



**Figure 27-1** Relationship between lipid bilayers and associated proteins in myelin within internodes. Myelin basic protein (MBP) is an intracellular protein that has a role in myelin compaction. Mutant forms of myelin protein zero (MPZ), peripheral myelin protein 22 (PMP22), and periaxin (PRX) cause some forms of Charcot-Marie-Tooth disease, a hereditary demyelinating neuropathy.

and with their conduction speeds. Thin unmyelinated fibers mediate autonomic functions as well as pain and temperature sensation and have the slowest conduction speeds. Large diameter axons with thick myelin sheaths transmit light touch and motor signals and have fast conduction speeds. In the case of myelinated axons, individual Schwann cells make exactly one myelin sheath that wraps around a single axon to create a myelinated segment called an *internode*. Internodes are separated by unmyelinated gaps referred to as *nodes of Ranvier*, which are uniformly spaced along the length of the axon. A number of specialized proteins are essential for normal assembly and function of myelin within internodes (Fig. 27-1). Unmyelinated axons are also intimately associated with Schwann cells but in a different arrangement in which one cell surrounds segments of multiple axons.

Most peripheral nerves carry out both motor and sensory functions and thus contain axons of varying diameter and myelin thickness. The axons are bundled together by three major connective tissue components: the *epineurium*, which encloses the entire nerve; the *perineurium*, a multilayered concentric connective tissue sheath that groups subsets of axons into fascicles; and the *endoneurium*, which surrounds individual nerve fibers.

## General Types of Peripheral Nerve Injury

### Axonal Neuropathies

**Axons are the primary target of the damage in this large group of peripheral neuropathies (Fig. 27-2).** The morphologic hallmarks of axonal neuropathies can be produced experimentally by cutting a peripheral nerve, which results in a prototypical pattern of injury described as *Wallerian degeneration*. Portions of axons that are distal to the point of transection are disconnected from the central neuron

and degenerate. Within a day of injury, the distal axons begin to fragment and the associated myelin sheaths unravel (Fig. 27-3) and disintegrate into spherical structures (*myelin ovoids*). Macrophages are recruited and they participate in the removal of axonal and myelin debris. Regeneration starts at the site of transection with the formation of a growth cone and the outgrowth of new branches from the stump of the proximal axon. Schwann cells and their associated basement membranes guide the sprouting axons, which grow at about 1 mm per day, toward their distal target. Continuous pruning of the sprouting axons removes misguided branches. The Schwann cells create new myelin sheaths around the regenerating axons, but these myelin internodes tend to be thinner and shorter than in the original ones. The repair process is successful only if the two transected ends remain closely approximated. A failure of the outgrowing axons to find their distal target can produce a “pseudotumor” termed *traumatic neuroma* – a nonneoplastic haphazard whorled proliferation of axonal processes and associated Schwann cells that results in a painful nodule (Fig. 27-4).

The changes observed following experimental nerve transections only partially resemble those seen in various axonal neuropathies. One key difference is that in these disease states (unlike nerve transection) damage occurs over an extended period of time. As a result, degenerating and regenerating axons co-exist in a single biopsy. With time, damage tends to outpace repair, resulting in progressive loss of axons. Consequently, the electrophysiologic hallmark of axonal neuropathies is a reduction in signal strength owing to the dropout of axons from affected peripheral nerves.

### Demyelinating Neuropathies

**In these disorders, Schwann cells with their myelin sheaths are the primary targets of damage (Fig. 27-2),**