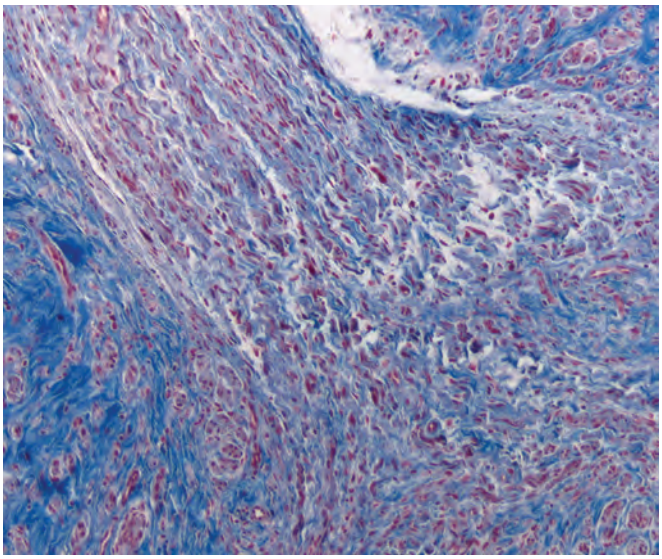

Figure 27-4 Trichrome-stained section of a traumatic neuroma showing the transition from normal nerve containing a parallel arrangement of axons (*upper left corner*) to a haphazard swirl of red stained axons associated with admixture of Schwann cells and blue-staining connective tissue.

whereas axons are relatively preserved. This definition is similar to that of demyelinating diseases that affect the central nervous system (Chapter 28). Individual myelin sheaths degenerate in a seemingly random pattern, resulting in discontinuous damage of myelin segments. In response to this damage, Schwann cells or Schwann cell precursors proliferate and initiate repair through the formation of new myelin sheaths, but these again tend to be shorter and thinner than the original ones. The electrophysiologic hallmark of these disorders is slowed nerve conduction velocity, reflective of the loss of myelin.

Neuronopathies

Neuronopathies result from destruction of neurons, leading to secondary degeneration of axonal processes. Infections like herpes zoster and toxins like platinum compounds are examples of insults that may lead to neuronopathies. Because the damage is at the level of the neuronal cell body, peripheral nerve dysfunction caused by neuronopathies is equally likely to affect proximal and distal parts of the body (unlike peripheral axonopathies which preferentially affect the distal extremities).

Anatomic Patterns of Peripheral Neuropathies

Peripheral neuropathies can be separated into several groups according to the anatomic distribution of involvement and the associated neurological deficits. This approach can be helpful clinically, since each pattern has a different set of potential underlying causes. These anatomic patterns of injury are as follows:

- *Mononeuropathies* affect a single nerve and result in deficits in a restricted distribution dictated by normal anatomy. Trauma, entrapment, and infections are common causes of mononeuropathy.
- *Polyneuropathies* are characterized by involvement of multiple nerves, usually in a symmetric fashion. In most cases axons are affected in a length dependent fashion leading to deficits that start in the feet and ascend with disease progression. The hands often start to show involvement by the time deficits extend to the level of the knee, resulting in a characteristic "stocking and glove" distribution of sensory deficits.
- *Mononeuritis multiplex* describes a disease process that damages several nerves in a haphazard fashion. An affected patient might have a right wrist drop from involvement of the right radial nerve and a left foot drop from peroneal nerve damage. Vasculitis is a common cause of this pattern of injury.
- *Polyradiculoneuropathies* affect nerve roots as well as peripheral nerves, leading to diffuse symmetric symptoms in proximal and distal parts of the body.

Specific Peripheral Neuropathies

Many different types of disease processes can damage peripheral nerves, including inflammatory diseases, infections, metabolic changes, toxic injury, trauma, (para)neoplastic disease, and inherited gene defects.

Inflammatory Neuropathies

Guillain-Barré Syndrome (Acute Inflammatory Demyelinating Polyneuropathy)

Guillain-Barré syndrome is a demyelinating peripheral neuropathy that may lead to life-threatening respiratory paralysis. The overall annual incidence is approximately one case per 100,000 persons. The disease is characterized clinically by weakness beginning in the distal limbs that rapidly advances to affect proximal muscle function ("ascending paralysis"). Histologic features are inflammation and demyelination of spinal nerve roots and peripheral nerves (radiculoneuropathy).

Pathogenesis. **In most cases, Guillain-Barré syndrome is thought to be an acute-onset *immune-mediated demyelinating neuropathy*.** Approximately two thirds of cases are preceded by an acute, influenza-like illness from which the affected individual has recovered by the time the neuropathy becomes symptomatic. Infections with *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr virus, and *Mycoplasma pneumoniae*, or prior vaccination, have significant epidemiologic associations with Guillain-Barré syndrome. No infectious agent has been demonstrated in affected nerves, and an immunologic reaction is favored as the underlying cause. A similar inflammatory disease of peripheral nerves can be reproduced in experimental animals by immunization with a peripheral nerve myelin protein. A T-cell–mediated immune response ensues, accompanied by segmental demyelination induced by activated macrophages. Transfer of these T cells to a naive animal results in comparable lesions. Moreover, lymphocytes from individuals with Guillain-Barré syndrome have been shown to produce demyelination in tissue cultures of myelinated nerve fibers. Circulating antibodies that cross-react with components of peripheral nerves may also play a role.