may harbor viral inclusions in progressive multifocal leukoencephalopathy. *Glial cytoplasmic inclusions*, primarily composed of α-synuclein, are found in oligodendrocytes in multiple system atrophy (MSA).

Ependymal cells, the ciliated columnar epithelial cells lining the ventricles, do not have specific patterns of reaction. When there is inflammation or marked dilation of the ventricular system, disruption of the ependymal lining is paired with proliferation of subependymal astrocytes to produce small irregularities on the ventricular surfaces *(ependymal granulations)*. Certain infectious agents, particularly CMV, may produce extensive ependymal injury, with viral inclusions in ependymal cells. However, neither oligodendrocytes nor ependymal cells mediate significant responses to most forms of injury in the CNS.

KEY CONCEPTS

Cellular Pathology of the Central Nervous System

- Each cellular component of the nervous system has a distinct set of patterns of response to injury.
- Neuronal injury commonly results in cell death, either by apoptosis or necrosis. Loss of neurons that is difficult to detect without formal quantification may still contribute to dysfunction.
- Astrocytes show morphologic changes including hypertrophy of the cytoplasm, accumulation of intermediate filament protein (GFAP), and hyperplasia.
- Microglia, the resident monocyte-lineage population of the CNS, proliferate and accumulate in response to injury.

Cerebral Edema, Hydrocephalus, and Raised Intracranial Pressure and Herniation

The brain and the spinal cord are encased and protected by the rigid skull and the bony spinal canal. The pressure within the cranial cavity may rise in one of three commonly observed clinical settings: generalized brain edema, increased CSF volume (hydrocephalus), and focally expanding mass lesions. Depending on the degree and rapidity of the pressure increase and the nature of the underlying lesion, the consequences range from subtle neurologic deficits to death.

Cerebral Edema

Cerebral edema (more precisely, brain parenchymal edema) is the result of increased fluid leakage from blood vessels or injury to various cells of the CNS. There are two main pathways of edema formation in the brain.

- *Vasogenic edema* is an increase in extracellular fluid caused by blood-brain barrier disruption and increased vascular permeability, allowing fluid to shift from the intravascular compartment to the intercellular spaces of the brain. The paucity of lymphatics greatly impairs the resorption of excess extracellular fluid. Vasogenic edema may be either localized (e.g., adjacent to inflammation or neoplasms) or generalized, as can follow ischemic injury.
- *Cytotoxic edema* is an increase in intracellular fluid secondary to neuronal, glial, or endothelial cell membrane injury, as might be encountered in someone with a generalized hypoxic/ischemic insult or with a metabolic derangement that prevents maintenance of the normal membrane ionic gradient.

In practice, conditions associated with generalized edema often have elements of both vasogenic and cytotoxic edema. In generalized edema, the gyri are flattened, the intervening sulci are narrowed, and the ventricular cavities are compressed. As the brain expands, herniation may occur.

Interstitial edema (hydrocephalic edema) occurs especially around the lateral ventricles when an increase in intravascular pressure causes an abnormal flow of fluid from the intraventricular CSF across the ependymal lining to the periventricular white matter.

Hydrocephalus

Hydrocephalus is the accumulation of excessive CSF within the ventricular system (Fig. 28-2). The choroid plexus within the ventricular system produces CSF, which normally circulates through the ventricular system and enters the cisterna magna at the base of the brain stem through the foramina of Luschka and Magendie. Subarachnoid CSF bathes the superior cerebral convexities and is absorbed by the arachnoid granulations. Most cases of hydrocephalus are a consequence of impaired flow and resorption of CSF; overproduction is a rare cause that can accompany tumors of the choroid plexus. An increased volume of CSF within the ventricles expands them and can elevate the intracranial pressure.

When hydrocephalus develops in infancy before closure of the cranial sutures, there is enlargement of the head,

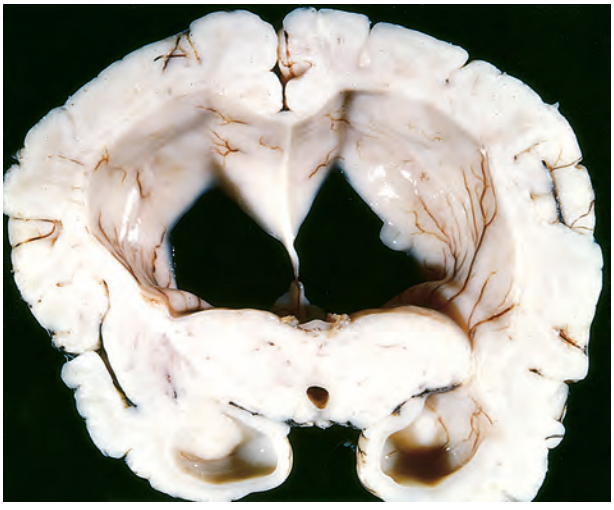

Figure 28-2 Hydrocephalus. Dilated lateral ventricles seen in a coronal section through the midthalamus.