traction or surgery may be required to relieve pressure and repair tissues. Glucocorticoids such as methylprednisolone may be administered to reduce edema and stabilize the vascular system. Other injuries require prompt treatment to minimize secondary damage caused by decreased oxygen or circulation.

Ongoing care is necessary to prevent the complications related to immobility. The leading cause of death now is pneumonia, rather than renal failure. Early, extensive rehabilitation is required to learn the best ways to use the remaining function, prevent complications, and maximize independence. A team of rehabilitation professionals including occupational therapists, physiotherapists, respiratory therapists (for lesions at C4 and above), and psychotherapists can assist the patient with performance of the activities of daily living, ventilation, and other body needs. Advances in technology have provided myriad assistive devices, which can be tailored to the patient's individual needs.

With improved treatment and rehabilitation, persons with SCI are living much longer, adding the complications of aging to those of SCI. These include skin breakdown, respiratory problems, digestive and urinary tract complications, and musculoskeletal problems such as carpal tunnel syndrome and torn rotator cuff.

THINK ABOUT 14-13

a. Compare the immediate and permanent effects on motor function of a lumbar spinal cord injury.
b. Explain why micturition may not occur immediately after an injury (urinary retention), but urinary incontinence may develop later.
c. Explain several reasons why a cervical injury is much more serious than a lumbar injury.
d. Explain the cause of spinal shock and its effects.

Congenital Neurologic Disorders

Down syndrome is discussed in Chapter 21.

Hydrocephalus

Pathophysiology

Hydrocephalus is a condition in which excess cerebrospinal fluid (CSF) accumulates within the skull, compressing the brain tissue and blood vessels. The condition is sometimes called "water on the brain." Because the cranial sutures have not yet closed, the infant's head enlarges beyond the normal size as the amount of fluid increases. Excess CSF accumulates because more is produced than is absorbed, often because of obstruction to the flow at some point. In the majority of cases, production of CSF is normal, but there is a reduction in the amount reabsorbed. Most cases are apparent shortly after birth, but some may not be diagnosed until later in childhood.

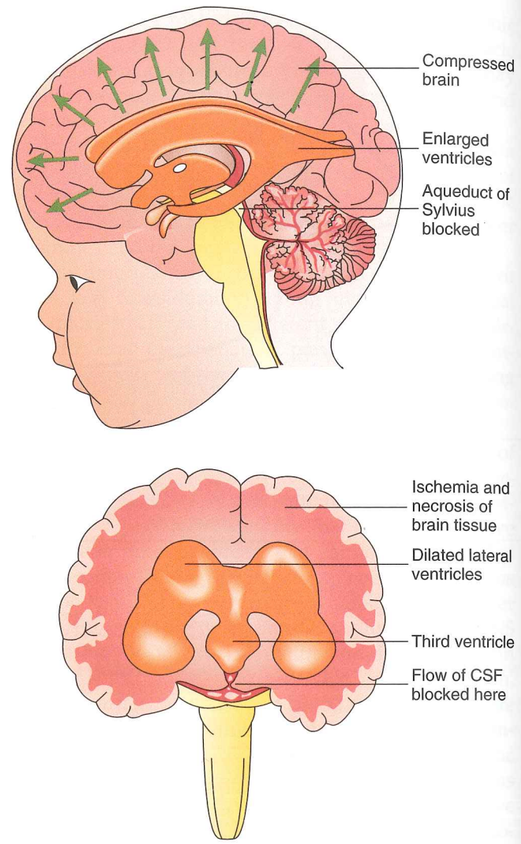

FIGURE 14-25 Hydrocephalus.

There are two types of hydrocephalus. *Noncommunicating* or *obstructive hydrocephalus* occurs in babies when the flow of CSF through the ventricular system is blocked, usually at the aqueduct of Sylvius or the foramen magnum (Fig. 14-25). This condition usually results from a fetal developmental abnormality, such as stenosis or a neural tube defect. In many neonates, an associated myelomeningocele or Arnold-Chiari malformation is present. The obstruction leads to increased back pressure of fluid in the ventricles of the brain, which gradually dilates or enlarges the ventricles and compresses the blood vessels and brain tissue.

In the second type, *communicating hydrocephalus*, the absorption of CSF through the subarachnoid villi is impaired, resulting in increased pressure of CSF in the system. In neonates, the skull can expand to some degree in the early stages of hydrocephalus to relieve the pressure, but if the condition is not treated quickly, the brain tissue is permanently damaged.

In older children and adults, intracranial pressure (ICP) increases more rapidly than in neonates, because the fused sutures of the skull prevent expansion to accommodate the increased volume of CSF. The amount of brain damage that results depends on the rate at which pressure increases and the time that elapses before relief occurs. Other factors that increase the risk of damage may also be present in a particular patient. Brain damage may result in major physical disability and intellectual impairment because all areas of the brain are affected.

Etiology

Developmental abnormalities are the most frequent cause of hydrocephalus, particularly stenosis or **atresia** (the absence of a canal or opening) at the connecting channels between the ventricles or a thickened arachnoid membrane.

Obstruction may also develop at any age from tumors, infection, or scar tissue. Meningitis can cause obstructive hydrocephalus during the acute infection or lead to fibrosis in the meninges, impairing absorption.

Signs and Symptoms

The signs of increasing CSF depend on the age of the patient. In the *neonate* or young *infant*, in whom the sutures have not yet closed, the head can enlarge and the fontanels bulge in the early stages of hydrocephalus. Recording head size is a standard procedure after birth and often is done during routine examinations. With the currently brief periods of hospitalization after childbirth, this measurement may not be taken, but it can provide a basic reference point if a problem is suspected.

In the patient with hydrocephalus, scalp veins appear dilated and the eyes show the "sunset sign," in which the white sclera is visible above the colored pupil. Pupil response to light is sluggish. The infant is lethargic but irritable and difficult to feed. A high-pitched or shrill cry often occurs when the infant is moved or picked up. The condition must be diagnosed and treated as soon as possible to minimize brain damage. In older children and adults, the head cannot enlarge and the classical signs of increased ICP develop as the volume of CSF expands. These may include decreased memory, difficulty in coordination, and impaired balance. Often urinary incontinence is present. Depending on the underlying cause, other manifestations may be present.

Diagnostic Tests

A computed tomography (CT) or magnetic resonance imaging (MRI) scan can locate the obstruction or abnormal flow and determine the size of the ventricles.

Treatment

Surgery is usually performed to remove an obstruction or provide a shunt for CSF from the ventricle into the peritoneal cavity or other extracranial site, such as the right atrium of the heart. A shunt must be replaced as the child grows. Shunts are vulnerable to blockage or infection and thus require continued close monitoring to prevent further brain damage.

THINK ABOUT 14-14

a. Differentiate between communicating and noncommunicating hydrocephalus.
b. Explain the effects of ventricular dilation.
c. Explain why there are no focal signs of hydrocephalus in neonates.

Spina Bifida

Spina bifida refers to a group of neural tube defects that are congenital anomalies of varying severity. They are a common developmental defect, myelomeningocele occurring in an estimated 1500 to 2000 of the 4 million live births per year in the United States. The incidence rate varies in different countries, with the incidence in Canada being slightly higher than that in the United States.

Pathophysiology

The neural tube develops during the fourth week of gestation, beginning in the cervical area and progressing toward the lumbar area. The basic problem in spina bifida is failure of the posterior spinous processes on the vertebrae to fuse, which may permit the meninges and spinal cord to herniate, resulting in neurologic impairment. Any number of vertebrae can be involved, and the lumbar area is the most common location.

Three types of spina bifida are common (Fig. 14-26*A*):

- *Spina bifida occulta* develops when the spinous processes do not fuse, but herniation of the spinal cord and meninges does not occur. The defect may not be visible, although often a dimple or a tuft of hair is present on the skin over the site. The defect may be diagnosed by means of routine x-ray examination or when mild neurologic signs manifest owing to tension on the cord during a growth period.
- *Meningocele* is the same bony defect, but herniation of the meninges occurs through the defect, and the meninges and CSF form a sac on the surface. **Transillumination** confirms the absence of nerve tissue in the sac. Neurologic impairment is usually not present, although infection or rupture of the sac may lead to neurologic damage.
- *Myelomeningocele* is the most serious form of spina bifida. Herniation of the spinal cord and nerves along with the meninges and CSF occurs, resulting in considerable neurologic impairment (see Fig. 14-26*C*). The location and extent of the herniation determine how much function is lost. This defect is often seen in conjunction with hydrocephalus.

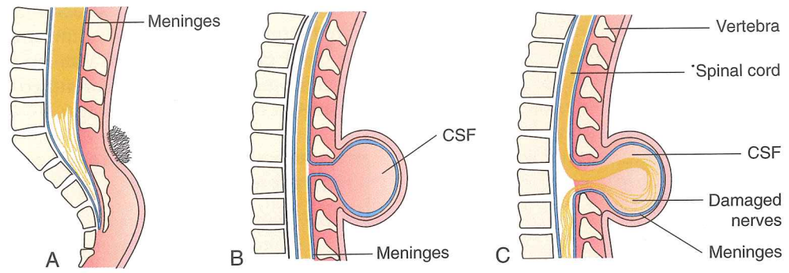

FIGURE 14-26 Spina bifida.

Diagnostic Tests

Alpha-fetoprotein (AFP) that has leaked from the defect results in an elevated level in maternal blood in a specimen obtained at 16 to 18 weeks' gestation. Amniocentesis detects the presence of AFP that has leaked into the amniotic fluid surrounding the fetus. The presence of spina bifida can be diagnosed prenatally by ultrasound.

Etiology

Spina bifida appears to have a multifactorial basis, with a combination of genetic and environmental factors contributing to its development. There is a high familial incidence of spina bifida and associated defects, such as **anencephaly** (absence of the cerebral hemispheres and superior cranial vault).

Environmental factors include exposure to radiation, gestational diabetes, and deficits of vitamin A or folic acid. Folic acid supplements are recommended before conception and for the first 6 weeks of pregnancy as a preventive measure. Research has shown that such supplementation reduces the incidence rate of the disorder.

Signs and Symptoms

Meningocele and myelomeningocele are visible as a protruding sac over the spine. In myelomeningocele, the extent of the neurologic deficit depends on the level of the defect (see Fig. 14-4) and the status of the nerve tissue; sensory and motor function at and below the level of the herniation is impaired. Some degree of muscle weakness or paralysis is present. Bladder and bowel control is usually impaired. Depending on the level of damage and the availability of reflex and sphincter control, there may be fecal and urinary incontinence.

Treatment

Some surgical repair of spina bifida has been done successfully in utero before birth.

Controversy continues about the timing of the surgical repair of the sac if done postnatally—whether it should take place immediately or be delayed. Rupture and infection are potential complications when repair is delayed. The decision regarding surgery also depends on the presence of other **anomalies** (abnormal structures) that may be present in the infant. After repair, ongoing assistance and occupational and physical therapy are required to manage the neurologic deficits. Local community services and the Spina Bifida Association, which has many local chapters, provide continuing support for the parents and the child.

Cerebral Palsy

Cerebral palsy (CP) is a group of disorders marked by some degree of motor impairment, caused by genetic mutations, abnormal fetal formation of functional brain areas, infection, or brain damage in the perinatal period. In addition, damage usually occurs in other areas of the brain, resulting in a clinical presentation that is highly variable, depending on the specific areas affected and the severity of the trauma. The damage may occur before, during, or shortly after birth and is nonprogressive. It is estimated that there are about 500,000 individuals with CP in the United States, with approximately 10,000 children developing CP each year. With improved treatment, rehabilitation, and education, many individuals with CP live into adulthood.

Pathophysiology

Pathologically, the brain tissue is altered by malformation, mechanical trauma, hypoxia, hemorrhage, hypoglycemia, hyperbilirubinemia, infection, or some other factor, resulting in necrosis. In some cases, generalized necrosis and atrophy of brain tissue have occurred, whereas in other cases only one or two localized areas of the brain are affected. Although all children have some degree of altered mobility, which provides the basis for classifying cerebral palsy, an assortment of other problems is present in individual cases.

Etiology

Single or multiple factors may be implicated in the development of cerebral palsy. Hypoxia or ischemia is the major cause of brain damage; it may occur prenatally, perinatally, or postnatally. Hypoxia may be caused by placental complications or a difficult delivery or by vascular occlusion, hemorrhage, aspiration, or respiratory impairment in the premature infant. High bilirubin levels, resulting from problems such as prematurity or Rh blood incompatibility may cause *kernicterus*, in which accumulated bilirubin crosses the blood-brain barrier and damages the neurons. Other causes of cerebral palsy include infection or metabolic abnormalities, such as hypoglycemia, in either the mother or the child.

Signs and Symptoms

In some cases the effects are evident at birth, whereas in others the delay in motor development or abnormal muscle tone does not become apparent for several months. Persistence of early reflexes, such as the Moro reflex, may indicate cerebral palsy.

Cerebral palsy is classified either on the basis of area affected (e.g., quadriplegia or diplegia) or on the basis of the motor disability that results (Table 14-9). Three major groups of motor disability have been identified:

- The first and largest group includes those with *spastic paralysis*, which results from damage to the pyramidal tracts (diplegia) or the motor cortex (hemiparesis), or from general cortical damage (quadriparesis). As the name indicates, this form is characterized by **hyperreflexia** (excessive reflex response). For example, crossed legs are apparent when the child is held up or a child with some mobility walks with a typical scissors gait (i.e., on the toes and with crossed legs).
- The second group is *dyskinetic* disease, which results from damage to the extrapyramidal tract, basal nuclei, or cranial nerves. This form of cerebral palsy is manifested by **athetoid** or **choreiform** involuntary movements and loss of coordination with fine movements.
- The third group, *ataxic* cerebral palsy, commonly develops from damage to the cerebellum and manifests as loss of balance and coordination.
- Spasticity is manifested by increased muscle tone or resistance to passive movement, with excessive reflex responses. Unilateral use of the hands or feet and asymmetric body movements are indications of abnormality. Writhing movements or facial grimaces may indicate athetoid cerebral palsy. Feeding difficulties and constant tongue thrusting are signs of motor dysfunction and may interfere with nutrition and growth. The position of the child's limbs when resting or when held up is often unusual (e.g., scissors position of the legs).

TABLE 14-9 Cerebral Palsy

Type	Percentage of Cases	Area of Damage	Effects
Spastic	65%-75%	Motor cortex or pyramidal tracts	Paralysis Hyperreflexia and increased muscle tone
Dyskinetic	20%-25%	Basal nuclei or extrapyramidal tracts	Loss of motor control and coordination Athetoid or choreiform movements
Ataxic	5%	Cerebellum	Gait disturbance Loss of balance
Mixed	13%	All of above	Some of each of above

In addition to the motor deficit, cerebral palsy may be accompanied by many other problems, which depend on the other areas of brain damage. A few common areas of dysfunction are:

- Intellectual function
- Communication and speech
- Seizures
- Visual problems

With regard to cognitive function, one third of persons with cerebral palsy are considered to have normal intelligence, one third are mildly impaired, and one third are severely cognitively disabled.

Communication and speech development are difficult because of motor disability, possible impaired mentation, and visual or hearing deficits. A number of children have learning disabilities and behavioral problems, such as attention deficit disorder, spatial disorientation, and hyperactivity.

Seizures, primarily of the generalized tonic-clonic type, are common. Visual problems, such as astigmatism and strabismus, occur frequently.

Treatment

Because each infant has a unique set of problems, individualized and immediate therapy is necessary. Early stimulation programs with a team of health professionals are helpful in encouraging motor skills, coordination, and intellectual development. Assessment and therapy by speech and language pathologists can assist parents in dealing with feeding and swallowing problems, positioning the child correctly, reducing the effects of tongue thrusting, and encouraging communication.

Physical therapy is essential to maximize physical development. Regular exercise therapy and use of devices such as braces can improve mobility and reduce deformities. A program called MEDEK (CME) is a therapeutic exercise program offered by trained professionals to some infants and young children with developmental problems involving skeletal muscle, particularly hypotonia. This is a strenuous program of repetitive exercises designed to promote strength, mobility, and

independence. No devices or machines are used. The program may be offered in private clinics or combined with traditional therapies, which are required for older children. Family members can be trained to provide regular exercise and thus reduce the incidence of complications.

Occupational therapy works with the child to maximize hand function, teach the use of adaptive devices, and facilitate the development of skills associated with normal development and academic work, as well as providing adaptive devices to maximize mobility and independence.

Specialists in early education for developmentally handicapped children can work with the child and the family to develop and maximize motor skills, eye-hand coordination, and reflex responses. As the child develops, simple exercises can be instituted to help in learning to recognize familiar objects or sounds, associating cause with effect, and identifying likes and dislikes. Appropriate medication to control seizures prevents complications.

Hearing and vision require monitoring in the early stages, and some form of communication must be developed as soon as possible. Many new devices and techniques are now available to promote communication. Technologic advances, including computers, provide aids for many different problems and enable many individuals to live more independently and develop individual interests and skills. In many areas, children with cerebral palsy are being integrated into mainstream classes in schools and other activities.

THINK ABOUT 14-15

a. Compare Down syndrome (see Chapter 21) and cerebral palsy with regard to cause and effects on motor and cognitive abilities.
b. Describe the factors that could interfere with communication in a child with cerebral palsy.
c. Discuss how technology may provide accommodation for communication deficits.

Seizure Disorders

Seizures result from uncontrolled, excessive discharge of neurons in the brain. The activity may be localized or generalized. They have many possible causes. Seizure disorders are characterized by recurrent seizures, sometimes called convulsions. It is estimated that 3 to 6 million affected individuals exist in the United States. The onset occurs before age 20 in 75% of cases. *Epilepsy* is the old term for recurrent seizures, rarely used today because of the stigma once attached to the term.

Seizure disorders are classified by their location in the brain and their clinical features, including characteristic EEG patterns during and between seizures. The international classification of seizures is summarized in Box 14-1, a commonly accepted classification that incorporates current terminology and divides seizures into two basic categories, generalized and partial.

BOX 14-1 Classification of Seizures

I. Partial seizures (focal)
  a. Simple
    1. Motor (includes jacksonian)
    2. Sensory (e.g., visual, auditory)
    3. Autonomic
    4. Psychic
  b. Complex (impaired consciousness)
    1. Temporal lobe or psychomotor
  c. Partial leading to generalized seizures
II. Generalized (both hemispheres affected with loss of consciousness)
  a. Tonic-clonic (grand mal)
  b. Absence (petit mal)
  c. Myoclonic
  d. Infantile spasms
  e. Atonic (akinetic)
  f. Lennox-Gastaut syndrome (febrile seizures)
III. Unclassified

Generalized seizures have multiple foci or origins in the deep structures of both cerebral hemispheres and the brain stem and cause loss of consciousness, whereas *partial seizures* have a single or focal origin, often in the cerebral cortex, and may or may not involve altered consciousness. However, partial seizures may progress to generalized seizures.

Seizures may be primary (idiopathic) or secondary (acquired) with an identified cause, such as posttraumatic syndrome. Seizures can be categorized on other grounds because they may result from an abnormality in the brain or from systemic causes, such as hypoglycemia or withdrawal from certain drugs. They may be a temporary problem, such as febrile seizures in an infant, or they may be chronic and frequent. An individual can have more than one type of seizure. For example, absence seizures, which are common in children, may decrease or be replaced by tonic-clonic or psychomotor seizures. Common types of seizures are described in the section on signs and symptoms.

Pathophysiology

A seizure results from a sudden, spontaneous, uncontrolled depolarization of neurons, which causes abnormal motor or sensory activity and possibly loss of consciousness. The neurons in the epileptogenic focus are hyperexcitable and have a lowered threshold for stimulation. Any physiologic change, such as alkalosis or other sensory stimulus—for example, flashing lights—can easily activate the "irritable" neurons. These focal cells stimulate the surrounding normal cells, spreading the activity. There are various theories about the specific mechanism for seizure activity, including altered permeability of the neuronal membrane, reduced inhibitory control of neurons, or a transmitter imbalance.

Each seizure lasts for a few seconds or minutes, and the excessive activity of the neurons then ceases *spontaneously*. The altered pattern of electrical activity, or brain waves, during a seizure can be demonstrated on an EEG, indicating the type of seizure and its focus. Also, observation and description of the seizure by bystanders, particularly its initial effects, is useful in identifying the origin or focus of the seizure.

Complications may arise from generalized tonic-clonic (grand mal) seizures that are severe and frequent. Injuries may occur during a seizure.

Recurrent or continuous seizures without recovery of consciousness are termed *status epilepticus*. This condition may lead to serious consequences if it is not treated promptly. Respiration is impaired during a generalized tonic-clonic seizure and skeletal muscle activity is intense; the combination of these events in status epilepticus can lead to severe hypoxia, hypoglycemia, acidosis, and decreased blood pressure, potentially resulting in brain damage.

Etiology

Many seizure disorders are idiopathic. To date, four genes have been identified as having a role in seizure disorders. Familial incidence is more evident in young children.

Children with congenital disorders, such as cerebral palsy, may have seizures resulting from the brain damage. Acquired seizures that occur after head injury or infection are more common now because improved treatment of these primary conditions has led to a higher survival rate. A seizure may be initiated by a tumor, infection, or hemorrhage in the brain, or by a high fever in an infant or young child (febrile seizure). Some systemic disorders, such as renal failure or hypoglycemia, may precipitate a seizure in an individual who has no previous history of seizures. Sudden withdrawal from sedatives or alcohol can precipitate seizures as well as drugs such as cocaine.

Precipitating factors, or triggers, of an individual seizure may include physical stimuli, such as loud noises or bright lights, or biochemical stimuli, such as stress, excessive premenstrual fluid retention, hypoglycemia, change in medication, or hyperventilation (alkalosis). Awareness and avoidance of the potential precipitating factors in an individual can reduce the frequency of seizures. The medical history should be updated frequently to note changes in precipitating factors and the type of seizure.

Signs and Symptoms

Generalized Seizures.

Absence (petit mal) seizures are generalized seizures that are more common in children than adults, beginning about age 5. The seizure lasts for 5 to 10 seconds and may occur many times during the day. There is a brief loss of awareness and sometimes transient facial movements, such as twitches of the eyelids or lip smacking. Usually the child simply stares into space for a moment and then resumes the activity previously pursued. No memory of the episode is retained.

Tonic-clonic (grand mal) seizures are generalized seizures that may occur spontaneously or after simple seizures. There is a pattern for this type of seizure, which usually ends spontaneously:

- **Prodromal** signs occur in some individuals, such as nausea, irritability, depression, or muscle twitching some hours before the seizure.
- An **aura**, such as a peculiar visual or auditory sensation, immediately precedes the loss of consciousness in many persons.
- Loss of consciousness occurs, and the individual falls to the floor.
- Strong **tonic** muscle contraction, resulting briefly in flexion, is followed by extension of the limbs and rigidity in the trunk (ictal phase).
- A cry escapes as the abdominal and thoracic muscles contract, forcing air out of the lungs. The jaws are clenched tightly, and respiration ceases.
- The **clonic** stage follows, in which the muscles alternately contract and relax, resulting in a series of forceful jerky movements that involve the entire body. Increased salivation (foaming at the mouth) and bowel and bladder incontinence may occur.
- Contractions gradually subside spontaneously in several minutes; the body is limp and consciousness slowly returns.
- The person is confused and fatigued, with aching muscles, and falls into a deep sleep in this **postictal** period.

EMERGENCY TREATMENT FOR SEIZURES

1. If possible, clear a space and gently place the person on the floor, positioning him or her on the side, cushioning the head, and loosening neckwear.
2. Move potentially harmful objects away from the patient.
3. Do not force a specific position or unduly restrain the person, which can cause injury.
4. Do not put anything in the person's mouth.
5. When the seizure ends, offer reassurance and check breathing and patient orientation to surroundings.
6. If the seizure continues or immediately repeats, seek medical assistance.

The prodromal indications and occasionally the aura may be remembered by the person but not the entire seizure (amnesia). Hypoxia is common at this time because of interference with respiration during the seizure and because some airway obstruction may be

present, owing to excess saliva or tongue position. Also, the contracting muscles present an increased demand for oxygen during the seizure. Increased levels of lactic acid and carbon dioxide in the body fluids contribute to acidosis. Recurrent tonic-clonic seizures without full return to consciousness are termed *status epilepticus* and carry an increased risk of complications.

■ *Partial Seizures.* Simple partial or focal seizures arise from an epileptogenic focus, often related to a single area of damage in the cortex. They are manifested by repeated motor activity, such as jerking or turning the head or eye aside, jerky movements of a leg, or by a sensation such as tingling that begins in one area and may spread. Auditory or visual experiences, such as ringing in the ears or a sensation of light, may occur if the focus is in the related area. Memory and consciousness remain, although awareness is reduced. A *jacksonian seizure* is a focal motor seizure in which the clonic contractions begin in a specific area and spread progressively; for example, the contractions "march" up the arm and then to the face.

Children and adults may have complex partial, temporal lobe, or psychomotor seizures. They usually arise from the temporal lobe, but may involve the limbic system or frontal lobe. Sometimes an aura is present, such as the perception of an odd odor. The seizure itself consists of bizarre behavior, perhaps repetitive and purposeful but *inappropriate*; for example, waving or clapping the hands. Frequently visual or auditory hallucinations or feelings of déjà vu (perceiving strange surroundings as familiar) occur. The person is unresponsive to people or activities during the seizure, and afterward he or she is amnesic and drowsy.

Diagnostic Tests

A detailed medical history and description of the seizure is required. An EEG will determine the type and location of the seizure. An MRI can detect any structural abnormality in the brain.

Treatment

Any primary cause should be treated, and the specific factors that precipitate seizures should be identified and avoided.

Anticonvulsant drugs, such as phenytoin (Dilantin), are prescribed to raise the threshold for neuronal stimulation and prevent seizures. A choice of anticonvulsant drugs is available to treat different types of seizures and for optimum control in an individual patient. In many cases, anticonvulsant drugs are combined with sedatives, such as phenobarbital, to allow a reduction in the dosage and side effects of the drugs, while simultaneously decreasing the occurrence of seizures. Phenobarbital increases liver enzyme activity, and therefore may affect the dosage of other medications. Phenytoin may cause gingival hyperplasia (Fig. 14-27), which can cause

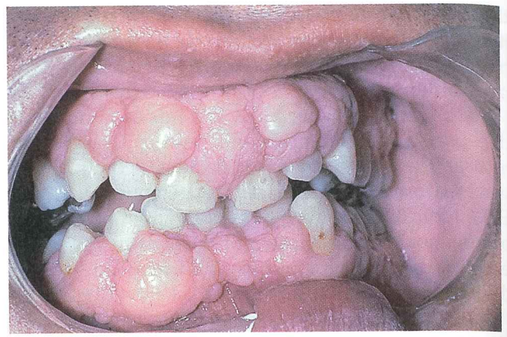

FIGURE 14-27 An example of gingival hyperplasia associated with the medication phenytoin (Dilantin) used to treat seizures. Compare with normal gingiva in Figure 20-7*A*. *(Courtesy of Evie Jesin, RRDH, BSe, George Brown College of Applied Arts and Technology, Toronto, Ontario, Canada.)*

difficulty in maintaining good oral hygiene and create a cosmetic problem for the patient. Many anticonvulsant drugs reduce leukocyte counts, thus predisposing the patient to infection. Several drugs reduce blood-clotting capability. It is essential to continue medication as prescribed at set intervals and without omissions, because sudden withdrawal can cause more severe seizures or status epilepticus, with its risk of brain damage.

Once a seizure begins it cannot be stopped. Single episodes require no additional medical treatment unless the individual continues to be disoriented. Prolonged or recurrent seizures (status epilepticus) are life threatening and require hospital treatment with medications such as intravenous diazepam, oxygen, and fluids.

During pregnancy, some women have an increased number of seizures. There is an increase in the incidence of congenital abnormalities in children born to mothers with seizure disorders; this is probably related to drug therapy.

THINK ABOUT 14-16

a. Describe how a seizure develops in the brain tissue.
b. Differentiate a partial seizure from a general seizure and give an example of each.
c. Describe factors that should be avoided if a patient has a history of seizures.
d. List the sequence of events in a generalized tonic-clonic seizure.

Chronic Degenerative Disorders

Multiple Sclerosis

Multiple sclerosis (MS) involves a progressive demyelination of the neurons of the brain, spinal cord, and

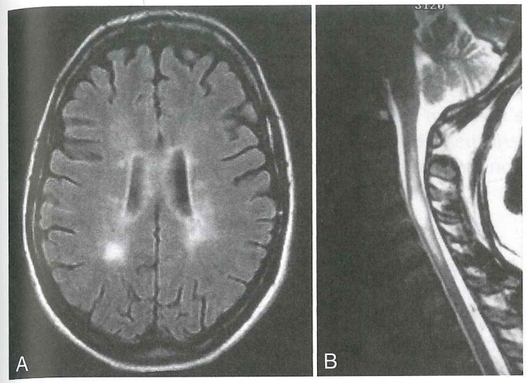

FIGURE 14-28 **A**, Typical white matter changes around the ventricles shown on MRI in multiple sclerosis. **B**, Change in the spinal cord in multiple sclerosis. *(From Perkin GD:* Mosby's Color Atlas and Text of Neurology, *ed 2, London, 2002, Mosby.)*

cranial nerves. There are a number of types of MS with considerable variation in the effects, severity, and progression in any one individual. Multiple sclerosis is characterized by remissions and exacerbations, but nevertheless is marked by progressive degeneration. Estimated incidence runs from 30 to 100 per 100,000 persons. It is the second most common cause of disability in the United States; motor vehicle accidents are the first.

Pathophysiology

Loss of myelin interferes with the conduction of impulses in the affected fibers. It affects all types of nerve fibers—motor, sensory, and autonomic—and occurs in diffuse patches throughout the nervous system (Fig. 14-28). Recent research has shown that cognitive function can be impaired in the client with MS, particularly with respect to attention to tasks and memory.

The earliest lesion occurs as an inflammatory response as cells that normally do not enter the brain or spinal cord do so and attack neurons, with loss of myelin in the white matter of the brain or spinal cord. Recent research has identified a protein in the body's blood clotting mechanism as a potential trigger of the immune response. Later larger areas of inflammation and demyelination, termed *plaques*, become visible, frequently beside the lateral ventricles in the brain, in the brain stem, and in the optic nerves.

Initially the area of plaque appears pinkish and edematous, but then it becomes gray and firm. Each plaque varies in size, and several may coalesce into a single patch. The initial inflammation may subside, and neural function may return to normal for a short time, until another exacerbation occurs. In time neural degeneration becomes irreversible, and function is lost permanently. With each recurrence, additional areas of the central nervous system (CNS) are involved. Multiple sclerosis varies in severity, occurring in mild and slowly progressive patterns in some individuals and in rapidly progressive forms in others.

Etiology

The onset of symptoms usually occurs in individuals between ages 20 and 40, with a peak at 30 years. The disease is more common in women by a 2:1 ratio. The cause is unknown, although many researchers believe it is an autoimmune disorder. However it may be even more complex in its origins. Multiple sclerosis appears to have genetic, immunologic, and environmental components. Multiple sclerosis occurs more frequently in people of European descent, and there is an increased risk for close relatives of affected individuals. The environmental factors have not yet been determined, although it is thought that climate may play a role because the disease is more common in temperate zones (northern United States and Canada) and in individuals who grow up in temperate climates. However there are exceptions to this factor, where MS occurs in warm climates. Viral infection and an abnormal immune response have also been suspected.

Signs and Symptoms

The manifestations of MS are determined by the areas that are demyelinated in each individual (Fig. 14-29). Blurred vision is a common early sign. Initially weakness in the legs often occurs, resulting from plaques on the corticospinal tract. If the cranial nerves are affected, diplopia (double vision), **scotoma** (a spot in the visual field), or dysarthria (poor articulation) may occur. Paresthesias, areas of numbness, burning, or tingling develop if the sensory nerve fibers are damaged. As the number of plaques increases with each exacerbation, progressive weakness and paralysis extending to the upper limbs, loss of coordination, and bladder, bowel, and sexual dysfunction occur. Chronic fatigue is common. Sensory deficits include paresthesias and loss of position sense in the upper body, face, and legs. The clinical picture and mode of progression vary greatly among individuals. Later in the course of the disease, depression or euphoria may develop. Complications related to immobility, such as respiratory infection, decubitus ulcers, and contractures, are common as the disease progresses.

Diagnostic Tests

There is no definitive test for multiple sclerosis, and a long delay may precede the diagnosis. A history of exacerbations and remissions, involvement of multiple focal areas, progression, and absence of other neurologic diagnostic criteria are often the basis for an initial diagnosis of MS. Magnetic resonance imaging studies are best for diagnosis and monitoring and are able to detect multiple CNS lesions. Often patients have elevated protein, gamma globulin, and lymphocytes levels in the CSF.

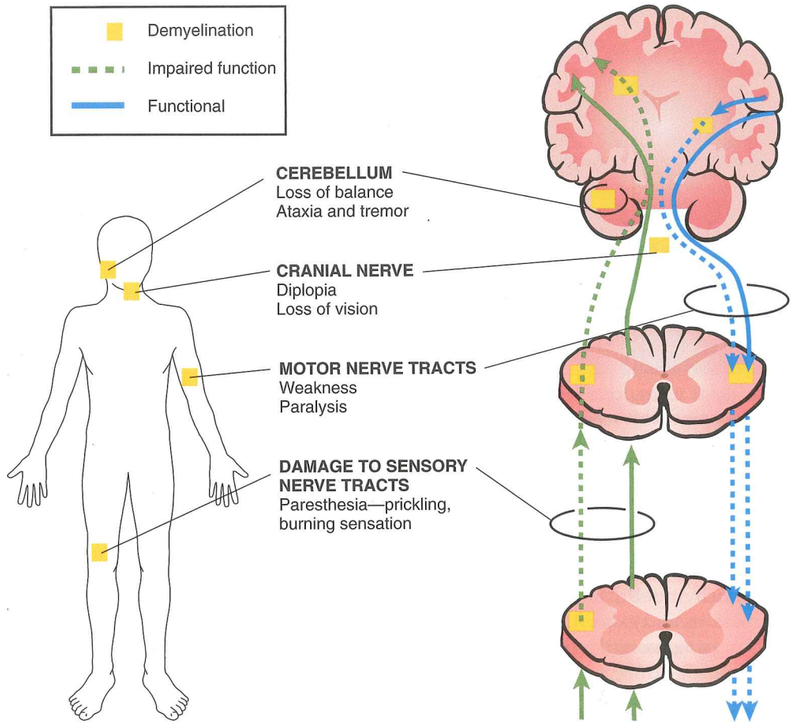

FIGURE 14-29 Multiple sclerosis—distribution of lesions.

Treatment

No specific treatment is available at this time, although new measures are always being investigated. Interferon beta-1b (Betaseron) appears to reduce the frequency and severity of exacerbations through its effects on the immune system. Glucocorticoid agents may help to control acute signs during exacerbations. Drugs to target the abnormal clotting proteins in the brain are being developed. Additional drugs may be prescribed as muscle relaxants or for other complications. The number of exacerbations can be reduced by avoiding excessive fatigue, stress, injury, or infection.

Therapy includes physical therapy and exercise to maintain mobility. Occupational therapy is essential in assessing the need for and provision of adaptive devices to simplify work and reduce fatigue. Special problems, such as constipation or incontinence, require individual attention. Communication and interest must be maintained by addressing issues such as visual impairment or speech disorders early in the course of the disease. Early intervention by a speech and language pathologist can maximize communication and assist with some feeding problems. As with any disabling condition, rehabilitation and psychosocial support are essential in maximizing function.

THINK ABOUT 14-17

a. Relate the following early signs of multiple sclerosis to the location of plaques: diplopia, tremors in the legs, facial weakness.
b. Relate the frequency of exacerbations to the progress of the disease.

Parkinson's Disease (Paralysis Agitans)

Parkinson's disease is a progressive degenerative disorder, affecting motor function through loss of extrapyramidal activity. It is estimated that 5000 individuals develop Parkinson's disease each year and that between 500,000 and 1.5 million Americans have Parkinson's disease.

Pathophysiology

In Parkinson's disease, dysfunction of the *extrapyramidal motor system* occurs because of progressive degenerative changes in the basal nuclei, principally in the *substantia nigra.* In this condition, a decreased number of neurons in the substantia nigra secrete dopamine, an inhibitory neurotransmitter, leading to an imbalance between excitation and inhibition in the basal nuclei. The excess stimulation affects movement and posture by increasing muscle tone and activity, leading to resting tremors, muscular rigidity, difficulty in initiating movement, and postural instability. Many patients with Parkinson's disease have a reduced number of cortical neurons, which is characteristic of dementia. Diagnosis depends on the physical manifestations and clinical history.

Etiology

Primary or idiopathic Parkinson's disease usually develops after age 60 and occurs in both men and women. Several genes have been identified in cases of familial Parkinson's disease, but a common focus of research is the possible damaging effects of viruses or toxins on cells. Recent research has focused on the mitochondrial changes in cells from patients with Parkinson's disease; these changes suggest periods of significant oxidative stress leading to the accumulation of free radicals within the cells.

Secondary Parkinsonism may follow encephalitis, trauma, or vascular disease. Drug-induced Parkinson's disease is linked particularly to use of the phenothiazines (e.g., chlorpromazine). The effects may be reversible or diminished when the drug is discontinued.

Signs and Symptoms

Early signs include fatigue, muscle weakness, muscle aching, decreased flexibility, and less spontaneous change in facial expression. More obvious signs are tremors in the hands at rest and a repetitive "pill-rolling" motion of the hands. Tremors cease with voluntary movement and during sleep. As the disease advances, tremors affect the hands and feet, the face, tongue, and lips. Further motor impairment, increased muscle rigidity, difficulty in initiating movement, slow movements (bradykinesia), and a lack of associated involuntary movement occurs; for example, loss of arm-swinging when walking or spontaneous postural adjustments when sitting. The characteristic standing posture is stooped, leaning forward with the head and neck flexed (Fig. 14-30). Festination, or a propulsive gait (short, shuffling steps with increasing acceleration), occurs as postural reflexes are impaired, leading to falls. Complex activities, such as getting up out of a chair, become slow and difficult.

Other functions are affected as the voice becomes low and devoid of inflection (the person speaks in a quiet monotone) and dysarthria develops. Chewing and swallowing become difficult, prolonging eating time and causing recurrent drooling. The face of the patient resembles a mask, and blinking of the eyelids is reduced, resulting in a blank, staring face. Autonomic dysfunction is manifested in the later stages by urinary retention, constipation, and orthostatic hypotension. As orthostatic hypotension develops, the threat of falls increases. Urinary tract and respiratory infections are common complications. Dementia develops late in the course of the disease in 20% of affected persons.

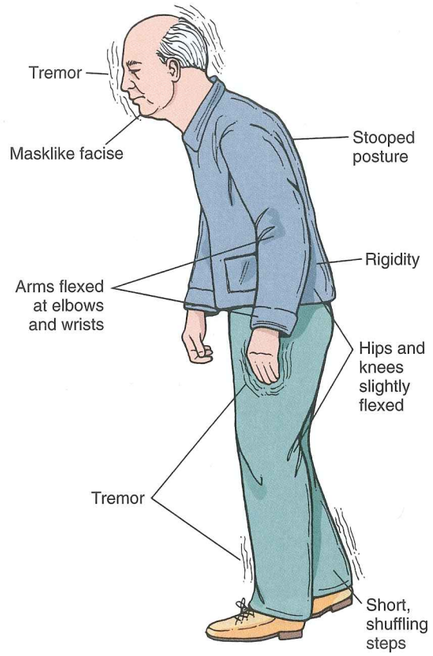

FIGURE 14-30 Parkinson's disease. *(From Monahan FD, Drake T, Neighbors M:* Nursing Care of Adults, *Philadelphia, 1994, Saunders.)*

Treatment

Dopamine replacement therapy has been used to reduce motor impairment. Levodopa (l-dopa), a **precursor** of dopamine, is administered because dopamine itself does not cross the blood-brain barrier. Selegiline (Eldepryl), a drug that blocks the breakdown of l-dopa in the brain, has resulted in improvement for some individuals. Anticholinergic drugs are also helpful. Several drugs are under investigation, as are new surgical procedures and transplants of fetal dopamine-producing cells or adult stem cells. Drug treatment may also include the use of antidepressant drugs to deal with the depression that often develops as the disease progresses.

Swallowing and speech impairments require early attention from a speech and language pathologist to maintain function as long as possible. Physical therapy is helpful in maintaining general mobility. Exercise that promotes the use of the arms and forceful movements are helpful. Occupational therapists work to improve balance, coordination, and safe use of adaptive devices.

Constant monitoring and immediate treatment of respiratory and urinary tract infections can reduce the risk of damage to the organs involved.

THINK ABOUT 14-18

a. Describe the pathophysiology of Parkinson's disease.
b. Describe three common manifestations that can be observed in a person with Parkinson's disease.
c. Explain why adequate nutrition and hydration may be difficult to maintain in a person with Parkinson's disease.
d. If adequate nutrition and hydration are not maintained, what potential complications may ensue?

Amyotrophic Lateral Sclerosis

The name of this disease, amyotrophic lateral sclerosis (ALS), is indicative of the pathology: amyotrophic means "muscle wasting" and sclerosis refers to the degenerative "hardening" of the lateral corticospinal tracts. The cause has not been identified, although a number of genes on various chromosomes have been linked to the disease. Ten percent of cases are considered familial. Most cases are random and do not reflect any ethnic trends in incidence. The disease is invariably fatal over time.

The disease, also called Lou Gehrig's disease, primarily affects individuals between the ages of 40 and 60, particularly men. The prevalence is 6 to 8 per 100,000. Although the disease is not common, it has attracted public attention because there is no means of preventing the continuous and rapid decline of motor and respiratory function, whereas cognitive function remains intact. Amyotrophic lateral sclerosis has been the focus of debate by the public and legislative and medical groups regarding ethical issues surrounding euthanasia for patients with such diseases.

Pathophysiology

Amyotrophic lateral sclerosis is a progressive degenerative disease affecting both upper motor neurons in the cerebral cortex and lower motor neurons in the brain stem and spinal cord. There is no indication of inflammation around the nerves. Recent studies have shown that supportive glial cells called *astrocytes* secrete a neurotoxin leading to the death of motor neurons. The loss of upper motor neurons leads to spastic paralysis and hyperreflexia; damage to lower motor neurons results in **flaccid** paralysis, with decreased muscle tone and reflexes. Sensory neurons, cognitive function, and cranial nerves III, IV, and VI to the eye muscles are not affected. The loss of neurons occurs in a diffuse and asymmetric pattern but proceeds without remission. Progressive muscle weakness eventually affects respiratory function. Although a specific diagnostic test has not been available to confirm the presence of the disease, many tests are required to eliminate other possible diagnoses. At present, a new test for specific biomarkers in CSF is under evaluation. Nerve conduction velocity tests and tests of muscle response to electrical stimulation are also used to evaluate the patient's myoneural function.

Signs and Symptoms

Initially in most cases, the upper extremities, particularly the hands, manifest weakness and muscle atrophy, with loss of fine motor coordination commencing with the distal fibers. Stumbling and falls are common. Muscle cramps or twitching may result from an imbalance of antagonistic muscles. The weakness and paralysis progress throughout the body. Dysarthria develops as the cranial nerves controlling speech are lost. Eventually swallowing and respiration are impaired, and a ventilator is required.

Treatment

At this time, no specific treatment is available to slow the degenerative process. Stem cell therapy is under investigation. A new drug, Rilutek (riluzole) has been developed to slow further damage to neurons; this can assist with maintaining swallowing and ventilation reflexes. A well-balanced program of moderate exercise and rest is helpful. Electronic communication devices are recommended for use relatively early in the course of the disease. A team approach to care can minimize the complications of immobility, sustain function as long as possible, and support the family. The team includes a respiratory therapist, nutritionist, speech pathologist, occupational therapist, physical therapist, psychologist, and social worker. In most cases respiratory failure occurs in 2 to 5 years, although some individuals survive for a longer period.

Myasthenia Gravis

Myasthenia gravis is an autoimmune disorder that impairs the receptors for acetylcholine (ACh) at the neuromuscular junction. The specific cause is not known, although many patients have thymus disorders, such as hyperplasia or benign tumors. Women are more frequently affected than men, and the age of onset is between ages 20 and 30 for women and greater than age 50 for men.

Pathophysiology

In myasthenia gravis, IgG autoantibodies to ACh receptors form, blocking and ultimately destroying the receptor site, thus preventing any further stimulation of the muscle. This change leads to skeletal muscle weakness and rapid fatigue of the affected muscles. The facial and ocular muscles are usually affected initially, followed by the arm and trunk muscles.

Diagnostic Tests

Several tests are available, including electromyography, to test for muscle fatigue, and an assay of serum antibodies. One test uses edrophonium chloride (Tensilon), a short-acting anticholinesterase inhibitor, to prolong the action of ACh at the myoneural junction, resulting in a short period of increased skeletal muscle function.

Signs and Symptoms

Muscle weakness is noticeable in the face and eyes, and fatigue develops quickly when the muscles are being used. Diplopia and ptosis impair vision, and speech becomes a nasal monotone. Spontaneous facial expressions are lost, and the face appears to droop with sadness. Attempts to smile may result in what appears to be a snarl. Chewing and swallowing become difficult as the weakness progresses and the risk of aspiration increases. The head droops as the neck muscles become involved. As the arms become weaker, it is difficult for the person to comb hair, brush teeth, or prepare and eat food. Muscle fatigue becomes more marked as the day progresses. Upper respiratory infections occur frequently and tend to be prolonged, because it becomes more difficult to remove secretions. *Myasthenic crisis*, which may occur when there is added stress—such as infection, trauma, or alcohol intake—involves an increase in weakness and fatigue, and respiratory impairment may develop.

Treatment

Anticholinesterase agents, such as pyridostigmine (Mestinon) or neostigmine (Prostigmin), may be used to temporarily improve neuromuscular transmission. These agents prolong the action of ACh at the neuromuscular junction and facilitate eating and swallowing. Glucocorticoids such as prednisone are effective in suppressing the immune system. Plasmapheresis, a process that removes antibodies from the blood, may help temporarily. Thymectomy may be helpful in reducing symptoms if hyperplasia or an adenoma is present. The long-term prognosis is increasing generalized weakness with eventual weakness of respiratory muscles.

THINK ABOUT 14-19

a. Explain why a person with myasthenia gravis might prefer a soft diet. List several potential complications of a continued soft diet.
b. Describe how oral hygiene might be affected by myasthenia gravis.
c. Compare the pathophysiology, significant early signs or symptoms, and course of amyotrophic lateral sclerosis, myasthenia gravis, multiple sclerosis, and Guillain-Barré syndrome

Huntington Disease

Huntington disease (HD), or Huntington's chorea, is an inherited disorder that does not manifest until midlife. Maternal inheritance delays onset longer than inheritance from fathers. It has a prevalence of 5 per 100,000 people and affects all ethnic groups. It is estimated that 15,000 people have HD in the United States and greater than 150,000 individuals face a 50% chance of inheriting the disorder.

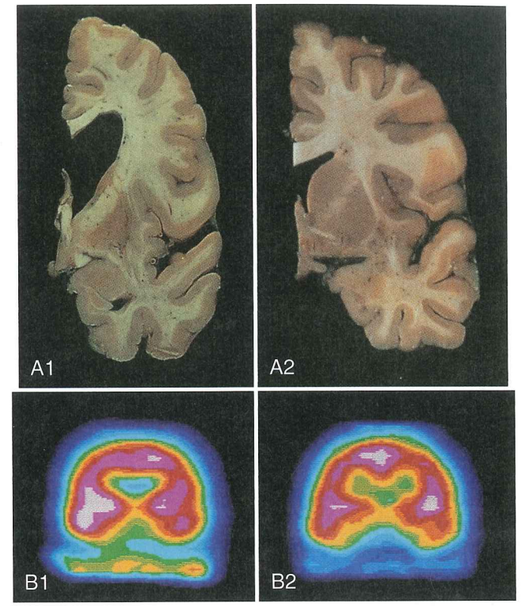

FIGURE 14-31 **Huntington's Disease A,** Coronal section of the brain shows a dilated lateral ventricle with caudate and lentiform atrophy on the left compared with a normal brain on the right. **B,** Reduced caudate blood flow shown on the left, compared to normal blood flow on the right, shown in single photon emission CT scan. *(From Perkin GD:* Mosby's Color Atlas and Text of Neurology, *ed 2, St. Louis, 2002, Mosby.)*

Pathophysiology

Progressive atrophy of the brain occurs, with degeneration of neurons, particularly in the basal ganglia and the frontal cortex. The ventricles are dilated (Fig. 14-31). There is depletion of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter in the basal nuclei and substantia nigra. Levels of ACh in the brain also appear to be reduced.

Etiology

This condition is inherited as an autosomal-dominant trait (about a 50% probability of having an affected child) and is carried on chromosome 4. Until recently there were no diagnostic tests available to identify affected individuals before the onset of symptoms; therefore children with a high risk of inheritance were once born to affected parents before the disease was diagnosed in the parents. This combination of factors increased the incidence of the disorder. That trend is

changing because testing and genetic counseling are available. However, in one in three newly diagnosed cases there is no record of family members with the disorder.

Signs and Symptoms

At the onset, mood swings and personality changes develop, as well as restlessness and choreiform (rapid, jerky) movements in the arms and face. There may also be early indications of intellectual impairment, such as difficulty learning new information, loss of problem-solving skills, poor judgment, inability to concentrate, and memory lapses. With progressive degeneration, rigidity and akinesia develop, making any movement difficult. Personality changes, moodiness, and behavioral disturbances become more marked as dementia progresses.

Diagnostic Tests

The presence of the defective gene can be detected by DNA analysis.

Treatment

No therapy is available to slow the progress of the disease. Symptomatic therapy, such as physiotherapy or tetrabenazine, a new drug approved in 2008, may reduce the choreiform movements and maintain mobility for a longer time. Other drugs may be used to treat behavior changes. In later stages the patient with HD requires significant supportive care for physical needs.

Dementia

There are many formal definitions of dementia, based on the following characteristics. It is a progressive chronic disease, in which cortical function is decreased, impairing cognitive skills such as language and innumeracy, logical thinking and judgment, ability to learn new information, as well as motor coordination. Loss of memory affects primarily short-term or recent memory, but includes confusion about the events in long-term memory. Memory loss is often progressive, leading to long-term as well as short-term memory loss. Behavioral and personality changes are usually present. These changes lead to inability to work and perform activities of daily living.

Tests are available for a behavioral assessment and to distinguish between "normal forgetfulness" and memory loss related to dementia. For example, forgetful people can remember when clues are available, handle finances, and function independently. In a person with dementia, recall does not occur after being given clues, the day cannot be identified, calculations are difficult, and reminders are needed for meals and hygiene.

There are many causes of dementia, including vascular disease (e.g., arteriosclerosis), infections, toxins, and genetic disorders. Alzheimer's disease accounts for more than 50% of those affected with dementia with vascular causes of dementia in second place.

Alzheimer's Disease

Approximately 10% of the population greater than 65 years of age has Alzheimer's disease (AD), and this increases to over 25% in the age group greater than 85 years. Females are affected more than males. It is estimated that between 4.5 and 5.4 million Americans are affected by AD.

In Alzheimer's disease there is a progressive loss of intellectual function that eventually interferes with work, relationships, and personal hygiene. Personality changes, lack of initiative, and repetitive behavior and impairments in judgment, abstract thinking, and problem-solving abilities are characteristic of the disease.

Pathophysiology

Typical changes in Alzheimer's disease include progressive cortical atrophy, which leads to dilated ventricles, and widening of the sulci (Fig. 14-32). Neurofibrillary tangles in the neurons and senile plaques are found in large numbers in the affected parts of the brain. The plaques, which disrupt neural conduction, contain fragments from beta-amyloid precursor protein (βAPP); the role of this protein is a focus of research. Some neurofibrils and plaques have been found in the brains of elderly people whose cognitive function is not impaired, and therefore it appears that the numbers and distribution of the plaques are the significant factors. A deficit of the neurotransmitter ACh also occurs in the affected brain.

No definitive diagnostic tests are available; the diagnosis is based on observations and ruling out other possible causes. Progressive tests of memory are very helpful in making a probable diagnosis of AD. Some cases of dementia have been labeled Alzheimer's disease, and then later classified as another form of dementia.

Etiology

The specific cause is unknown.

At least four defective genes located on different chromosomes have been associated with AD. Three gene mutations on chromosomes 1, 14, and 21 are inherited as autosomal dominant traits resulting in early onset AD. The genetic factor is also supported by the high incidence in older persons with Down syndrome (trisomy 21). One form of late onset AD has been linked to a mutation on chromosome 19. Other forms of Alzheimer's disease appear to be multifactorial in origin. The National Institute on Aging has launched major research investigations into genetic and other suspected factors, including exposure to metals, viruses, and metabolic syndrome.

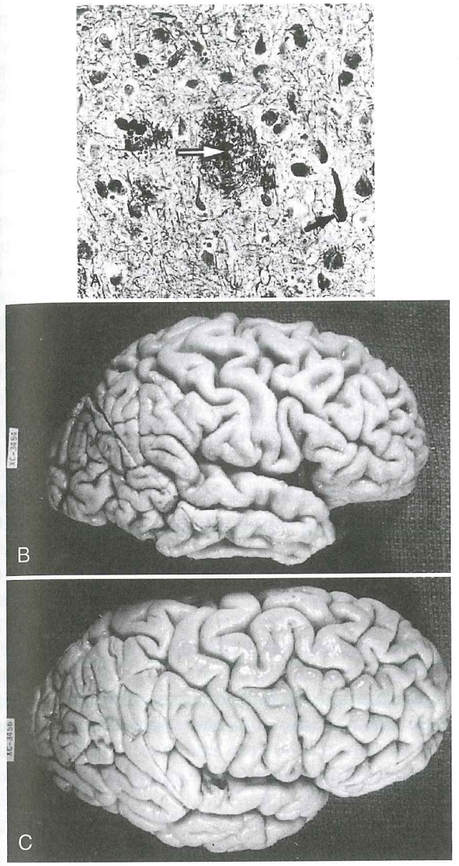

FIGURE 14-32 **Pathologic Changes in Alzheimer's Disease A,** A mature plaque with central amyloid core (*white arrow*) next to a neurofibrillary tangle (*black arrow*). **B,** Alzheimer's disease: brain is smaller with narrower gyri and wider sulci, particularly in frontal and temporal lobes. **C,** Comparable normal brain. *(From Damjanov I, Linder J:* Anderson's Pathology, *ed 10, St. Louis, 1996, Mosby.)*

Signs and Symptoms

There is less emphasis on differentiating the pathophysiology and signs of early versus late-onset disease. Several research projects are, however, focused on defining the signs at the time of onset and through the stages to determine the pattern of neurologic damage.

Onset tends to be insidious. The course may extend over 10 to 20 years:

- In the early stage, gradual loss of memory and lack of concentration become apparent. Ability to learn new information and to reason is impaired and behavioral changes, such as irritability, hostility, and mood swings, are common.
- Cognitive function, memory, and language skills continue to decline. Problem solving, mathematical ability, and judgment are poor. Apathy, indifference, and confusion become more marked. Managing the activities of daily living becomes difficult, affecting meal preparation, dressing, and personal hygiene. Wandering is common and the person may become confused and lost, even in familiar territory.
- In the late stage, the person does not recognize his or her family, lacks awareness or interest in the environment, is incontinent, and is unable to function in any way. Degenerative changes may gradually interfere with motor function.

Treatment

Although no specific treatment is available to reverse the effects of AD, occupational therapy is important in assessment and provision of adaptive devices to provide for a safe environment as long as is possible. Specific problems, such as depression or anxiety, are treated symptomatically. Many drugs are contraindicated because they add to mental confusion. Anticholinesterase drugs, such as donepezil (Aricept), have led to some temporary improvement resulting from improved cholinergic transmission.

Moderate stimulation, perhaps in a daycare setting, is helpful, while maintaining a daily routine and exercise program is also advisable. A team approach to care is helpful in prolonging independence and supporting the family. Social workers, occupational therapists, psychologists, and speech therapists can provide direction and assistance. A daily routine and secure surroundings facilitate compliance with care. Often the primary caregiver is included in such therapy programs. Survival ranges up to 20 years, with an average of 7 years.

THINK ABOUT 14-20

a. List the early signs of Alzheimer's disease.
b. Describe three ways that AD can interfere with activities of daily living.
c. Compare the effects of AD, HD, ALS, and Parkinson's disease.

Other Forms of Dementia

Vascular Dementia

Vascular dementia is a form of dementia that is caused by cerebrovascular disease and frequently is a result of multiple small brain infarctions. It is common in persons older than age 70, particularly those with hypertension. Onset is insidious, with memory loss, apathy, and inability to manage daily routines. Progression may be in stages that are connected to the infarctions and loss of brain tissue. Other neurologic impairment is common.

Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is a rare, but rapidly progressive, form of dementia caused by infection by a prion, an altered infectious protein particle (PrP) with a preference for nervous tissue. The infecting protein appears to alter normal host PrP or the coding gene for protein shape. Often the origin of the infection is not identified. Some cases show a familial incidence (defect in human prion protein gene) and some have been iatrogenic, including sources such as surgery, corneal transplants, or other invasive procedures. Most are sporadic. Creutzfeldt-Jakob disease is more common in older individuals.

Creutzfeldt-Jakob disease has a very long incubation period after its introduction into the brain, where more abnormal prions are produced. This is followed by rapid destruction of neurons, formation of plaques and vacuoles (empty spaces) in the neurons (spongiform encephalopathy). Early indicators are memory loss, behavioral changes, motor dysfunction, and progressive dementia. An EEG and MRI study aids the diagnosis. The course is 6 to 12 months. No treatment is available at this time.

The prions resist common methods of sterilization and disinfection. A link has been established between bovine spongiform encephalopathy (BSE, or mad cow disease) and a variant form of CJD (vCJD), with transmission by infected beef.

AIDS Dementia

Dementia is common in the later stages of AIDS (see Chapter 7). The virus itself invades brain tissue and may be exacerbated by other infections, including those of *Candida* or *Toxoplasma* species, and by tumors, such as lymphomas. Gradual loss of memory and cognitive ability and impaired motor function (e.g., ataxia, weakness, and abnormal reflexes) are typical.

In children with congenital HIV infection, the brain is frequently affected, causing mental retardation and delayed motor development.

Mental Disorders

Mental illness is classified using the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*, published by the American Psychiatric Association. Mental health problems involve significant dysfunction in the areas of behavior or personality that interferes with the person's ability to function. Biochemical and structural abnormalities in the brain appear to contribute to these pathologies. Many disorders have a genetic component. Stressors may play a role in the development of the illness. Psychotic illness includes the more serious disorders, such as schizophrenia, delusional disorders, and some affective or mood disorders. Many patients with psychotic disorders receive large doses of drugs with obvious side effects. Other common mental disorders include anxiety and panic disorders, which are less severe but nevertheless disruptive. This section provides a brief introduction to the pathophysiology of several common mental disorders. Further information can be obtained from texts focusing on mental health.

Schizophrenia

Pathophysiology

Schizophrenia affects approximately 1.3% of the population and includes a variety of syndromes, which present differently in each individual. Although the etiology and pathogenesis have not been fully determined, some common changes do occur in the brains of schizophrenic patients, including reduced gray matter in the temporal lobes, enlarged third and lateral ventricles, abnormal cells in the hippocampus (part of the limbic system), excessive dopamine secretion, and decreased blood flow to the frontal lobes. Some of these changes appear to be linked to the neurologic manifestations seen in schizophrenic patients, such as abnormal eye movements (staring or periodic jerky eye movements).

Etiology

Theories about the cause of schizophrenia focus on a genetic predisposition along with brain damage in the fetus caused by perinatal complications or viral infection in the mother during pregnancy. Twin studies show a high concordance in both monozygotic and dizygotic twins pointing to a genetic component. Onset of schizophrenia usually occurs between ages 15 and 25 in men and 25 and 35 in women. Stressful events appear to initiate the onset and recurrences.

Signs and Symptoms

Symptoms may be grouped as positive (e.g., delusions, bizarre behavior) or negative (e.g., flat emotions, decreased speech). Both the excesses and the deficits may appear in one patient. Subtypes are based on the predominant characteristics.

Generally disorganized thought processes are the basic problem. Communication is often impaired by inadequate language skills, including lack of appropriate association of thoughts, meaningless repetition of words or thoughts, or development of new words without accepted meanings (neologisms). Delusions or false beliefs and ideas are persistent. Delusions may include a belief in persecution by others or ideas of grandeur or power over others. Problem-solving ability is impaired, and the attention span is brief. Hallucinations or abnormal sensory perceptions are common. The patient may withdraw socially from people and show little emotion but also may experience mood swings and become anxious. Often self-care is neglected.

Treatment

Drugs are the major therapeutic modality, often in conjunction with psychotherapy and psychosocial rehabilitation. The antipsychotic drugs (major tranquilizers or neuroleptics), chlorpromazine (Thorazine), fluphenazine (Prolixin, Moditen), haloperidol (Haldol), and clozapine (Clozaril), act by decreasing dopamine activity in the brain. These drugs frequently cause side effects related to excessive extrapyramidal activity (or parkinsonian signs). Dystonia and tardive dyskinesia cause involuntary muscle spasms in the face, neck, arms, or legs. Tardive dyskinesia may present as chewing or grimacing, repetitive jerky or writhing movements of the limbs, tremors, or a shuffling gait. With prolonged use and high doses of these drugs, tardive dyskinesia may be irreversible. Some of these side effects may be reduced by anti-Parkinson agents (anticholinergics), but these drugs also have adverse effects, such as blurred vision and dry mouth.

Depression

Depression is classified as a mood disorder, of which there are several subgroups. Major depression, or unipolar disorder, is endogenous, and a precise diagnosis is based on biologic factors or personal characteristics. Etiologic factors include genetic, developmental, and psychosocial stressors. Bipolar disorder involves alternating periods of depression and mania. Depression may also occur as an exogenous or reactive episode, a response to a life event, or secondarily to many systemic disorders, including cancer, diabetes, heart failure, and systemic lupus erythematosus. Depression is a common problem, and many patients with milder forms may be misdiagnosed and not receive treatment.

Pathophysiology

Depression is classified as an affective or mood disorder on the basis of characteristic disorganized emotions. It results from decreased activity by the excitatory neurotransmitters, norepinephrine and serotonin, in the brain. The exact mechanism has not yet been established, but twin studies do suggest a genetic component. The depressed client often has a history of major psychosocial trauma, which may contribute to the development of the disorder.

Signs and Symptoms

Depression is indicated by a prolonged period of profound sadness marked by hopelessness and an inability to find pleasure in any activity. Lack of energy and loss of self-esteem and motivation interfere with daily activity. Some individuals may be irritable and agitated. The individual has difficulty in concentrating and solving problems. Sleep disorders, such as insomnia or, occasionally, excessive sleep, usually accompany depression. Loss of appetite and libido (sex drive) are common. The degree to which the individual is affected varies over time and between individuals. In some cases disability results as the individual is unable to meet the demands of daily life.

Treatment

Antidepressant drugs that increase norepinephrine activity are effective in treating many cases of depression. There is concern about the increased risk of suicide in children and adolescents taking antidepressant medications without concurrent psychiatric counselling.

A group of drugs in common use, the selective serotonin reuptake inhibitors (SSRIs), including fluoxetine (Prozac), have fewer cardiovascular side effects than drugs that block norepinephrine uptake. They prolong the activity at serotonin receptors, with antidepressant and anxiolytic effects. A new class, called serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine [Effexor]), may be more selective in receptor action and have fewer side effects.

The tricyclic antidepressants (TCAs), such as amitriptyline (Elavil), block the reuptake of the neurotransmitters, particularly norepinephrine, into the presynaptic neuron. These mechanisms allow the stimulation by excitatory neurotransmitters to continue in the brain.

Monoamine oxidase (MAO) inhibitors, such as tranylcypromine (Parnate), block the destruction of norepinephrine and serotonin by the enzyme MAO at the synapse. Monoamine oxidase inhibitors cause many interactions involving certain foods and other drugs that may result in a hypertensive crisis (marked increase in high blood pressure). Foods to be avoided include tyramine-containing substances, such as chocolate, aged cheese, beer, and red wine. Monoamine oxidase inhibitors are not taken with SNRIs or SSRIs due to dangerous synergistic effects.

Another treatment of severe depression involves electroconvulsive therapy (ECT, shock treatments), which increases norepinephrine activity, but may result in some memory loss.

Panic Disorder

Panic attacks are common but do not necessarily lead to panic disorder. *Panic attack* refers to a sudden brief episode of discomfort and anxiety. Panic disorder, an anxiety disorder, develops when panic attacks are frequent or prolonged. These attacks occur in situations that most individuals would not find threatening.

Pathophysiology

A genetic factor has been implicated. An increased discharge of neurons may occur in the temporal lobes. Biochemical abnormalities involving the neurotransmitters norepinephrine, serotonin, and GABA may also be involved. Patients are fearful of having another panic attack, leading to increased irritability of the limbic system.

Creutzfeldt-Jakob Disease

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The prions resist common methods of sterilization and disinfection. A link has been established between bovine spongiform encephalopathy (BSE, or mad cow disease) and a variant form of CJD (vCJD), with transmission by infected beef.

AIDS Dementia

Dementia is common in the later stages of AIDS (see Chapter 7). The virus itself invades brain tissue and may be exacerbated by other infections, including those of *Candida* or *Toxoplasma* species, and by tumors, such as lymphomas. Gradual loss of memory and cognitive ability and impaired motor function (e.g., ataxia, weakness, and abnormal reflexes) are typical.

In children with congenital HIV infection, the brain is frequently affected, causing mental retardation and delayed motor development.

Mental Disorders

Mental illness is classified using the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*, published by the American Psychiatric Association. Mental health problems involve significant dysfunction in the areas of behavior or personality that interferes with the person's ability to function. Biochemical and structural abnormalities in the brain appear to contribute to these pathologies. Many disorders have a genetic component. Stressors may play a role in the development of the illness. Psychotic illness includes the more serious disorders, such as schizophrenia, delusional disorders, and some affective or mood disorders. Many patients with psychotic disorders receive large doses of drugs with obvious side effects. Other common mental disorders include anxiety and panic disorders, which are less severe but nevertheless disruptive. This section provides a brief introduction to the pathophysiology of several common mental disorders. Further information can be obtained from texts focusing on mental health.

Schizophrenia

Pathophysiology

Schizophrenia affects approximately 1.3% of the population and includes a variety of syndromes, which present differently in each individual. Although the etiology and pathogenesis have not been fully determined, some common changes do occur in the brains of schizophrenic patients, including reduced gray matter in the temporal lobes, enlarged third and lateral ventricles, abnormal cells in the hippocampus (part of the limbic system), excessive dopamine secretion, and decreased blood flow to the frontal lobes. Some of these changes appear to be linked to the neurologic manifestations seen in schizophrenic patients, such as abnormal eye movements (staring or periodic jerky eye movements).

Etiology

Theories about the cause of schizophrenia focus on a genetic predisposition along with brain damage in the fetus caused by perinatal complications or viral infection in the mother during pregnancy. Twin studies show a high concordance in both monozygotic and dizygotic twins pointing to a genetic component. Onset of schizophrenia usually occurs between ages 15 and 25 in men and 25 and 35 in women. Stressful events appear to initiate the onset and recurrences.

Signs and Symptoms

Symptoms may be grouped as positive (e.g., delusions, bizarre behavior) or negative (e.g., flat emotions, decreased speech). Both the excesses and the deficits may appear in one patient. Subtypes are based on the predominant characteristics.

Generally disorganized thought processes are the basic problem. Communication is often impaired by inadequate language skills, including lack of appropriate association of thoughts, meaningless repetition of words or thoughts, or development of new words without accepted meanings (neologisms). Delusions or false beliefs and ideas are persistent. Delusions may include a belief in persecution by others or ideas of grandeur or power over others. Problem-solving ability is impaired, and the attention span is brief. Hallucinations or abnormal sensory perceptions are common. The patient may withdraw socially from people and show little emotion but also may experience mood swings and become anxious. Often self-care is neglected.

Treatment

Drugs are the major therapeutic modality, often in conjunction with psychotherapy and psychosocial rehabilitation. The antipsychotic drugs (major tranquilizers or neuroleptics), chlorpromazine (Thorazine), fluphenazine (Prolixin, Moditen), haloperidol (Haldol), and clozapine (Clozaril), act by decreasing dopamine activity in the brain. These drugs frequently cause side effects related to excessive extrapyramidal activity (or parkinsonian signs). Dystonia and tardive dyskinesia cause involuntary muscle spasms in the face, neck, arms, or legs. Tardive dyskinesia may present as chewing or grimacing, repetitive jerky or writhing movements of the limbs, tremors, or a shuffling gait. With prolonged use and high doses of these drugs, tardive dyskinesia may be irreversible. Some of these side effects may be reduced by anti-Parkinson agents (anticholinergics), but these drugs also have adverse effects, such as blurred vision and dry mouth.

Depression

Depression is classified as a mood disorder, of which there are several subgroups. Major depression, or unipolar disorder, is endogenous, and a precise diagnosis is based on biologic factors or personal characteristics. Etiologic factors include genetic, developmental, and psychosocial stressors. Bipolar disorder involves alternating periods of depression and mania. Depression may also occur as an exogenous or reactive episode, a response to a life event, or secondarily to many systemic disorders, including cancer, diabetes, heart failure, and systemic lupus erythematosus. Depression is a common problem, and many patients with milder forms may be misdiagnosed and not receive treatment.

Pathophysiology

Depression is classified as an affective or mood disorder on the basis of characteristic disorganized emotions. It results from decreased activity by the excitatory neurotransmitters, norepinephrine and serotonin, in the brain. The exact mechanism has not yet been established, but twin studies do suggest a genetic component. The depressed client often has a history of major psychosocial trauma, which may contribute to the development of the disorder.

Signs and Symptoms

Depression is indicated by a prolonged period of profound sadness marked by hopelessness and an inability to find pleasure in any activity. Lack of energy and loss of self-esteem and motivation interfere with daily activity. Some individuals may be irritable and agitated. The individual has difficulty in concentrating and solving problems. Sleep disorders, such as insomnia or, occasionally, excessive sleep, usually accompany depression. Loss of appetite and libido (sex drive) are common. The degree to which the individual is affected varies over time and between individuals. In some cases disability results as the individual is unable to meet the demands of daily life.

Treatment

Antidepressant drugs that increase norepinephrine activity are effective in treating many cases of depression. There is concern about the increased risk of suicide in children and adolescents taking antidepressant medications without concurrent psychiatric counselling.

A group of drugs in common use, the selective serotonin reuptake inhibitors (SSRIs), including fluoxetine (Prozac), have fewer cardiovascular side effects than drugs that block norepinephrine uptake. They prolong the activity at serotonin receptors, with antidepressant and anxiolytic effects. A new class, called serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine [Effexor]), may be more selective in receptor action and have fewer side effects.

The tricyclic antidepressants (TCAs), such as amitriptyline (Elavil), block the reuptake of the neurotransmitters, particularly norepinephrine, into the presynaptic neuron. These mechanisms allow the stimulation by excitatory neurotransmitters to continue in the brain.

Monoamine oxidase (MAO) inhibitors, such as tranylcypromine (Parnate), block the destruction of norepinephrine and serotonin by the enzyme MAO at the synapse. Monoamine oxidase inhibitors cause many interactions involving certain foods and other drugs that may result in a hypertensive crisis (marked increase in high blood pressure). Foods to be avoided include tyramine-containing substances, such as chocolate, aged cheese, beer, and red wine. Monoamine oxidase inhibitors are not taken with SNRIs or SSRIs due to dangerous synergistic effects.

Another treatment of severe depression involves electroconvulsive therapy (ECT, shock treatments), which increases norepinephrine activity, but may result in some memory loss.

Panic Disorder

Panic attacks are common but do not necessarily lead to panic disorder. *Panic attack* refers to a sudden brief episode of discomfort and anxiety. Panic disorder, an anxiety disorder, develops when panic attacks are frequent or prolonged. These attacks occur in situations that most individuals would not find threatening.

Pathophysiology

A genetic factor has been implicated. An increased discharge of neurons may occur in the temporal lobes. Biochemical abnormalities involving the neurotransmitters norepinephrine, serotonin, and GABA may also be involved. Patients are fearful of having another panic attack, leading to increased irritability of the limbic system.

Signs and Symptoms

Repeated episodes of intense fear without provocation, which may last for minutes or hours, characterize this disorder. Palpitations or tachycardia, hyperventilation, sweating, sensations of choking or smothering, and nausea accompany the feeling of terror. Patients who anticipate attacks may develop a fear of open spaces (agoraphobia) or a fear of being in a place where no help is available and may refuse to leave their homes.

Treatment

Treatment consists of psychotherapy combined with drug therapy, usually antianxiety agents, such as alprazolam (Xanax) or diazepam (Valium). Antianxiety agents or minor tranquilizers, such as the benzodiazepines, potentiate the activity of GABA, an inhibitory neurotransmitter. Large doses may be necessary, which can cause drowsiness and ataxia. These drugs have a wide safety margin when used appropriately. In some patients, antidepressants may be prescribed.

THINK ABOUT 14-21

a. Compare three signs of schizophrenia with three signs of depression.
b. Explain how antipsychotic drugs act to reduce signs of mental illness.
c. Describe common signs of extrapyramidal side effects of antipsychotic drugs.
d. Describe a panic attack.

Spinal Cord Disorder

Herniated Intervertebral Disc

Pathophysiology

The vertebrae are separated by cartilaginous discs, which act as cushions and provide some flexibility to the spinal column. Herniation involves protrusion of the nucleus pulposus, the inner gelatinous component of the intervertebral disc, through a tear in the annulus fibrosus, the tough outer covering of the disc (Fig. 14-33). Such protrusions into the extradural space, usually laterally exert pressure on the spinal nerve root or spinal cord at the site, interfering with nerve conduction. The tear in the capsule may occur suddenly or develop gradually. Depending on which site is involved, sensory, motor, or autonomic function can be impaired. The most common location is the lumbosacral discs, at L4 to L5 or L5 to S1. Some herniations involve cervical discs between C5 and C7. If pressure on the nerve tissue or blood supply is prolonged and severe, permanent damage to the nerve may result.

Etiology

A person may be predisposed to herniation because of degenerative changes in the intervertebral disc,

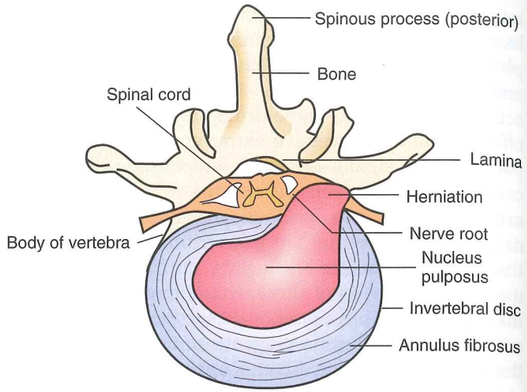

FIGURE 14-33 Herniated intervertebral disc.

resulting from age or metabolic changes. The herniation usually is caused by trauma or poor body mechanics, leading to excessive stress on the muscles, for example, by improper lifting or transfer of patients. Trauma accounts for about 50% of herniations.

Signs and Symptoms

Signs depend on the location and extent of the protrusion (see Figs. 14-4 and 14-23). In most cases, the effects are unilateral; however, large protrusions may cause bilateral effects. Because of pressure on the sensory nerve fibers in the dorsal root, lumbosacral herniations cause pain in the lower back, radiating down the posterior aspect of one or both legs (sciatic nerve pain). Actions such as coughing or straight leg-raising usually aggravate the pain. Paresthesia or numbness and tingling may occur. If the nerve compression is extensive, muscle weakness develops. Interference with micturition (bladder emptying) may develop.

Similarly a herniated disc in the cervical region causes pain in the neck and shoulder that radiates down the arm. Sensory impairment, reduced neck movement, and weakness may accompany the pain. The pressure may lead to skeletal muscle spasm in the neck or back, further increasing the pain.

Diagnostic Tests

Myelography with contrast dye, CT scans, and MRI confirm the herniation.

Treatment

Conservative treatment, including bed rest; application of heat, ice, or traction; or drugs, such as analgesics, anti-inflammatory agents, and skeletal muscle relaxants, are the initial approach. Back education programs are helpful in establishing appropriate positions for rest and activity. It is important to note that the pressure on the disks is highest in the sitting position. Physiotherapy

and an appropriate program of exercise are usually undertaken. An occupational therapist can recommend appropriate modifications to daily life and workplace activities. Surgery may be considered in selected cases of unremitting chronic back pain and includes laminectomy or diskectomy. Spinal fusion is required if several vertebrae are involved creating added instability.

THINK ABOUT 14-22

Explain how a herniated intervertebral disc causes pain in the leg.

CASE STUDY A

Brain Tumor

Mr. A.H., age 44, had a generalized tonic-clonic seizure unexpectedly at work. He had no history of seizures, trauma, infection, or other illness. Investigation revealed a tumor in the right parietal lobe. This was removed surgically, although the diffuse nature of the malignant mass prevented its complete elimination. Follow-up radiation treatment was recommended.

1. Describe briefly several diagnostic tests that would be of value in this case.
2. Explain the basis of this seizure activity, and describe how it might be controlled.
3. Describe each stage, in sequence, of a generalized tonic-clonic seizure.

After surgery, Mr. A.H. demonstrated considerable weakness and sensory loss on his left side.

4. Match each of these effects with the functional areas of the brain that control them.

A few days after surgery, Mr. A.H. developed a bacterial infection at the operative site.

5. Explain why this infection is likely to increase motor and sensory deficits.

The infection was eradicated quickly with treatment, but the tumor did not respond to radiation and chemotherapy. As a result, several tumors in the brain grew relatively large during the next 2 months.

6. The cancer treatments caused severe anemia, nausea, and vomiting. Explain how these side effects could cause other complications for Mr. A.H.; describe these complications clearly.
7. Suggest several types of therapy or assistance that would be helpful to Mr. A.H. during this period. (Extend this question to focus on your specialty area, when possible.)

Mr. A.H. developed severe headaches and diplopia and became increasingly lethargic, and his seizures increased in frequency despite anticonvulsant medication. He was given medication to reduce the frequency of vomiting.

8. Explain the specific rationale for each of his manifestations.

As the tumors increased in size Mr. A.H.'s vital signs indicated increased pulse pressure.

9. Explain the cause of each of this sign.
10. Describe the changes that are likely to occur as coma develops in Mr. A.H.

CASE STUDY B

Spinal Cord Injury

B.L., age 17, has a compression fracture at C5 to C6, a result of diving from a bridge into a river and hitting a submerged rock. Fortunately a companion who had first aid training as a lifeguard rescued her and tried to minimize any secondary damage. In the emergency department, B.L. could not move her limbs or sense touch and lacked reflexes in her limbs.

1. Explain why caution is needed when handling a person with possible spinal cord injury.
2. Describe a compression fracture and how it can affect neurologic function.
3. Explain why reflexes are absent in B.L. at this early stage. What type of paralysis is present?
4. Explain why and how B.L.'s respiratory function may be impaired at any time.
5. Explain why the full extent of permanent damage cannot be estimated in this initial period.

Surgery was performed to relieve pressure and stabilize the fracture site.

6. Describe several additional factors that may result in secondary damage to the spinal cord.
7. Explain the anticipated effect in the immediate period of this injury on B.L.'s blood pressure and bladder function.

Several weeks later, routine examination indicated that some spinal cord reflexes were returning in the lower extremities.

8. Explain the significance of the returning reflexes.
9. Explain why each of the following complications could develop in B.L. and state the early signs for each:
   a. pneumonia
   b. decubitus ulcer
   c. muscle atrophy
   d. contracture
10. Briefly describe how the risk for each of the above complications could be minimized.

Gradually more reflexes returned. Some muscle tone and movement of the shoulder and upper arm became apparent, but no other function returned.

11. Explain how the dermatomes can assist in detecting functional areas.
12. Describe the change to be expected in bowel and bladder function as reflexes return.

One day, B.L. suddenly developed a severe headache and blurred vision. Her blood pressure was 210/120 mmHg and her pulse was 62 beats per minute.

13. What has probably caused this effect, and what action needs to be taken?
14. Suggest the specific components for a rehabilitation program for B.L. Expand your comments in areas of particular concern to you.

CASE STUDY C

Increased Intracranial Pressure

R.T. is a 16-year-old girl who has just received her driver's license. She has taken several friends to a "bush party" at a classmate's farm where beer and liquor were available. She leaves the party at 2:00 AM after having several drinks. Her

friends tease her as she attempts to put on her seat belt and one calls her a sissy. She begins driving home without a seat belt. Her car drifts across the median and is involved in a head-on collision. Her most serious problem appears to be severe brain injury following ejection from the car. She is transported to the area trauma center, where treatment begins immediately.

1. Examination indicates papilledema in the right eye, a subdural hematoma in the temporal region, loss of consciousness and decreased responsiveness to painful stimuli. Explain how each symptom or sign is related to increased intracranial pressure.
2. Describe a subdural hematoma, its location, and how it developed and caused ICP.
3. R.T. develops bilaterally dilated pupils and a CT scan shows ventricular shift. What are the implications of these findings?
4. Surgery is performed to reduce the pressure in her cranium and R.T. recovers but requires rehabilitation for several deficits, including problems with hearing and memory as well as comprehension of speech. How will these deficits affect her academic work? Which regions of the cortex have been damaged?

One year after the accident, R.T. returns to high school and with the aid of a special education program for with head injuries, she graduates.

CASE STUDY D

Multiple Sclerosis

W.H., a woman, age 36, has received a diagnosis of multiple sclerosis. She has lost part of her left visual field and has weakness in her left leg. W.H.'s mother had multiple sclerosis.

1. State the factors in the history and the diagnostic tests that would indicate multiple sclerosis as a diagnosis.
2. Describe the pathophysiology of multiple sclerosis.
3. State the possible locations of the lesions that have caused visual and motor deficits.
4. Describe the typical course of multiple sclerosis that W.H. can expect in future.
5. Suggest several measures that can be used to minimize exacerbations.
6. Explain why adequate nutrition and hydration are important in patients with chronic neurologic conditions, including specific potential complications that may be avoided.
7. Explain why a program of moderate activity is important for W.H.

CASE STUDY E

Alzheimer's Disease

D.N. developed Alzheimer's disease at age 50. Early signs were vague and included occasional errors in judgment and increased criticism of others, noted only in retrospect. Several years later, following several episodes of extreme anger, a diagnosis of Alzheimer's disease was made. At this time, it was suspected that his father had also had AD, but had died from an unrelated cause before a diagnosis could be made.

1. Why is a diagnosis difficult in the early stage of AD?
2. Could there be a familial factor?
3. Describe the pathologic changes that occur in the brain with AD.

The neurologist prescribed galantamine (Reminyl), an anticholinesterase inhibitor and regular attendance at a group center offering appropriate activities.

4. How would this drug be useful in treating AD?

The degeneration progressed rapidly over the next 2 years. The maximum dose of galantamine is no longer effective. He is confused about any change and not capable of performing simple activities. Communication is impaired, including that with family members.

5. Describe what might be expected in the final stage of AD.

CHAPTER SUMMARY

The brain and spinal cord are mapped in specific areas related to functions. Damage to a certain area results in a precise dysfunction and manifestations (focal signs) regardless of the exact cause. Damage to the right side of the brain (motor or sensory cortex) affects the contralateral side of the body. Loss of consciousness occurs when the RAS is depressed or large areas of the cerebral cortex are damaged. Aphasia, the inability to communicate, may be expressive, receptive, or a combination, and is often related to damage in Broca's area or Wernicke's area in the dominant hemisphere (left). Regeneration or replacement of neurons does not occur in the CNS.

Increased Intracranial Pressure

- The manifestations of *ICP* are common to all types of lesions in the brain and include a decreasing level of consciousness; headache; vomiting; increasing pulse pressure; papilledema; fixed, dilated pupil; and increasing CSF pressure.
- *Brain tumors*, both benign and malignant, cause focal effects and increased ICP, and are often life threatening.

Vascular Problems

- *Transient ischemic attacks* are caused by temporary reductions in blood supply, causing brief impairment of speech or motor function. They may serve as a warning of impending obstruction of blood flow.
- *Cerebrovascular accident* may result from atheroma, embolus, or hemorrhage causing total loss of blood supply to an area of the brain and subsequent infarction. Cerebral edema adds to the neurologic deficit during the first 48 hours. The presence of collateral circulation or immediate clot dissolution may minimize permanent damage.
- *Cerebral aneurysm* is frequently asymptomatic and undiagnosed until it is very large or rupture occurs.

Infections

- *Meningitis* is frequently caused by meningococcus, often carried in the upper respiratory tract, but a variety of other microbes may cause infection depending on the individual circumstances. Inflammation and swelling of the meninges leads to increased ICP, but no focal signs are present. Typical signs are severe headache, nuchal rigidity, photophobia, lethargy, and vomiting.

Injuries

- *Brain injury* may be mild with only transient dysfunction (e.g., concussion) or very serious with extensive damage to brain tissue (e.g., compound skull fracture). Inflammation and bleeding will create increased ICP and focal signs will reflect both the primary site and contrecoup injury. Secondary brain damage may be caused by hematoma formation, infection, or ischemia due to shock or other systemic factors.
- *Spinal cord injury* may result from a dislocation or fracture of a vertebra related to flexion, hyperextension, compression, or penetration injury. Additional neurologic damage is caused by hemorrhage, inflammation, or vasospasm. Immediately after the injury, a period of spinal shock develops in which reflexes and all functions cease at and below the level of injury. Following this period, reflexes return below the level of injury, and other functions may return, depending on the extent of spinal cord damage and the level of the injury. Cervical injury is particularly dangerous because of the risk of respiratory failure related to phrenic nerve dysfunction.

Congenital Neurologic Disorders

- *Hydrocephalus* occurs in the neonate when excessive amounts of cerebrospinal fluid force separation of the cranial bones, enlargement of the head, and compression of brain tissue. A shunt may be used to reroute CSF to prevent continued damage.
- *Spina bifida* involves a number of developmental neural tube defects. In *myelomeningocele*, the most serious form, the spinal cord and nerves as well as meninges and CSF herniate through the vertebral defect, resulting in neurologic dysfunction at and below that level of the spinal cord.
- *Cerebral palsy* refers to a group of disorders resulting from brain damage during fetal development or in the neonate, all of which involve a motor disability. A variety of other abnormalities (e.g., seizures or cognitive impairment) is present in each child depending on the areas of the brain that are damaged.

- *Seizure disorders* consist of a diversity of conditions caused by intermittent episodes of excessive uncontrolled neuronal discharge in the brain. Generalized seizures of the tonic-clonic type (grand mal) follow a typical pattern of initial aura, loss of consciousness, tonic muscle contraction, a cry, clonic muscle contraction, cessation, and postictal recovery.

Chronic Degenerative Diseases

- *Multiple sclerosis* is marked by progressive loss of myelin from nerves in the CNS, resulting in a loss of motor, sensory, and autonomic functions. The clinical effects vary with the individual, depending on the specific areas affected and the number of exacerbations.
- *Parkinson's disease* involves a deficit of dopamine caused by degenerative changes in the basal nuclei. Extrapyramidal dysfunction leads to tremors, muscular rigidity, and loss of the commonly associated involuntary movements such as arm swinging.
- *Amyotrophic lateral sclerosis* is a disorder marked by degeneration of upper and lower motor neurons, hence by progressive wasting of skeletal muscle, whereas other functions such as intellect persist.
- *Huntington's disease* is unusual because the effect of the autosomal dominant trait is not evident until midlife. Atrophy of the brain and decreased neurotransmitters cause choreiform movements and progressive cognitive impairment.
- *Alzheimer's disease* is a form of dementia or progressive loss of intellectual function and personality changes. Cortical atrophy and other pathologic changes in the neurons disrupt conduction, and in time all functions deteriorate.

Mental Disorders

- *Schizophrenia* is linked to specific chemical and physical abnormalities in the brain, resulting in disorganized thought processes, delusions, or decreased responsiveness.
- *Depression* encompasses a number of mood disorders linked to deficits of excitatory neurotransmitters. It may also develop secondary to a number of systemic disorders.
- *Panic disorder* is diagnosed when panic attacks, periods of intense fear and anxiety, occur at frequent intervals and persist. Chemical imbalance is considered to be the underlying cause.

Spinal Cord

- *Herniated intervertebral disc* is a common problem in older individuals or in cases of spinal trauma or undue stress. A tear occurs in the annulus fibrosis, allowing the inner nucleus pulposus to protrude and exert pressure on the spinal nerve or root, causing pain and weakness.