further lower the seizure threshold and are associated with more seizures in people with epilepsy (Table 118-1).

Seizures can occur at any time. Ten percent of the population in developed countries has a seizure at some time during their life. In contrast, 0.7% to 1% has current epilepsy (prevalence) and 3% to 4% has epilepsy at some time during their life (lifetime prevalence). In the United States, there are approximately 125,000 new cases of epilepsy diagnosed each year (incidence). The incidence and prevalence are biphasic, with epilepsy being more common in childhood (primarily because of perinatal injury, infections, and genetic factors) and in old age (because of stroke, tumors, and dementia) (Fig. 118-1). In developing countries the frequency of epilepsy is higher because of factors such as increased brain infections with organisms such as cysticercosis.

PATHOLOGY

Prior to the 1990s, the underlying cause was not determined in most people with epilepsy. The advent of MRI and, more recently, genetic analysis has substantially improved our ability to identify the cause of many types of epilepsy. About 70% of adults and 40% of children with new-onset epilepsy have partial (focal) seizures implying a cerebral injury or lesion. The most common lesions are hippocampal sclerosis, neuronal and glial tumors, vascular malformations, neuronal migration disorders (e.g., cortical dysplasia), hamartomas, encephalitis, autoimmunity, cerebral trauma, embolic stroke, and hemorrhage. Hippocampal sclerosis (sometimes referred to as mesial temporal sclerosis) is particularly common and can occur in isolation or secondary to another epileptogenic lesion (dual pathology). It consists of loss of pyramidal cells and gliosis in several hippocampal subfields. Hippocampal sclerosis is associated with temporal lobe epilepsy and short-term memory dysfunction. Not all patients with cerebral lesions develop epilepsy; how or why a particular lesion becomes epileptogenic is poorly understood.

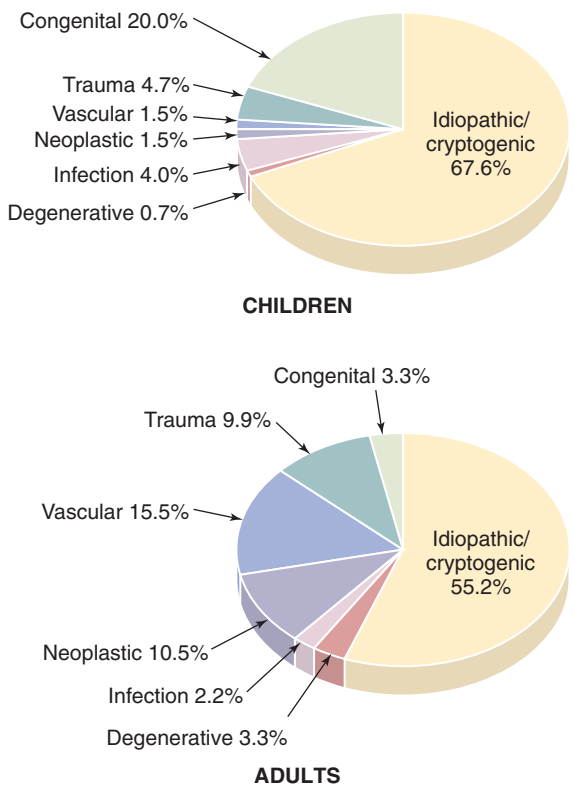

FIGURE 118-1 Etiology of epilepsy, according to age, in all newly diagnosed cases in Rochester, Minnesota, 1935–1984. (Modified from Hauser WA, Annegers JF, Kurland LT: Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984, Epilepsia 34:453–468, 1993.)

Hereditary influences have long been associated with epilepsy. During the past several decades, a number of gene mutations have been associated with specific epilepsy syndromes, both focal and generalized. Many of the mutations occur in ion channels, which, not surprisingly, lead to neuronal dysfunction and epilepsy. Two important phenotypic examples of channelopathies are genetic (generalized) epilepsy with febrile seizures plus (GEFS+) and Dravet syndrome (also known as severe myoclonic epilepsy of infancy). GEFS+ is typically associated with a partial loss of function mutation in the voltage-gated sodium channel gene, *SCN1A*, whereas a complete loss of function mutation in the same gene results in Dravet syndrome. Less commonly, mutations in other ion channel genes can lead to the same phenotypic expressions. GEFS+ can begin at any age, although is usually evident in childhood, with various seizure types in different affected family members; some may have febrile seizures after age 6 years (febrile seizures plus), whereas others may have myoclonic, absence, or partial seizures. In contrast, Dravet syndrome typically presents at 6 to 8 months of age with prolonged hemiclonic seizures associated with an intercurrent fever. Adults with Dravet syndrome are typically mentally retarded with spasticity or ataxia, gait dysfunction, and occasion nocturnal clonic seizures as well as other seizure types. Recognition of Dravet syndrome is important because certain antiepileptic drugs (AEDs) can cause permanent clinical deterioration (e.g., lamotrigine, phenytoin), whereas others are particularly beneficial (e.g., topiramate, levetiracetam, valproate, benzodiazepines).

CLINICAL PRESENTATION

Classification and Clinical Manifestations

Seizures are classified by their clinical symptoms and signs. The manifestations of a seizure depend on whether its onset includes most or only a part of the cerebral cortex, on the functions of the involved cortical areas, and on the subsequent pattern of spread within the brain. Seizures are of two broad types: those with onset limited to a specific region of cerebral cortex *(partial or focal seizures)* and those with onset that involves the cerebral cortex diffusely *(generalized seizures)*. Seizures are dynamic with an evolving electrical discharge. Thus, highly focal *(simple partial)* seizures can progress into more widespread *(complex partial)* seizures and partial seizures can evolve into secondarily generalized tonic-clonic seizures.

In an individual, seizures are typically stereotyped, although a person can have more than one seizure type and a specific seizure type can have varying intensities. The behaviors that occur during the seizure are termed the *seizure semiology*. The seizure itself is referred to as the ictus and the period of time during which the seizure occurs is termed the *ictal phase*. The time after the seizure, until the patient is fully recovered, is the *postictal phase* and the