protoplasmic astrocytes (2), an oligodendrocyte (3), and blood capillaries (4). A nerve cell normally has several branching dendrites (5) and an axon (6). Short, cut boutons terminaux (7) of other nerve cells are located both on dendrites and on the axon, forming synapses with the depicted neuron.

Near the nerve cells are located two astrocytes (2) with their processes (8). These processes are of variable length and have footlike or platelike terminations (9), which are in contact both with the nerve cell (1) and, as perivascular feet, with the capillaries (4). The astrocytes contact one another at the site indicated by an arrow. The perivascular feet of astrocytes, as the membrana limitans gliae perivascularis, cover about 80% of the capillary surface. Areas not covered by the membrane (10), where only the capillary basal lamina is present, are uncommon.

Short, rounded protrusions (11) also form on the body of astrocytes and serve as supports for the numerous processes of the various nerve cells.

An oligodendrocyte (3) surrounds an axonal segment with its myelin sheath (12). Below the node of Ranvier (13), another oligodendrocyte supplies the neuron with a myelin sheath.

To avoid misinterpretation of this plate, it should be noted that great numbers of many different kinds of cell processes occur between the cells and capillaries—the so-called neuropil. These processes have been omitted here for the sake of clarity. The actual appearance of a section through the close cell union of the nervous tissue has already been shown in Plate 2.

Magnification: \( \times 2,700 \)

**REFERENCES**


A protoplasmic astrocyte (1) is a relatively large, stellate cell that predominantly occurs in the gray matter of the brain and spinal cord. The cell body contains a large, spherical nucleus with very finely dispersed chromatin, which facilitates identification of astrocytes in the electron microscope. Around the nucleus, several short cisternae of rough endoplasmic reticulum and a medium-sized Golgi apparatus are found. In addition to a small number of mitochondria, glycogen particles and centrioles occur in the slightly osmiophilic cytoplasm, since astrocytes are capable of division under certain circumstances.

Gliofibrils (2) are particularly characteristic of astrocytes; they are seen in sections to run transversely and longitudinally, largely in the vicinity of the nucleus, whence they extend into the processes. Gliofibrils, which probably have a mechanical function, are composed of 5- to 10-nm-thick gliofilaments consisting of gli fibrillary acidic protein.

The short processes of a protoplasmic astrocyte extend on one side to the nerve cells (3) and on the other to the blood capillaries (4). Whereas capillaries and perivascular feet (5) are separated by a 30- to 50-nm-thick capillary basal lamina (6), the cytoplasmic end plates (7) approach the nerve cells at a distance of less than 20 nm. Thus, some axosomatic synapses (8) become covered by astrocyte extensions.

Many unmyelinated (9) and myelinated nerve fibers (10) as well as nerve endings (11) are found around the body of the astrocyte at a distance of only 20 nm. They indent the surface of the cell body somewhat, giving rise to many small platelike cytoplasmic processes. It is, therefore, supposed that an astrocyte is also able to embrace various synapses (e.g., axodendritic synapses, 12; axospinous synapses, 13) in addition to surrounding nerve fibers. A few denticular spines (14) can also be observed outside the astrocyte.

The presence of glycogen in the cytoplasm of astrocytes and the high phosphorylase activity indicate that these cells are of major importance in the metabolism of carbohydrates in the central nervous system. In contrast to nerve cells, glial elements do not show any acetycholinesterase activity, though they do have an increased concentration of adenosine triphosphate (ATP) bound to the cell membrane. As a result of their energetic involvement in the sodium pump, astrocytes play an important role in ionic regulation of the CNS. Hitherto, there has been little evidence of phagocytic activity of astrocytes.

Magnification: \( \times 10,000 \)

REFERENCES
Duncan D, Morales R (1973) Fine structure of astrocyte mitochondria in the spinal cord of the dog, cat, and monkey. Annt Res 175:519-528
Phillips DE (1973) An electron microscopic study of macroglia and microglia in the lateral funiculus of the developing spinal cord in the fetal monkey. Z Zellforsch 140:145-167
NERVOUS TISSUE

Plate 151. Glia of the Central Nervous System. Fibrous Astrocyte

The 8- to 10-μm-wide fibrous astrocytes occur, as stated in Plate 148, predominantly in the white matter of the central nervous system. These cells are characterized by 20-40 wirelike, occasionally branched processes (1) of various lengths (10–50 μm) that are inserted between myelinated (2) and unmyelinated (3) nerve fibers. The longer processes run parallel with the nerve fibers, whereas many of the transverse processes (arrow) contact blood capillaries (4).

The astrocyte body contains a nucleus with homogeneously dispersed heterochromatin. Moderately developed organelles, a few lysosomes, and small clusters of glycogen particles (5) occur in the cytoplasm. As in protoplasmic astrocytes, gliofibrils (6), made up of gliofilaments, represent specific differentiations in fibrous astrocytes. Gliofilaments form a mechanically resistant skeleton in the perikaryon and its processes.

Fibrous astrocytes fulfill the same histophysiological functions in the white matter of the central nervous system as the protoplasmic astrocytes do in the gray. It has been proved that the two are variations of the same cell type which have adapted to different environments.

Following loss of nervous tissue, it is largely the function of fibrous astrocytes to replace the damaged or affected area. Though the ability of glia cells to divide is slight after birth, it is possible in the case of damage for mitoses to take place. Scar formation then occurs in the CNS and is termed gliosis.

Two nodes of Ranvier (7) can be recognized on myelinated nerve fibers. (See Plate 68 in Krsćić 1979.)

Magnification: × 8,000

REFERENCES
In the two previous plates, it was seen how protoplasmic and fibrous astrocytes affix nerve cells and nerve fibers by their processes. All these elements, together with the microglia cells and capillaries, form the neuropil—a densely packed cellular conglomerate which fills spaces between the perikarya of the nerve cells of the CNS. This figure shows that astrocytes also play a mechanical and metabolic role in the extensive synaptic regions. The light-microscopic morphology of velate astrocytes in the granular layer of the cerebellum has already been seen in Plate 148. The cells appear stellate following special staining techniques, though the number of their processes is relatively small. Electron-microscopic studies have shown that these cells are a specially differentiated type of astrocyte which have winglike processes, similar to cabbage leaves in appearance (arrows), instead of cylindrical processes. With these cytoplasmic sheets, the cells envelop capillaries (1) and nerve cells (2, here a small granule cell), as well as parts of the cerebellar glomeruli (3), which are characteristic of the granular layer of the cerebellar cortex. Under the light microscope, these cerebellar glomeruli appear as pale anuclear areas (see Plate 148); electron-microscopically, it has been determined that in these structures, synaptic contacts exist between mossy fibers (4) and dendrites (5) of the small granule cells. These complex structures are thus more or less bounded by the astrocyte extensions. It is assumed that some dendrites and/or axons (6) of nerve cells may pass through the astrocyte processes. The cytoplasmic sheets appear free in this plate though they do of course surround other nerve cells or cerebellar glomeruli, which have been omitted for the sake of clarity. From the behavior of the processes of this type of astrocyte, it is evident that these cells are not solely involved in the metabolism of nerve cells, but also supply the synapses with energy. The basal lamina (7) can be observed between the astrocyte processes and the non-fenestrated blood capillary.

Magnification: \( \times 5,000 \)

REFERENCES


NERVOUS TISSUE

Plate 153. Glia of the Central Nervous System. Membrana Limitans Gliae Superficialis and Perivascularis

In addition to other functions, astrocytes provide a boundary to the tissue of the CNS against the blood vessels that supply it and other adjacent tissues. The structure of these boundaries is as follows. With their processes, protoplasmic astrocytes (1) form a three-dimensional network, the interstices of which contain neurons (not shown). All footlike astrocyte processes that extend to the surface of the brain are arranged adjacent to one another such that a membrana limitans gliae superficialis (2) forms. The innermost of the leptomeninges, the pia mater (3), is closely apposed to this membrane. Above the pia mater is found a connective tissue layer poor in blood vessels, the arachnoid membrane (4), connected to the pia mater by a loose trabecular framework (5). Thus, between the two leptomeninges there is a space containing numerous blood vessels (6), termed the subarachnoid space (7). Between the arachnoid and the dura mater (8), which is composed of dense connective tissue, occurs the slitlike subdural space (9).

Extensions of the subarachnoid space, the Virchow-Robin spaces (10), accompany the penetrating blood vessels (11) to a certain depth. These spaces contain collagen and reticular fibers, which gradually diminish with the reduction in blood vessel diameter until eventually the capillaries (12) completely lack a connective tissue envelope. In its place, as already mentioned in Plates 149 and 150, the astrocyte perivascular feet form a membrana limitans gliae perivascularis (13). The two glial membranes provide the essential specific environment and isolation for the nervous tissue of the CNS. Here, the membrana limitans gliae perivascularis is important since it forms part of the blood-brain barrier.

The structures in insets A and B are enlarged in the corresponding figures of Plate 154.

Magnification: × 1,000

REFERENCES

The end feet (Fig. A1) of the astrocytes contact one another by means of a nexus (Fig. A2) and form the membrana limitans gliae superficialis. The glial processes are separated from the pia mater (Fig. A3) and its collagen microfibrils (Fig. A4), fibrocytic processes (Fig. A5), and blood capillaries (Fig. A6) by a basal lamina (Fig. A7). Beneath the surface glial membrane are located numerous processes (Fig. A8) of nerve and glia cells belonging to the neuropil.

The membrana limitans gliae perivascularis is, as already mentioned, made up of the perivascular feet (Fig. B1) of astrocytes. The perivascular glial layer is separated from a nonfenestrated brain capillary (Fig. B2) and its pericyte (Fig. B3) by a 20- to 50-nm-thick basal lamina (Fig. B4). Outside the membrana limitans gliae perivascularis is the neuropil (Fig. B5). Calculations have shown that 25%-80% of the neuropil volume of the rat consists of glia cell processes. The inset in Fig. B corresponds to Fig. C.

It has been known for some time that vital stains, e.g., trypan blue, which is capable of staining certain cells blue, are unable to penetrate the brain, with the exception of a few restricted areas. The same applies to some substances circulating in the blood plasma. This selectivity of the brain, which affects metabolic processes, is termed the blood-brain barrier (BBB). Morphologically, the BBB consists of zonulae occludentes (Fig. C1) joining nonfenestrated endothelial cells (Fig. C2), a basal lamina (Fig. C3), and the perivascular feet (Fig. C4) of astrocytes. The absence of pericapillary spaces is very characteristic of the BBB.

The extracellular spaces in the CNS according to a recent estimation comprise 17%-20% of the total volume of the brain. Investigations have shown that these spaces hold a proteoglycan-containing ground substance which could hinder free ionic diffusion. In addition, endothelial cells and astrocytes are able to regulate the selectivity of the BBB. It is assumed that some endothelial cells exhibit polar differentiation and transport certain substances only in one direction. (See physiology texts for further information.)

There are also, however, areas of the brain which lack a BBB. Here, the capillaries are fenestrated and surrounded by broad pericapillary spaces; the membrana gliae perivascularis is only partially present. Such structural features appear in the choroid plexus (Fig. D1), pineal body (Fig. D2), subcommissural organ (Fig. D3), area postrema (Fig. D4), neurohypophysis (Fig. D5), median eminence (Fig. D6), and infundibulum.

The BBB is in practice of great importance in the medical treatment of cerebral diseases, since it can prevent the passage of drugs into nervous tissue. (See Plates 148, 150 in Krstic 1979.)

Magnifications: Figs. A, B, × 10,000; Fig. C, × 40,000

REFERENCES
Plate 155. Glia of the Central Nervous System. Oligodendrocytes

The 6- to 8-μm-large oligodendrocytes are found in the direct vicinity of nerve cells and their processes and blood capillaries. The light-microscopic appearance of these cells has already been shown in Plate 148. Oligodendrocytes (Fig. A1) usually appear in the electron microscope as ovoid or elliptoidal cells with a large heterochromatin-rich nucleus. A few mitochondria and relatively voluminous Golgi complexes are present in the narrow belt of cytoplasm. Owing to the large numbers of cisternae of rough endoplasmic reticulum and free ribosomes, the cytoplasm of oligodendrocytes appears significantly darker than that of astrocytes. Oligodendrocytes bear only a few relatively short conical and platelike processes. Functionally, these processes are of particular importance in forming the myelin sheaths in the CNS. It is assumed that the leaflike processes with their tongue-like cytoplasmic thickenings (Fig. A2) roll around the axons (Fig. A3), though the exact manner is unknown. One oligodendrocyte can provide a segment or internode of the myelin sheath (Fig. A4) for several axons. The nodes of Ranvier (arrows) are sites where the myelin sheath is lacking. At these places, the axons are in direct contact with their environment, e.g., with boutons terminaux (Fig. A5). Schmidt-Lantermann incisures are almost never present in the myelin sheaths of the CNS. In the upper right of the drawing, a cut-away section of a nerve cell (Fig. A6) and the axon hillock (Fig. A7) can be seen. Several boutons terminaux (Fig. A8) are in contact with the neuron. Figure B shows the development of the myelin sheath as currently understood, which is based on the fact that the innermost myelin lamella is always the shortest. It is supposed that the lamellar oligodendrocyte processes (Fig. B1) have a trapezoid form with the broader base (Fig. B2) toward the cell. Following attachment of the shorter side (Fig. B3) to the axon (Fig. B4), the cell process then probably rotates about the axon, thus forming the myelin sheath. The peculiar contractions of oligodendrocytes observed in tissue culture for the main part remain to be clarified. (See Plate 89 in Krstić 1979.)

Magnification: Fig. A, × 14,000

REFERENCES
Plate 156. Glia of the Central Nervous System. Microglia
(Modified from HAGER 1968)

Following special impregnation methods, microglia, mesoglia, or Hortega cells (Figs. A1, B1) appear in all regions of the CNS, predominantly however near capillaries. Irregular, sometimes bushlike processes extend from the long cell body (Fig. A).

In the electron microscope, microglia appear as very irregular elements with an ellipsoidal nucleus containing dispersed chromatin. The dense, ribosome-rich cytoplasm contains a moderately to well-developed Golgi apparatus, a variable number of mitochondria and cisternae of rough endoplasmic reticulum, and peripheral vacuoles (Fig. B2). Particularly characteristic of Hortega cells is the presence of several lysosomes (Fig. B3), phagolysosomes (Fig. B4), and residual bodies (Fig. B5).

Microglia are able to move in ameboid fashion and can thus move away from the capillaries. In doing so, they perforate the basal lamina (Fig. B6) at the sites marked by arrows, force their way between the astrocyte end feet (Fig. B7) of the membra limitans gliae perivascularis to the neuropil (Fig. B8), and then enter areas of dead nervous tissue and phagocytize the cell debris. Hortega cells are also distinguished by their ability to store iron and pigments.

The origin of microglia has not yet been conclusively demonstrated. Since they largely wander out of the capillary region, some investigators believe that these cells are specially differentiated pericytes (so-called perivascular microglial cells). If a pericyte (Fig. B9) is compared with a microglial cell, it is certainly possible to recognize several morphological similarities. According to another interpretation, small, rounded cells (Fig. B10) in the neuropil with a spherical nucleus and dense cytoplasm (so-called intermediate microglial cells) are able to differentiate into Hortega cells. The assertion that these cells develop from monocytes has likewise not been proven. It is, however, certain that microglia stem from the mesoderm of the neural crest and migrate to the CNS with the blood vessels.

Magnifications: Fig. A, ×1,500; Fig. B, ×10,000

REFERENCES
Baron M, Gallego A (1972) The relation of the microglia with the pericytes in the cat cerebral cortex. Z Zellforsch 128:42-57
Plate 157. Form of Nerve Cells Under the Light Microscope

Excitability, conduction, and processing of information are the basic properties of nerve cells (neurocytes, ganglion cells). Their morphology can be studied following Golgi staining.

As was evident in the previous plates, both simple and complex ganglion cells exist, however they are always constructed according to the same principle. The structure of a ganglion cell will be discussed with the example of a simple bipolar nerve cell (Fig.A1) from Corti’s ganglion.

The dendrite (Fig.A2) conducts the stimulus in the direction of the arrows toward the cell body, i.e., it is the receptive part of the cell. In the perikaryon, the information is processed, altered, and then conducted to the axon (Fig.A3), also in the direction of the arrow. An axon thus has an effector function. The framework of neurofibrils (Fig.A4), which occurs in all nerve cells, can also be seen.

Nerve cells with all their processes represent genetic, morphological, biological, and regenerative units of the nervous tissue which are termed neurons. Together with elements of the neuroglia they form the nervous system.

The behavior of the processes and the form of the perikaryon of a nerve cell can vary considerably according to function. Thus, e.g., multipolar ganglion cells from the spinal cord are distinguished by an irregular perikaryon (Fig.D1); they have many dendrites (Fig.D2) extending in various directions and only one, occasionally 1-m-long, axon (Fig.D3) with lateral ramifications, the collaterals or paraxons (Fig.D4). It is apparent that the axon, in contrast to the dendrites, always has the same diameter.

Pyramidal cells from the gray matter of the cerebrum can be observed in section to have a triangular perikaryon (Fig.E1) and numerous horizontally branching dendrites (Fig.E2), bearing small dendritic spines. At the base of the triangle, an axon and its paraxons (Fig.E3) leave the perikaryon.

The body of Purkinje cells (Fig.G1) from the cerebellum is in the form of a pear and the branching dendrites (Fig.G2), with great numbers of spinous processes (Fig. G, arrows), give the cell a tree-like appearance. There is one long axon (Fig.G3). These cells belong to the Golgi type I neurons, i.e., nerve cells that are characterized by many dendrites and long axons that run into the white matter.

Small neurons, e.g., basket cells (Fig.F) and granule cells (Fig.H) of the cerebellum, are rich in dendrites (Figs.F1, H1) but only bear short axons (Figs.F2, H2), which never leave the gray matter. They are termed Golgi type II neurons and serve to conduct impulses to several neurons within the gray matter.

This plate also shows two exceptions to the rule according to which every nerve cell has one axon and several dendrites. Spinal ganglion cells (Fig.B) are considered biaxonal and dendritic, and amacrine cells (Fig.C) from the retina are nerve cells that apparently only possess dendrites.

Magnifications: Figs. A–H, × 600

REFERENCES
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Plate 158. Various Types of Nerve Cell

According to the criteria of shape of the cell body and the number of processes, the following types of neuron can be distinguished.

A. Apolar nerve cells are neurocytes without dendrites and axons which only occur at the beginning of histogenesis (Fig. A1). Subsequently, they develop into the various nerve cells (Fig. A2) listed below. Broadly speaking, the hair cells (Fig. A3) of the vestibulocochlear organ and taste buds can also be classed as apolar cells.

B. Unipolar nerve cells only appear in the form of rod (Fig. B1) and cone cells (Fig. B2) of the retina. Both have axonlike processes (arrows) stemming from a single cell pole.

C. Pseudounipolar nerve cells are initially bipolar neurons (Fig. C1) whose processes gradually join together close to their points of origin (Fig. C2, in the direction of the arrows) as a result of asymmetrical cell growth. The T-shaped process (Fig. C3) then develops that is characteristic of the ganglion cells of the spinal ganglia and ganglia of the cerebral nerves, except for the ganglion of the vestibulocochlear nerve.

D. Bipolar nerve cells have one dendrite (Fig. D1) and one axon (Fig. D2), which are very difficult to differentiate morphologically. Bipolar nerve cells are found in the retina (as the second neuron of the visual pathway) and as the first neurons of the vestibulocochlear organ.

E. Multipolar nerve cells are the most frequent kind of neuron. As stated in the previous plate, there are two types of multipolar neuron: Golgi type I, with long axons, and Golgi type II, with short axons.

REFERENCES


Plate 159. Arrangement of Nerve Cells

In the gray matter of the cerebrum and cerebellum, the neurons form more or less well-defined layers. In other parts of the central nervous system, they occur in groups or nuclei in which nerve cells do not have a particular order within the neuropil. Purkinje cells (1) of the cerebellum, however, are an exception to this rule.

In plan view, these neurons appear as already depicted in Plate 157. Purkinje cells have been shown to be completely flattened elements, tightly packed and arranged in a consecutive fashion. Their highly branching dendrites (2), with dendritic spines (3), run in a plane perpendicular to the axis of the folia of the cerebellum. Transverse sections show the Purkinje cells (1a) to be spindle- or bottle-shaped, narrow, and with poorly developed dendrites.

A small granule cell (4) makes synaptic contact by means of its T-shaped branched axon (5) with large numbers of apposed Purkinje cells.

Magnification: × 1,500

REFERENCES
Several dendrites (1) and a myelinated axon (2) leave the voluminous perikaryon of a pyramidal cell. The cytoplasm of the nerve cells, here termed neuroplasm, contains a nucleus (3), with a distinct nucleolus (4), and a well-developed, frequently multiple Golgi apparatus (5). Cisternae of rough endoplasmic reticulum are also developed to a high degree and largely occur as groups of parallel double lamellae which form the characteristic Nissl bodies (6). They are abundant throughout the whole of the neuroplasm and dendrites. Nissl bodies are only absent from the axon and from the small zone where the axon leaves the cell body, the axon hillock (7). Many mitochondria, lysosomes, and occasionally lipofuscin granules can be seen between the lamellae of rough endoplasmic reticulum.

The 20-nm-thick neurotubules and approximately 7-nm-thick neurofilaments, which are very numerous in the neuroplasm, together form the light-microscopically visible neurofilaments. Since nerve cells have completely lost the ability to divide, centrioles are not found in the neuroplasm.

Large numbers of boutons terminaux (8) and several astrocyte processes (9) are in contact with the plasmalemma of nerve cells. One of these processes (arrow) simultaneously contacts the neurocyte and a capillary (10).

The pyramidal cell in this plate has been drawn so that it projects from the tightly packed neuroplasm (II), which has here been cut as a cube. In this way, it is easier to follow the path of the glial and nerve cell processes and obtain a clearer impression of the closed cellular union which is the nervous tissue of the CNS. (See Plates 44, 45, 119–121 in Krstić 1979.)

Magnification: \( \times 3,500 \)

REFERENCES


Plenzinger KH (1973) Synaptic morphology and cytochemistry. Progr Histochem Cytochem 5:1–86
NERVOUS TISSUE

Plate 161. Nerve Cell. Neurofibrils

The light-microscopic appearance of neurofibrils has already been depicted in Plate 157. The present, somewhat schematized, reconstruction was prepared from a study of 2- to 3-μm-thick sections in the high-voltage electron microscope. The nucleus (1) is located in the center of the nerve cell body and is surrounded by flattened, perforated lamellae of the multiple Golgi apparatus (2). These lamellae, recognizable in sections as Golgi fields, are connected by means of numerous thin tubules (3). Neurofibrils (4), which are made up of neurofilaments, run through all parts of the perikaryon and extend into the dendrites (5) and axon (6). In this manner, a fibrillar framework develops within every nerve cell, which not only imparts mechanical strength, but is possibly also responsible for conducting vesicular structures and impulses through the cell body. Mitochondria (7) are contained within the interstices of the neurofibrillar network.

(See Plates 31-33, 66 in KRSTIĆ 1979.)

Magnification: \( \times 4,000 \)

REFERENCES

Plate 162. Neurosecretory or Neuroendocrine Nerve Cells.

Example: Cells of the Nucleus Supraopticus and Paraventricularis

Certain nerve cells respond to stimuli not by producing bioelectric impulses but by secretory activity. These so-called neuroendocrine cells occur in groups, nuclei, predominantly in the hypothalamus (Fig. A, inset). A three-dimensional, schematic section of the hypothalamus is presented in Fig. B.

Several boutons terminaux (Fig. B1) of other nerve cells make synaptic contacts with the stellate neurons of the nucleus supraopticus (NSO) and nucleus paraventricularis (NPV). A few dendritic processes (Fig. B2) of neurons situated in the vicinity of the ventricular wall project through the ependyma (Fig. B3) and reach the cerebrospinal fluid; the cells concerned are neurosecretory cerebrospinal fluid-contacting neurons (see Plate 147). Axons (Fig. B4) of NSO and NPV neurons extend to the neurohypophysis (Fig. B5). Some of these axons come into contact with capillary loops (Fig. B6) of the hypophyseal stalk, whereas the expanded terminations of other axons rest on capillaries (Fig. B7) of the neurohypophysis. A series of numerous thickenings, Herring bodies (Fig. B8), can be seen along the axons. All these axons together comprise the neurosecretory hypothalamohypophyseal tract (Fig. B9).

Special staining techniques reveal neurosecretory cells (Fig. C) to be spindle-shaped or stellate elements, usually close to capillaries. Axons (Fig. C1) rich in secretory product run between the nerve cells. The inset in Fig. C corresponds to Fig. D. Like all nerve cells, neurosecretory cells contain Nissl bodies (Fig. D1), mitochondria, and lysosomes. Osmiophilic, 100- to 200-nm-wide, secretory granules (Fig. D2), containing neurohormones and surrounded by a unit membrane, detach themselves from the Golgi apparatus and move into the axon (Fig. D3). The neurosecretory cell is separated from the capillary (Fig. D4) by an extremely thin investment of astrocytes (Fig. D5) and two basal laminae (Fig. D6). Boutons terminaux (Fig. D7) are located on the cell body and its processes.

Figure E is a continuation of Fig. D and shows a small Herring body, which contains numerous neurosecretory granules (Fig. E2) as well as mitochondria and cisternae of smooth endoplasmic reticulum (Fig. E8). Neurohormones in the neurosecretory granules are bound to a carrier, neurophysin.

Lower down, the neurosecretory axon (Fig. F3) terminates in the immediate proximity of a capillary (Fig. F9) with fenestrated endothelium. The nerve ending contains mitochondria, cisternae of smooth endoplasmic reticulum, neurotubules, many neurosecretory granules, and synaptoid vesicles (Fig. F10). Synapses (Fig. F11) with other axons also exist.

Neurosecretory granules (Fig. F2) when required are expelled from the nerve endings into the pericapillary spaces (Fig. F12) by exocytosis. From here, the neurohormones, now freed from the neurophysin, enter the blood circulation and are transported to the effectector cells, where they carry out their specific function.

The neurosecretory cells of the NSO synthesize anti-diuretic hormone, and those of the NPV oxytocin. (See Plates 32, 33, 64 in KRSTIĆ 1979.)

Magnifications: Fig. C, ×400; Figs. D–F, ×17,000

REFERENCES

Plate 163. Neurosecretory Nerve Cell. Simplified General Scheme of the Mode of Action of Polypeptide Hormones

Advances in neuroendocrinology have shown that neurosecretory cells are at the beginning of a chain of hormonal events. Recently, the mode of action of hormones has been investigated more closely at the molecular level. This simplified scheme of the mechanisms of action of polypeptide hormones was prepared on the basis of these new findings.

Synaptic contacts (1), as mentioned in Plate 162, and other possible sources of excitation cause the neuroendocrine cell (2) to be stimulated in the direction of the unshaded arrows. The cell synthesizes its hormone and secretes it (symbolized as black spherules, 3) into the blood circulation. Since the hormone carries information determining the behavior of certain cells, it is termed a "first messenger." Of particular importance in the further action of the hormone is a specific union between the hormone and a genetically determined receptor sites in the plasmalemma of the target cell. Several such receptor sites can be seen as hemispherical indentations (4) at the level of the outer layer of the cell membrane (5). Thus, "recognition" of the hormone is dependent on the form of the receptor on the target cell membrane: It is believed that the hormone fits into the receptor sites like a key into a lock.

The hormone-receptor complex (6) activates an enzyme, adenyl cyclase (7), located on the inner side of the cell membrane, which forms cyclic adenosine monophosphate (cAMP) from adenosine triphosphate (ATP) in the presence of Mg$^{2+}$ ions. In this way, the hormonal information becomes amplified $10^3$- to $10^4$-fold and is transferred to the cytoplasm without the hormone itself entering the cell. Since cAMP occurs in practically all the cells it is referred to as the "second messenger." It activates the specific enzymes and/or genes of target cells, in addition to affecting their permeability. As a response, the target cells secrete specific products (8) which can act on other cells (9) or inhibit the activity of the hormone-producing cells in the form of a negative feedback (10). After stimulation of adenyl cyclase by the hormone-receptor complex, the hormone becomes inactivated (11). The high specificity of the hormone is also indicated in this plate. It is clear that the morphological (and chemical) receptors of the other two cells (12, 13) are incapable of binding the structurally different hormone.

This scheme applies to the action of epinephrine and all polypeptide hormones. For all practical purposes, it can be assumed that the mode of action of neurohormones is based on the same mechanism. A discussion of the mechanism of action of steroid hormones is beyond the scope of this book. (See Plates 153, 154 in Kurić 1979 and biochemistry and physiology texts for further information.)

REFERENCE