complex lipids (lipofuscin), proteins, or carbohydrates. Abnormal cytoplasmic deposition of complex lipids and other substances also occurs in genetically determined disorders of metabolism in which substrates or intermediates accumulate (Chapter 5). Viral infection can lead to abnormal intranuclear inclusions, as seen in herpetic infection (Cowdry body), cytoplasmic inclusions, as seen in rabies (Negri body), or both nucleus and cytoplasm as in cytomegalovirus infection.

Some degenerative diseases of the CNS are associated with neuronal intracytoplasmic inclusions, such as neurofibrillary tangles of Alzheimer disease and Lewy bodies of Parkinson disease; others cause abnormal vacuolization of the perikaryon and neuronal cell processes in the neuropil (Creutzfeldt-Jakob disease).

Reactions of Astrocytes to Injury

Gliosis is the most important histopathologic indicator of CNS injury, regardless of etiology, and is characterized by both hypertrophy and hyperplasia of astrocytes. The astrocyte derives its name from its star-shaped appearance. These cells have multipolar, branching cytoplasmic processes that emanate from the cell body and contain glial fibrillary acidic protein (GFAP), a cell type-specific intermediate filament (Fig. 28-1). Astrocytes act as metabolic buffers and detoxifiers within the brain. Additionally, through the foot processes, which surround capillaries or extend to the subpial and subependymal zones, they contribute to barrier functions controlling the flow of macromolecules between the blood, the cerebrospinal fluid (CSF), and the brain. In gliosis, the nuclei of astrocytes, which are typically round to oval (10 μm wide) with evenly dispersed, pale chromatin, enlarge, become vesicular, and develop prominent nucleoli. The previously scant cytoplasm expands to a bright pink, somewhat irregular swath around an eccentric nucleus, from which emerge numerous stout, ramifying processes; these cells are called *gemistocytic astrocytes*.

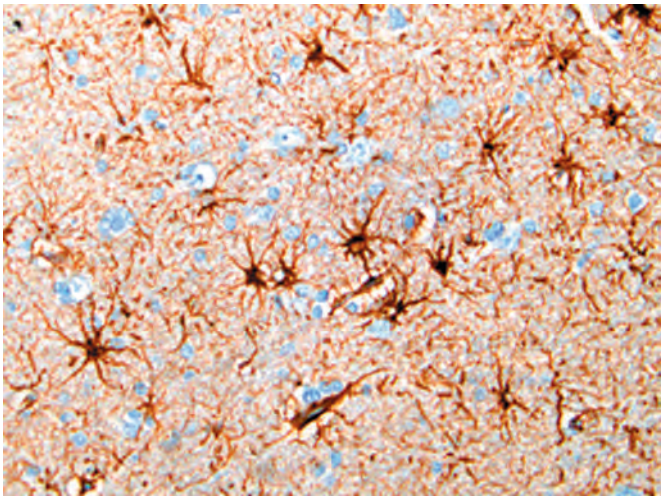

Figure 28-1 Astrocytes and their processes. Immunohistochemical staining for glial fibrillary acidic protein reveals astrocytic perinuclear cytoplasm and well-developed processes *(brown)*.

Acute cell injury, as occurs in hypoxia, hypoglycemia, and toxic injuries, is manifested by cellular swelling, as in other cells (Chapter 2). The *Alzheimer type II astrocyte* (unrelated to Alzheimer disease but first described by the same individual) is a gray matter cell with a large (two to three times normal) nucleus, pale-staining central chromatin, an intranuclear glycogen droplet, and a prominent nuclear membrane and nucleolus. This type of change is mainly seen in individuals with long-standing hyperammonemia due to chronic liver disease, Wilson disease, or hereditary metabolic disorders of the urea cycle.

Other types of cell injury lead to the formation of cytoplasmic inclusion bodies. *Rosenthal fibers* are thick, elongated, brightly eosinophilic, irregular structures that occur within astrocytic processes, and contain two heat-shock proteins (αB-crystallin and hsp27) as well as ubiquitin. Rosenthal fibers are typically found in regions of long-standing gliosis; they are also characteristic of one type of glial tumor, pilocytic astrocytoma. In *Alexander disease*, a leukodystrophy associated with mutations in the gene encoding GFAP, abundant Rosenthal fibers are found in periventricular, perivascular, and subpial locations. More commonly seen are *corpora amylacea*, or polyglucosan bodies. These are round, faintly basophilic, periodic acid-Schiff (PAS)-positive, concentrically lamellated structures of 5 to 50 μm in diameter that are located wherever there are astrocytic end processes, especially in the subpial and perivascular zones. They consist primarily of glycosaminoglycan polymers, as well as heat-shock proteins and ubiquitin. They occur in increasing numbers with advancing age and are thought to represent a degenerative change in the astrocyte. The *Lafora bodies* that are seen in the cytoplasm of neurons (as well as hepatocytes, myocytes, and other cells) in myoclonic epilepsy (Lafora body myoclonus with epilepsy) have a similar structure and biochemical composition.

Reactions of Microglia to Injury

Microglia are mesoderm-derived phagocytic cells that serve as the resident macrophages of the CNS. They share many surface markers with peripheral monocytes/macrophages (e.g., CR3 and CD68). They respond to injury by (1) proliferating; (2) developing elongated nuclei *(rod cells)*, as in neurosyphilis; (3) forming aggregates around small foci of tissue necrosis *(microglial nodules)*; or (4) congregating around cell bodies of dying neurons *(neuronophagia)*. In addition to resident microglia, blood-derived macrophages may also be present in inflammatory foci.

Reactions of Other Glial Cells to Injury

Oligodendrocytes are cells that wrap their cytoplasmic processes around axons and form myelin. Each oligodendrocyte myelinates numerous internodes on multiple axons, in contrast to the myelinating Schwann cell in peripheral nerve, which has a one-to-one correspondence between cells and internodes. Injury or apoptosis of oligodendroglial cells is a feature of acquired demyelinating disorders and leukodystrophies. Oligodendroglial nuclei