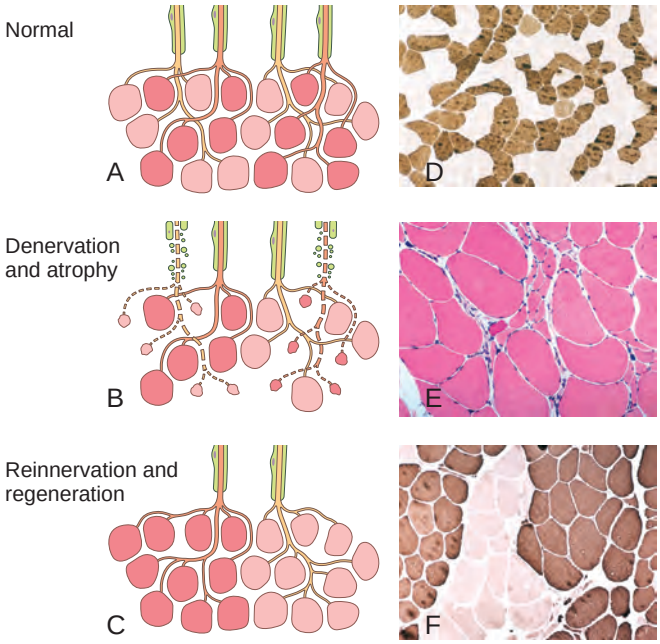

Figure 27-7 **A,** This diagrammatic representation of four normal motor units shows a normal checkerboard type admixture of light and dark stained fibers of opposite type. **B,** Damage to innervating axons leads to loss of trophic input and atrophy of myofibers. **C,** Reinnervation of myofibers can lead to a switch in fiber type and segregation of fibers of like type. As illustrated here, reinnervation is also often associated with an increase in motor unit size, with more myofibers innervated by an individual axon. **D,** Normal muscle has a checkerboard type distribution of type I (light) and type II (dark) fibers on this ATPase reaction (pH9.4) corresponding to findings in **A. E,** Clustered flattened "angulated" atrophic fibers (*group atrophy*) are a typical finding associated with disrupted innervation. **F,** With ongoing denervation and reinnervation, large clusters of fibers appear that all share the same fiber type (*type grouping*).

regeneration. Fusion of activated satellite cells to damaged myofibers is an important step for regeneration. Eventually, new sarcomeres are generated and the continuity of the original myofiber is restored. *Regenerating myofibers* are rich in RNA and therefore blue (basophilic) in hematoxylin and eosin stained sections. They have enlarged nuclei with prominent nucleoli that are often randomly distributed in the cytoplasm, instead of being in their normal subsarcolemmal location. Depending on the nature of the primary insult, atrophic myofibers may also be seen. Regeneration can restore muscle to normal following an acute, transient injury, but in chronic disease states regeneration often fails to keep pace with damage. In this setting, muscles often show endomysial fibrosis (collagen deposition), dropout of myofibers, and fatty replacement.

- *Myofiber hypertrophy* can be seen as a physiologic adaptation to exercise or in association with certain chronic myopathic conditions.
- *Cytoplasmic inclusions* in the form of vacuoles, aggregates of proteins, or clustered organelles are characteristic of several primary forms of myopathy.

Inflammatory Myopathies

Historically, polymyositis, dermatomyositis, and inclusion body myositis have been considered the three main primary inflammatory myopathies; however, inclusion body myositis is an enigmatic condition (discussed later) in which the role of inflammation is uncertain. In contrast, polymyositis and dermatomyositis show typical features of autoimmune inflammatory diseases, including associations with certain autoantibodies, particular HLA-DR genotypes, and other autoimmune disorders. In addition to prototypical presentations, there are overlapping forms and cases that defy precise classification. Other immune-mediated disorders, such as systemic lupus erythematosus, systemic sclerosis, and sarcoidosis (Chapter 6), as well as certain infectious agents (Chapter 8), can also cause myositis and are discussed elsewhere.

Dermatomyositis

Dermatomyositis is a systemic autoimmune disease that typically presents with proximal muscle weakness and skin changes.

Pathogenesis. **Dermatomyositis is an immunologic disease in which damage to small blood vessels contributes to muscle injury.** The vasculopathic changes can be seen as *telangiectasias* (dilated capillary loops) in the nail folds, eyelids, and gums, and as dropout of capillary vessels in skeletal muscle. Biopsies of muscle and skin may show deposition of the complement membrane attack complex (C5b-9) within capillary beds in both tissues. An inflammatory signature enriched for genes that are upregulated by type I interferons is seen in muscle and in leukocytes. The prominence of this signature appears to correlate with disease activity. Various autoantibodies are often detected by serologic studies, and B lymphocytes as well as plasma cells are part of the inflammatory infiltrate that is seen in muscles. Certain autoantibodies tend to be associated with specific clinical features:

- *Anti-Mi2 antibodies* (directed against a helicase implicated in nucleosome remodeling) show a strong association with prominent Gottron papules and heliotrope rash (described later).
- *Anti-Jo1 antibodies* (directed against the enzyme histidyl t-RNA synthetase) are associated with interstitial lung disease, nonerosive arthritis, and a skin rash described as "mechanic's hands."
- *Anti-P155/P140 antibodies* (directed against several transcriptional regulators) are associated with paraneoplastic and juvenile cases of dermatomyositis.

A direct link between these autoantibodies and disease pathogenesis has not yet been established.

MORPHOLOGY

Muscle biopsies of affected patients show infiltrates of mononuclear inflammatory cells that tend to be most pronounced in the perimysial connective tissue and around blood vessels. Sometimes there is a distinctive pattern in which myofiber atrophy is accentuated at the edges of the fascicles—**perifascicular atrophy** (Fig. 27-8*B*). Segmental fiber necrosis and regeneration may also be seen. Immunohistochemical