The Nervous System

The nervous system is a highly complex and interconnected network of neurons and supporting neuroglia. Neural tissue is extremely delicate, and the characteristics of the extracellular environment must be kept within narrow homeostatic limits. When homeostatic regulatory mechanisms break down, under the stress of environmental factors, infection, or trauma, symptoms of neurological disorders appear.

There are literally hundreds of different disorders of the nervous system. A neurological examination attempts to trace the source of the problem through evaluation of the sensory, motor, behavioral and cognitive functions of the nervous system. Figure A-25 introduces several major categories of nervous system disorders. Many of these examples will be discussed in the sections that follow. Table A-17 summarizes representative infectious diseases of the nervous system.

THE SYMPTOMS OF NEUROLOGICAL DISORDERS

The nervous system has varied and complex functions, and the systems of neurological disorders are equally diverse. However, there are a few symptoms that accompany many different disorders.

- **Headache**: The majority of headaches (roughly 90 percent) are tension headaches due to muscle tension or migraine headaches that have both neurological and circulatory origins. Neither of these conditions is life-threatening.

- **Muscle weakness**: Muscle weakness can have an underlying neurologic basis, as noted in the section on muscle disorders (see Figure A-23, p. 64). The examiner must determine the origin of the symptom. Myopathies (muscle disease) must be differentiated from neurologic diseases such as demyelinating disorders, neuromuscular junction dysfunction, and peripheral nerve damage.

- **Paresthesias**: Loss of feeling, numbness, or tingling sensations may develop following damage to (1) a sensory nerve (cranial or spinal nerve) or (2) sensory pathways inside the CNS. The effects may be temporary or permanent. For example, a pressure palsy (p. 80) may last a few minutes, whereas the paresthesia that develops distal to an area of severe spinal cord damage (p. 75) will probably be permanent.
THE NEUROLOGICAL EXAMINATION

During a physical examination, information about the nervous system is obtained indirectly, by assessing sensory, motor, and intellectual functions. Examples of factors noted in the physical examination include:

- **State of consciousness:** There are many different levels of consciousness, ranging from unconscious and incapable of being aroused, to fully alert and attentive, to hyperexcitable.

- **Reflex activity:** The general state of the nervous system, and especially the state of peripheral sensory and motor innervation, can be checked by testing specific reflexes (p. 80). For example, the knee-jerk reflex will not be normal if damage has occurred in associated segments of the lumbar spinal cord, their spinal nerve roots, or the peripheral nerves involved in the reflex.

- **Abnormal speech patterns:** Normal speech involves intellectual processing, motor coordination at the speech centers of the brain, precise respiratory control, regulation of tension in the vocal cords, and adjustment of the musculature of the palate and face. Problems with the selection, production, or use of words often follow damage to the cerebral hemispheres, as in a stroke (p. 116).

- **Abnormal motor patterns:** An individual’s posture, balance, and mode of walking, or gait, are useful indicators of the level of motor coordination. Clinicians also ask about abnormal involuntary movements that may indicate a seizure, a temporary disorder of cerebral function (p. 77).

**Headaches**

Almost everyone has experienced a headache at one time or another. Diagnosis and treatment pose a number of problems, primarily because, as we noted earlier, headaches can be produced by a wide variety of underlying conditions. The most common causes of headache are either vascular or muscular problems.

Most headaches do not merit a visit to a neurologist. The vast majority of headaches are associated with muscle tension, such as tight neck muscles, but a variety of other factors may be responsible. For example, headaches may develop due to one of the following problems:

1. **CNS problems,** such as infections (meningitis, encephalitis, rabies) or brain tumors
2. **Trauma,** such as a blow to the head (p. 45)
3. **Cardiovascular disorders,** such as a stroke (p. 116)
4. **Metabolic disturbances,** such as low blood sugar
5. **Related muscle tension,** such as stiff neck or temporomandibular joint (TMJ) syndrome

<table>
<thead>
<tr>
<th>Disease</th>
<th>Organism(s)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hansen’s disease (leprosy)</td>
<td><em>Mycobacterium leprae</em></td>
<td>Progresses slowly; invades nerves and produces sensory loss and motor paralysis; cartilage and bone may degenerate. Inflammation of the spinal or cranial meninges</td>
</tr>
<tr>
<td>Bacterial meningitis</td>
<td><em>Haemophilus influenza</em></td>
<td><em>Haemophilus</em> meningitis; usually infects children (age 2 months–5 years); vaccine available</td>
</tr>
<tr>
<td></td>
<td><em>Neisseria meningitidis</em></td>
<td>Meningococcal meningitis; usually infects children and adults (age 5–40 years); treatment with antibiotics</td>
</tr>
<tr>
<td></td>
<td><em>Streptococcus pneumoniae</em></td>
<td>Streptococcal meningitis; usually infects adults over age 40; high mortality rate (40%)</td>
</tr>
<tr>
<td>Brain abscesses</td>
<td>Various bacteria</td>
<td>Infection increases in size and compresses the brain.</td>
</tr>
<tr>
<td><strong>Viral Diseases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Polioviruses</td>
<td>Polio has different forms; only one attacks motor neurons, leading to paralysis of limbs and muscle atrophy. Vaccine is available.</td>
</tr>
<tr>
<td>Rabies</td>
<td>Rabies virus</td>
<td>Virus invades the central nervous system through peripheral nerves. Untreated cases are fatal; treatment involves rabies antitoxin.</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>Various encephalitis viruses</td>
<td>Inflammation of the brain; fever and headache; no vaccine is available. Transmission occurs by mosquitoes. Eastern equine encephalitis is most lethal (50–75% mortality rate).</td>
</tr>
<tr>
<td><strong>Parasitic Diseases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African sleeping sickness</td>
<td><em>Trypanosoma brucei</em></td>
<td>Caused by a flagellated protozoan; infection occurs through bite of tsetse fly; infects blood, lymph nodes, and then nervous system. Symptoms include headache, tiredness, weakness, and paralysis, before coma and death; no vaccine is available.</td>
</tr>
</tbody>
</table>
Migraine headaches affect roughly 5 percent of the population. An individual with a classic migraine experiences visual or other sensory signals that an attack is imminent. The headache pain may then be accompanied by disturbances in vision or somatic sensation, extreme anxiety, nausea, or disorientation. The symptoms generally persist for several hours. A common migraine typically lacks any warning signs.

Evidence indicates that migraine headaches begin at a portion of the mesencephalon known as the dorsal raphe. Electrical stimulation of the dorsal raphe can produce changes in cerebral blood flow; several drugs with anti-migraine action inhibit neurons at this location. The most effective drugs stimulate a class of serotonin receptors that are abundant in the dorsal raphe.

The trigger for tension headaches probably involves a combination of factors, but sustained contractions of the neck and facial muscles are most commonly implicated. Tension headaches can last for days or can occur daily over longer periods, typically without the throbbing, pulsing sensations characteristic of migraine headaches. Instead, the person may complain of a feeling of pressure or viselike compression. Some tension headaches do not involve the muscles but accompany severe depression or anxiety.

Demyelination Disorders

Demyelination disorders are linked by a common symptom: the destruction of myelinated axons in the CNS and PNS. The mechanism responsible for this symptom differs in each of these disorders. We will consider only the major categories of demyelination disorders in this section.

- **Heavy metal poisoning**: Chronic exposure to heavy metal ions, such as arsenic, lead, or mercury, can lead to damage of neuroglia and to demyelination. As demyelination occurs, the affected axons deteriorate, and the condition becomes irreversible. Historians note several examples of heavy metal poisoning with widespread impact. For example, lead contamination of drinking water has been cited as one factor in the decline of the Roman Empire. In the seventeenth century, the great physicist Sir Isaac Newton is thought to have suffered several episodes of physical illness and mental instability brought on by his use of mercury in chemical experiments. Well into the nineteenth century, mercury used in the preparation of felt presented a serious occupational hazard for those employed in the manufacture of stylish hats. Over time, mercury absorbed through the skin and across the lungs accumulated in the CNS, producing neurological damage that affected both physical and mental function. (This effect is the source of the expression “mad as a hatter.”) More recently, Japanese fishermen working in Minamata Bay, Japan, collected and consumed seafood contaminated with mercury discharged from a nearby chemical plant. Levels of mercury in their systems gradually rose to the point that clinical symptoms appeared in hundreds of people. Making matters worse, mercury contamination of developing embryos caused severe, crippling birth defects.

- **Diphtheria**: Diphtheria (dif-THÊ-ri-uh; diphtheria, membrane + -ia, disease) is a disease that results from a bacterial infection of the respiratory tract. In addition to restricting airflow and sometimes damaging the respiratory surfaces, the bacteria produce a powerful toxin that injures the kidneys and adrenal glands, among other tissues. In the nervous system, diphtheria toxin damages Schwann cells and destroys myelin sheaths in the CNS. This demyelination leads to sensory and motor problems that may ultimately produce a fatal paralysis. The toxin also affects cardiac muscle cells, and heart enlargement and failure may occur. The fatality rate for untreated cases ranges from 35 to 90 percent, depending on the site of infection and the subspecies of bacterium. Because an effective vaccine exists, cases are relatively rare in countries with adequate health care.

- **Multiple sclerosis**: Multiple sclerosis (skler-Ö-sis; sklerosis, hardness), or MS, is a disease characterized by recurrent incidents of demyelination affecting axons in the optic nerve, brain, and/or spinal cord. Common symptoms include partial loss of vision and problems with speech, balance, and general motor coordination. The time between incidents and the degree of recovery varies from case to case. In about one-third of all cases, the disorder is progressive, and each incident leaves a greater degree of functional impairment. The average age at the first attack is 30–40; the incidence in women is 1.5 times that among men. Treatment with corticosteroid injections and interferon slow the progression of the disease in some patients. MS is discussed in more detail in a later section (p. 82).

- **Guillain-Barré syndrome**: Guillain-Barré syndrome is characterized by a progressive but reversible demyelination. Symptoms initially involve weakness of the legs, which spreads rapidly to muscles of the trunk and arms. These symptoms usually increase in intensity for 1–2 weeks before subsiding. The mortality rate is low (under 5 percent), but there may be some permanent loss of motor function. The cause is unknown, but because roughly two-thirds of Guillain-Barré patients develop symptoms within two months after a viral infection, it is suspected that the condition may result from a malfunction of the immune system. (The mechanism involved is considered in Chapter 14 of the text; see p. 446.)
Drugs and Synaptic Function

Many drugs interfere with key steps in the process of synaptic transmission. These drugs may (1) interfere with transmitter synthesis, (2) alter the rate of transmitter release, (3) prevent transmitter inactivation, or (4) prevent transmitter binding to receptors. The discussion that follows is limited to clinically important compounds that exert their effects at cholinergic synapses. Their sites of activity are indicated in Figure A-26.

Botulinus toxin is responsible for the primary symptom of botulism, a widespread paralysis of skeletal muscles. Botulinus toxin blocks the release of ACh at the presynaptic membrane of cholinergic neurons. The venom of the black widow spider has the opposite effect. It causes a massive release of ACh that produces intense muscular cramps and spasms.

Anticholinesterase drugs, sometimes called cholinesterase inhibitors, block the breakdown of ACh by acetylcholinesterase. The result is an exaggerated and prolonged stimulation of the postsynaptic membrane. At the neuromuscular junctions, this abnormal stimulation produces an extended and extreme state of contraction. Military nerve gases block cholinesterase activity for weeks, although few persons exposed are likely to live long enough to regain normal synaptic function. Most animals utilize ACh as a neurotransmitter, and anticholinesterase drugs, such as malathion, are in widespread use in pest-control projects.

Drugs such as atropine or d-tubocurarine prevent ACh from binding to the postsynaptic receptor. The latter compound is a derivative of curare, a plant extract used by certain South American tribes to paralyze their prey. Curare and related compounds induce paralysis by preventing stimulation of the neuromuscular junction by ACh. Atropine can also be administered intentionally to counteract the effects of anticholinesterase poisoning. Other compounds, including nicotine, an active ingredient in cigarette smoke, bind to the receptor sites and stimulate the postsynaptic membrane. There are no enzymes to remove these compounds, and the effects are relatively prolonged.

Table A-18 provides additional information on specific chemical compounds, their uses, and their sites of action.

Spinal Anesthesia

Injecting a local anesthetic around a nerve produces a temporary blockage of nerve function. This can be done peripherally, as when sewing up skin lacerations, or at sites around the spinal cord to obtain more widespread anesthetic effects. Although an epidural block, the injection of an anesthetic into the epidural space, has the advantage of affecting only the spinal nerves in the immediate area of the injection, epidural anesthesia may be difficult to achieve in the upper cervical, midthoracic, and lumbar regions, where the epidural space is extremely narrow. Caudal anesthesia involves the introduction of anesthetics into the epidural space of the sacrum. Injection at this site paralyzes lower abdominal and perineal structures. Caudal anesthesia may be used instead of epidural blocks in the lower lumbar or sacral regions to control pain during childbirth.

Local anesthetics may also be introduced into the subarachnoid space of the spinal cord. However, the effects spread as CSF circulation and diffusion distributes the anesthetic along the spinal cord. As a result, precise control of the regional effects can be difficult to achieve. Problems with overdosing are seldom serious, because the diaphragmatic breathing muscles are controlled by upper cervical spinal nerves. Thus respiration continues even when the thoracic and abdominal segments have been paralyzed.

Epidural and Subdural Hemorrhages

The most common cases of epidural bleeding, or epidural hemorrhage, involve a traumatic arterial leak. The arterial blood pressure usually forces considerable quantities of blood into the epidural...
space, distorting the underlying soft tissues of the brain. The individual loses consciousness from minutes to hours after the injury, and death follows in untreated cases.

An epidural hemorrhage involving a damaged vein does not produce massive symptoms immediately, and the individual may not develop symptoms until several hours to several days or even weeks after the original incident. Consequently, the problem may not be diagnosed until the nervous tissue has been severely damaged by distortion, compression, and secondary hemorrhaging. Epidural hemorrrages are rare, occurring in fewer than 1 percent of head injuries. This is rather fortunate, for the mortality rate is 100 percent in untreated cases and over 50 percent even after removal of the blood pool and closure of the damaged vessels.

In a subdural hemorrhage the blood accumulates between the dura and the arachnoid. Subdural hemorrhages are roughly twice as common as epidural hemorrhages. The most common source of blood is a small meningeal vein or one of the dural sinuses. Because the blood pressure is somewhat lower in the venous system, the extent and effects of this condition are more variable than those of the epidural hemorrhages.

### Meningitis

The warm, dark, nutrient-rich environment of the meninges provides ideal conditions for a variety of bacteria and viruses. Microorganisms that cause meningitis include bacteria associated with middle ear infections; pneumonia, streptococcal ("strep"), staphylococcal ("staph"), or meningococcal infections; and tuberculosis. These pathogens may gain access to the meninges by traveling within blood vessels or by entering at sites of vertebral or cranial

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### Table A-18 Drugs Affecting Acetylcholine Activity at Synapses

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Effects</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemicholinium</td>
<td>Blocks ACh synthesis</td>
<td>Produces symptoms of synaptic fatigue</td>
<td>Produced by bacteria; responsible for a deadly type of food poisoning</td>
</tr>
<tr>
<td>Botulinus toxin</td>
<td>Blocks ACh release directly</td>
<td>Paralyzes voluntary muscles</td>
<td>Administered as sedatives and anesthetics</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Decrease rate of ACh release</td>
<td>Muscular weakness, depression of CNS activity</td>
<td></td>
</tr>
<tr>
<td>Procaine (Novocain®, Lidocaine)</td>
<td>Reduces membrane permeability to sodium</td>
<td>Prevents stimulation of sensory neurons</td>
<td></td>
</tr>
<tr>
<td>Tetrodotoxin (TTX)</td>
<td>Blocks sodium ion channels</td>
<td>Eliminates production of action potentials</td>
<td>Produced by some marine organisms during normal metabolic activity</td>
</tr>
<tr>
<td>Saxitoxin (STX)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciguatoxin (CTX)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neostigmine</td>
<td>Prevents ACh inactivation by cholinesterase</td>
<td>Sustained contraction of skeletal muscles; other effects on cardiac muscle, smooth muscle,</td>
<td>Used clinically to treat myasthenia gravis and to counteract overdoses of tubocurarine</td>
</tr>
<tr>
<td>Insecticides (malathion, parathion, etc.), and nerve gases</td>
<td>As above</td>
<td>as above</td>
<td>Related compounds used in military nerve gases</td>
</tr>
<tr>
<td>d-tubocurarine</td>
<td>Prevents ACh binding to postsynaptic receptor sites</td>
<td>Paralysis of voluntary muscles</td>
<td>Curare produced by South American plant</td>
</tr>
<tr>
<td>Nicotine</td>
<td>Binds to ACh receptor sites</td>
<td>Low doses facilitate voluntary muscles; high doses cause paralysis</td>
<td>An active ingredient in cigarette smoke; very addictive</td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>Reduces sensitivity to ACh</td>
<td>Paralysis of voluntary muscles</td>
<td>Used to produce muscular relaxation during surgery</td>
</tr>
<tr>
<td>Atropine</td>
<td>Competes with ACh for binding sites on postsynaptic membrane</td>
<td>Reduced heart rate, smooth muscle activity; skeletal muscle weakness develops at high doses</td>
<td>Produced by deadly nightshade plant</td>
</tr>
</tbody>
</table>
injury. Headache, chills, high fever, disorientation, and rapid heart and respiratory rates appear as higher centers are affected. Without treatment, delirium, coma, convulsions, and death may follow within hours.

The most common clinical assessment involves checking for a “stiff neck” by asking the patient to touch chin to chest. Meningitis affecting the cervical portion of the spinal cord results in a marked increase in the muscle tone of the extensor muscles of the neck. So many motor units become activated that voluntary or involuntary flexion of the neck becomes painfully difficult if not impossible.

The mortality rate for viral and bacterial meningitis ranges from 1 to 50 percent or higher, depending on the type of virus or bacteria, the age and health of the patient, and other factors. There is no effective treatment for viral meningitis, but bacterial meningitis can be combated with antibiotics and the maintenance of proper fluid and electrolyte balance. The incidence of the most common form of bacterial meningitis, caused by *Haemophilus influenzae*, has been dramatically reduced by immunization.

**Spinal Cord Injuries and Experimental Treatments** EAP p. 240

At the outset, any severe injury to the spinal cord produces a period of sensory and motor paralysis termed *spinal shock*. The skeletal muscles become flaccid; neither somatic nor visceral reflexes function; and the brain no longer receives sensations of touch, pain, heat, or cold. The location and severity of the injury determine how long these symptoms persist and how completely the individual recovers.

Violent jolts, such as those associated with blows or gunshot wounds near the spinal cord, may cause *spinal concussion* without visibly damaging the spinal cord. Spinal concussion produces a period of spinal shock, but the symptoms are only temporary and recovery may be complete in a matter of hours. More serious injuries, such as vertebral fractures, usually involve physical damage to the spinal cord. In a *spinal contusion* hemorrhages occur in the meninges, pressure rises in the cerebrospinal fluid, and the white matter of the spinal cord may degenerate at the site of injury. Gradual recovery over a period of weeks may leave some functional losses. Recovery from a *spinal laceration* by vertebral fragments or other foreign bodies will usually be far slower and less complete. *Spinal compression* occurs when the spinal cord becomes physically squeezed or distorted within the vertebral canal. In a *spinal transection* the spinal cord is completely severed. At present surgical procedures cannot repair a severed spinal cord, but experimental techniques may restore partial function.

Spinal cord injuries often involve some combination of compression, laceration, contusion, and partial transection. Relieving pressure and stabilizing the affected area through surgery may prevent further damage and allow the injured spinal cord to recover as much as possible.

Two avenues of research are being pursued, one biological and the other electronic.

**Biological Methods.** A major biological line of investigation involves the introduction of stem cells and the biochemical control of nerve growth and regeneration. Treated with embryonic stem cells at the injury site 9 days after a crushing injury to the spinal cord, laboratory rats recovered some limb mobility and strength. Oligodendrocytes, astrocytes, and functional neurons developed at the injury site. Neural stem cells have also been proposed for the treatment of strokes, Parkinson’s disease, and Alzheimer’s disease. The recent discovery that the adult brain contains inactive stem cells has opened a new line of investigation: What are the factors that activate resident stem cells?

Neurons are influenced by a combination of growth promoters and growth inhibitors. Damaged myelin sheaths apparently release an inhibitory factor that slows the repair process. Researchers have made an antibody, IN-1, that inactivates the inhibitory factor released in the damaged spinal cords of rats. The treatment stimulates repairs, even in severed spinal cords.

A partial listing of compounds known to affect nerve growth and regeneration includes *nerve growth factor* (NGF), *brain-derived neurotrophic factor* (BDNF), *neurotrophin-3* (NT-3), *neurotrophin-4* (NT-4), *glial growth factor*, *glial maturation factor*, *cilary neurotrophic factor*, and *growth-associated protein 43* (GAP-43). Many of these factors have now been synthesized by means of gene-splicing techniques, and sufficient quantities are available to permit their use in experiments on humans and other mammals. Initial results are promising, and these factors in various combinations are being evaluated for treatment of CNS injuries and the chronic degeneration seen in Alzheimer’s disease and Parkinson’s disease.

**Electrical Methods.** Several research teams are experimenting with the use of computers to stimulate specific muscles and muscle groups electrically. The technique is called *functional electrical stimulation*, or FES. This approach commonly involves implanting a network of wires beneath the skin with their tips in skeletal muscle tissue. The wires are connected to a small computer worn at the waist. The wires deliver minute electrical stimuli to the muscles, depolarizing their membranes and causing contractions. With this equipment and lightweight braces, quadriplegics have walked several hundred yards and paraplegics several thousand. The Parastep™ system, which uses a microcomputer controller, is now undergoing clinical trials.

Equally impressive results have been obtained using a network of wires woven into the fabric of close-fitting garments. This provides the necessary stimulation without the complications and maintenance problems that accompany implanted wires. A
paraplegic woman in a set of electronic “hot pants” completed several miles of the 1985 Honolulu Marathon, and more recently a paraplegic woman walked down the aisle at her wedding.

Such technological solutions can provide only a degree of motor control without accompanying sensation. Everyone would prefer a biological procedure that would restore the functional integrity of the nervous system. For now, however, computer-assisted programs such as FES can improve the quality of life for thousands of paralyzed individuals.

**Hydrocephalus**

The adult brain is surrounded by the inelastic bones of the cranium. The cranial cavity contains two fluids, blood and cerebrospinal fluid (CSF), and the relatively firm tissues of the brain. Because the total volume cannot change, when the volume of blood or CSF increases, the volume of the brain must decrease. In a subdural or epidural hemorrhage the fluid volume increases as blood collects within the cranial cavity. The rising intracranial pressure compresses the brain, leading to neural dysfunction that, if not treated, ends in unconsciousness and death.

Any alteration in the rate of cerebrospinal fluid production is normally matched by an increase in the rate of removal at the arachnoid villi. If this equilibrium is disturbed, clinical problems appear as the intracranial pressure changes. The volume of cerebrospinal fluid will increase if the rate of formation accelerates or the rate of removal decreases. In either event the increased fluid volume leads to compression and distortion of the brain. Increased rates of formation may accompany head injuries, but the most common problems arise from masses, such as tumors or abscesses, or from developmental abnormalities or scarring after infection. These conditions have the same effect: they restrict the normal circulation and reabsorption of CSF. Because CSF production continues, the ventricles gradually expand, distorting the surrounding neural tissues and causing the deterioration of brain function.

Infants are especially sensitive to alterations in CSF volume that increase intracranial pressure, because the arachnoid villi, which reabsorb CSF, do not appear until roughly 3 years of age. As in an adult, if intracranial pressure becomes abnormally high, the ventricles will expand. But in an infant the cranial sutures have yet to fuse, and the skull can enlarge to accommodate the extra fluid volume. This can produce an enormously expanded skull, a condition called hydrocephalus, or “water on the brain.” Infant hydrocephalus (Figure A-27) often results from some interference with normal CSF circulation, such as blockage of the mesencephalic aqueduct or constriction of the connection between the subarachnoid spaces of the cranial and spinal meninges. Untreated infants often suffer some degree of mental retardation. Successful treatment usually involves the installation of a **shunt**, a bypass that either bypasses the blockage site or drains the excess cerebrospinal fluid. In either case, the goal is reduction of the intracranial pressure. The shunt may be removed if (1) further growth of the brain eliminates the blockage or (2) the intracranial pressure decreases following the development of the arachnoid villi at 3 years of age.

**Lumbar Puncture and Myelography**

Tissue samples, or biopsies, are taken from many organs to assist in diagnosis. For example, when a liver or skin disorder is suspected, small plugs of tissue are removed and examined for signs of infection or cell damage, or used to diagnose a tumor. Unlike many other tissues, however, neural tissue consists largely of cells rather than extracellular fluids or fibers. Tissue samples are seldom removed for analysis, because any extracted or damaged neurons will not be replaced. Instead, small volumes of cerebrospinal fluid (CSF) are extracted via a spinal tap and analyzed. CSF is intimately associated with the neural tissue of the CNS, and pathogens, cell debris, or metabolic wastes in the CNS will therefore be detectable in the CSF.

With the vertebral column flexed, a needle can be inserted between the lower lumbar vertebrae and into the subarachnoid spaces with minimal risk to the cauda equina. This procedure, known as a **lumbar puncture**, can be used to remove 3–9 ml of CSF from the subarachnoid space or to introduce anesthetic drugs.

**Myelography** involves the introduction of radiopaque dyes into the CSF of the subarachnoid space. Because the dyes are opaque to X-rays, the CSF appears white on an X-ray photograph, as in Figure A-27 Hydrocephalus

This infant suffers from hydrocephalus, a condition usually caused by impaired circulation and removal of cerebrospinal fluid. CSF buildup in infancy leads to distortion of the brain and enlargement of the cranium.
Figure A-28. Any tumors, inflammations, or adhesions that distort or divert CSF circulation will be shown in silhouette.

In the event of severe infection, inflammation, or leukemia (cancer of the white blood cells), antibiotics, steroids, or anticancer drugs can be injected into the subarachnoid space.

**Amnesia**

Amnesia may occur suddenly or progressively, and recovery may be complete, partial, or nonexistent, depending on the nature of the problem. In **retrograde amnesia** (retro-, behind), the individual loses memories of past events. Some degree of retrograde amnesia often follows a head injury, and accident victims are frequently unable to remember the moments preceding a car wreck. In **anterograde amnesia** (antero-, ahead), an individual may be unable to store additional memories, but earlier memories are intact and accessible. The problem appears to involve an inability to generate long-term memories. At least two drugs—**diazepam** (Valium) and **Halcion**—have been known to cause brief periods of anterograde amnesia. A person with permanent anterograde amnesia lives in surroundings that are always new. Magazines can be read, chuckled over, and then reread a few minutes later with equal pleasure, as if they had never been seen before. Physicians and nurses must introduce themselves at every meeting, even if they have been visiting the patient for years.

**Posttraumatic amnesia** (PTA) often develops after a head injury. The duration of the amnesia varies depending on the severity of the injury. PTA combines the characteristics of retrograde and anterograde amnesia; the individual can neither remember the past nor consolidate memories of the present.

**Seizures and Epilepsy**

A **seizure** is a temporary disorder of cerebral function, accompanied by abnormal, involuntary movements, unusual sensations, and/or inappropriate behavior. The individual may or may not lose consciousness for the duration of the attack. There are many different types of seizures. Clinical conditions characterized by seizures are known as **seizure disorders**, or **epilepsies**. The term **epilepsy** refers to more than 40 different conditions characterized by a recurring pattern of seizures over extended periods. In roughly 75 percent of patients, no obvious cause can be determined.

Seizures of all kinds are accompanied by a marked change in the pattern of electrical activity monitored in an electroencephalogram. The alteration begins in one portion of the cerebral cortex but may subsequently spread to adjacent regions, potentially involving the entire cortical surface. The neurons at the site of origin are abnormally sensitive. When they become active, they may facilitate and subsequently stimulate adjacent neurons. As a result, the abnormal electrical activity can spread across the entire cerebral cortex.

The extent of the cortical involvement determines the nature of the observed symptoms. A **focal seizure** affects a relatively restricted cortical area, producing sensory and/or motor symptoms. The individual usually remains conscious throughout the attack. If the seizure occurs within a portion of the primary motor cortex, the activation of pyramidal cells will produce uncontrollable movements. The muscles affected or the specific sensations experienced provide an indication of the precise region involved. In a **temporal lobe seizure** the disturbance spreads to the sensory cortex and association areas, so the individual also experiences unusual memories, sights, smells, or sounds. Involvement of the limbic system may also produce sudden emotional changes. Often the individual will lose consciousness at some point during the incident.

**Convulsive seizures** are associated with uncontrolled muscle contractions. In a **generalized seizure** the entire cortical surface is involved.
Generalized seizures may range from prolonged, major events to brief, almost unnoticed incidents. Only two examples will be considered here, grand mal and petit mal seizures.

Most readers will think of an epileptic attack as involving powerful, uncoordinated muscular contractions affecting the face, eyes, and limbs. These are symptoms of a grand mal seizure. During a grand mal attack, the cortical activation begins at a single focus and then spreads across the entire surface. There may be no warning, but some individuals experience a vague apprehension or awareness that a seizure is about to begin. There follows a sudden loss of consciousness, and the individual drops to the floor as major muscle groups go into tonic contraction. The body remains rigid for several seconds before a rhythmic series of contractions occurs in the limb muscles. Incontinence may occur. After the attack, subsides, the individual may appear disoriented or sleep for several hours. Muscles or bones subjected to extreme stresses may be damaged, and the person will probably be rather sore for days after the incident.

Petit mal epileptic attacks are very brief (under 10 seconds in duration) and involve few motor abnormalities. Typically the individual simply loses consciousness suddenly, with no warning. It is as if an internal switch were thrown and the conscious mind turned off. Because the individual is “not there” for brief periods during petit mal attacks, the incidents are also known as absence seizures. During the seizure there may be small motor activities, such as fluttering of the eyelids or trembling of the hands.

Petit mal attacks usually begin between the age of 6 and 14 years. They can occur hundreds of times per day, so that the child lives each day in small segments separated by blank periods. The victim is aware of brief losses of consciousness that occur without warning but seldom seeks help because of embarrassment. Often he or she becomes extremely anxious about the timing of future attacks. However, the motor signs are so minor as to go completely unnoticed by other family members, and the psychological stress caused by this condition is often overlooked. The initial diagnosis is frequently made during counseling for learning problems. (You have probably taken an exam after missing 1 or 2 lectures of 20. Imagine taking an exam after missing every third minute of every lecture.)

Both petit mal and grand mal epilepsy can be treated with barbiturates or other anticonvulsive drugs, such as phenytoin sodium (dilantin).

The Basal Nuclei and Parkinson’s Disease

The basal nuclei contain two discrete populations of neurons. One group stimulates motor neurons by releasing acetylcholine (ACh), and the other inhibits motor neurons by the release of gamma aminobutyric acid (GABA). Under normal conditions the excitatory neurons remain inactive, and the descending tracts are primarily responsible for inhibiting motor neuron activity. If the descending tracts are severed in an accident, the loss of inhibitory control leads to a generalized state of muscular contraction known as decerebrate rigidity.

The excitatory neurons are quiet because they are continually exposed to the inhibitory effects of the neurotransmitter dopamine. This compound is manufactured by neurons in the substantia nigra and carried to synapses in the basal nuclei. If the ascending tract or the dopamine-producing neurons are damaged, this inhibition is lost and the excitatory neurons become increasingly active. This increased activity produces the motor symptoms of Parkinson’s disease, or paralysis agitans.

Parkinson’s disease is characterized by a pronounced increase in muscle tone. Voluntary movements become hesitant and jerky, a condition called spasticity, for a movement cannot occur until one muscle group manages to overpower its antagonists. Individuals with Parkinson’s disease show spasticity during voluntary movement and a continual tremor when at rest. A tremor represents a tug of war between antagonistic muscle groups that produces a background shaking of the limbs, in this case at a frequency of 4–6 cycles per second. Individuals with Parkinson’s disease also have difficulty starting voluntary movements. Even changing one’s facial expression requires intense concentration, and the individual acquires a blank, static expression. Finally, the positioning and preparatory adjustments normally performed automatically no longer occur. Every aspect of each movement must be voluntarily controlled, and the extra effort requires intense concentration that may prove tiring and extremely frustrating. In the late stages of this condition, other CNS effects, such as depression, hallucinations, and dementia often appear.

Providing the basal nuclei with dopamine can significantly reduce the symptoms for two-thirds of Parkinson’s patients, but intravenous dopamine injection is not effective, because the molecule cannot cross the blood-brain barrier. The most common procedure involves the oral administration of the drug L-DOPA (levodopa), a related compound that crosses the capillaries and is then converted to dopamine. Unfortunately, it appears that with prolonged treatment, the capillaries become less permeable to L-DOPA, so the required dosage increases. Surgery to control Parkinson’s symptoms has focused on the destruction of large areas within the basal nuclei or thalamus to control the motor symptoms of tremor and rigidity. The high rate of success for drug therapy has greatly reduced the number of surgical procedures. In 2001, electrical stimulation of the deep brain subthalamic nucleus by implanted wires and a pacemaker-like power pack to dramatically improved motor function in some patients. Recent attempts to transplant tissues producing dopamine or related compounds into the basal nuclei have met with limited success.
Variable results have been obtained with the transplantation of tissue from the adrenal gland. The transplantation of fetal tissue into adult brains has been more successful. Most individuals with Parkinson’s disease are elderly. However, since 1983 an increasing number of young people have developed this condition. In that year a drug appeared on the streets rumored to be “synthetic heroin.” The drug contained the contaminant named MPTP. This accidental by-product of the synthetic process destroys neurons of the substantia nigra, eliminating the manufacture and transport of dopamine to the basal nuclei. As a result of exposure to this drug, approximately 200 young, healthy adults developed symptoms of severe Parkinson’s disease. Why MPTP targets these particular neurons, and not all of the CNS neurons that produce dopamine, remains a mystery. MPTP has been used to give experimental animals Parkinson’s disease. Testing the animals speeds the development of more effective treatments.

### Huntington’s Disease

_Huntington’s disease_ is an inherited disease marked by a progressive deterioration of mental abilities. There are approximately 25,000 Americans with this condition. In Huntington’s disease the basal nuclei show degenerative changes, as do the frontal lobes of the cerebral cortex. The basic problem is the destruction of ACh-secreting and GABA-secreting neurons in the basal nuclei. The cause of this deterioration is not known. The first signs of the disease usually appear in early adulthood. As you would expect in view of the areas affected, the symptoms involve difficulties in performing voluntary and involuntary patterns of movement and a gradual decline in intellectual abilities leading eventually to dementia and death.

Tests can now detect the presence of the gene for Huntington’s disease, which is an autosomal dominant gene located on chromosome 4. In people with Huntington’s disease, a gene of uncertain function contains a variable number of repetitions of the nucleotide sequence CAG. This DNA segment appears to be unstable, and the number of repetitions can change from generation to generation. The duplication or deletion is thought to occur during gamete formation. For the larger the number of repetitions, the earlier in life the symptoms appear and the more severe the symptoms. The link between the multiple copies of the CAG nucleotide and the disorder has yet to be understood. There is no effective treatment. A victim’s children have a 50 percent risk of receiving the gene and developing Huntington’s disease.

### Cerebellar Dysfunction

Cerebellar function may be permanently altered by trauma or a stroke, or temporarily by drugs such as alcohol. Such alterations can produce disturbances in motor control. In severe ataxia balance problems are so great that the individual cannot sit or stand upright. Less-severe conditions cause an obvious unsteadiness and irregular patterns of movement. The individual often watches his or her feet to see where they are going and controls ongoing movements by intense concentration and voluntary effort. Reaching for something becomes a major exertion, for the only information available must be gathered by sight or touch while the movement is taking place. Without the cerebellar ability to adjust movements while they are occurring, the individual becomes unable to anticipate the time course of a movement. Most often, a reaching movement ends with the hand overshooting the target. This inability to anticipate and stop a movement precisely is called dysmetria (dis-MET-uh; dys- = bad + metron, measure). In attempting to correct the situation, the hand usually overshoots again in the opposite direction, and then again. This leaves the hand oscillating back and forth until either the object can be grasped or the attempt is abandoned. This oscillatory movement is known as an intention tremor.

Clinicians check for ataxia by watching an individual walk in a straight line; the usual test for dysmetria involves touching the tip of the index finger to the tip of the nose. Because many drugs impair cerebellar performance, the same tests are used by police officers to check drivers suspected of alcohol or other drug abuse.

### Shingles and Hansen’s Disease

In _shingles_, or _herpes zoster_, the _herpes varicella-zoster_ virus attacks neurons within the dorsal roots of spinal nerves and sensory ganglia of cranial nerves. This disorder produces a painful rash whose distribution corresponds to that of the affected sensory nerves (Figure A-29). Shingles develops in adults who were first exposed to the virus as children. The initial infection produces symptoms known as chicken pox. After this encounter the virus remains dormant within neurons of the anterior gray horns of the spinal cord. It is not known what triggers reactivation of this pathogen. Fortunately for those affected, attacks of shingles usually heal and leave behind only unpleasant memories.

Most people suffer only a single episode of shingles in their adult lives. However, the problem may recur in people with weakened immune systems, including those with AIDS or some forms of cancer. Treatment typically involves large doses of the antiviral drug acyclovir (Zovirax).

The condition traditionally called _leprous_, now more commonly known as _Hansen’s disease_, is an infectious disease caused by a bacterium, _Mycobacterium leprae_. It is a disease that progresses slowly, and symptoms may not appear for up to 30 years after infection. The bacterium invades peripheral nerves, especially those in the skin, producing sensory losses. Over time motor paralysis develops, and the combination of sensory and
motor loss can lead to recurring injuries and infections. The eyes, nose, hands, and feet may develop deformities as a result of neglected injuries. There are several forms of this disease; peripheral nerves are always affected, but some forms also involve extensive skin and mucous membrane lesions.

Only about 5 percent of those exposed develop symptoms; people living in the Tropics are at greatest risk. There are about 2000 cases in the United States, and an estimated 12–20 million cases worldwide. If detected before deformities occur, the disease can usually be treated successfully with drugs such as rifampin and dapsone. Treated individuals are not infectious, and the practice of confining "lepers" in isolated compounds has been discontinued.

Palsies

Peripheral nerve palsies, or peripheral neuropathies, are characterized by regional losses of sensory and motor function as the result of nerve trauma or compression. Brachial palsies result from injuries to the brachial plexus or its branches. Crural palsies involve the nerves of the lumbosacral plexus.

Although palsies may appear for several reasons, the pressure palsies are especially interesting. A familiar but mild example is the experience of having an arm or leg “fall asleep.” The limb becomes numb, and afterwards an uncomfortable “pins-and-needles” sensation, or paresthesia, accompanies the return to normal function.

These incidents are seldom of clinical significance, but they provide graphic examples of the effects of more serious palsies that can last for days to months. In radial nerve palsy, pressure on the back of the arm interrupts the function of the radial nerve, so that the extensors of the wrist and fingers are paralyzed. This condition is also known as “Saturday night palsy,” for falling asleep on a couch with your arm over the seat back (or beneath someone’s head) can produce the right combination of pressures. Students may also be familiar with ulnar palsy, which can result from prolonged contact between elbow and desk. The ring and little fingers lose sensation, and the fingers cannot be adducted.

Men with large wallets in their hip pockets may develop symptoms of sciatic compression after driving or sitting in one position for extended periods. As nerve function declines, the individuals notice some lumbar or gluteal pain, a numbness along the back of the leg, and a weakness in the leg muscles. Similar symptoms result from compression of the sciatic nerve by a distorted lumbar intervertebral disc. This condition is termed sciatica, and one or both legs may be affected, depending on the site of compression. Finally, sitting with your legs crossed may produce symptoms of a peroneal palsy. Sensory losses from the top of the foot and side of the leg are accompanied by a decreased ability to dorsiflex or evert the foot.

Reflexes and Diagnostic Testing

Many reflexes can be assessed through careful observation and the use of simple tools. The procedures are easy to perform, and the results can provide valuable information about damage to the spinal cord or spinal nerves. By testing a series of spinal and cranial reflexes, a physician can assess the function of sensory pathways and motor centers throughout the spinal cord and brain.

Neurologists test many different reflexes; only a few are so generally useful that physicians make them part of a standard physical examination. These reflexes are shown in Figure A-30.

The ankle jerk (Figure A-30a), biceps reflex (Figure A-30b), and triceps reflex (Figure A-30c) are stretch reflexes controlled by specific segments of the spinal cord. Testing these reflexes provides information about the corresponding spinal segments. For example, a normal patellar reflex, or knee jerk, indicates that spinal nerves and spinal segments L2-L4 are undamaged. The abdominal reflex (Figure A-30d), present in the normal adult, results from descending spinal facilitation. In this reflex, a light stroking of the skin produces a reflexive twitch in the abdominal muscles that moves the navel toward the stimulus. This reflex disappears following damage to descending tracts.

Abnormal Reflex Activity

In hyporeflexia normal reflexes are weak, but apparent, especially with reinforcement. In areflexia (a-re-FLEK-se-uh; a-, without) normal reflexes fail to appear, even with reinforcement. Hyporeflexia or areflexia may indicate temporary or permanent damage to skeletal muscles, dorsal or ventral nerve roots, spinal nerves, the spinal cord, or the brain.

Hyperreflexia occurs when higher centers maintain a high degree of facilitation along the spinal cord. Under these conditions reflexes are easily triggered, and the responses may be grossly exaggerated. This effect can also result from spinal cord compression or diseases that target

Figure A-29 Shingles

The left side of a person with shingles. The skin eruptions follow the distribution of dermatomal innervation.
higher centers or descending tracts. One potential result of hyperreflexia is the appearance of alternating contractions in opposing muscles. When one muscle contracts, it stimulates the stretch receptors in the other. The stretch reflex then triggers a contraction in that muscle, and this stretches receptors in the original muscle. This self-perpetuating sequence, which can be repeated indefinitely, is called clonus (KŁÖ-nūs). In a hyperreflexive person, a tap on the patellar tendon will set up a cycle of kicks, rather than just one or two.

A more extreme hyperreflexia develops if the motor neurons of the spinal cord lose contact with higher centers. Often, following a severe spinal injury, the individual first experiences a temporary period of areflexia known as spinal shock (p. 75). When the reflexes return, they respond in an exaggerated fashion, even to mild stimuli. For example, the lightest touch on the skin surface may produce a massive withdrawal reflex. The reflex contractions may occur in a series of intense muscle spasms potentially strong enough to break bones. In the mass reflex, the entire spinal cord becomes hyperactive for several minutes, issuing exaggerated skeletal muscle and visceral motor commands.

**Multiple Sclerosis**

Multiple sclerosis (MS), introduced in the discussion of demyelination disorders, is a disease that produces muscular paralysis and sensory losses through demyelination. The initial symptoms appear as the result of myelin degeneration within the white matter of the lateral and posterior columns of the spinal cord or along tracts within...
the brain. For example, spinal cord involvement may produce weakness, tingling sensations, and a loss of “position sense” for the limbs. During subsequent attacks the effects become more widespread, and the cumulative sensory and motor losses may eventually lead to a generalized muscular paralysis.

Recent evidence suggests that this condition may be linked to a defect in the immune system that causes it to attack myelin sheaths. MS patients have lymphocytes that do not respond normally to foreign proteins, and because several viral proteins have amino acid sequences similar to those of normal myelin, it has been proposed that MS results from a case of mistaken identity. For unknown reasons MS appears to be associated with cold and temperate climates. It has been suggested that individuals developing MS may have an inherited susceptibility to the virus that is exaggerated by environmental conditions. The yearly incidence within the United States averages around 50 cases for every 100,000 in the population. Improvement has been noted in some patients treated with interferon, a peptide secreted by cells of the immune system, and recently corticosteroid treatment has been linked to a slowdown in the progression of MS.

**Alzheimer’s Disease**  
**EAP p. 268**

In its characteristic form, Alzheimer’s disease produces a gradual deterioration of mental organization. The afflicted individual loses memories, verbal and reading skills, and emotional control. Initial symptoms are subtle—moodiness, irritability, depression, and a general lack of energy. These symptoms are often ignored, overlooked, or dismissed. Elderly relations may be viewed as “eccentric” or “irascible,” and humored whenever possible.

As the condition progresses, however, it becomes more difficult to ignore or accommodate. The victim has difficulty making decisions, even minor ones. Mistakes—sometimes dangerous ones—are made, either through bad judgment or simple forgetfulness. For example, the person might decide to make dinner, light the gas burner, place a pot on the stove, and go into the living room. Two hours later, the pot, still on the stove, melts into a shapeless blob and starts a fire that destroys the house.

As memory losses continue, the problems become more severe. The affected person may forget relatives, her home address, or how to use the telephone. The memory loss often starts with an inability to store long-term memories, followed by the loss of recently stored memories, and eventually the loss of basic long-term memories, such as the sound of the victim’s own name. The loss of memory affects both intellectual and motor abilities, and a patient with severe Alzheimer’s disease has difficulty in performing even the simplest motor tasks. Although by this time victims are relatively unconcerned about their mental state or motor abilities, the condition can have devastating emotional effects on the immediate family.

Individuals with Alzheimer’s disease show a pronounced decrease in the number of cortical neurons, especially in the frontal and temporal lobes. This loss is correlated with inadequate ACh production in the nucleus basalis of the cerebrum. Axons leaving this region project throughout the cerebral cortex, and when ACh production declines, cortical function deteriorates.

Most cases of Alzheimer’s disease are associated with unusually large concentrations of neurofibrillary tangles and plaques in the nucleus basalis, hippocampus, and parahippocampal gyrus. The tangles are intracellular masses of abnormal microtubular proteins. The plaques are extracellular masses that form around a core that consists of an abnormal protein called beta-amyloid. Beta amyloid is also found in other tissues, including the skin, blood vessels, subcutaneous layer, and intestine. Familial cases of Alzheimer’s disease are associated with mutations on either chromosome 21 or a small region of chromosome 14. A number of experimental protocols are undergoing clinical trials, but as yet there is no effective treatment for this condition.

**PROBLEMS WITH SENSORY SYSTEMS**  
**EAP p. 278**

A recurring theme of the text is that an understanding of how a system works enables you to predict how things might go wrong. You are already familiar with the organization and physiology of sensory systems, and some of the most important clinical problems were discussed in clinical comments on the preceding pages. Placing the entire array into categories provides an excellent example of a strategy that can be used to analyze any system in the body.

Every sensory system contains peripheral receptors, afferent fibers, ascending tracts, nuclei, and areas of the cerebral cortex. Any malfunction affecting the system must involve one of those components. Any clinical diagnosis requires seeking answers to a series of yes or no questions, eliminating one possibility at a time until the nature of the problem becomes apparent. Figure A-31 organizes the disorders considered in this chapter into a “trouble-shooting” format similar to that used to diagnose problems with automobiles or other mechanical devices.

**The Control of Pain**  
**EAP p. 278**

Pain management poses a number of problems for clinicians. Painful sensations can result from tissue damage or sensory nerve irritation; it may originate where it is perceived, be referred from another location, or represent a false signal generated along the sensory pathway (see Figure A-2, p. 12). The treatment differs in each case, and an accurate diagnosis is an essential first step.

When pain results from tissue damage, the most effective solution is to stop the damage and end the stimulation. This is not always possible.
Alternatively, the painful sensations can be suppressed at the injury site. Topical or locally injected anesthetics inactivate nociceptors in the immediate area. Aspirin and related analgesics reduce inflammation and suppress the release of irritating chemicals, such as enzymes or prostaglandins, in damaged tissues.

Pain can also be suppressed by inhibition of the pain pathway. Analgesics related to morphine reduce pain by mimicking the action of endorphins. Surgical steps can be taken to control severe pain, including (1) the sensory innervation of an area can be destroyed by an electric current, (2) the dorsal roots carrying the painful sensations can be cut (a rhizotomy), (3) the ascending tracts in the spinal cord can be severed (a tractotomy), or (4) thalamic or limbic centers can be stimulated or destroyed. These options, listed in order of increasing degree of effect, surgical complexity, and associated risk, are used only when other methods of pain control have failed to provide relief.

The Chinese technique of acupuncture to control pain has recently received considerable attention. Fine needles are inserted at specific locations and are either heated or twirled by the therapist. Several theories have been proposed to account for the positive effects, but none is widely accepted. It has been suggested that the pain relief may follow endorphin release, but it is not known how acupuncture stimulates endorphin release; the acupuncture points do not correspond to the distribution of any of the major peripheral nerves.

Many other aspects of pain generation and control remain a mystery. Up to 30 percent of patients experience a significant reduction in pain after receiving a nonfunctional medication. It has been suggested that this “placebo effect” results from endorphin release triggered by the expectation of pain relief. Although the medication has no direct effect, the indirect effect can be quite significant.

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**Assessment of Tactile Sensitivities**

Regional sensitivity to light touch can be checked by gentle contact with a fingertip or a slender wisp of cotton. The two-point discrimination test provides a more detailed sensory map for tactile receptors. Two fine points of a drawing compass, bent paper clip, or other object are applied to the skin surface simultaneously. The subject then describes the contact. When the points fall within a single...
receptive field, the individual will report only one point of contact. A normal individual loses two-point discrimination at 1 mm (0.04 in.) on the surface of the tongue, at 2–3 mm (0.08–0.12 in.) on the lips, at 3–5 mm (0.12–0.20 in.) on the backs of the hands and feet, and at 4–7 cm (1.6–2.75 in.) over the general body surface.

Vibration receptors are tested by applying the base of a tuning fork to the skin. Damage to an individual spinal nerve produces insensitivity to vibration along the paths of the related sensory nerves. If the sensory loss results from spinal cord damage, the injury site can often be located by walking the tuning fork down the spinal column, resting its base on the vertebral spines.

Descriptive terms are used to indicate the degree of sensitivity in the area considered. Anesthesia implies a total loss of sensation; the individual cannot perceive touch, pressure, pain, or temperature sensations from that area. Hypesthesia is a reduction in sensitivity, and paresthesia is the presence of abnormal sensations, such as the pins-and-needles sensation when an arm or leg “falls asleep” due to pressure on a peripheral nerve. (Several types of pressure palsies producing temporary paresthesia were discussed on p. 80.)

Conjunctivitis

Problems with the accessory structures of the eye and ear are more common causes of abnormal sensory function than damage to the receptors or the innervation. The term conjunctivitis is more useful as the description of a symptom than as a name for a specific disease. A great variety of pathogens, including bacteria, viruses, and fungi, can cause conjunctivitis, and a temporary form of the condition may be produced by chemical or physical irritation (including even such mundane experiences as prolonged crying or peeling an onion).

Chronic conjunctivitis, or trachoma, results from bacterial or viral invasion of the conjunctiva. Trachoma is often highly contagious. Severe cases may disrupt the corneal surface and affect vision. The pathogen most often involved is *Chlamydia trachomatis*. Trachoma is a relatively common problem in southwestern North America, North Africa, and the Middle East. The condition must be treated with topical and systemic antibiotics to prevent scleral damage, eventual corneal damage, and vision loss.

Corneal Transplants

The cornea has a very restricted ability to repair itself, so corneal injuries must be treated immediately to prevent serious visual losses. To restore vision after corneal scarring, it is usually necessary to replace the cornea through a corneal transplant. Corneal replacement is probably the most common form of transplant surgery. Corneal transplants can be performed between unrelated individuals because there are no corneal blood vessels, and white blood cells that would otherwise reject the graft are unlikely to enter the area. Corneal grafts are obtained by posthumous donation; for best results the tissues must be removed within 5 hours after the donor’s death.

Glaucoma

If aqueous humor cannot enter the canal of Schlemm, the condition of glaucoma develops. Although drainage is impaired, production of aqueous humor continues, and the intraocular pressure begins to rise. The fibrous scleral coat cannot expand significantly, so the increasing pressure begins to distort soft tissues within the eye.

The optic nerve is not wrapped in connective tissue, for it penetrates all three tunics. When intraocular pressures have risen to roughly twice normal levels, distortion of the nerve fibers begins to affect visual perception. If this condition is not corrected, blindness eventually results.

Glaucoma affects roughly 2 percent of the population over 35, and in most cases the primary factors responsible cannot be determined. Because it is a relatively common condition—over 2 million cases in the United States alone—most eye exams include a test of intraocular pressure. Glaucoma may be treated by the application of drugs that constrict the pupil and tense the edge of the iris, making the surface more permeable to aqueous humor. Surgical correction involves perforating the wall of the anterior chamber to encourage drainage. This procedure is now performed by laser surgery on an outpatient basis.

Otitis Media and Mastoiditis

Otitis media is an infection of the middle ear, frequently of bacterial origin. Acute otitis media typically affects infants and children, and is occasionally seen in adults. The pathogens usually gain access via the auditory tube, usually during an upper respiratory infection. As the pathogen population rises in the tympanic cavity, white blood cells rush to the site, and the middle ear becomes filled with pus. Eventually the tympanum may rupture, producing a characteristic oozing from the external auditory canal. The bacteria can usually be controlled by antibiotics, the pain reduced by analgesics, and the swelling reduced by decongestants. In the United States it is rare for otitis media to progress to the stage at which tympanic rupture occurs.

Otitis media is extremely common in underdeveloped countries where medical care and antibiotics are not readily available. Both children and adults in these countries often suffer from chronic otitis media, a condition characterized by chronic or recurring bouts of infection. This condition produces scarring or perforation of the tympanic membrane, which leads to some degree of hearing loss. Resulting damage to the inner ear or the auditory ossicles may further reduce auditory sensitivity.
If the pathogens leave the middle ear and invade the air cells within the mastoid process, mastoiditis develops. The connecting passageways are very narrow, and as the infection progresses, the subject experiences severe earaches, fever, and swelling behind the ear in addition to symptoms of otitis media. Prompt antibiotic therapy is needed, and if the problem remains, the person may have to undergo mastoidectomy (opening and drainage of the mastoid sinuses). The major risk of mastoiditis is the spread of the infection to the brain by the connective tissue sheath of the facial nerve (N VII). Recurrent otitis media may be treated by myringotomy (drainage of the middle ear through a surgical opening in the tympanic membrane) with placement of a temporary tube in the tympanic membrane.

**Vertigo** EAP p. 299

The term vertigo describes an inappropriate sense of motion. This meaning distinguishes it from "dizziness," a sensation of light-headedness and disorientation that often precedes a fainting spell. Vertigo can result from abnormal conditions in the inner ear or from problems elsewhere along the sensory pathway. It can accompany CNS infection, and many people experience vertigo when they have high fevers.

Any event that sets endolymph into motion can stimulate the equilibrium receptors and produce vertigo. Placing an ice pack in contact with the temporal bone or flushing the external auditory canal with cold water may chill the endolymph in the outermost portions of the labyrinth and establish a temperature-related circulation of fluid. A mild and temporary vertigo is the result. Consumption of excessive quantities of alcohol and exposure to certain drugs can also produce vertigo by changing the composition of the endolymph or disturbing the hair cells.

Acute vertigo can also result from damage caused by abnormal endolymph production, as in Ménière’s disease. Probably the most common cause of vertigo is motion sickness. Motion sickness appears to develop when central processing stations receive conflicting sensory information. When you read in a boat or plane, for example, your eyes (which are tracking lines on a page) report that the book isn’t moving, but your inner ear reports that your body is lurching and turning. Why and how these conflicting reports result in nausea, vomiting, and other symptoms is not known.

**Testing and Treating Hearing Deficits** EAP p. 304

In the most common hearing test, a subject listens to sounds of varying frequency and intensity generated at irregular intervals. A record is kept of the responses, and the graphed record, or audiogram, is compared with that of an individual with normal hearing (Figure A-32). Bone conduction tests are used to discriminate between conductive and nerve deafness. If you put your fingers in your ears and talk quietly, you can still hear yourself because the bones of the skull conduct the sound waves to the cochlea, bypassing the middle ear. In a bone conduction test the physician places a vibrating tuning fork against the skull. If the subject hears the sound of the tuning fork in contact with the skull, but not when held next to the auditory meatus, the problem must lie within the external or middle ear. If the subject remains unresponsive to either stimulus, the problem must be at the receptors or along the auditory pathway.

Several effective treatments exist for conductive deafness. A hearing aid overcomes the loss in sensitivity by simply increasing the intensity of sound. Surgery may repair the tympanic membrane or free damaged or immobilized ossicles. Artificial ossicles may also be implanted if the originals are damaged beyond repair.

There are few possible treatments for nerve deafness. Mild conditions may be overcome by the use of a hearing aid if some functional hair cells remain. In a cochlear implant a small battery-powered device is inserted beneath the skin behind the mastoid process. Small wires run through the round window to reach the cochlear nerve, and when the implant “hears” a sound, it stimulates
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Increasing the number of wires and varying their implantation sites make it possible to create a number of different frequency sensations. Those sensations do not approximate normal hearing, because there is as yet no way to target the specific afferent fibers responsible for the perception of a particular sound. Instead, a random assortment of afferent fibers are stimulated, and the individual learns to recognize the meaning and probable origin of the perceived sound. Radio personality Rush Limbaugh received a multichannel cochlear implant in 2002, and congenitally deaf children with implants have learned normal speech.

A new approach involves inducing the regeneration of hair cells of the organ of Corti. Researchers working with other mammals have been able to induce hair-cell regeneration both in cultured hair cells and in living animals. This is a very exciting area of research, and there is hope that it may ultimately lead to an effective treatment for human nerve deafness.

CRITICAL-THINKING QUESTIONS

4-1. Ten-year-old Christina falls while climbing a tree and lands on her back. Her frightened parents take her to the local emergency room, where she is examined. Her knee-jerk reflex is normal, and she exhibits a plantar reflex (negative Babinski reflex). These results suggest that:

a. Christina has injured one of her descending nerve tracts.
b. Christina has injured one of her ascending nerve tracts.
c. Christina has a spinal injury in the lumbar region.
d. Christina has a spinal injury in the cervical region.
e. Christina has suffered no damage to her spinal cord.

4-2. Susan brings her husband, Jim, age 32, to the emergency room. Jim has been complaining of a severe headache for the last 12 hours. He has a temperature of 39°C (102°F) and a “stiff” neck and complains of pain when he moves his chin to chest. His reflexes are normal. A lumbar puncture is performed; the results of CSF analysis are reported as follows:

Analysis of CSF
- Microorganism: presence of *Streptococcus pneumoniae* (bacteria) detected by rapid latex agglutination tests for bacterial antigens
- Pressure of CSF: 201 cm H₂O
- Color of CSF: cloudy
- Glucose: 50 mg/dl
- Protein: 47 mg/dl
- Cell count (lymphocytes): 550 mm³

What is the likely diagnosis?

a. brain tumor
b. meningitis
c. cerebrovascular accident
d. multiple sclerosis

4-3. Tapping the calcaneal tendon of a normal individual with a rubber hammer will produce a reflex response. What response would you expect? What type of reflex is this? Describe the steps involved in the reflex. Discuss other reflexes of this type, and what can be learned by reflex testing.

4-4. Mrs. Glenn, 73 years old, has recently had trouble controlling her movements. Even when resting, she has continual, slight tremors and increased muscle tone to the point of rigidity. She visits her physician, who conducts a series of tests, including an assessment of her reflexes. What change or changes would you expect to see in Mrs. Glenn’s spinal reflexes?

4-5. Chelsea is mountain climbing with a group of friends when she slips, falls, and bumps the left side of her head on a rock. She gets up slowly and is dazed but otherwise appears unhurt. She feels able to proceed, and the climb continues. An hour later, Chelsea gets a severe headache and experiences a ringing in her ears. She starts having trouble speaking and soon loses consciousness. Before medical personnel can reach the scene, Chelsea dies. What was the likely cause of death?

4-6. Dave has a hypothalamic tumor that compresses the right medial surface of the optic chiasm posterior to the decussation. How would this condition affect his vision?

4-7. Mr. Romero, 62 years old, has trouble hearing people during conversations, and his family persuades him to have his hearing tested. How can the physician determine whether Mr. Romero’s problem results from nerve deafness or conductive deafness?