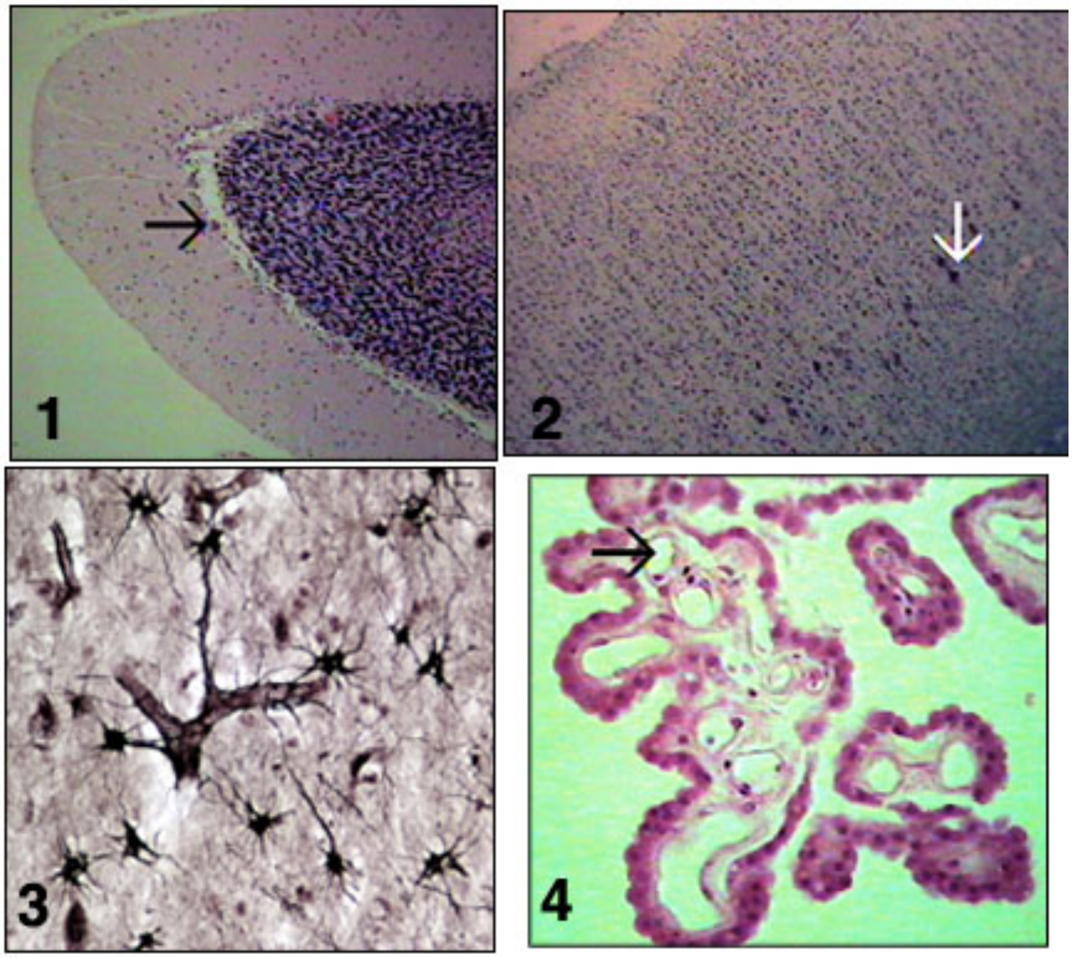
Cerebellar and Cerebral Cortex



1. Cerebellar cortex. Note the trilaminar appearance and the Purkinje cell layer (arrow).
2. Cerebral cortex. Note the multilaminar appearance and in this specific region of the cortex (frontal lobe) the presence of Betz cells (arrow).
3. Astrocytes (stained black) within the cerebral cortex.
4. Choroid plexus. Note the capillaries (arrow).

The cerebellar and cerebral hemispheres differ from the spinal cord in that the gray matter is located at the periphery and the white matter lies centrally. Both regions of the brain consist of an outer cortex of gray matter and a subcortical region of white matter.

Cerebral Cortex

The cerebral cortex is 1.5 to 4.0 mm thick and contains about 50 billion neurons plus nerve processes and supporting glial cells. In all but a few regions it is characterized by a laminated appearance. Perikarya generally are organized into five layers. Starting at the periphery of the cerebral cortex, the general organization of neurons is molecular layer (I), external granular layer (II), external pyramidal layer (III), internal granular layer (IV), internal pyramidal layer (V), and multiform layer (VI).

The molecular layer (I) is a largely perikaryon-free zone just below the surface of the cortex. Neurons of similar type tend to occupy the same layer in the cerebral cortex, although each cellular layer is composed of several different cell types. For convenience of description, these neurons often are placed in two major groups: pyramidal cells and stellate or nonpyramidal cells. The perikarya of pyramidal cells are pyramidal in shape and have large apical dendrites that usually are oriented toward the surface of the cerebral cortex and enter the overlying layers; the single axons enter the subcortical white matter. They are found in layers II, III, V, and, to a lesser extent, layer VI. Very large pyramid-shaped neurons (Betz cells) are present in the internal pyramidal layer (V) of the frontal lobe. Stellate (nonpyramidal) cells lack the pyramid-shaped perikarya and the large apical dendrite. They occur in all layers of the cerebral cortex but are concentrated in the internal granular layer (IV). Impulses entering the cortex are relayed primarily to stellate cells and then transmitted to pyramidal cells in the various layers by the vertical axons of the stellate cells. Axons of pyramidal cells generally leave the cortex and extend to other regions of the brain and spinal cord.
The cerebral cortex functions in vision, hearing, speech, voluntary motor activities, and learning.

Cerebellar Cortex

Three layers characterize the cerebellar cortex: an outer molecular layer, a middle Purkinje cell layer, and an inner granule cell layer.
The molecular layer is mainly a synaptic area with relatively few nerve cell bodies. It consists primarily of unmyelinated axons from granule cells, the axons running parallel to the cortical surface. It also contains large dendrites of the underlying Purkinje cells and in its superficial portion contains small-scattered neurons called stellate cells. Other small neurons located deep in this layer and adjacent to Purkinje cells are called basket cells.
The Purkinje cell layer is formed by the cell bodies of Purkinje cells - large, pear-shaped neurons aligned in a single row and characterized by large branching dendrites that lie in the molecular layer. They represent Golgi type I neurons and number about 15 million. Three-dimensionally, the large dendritic trees occupy a narrow plane, reminiscent of fan coral, and are so arranged that each dendritic tree is parallel to its neighbor. A single small axon from the Purkinje cell passes through the granule cell layer and synapses with neurons in the central cerebellar area.
The granule cell layer consists of numerous closely packed, small neurons whose axons enter the molecular layer to synapse with dendrites of Purkinje cells. The granule cells represent Golgi type II neurons. They have small, round nuclei with coarse chromatin patterns and only scant cytoplasm; dendrites are short and clawlike. The axons enter the molecular layer, bifurcate, and run parallel to the surface but perpendicular to the wide plane of the Purkinje dendritic tree. The axons of granule cells synapse with about 450 Purkinje cells in a relationship similar to that of wires coursing along telephone poles. Axons of granule cells also synapse with stellate and basket neurons in the molecular layer. Another type of small neuron, the Golgi cell, is found in the outer zone of the granule cell layer.
Two types of afferent nerve fibers enter the cerebellar cortex from outer regions of the central nervous system. These are the mossy fibers, which synapse with granule cells, and the climbing fibers, which enter the molecular layer and wind about the dendrites of Purkinje cells.
The cerebellum functions primarily in the modulation of skeletal muscle activity such as the coordination of limb movement and balance.

The gray matter of the spinal cord, cerebrum, and cerebellum consists of a complex, highly ordered meshwork of dendritic, axonal, and glial processes that envelop the perikarya of associated neurons. This network, called the neuropil, provides a vast area for synaptic contact and interaction between nerve processes and forms an organizing framework. It is important for coordinating activities in the central nervous system.

Meninges

In addition to the covering of bone formed by the skull and vertebral column, the central nervous system is contained within three connective tissue membranes called meninges. The outermost, the dura mater, consists primarily of dense collagenous connective tissue. Around the brain it forms two layers and serves as a periosteum for the cranium and as the covering of the brain. The periosteal layer is rich in blood vessels, nerves, and cells. The inner layer is less vascular, and its interior surface is lined by a simple squamous epithelium. Where it covers the spinal cord, the dura is a single layer of dense irregular connective tissue that contains scattered elastic fibers. The outer surface is covered by a simple squamous epithelium, separated from the periosteum of the vertebrae by an epidural space filled by loose connective tissue that is rich in fat cells and veins. The inner surface of the dura of the spinal cord is lined by a simple squamous epithelium. Between it and the next meninx, the arachnoid, is a narrow, fluid-filled subdural space.

The arachnoid is a thin, weblike, avascular membrane made up of fine collagenous fibers and scattered elastic fibers. The outer region forms a smooth sheet, while the inner surface gives rise to numerous strands (trabeculae) that extend into and blend with the underlying pia mater. The inner surface of the arachnoid, the trabeculae, and the external surface of the pia are covered by a simple squamous epithelium that also lines a large space, the subarachnoid space, which contains cerebrospinal fluid.

The pia mater is a thin, vascular membrane that closely invests the brain and spinal cord. Because the pia and arachnoid are closely related, they often are considered together as the pia arachnoid. The pia consists of delicate collagenous and elastic fibers, fibroblasts, macrophages, and scattered mesenchymal cells. A sheath of pia mater invests blood vessels entering and leaving the brain substance. A perivascular space surrounds the vessels as they extend into the substance of the central nervous system and is continuous with the subarachnoid space.

Ependyma

The ependyma lines the central canal of the spinal cord and ventricles of the brain. It consists of a simple epithelium in which the closely packed cells vary from cuboidal to columnar. The luminal surfaces of the cells show large numbers of microvilli and, depending on the location, may show cilia. Adjacent cells are united by desmosomes and zonula adherens; zonula occludens generally are not seen. Hence, cerebrospinal fluid in the central canal and ventricles can pass between ependymal cells to enter the parenchyma of the central nervous system. The bases of ependymal cells have long, threadlike processes that branch, enter the substance of the brain and spinal cord, and may extend to the external surface, where they contribute end feet to the glia limitans. The ependyma forms a secretory epithelium in the ventricles of the brain, where it is in direct contact with a highly vascular region of the pia mater; the tela choroidea. The modified ependyma called choroid epithelial cells and the tela choroidea form the choroid plexus, which secretes cerebrospinal fluid.

Choroid epithelial cells of the choroid plexus are columnar and closely packed and bear numerous microvilli. Unlike those in other regions of the ependyma, cell apices here are joined by zonula occludens, which prevent passage of material between cells. Choroid epithelial cells lie on a continuous basal lamina that separates them from a connective tissue that contains small bundles of collagenous fibers, pia-arachnoid cells, and numerous blood vessels. Capillary endothelial cells in this region, unlike those elsewhere in the brain, have numerous fenestrations. Fluid readily moves through the capillary wall but is prevented from entering the ventricles by the zonula occludens. Choroid epithelial cells secrete sodium ions into the ventricles, and chloride ions, water, and other substances follow passively. Protein and glucose concentrations are relatively low. Cerebrospinal fluid is formed continuously, moves slowly through the ventricles of the brain, and enters the subarachnoid space. It surrounds and protects the central nervous system from mechanical injury and is important in the metabolic activities of the central nervous system.

Certain substances in the blood are prevented from entering the central nervous system, although they readily gain access to other tissues. The end feet of astrocytes sheath capillaries deep in the spinal cord and brain, and occluding tight junctions unites the nonfenestrated endothelial cells. The endothelial cells do not exhibit trans-endothelial transport vesicles typical of endothelial cells found in capillaries elsewhere. Additionally, the internal plasmalemma of the endothelial cells is thought to have special properties that prevent passage of some substances. Together the tight junctions and internal plasmalemma of the endothelial cells form the blood-brain barrier.

Highly vascularized areas - *the circumventricular organs* - are present in specific regions along the midline of the walls of the ventricles. These organs include the organum vasculosum, lamina terminalis, subfornical organ, subcommissural organ, and area postrema. Except for the subcommissural organ, the ependymal cells of these areas are modified and appear as stellate cells called tanycytes, which are thought to transport cerebrospinal fluid to neurons in the hypothalamus. Such regions are devoid of an internal (subependymal) layer and the external (subpial) layer of glial processes. The underlying capillaries are lined by a fenestrated endothelium. These regions lack the morphologic elements of a true blood-brain barrier and, except for the subcommissural organ, are able to accumulate vital dyes. Large molecules are thought to traverse these regions, which provide areas of exchange between the central nervous system and blood.