

in the first year after fracture compared with those without fracture. Delay until surgery after hip fracture increases mortality significantly.³¹⁹ Older women (more than 65 years) who survive the first year after a hip fracture may be at increased risk of death up to 5 years after the injury.^{207,300}

Many people are at high risk for premature death or loss of independence following fracture; mortality after fracture is higher among men than among women.^{41,46} Less than 50% of older adults with a hip fracture will regain their prior level of function.⁴⁵⁷ The inability to stand up, sit down, or walk 2 weeks after surgery is the strongest predictor for mortality among older adults with surgically repaired hip fractures.^{187,490}

A person's condition before fracture (especially that of older adults with hip fractures) has important prognostic implications. Older adults who fall within 6 months following a hip fracture are more likely to demonstrate poorer balance, slower gait speed, and greater decline in ADL from the prefracture level than those who do not fall.⁴⁵⁷

Healthy functional status contributes to faster recovery time with fewer complications and reduced medical expenses.⁸⁸ Negative predictors for healing include medications such as calcium channel blockers and NSAIDs, renal or vascular insufficiency, smoking, alcoholism, and diabetes mellitus. Treatment can also affect healing via inadequate reduction, poor stabilization and fixation, distraction damage to blood supply, and postoperative infection.

Associated complications such as nerve injury can occur, and it can take up to 12 to 18 months before reinnervation of the motor endplate is complete. Return of function is dependent upon this factor. If there are no signs of improvement by 7 months, spontaneous recovery is unlikely.⁵⁴⁰ Exploratory surgery may be indicated at that time.

SPECIAL IMPLICATIONS FOR THE THERAPIST 27-17

Fracture

PREFERRED PRACTICE PATTERNS

Besides the obvious practice patterns, complications from the fracture or the treatment for the fracture can result in skin, vascular, neurologic, and joint involvement beyond the effects associated with bony injury. In such cases, other corresponding practice patterns may apply. Criteria for fractures of the skull may be best described by the neuromuscular practice patterns.

4G: Impaired Joint Mobility, Muscle Performance, and Range of Motion Associated with Fracture

4H: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Joint Arthroplasty

4I: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Bony or Soft Tissue Surgery

7A: Primary Prevention/Risk Reduction for Integumentary Disorders

There are excellent resources regarding fractures available for the therapist managing fractures, including special considerations, orthopedic intervention, rehabilitation considerations, precautions, goals, and therapeutic exercise with expected time frames for healing and rehabilitation.^{61,202,259,430,440}

For the older adult, there are many potential consequences of fractures. These include biomechanical, functional, and psychologic effects that can limit function and result in considerable disability. Biomechanical consequences can include anorexia and weight loss, compression of abdominal contents and decreased lung function from kyphotic posture, and the risk of more fractures.

Chronic, debilitating pain and increased dependence on family and friends occur as part of the functional consequences. Often there is a significant decrease in the individual's ability to perform ADLs because of impaired physical function. These factors combined with depression and anxiety (and for some people, sleep disorders) results in psychologic consequences.⁴⁰⁴ The therapist must remain alert to all of these potential consequences when evaluating each client and planning the best approach to clinical management.

Tobacco use, especially cigarette smoking (both the nicotine and the smoke itself) exposes individuals to toxins that can delay bone healing considerably. Nicotine occupies receptor sites on the stem cells' surface that are intended for acetylcholine, a chemical that helps nerve cells communicate. Normally, stem cells turn into cartilage-forming cells needed to create the scaffold for callus development over the break.

Nicotine's effect on stem cells is to cause them to produce too much cartilage while at the same time blocking nerve transmission and delaying or preventing bone healing. Therapists should review the hazards of smoking with clients who have fractures and encourage smoking cessation or reduction. Using nicotine patches or gum immediately after bone injury may have the same negative effect as continuing to smoke.

Fall (Fracture) Prevention

Physical therapists can have a major impact on fall prevention, contributing to the savings of high costs to the health care industry by assessing for risk factors and preventing falls that lead to fractures (see Boxes 27-19 and 27-20).

Given the risk for fracture and other complications and associated emotional and monetary costs, falls are of significant concern for older adults, their families, and the health care system. Complications caused by falls are the leading cause of death from injury in men and women older than 65 years⁴³⁹; a cluster of falls has been observed in older individuals during the months preceding death.¹⁶⁰

INCIDENCE

Half of all older adults who fall die as a direct or indirect result of that fall; men are more likely to die after

Continued.

a fall than women. The fall rates and mortality rates from falls are on the rise in the United States.^{3,63,392} Other important statistics include the following:

- 13,700 people aged 65 years and older died from falls last year in the United States.⁷³
- At least one out of every four adults aged 65 and older will fall at least once during the next year; it is likely that older adults are falling even more often than is generally reported.⁵⁰
- Some sources say that one out of every three adults 65 years of age and older fall each year.^{181,203}
- 14% of adults who fall return to the hospital within 2 weeks.
- Falls are the second leading cause of traumatic brain injury among persons age 65 and older.^{91,352}
- Older adults who fall often sustain more severe head injuries than their younger counterparts.
- Falls are a major cause of intracranial lesions among older persons because of their greater susceptibility to subdural hematoma.⁹¹
- Even among older adults who do not sustain an injury during a fall, half cannot get up off the floor; this is a predictive factor for functional decline and/or death.^{500,503}
- The complaint of dizziness is one of the most common reasons older adults visit the doctor; the incidence of dizziness doubles, triples, and quadruples decade by decade from 60 to 80 years of age.⁵⁴¹
- Less than half (45%) of these cases (dizziness) are caused by vestibular problems.

RISK FACTORS AND RED FLAGS

Complex layers of skill are required to maintain balance in the upright position. Strength, coordination, endurance, flexibility, vision, vestibular control, and hearing are just a few of the skills involved.

At the same time, there are more than 400 risk factors identified for falls. It may be best to focus on the most common risk factors that are modifiable. Age is certainly a primary risk factor, and although age itself is not modifiable, we must be very aware of which adults are at risk requiring screening and intervention (Box 27-20). The rates of falls and fall injuries increase with age; adults 85 and older are four to five times more likely to injure themselves in a fall than adults ages 65 to 74; the risk of being seriously injured in a fall increases with age.⁴⁷⁷

Movement impairments, cognitive deficits, errors in judgment, and an unsafe environment are common hazards for the aging adult. Gait changes such as an increase in base of support or stride width increases the risk of falls.²⁶² The use of an assistive device such as a cane or walker is a risk factor, especially when learning to use it for the first time. Incontinence (including functional incontinence) is a risk factor by itself but when combined with any of these other risk factors raises the risk even more.

Gait or balance instability combined with muscle weakness is among the highest risk factors.¹⁶ Combine any one of these with side effects of medication, the use of alcohol or other drugs (especially when

Box 27-20

RISK FACTORS FOR FALLS

Age Changes

- Muscle weakness or imbalance
- Decreased balance
- Age-related changes in peripheral vestibular mechanisms
- Impaired proprioception or sensation
- Delayed muscle response, increased reaction time

Pathologic Conditions

- Pathologic fractures
- Vestibular disorders
- Orthostatic hypotension (especially before breakfast)
- Dehydration
- Neuropathies
- Osteoporosis
- Arthritis
- Amputation
- Visual or hearing impairment
- Cardiovascular disease
- Urinary incontinence
- Central nervous system disorder (e.g., stroke, Parkinson's disease, multiple sclerosis, traumatic brain injury, spinal cord injury, amyotrophic lateral sclerosis)
- Altered neuromuscular reflexes
- Depression; dementia or other cognitive impairments
- Anemia

Medications

- Antihypertensives
- Sedatives-hypnotics
- Tricyclic antidepressants
- Diuretics
- Narcotics
- Benzodiazepines (antianxiety)
- Phenothiazines
- Polypharmacology (use of more than four medications)

Environmental

- Poor lighting
- Throw rugs, loose carpet, complex carpet designs
- Cluster of electrical wires or cords
- Stairs without handrails
- Bathrooms without grab bars
- Slippery floors (water, urine, floor surface)
- Restraints
- Footwear, especially slippers

Other

- History of falls (past month)
- Abuse or assault of older persons
- Sedentary lifestyle
- Nonambulatory status requiring transfers
- Gait changes or limitations
 - Decreased stride length or speed
 - Increased stride width
 - Muscular weakness
- Postural instability
- Fear of falling⁵⁰⁶
- Use of assistive devices (e.g., walkers, cane)
- Use of alcohol or other drugs
- Sleep disturbance, sleep disorder, or insomnia

combined with medications), and multiple comorbidities and the risk for falls increases disproportionately.

Many gait disturbances really are a reflection of underlying red flag histories and risk factors. For example, visual impairments can cause increased sway and increased stride width. A past history of falls is a predictor of fear of falling, and a fear of falling will lead to changes in gait such as shorter stride length and slower speed.

Past history of joint replacement (knee) increases the risk of tripping, which increases the risk of falling and injury.³¹⁵ Painful feet from bunions, corns, overgrown or ingrown toenails, and other podiatric conditions are reported by 50% of older adults when asked. Loss of protective sensation in the feet occurs with diabetes or other peripheral neuropathies.

Neuromusculoskeletal impairments such as muscular weakness, loss of motion, and balance instability, especially when combined with comorbidities such as arthritis, Parkinson's disease, multiple sclerosis, stroke, and so on, can result in positive Trendelenburg's sign, uneven stride length, limping, uneven weight bearing, and many other changes in gait pattern.

Comorbidities such as osteoporosis, arthritis and other orthopedic problems, limb amputation, diabetes, dementia, chronic lung disease, stroke, and heart disease are actually more important than polypharmacy (use of four or more medications of any kind) as risk factors for falls, although polypharmacy is still an important risk factor.²⁷²

Many of the risk factors fall under the category of red flag histories, too. A past history of falls is one of the most important red flag histories. Obtaining an accurate history can be very challenging. Older adults may forget or deny problems with balance, coordination, and falls (or near falls). They may have lost self-confidence or experience postfall anxiety. Often they modify their behavior and activity level to avoid anything that might cause a fall, so they can honestly answer that they are not having any trouble with falls and have not fallen in the last weeks to months.

Meanwhile, their hygiene is poor because they are afraid to get in and out of the tub or shower. They may restrict and even eliminate community activities for fear of falling. Fear of falling (and especially the fear of not being able to get up) leads to self-imposed functional limitations such as prolonged sitting and all of the natural sequelae that come with an increasingly sedentary lifestyle. Predictors of fear of falling include the following:

- Past history of falls
- Use of assistive device
- Balance or gait instability
- Depression or anxiety

Gait and Movement Characteristics Associated with Falls

In the older adult, gait disturbances and gait changes are often an outward manifestation of an inward or other problem. The therapist should not seek to change the gait pattern *until* the underlying cause of the problem is known. Consider all of the following gait

characteristics associated with falls and assess carefully. Here are just a few³¹:

- Decreased gait speed and stride length (linked with weak hip extensors and ankle plantar flexors, reduced push-off phase, reduced ability to propel the body forward during gait)
- Increased stride frequency (linked with muscle weakness and impaired balance requiring increased duration of double support)
- Increased (wider) stance (neurologic changes in diabetes or other conditions, muscle weakness)
- Unsteady gait (speed changes abruptly when unintended and/or person cannot adopt new movement patterns when the task requires it; alcohol or other drug use, dizziness, side effect of medication, decreased ankle/knee proprioception)
- Grabbing for support or stumbling
- Decreased medial-lateral sway (gluteus medius weakness)
- Unsafe or incomplete transfers
- Poor sitting balance; difficulty sitting or unsafe sitting down
- Difficulty rising from a seated position

Visual Impairment

Bifocal or multifocal eyeglasses combined with decreased contrast sensitivity and decreased depth perception lead to bending the head up and down to see the edge of a step. Decreased peripheral vision results in increased postural sway necessary to find center; with decreased reaction times, client cannot regain lost balance, resulting in an injurious fall.

Blindness and visual impairment are among the 10 most common causes of disability in the United States, associated with shorter life expectancy and lower quality of life.³⁵³ Visual impairment (especially combined with cognitive deficits) can lead to errors in judgment such as climbing up on counters, overreaching, and the use of step stools, resulting in falls.

The therapist can assist in identifying possible untreated visual impairment by asking a few simple visual screening questions and making an appropriate referral when indicated:

- How much difficulty would you have recognizing a friend across the street? [Choose one.]

| | |
|---------------------|--------------------|
| No difficulty | Some difficulty |
| Moderate difficulty | Extreme difficulty |

- How much difficulty do you have watching television? [Choose one.]

| | |
|---------------------|--------------------|
| No difficulty | Some difficulty |
| Moderate difficulty | Extreme difficulty |

- When was the last time you had an eye examination in which the pupils were dilated (you had to wear the wraparound sunglasses after the examination)?

SCREENING QUESTIONS TO IDENTIFY HISTORY OF FALLS

It may be best to avoid asking the question, Do you have a fear of falling? It is less threatening to ask about

Continued.

the *degree of confidence* in performing an activity, especially for people who view admitting fear as a sign of weakness.^{302,502} It may be better to ask questions with answers on a continuum from "no confidence" to "complete (100%) confidence." For example:

- How confident are you when walking on sidewalks, grass, or uneven surfaces? [Choose one.]

| | |
|----------------------|----------------------|
| Not confident at all | Slightly confident |
| Moderately confident | Completely confident |

- How confident are you when getting in and out of a car? [Choose one.]

| | |
|----------------------|----------------------|
| Not confident at all | Slightly confident |
| Moderately confident | Completely confident |

- How confident are you when using a public restroom? [Choose one.]

| | |
|----------------------|----------------------|
| Not confident at all | Slightly confident |
| Moderately confident | Completely confident |

Follow-up questions may include the following:

- In the past month, have you had any falls?
- In the last month, have you slipped or tripped or lost your balance and almost fallen?
- In the last month, have you hit against furniture and bruised yourself?
- In the past month, have you landed on the floor? If yes, were you able to get up by yourself or without help?

TESTING

Tests and measures are important in identifying individuals at risk for falls and finding ways to reduce risk factors and prevent falls. The therapist should collect baseline data using validated, reliable tests, keeping in mind that many tests do not identify why the individual is at risk or what intervention strategies would be most effective.

Advances in technology are beginning to provide computerized assessments of sensory integration and motor control that can objectively identify and differentiate balance system disorders (e.g., NeuroCom, Biologix). Since these are not yet available in all facilities, other test measures must be relied upon. For example, the Semmes-Weinstein monofilament test (see Fig. 11-15) can be used to check the protective level of sensation in the feet; impairment of this peripheral system could be the primary risk factor for falls and subsequent fracture.

Decreased sensation in the feet associated with diabetic neuropathy can affect both the timing and quality of gait, requiring retraining of the somatosensory and vestibular systems to help compensate for the somatosensory deficit.^{398,359,541} A neurologic miscue can create footdrop and the toe hitting the ground can cause a fall, easily leading to a hip fracture or broken arm.

A loss of protective sensation and diminished information being received by the brain about how much muscle to use at corresponding sequences of toe-offs during gait can occur. Gait and strength training are important in the management of large fiber neuropathies

when impaired vibration, depressed tendon reflexes, and shortening of the Achilles tendon occur.⁵²⁸

At the same time, keep in mind that diabetes gait may occur independent of sensory impairment. The increased joint movement, wider stance, and slower pace demonstrated in some individuals with type 2 diabetes may be neurologic in origin and not related to muscle weakness or loss of sensation in the feet.^{398,399}

Test for ankle and knee proprioception. Determine the lowest threshold for detecting joint movement, determine the accuracy of joint position sense by comparing or matching each joint to the contralateral joint, and perform the joint repositioning test (test limb segment repositioning without the aid of vision).

Dizziness can be due to benign paroxysmal positional vertigo (BPPV) caused by particles containing calcium collected in a semicircular canal provoking episodes of spinning vertigo when the head is moved into certain positions. A canalith repositioning procedure (e.g., Epley maneuver, canalith repositioning treatment or CRT, liberatory maneuver) "cures" this problem by repositioning the person (from sitting to side lying or supine) to move particles out of the canal into the utricle, where they can be reabsorbed.

Test for BPPV by performing the Dix-Hallpike maneuver: assist the patient from sitting to supine with the head extended over the edge of the treatment table and rotated 45 degrees to the side of the suspected ear. A positive test result is present when nystagmus is induced after a delay of about 10 seconds. See further discussion in Chapter 38.

TEST FUNCTIONAL LIMITATIONS

The therapist should use a standardized fall assessment tool and use it consistently. An excellent resource for test tools is available: Falls Prevention for Older People: Resources: Screening Tools (<http://www.fallsprevention.org.au/resources.htm>; accessed July 17, 2007).

Tests for functional limitations are useful but do not necessarily identify the cause(s) of balance dysfunction. Many tests are available; the therapist should choose one that best matches the individual's current level of functioning. Some examples include the following:

- Berg Balance Scale: 14-item test measures balance on a continuum from sitting to standing. Valid and reliable measure of balance in older adults; predictive of individuals at risk; helps goal setting and directs intervention; use with lower-functioning patients.
- Timed Up and Go Test (TUGT): used to screen individuals at risk for falls. The client must be able to follow directions. Score of 13.5 seconds indicates that the individual is at risk for falls.
- One-Legged Stance Test: measures postural stability needed to make turns, climb stairs, get dressed, get in a car, step into a bathtub, or step up onto a curb. Risk of falls increases two times if test score is less

than 5 seconds; client is at risk if response is 12 seconds or less; marginal risk if response is 13 to 20 seconds; 20+ is considered "safe"; the individual must not sway more than 45 degrees to remain in the "safe" category.

- Sit-to-Stand: must be able to rise from a chair 10 times without using the arms in less than 20 seconds.
- Four Square Step Test (FSST): reliable, valid, easy to administer and score; timed test to assess the rapid change in direction while stepping over low objects and movement in four directions; requires higher level of cognitive function and ability to shift weight from one foot to the other while changing direction. Consider using with adults who report falls or near loss of balance as a result of hurrying. Correlates with Functional Reach Test and Timed Up and Go Test]; this means the tests measure similar constructs, so only one of the tests needs to be administered.¹⁰⁵

Predictive fall risk information can also be obtained and can be useful when putting together the plan of care; fall risk assessment for use with the acute care inpatient population and assessing fear of falling may be appropriate (Box 27-21). No one scale best predicts falls risk in older adults. The Activities-Specific Balance Confidence (ABC) Scale and Falls Efficacy Scale (FES) are highly correlated with each other. These two tests are moderately correlated with Survey of Activities and Fear of Falling in the Elderly (SAFE).²⁰⁵

The therapist should adopt a task- or function-oriented approach. This requires analysis of all the systems involved in the required movement. Rather than focus on individual exercise movements, identify the systems involved in the task and direct intervention to each of those systems.

For example, suppose the patient's goal is to be able to pick up objects from the floor. Physical therapy goals are to improve reactive responses to external challenge during stance and ambulation activities as measured by the following: Goal 1—Increase Berg Balance Scale score from 34/56 to 50/56 in 6 weeks; Goal 2—Increase Tinetti's Performance-Oriented Mobility Assessment (POMA) score from 19/28 to 24/28.

The intervention should be customized for each individual, targeting the specific underlying impairments, which may include the following:

- Task-specific activities in sitting, standing, and walking (including reaching; weight shifting; progressing from flat surfaces to rocker board, curbs)
- Functional strengthening of the ankle, hip, and trunk muscles
- Range of motion in the trunk, hip, lower extremity (especially ankle)
- Static and dynamic balance activities with lateral sway, reach, grasp, manipulation of arms
- Treadmill training

Keep in mind that general strengthening is not enough. Specific muscle groups must be targeted and given enough resistance to build strength. The ankle is considered the most important joint governing

Box 27-21

PREDICTIVE FALL RISK ASSESSMENT

- Functional reach test: must be able to reach 6 or more inches
- Tinetti's Performance-Oriented Mobility Assessment (POMA)/Tinetti's Balance Index: objectify gait and balance; predict risk of falls; can be used with people who have an assistive device; does not detect small changes in gait deviation—Gait Abnormality Rating Scale (GARS) is better for assessing early, minute gait deviations
- Dynamic Gait Index: provides predictive fall-risk information
- Gait Abnormality Rating Scale—Modified (GARS-M): used to assess risk of falling in community-dwelling, frail older adults based on several gait variables
- Physiologic Profile Assessment (PPA): series of simple tests of vision, peripheral sensation, muscle force, reaction time, and postural sway that are easy to administer quickly with minimal equipment²⁹⁰
- Measurement of vital signs and assessment for postural hypotension: these are important assessment tools in predicting falls

For Use with Acute Care Inpatient Population—Fall Risk Assessment

- STRATIFY: St. Thomas's Risk Assessment Tool in Falling Elderly Inpatients
- Hendrich II Fall Risk Model (<http://www.hartfordign.org/publications/trythis/issue08.pdf>)

Fear of Falling

- Falls Efficacy Scale (FES): good for adults who are frail
- Survey of Activities and Fear of Falling in the Elderly (SAFE): assesses 11 activities of daily living
- Activities-Specific Balance Confidence Scale (ABC): measure of balance confidence; good with higher functioning older adults; used in studies of amputee populations

balance.⁵⁵⁹ Older folks often have reduced ankle motion and strength; these deficits are linked with reduced balance.³²⁵ Check for loss of ankle motion; mobilize the calcaneus before stretching. Resistive exercises that produce overload of the hip extensors or ankle dorsiflexors are more effective in improving balance and reducing falls than general low-resistance exercises for the lower extremities.⁹⁵

EXERCISE AND FALL PREVENTION

Three types of exercise that can help prevent falls and fractures are balance training (prevents falls), strength training (builds bone and muscle), and aerobic training (builds muscle and endurance).

Walking while performing an additional attention-demanding cognitive task is a means to measure whether the client is able to walk automatically. The therapist can assess for dual-task interference, which is the worsening of performance of the main task (e.g., walking) as a result of simultaneously performing an attention-demanding cognitive task (e.g., counting backward).

Automaticity of the main task is reflected by a low or absent dual-task interference effect. Nonautomaticity

Continued.

can have an impact on daily living; gait changes caused by performing an additional cognitive task while walking are associated with increased risk of falling among older adults.^{36,520}

STEPS TO TAKE

Almost all hip fractures in older adults (over 65 years) are caused by falls, and very few are spontaneous, answering the question of whether falls are the result of fractures or vice versa.³⁷⁶ Hip fractures among older adults occur mainly in well-known environments, during everyday activities, and without overwhelming hazards, emphasizing again the importance of fall prevention/fracture reduction programs for all adults over age 65 years.

The CDC has recommended community-based falls prevention programs as an effective strategy based on research identifying interventions that can reduce falls. The therapist can be very instrumental in falls prevention by reviewing each of these with all clients age 65 and older. Four key fall prevention strategies are the following:

- Review of medications to reduce side effects and interactions
- Annual eye examination
- Regular exercise
- Reduction of fall hazards in every room of the home or facility

Modifying the environment is important; it may not prevent falls but it may reduce the severity of injury. The therapist should have the client and/or family complete an environmental safety check. Some studies show that this step is more effective when people are provided with a checklist and encouraged to make the changes themselves. An excellent checklist is available.³⁷¹

Fall-proofing homes; fall prevention education; osteoporosis and fall assessment; osteoporosis prevention (see Chapter 24); and exercise programs to improve balance, coordination, flexibility, strength, endurance, breathing, and posture are all important components of fall prevention and subsequent fracture prevention. Exercise to address all these components is key in fall prevention.⁴⁵⁸ For example, lower extremity weakness or loss of motion, particularly at the ankle and knee, is significantly associated with recurrent falls in the older adult population.^{323,539}

Specific intervention programs,³⁰⁴ exercise suggestions,^{162,170,450} and educational materials^{18,216} are available (Box 27-22). Sometimes even the simple step of teaching clients adequate hydration can improve their muscle strength, coordination, and balance, reducing risk for falls (see the section on Dehydration in Chapter 5).

Computerized assessments of sensory integration and motor control can objectively identify and differentiate balance system disorders. Through advances in technology, therapists are now better able to identify the underlying impairments that may increase a person's risk for falling.^{368,525} In addition, clinical risk factors predictive of fracture (e.g., age, gender, height, weight, use of walking aid, current smoking) have

Box 27-22

RESOURCES FOR FALLS ASSESSMENT AND PREVENTION

1. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention: Guidance for prevention of falls in older persons, *Ann Long Term Care* 9:42-47, 2001. Available on-line at http://www.healthinaging.org/public_education/falls_index.php. Accessed June 1, 2008.
 - Falls: General information
 - Medical Evaluation of Falls
 - Choosing a Cane or Walker
 - Choosing and Starting an Exercise Program
 - Improve Your Balance in 10 Minutes/Day
 - Decrease Your Risk of Falling
 - Tips for Patients with Low Vision
2. Department of Health and Human Services (HHS), Bureau of Primary Health Care: Lower Extremity Amputation Prevention (LEAP) program. Available on-line at www.hrsa.gov/leap. Accessed June 1, 2008.
3. Falls Prevention Project for Older Adults offers program manuals and training resources. Available on-line at www.temple.edu/older_adult. Accessed June 1, 2008.
4. Fall Risk Assessment for Older Adults: The Hendrich II Model. Available on-line at <http://www.hartfordign.org/publications/trythis/issue08.pdf>. Accessed June 1, 2008.
5. Falls Prevention for Older People: Resources: Screening tools. Available on-line at <http://www.fallsprevention.org.au/resources.htm>. Accessed June 1, 2008. Excellent web page that describes various testing tools for falls.
6. National Center for Injury Prevention and Control (NCIPC): Preventing falls among older adults. Available on-line at <http://www.cdc.gov/ncipc/duip/preventadultfalls.htm>. Accessed June 1, 2008. Lots of great patient education materials, checklists, posters, prevention strategies.
7. National Safety Council: Falls in the home and community. Available on-line at <http://www.nsc.org/issues/fallstop.htm>. Accessed June 1, 2008.
8. Stevens JA: Falls among older adults—risk factors and prevention strategies. Falls free: promoting a national falls prevention action plan. Washington, DC, 2005, National Council on Aging. Brochures and posters available in English, Spanish, and Chinese are available at <http://www.cdc.gov/ncipc/pub-res/toolkit/brochures.htm> with additional information at <http://www.cdc.gov/ncipc/pub-res/toolkit/toolkit.htm>. Accessed June 1, 2008.

been identified. The presence of five or more of these factors increases the rate of fracture (tested in white women).³³¹ These models have not been validated in other population groups.

Instituting and following a fall protocol in an extended or acute care facility may be able to reduce the incidence of repeated falls. The therapist can help staff set up a study to find out what time of day most falls occur and establish well-supervised small group activities during those times, especially for residents with dementia who are more likely to be put by themselves, get bored, and attempt to get up without assistance and fall. Residents of long-term care facilities may require individualized exercise interventions that can be adapted to their changing needs in reducing falls.³⁷⁵

Current use of physical restraints with acute care clients or residents of long-term care facilities is based largely on the assumption that these devices prevent falls and fall-related injuries. Numerous studies have reported a significant incidence of falls and injuries in restrained older adults rather than a lower risk of falls and injuries. With growing acceptance of restraint-free care as a standard of practice, therapists can be instrumental in educating personnel in these facilities of these findings when instituting a program.^{68,505}

A THERAPIST'S PERSPECTIVE

The vestibular system controls head, neck, and eye movements and is certainly an important component of balance and falls prevention. The three semicircular canals positioned in each spatial plane accurately sense head position and rapidly send signals to the eyes to keep our vision stable. After the age of 40, the number and size of vestibular neurons decrease. In individuals over the age of 70, 40% of the vestibular sensory cells are gone.^{40,471}

Vestibular impairment or dysfunction is certainly a possible cause of falls, and the therapist should test for this and intervene appropriately, but often the underlying etiologies are impairments of the peripheral systems feeding into the vestibular system. The vestibular system may react too little or inappropriately because external stimuli are deficient. Keep in mind that there may be other causes of vestibular system failure, which may not be failure at all but merely compensation for impairment or failure of other systems.

Take into consideration motor, visual, and especially oculomotor, vestibulomotor, and oculovestibular reflexes; it is not a single-system issue. The *visual* or *ocular system* determines movement and position in space and provides visual reference points. And the *proprioceptive* or *somatosensory* system consisting of pressure sensors in muscles, tendons, and joints (especially in the lower extremities) senses gravity and joint position. Any change in these systems can result in dizziness, fear of falling, and limited activity, leading to increased postural instability and contributing to further weakness and imbalance in a downward declining spiral of events.

Consider the effects of macular degeneration, loss of peripheral vision, and the loss of visual cueing mechanisms from these systems. A person may be able to compensate with one problem or system dysfunction, but when all three systems are impacted, it is much more difficult. The person starts to experience dizziness as the vestibular system tries to increase input. The person's natural tendency is to sit more to avoid dizziness and falls.

Sometimes use of a simple cane to increase peripheral messages can make a big difference. But what is the typical response to this? "That will make me look old." "I'd rather fall than use that thing." Issues of pride enter in; the individual is unwilling to use a cane to help increase proprioceptive cues to make up for a loss of vestibular, visual, or motor input. You may need to have an honest, frank discussion with that

person. Try to reframe the client's view of the situation into something more acceptable; for example, help the individual see this as a short-term situation or even consider using a more direct approach. For instance, convey the following information to your patient/client:

Studies show that 50% of the people over 65 who fall fracture their hip and do not return home from the hospital. They often end up in a nursing home or extended care facility. Fifty percent of those people die within 1 year. Are you going to let a simple cane keep you from going home? If you do not want to use a cane, then how about getting a walking stick and letting me help you learn how to use it to your best advantage?

The therapist can also help older adults determine their own problem list and solutions in order to effect successful changes in behavior by asking the following questions²⁷¹:

- What do you think is the problem?
 - What can be done to change your situation?
- Alternatively: What do you think will help?

- What needs to happen for you to be able to _____ (repeat what the person just told you)?
- Can you do it? Can you _____ (repeat back what the person said needs to happen).
- Will you do it?

If the patient/client hesitates, you can ask, "What is one thing you CAN do to improve matters?"

The therapist can also make some changes in how he or she practices in regards to screening individuals for falls risk, reducing or modifying risk factors, and preventing falls leading to fractures. If implementing a falls screening and prevention program for your facility seems too overwhelming, then at least choose one test and perform it consistently for 6 months or 1 year. Consider providing and/or participating in health fairs offering balance and posture screening.

Put together a task force with the express purpose of developing a screening checklist to fit your population base. Complete the checklist for every patient/client and conduct appropriate test measures. Make an appropriate referral sooner rather than later.

Stress Reaction/Fracture

In the case of individuals reporting isolated or pinpoint pain of the lower extremity associated with overuse in the presence of negative radiographic examination (x-ray), the therapist may need to assess further for the possibility of a stress fracture. This is also true for the client who shows minimal improvement (or a worsening of symptoms) following therapy intervention.

Applying a translational, rotational, or impact stress to the bone often reproduces the symptoms when the stressed bone lies deep within the tissue. Testing may start by applying a striking (percussive/compressive) force through the heel as the client lies supine and

Continued.

Box 27-23**DIFFERENTIATION OF STRESS REACTION/FRACTURE****Pubic Ramus**

- Adductors may be in spasm (adductor avulsion from stress fracture at the inferior ramus); limited abduction
- Negative heel strike/percussion test result
- Pain with activity that is relieved with rest, usually no pain at night
- Pain with resistance to the muscles of adduction and external rotation; positive Patrick's or FABER (hip and knee flexion, hip abduction, hip external rotation) test (e.g., pain is reproduced as the person tries to internally rotate from a position of external rotation)
- Gait may be normal or antalgic depending on the fracture location

Femoral Neck

- Vague, nonspecific description and onset of pain; unrelieved by rest; aggravated at night by rolling onto that side
- Positive Trendelenburg's sign (see Fig. 23-14) with compensated gait pattern
- Positive heel strike/percussion test; symptoms reproduced with hopping
- Positive test of femoral neck integrity (pain as person tries to externally rotate from an internally rotated position; may be unable to even assume test position in passive internal or medial rotation)*
- Noncapsular pattern (capsular pattern of the hip is defined as gross limitation of flexion, abduction, and medial rotation and slight limitation of extension with little or no limitation of lateral rotation)
- Localized tenderness at the greater trochanter unrelieved by treatment intervention for bursitis; pain may occur in the buttocks and/or groin

Tibia

- Painful pinpointed symptoms reproducible on palpation, frequently bilateral (one side more symptomatic than the other side); must be differentiated from shin splints
- Increased pain on weight bearing and walking (person assumes a wide-based waddling gait)
- May have a positive reaction to painful heel strike (more common in a hip fracture); symptoms reproduced with hopping

Adapted from Ozburn MS, Nichols JW: Pubic ramus and adductor insertion stress fractures in female basic trainees, *Mil Med* 146(5):332-334, 1981.

*This may be differentiated from trochanteric bursitis, which is characterized by painful hip abduction and lateral rotation (but not medial rotation).

observing for any associated increase in painful symptoms, especially at the hip or groin. Pull the leg into a position of internal rotation and resist as the person tries to externally rotate the leg; then move the leg into external rotation as the person tries to internally rotate the leg. For a differentiation of stress reactions of the femoral neck versus the pubic ramus, see Box 27-23.

Any suspicion of stress reaction/fracture warrants communication with the physician. Further imaging studies may be necessary. Any woman with a stress fracture should be evaluated for the female athlete

triad (amenorrhea, eating disorder, osteoporosis). Treatment of the underlying factors that contribute to the injury is important, including these three factors.⁵⁵⁰

Rehabilitation will vary depending on the age, condition, and goals of the affected individual. For example, rehabilitation for military personnel will differ greatly from that prescribed for a postmenopausal woman. Specifics of progressing an exercise program are available.⁴²⁷

Acute Care and Complications

Complications of fractures require vigilance on the therapist's part and possibly quick action. Significant swelling can occur around the fracture site, and if the swelling is contained within a closed soft tissue compartment, compartmental syndrome may occur (see the section on Soft Tissue Injuries in this chapter). Because of the progressively increased intra-compartmental pressure, nerve and circulatory compromise can occur. This condition may be acute or chronic. The compartment becomes exquisitely painful.

A thorough sensory and motor examination may be warranted. If the therapist notes skin changes, decreased motor function, burning, paresthesia, or diminished reflexes, physician contact is necessary. Permanent damage and loss of function may result if this condition is not treated. The therapist's examination may be helpful in establishing the extent of the injury and baseline function.⁵⁵¹

Another complication associated with fractures is fat embolism, a potentially fatal event. The risk of developing this condition is related to fracture of long bones and the bony pelvis, which contain the most marrow. The fat globules from the bone marrow (or from the subcutaneous tissue at the fracture site) migrate to the lung parenchyma and can block pulmonary vessels, decreasing alveolar diffusion of oxygen.

The initial symptoms typically appear 1 to 3 days after injury, but this complication can occur up to a week later. Subtle changes in behavior and orientation occur if there are emboli in the cerebral circulation. There may also be complaints of dyspnea and chest pain, diaphoresis, pallor, or cyanosis. A rash on the anterior chest wall, neck, axillae, and shoulders may develop. The onset of any of these symptoms warrants immediate physician contact.

Individuals with acute VCFs (see Fig. 24-5) can be difficult to treat, because pain and fear can be severe. Even when extra care is taken with logrolling techniques, transitional movements can be exquisitely painful, with the client crying and begging the therapist to stop.

Arranging for premedication 45 to 60 minutes before treatment is advised, followed by modalities to modulate the pain and promote relaxation before attempting movement or exercise. Adaptive equipment, from wheelchair modifications to spinal orthotics to assistive devices (e.g., reachers/grabbers, stocking aids, raised toilet seats, bed grab bars), helps

to improve posture, function, mobility, confidence, and independence.

The therapist must be alert to other complications that can occur following fracture, such as breakage of wires, displacement of screws, loss of fixation, refracture, delayed union and malunion, and infection.⁴⁵¹ Anyone on bed rest is at risk for complications from immobility, including constipation, deep vein thrombosis, pulmonary embolism, and pneumonia.

Fracture Rehabilitation

Like medical treatment, fracture rehabilitation is shaped by fracture type, need for reduction, presence of instability after reduction, and functional requirements of the affected individual. Postoperative rehabilitation begins anywhere from immediately to within 1 week after surgery depending on the physician's protocol.

There are some widely accepted guidelines and rehabilitation protocols for various types of fractures (e.g., Neer rehabilitation program for shoulder fractures, Vanderbilt program, Tinetti protocol of balance exercises for rehabilitation from hip fractures).^{280,501} The American Academy of Orthopaedic Surgeons offers guidelines for the rehabilitation of many different types of fractures. Several publications with fracture rehabilitation protocols are available specifically for the physical therapist.^{55,279,281,517,382}

Mortality rates following hip fractures in older adults may be improved by a more intensive rehabilitation program immediately after the operation. The best predictor of mortality immediately after hip fracture up to 1 year after fracture is the inability to stand up, an indicator of frailty.¹⁸⁷

Older adults admitted for care of a fall-related hip fracture should be evaluated early in their hospital stay to determine risk for falls following discharge. Indicators may include a previous history of falls and pre-fracture use of an assistive device for ambulation. The plan of care should include balance and mobility training to prevent future falls. A previous history of falls is a risk factor for future falls; poor balance, slow gait speed, and decline in ADLs have been identified in older adults who fall within 6 months following a hip fracture.⁴⁵⁷

Early mobilization accompanied by transfer training, and maintaining strength and range of motion after fracture surgery are essential to reduce the risk of deep vein thromboembolism, pulmonary or infectious complications, skin breakdown, and decline in mental status.

Following a fracture anywhere in the lower extremity (including the hip), some orthopedic surgeons advocate unrestricted weight bearing, advising the client to decide himself or herself how much weight to put on the leg. Stable fractures can usually tolerate weight bearing. Rotationally stable but potentially long unstable femur fracture may be allowed toe-touch weight bearing. Clients with vertically and rotationally unstable femoral fractures may be restricted to non-weight-bearing status using a wheelchair or electric scooter (if not in a spica hip cast).⁴¹⁴

Although immediate weight bearing may cause initial bone loss, the long-term success of achieving bone growth remains unchanged,⁴⁵⁴ and the short-term benefits of functional recovery and quicker return to independent living that accompany unrestricted weight bearing are important.^{257,391}

Again, depending on the type of fracture, some movements may be restricted to allow for proper fracture consolidation. Most importantly, a non-weight-bearing status can actually place greater forces on the hip as a result of the biomechanics involved in maintaining correct positioning of the lower extremity.^{208,357} In the case of femoral neck or intertrochanteric fractures, there is little biomechanical justification for restricted weight bearing; indeed, there is far greater pressure generated from performing a hip bridge while using a bedpan (almost equivalent to the effect of unsupported ambulation).²⁵⁷

Partial weight bearing is usually considered 30% to 50% of body weight. Touch or touch-down weight bearing is 10% of body weight, but this is a subjective decision that is not easily determined. Allowing for unrestricted weight bearing according to the client's tolerance (WBAT) is less restrictive, but the therapist must assess for intact cognition and decision-making abilities, intact sensation, upper body strength, vestibular function and balance, and proprioception before allowing unsupervised WBAT.

Early repair and physical therapy have been shown to reduce hospital stays, increase chances of returning home (rather than being discharged to a nursing facility or rehabilitation facility), reduce complications, and improve functional mobility and independence at discharge,^{163,250} and are associated with higher rates of 6-month survival.^{88,198} Therapists are encouraged to share the results of studies such as these with hospital administrators when developing fall and fracture prevention programs.

The literature supports recommending follow-up for strength and functional assessment 7 to 9 months after fracture.^{438,454} Muscle strength around the hip remains weak after hip fracture, with joint arthroplasty requiring an exercise program for strengthening for 1 year or longer.^{218,456} Short-term intervention with a therapist can be very cost effective in reducing refracture rates.^{454,455}

Older adults who receive physical therapy while still in the hospital following hip replacement for hip fracture are more likely to be discharged directly home rather than to a rehabilitation or assisted living facility.¹⁷⁵ People with hip fractures who receive additional home health visits are less likely to be hospitalized and more likely to need fewer medical visits, which usually translates into lower Medicare costs.²²¹

For clients with VCFs, the plan of care should include trunk extension strengthening and a cognitive-behavioral component to improve coping, especially for older adults. Improvements have been retained for at least 6 months in one randomized, controlled trial.¹⁵⁰

Osteochondroses

A number of clinical disorders of ossification centers (epiphyses) in growing children share the common denominator of avascular necrosis and its sequelae. These disorders are grouped together and referred to as the *osteochondroses*⁴³⁰ with multiple synonyms (epiphysitis, osteochondritis, aseptic necrosis, ischemic epiphyseal necrosis). There are additional eponyms based on the name of the person or persons who described the disorder as well, such as Kohler's disease (tarsal-navicular bone disease), Osgood-Schlatter disease, and Legg-Calve-Perthes disease.

The underlying etiologic factors and pathogenesis are similar in all these entities, and the clinical manifestations are determined by the stresses and strains present. Most susceptible areas are the epiphyses, which are entirely covered by articular cartilage and therefore poorly vascularized.

Osteochondritis Dissecans

Osteochondritis dissecans (OCD) is a disorder of one or more ossification sites with localized subchondral necrosis followed by recalcification. This condition affects the subchondral bone and the layer of articular cartilage just above. A piece of articular cartilage and fragment of bone separate and pull away from the underlying bone. These fragments can become loose bodies in the joint; the most common site of involvement is the medial femoral condyle.

OCD is caused by repetitive microtrauma resulting in ischemia and disruption of the subchondral growth. The articular cartilage softens, and fragment separation leads to cartilage injury that can progress to form a crater. Activity-related pain, swelling, and giving way are common symptoms. Pain is increased with passive knee extension and tibial internal rotation and relieved with tibial external rotation (Wilson's sign).

X-rays and MRI help confirm the diagnosis. Management varies with the person's age and the severity of the lesion and includes nonoperative management (activity modification, protected weight bearing, immobilization for 4 to 6 weeks) and operative treatment. Quadriceps strengthening and gradual return to activities follow immobilization. If conservative care is unsuccessful in bringing about healing, then surgery may be needed (e.g., microfracture, implant tissue to stimulate cartilage and bone growth).

Osteonecrosis

Overview and Incidence

The term *osteonecrosis* refers to the death of bone and bone marrow cellular components as a result of loss of blood supply in the absence of infection. *Avascular necrosis* and *aseptic necrosis* are synonyms for this condition.

The femoral head is the most common site of this disorder (sometimes called Chandler's disease), but other sites can include the scaphoid, talus, proximal humerus, tibial plateau, and small bones of the wrist and foot. Avascular necrosis is the underlying cause for 10% of

Box 27-24

CONDITIONS ASSOCIATED WITH OSTEONECROSIS

- Idiopathic
- Trauma (e.g., fall)
- Systemic lupus erythematosus
- Pancreatitis
- Diabetes mellitus
- Hyperlipidemia
- Cushing's disease
- Gout
- Sickle cell disease
- Alcoholism
- Obesity
- Pregnancy
- Medications
 - Oral contraceptives
 - Corticosteroids
 - Bisphosphonates (under investigation)
- Organ transplantation (medication related)
- Human immunodeficiency virus (HIV) infection
- Radiation therapy (less common)
- Dysbaric disease (deep sea diving; rare)

total hip replacement surgeries³⁶² and overall affects approximately 20,000 people annually, often between the second and fifth decades of life.²⁷⁰

Etiologic and Risk Factors

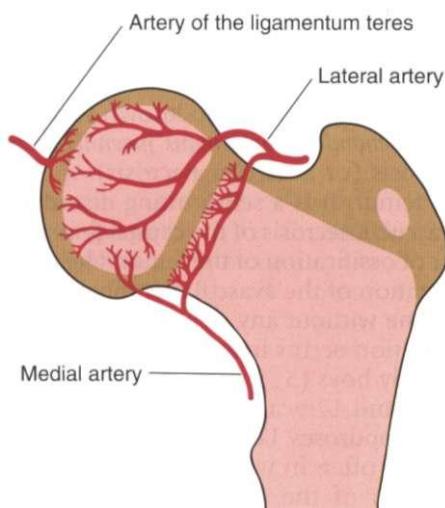
Osteocytic necrosis results from tissue ischemia brought on by the impairment of blood-conducting vessels. A minimum of 2 hours of complete ischemia and anoxia is necessary for permanent loss of bone tissue.²²⁴ The bony ischemia may be secondary to trauma disrupting the arterial supply or to thrombosis disrupting the microcirculation.

Bones or portions of bones that have limited collateral circulation and few vascular foramina are susceptible to avascular necrosis. Box 27-24 lists conditions associated with osteonecrosis. A number of these conditions are linked to osteonecrosis by the development of fat emboli (caused by altered fat metabolism) in the vascular tree of the involved bone.

The conditions associated with the development of fat emboli include alcoholism, obesity, pregnancy, pancreatitis, medications (e.g., oral contraceptives, corticosteroids), and unrelated fractures. Many cases of femoral head osteonecrosis are idiopathic (i.e., no known cause or risk factor can be identified).

Osteonecrosis has also been recognized as a complication in HIV-positive individuals; in fact, individuals who are HIV positive have a 100-fold greater risk of developing osteonecrosis than the general population.³⁵⁶ The exact mechanism for this remains unknown. It may be due to hyperlipidemia secondary to the use of protease inhibitors; however, avascular necrosis was reported before the era of highly active antiretroviral therapy (HAART).⁴¹⁶ It does not appear to be related to the degree of immunodeficiency.

More recently, the use of bisphosphonates has been linked with osteonecrosis of the jaw (sometimes referred

**Figure 27-26**

Blood supply to the femoral head in a child. (From Bullough PG: *Orthopaedic pathology*, ed 3, London, 1997, Mosby-Wolfe, p 263.)

to as "dead jaw syndrome"), especially after trauma to the teeth or bones of the jaw such as occurs with dental surgery (e.g., tooth extraction). The reason this happens is not entirely clear. Scientists hypothesize that since the jaw has a high rate of bone renewal in response to stress via generation of an inflammatory response by the gums and teeth, bisphosphonates keep osteoclasts from reabsorbing damaged bone cells in the jaw. The damaged bone builds up and eventually results in osteonecrosis.

This phenomenon is most likely to occur in individuals treated for bone cancer with intravenous bisphosphonates. The dosage of intravenous bisphosphonates can be as much as 12 times more than the oral bisphosphonate dosage prescribed for osteoporosis. Individuals with cancer treated this way also undergo other bone-weakening treatments (e.g., chemotherapy, radiation therapy).

Pathogenesis

Certain bones are more vulnerable to osteonecrosis than others. These bones are covered extensively by cartilage, have few vascular foramina, and have limited collateral circulation. The femoral head is a prime example of a bone at risk. The superolateral two thirds of the femoral head receives its blood supply almost entirely from the lateral epiphyseal branches of the medial femoral circumflex artery (Fig. 27-26).

The only other source of blood for the femoral head is the medial epiphyseal artery (contained within the ligamentum teres), which has limited anastomoses with the lateral epiphyseal vessels. Hip dislocation or fracture of the neck of the femur can compromise the precarious vascular supply to the head of the femur. The talus, scaphoid, and proximal humerus are also susceptible to osteonecrosis.

As the ischemia progresses, repair processes occur but are not capable of preventing necrosis and deformation of the bone, such as flattening and collapse of the femoral head. The articular cartilage and acetabulum are usually spared until late in the disease process, but the articular cartilage may be lifted off the underlying bone, resulting

in irreparable damage to the joint.²⁰¹ The entire process extends over many years, and unlike in osteochondrosis of immature bone (e.g., Legg-Calve-Perthes disease), spontaneous healing never occurs.

Clinical Manifestations

Often no symptoms are observed during the initial development of osteonecrosis even though an ischemic condition of the bone exists.²⁰¹ Hip pain is the usual initial presenting complaint, with a gradual onset, sometimes of many weeks' duration, before diagnosis. The pain may be mild and intermittent initially but will progress to become severe, especially during weight-bearing activities.

If the femur is involved, the pain may be noted in the groin, thigh, or medial knee area. An antalgic gait is noted, and pain provocation occurs with weight-bearing activities and hip range-of-motion exercises, especially internal rotation and flexion and adduction. The affected individual will report a slowly progressive stiffening of the joint. When fracture occurs, it is usually at the junction between necrotic bone and reparative bone, possibly extending down through the reparative interface to the healthy inferior cortex of the femoral neck.³⁴⁰

Eventually degenerative joint changes and osteoarthritis occur at the involved hip joint; the pathologic process is often relentless, with collapse of the femoral head imminent in spite of medical intervention.²⁰¹

Osteonecrosis of the jaw is characterized by exposed bone in the mouth, numbness or heaviness in the jaw, pain, swelling, infection, and loose teeth. Delayed or poor wound healing after dental surgery may be the first indication of a problem. Crepitus as the jaw opens and closes may be present and is often described as like the sound of someone walking on ice.

MEDICAL MANAGEMENT

DIAGNOSIS. Plain films may be normal initially. Bone scan, MRI, and CT scans are much more sensitive procedures and detect subtle bony changes.

TREATMENT. The choice between conservative and surgical intervention depends on the size of the lesion, how early the diagnosis is made, and whether bony collapse has occurred. If surgery is not indicated, protected weight bearing is essential to prevent collapse of the lesion.

Surgical intervention may consist of core decompression for small lesions without evidence of structural collapse (most common procedure in early diagnosis) to relieve pain and delay or prevent structural collapse, hemiarthroplasty, or total joint replacement.²⁰² Core decompression removes a core of bone from the femoral head and neck in an attempt to relieve intermedullary pressure, thereby promoting revascularization. This may be accompanied by bone grafting.⁴⁷⁵

Joint replacement may be required if femoral head collapse occurs or in order to prevent this complication. However, this procedure is limited by young age and high activity level as well as the limited life expectancy of the prosthesis.

New techniques for bone stimulation may be used, such as replacing the dead bone with living bone from

the individual's fibula to give added strength to the damaged area and possibly prevent or postpone joint arthroplasty in young individuals; see also the section on Fracture: Treatment in this chapter.

An osteotomy may be performed to shift the site to where maximal weight bearing occurs on a particular joint surface. Analgesics and NSAIDs are used for symptomatic relief of pain.

PROGNOSIS. The prognosis depends on the extent of damage that has occurred before diagnosis in the case of nontraumatic disease. Unfortunately, many cases are diagnosed in an advanced stage of disease, when minimally invasive surgical procedures are no longer helpful.²⁷⁰ Early intervention (both surgical and nonsurgical) has definitely improved the outcome, but many people with femoral head osteonecrosis experience irreversible damage to the joint and will need total arthroplasty.

SPECIAL IMPLICATIONS FOR THE THERAPIST 27-18

Osteonecrosis

PREFERRED PRACTICE PATTERNS

4G: Impaired joint Mobility, Muscle Performance, and Range of Motion Associated with Fracture

4H: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Joint Arthroplasty

4I: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Bony or Soft Tissue Surgery

Therapists are always advised to obtain a thorough and complete history from clients, especially in the presence of musculoskeletal manifestations of apparently unknown cause. Because osteonecrosis is difficult to identify early, knowledge of causative factors (see Box 27-24) is important. Differential diagnosis of lumbar, hip, thigh, groin, or knee pain is essential, because osteonecrosis may present referred pain and symptoms as if coming from any one of these.

When treating people at risk for osteonecrosis, therapists must consider the possibility of fracture if there is a sudden worsening of pain complaints followed by a sudden, dramatic loss in range of motion. Once the diagnosis is made, close communication with the physician is important for safe progression of weight bearing and exercise.

Following surgical intervention, the usual postoperative precautions and indications apply for minimization of complications (e.g., deep vein thrombosis), early mobilization, assessment for gait-assistive devices, gait training, demonstration of motion restrictions, and pain management.

In the case of microvascular bone transplantation, some physicians caution clients to avoid high-impact activities such as jumping, skiing, competitive tennis, and carrying more than 100 lb, although long-term studies of these stresses on repaired or reconstructed bones have not been carried out.

Legg-Calve-Perthes Disease

Definition and Overview

Legg-Calve-Perthes disease, also known as *coxa plana* (flat hip) and *osteochondritis deformans juvenilis*, is epiphyseal aseptic necrosis (or avascular necrosis) of the proximal end of the femur. It is a self-limiting disorder characterized by avascular necrosis of the capital femoral epiphysis (the center of ossification of the femoral head). Complete revascularization of the avascular epiphysis occurs over a period of time without any treatment.

This condition occurs in approximately 1 in 1200 children, primarily boys (5:1 ratio of boys to girls) between the ages of 3 and 12 years, making it the most common of the osteochondroses. Legg-Calve-Perthes disease occurs 10 times more often in whites than in blacks.

Deformation of the epiphysis with changes in the shape of the femoral head and the acetabulum occur during the process of revascularization in a significant portion of affected individuals. This may lead to degenerative arthritis in young adult life.²⁷² Changes in the shape of the acetabulum can be classified as type I (normal, concave acetabular margin), type II (flat, horizontal lateral acetabular margin), or type III (convex, sloping acetabular margin).¹⁶¹

Etiologic Factors

The direct cause is a reduction in blood flow to the joint, though what causes this is unknown. It may be that the artery of the ligamentum teres femoris closes too early, not allowing time for the circumflex femoral artery to take over. Genetic coagulopathy has been suggested,¹⁷⁶ possibly triggered by exposure to cigarette smoke in utero and during childhood.¹⁴⁹

Delay in bone age relative to the child's chronologic age suggests a possible general disorder of skeletal growth with focal expression in the hip. Mechanisms proposed to explain the delay in bone maturation include genetic, endocrine, nutritional, and socioeconomic factors.²⁷⁴

Pathogenesis

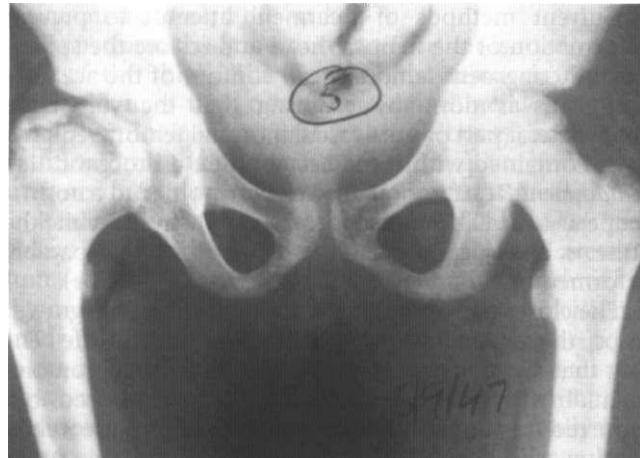
The disease process consists of four stages lasting from 2 to 5 years (Table 27-3 and Fig. 27-27). Because the growth plate of the femoral head lies above the insertion of the capsule of the hip joint in children and because the epiphyseal plate acts as a firm barrier to blood flow between the metaphysis and epiphysis, the femoral head depends on vessels that track along the surface of the neck of the femur to enter the epiphysis above the growth plate.

Injection studies have demonstrated that the most important vessels supplying the epiphysis are the lateral epiphyseal vessels. These vessels are vulnerable to interruption of blood flow by trauma or by increased intraarticular pressure. It is possible that in Legg-Calve-Perthes disease the ischemic events are episodic in nature and result from increased intraarticular pressure.⁶⁰

Delays in bone maturation observed with this disease are correlated with the stage of the disease. The decrease in bone age delay in the later stages of the disease indicates that as the disease progresses, bone maturation accelerates and tries to catch up with the chronologic age.

Table 27-3 Stages of Legg-Calvé-Perthes Disease

| Stage | Time Period | Pathogenesis |
|---|--------------|---|
| Avascular (stage I) | 1-2 wk | Quiet phase: spontaneous vascular interruption to the epiphysis causes necrosis of the femoral head with degenerative changes; hip synovium and joint capsule are swollen, edematous, and hyperemic; joint space widens; cells of the epiphysis die, but bone remains unchanged. |
| Revascularization (stage II; fragmentation stage) | 6-12 mo | Vascular reaction: new blood supply causes bone resorption and deposition of new bone cells; deformity from pressure on weakened area occurs; the entire or anterior one half of the epiphysis of the femoral head is necrotic; increased blood supply and decalcification of bone cause softening at the junction of the femoral neck and the capital epiphyseal plate; granulation tissue and blood vessels invade the dead bone, now detectable on radiographic examination. |
| Reparative (stage III; residual stage) | 2-3 yr | New bone replaces necrotic bone; the necrotic femoral head is replaced or surrounded by new bone (sometimes giving it an appearance of a head inside a head (see Fig. 27-27); collapse and flattening of the femoral head causes the femoral neck to become short and wide, with subluxation, progressive deformity, and even fracture possible. |
| Regenerative (intravascular) | Final months | Completion of healing or regeneration gradually reforms the head of the femur into live spongy bone; restoration of the femoral head to a normal shape is more likely in younger children and only if the anterior epiphysis was involved; residual deformity may exist in some cases that can lead to the gradual development of joint disease (osteoarthritis). |

**Figure 27-27**

Radiograph of lower pelvis in Legg-Calvé-Perthes disease after revascularization of the necrotic femoral head shows enlargement of the head, with the original necrotic ossification center seen as a "head within a head." (From Bullough PG: *Orthopaedic pathology*, ed 3, London, 1997, Mosby-Wolfe, p 263.)

This phenomenon is referred to as *bone maturation acceleration*. This process occurs earlier in the epiphyses of the lower ends of the radius and ulna and short bones of the hands compared to the carpal bones.²⁷⁴

Clinical Manifestations

The Legg-Calvé-Perthes condition is characterized by insidious onset, initially presenting as the intermittent appearance of a limp on the involved side with hip pain described as soreness or aching with accompanying stiffness. The pain may be present in the groin and along the entire length of the thigh following the path of the

obturator nerve or referred pain just in the area of the knee. There is usually pinpoint tenderness over the hip capsule.

Painful symptoms are aggravated by activity and fatigue and relieved somewhat by rest. Mild Legg-Calvé-Perthes disease is characterized by partial femoral head collapse, retention of a full range of hip abduction and rotation, and lack of subluxation on radiographic examination.

Delay in bone maturation is a common feature of this condition. Skeletal development is unevenly timed in the growing bones, with the maximum delay occurring in the distal limb segments. As the condition progresses, there are decreases in active and passive range of motion, as well as limited physiologic (accessory) motion affecting walking and running.

Severe Legg-Calvé-Perthes disease begins later and involves collapse of the whole femoral head, stiffness, and subluxation. Atrophy of the thigh musculature and restriction of hip abduction and rotation may develop. Short stature may develop as a result of epiphyseal dysplasia, and in those individuals who are left untreated, a flat femoral head will develop that is prone to degenerative joint disease.⁴¹³

Late complications in adults with a childhood history of Legg-Calvé-Perthes include early OA of the hip and acetabular labral tears. Hip, groin, or back pain may be the first symptom in affected adults. Postural asymmetry, leg length discrepancy, decreased range of motion, and decreased strength may be accompanied by an abnormal gait pattern.³⁷

MEDICAL MANAGEMENT

DIAGNOSIS. Physical examination, clinical history, and radiographic examination (Fig. 27-28) confirm the

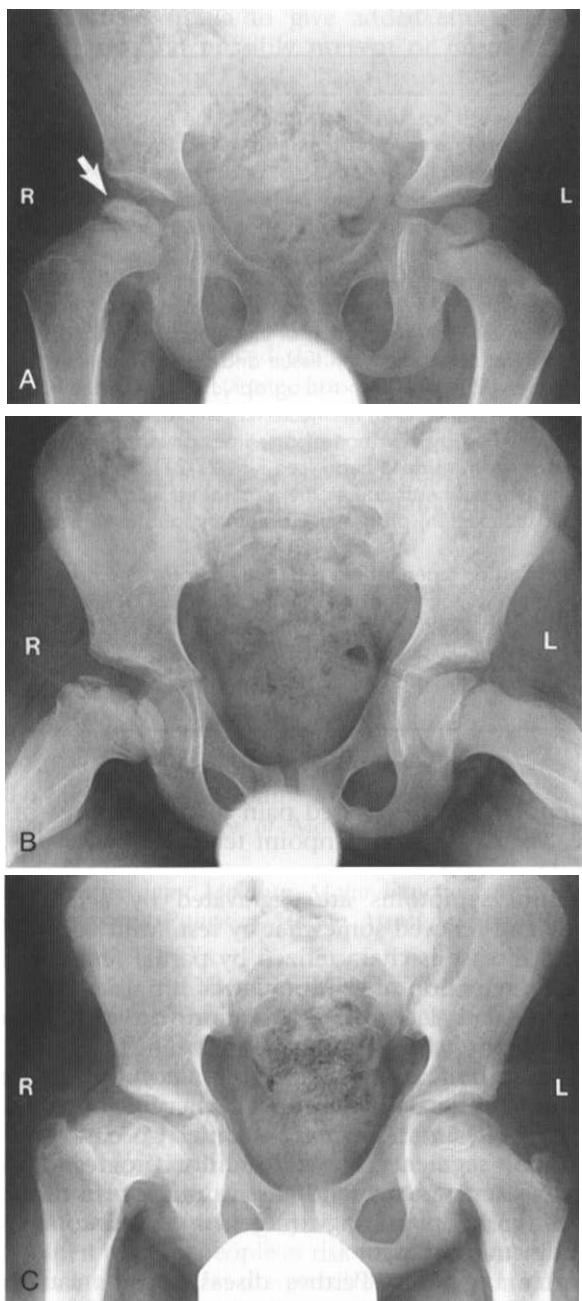


Figure 27-28

Legg-Calvé-Perthes disease. **A**, Anterior view of the pelvis demonstrates fragmentation and sclerosis of the right femoral epiphysis (arrow) in a 6-year-old male. **B**, Follow-up film obtained 8 years later shows continuing deformity resulting from osteonecrosis. **C**, The child developed significant degenerative arthritis by age 12. (From Mettler FA: Primary care radiology, Philadelphia, 2000, Saunders.)

diagnosis. MRI is widely accepted as the imaging method of choice, allowing early diagnosis and providing staging information necessary for adequate management.

There are several different classifications used to determine severity of disease and prognosis. The Catterall classification specifies four different groups defined by radiographic appearance during the period of greatest bone loss.

The Salter-Thomson classification simplifies the Catterall classification by reducing it down to two groups: group A (Catterall I, II), in which less than 50% of the ball is involved, and group B (Catterall III, IV), in which more than 50% of the ball is involved. Both classifications share the view that if less than 50% of the ball is involved, the prognosis is good, while more than 50% involvement indicates a potentially poor prognosis.

The Herring classification studies the integrity of the lateral pillar of the ball. In lateral pillar group A, there is no loss of height in the lateral one third of the head and little density change. In lateral pillar group B there is a lucency and loss of height of less than 50% of the lateral height. Sometimes the ball is beginning to extrude the socket. In lateral pillar group C there is more than 50% loss of lateral height.^{410a}

Many doctors utilize these classifications as they provide an accurate method of determining prognosis and help in determining the appropriate form of treatment.

TREATMENT. The goal of treatment is to limit deformity and preserve the integrity of the femoral head. Mild disease may not require intervention, but careful follow-up with radiographic examination every 3 months is needed to observe for deterioration and progression of the disease.³²⁷

Current methods of treatment attempt to prevent deformation of the femoral head and restore the spherical and congruent femoral head contour of the acetabulum. This is done by ensuring that the vulnerable anterolateral part of the avascular capital femoral epiphysis is contained within the acetabulum, a process called *containment*. The femoral head can be molded to a normal shape as it heals. The idea is to accomplish this while the bone is biologically plastic and before it is irreparably deformed.²³²

The closer to normal the femoral head is when growth stops, the better the hip will function in later life. The way that surgeons achieve this goal is through containment. In the past, weight bearing was minimized, but more recently, therapy allows the child to continue weight bearing with the femur in an abducted and internally rotated position. Keeping the head of the femur well seated in the acetabulum decreases focal areas of increased load and minimizes distortion, thereby maintaining range of motion and preventing deformity.

The femoral head must be held in the joint socket (acetabulum) as much as possible. It is better if the hip is allowed to move and is not held completely still in the joint socket. Joint motion is necessary for nutrition of the cartilage and for healthy growth of the joint. All treatment options for Legg-Calve-Perthes disease try to position and hold the hip in the acetabulum as much as possible. This healing process can take several years.

Conservative care is usually continued for 2 to 4 years. A variety of splints, braces, and positional devices may be used to maintain the proper position. When lack of motion has become a problem, the child may be admitted to the hospital and placed in traction. Traction is used to quiet the inflammation. Antiinflammatory medications may be prescribed. Physical therapy is used to

restore the hip motion as the inflammation comes under control. This process usually takes about a week. Home traction may also be an option.

In some cases, surgery will be required to obtain adequate containment. Sometimes, adequate motion cannot be regained with traction and physical therapy alone. If the condition is longstanding, the muscles may have contracted or shrunk and cannot be stretched back out.

To help restore motion, the surgeon may recommend a *tenotomy* of the contracted muscles. When a tenotomy is performed, the tendon of the muscle that is overly tight is cut and lengthened. This is a simple procedure that requires only a small incision. The tendon eventually scars down in the lengthened position, and no functional loss is noticeable.

Surgical treatment for containment may be best in older children who are not compliant with brace treatment or where the psychologic effects of wearing braces may outweigh the benefits. Surgical containment does not require long-term use of braces or casts. Once the procedure has been performed and the bones have healed, the child can pursue normal activities as tolerated.

Surgical treatment for containment usually consists of procedures that realign either the femur (thighbone), the acetabulum (hip socket), or both. Realignment of the femur is called a *femoral osteotomy*. This procedure changes the angle of the femoral neck so that the femoral head points more toward the socket.

To perform this procedure, an incision is made in the side of the thigh. The bone of the femur is cut and realigned in a new position. A large metal plate and screws are then inserted to hold the bones in the new position until the bone has healed. The plate and screws may need to be removed once the bone has healed.

Realignment of the acetabulum is called a *pelvic osteotomy*. This procedure changes the angle of the acetabulum (socket) so that it covers or contains more of the femoral head. To perform this procedure, an incision is made in the side of the buttock. The bone of the pelvis is cut and realigned in a new position. Large metal pins or screws are then inserted to hold the bones in the new position until the bone has healed. The pins usually must be removed once the bone has healed.

If there is a serious structural change in the anatomy of the hip, there may need to be further surgery to restore the alignment closer to normal. This is usually not considered until growth stops. As a child grows, there will be some remodeling that occurs in the hip joint. This may improve the situation such that further surgery is unnecessary.

In severe cases, both femoral osteotomy and pelvic osteotomy may be combined to obtain even more containment.

PROGNOSIS. Legg-Calve-Perthes disease may vary in severity from a mild self-healing problem with no sequelae to a condition that will destroy the hip unless serious action is taken. Early on, it may be difficult to determine which course the disease will follow.

Even though the disease is self-limiting, the prognosis varies according to the age of onset (better prognosis in children whose onset is before age 5 years). Children over

the age of 8 years at the time of onset have a better outcome with surgical treatment than with nonoperative care.¹⁹¹ There is some evidence to suggest that early delay in bone age (stage I of the disease) is linked with more severe disease.²⁷⁴

Older age, complete involvement of the femoral head, and noncompliance with treatment contribute to a poorer prognosis. Although girls are less likely to develop Legg-Calve-Perthes disease compared to boys, they often have a poorer prognosis. The reason for this difference is unknown.

A delay in bone age maturation of more than 2 years in stage I of the disease has been linked with greater severity of the disease. However, children with Legg-Calve-Perthes disease have a normal onset of puberty, and by the time they are 12 to 15 years old, their stature and bone age are the same as those of their peers.²⁶²

SPECIAL IMPLICATIONS FOR THE THERAPIST 27-19

Legg-Calve-Perthes Disease

PREFERRED PRACTICE PATTERNS

4B: Impaired Posture

4D: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Connective Tissue Dysfunction

4I: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Bony or Soft Tissue Surgery

Therapists may be involved in gait training, aquatic therapy, and range of motion exercises during this period. It should be emphasized to the child and family that Legg-Calve-Perthes disease is a long-term problem with treatment aimed at minimizing damage while the disease runs its course. Performing exercises daily is essential during the healing process to ensure that the femur and hip socket have a perfectly smooth interface. This will minimize the long-term effects of the disease. As sufferers age, problems in the knee and back can arise as a result of the abnormal posture and stride adopted to protect the affected joint.

Surgery may be performed to contain the femoral head in the acetabulum, especially in children older than 6 years with serious involvement of the femoral head. Hip replacements are relatively common during the sixth decade as the already damaged hip suffers routine wear; this varies from individual to individual.

See also Special Implications for the Therapist: Developmental Hip Dysplasia in Chapter 23. For specific intervention guidelines, the reader is referred to a more appropriate text.
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Osgood-Schlatter Disease

Overview

Osgood-Schlatter disease (osteochondrosis) results from fibers of the patellar tendon pulling small bits of immature bone from the tibial tuberosity. In the past,

Osgood-Schlatter was considered a form of osteochondritis (inflammation of bone and cartilage), but more recent thinking suggests that the process is one part of the spectrum of mechanical problems related to the extensor mechanism. Rather than being an actual degenerative "disease," Osgood-Schlatter is considered a form of tendinitis of the patellar tendon.

It is most commonly seen in active adolescent boys ages 10 to 15 years but can also affect girls ages 8 to 13 years. The ratio of boys to girls affected by Osgood-Schlatter disease is 3:1.

Etiologic Factors and Pathogenesis

Osgood-Schlatter disease is probably the result of indirect trauma (force produced by the sudden, powerful contraction of the quadriceps muscle during an activity) or repetitive stress (repeated knee flexion against a tight quadriceps muscle) before complete fusion of the epiphysis to the main bone has occurred. It is further aggravated by the longitudinal traction associated with bone growth in adolescents and the presence of external tibial torsion. Other causes include local deficient blood supply and genetic factors.

Another possible cause of Osgood-Schlatter lesions is abnormal alignment in the legs. Children who are knock-kneed or flat-footed seem to be most prone to the condition. These postures put a sharper angle between the quadriceps muscle and the patellar tendon. This angle is called the *Q angle*. A large Q angle puts more tension on the bone growth plate of the tibial tuberosity, increasing the chances for an Osgood-Schlatter lesion to develop. A high-riding patella, called *patella alta*, is also thought to contribute to development of Osgood-Schlatter lesions.³²⁶

In young athletes, the tendon is attached to prebone, which is weaker than normal adult bone. With excessive stresses on the tendon from running and jumping, the structure becomes irritated and a tendinitis begins. Often fragments representing cartilage or bone formations are found on the surface of the patellar tendon and are a potential cause of pain. These patellar tendon fibers can actually pull fragments away from the tibial epiphysis (Fig. 27-29).

Clinical Manifestations

Clinically, clients report constant aching and pain at the site of the tibial tubercle (just below the kneecap), which is often enlarged on visual examination. Symptoms are aggravated by any activity that causes forceful contraction of the patellar tendon against the tubercle, such as active knee extension or resisted knee flexion (e.g., going up or down stairs, running, jumping, biking, hiking, kneeling, squatting).

Besides the obvious soft tissue swelling, there may be localized heat and tenderness, the latter elicited with direct pressure over the tibial tubercle. Many children with this condition also have significant tightness in the hamstrings, iliotibial band, triceps surae (bellies of the gastrocnemius and soleus), and quadriceps muscles. Tightness in these areas can potentially increase the flexion moment and subsequent stresses at the tibial tubercle.

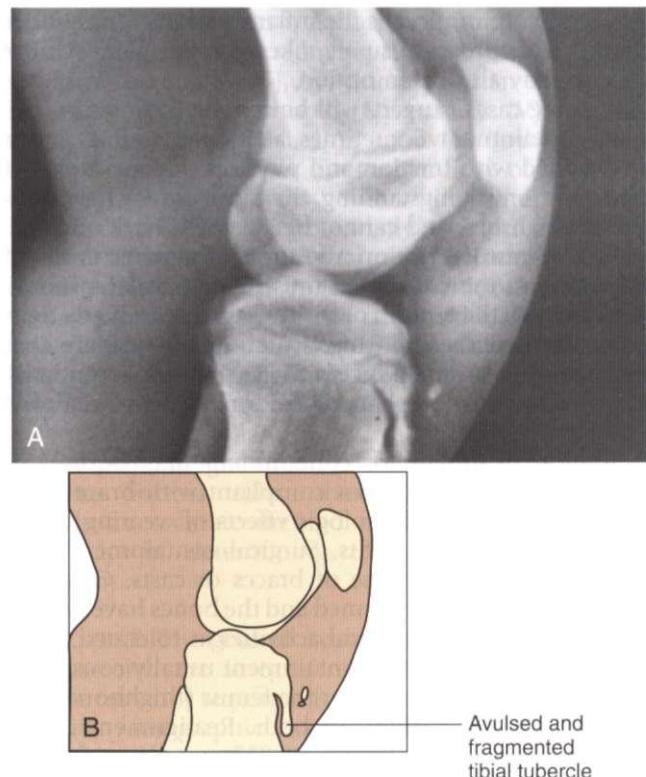


Figure 27-29

Clinical radiograph of the knee in a 12-year-old child shows fragmentation and avulsion of the tibial tubercle. Swelling below the knee and an enlarged tibial tuberosity may be observed clinically. This condition, known as Osgood-Schlatter disease, is probably posttraumatic. (From Bullough PG: *Orthopaedic pathology*, ed 3, London, 1997, Mosby-Wolfe, p 98.)

MEDICAL MANAGEMENT

DIAGNOSIS. On physical examination, the examiner forces the tibia into internal rotation while slowly extending the child's knee from 90 degrees of flexion; at about 30 degrees of knee flexion pain is reproduced that can be relieved by externally rotating the tibia.

Clinical diagnosis may be confirmed by radiograph (or ultrasonography to avoid exposure to x-ray), since many conditions are very similar (e.g., patellar tendinitis, chondromalacia patella, synovial plica). Although the films may be normal, epiphyseal separation, soft tissue swelling, and bone fragmentation can be visualized in many cases.

TREATMENT AND PROGNOSIS. Immobilization is no longer advocated with this condition, although rest from aggravating activities and/or activity modification is recommended until symptoms have subsided. This time frame ranges anywhere from 2 to 3 weeks in some individuals to 2 to 3 months or more in others. Enough time must be allowed for revascularization, healing, and ossification of the tibial tubercle before resumption of unrestricted athletic participation. NSAIDs and ice are used regularly.

Treatment should include exercises to address the mechanical inefficiencies of the extensor mechanism, stretching for any areas of inflexibility, and strengthening areas of weakness (e.g., ankle dorsiflexion, pain-free quadriceps strengthening).

Balance and coordination should be assessed and rehabilitation provided as appropriate. Support may be provided through the use of a knee sleeve, brace, or narrow strap around the leg placing pressure over the tibial tubercle. This latter device is used to reduce the pulling stresses of the patellar tendon on the tubercle and subsequently reduce pain.

About 90% of children with this condition respond well to nonoperative treatment. Complete recovery is expected with closure of the tibial growth plate.¹⁴⁷ Conservative measures are usually sufficient to provide pain relief and resolution of local swelling. Some individuals experience mild discomfort in kneeling;

activity restriction is imposed until the individual is symptom free.

When conservative care fails to resolve painful symptoms, full-extension immobilization of the leg through reinforced elastic knee support, cast, or splint may be prescribed for 6 to 8 weeks. In chronic, unresolved cases, surgery may be necessary to remove the epiphyseal ossicle that forms in the tendon. In extreme cases, the epiphysis may actually be removed or holes drilled into the tibial tubercle to facilitate revascularization of the area.

References

To enhance this text and add value for the reader, all references are included on the companion Evolve site that accompanies this textbook. The reader can view the reference source and access it on-line whenever possible. There are a total of 550 cited references and other general references for this chapter.

SECTION 4 PATHOLOGY OF THE NERVOUS SYSTEM

CHAPTER 28

Introduction to Central Nervous System Disorders

KENDA S. FULLER

OVERVIEW

The central nervous system (CNS) controls and regulates all mental and physical functions. The nervous system is unparalleled among organ systems in terms of diversity of cellular constituents. It is composed of a network of neural tissue that includes both receptors and transmitters. There is a complex interaction among the areas that control different functions. A variety of neurons provide transmission of specific information throughout the nervous system. Disease or trauma of the CNS may affect the nervous system through damage to several types of tissues in a local area, such as in stroke, or it may cause dysfunction in one type of tissue throughout many areas of the CNS such as in multiple sclerosis. Dysfunction of the neurons in an area of the brain can disrupt the complex organization of firing, resulting in abnormal perception of the environment, uncoordinated movement, loss of force production, and decreases in cognition.

Behavior, including thought and movement, is shaped by the interplay between genes and the environment. There are genes that control entry into the cell cycle where cells synthesize DNA and undergo mitosis. Proliferation can be triggered by internal signals or in response to external growth factor stimulation. There is a complex spectrum of alterations produced by aging, disease, and neoplastic transformation. Neoplastic transformation, which is the basis of cancer, is characterized by mutations of genes regulating cell growth, differentiation, and death. A set of genes appears to inhibit cellular proliferation; these genes are the "brakes" of the cell cycle, and loss of these genes may lead to tumor growth.¹⁶

Inherited patterns of deoxyribonucleic acid (DNA) expression appear to cause a predisposition for neurologic disease and affect the ability to repair damage from an insult in the nervous system. Genetic information is stored in the chromosomes within each individual cell in the body; about 80,000 genes are represented and arranged in a precise order. More than one-third of the genes are expressed as messenger ribonucleic acid (RNA) in the brain, more than in any other part of the body. An anomaly or alternative gene version is referred to as an *allele*. Single-gene mutations or alleles have been identified and can be associated with degenerative neurologic

disease such as Huntington's disease. However, for most chronic disorders, there appear to be multiple abnormalities, and it is clear that environmental conditions have an effect on how the abnormality is manifested.²

Pathologic derangements of normal cellular processes are a way of looking at possible causes of disease. Diseases in which cells are lost are characterized as necrotic and apoptotic. Both necrosis and apoptosis underlie diseases as diverse as stroke, trauma, demyelinating disorders, infections, and neurodegenerative disorders.

PATHOGENESIS

Cellular Dysfunction

Neuronal cell death is a hallmark of many disorders of the nervous system through the processes of necrosis and apoptosis. When cell death is caused by necrosis, there is cellular swelling, fragmentation, and cell disintegration. Necrosis causes the internal structure of the cell to swell as water enters the cell through osmosis and cell membranes to rupture. Lymphocytes and polynuclear cells can cause inflammatory cells to surround the necrotic debris, resulting in release of cytotoxic compounds and destruction of neighboring cells. Excitotoxicity results from the inappropriate activation of excitatory amino acid receptors leading to the entry of calcium ions into the cell. The calcium activates intracellular function. Damaged cells release excitotoxins that damage surrounding cells.¹⁶

Apoptosis is programmed cell death, or a type of cellular suicide, but apoptosis does not cause inflammatory responses. It is a more organized process with fragmentation of the cells and degradation of the DNA. It is common during the development of cells to eliminate the overproduction of one cell type. The biochemical pathway is present in all cells of the body and is used normally in the maturation and regulation of the nervous system with systematic removal of neurons from the brain. In apoptosis, the cell is removed by macrophages and leaves no residual damage to other components of the CNS. If the cell sustains genetic damage through neurodegenerative disease or injury and cannot be repaired by the system, the cell dies. Damage to the CNS can cause excessive apoptosis through the process of trophic factor withdrawal, oxidative insults, metabolic compromise,

overactivation of glutamate receptors, and exposure to bacterial toxins.³⁶ These processes are described in the next paragraphs.

The intensity of cellular injury determines whether the cell dies or is able to survive. Very severe injury leads to the passive process of necrosis, less severe but irreparable injury leads to the active process of apoptosis, and survivable injury leads to reactive changes such as gliosis or scarring.

Free radical formation is a by-product of excitotoxicity. Free radicals are capable of destroying cellular components and triggering apoptosis. Free radicals are molecules with an odd number of electrons. The odd, or unpaired, electron is highly reactive as it seeks to pair with another free electron. Free radicals are generated during oxidative metabolism and energy production in the body. Free radicals are related to normal metabolism but can be the cause of oxidative stress in brain injury and disease. Oxidative stress refers to cells and tissues that have been altered by exposure to oxidants. Oxidation of lipids, proteins, and DNA leads to tissue injury. Nitrogen monoxide (nitric oxide [NO]) is a free radical generated by NO synthase (NOS). This enzyme modulates physiologic responses, such as vasodilation or signaling, in the brain. Oxidative stress, rather than being the primary cause, appears to be a secondary complication in many progressive disorders, such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS), as well as disorders of mental status. An enhanced antioxidant status is associated with reduced risk of several diseases.⁴⁴

The blood-brain barrier is made from endothelial cells and its tight junctions, so that substances can pass only through the cell and not in between cells. Drug entry into the CNS is determined by the drug's lipid solubility. Glucose and amino acid cross the endothelial cell barrier via protein transporters.

The ependyma cells line the ventricles and spinal canal and regulate metabolism between the channels of the extracellular space and the ventricles. Ependyma forms the basis of the cerebral spinal fluid barrier. There is movement of molecules through the extracellular space with the possibility of long range and relatively diffuse actions of neurotransmitters released into the extracellular space. This type of signaling is known as *volume transmission* and may have a major role in setting large-scale neuronal excitability or inhibition.¹⁶

Dysfunction within the nervous system can affect either or both of the two main classes of cells: the glial cells and the neurons. Stem cells create new glia and new neurons. The region immediately beneath the ependymal cell layer produces new cells at a very low rate in the adult compared to the amount created during neurogenesis in early development. They migrate widely through the brain and conform phenotypically to the regions where they end up.

Glial Cells

Aside from neurons, macroglia and microglia are the two primary cell types located throughout the CNS. The macroglia are derived from a nerve cell lineage and are classified into three distinct subtypes: astrocytes,

oligodendrocytes, and Schwann cells. These macroglia are the most populous cells of the CNS and support and maintain neuronal plasticity throughout the CNS. Glial cells are often implicated in the disease process that affects brain tissue.²⁶

Microglia are the resident immune cells of the brain. Microglia also are interspersed throughout the brain and represent approximately 10% of the CNS population. Microglia differ from the macroglia because they are derived from a monocyte cell lineage. Microglia respond to CNS insult both by diffuse proliferation and infiltration of CNS tissue. Microglia are pivotal in innate immune activation and function to modulate neuroinflammatory signals throughout the brain. In the absence of stimulus, microglia are dormant.

During an immune response, microglia are activated. Inflammatory cytokines produced within the CNS target neuronal substrates, triggering a response of fever, increased sleep, reduced appetite, and lethargy. Collectively, these behavioral symptoms of sickness are evolutionarily conserved and function to increase the metabolic demand for clearance of pathogens via the microglia.²⁰ Active microglia show macrophage-like activities, including scavenging, phagocytosis, antigen presentation, and inflammatory cytokine production. Microglia recruit and activate astrocytes to propagate these inflammatory signals further. Normally, these neuroinflammatory changes are transient and beneficial, with microglia returning to the dormant state after the resolution of the immune challenge. Aging, however, may provide a brain environment in which microglia activation is not resolved, leading to a heightened sensitivity to immune activation; this lack of resolution may contribute to the pathogenesis of neurologic disease.⁵⁵

Activated microglia and monocytes coming in from the bloodstream can assume the form of macrophages, or giant multinucleated cells filled with ingested debris. Nearby neurons may be damaged by toxins released from activated macrophages and microglia.

Astrocytes are named because they look like star cells. They are the most numerous cells in the brain and outnumber neurons 10:1. Fig. 28-1 shows the relationship of the glial cell to the neuron. The glial cells provide support and structure for the CNS and play the role that connective tissue performs in other parts of the body. The glial cells are active in the system but are not involved in signaling information. The neurons communicate information to one another in order to process sensory information, program motor and emotional responses, and store information through memory.

In addition to their support function, the cells serve a nutritive function, since they connect to the capillary wall and to the nerve cell. They may be responsible for the release of nerve growth factor. Astrocytes are permeable to potassium and therefore are involved in maintaining the correct potassium balance in the extracellular space. Astroglia have the ability to monitor and remove extracellular glutamate and other residual neuronal debris after brain injury and can seal off damaged brain tissue.^{26,52} When the astroglial cells become dysfunctional as part of an injury or degenerative process, it may reinforce neuronal damage. Astroglial changes are widely recognized

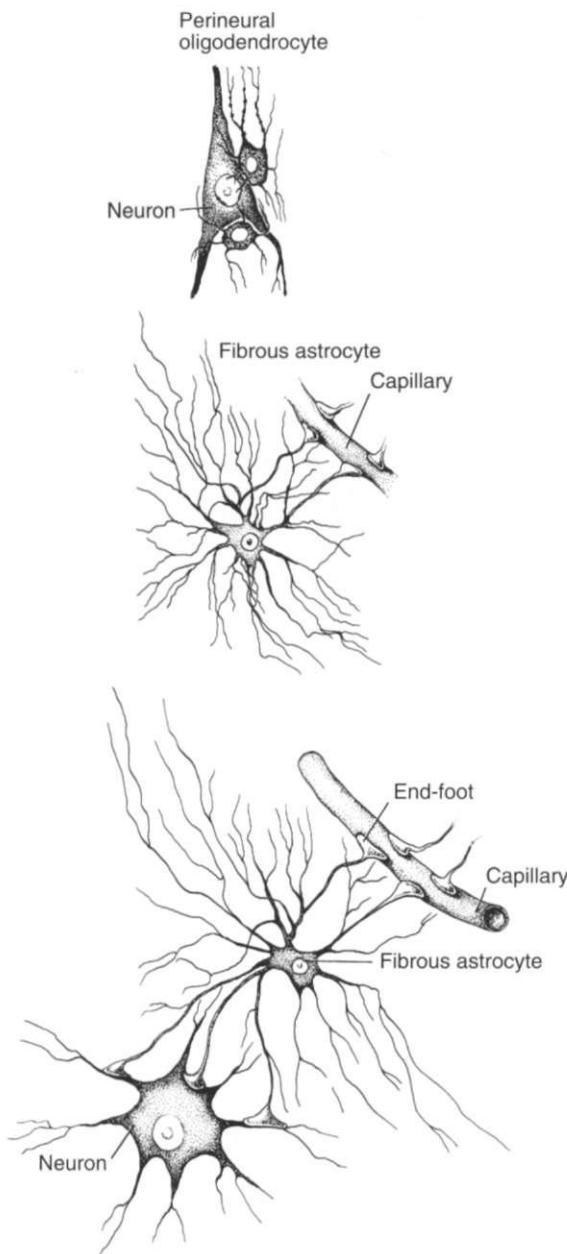


Figure 28-1

The relationship of the glial cells (astrocytes, oligodendrocytes) to the neurons and capillaries. [From Kandel ER, Schwartz JH: *Principles of neural science*, ed 2, New York, 1985, Elsevier.]

to be one of the earliest and most remarkable cellular responses to CNS injury.⁴² Astrocyte swelling is a common pathologic finding and is often seen at the interface with the vascular system. The swelling may be a factor in gliosis, a reaction of the glial cells that produces tissue that is laid down in a scarlike manner, producing glial scarring.⁴³ Astroglial cell tissue can be the site of neoplastic disorders that disrupt nerve cell function by compressing the neurons and blood supply in the surrounding area (see Chapter 30).

The two other glial cell types, the oligodendrocyte, a part of the CNS, and the Schwann cell found in the peripheral nervous system are responsible for the produc-

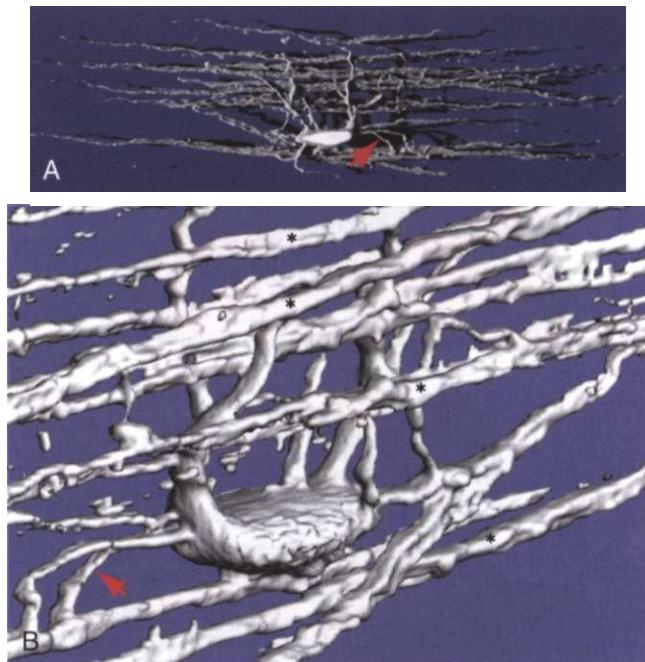


Figure 28-2

A, Single oligodendrocyte from a rat. **B**, More magnified view showing the process as they emerge from the cell body. [From Nolte J: *The human brain: An introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby. Courtesy Dr. Peter S. Egli, Institute of Anatomy, University of Bern, Bern, Switzerland.]

tion of the myelin sheath, which surrounds the axon. (See Chapter 39 for information on the peripheral disorders that are associated.) Demyelinating disorders that target the CNS, such as multiple sclerosis, are often the result of disrupted function of the oligodendrocyte.¹ This process is further described in the section on multiple sclerosis in Chapter 31. Figs. 28-2 and 28-3 show the oligodendrocyte and describe the process of myelination.⁴⁴

Pain was classically viewed as being mediated solely by neurons, as are other sensory phenomena. Spinal cord glia amplify pain and are activated by certain sensory signals arriving from the periphery. These glia express characteristics in common with immune cells in that they respond to viruses and bacteria, releasing proinflammatory cytokines, which create pathologic pain. (See Chapter 7 for more information about interactions between the immune system and the CNS.) Altering glial function has become a new approach to pain control.⁶⁴

Nerve Cells

There are many mechanisms of communication between nerve cells related to the structure and function of each cell type. The location in the nervous system, the input cells, and the target cells will determine how a cell communicates. The cell body size and the shape and configuration of dendrites and axons will also affect the method of communication. However, almost all neurons will typically fire through a manner that can be described schematically. Essentially, the chemical information encoded by a gene within one nerve cell is delivered to the appropriate postsynaptic genome through a series of

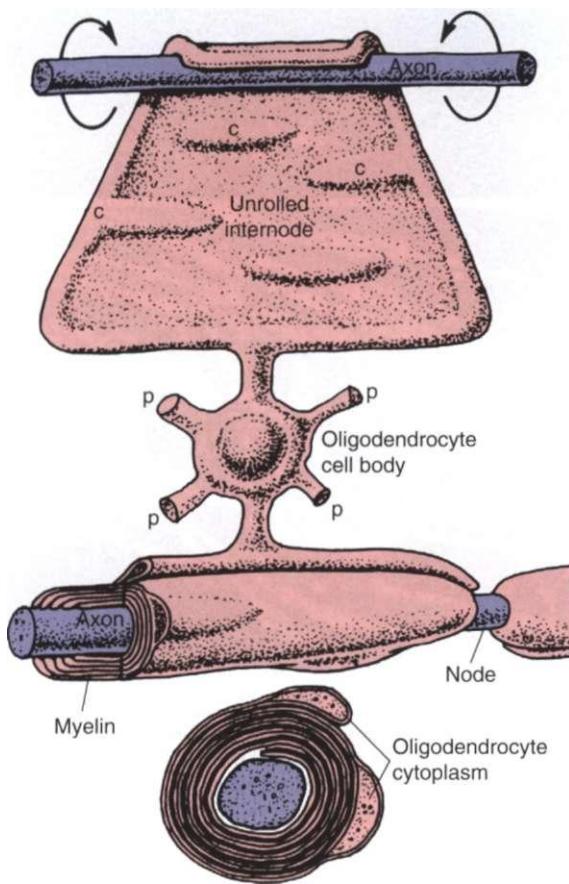


Figure 28-3

Schematic diagram of the formation of myelin in the central nervous system (CNS). (From Nolte J: *The human brain: An introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby. Redrawn from Krstić RV: *Illustrated encyclopedia of human histology*, Berlin, 1984, Springer-Verlag.)

molecular reactions.⁵⁶ Information is transferred via electrical signals that travel along the neuron and is carried to the next neuron through a series of biochemical events that will influence the behavior of the second-order neuron.

The cell body of the neuron is the metabolic center of the neuron and includes the nucleus where the genetic material is located. The gene expressed in a cell directs the manufacture of proteins that determine the structure, function, and regulation of the neural circuits. Mutation, or changes in the structure of the DNA, can lead to the production of abnormal proteins that can be associated with vulnerability to neurologic disease. Abnormalities within the gene structure leading to predisposition for mutations can be inherited. Toxicity or abuse of drugs can also affect the ability of the DNA to replicate in a normal manner and can cause long-term dysfunction of the nervous system. Cell body inclusions are growths that occur within the cell body as a part of aging, such as Lewy bodies, but can also be a part of the disease process and can cause loss of function of the cell as a result of the obliteration of the nucleus of the cell.⁴⁴

The cell body generates electrical activity through action potentials. A transient increase in sodium perme-

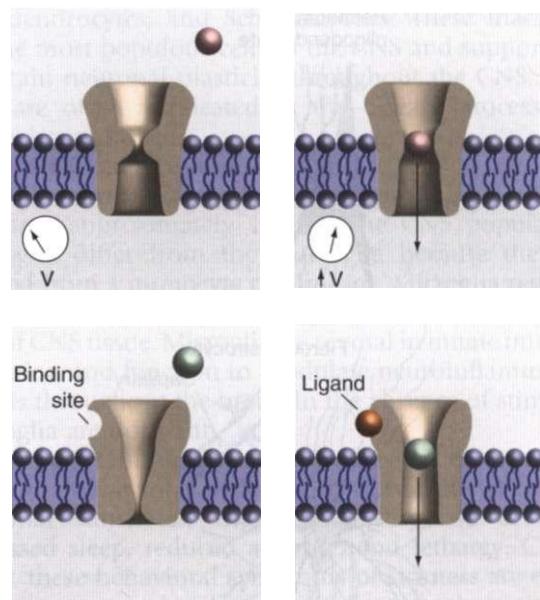


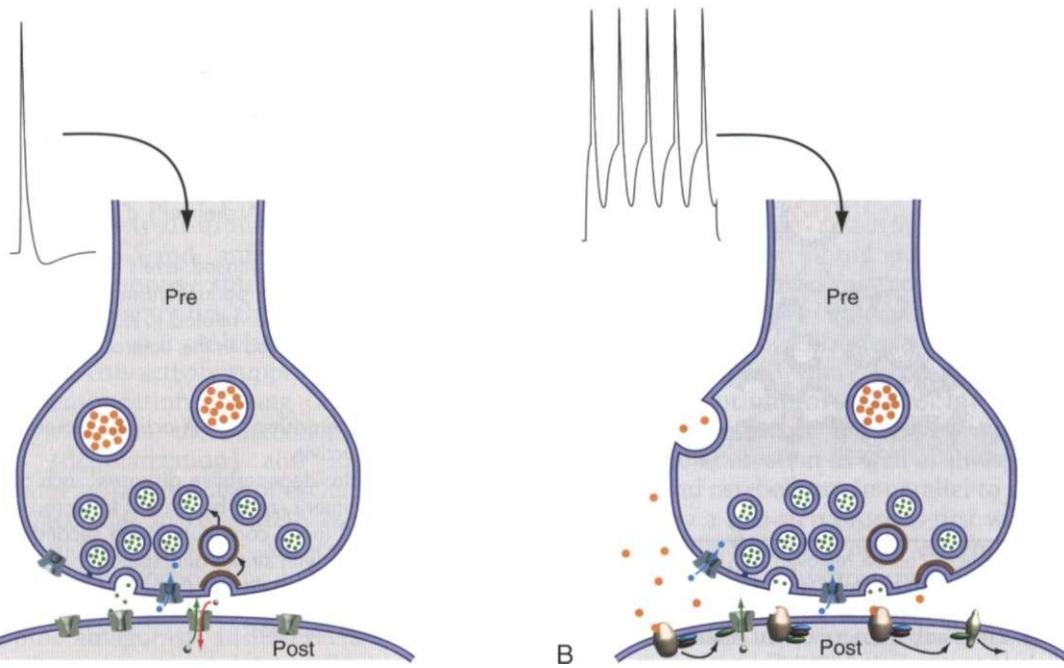
Figure 28-4

Ion channels respond to the changes in voltage. **A** represents the closed state, and **B** represents the open state that allows neurotransmitters to gain entry into the cell. **C** and **D** represent the opening based on the ligand attaching to the protein that causes the channel to open. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

ability is the molecular foundation of the action potential. The increase in sodium permeability causes this ion to be dominant and establishes the membrane potential as +40 mV, or action potential. This is transient and soon closed as the potassium channels open and resting potential is restored.

Ion channels are proteins that span the cell membrane and are able to conduct ions through the membrane. The ion channels recognize and select specific ions for transfer. They are able to open and close in response to specific electrical, mechanical, or chemical signals. Fig. 28-4 describes the gating properties.⁴¹ Sodium channel blockers bind the outer axonal surface of the channel and prevent the flux of sodium. The nerve cells sequentially generate four different signals at different sites within the cell: an input signal, a trigger signal, a conducting signal, and an output signal. The input signal depolarizes the cell membrane. Dendrites are typically the site for receiving incoming signals from other neurons. It is in the trigger zone on the initial segment of the axon that the receptor signals are summed, and the neuron then fires an action potential through the length of the axon. The intensity of the conducting signals is determined by the frequency of individual action potentials. As the action potential reaches the neuron's terminal, it stimulates the release of a chemical neurotransmitter cell through the presynaptic terminals.²⁶ Fig. 28-5 shows the processes related to transmitter release.⁴¹

The axon serves as the entry route of a number of pathogens and toxins and presents a large target as a result of its large volume. Excitatory synapses are distributed distally in the dendritic receptive field, and inhibitory synapses exist in the proximal dendritic field or on

**Figure 28-5**

A, Depolarization of the terminal causes sodium influx and opening of the channels in the postsynaptic neuron. **B**, Release of transmitters from large and small vesicles, the status of the postsynaptic proteins will affect the binding capability. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

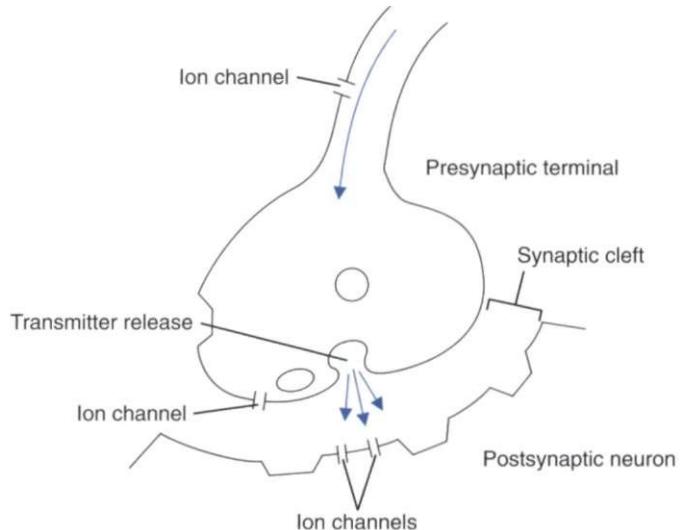
the cell body. The combined firing creates modulation of input.

The axon of the nerve can selectively be damaged, without destruction of the cell body, causing a decrease or loss of presynaptic activity. The stretch damage to the axon is responsible for the abnormal or delayed firing associated with damage to the brainstem in head trauma. Axonal spheroid formation is a reaction to injury resulting in formation of axon retraction balls and can be seen in radiation necrosis and traumatic brain injury. Axon degeneration plays a part in multiple sclerosis.¹⁶

Neurotransmission

By means of its axonal terminals, one neuron contacts and transmits information to the receptive surface of another neuron. The release of neurotransmitter from the presynaptic terminal and the uptake of that substance in the postsynaptic receptor are known as a synapse. A simplified diagram is shown Fig. 28-6. Virtually all communication between neurons occurs via chemicals. The chemical communication involved in this process is universally known as either neurotransmission or neuro-modulation.²⁷ Changes in neurotransmitter substances in the space surrounding the neurons have been implicated in many nervous system disease processes.

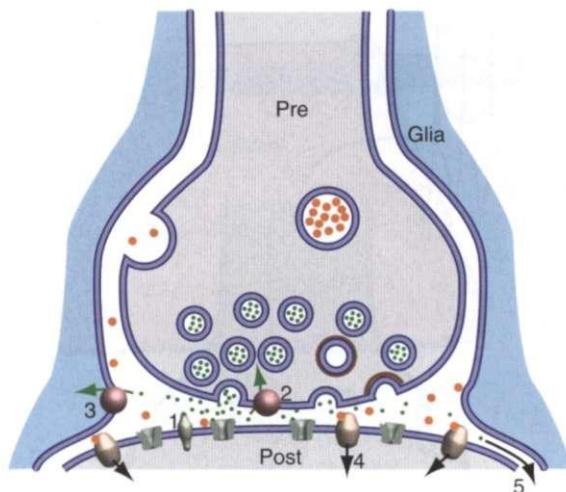
Neurotransmitters are synthesized within each neuron, stored in presynaptic vesicles, and released from depolarized nerve terminals. They bind specifically to presynaptic or postsynaptic receptors, which recognize the neurotransmitter's chemical conformation. A single neuron can release several different neurotransmitter substances, and a single neuron can be selectively receptive to differ-

**Figure 28-6**

Schematic representation of the postsynaptic neuron and the presynaptic terminal. Transmitter substances are synthesized in presynaptic terminals, released into the synaptic cleft, and occupied in the postsynaptic terminal.

ent types of neurotransmitters because of the differences in ion channels.²⁷ Activation of a receptor in response to neurotransmitter can cause changes in a variety of molecules. Modification, or modulation, of the system can take place presynaptically, postsynaptically, or within the cell body.

Changes in the target cell can cause abnormal responses to normal levels of transmitters. The amount of

**Figure 28-7**

The transmitter substances can be removed by (1) enzymatic inactivation of neurotransmitter, (2) reuptake of the neurotransmitter by the presynaptic terminal, (3) removal by the nearby glial cells, (4) uptake by the postsynaptic terminal, or (5) it may just move out of the synaptic space into adjoining spaces. [From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.]

neurotransmitter released in the synaptic cleft is determined by the neuronal firing rate, the quantity of transmitter in the nerve terminal, and the cumulative regulatory actions of excitatory and inhibitory neurotransmitters. These biochemical actions alter the electrical activity of the postsynaptic neurons.

One aspect of chemical transmission that is extremely important in signaling is the time course of transmitter in the synaptic cleft. The breakdown of a transmitter is an important variable and can change the concentration of the substance in the synaptic cleft.²² Control of the neurotransmitter in the synaptic cleft is the basis for pharmacologic treatment in degenerative neurologic disease. Fig. 28-7 diagrams the various ways that the substances in the synaptic cleft can be removed.⁴¹

An important concept for all neurotransmitters is that the final result of either hyperpolarization or depolarization depends on both the transmitter and its receptor. The concept of an inhibitory transmitter should be abandoned for the more accurate concept of an inhibitory interaction between neurotransmitter and receptor.

A wide range of substances makes up the neurotransmitter substances used by the nervous system. In some cases, they can coexist in the same neuron. Box 28-1 represents some typical substances that can be used as neurotransmitters. These substances can be used by neurons in different ways, according to the function of the specific neuron. To be used as a neurotransmitter, these substances are packaged in vesicles within the neuron and respond to the particular enzymes that are specific to that neuron.⁵⁷

Amino Acids. One of the small-molecule neurotransmitters, glutamate, is an excitatory amino acid transmitter used throughout the brain and spinal column. It is an intermediate transmitter in cellular metabolism, so the presence of glutamate in a cell does not necessarily suggest

Box 28-1**NEUROTRANSMITTERS AND ASSOCIATED RESPONSES****Amines**

- Acetylcholine: decreases in production associated with diseases such as Alzheimer's disease and myasthenia gravis
- Catecholamines
 - Dopamine: decreased levels responsible for symptoms associated with parkinsonism
 - Norepinephrine: related to cocaine or amphetamine
 - Serotonin: involved in the control of mood and anxiety

Amino Acids

- GABA: increasing GABA activity decreases incidence of seizure activity
- Glutamate: degenerative diseases, such as Parkinson's, ALS, or Alzheimer's, may be related to increases in glutamate; increased levels contribute to the secondary damage associated with stroke and spinal cord injury
- Glycine: more active in the spinal cord than CNS

Neuroactive Peptides*

- Enkephalins and β -endorphins: pain control achieved by use of drugs (opiates) that bind to endorphin and enkephalin receptors
- Substance P: involved in pain pathways

GABA, γ -Aminobutyric acid; ALS, amyotrophic lateral sclerosis; CNS, central nervous system.

*Over 50 neuroactive peptides have been identified, these are most typical.

neurologic activity. Glutamate functions with its receptors in an excitatory or depolarizing system at primary afferent nerve endings, the granule cells of the cerebellum, the dentate gyrus, and the corticostriatal and subthalamopallidal pathways important to basal ganglia function. When the levels of glutamate rise above normal, it can become neurotoxic and cause cell death. Glutamate opens ion channels to bring calcium into the cell. In the case of excess glutamate, too much calcium is allowed into the cell, and the calcium eventually destroys the cell. Excess glutamate can be an effect of neuronal injury, as in stroke, brain, or spinal cord injury. It appears that the genes in the nerve cell body may trigger this excitotoxic mechanism, resulting in release of excess glutamate that may lead to the degenerative processes associated with diseases such as ALS, Alzheimer's, Huntington's, and Parkinson's.⁴³ Part of the activation of seizure is due to glutamate receptors. Toxins or drug abuse can also trigger an excitotoxic level of glutamate.⁵⁶

γ -Aminobutyric acid (GABA) is a tiny amino acid that serves both as a neurotransmitter and as an intermediate metabolite in the normal function of cells. GABA is synthesized from glutamate by way of the vitamin B6-dependent enzyme, glutamate decarboxylase. GABA is the major transmitter for brief inhibitory synapses. GABAergic cells have a dense representation within the basal ganglia.²¹ Loss of GABAergic neurons that inhibit glutamate results in increased excitation. Glycine is another amino acid neurotransmitter that is the transmitter at some inhibitory CNS synapses. The distributions of GABA

and glycine synapses overlap, but glycine is more prominent in the spinal cord.¹⁴

The N-methyl-D-aspartate (NMDA) receptor has a complex process using glutamate and glycine activation at the same time but also requiring membrane polarization to remove magnesium from inside the cell, so that the cell can allow sodium to be active within the cell. NMDA receptors are widely distributed throughout the neocortex, hippocampus, and anterior horn motor neurons. The NMDA response thus works when the membrane bearing the receptor has already been depolarized by another stimulus, so it prolongs or augments the initial depolarization. This activity supports the activities of learning and memorization. During cellular energy failure induced by ischemia, there is collapse of membrane potentials (depolarization) and uncontrolled synaptic and transmembrane release of excitatory amino acids into the extracellular space. NMDA receptors will open and allow calcium into the intracellular space causing damage to the mitochondria, limiting the production of adenosine triphosphate (ATP). Drugs that are NMDA receptor antagonists include ketamine and eliprodil. Antiepileptic drugs, such as felbamate and lamotrigine, block the glutamate and glycine activity at the NMDA receptors.¹⁶

Amines. Cholinergic neurons play two different roles in the nervous system. Acetylcholine was the first neurotransmitter discovered and has primary activity at the level of the peripheral nervous system. It is the transmitter released by the motor neurons at neuromuscular junctions and within the autonomic nervous system. Disorders related to acetylcholine are discussed in Chapter 39. The role of the cholinergic neurons in the CNS is quite different because it is involved with the regulation of the general level of activity. Cholinergic systems can be mapped to the medial cortex and to the areas responsible for information flow to the hypothalamus and amygdala through the reticular formation. They also constitute a major element of the autonomic nervous system as pre-ganglionic neurons of sympathetic ganglia and postganglionic parasympathetic neurons. The cholinergic and biogenic amine systems appear to establish the activity set point of the cortex and basal ganglia rather than point to point neural firing.¹⁶ Biogenic amines are synthesized from amino acid precursors, dopamine, serotonin, and norepinephrine. Two transmitters known as catecholamines are dopamine and norepinephrine.

Dopamine is synthesized in four major CNS pathways. The most important and most widely understood involves the nigrostriatal pathway of the basal ganglia. Dopaminergic function is decreased in individuals with Parkinson's disease and attention disorders affecting the frontal lobe. The synthetic pathway for dopamine is tyrosine to dopa to dopamine.

Norepinephrine is a neurotransmitter found in the hypothalamus and the locus ceruleus in the brainstem. It is synthesized from dopamine and therefore shares the same enzymes, including the rate-limiting tyrosine hydroxylase. Like dopamine, norepinephrine is removed from the synapse by active reuptake into the presynaptic cell and then is metabolized by two enzymes, monoamine oxidase (MAO) and catechol O-methyltransferase

(COMT).²¹ Dopamine and norepinephrine are the primary neurotransmitters associated with the task of attending. Both need to be enhanced to achieve sustained clinical benefit.

The catecholamines appear to have an important role in working memory. The cholinergic system appears to be critical for the acquisition of long-term declarative memories. Cholinergic function decreases somewhat with age and greatly in individuals with Alzheimer's disease, and these changes may contribute importantly to corresponding reductions in declarative memory ability. Newer centrally acting cholinesterase inhibitors that can be administered orally have been developed that have been marketed for improvement of memory.

Serotonin has its main cell bodies in the dorsal raphe nucleus of the brain stem as well as the spinal cord, hippocampus, and cerebellum. In parallel to dopamine, it is synthesized by a two-step process, first with a rate-limiting enzyme and then a general enzyme. The first step takes tryptophan to 5-hydroxytryptophan (5-HTP) with the rate-limiting enzyme, tryptophan hydroxylase. The second step takes this intermediate to serotonin (5-hydroxytryptamine [5-HT]) by aromatic amino acid decarboxylase, which is the same enzyme involved in dopamine synthesis. There are several types of serotonin receptors spread throughout the brain. Serotonin is metabolized like the catecholamines by active reuptake into the presynaptic cell and then metabolism by MAO. Serotonin is removed from the synaptic cleft by reuptake pumps rather than by degradation. Tricyclic antidepressants work by inhibiting this reuptake.¹⁶

Neuropeptides. Neurons can secrete hormones, or neuropeptides, and most or all of them can function as neurotransmitters. Neuropeptides are metabolically difficult for cells to make and transport, and can be effective at very low concentrations. Synthesis of neuropeptides begins in the nucleus of the cell, where the gene is transcribed into RNA. In the endoplasmic reticulum the RNA is translated into the neuropeptide transmitter. When they have been activated and used to produce a signal, a new supply must be produced in the cell body. Neuropeptides coexist in neurons with both amino acid and amine neurotransmitters. Neuroactive peptides are involved in modulating sensibility and emotions.

Gaseous Neurotransmitters and Others. NO and carbon monoxide (CO) are gases than can diffuse easily through neuronal membranes and can influence subsequent transmitter release. Astrocytes may be the target, mediating cell to cell communication between vessel endothelium and smooth muscle and are critical in vaso-motor control, inflammation and neuronal communication. NO sets the functional state of adjacent cells and has a short half-life. NO released from endothelial cells acts on vascular smooth muscle causing vasodilatation. NO released from inflammatory cells occurs in high concentrations and kills cells. NO may play a role in neurodegeneration, and acute elevations may contribute to damage in ischemia and trauma. NO synthesis is augmented by NMDA receptor activation by glutamate, therefore NO may synergize excitotoxicity.²⁷

Neurotrophic factors are essential to maintenance and survival of neurons and their terminals but are produced

by the body in a limited supply. Four major neurotrophins have been identified in humans: nerve growth factor, brain-derived neurotrophic factor, neurotrophin 3, and neurotrophin 4/5. Neurotrophins interact with receptor cells to prolong the life of the neuron. Although this class of substances is also not fully understood, it is clear that it plays a role in the development of the nervous system. It appears to work by suppressing the pathway that leads to apoptosis.²⁶

CLINICAL MANIFESTATIONS

Sensory Disturbances

The skin, muscles, and joints contain a variety of receptors that create electrical activity as described previously^{3,54} (see Chapter 39). The electrical input is carried to the CNS through the *afferent axons* via the spinal cord. The cell bodies rest in the ganglion of the dorsal root that lies adjacent to the spinal cord. The afferent fibers are arranged somatotopically in the spinal column and ascend to the brainstem and the sensory cortex. Fig. 28-8 shows the simplified synapse.⁴¹ A characteristic of the fibers that run in the dorsal column of the spinal cord is that they synapse at the level of the brainstem nuclei, where they cross over to the contralateral (opposite) hemisphere of the brain. This phenomenon is illustrated in Fig. 28-9.⁴¹ When there is a disorder of the brain that affects the afferent system above the level of the brainstem, symptoms occur on the side contralateral to the lesion.^{26,41}

The brainstem receives information from specialized senses. For example, vestibular information is received via cranial nerve VIII and integrated through the brainstem nuclei, contributing to postural control and locomotion. Disorders of the afferent nerve, dorsal columns of the spinal cord, and brainstem result in changes in the sensory input available. This can manifest as lack of cutaneous sensation, numbness, tingling, paresthesias, or dysesthesias in the distribution of the nerves affected. Sensory input from the joints and muscles is known as *proprioception*. When this sensory function is lost or disturbed, the person will have difficulty maintaining the body in the appropriate position for the voluntary and involuntary movements necessary for most functional activities, especially those required for postural control. Movements become ataxic or uncoordinated because of the loss of feedback on position from the joints.³

The nervous system has several pain-control pathways available, some of which suppress and some of which facilitate the experience of pain. Modulation of noxious stimuli is directed by the reticular formation. Noxious stimuli can be experienced as more or less painful, depending on the individual's circumstances. If an individual is focused on a task during an injury, such as a soldier or athlete, the pain of the injury may be suppressed until the task is completed. When a lesion affects the midbrain areas that modulate and interpret sensory input, such as the thalamus, the result can cause exaggeration of sensory stimuli.

Disruption of the sensory input provided by the optic nerve is evident in some disorders of the brain and will result in loss of vision in some or all of a field of view.

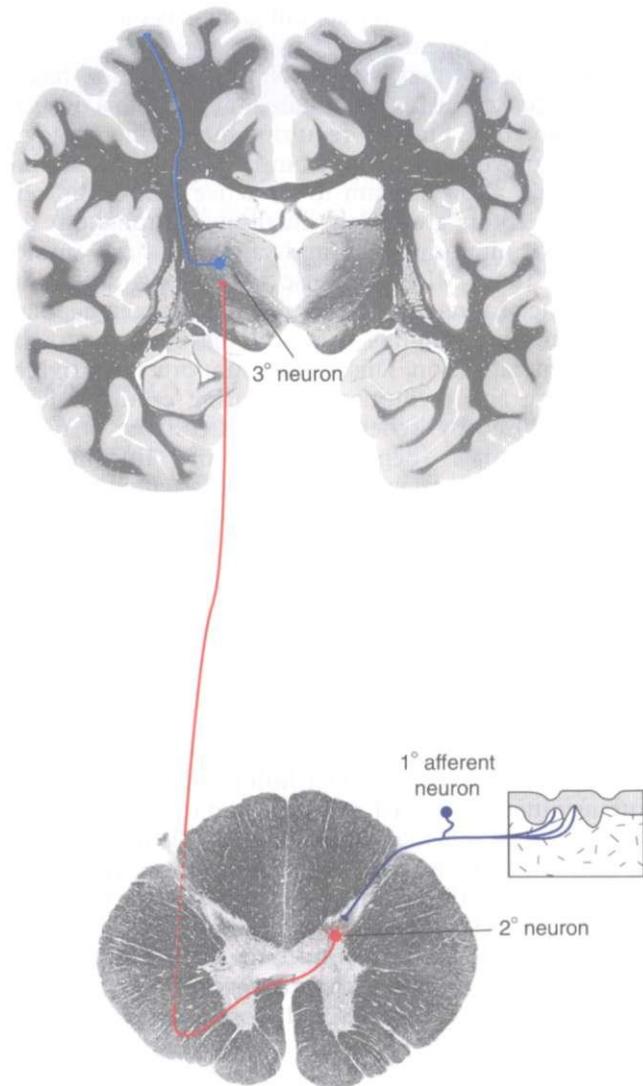


Figure 28-8

The minimum sensory pathway from the periphery to the cerebral cortex. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

Visual-field cuts are common with stroke (see Chapter 32). Visual hallucinations can also be part of a CNS disorder when the optic radiations or occipital lobe is disrupted, which may also be caused by stroke or a degenerative disease such as multiple sclerosis.

Brainstem Dysfunction

The brainstem contains the lower motor neurons for the muscles of the head and does the initial processing of general afferent information concerning the head. The cranial nerves enter the system at the brainstem through the respective nuclei and provide sensation and motor control of the head and neck. An anatomic view of the cranial nerves and the relationship of the nuclei to central structures is provided in Fig. 28-10.⁴¹ The sensory and motor functions of the cranial nerves are outlined in

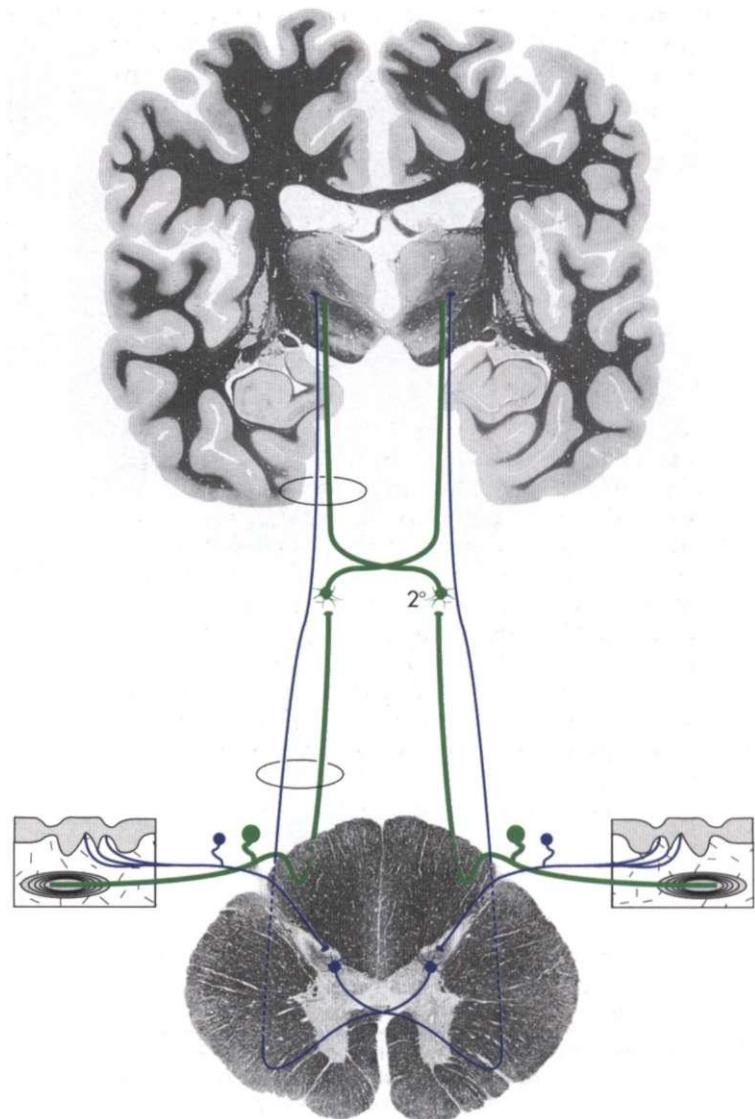


Figure 28-9

A, In the spinal cord, a lesion would result in decreased touch on the same side of the lesion and decreased pain sensation on the contralateral side. **B**, A lesion above the medulla would cause decreased touch and pain on the contralateral side. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

Table 28-1. A working knowledge of the attributes of the cranial nerves assists in the understanding of the level and impact of lesions within the CNS.

Distinctive brainstem functions include a conduit for spinal cord activity in both ascending sensory tracts and descending motor tracts. The nuclei in the brainstem provide relay functions to divert the information to the appropriate higher level structures for further modification.

The brainstem has been divided into three major subdivisions related to a characteristic set of features. The medulla, attached directly to the spinal cord, houses the inferior olfactory nucleus that has direct output connections to the cerebellum and gets direct input from the spinal cord and cerebellum. The pons extends from the medulla and is attached to the cerebellum through both the middle and superior cerebellar peduncles receiving major outflow from the cerebellum. Vestibular nuclei sit within the pons, making it the center for integration of vestibular input.

The third level of the brainstem, the midbrain, contains the red nucleus with fibers that connect the cerebellum to the thalamus. The substantia nigra found here connects to the basal ganglia structures and shares the dopamine pathway related to the initiation and control of movement. It is also connected to the cortex through the cerebral peduncle containing descending fibers.

The reticular formation is a diffuse network of neurons, extending through the brainstem to higher levels, and is important in influencing movement. The reticular regions are closely related to the cerebellum, basal ganglia, vestibular nuclei, and substantia nigra and involved with complex movement patterns. It is through the reticular formation that there is inhibition of flexor reflexes, so that only noxious stimulus can evoke the flexor response such as the reflexive pulling a hand away from a hot stove.

This is a brief reflection of the complexity of the brainstem and is not intended to be comprehensive. However, it is clear that advanced knowledge of the interface and

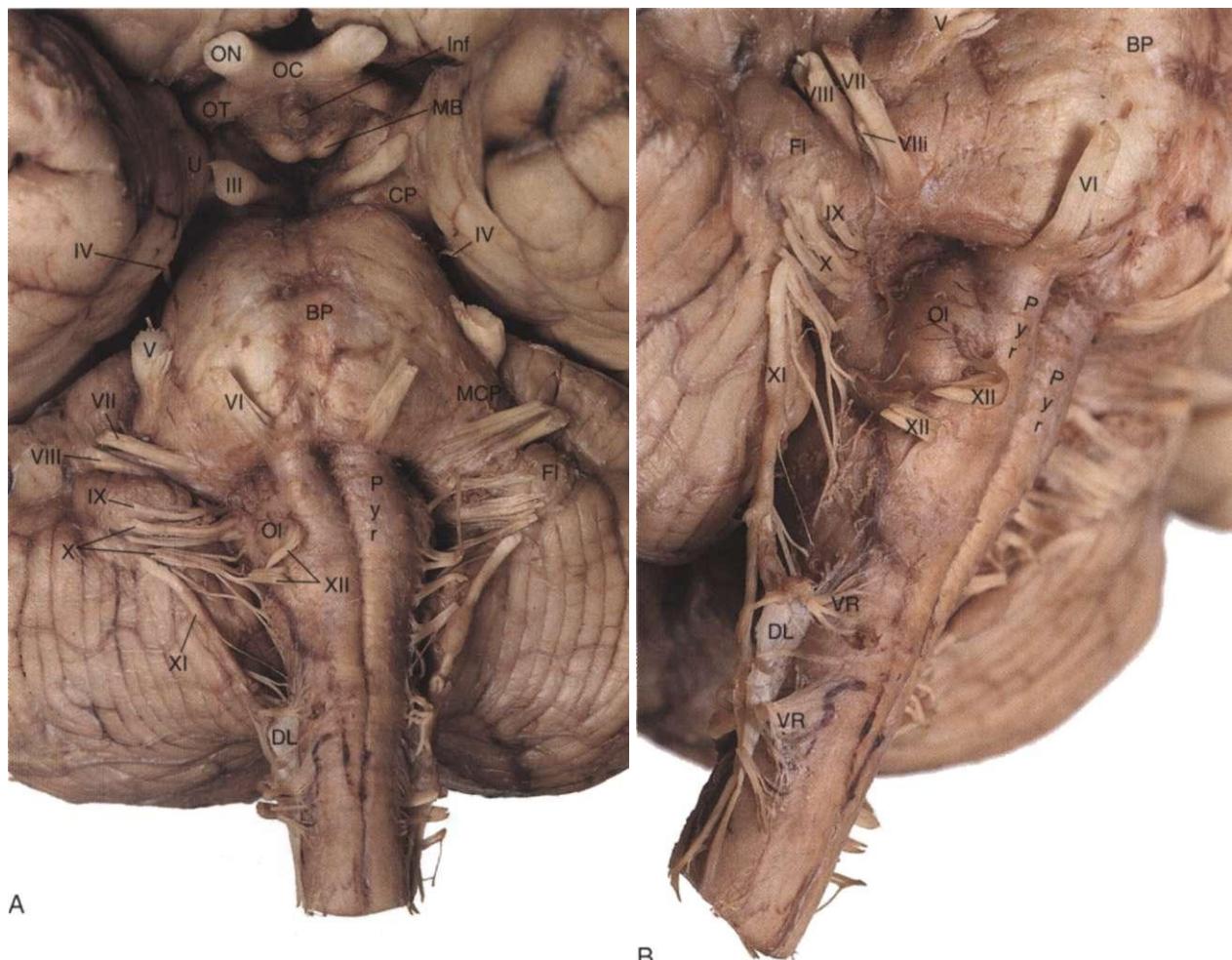


Figure 28-10

Representation of the cranial nerves III through XII. ON, Optic nerve; OC, optic chiasm; OT, optic tract; U, uncus; BP, basal pons; CP, cerebral peduncle; DL, dentate ligament (supports spinal cord); FL, flocculus of cerebellum; Pyr, (pyramids); OL, olive; MCP, middle cerebellar peduncle. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby. Dissection by Dr. Norman Koeling, The University of Arizona College of Medicine, Tucson, AZ.)

connections of the brainstem helps the therapist understand the functions that are described throughout this text.

Movement Disorders

Control of movement is accomplished by the cooperative effort of many brain structures.^{8,54} Activity initiated in the cerebral cortex triggers interneurons that regulate interaction of the lower motor neurons. The parietal and premotor areas of the cerebral cortex are involved in identifying targets in space, determining a course of action, and creating the motor program. The cortex determines strategies for movement. The brainstem and spinal cord are responsible for the execution of the task. The same signal may be processed simultaneously by many different brain structures for different purposes, showing parallel distributed processing. Various areas of the brain, such as the cerebellum and basal ganglia, interact to establish a motor program that modifies the hierarchic information going from the cortex to the spinal cord.

Abnormal movement patterns in neurologic disorders can result from lesions of the CNS at many levels. A simplified representation of the typical synaptic flow of neurons and interneurons is seen in Fig. 28-11. It is important to recognize that there are many synapses not represented here in the levels of the brainstem and central modulation centers of the basal ganglia and limbic lobes.

Damage at any level brings about the movement disorders that are related to the pathologies in the next chapters. Motor output is critically evaluated by the therapist, thus the knowledge of patterns of abnormal movement associated with disorders of the brain is part of the clinical expertise necessary to practice.

Disorders of Coordinated Movement

Lack of coordinated movement known as ataxia can occur with damage to a variety of structures of the nervous system, including sensory neuropathies, but is most commonly associated with cerebellar dysfunction. Damage to

Table 28-1 The Cranial Nerves and Their Functions

| Cranial Nerve | Component | Function |
|-------------------------|-----------|--|
| I: Olfactory | S | Olfaction |
| II: Optic | S | Vision |
| III: Oculomotor | M | Innervation of inferior oblique muscle and medial, inferior, and superior rectus muscles of eye |
| | A | Innervation of ciliary ganglion, which regulates pupillary constriction (pupillary constrictor muscle) and accommodation to near vision (ciliary muscle) |
| IV: Trochlear | M | Innervation of superior oblique muscle of eye |
| V: Trigeminal | S | Sensation (epicritic, protopathic) from face, nose, mouth, nasal and oral mucosa, anterior two-thirds tongue, and meningeal sensation, through all three divisions (ophthalmic, maxillary, mandibular) |
| | M | Innervation of muscles of mastication and tensor tympani muscle through mandibular division only |
| VI: Abducens | M | Innervation of lateral rectus muscle of eye |
| VII: Facial | S | Taste from anterior two-thirds tongue |
| | M | Innervation of muscles of facial expression and stapedius muscle |
| | A | Innervation of pterygopalatine ganglion, which innervates lacrimal and nasal mucosal glands, and submandibular ganglion, which innervates submandibular and sublingual salivary glands |
| VIII: Vestibulocochlear | S | Hearing (cochlear division), linear and angular acceleration, or head position in space (vestibular division) |
| IX: Glossopharyngeal | S | Taste and general sensation from posterior one-third tongue; sensation (epicritic, protopathic) from pharynx, soft palate, tonsils; chemoreception from carotid body and baroreception from carotid sinus (unconscious reflex sensory information) |
| | M | Innervation of pharyngeal muscles |
| X: Vagus | A | Innervation of otic ganglion, which supplies parotid gland |
| | S | Visceral sensation (excluding pain) from heart, bronchi, trachea, larynx, pharynx, GI tract to level of descending colon; general sensation of external ear; taste from epiglottis |
| | S | Visceral sensation (excluding pain) from heart, bronchi, trachea, larynx, pharynx, GI tract to level of descending colon; general sensation of external ear; taste from epiglottis |
| | M | Innervation of pharyngeal and laryngeal muscles and muscles at base of tongue |
| | A | Innervation of local visceral ganglia, which supply smooth muscles in respiratory, cardiovascular, and GI tract to level of descending colon |
| XI: Spinal accessory | M | Innervation of trapezius and sternocleidomastoid muscles |
| XII: Hypoglossal | M | Innervation of muscles of tongue |

S, Sensory nervous system; M, motor nervous system; A, autonomic nervous system; GI, gastrointestinal.

From Feiten DL, Feiten SY: A regional and systemic overview of functional neuroanatomy. In Farber SD: *Neurorehabilitation: a multisensory approach*, Philadelphia, 1982, Saunders, pp 53-54.

the input and output structures of the cerebellum, such as the thalamus and vestibular nuclei, can also cause ataxic movements.

Input regarding the position of the head, trunk, and extremities comes from the spinal cord in order to compare the resulting activity with the intended motor command. This input comes in rapidly because the relay involves only a few synapses. The input comes through the climbing fibers that connect the inferior olive to the Purkinje's cell or from mossy fibers that relay the remaining information.⁵ The deep cerebellar nuclei are the structures that communicate information from the Purkinje's cell to the various nuclei of the brainstem and thalamus.²⁶ The cerebellum has no direct synapse with the spinal cord but exerts its influence through the action on interneurons within the nuclei of the brainstem.

The medial region known as the *vestibule-cerebellum* connects with the cortex and brainstem through both its ascending and descending projections. The cerebellum

has influence on movement through the vestibulospinal and reticulospinal tracts. Lesions result in the inability to coordinate eye and head movement, postural sway, and delayed equilibrium responses.⁵ Postural tremor is present in some individuals with vestibulocerebellar lesions.

The spinocerebellum connects to the somatosensory tracts of the spinal cord. It receives input from the cortex regarding the ongoing motor command. Control of proximal musculature is achieved via the connections to the motor cortex. Lesions of the spinocerebellum can cause hypotonia and disruption of rhythmic patterns associated with walking. Precision of voluntary movements is lost when this area is dysfunctional.³⁸

The anterior lobe of the cerebellum is implicated in disorders of gait with loss of balance noted in stance. Proprioception may give inaccurate cues because the cerebellar relays become disrupted. Long loop reflexes lose adaptability and are unable to trigger appropriate responses in the lower leg to maintain balance when the

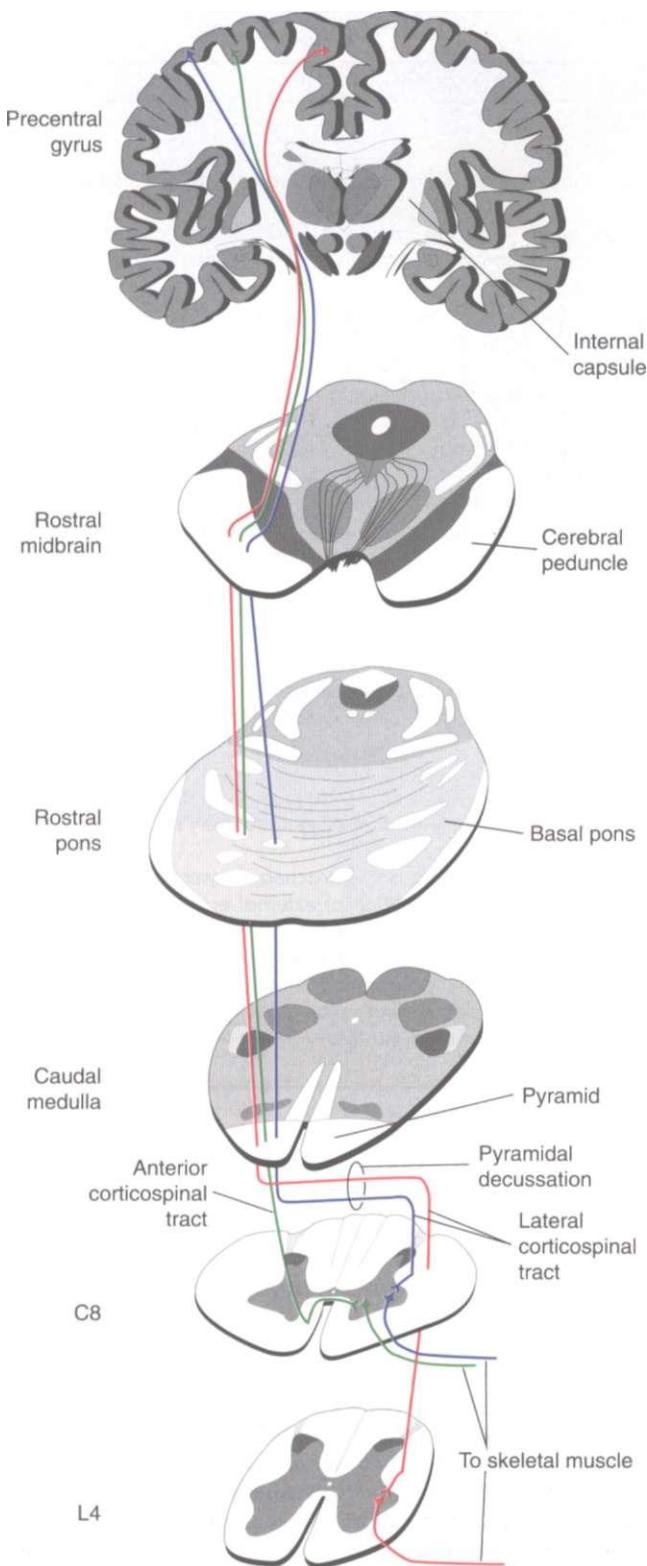


Figure 28-11

Pathway of the motor system from the cortex to the skeletal muscle as it courses through the brainstem structures and spinal cord. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

body sways or the surface is moving. The ability to modify reflexes is lost even when there are repeated trials.⁶⁰

In the cerebrocerebellum, or posterior lobes, connections are made to the cortex through the pons. The posterior lobes are involved in complex motor, perceptual, and cognitive tasks. Lesions of the cerebrocerebellum lead to a decomposition of movement and timing.

Hypotonicity, or decreased muscle tone, can occur on the side of the lesion or bilaterally if the lesion is central and is seen primarily in the proximal muscle groups. The person with hypotonicity is unable to fixate the limb posturally, leading to incoordination with movement. **Asthenia**, or generalized weakness, is sometimes seen in the person with cerebellar lesions. Hypotonicity and asthenia, however, do not always occur together. It is believed that both disorders represent loss of input from the cerebellum to the cerebral cortex, but they may represent loss of input to different areas of the cortex.

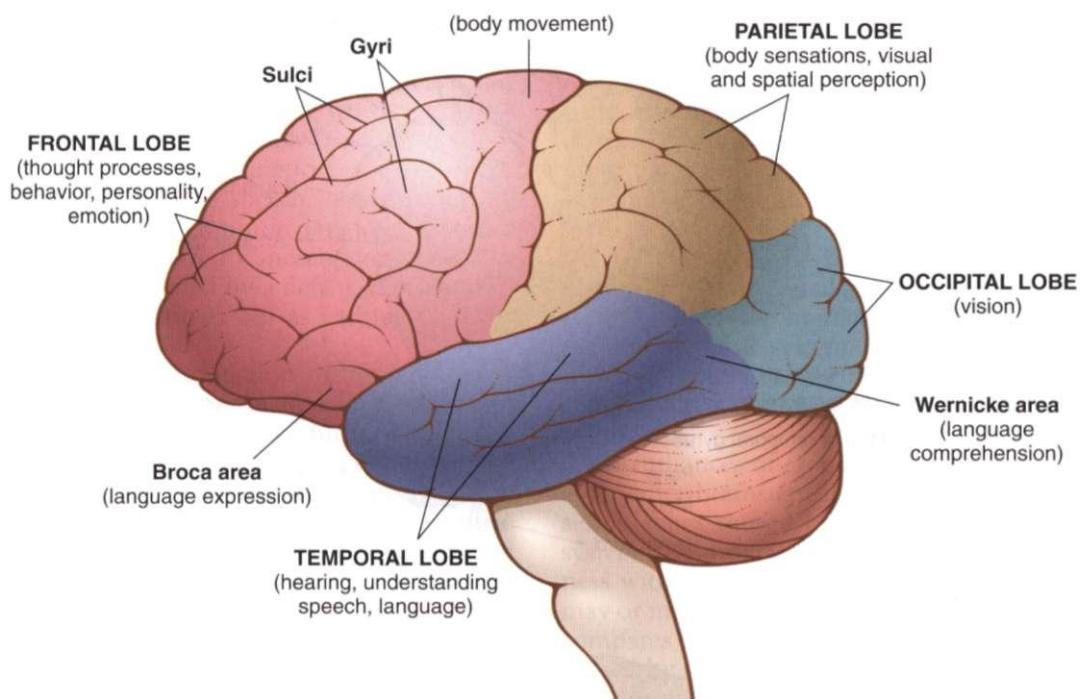
Dysmetria, the underestimation or overestimation of a necessary movement toward a target, is commonly seen with cerebellar disorders. There is an error in the production of force necessary to perform an intended movement. The initiation of movement is prolonged compared to normal, and the ability to change directions rapidly is impaired. The resulting overshoot and undershoot during movement are known as an *intention tremor*. **Dysdiadochokinesia**, the inability to perform rapidly alternating movements, is related to the inability to stop ongoing movement. The movement becomes slow, without rhythm or consistency.

Decomposition of movement is seen in persons with cerebellar dysfunction. Instead of performing a movement in one smooth motion, the person will move in distinct sequences to accomplish the motion. Multijoint movements are more affected than single-joint movements. Disruption in force and extent of movement will result in difficulty with grip control and maintaining static hold against resistance. When the resistance is removed, for example, the extremity will oscillate because of lack of feedback regarding position and force needed to maintain static hold.

Scanning speech is a component of cerebellar dysfunction representing complexity of the motor activity. Word selection is not affected, but the words are pronounced slowly and without melody, tone, or rhythm. This reflects the incoordination or hypotonicity of the muscles of the larynx in controlling the voice.

Eye movements are disrupted in the person with cerebellar dysfunction, in both a static head and eye position and with movement of the head. **Gaze-evoked nystagmus**, or nonvoluntary rhythmic oscillation of the eye, occurs when the cerebellum is unable to hold the gaze on an object, especially a lateral position. When looking at a lateral target, the eyes drift back toward midline and then immediately back to the target. Eyes flickering on and off the target, eyes fluttering around the target, or spastic bursts of eye oscillations may be present when there is brainstem or midline cerebellar lesions.

Ocular dysmetria is similar to the dysmetria seen in the extremities. This dysmetria is seen in cerebellar lesions when the eyes are moving from one target to another

**Figure 28-12**

Schematic representation of functional specialization in the cortex. (From Chabner DE: *The language of medicine*, ed 8, Philadelphia, 2007, Saunders.)

(known as *saccadic movement*) or when attempting to follow a target (known as *smooth pursuit*).

Vestibuloocular function is disrupted in medial lesions, and the ability to maintain eye stability during head movement is affected. See the section on Vestibular Dysfunction in Chapter 38 for more information on vestibuloocular dysfunction.

Gait disturbance is another disorder related to dysfunction of the cerebellum. The gait becomes wide based and staggering without typical arm swing. The step length is uneven, the step widths are inconsistent, and the feet are often lifted higher than necessary. Stance and swing become irregular, and there is loss of adaptation to changes in terrain. It becomes difficult to perform heel-to-toe walking or walking a straight line, which is the standard sobriety test. In some persons, there is a surprising ability to avoid a fall, although the standing balance is abnormal. When the person is able to perform compensatory movements of the upper body and limbs, falls can be avoided.¹⁹

The cerebellum plays a major role in motor learning. The cerebellum is vital in anticipatory, or feed-forward, activity and modification of response.²⁰ The cerebellum learns or memorizes small movements that are integrated into complex activity. During the acquisition phase of motor learning, the cerebellum is active.²⁴ Increased activity has also been noted during mental imagery or mental rehearsal of a motor program.⁴⁶ The cerebellum is active during cognitive and emotional processes, and lesions can cause difficulty in shifting attention from one sensory or thought domain to another.

Deficits of Higher Brain Function

The cortex has a great deal to do with the abilities and activities that are a part of the highest development in humans, including language and abstract thinking. Perception, movement, and adaptive response to the outside world depends on an intact cerebral cortex. As with other parts of the CNS, it is subdivided for ease of understanding the separate functions, although the structure and function is full of overlap. Fig. 28-12 represents some of the functional specialization of the brain. Fig. 28-13 describes the lobar relationship to the cerebellum and brainstem.

The *frontal lobe* is the largest single area of the brain, constituting nearly one-third of the brain's cortical surface. It is phylogenetically the youngest area of the brain and has major connections with all other areas of the brain. The frontal lobe is responsible for the highest levels of cognitive processing, control of emotion, and behavior. An individual's personality is established as a frontal lobe function, and one of the most disturbing deficits seen with lesions affecting the frontal lobe is change from the person's premorbid personality. A person's character and temperament are changed by damage to the frontal lobe. Slow processing of information, lack of judgment based on known consequences, withdrawal, and irritability can be the result of an insult to the frontal lobe. Lack of inhibition and apathy are common clinical problems related to frontal lobe damage. The person with a frontal lobe disorder may lack insight into the deficits, and therefore behavior can be difficult to control.

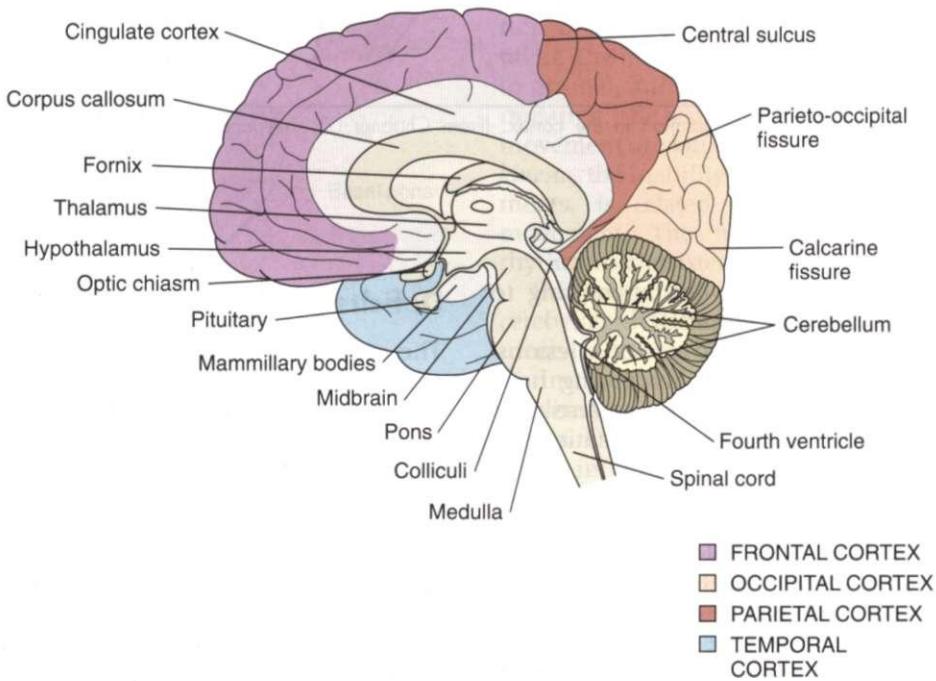
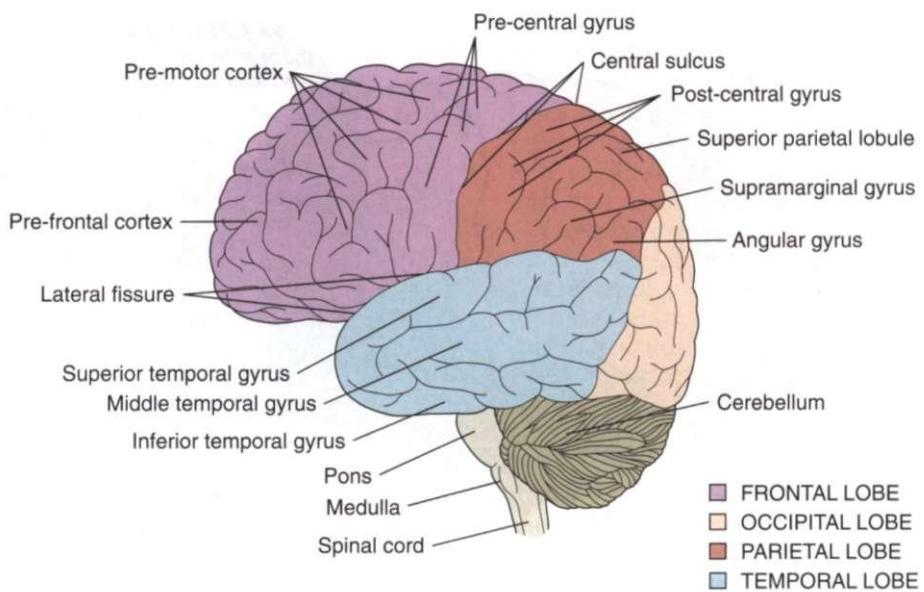


Figure 28-13

The lobes of the cortex and their relationship to the cerebellum, midbrain, and brainstem. (From Farber SD: *Neurorehabilitation: a multisensory approach*, Philadelphia, 1982, WB Saunders.)

The *right hemisphere syndrome* represents the inability to orient the body within external space and generate the appropriate motor responses. Hemineglect is one of the most common deficits seen with right hemisphere lesions. The individual does not respond to sensory stimuli on the left side of the body and does not respond to the environment surrounding the left side. Hemineglect is evident in the involved extremities and trunk during mobility and self-care activities. The ability to draw in two and three dimensions is lost along with other drawing skills, such as perspective and accurate copying. Spatial disorientation can result, with the person losing familiarity with the environment and becoming

lost in areas that should be familiar. Inability to read and follow a map can be an indication of right hemisphere deficit.¹³

Disorders of emotional adjustment often follow a lesion in the right hemisphere. These disorders are primarily in the affective domain of interpersonal relationships and socialization. Cortical control of the limbic system is believed to be responsible, but the exact mechanism of control of more complex emotional behavior is not completely understood at this time. There appears to be hemispheric lateralization of emotions with suggestions that the right hemisphere is the dominant hemisphere in controlling emotions.

Language is one of the higher functions of the brain that is affected in many disorders of the CNS. Speech is a more elementary capacity than language and refers to the mechanical act of uttering words using the neuromuscular structures responsible for articulation. *Dysarthria*, a disturbance in articulation, and *anarthria*, the lack of ability to produce speech, are disorders of speech not language. One common language disorder is *expressive aphasia*, a deficit in speech production or language output, accompanied by a deficit in communication, in which speech comes out as garbled or inappropriate words.

Localization of speech production in the left frontal lobe and impaired language comprehension in the temporal lobe demonstrate how higher functions can be related to brain regions. However, language control may be in different areas for different persons, and therefore damage to the same area of the brain may produce aphasia in some individuals whereas others may be spared. Left hand-dominant people may have right hemisphere dominance for language.³¹

Alexia is another symptom of higher brain dysfunction. It is the acquired inability to read. Alexia is typically caused by lesions in the left occipital lobe and the corpus callosum that prevent incoming visual information from reaching the angular gyrus for linguistic interpretation. *Agraphia* can be caused by lesions located anywhere in the cerebrum. Because writing is a motor skill, lesions of the corticospinal tract, basal ganglia, and cerebellum; myopathies; and peripheral nerve injuries can all cause abnormal or clumsy writing. These disorders may be seen in addition to neurobehavioral syndromes. Typically the features of agraphia tend to parallel the characteristics of aphasia.

Apraxia is an acquired disorder of skilled purposeful movement that is not a result of paresis, akinesia, ataxia, sensory loss, or comprehension. *Ideomotor apraxia* is the most common type and represents the inability to carry out a motor act on verbal command. Ideomotor apraxia appears to be caused by a lesion in the arcuate fasciculus. The anterior connection from the left parietal lobe may be disrupted, preventing the motor system from receiving the command to act. A lesion in the left premotor area can cause apraxia by directly interrupting the motor act. Damage to the anterior corpus callosum can lead to apraxia that is evident in the left hand only. *Ideational apraxia* is failure to perform a sequential act even though each part of the act can be performed individually. The lesion causing ideational apraxia appears to be in the left parietal lobe, as in hemiparesis, or in the frontal lobe, as in Alzheimer's disease. The syndrome is seen as well with diffuse cortical damage associated with degenerative dementia.

Agnosia is the inability to recognize an object; the previously acquired meaning of an object is no longer attached to it. Agnosia is associated with lesions of the sensory cortices involved with seeing, hearing, and feeling and with the loss of one sensory modality. It is difficult to assess because the person is often easily able to compensate. Although the ability to recognize an object by vision is gone, the ability to recognize that same object by hearing or feeling is retained.

Altered States of Consciousness

Alteration of consciousness is not considered an independent disease entity but a reflection of some underlying disease or abnormal state of brain function. The human brain possesses a mechanism that allows a waking and sleeping state (arousal), as well as a separate ability to focus awareness on relevant environmental stimuli (attention).^{13,37} To achieve a state of consciousness the cerebral cortex must be activated by the ascending reticular formation fibers in the brainstem. The fibers extend to the thalamus, limbic system, and cortex. The upper part of this system acts as an on/off switch for consciousness and controls the sleep-wake cycle. The lower part controls respiration.

Disturbances of arousal and attention can range from coma after brainstem injury (see Chapter 33) to confusional states caused by drug intoxication. Metabolic or systemic disorders generally cause depressed consciousness without focal neurologic findings.⁵⁹ CNS disorders may or may not have concomitant focal signs. Table 28-2 compares metabolic and drug-induced coma with coma caused by space-occupying lesions.

Clinical disorders of arousal may result in hyperaroused states and can appear as restlessness, agitation, or delirium. This is presumably a result of the loss of hemispheric inhibition of brainstem function. Hypoarousal can be described on a spectrum ranging from drowsiness to stupor and coma. Stupor is a state of unresponsiveness that requires vigorous stimulation to bring about arousal. Coma is a state of unarousable unresponsiveness. Small and restricted lesions of the brainstem can result in stupor and coma. Massive bilateral hemispheric lesions are necessary to cause coma.

Damage to the cerebral cortex can be caused by loss of blood flow, subarachnoid hemorrhage, anesthetic toxicity, hypoglycemia, hypothermia, or status epilepticus (see the section on Epilepsy in Chapter 36). If the link to the brainstem is destroyed, the person will remain in a persistent vegetative state (PVS). Although the person may make random movements and the eyes may open, mentation remains absent. Akinetic mutism, similar to PVS, reflects damage to the mediofrontal lobe and results in lack of motivation to perform any motor or mental activity (abulia). In the *locked-in syndrome*, there is damage to the pons resulting most often from thrombosis of the basilar artery. This is a remarkable impairment, involving no mental deficit at all but resulting in inability to move anything but the eyes. It is in essence the opposite of PVS.

Supratentorial lesions that cause increased pressure, such as hemorrhage, cerebral edema, or neoplasm, can cause coma by producing tentorial herniation and subsequent compression of the brainstem. There is usually a hemiparesis with a dilated pupil on the side of the lesion because of central compression involving the third cranial nerve by the herniation.

In infratentorial lesions, brainstem damage can be related to drugs, hemorrhage, infarction, or compression from the posterior fossa. Disruption of ocular movements is an early sign of brainstem involvement.⁶⁵ There is loss

Table 28-2 Characteristics of Comas

| Manifestations of Coma | Metabolic and Drug-Induced Comas | Comas from Space-Occupying Lesions |
|--------------------------------------|--|--|
| Onset | Behavioral changes, decreased attention and arousal | Usually severe headache, focal seizures |
| Pain response | Present and equal | May be different on each side |
| Reflexes | Intact deep tendon reflexes equal responses, | Deep tendon reflexes may be unequal; positive Babinski's sign (UMN lesion) |
| Pupillary reaction | Bilateral normal response | May be unequal |
| Size of pupil | May be at midpoint with anticholinergics; pinpoint from opiates; dilated from anoxia | Midbrain lesion: midpoint |
| Corneal reflex | Bilateral, intact | Pons lesion: pinpoint |
| Eye movement | Spontaneous movement without intention; no reaction to VOR | Herniation to brainstem: large |
| Decorticate or decerebrate posturing | Absent; movement is normal | Unequal, may be absent |
| Extremity movement | Equal movement on both sides | May have paresis of lateral gaze with cranial nerve III (oculomotor) compression |
| | | Posturing may be present, depending on level of lesion |
| | | Paresis may be unilateral |

UMN, Upper motor neuron; VOR, vestibuloocular reflex.

of the pupillary reaction to light while the corneal reflex remains intact.

Brain death relates to destruction of both the upper and lower parts of the reticular formation in the brainstem, which will eventually lead to death. Cortical electrical activity and spinal reflexes may be preserved, but these are of no consequence because they are unable to be used for thought or movement.

Attention is more difficult to relate to specific brain structure than arousal. However, the acute confusional state is one of the most common neurologic disorders encountered. Although there is not a clear understanding of the mechanism of attention from the neuroanatomic perspective, there appears to be a major role played by the parietal and frontal lobes. Frontal and prefrontal areas of the brain are responsible for mental control, concentration, vigilance, and performance of meaningful activity. Cognition and emotional control are established by extensive white matter connections between the frontal lobes and the remainder of the cerebrum.⁴⁸ Diseases that affect the white matter, such as multiple sclerosis, can affect the level of attention without decreasing arousal. Psychiatric disease has an effect on both arousal and attention⁴⁹. The acute confusional state may be the result of a number of causes. Intoxicants, metabolic disorders, infections, epilepsy, blood flow disorders, traumatic injuries, and neoplasms can all be responsible for the change in orientation or attention.

Emotional Instability

The orbital prefrontal region is especially expanded in the right cortex and is dominant for selectively attending to facial expressions. It has extensive connections with limbic and subcortical regions, important in regulation of emotional information and mediation of pleasure and pain. Primitive emotions that serve fundamental motivational and social communication functions and nonverbal affects are spontaneously expressed on the face. Psychic systems process unconscious information. Empathetic cognition and the perception of the emotional

states of other human beings are developed within the first 3 years of life. Control of vital functions enable the individual to cope actively with stress and external challenge. Self-regulation functions are learned through this region.⁴⁹

Although the limbic system defies exact definition, it is recognized as the area of control of human behavior and is widely studied in behavioral neurology. The limbic system, sometimes referred to as the limbic lobe, is generally considered to encompass part of the cortical, diencephalon, and brainstem structures. This system includes the orbitofrontal cortex, hippocampus, parahippocampal gyrus, cingulate gyrus, dentate gyrus, amygdala, septal area, hypothalamus, and portions of the thalamus. The limbic lobe structures are seen in Fig. 28-14.⁴¹ Working together, these structures provide the essential, need-directed motor activity necessary for survival. This is the area that integrates the motivation and intentional drive to trigger a motor act. Both the automatic and somatic systems are influenced by the limbic system.⁵² Limbic syndromes involve the primary emotions, which are those associated with pain, pleasure, anger, and fear. The processing of the limbic system is responsible for the fact that emotionally charged experiences will be more easily remembered than those with less emotional stimulation.¹³ In lower animals, the limbic system is concerned primarily with the sense of smell, and it is a common observation that smells can trigger a strong emotional response in humans.

The amygdala are nuclei located in the medial temporal lobe anterior to the hippocampus as illustrated in Fig. 28-15. The amygdala is involved in sensory processing and determining the value of the information received. The patterns of emotional memories are formed here, and this is the area that establishes the anxiety and panic or the pleasure that is unconsciously related to an experience that may or may not be remembered.³ The amygdala is richly connected with the prefrontal cortex, the thalamus, hypothalamus, and brainstem as seen in Fig. 28-16.⁴¹ Not represented here is the influence that the prefrontal cortex has on the amygdala, which is thought

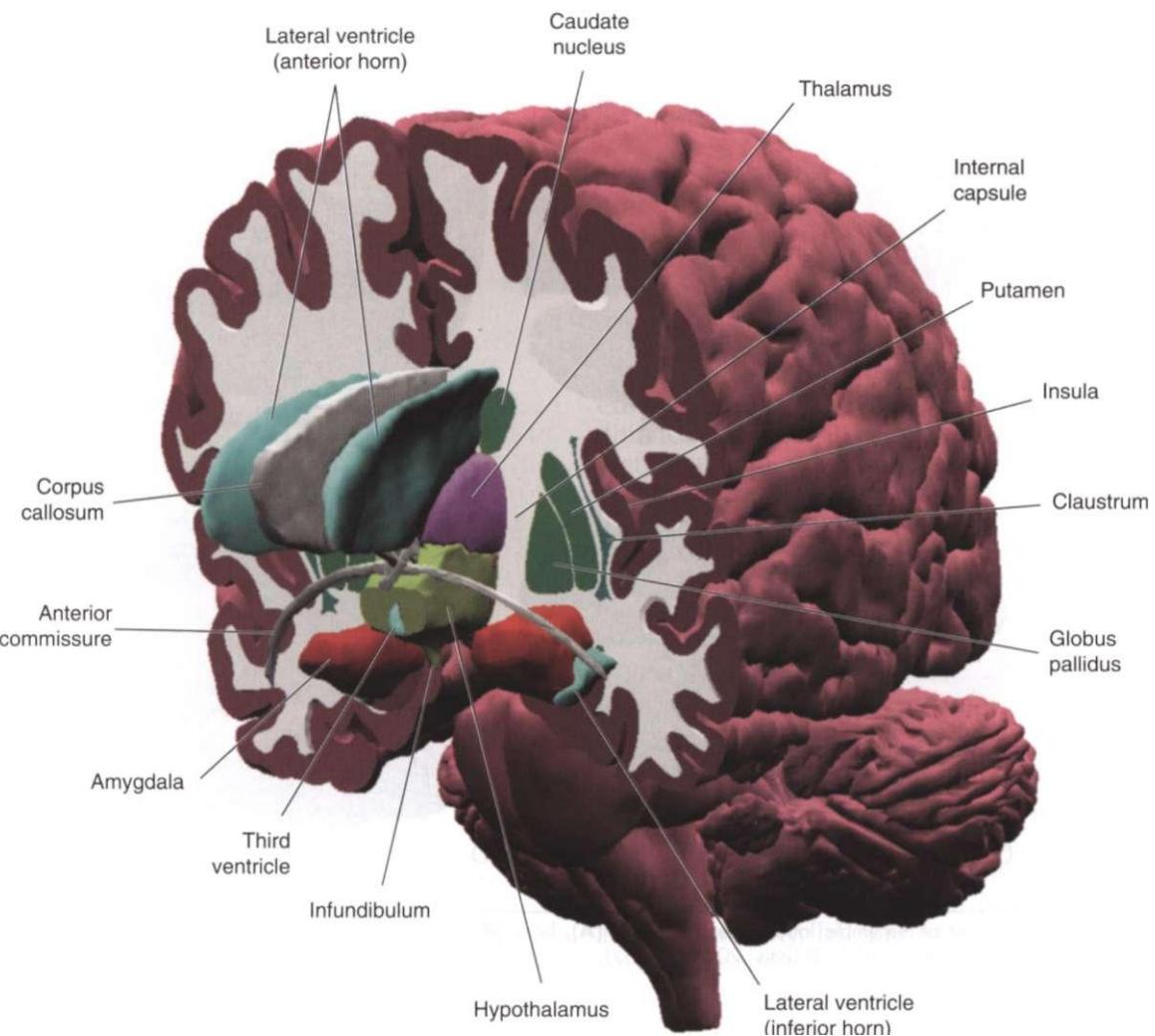


Figure 28-14

Three-dimensional representation of the structures of, and surrounding the limbic lobe. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

to be inhibitory. The amygdala is the central structure associated with the learning of fear, fearful responding, and associated autonomic and behavior responses.

Kindling is a term originally used to describe how sub-threshold seizure activity becomes increasingly active and severe with successive seizures. Partial kindling also can occur in the amygdala, and it appears related to increased defensive responses and anxiety-like behavior in animals. In humans the amygdala is involved in integrating emotional and contextual information that are parts of the human stress response. Amygdaloidal lesions result in hampered fear conditioning, whereas amygdaloidal stimulation results in classic fear responses such as defensive and aggressive behavior and autonomic reactivity. It has been demonstrated that the amygdala plays a role in conditioned fear responding in general and the startle response in particular.

Perhaps the best example of an anxiety disorder that seems to follow the classic fear-conditioning model is posttraumatic stress disorder (PTSD). Greater amygdala activations were identified in persons with PTSD than in

healthy controls. Activations in the amygdala correlated with weakened activation of the medial prefrontal cortex and hippocampus.³⁹ The prefrontal cortex is thought to be hypoactivated in PTSD, particularly during trauma memory activation. It is possible that such prefrontal cortex hypoactivation may be related to startle responses that are larger in PTSD when exposed to contexts in which they know they will be exposed to reminders of their trauma. Recent positron emission tomography (PET) studies have found that the amygdala is clearly active when individuals are thinking about their trauma.²⁸ The amygdala and the hippocampus play a crucial role in the pathophysiology of social phobia.

The thalamus is a two-lobed medial structure that sits just above the brainstem and is bounded on its dorsal surfaces by the lateral ventricles. The thalamus consists of multiple nuclei receiving input from sensory receptors and brainstem arousal systems and then relays this information to the frontal cortex, the cingulate gyrus, the amygdala, and the hippocampus. With the exception of olfaction, all sensory input goes through thalamic nuclei

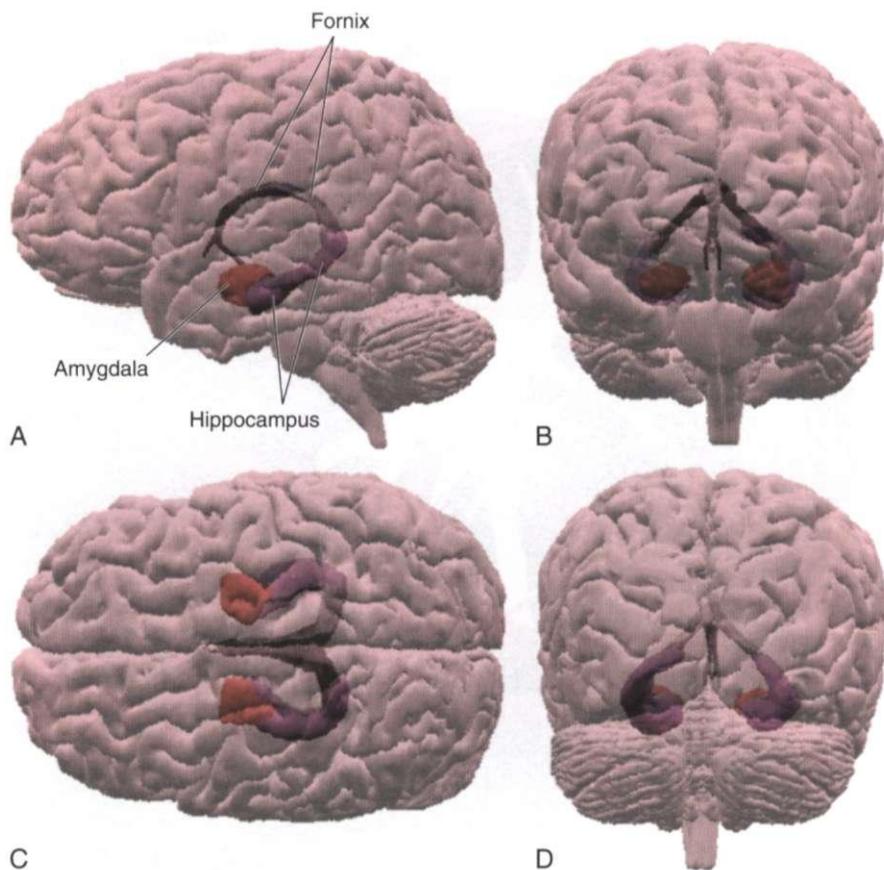


Figure 28-15

Placement of the main structures of the limbic lobe as seen from left (A), back (B), above (C), and behind (D). [From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.]

before being sent onto the cortex. The thalamus affects the quantity and quality of sensory processing. The fact that basic sensory information and arousal signals converge in the thalamus explains why even basic sensory signals can be distorted under conditions of high arousal. Although moderate arousal may facilitate transmission, conditions of high stress likely will distort or hinder transmissions to target structures throughout the brain.

Dissociative symptoms are common among survivors of trauma, and maladaptive levels of dissociation can develop alongside other pathologic responses to trauma. Dissociation is defined as a disruption in the usually integrated functions of consciousness, memory, identity, or perception of the environment, and the term *dissociative symptoms* in the literature have been used to capture a range of symptoms that can include changes in time perception, altered sensory perception, flashbacks, psychogenic amnesia, reduction in awareness, affective blunting, feelings of detachment, depersonalization, multiple identities, and derealization.^{15,28}

Although severe disturbances in sensory processing may occur under conditions of extreme stress, more subtle changes may occur even at baseline. The thalamus has rich bidirectional connections with the cingulate gyrus and the frontal cortex, two of the structures responsible for the prioritization and shifting of attention. During the extreme stress of an actual trauma, it is likely

that the thalamus impairs rather than facilitates the processing of environmental stimuli. In this sense, the thalamus has a role to play in amnesia for traumatic events. For example, disruption in the relay of contextual and traumatic information could contribute to the fragmentation and inaccuracies associated with traumatic memory. Unlike the role the hippocampus might play in fragmenting sensory elements of the memory, however, thalamic interference would result in an initial interference with basic stimulus encoding.²⁸

Levels of emotion that are generated and advanced by the limbic system, or more specifically the amygdala, can be described on a continuum. An emotion can be triggered as fear or frustration, which when heightened can manifest as anger. If the neurochemical activity continues to build and leads to internal chaos or conflict, it becomes rage. The motor response will become violent if there is a sufficient trigger. Genetics and environmental history will lead to differences in how a person moves from fear to violence. When there is damage to the area of the limbic lobe that results from injury or disease, there can be an increase in rage and easy progression to violence. The diffuse axonal damage of head injury can cause a tendency to become easily frustrated or to have unsubstantiated fears.

The different symptom dimensions of obsessive-compulsive disorder and other anxiety disorders are likely to

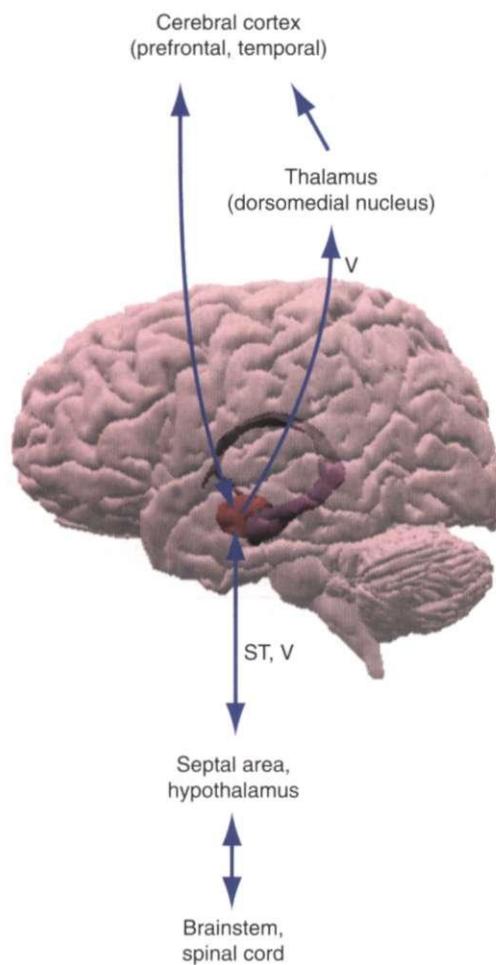


Figure 28-16

The limbic lobe gives input directed toward the cerebral cortex and the hypothalamus, brainstem, and spinal cord. [From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.]

share common neural substrates dedicated to general threat detection and emotional arousal because these reactions are adaptive and useful to deal with different kinds of threat. Research suggests that syndrome-specific neural substrates may have evolved to deal with specific threats. In evolutionary terms, general anxiety, which is common to individuals who have obsessive-compulsive disorder and other anxiety disorders, may have evolved to deal with nonspecific threats, for example, cleanliness is important for protection against infections; harming obsessions and checking rituals keep people safe; and hoarding helps people survive periods of scarcity. The neuroimaging findings, showing increased activation of limbic and ventral frontal-striatal regions in obsessive-compulsive disorder, could reflect exaggerations of normal emotional responses to biologically relevant stimuli rather than fundamentally abnormal neuronal responses.³⁵

Borderline personality disorder (BPD), including affective dysregulation, identity disturbance, and self-mutilating behaviors, were originally thought to involve

a disorder of character. In recent studies, it appears that BPD individuals are compromised significantly in executive skill and/or other frontal lobe functions, visuomotor speed, attention, and verbal memory. These fairly consistent neuropsychologic findings in adults are supported by developmental studies of children with borderline features. These children appear to have greater difficulty with executive skills, including planning, organizing, and sequencing; perceptual motor functioning; and memory proficiency.³⁹

Fear conditioning is a fast process, with a long-lasting effect, but repeated exposure to the conditioned stimulus in the absence of the unconditioned stimulus can lead to extinction. Extinction reduces the likelihood that the conditioned stimulus will elicit the fear response. The medial prefrontal and anterior cingulate cortices have been implicated in extinction learning. Understanding how learned fears are diminished and how extinction learning is changed in individuals who have anxiety disorders might be an important step in translating neurobiology research to diagnosis and treatment of these individuals.

Memory Problems

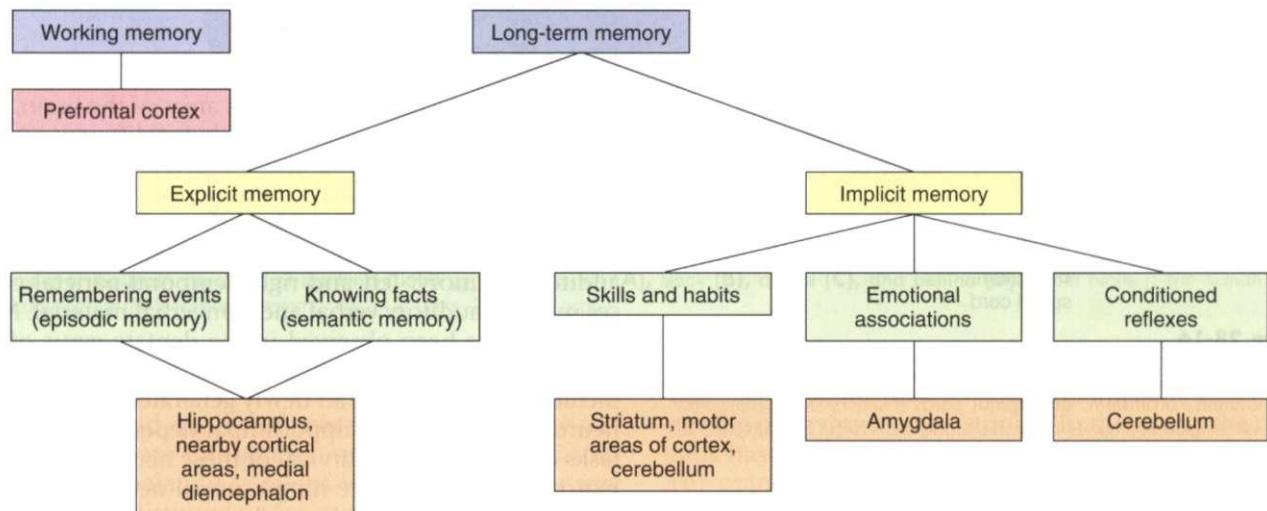
Memory is associated with various areas of the brain, and a particular area may be responsible for different aspects of memory. The hippocampus, the thalamus, and the basal forebrain are critical to the performance of recent memory (Table 28-3). Fig. 28-17 shows the relationship of learning strategies and brain regions. For immediate auditory memory, left and right temporal-parietal cortices mediate auditory verbal and nonverbal material. Neurogenesis has been observed in the dentate gyrus of the hippocampus throughout the lives of many species, including humans. Not all newly generated hippocampal neurons survive, but hippocampal-dependent memory tasks can enhance the survival of these neurons.²¹ Inflammatory cytokines reduce hippocampal neurogenesis and impair the ability to maintain long-term potentiation in the hippocampus, which is a critical physiologic process involved in memory consolidation.²⁰

Working memory, the ability to hold information in short-term storage while permitting other cognitive operations to take place, appears to depend on the prefrontal cortex. Keeping a spatial location in mind may involve a right frontal area that directs the maintenance of that information in a right parietal area, whereas keeping a word in mind may involve a left frontal area that directs the maintenance of that information in a left temporal or parietal area. Specific basal ganglia and cerebellar areas appear to support the working memory capacity of particular frontal regions.

Disorders of recent memory, known as *amnesia*, are a significant neurobehavioral phenomenon and common in persons after traumatic brain injury. *Declarative memory* is retention of facts and events of a prior experience or the memory of what has occurred and is related to explicit learning. *Procedural memory* describes the learning of skills and habits, or how something is done. Implicit learning is based on procedural memory. The relationship to memory and relearning motor skills is discussed in the

Table 28-3 Correlation of Anatomic Site to Disorders of Memory and Other Neurologic Findings

| Anatomic Site of Damage | Memory Finding | Other Neurologic and Medical Findings |
|---|---|---|
| Frontal lobe | Lateralized deficit in working memory. Right spatial defects, left verbal defects, impaired recall with spared recognition | Personality change Perseveration Chorea, dystonia Bradykinesia, tremor, rigidity |
| Basal forebrain | Declarative memory deficit | |
| Ventromedial cortex | Frontal lobe-type declarative memory deficit | Upper visual field defects |
| Hippocampus and parahippocampal cortex | Bilateral lesions yield global amnesia, unilateral lesions show lateralization of deficit. | |
| Fornix | Left: verbal deficit; right: spatial deficit | |
| Mammillary bodies | Global amnesia | |
| Dorsal and medial dorsal nucleus thalamus | Declarative memory deficit | |
| Anterior thalamus | Declarative memory deficit | |
| Lateral temporal cortex | Deficit in autobiographical memory | |

**Figure 28-17**

Anatomic correlates for explicit and implicit learning. (From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.)

Special Implications for the Physical Therapist: Motor Learning Strategies in this chapter.

Anterograde amnesia is the failure of new learning or formation of new memory. *Retrograde amnesia* is the loss of ability to recall events. The inability to acquire new learning is often accompanied by *confabulation*, the fabrication of information in response to questioning. *Traumatic amnesia* refers to an individual's inability to recall significant aspects of their traumatic experience. Traumatic memories are reported to be fragmented, compartmentalized, and disintegrated, suggesting that the hippocampus still may have a role to play in the phenomena of traumatic amnesia. Dysregulation in the hippocampal system has the potential to generate narratives of traumatic events that are spotty and unreliable.

Neuromodulators, such as norepinephrine, have the potential to affect hippocampal functioning in a more

dynamic fashion. The locus ceruleus, located in the brainstem, for example, projects directly to the hippocampus and modulates its functioning through norepinephrine release. The effects of such a network are unclear, although the implications are that stress-related memory alterations might occur on a split-second basis and deficient or extreme locus ceruleus input may disrupt normal hippocampal processing severely. Given that the hippocampus plays a role in integrating input from diverse sources when encoding memory, disruptions in its functioning may lead to memories that seem fragmented and nonlinear. Over time, fragments of the memory may become consolidated, vivid, and easily recalled, while other fragments rarely are accessed.²⁸

The role of stress in neurologic disease often is overlooked. Several chronic neurologic disease states, such as Alzheimer's disease, are associated with elevated

secretion of stress hormones, in particular Cortisol, which results from overactivity of the hypothalamic-pituitary-adrenal (HPA) axis. The stress or perceived threat activates the hypothalamus, triggering release of hormones that cause increased adrenal output of Cortisol.⁴⁷ Stress also can trigger or exacerbate symptom onset and perhaps progression of chronic illness such as Parkinson's disease. Stress hormones also can mitigate the impact of acute neurotrauma; for example, there is a positive correlation between Cortisol levels and mortality after head injury. Thus neurologic disease states can occur within a context of elevated glucocorticoids, which may have profound influences on recovery and neuroplasticity. In addition, abnormal regulation of glucocorticoid release is associated with many affective disorders, such as depression and PTSD, that are overrepresented in populations with neurologic disease; Parkinson's disease is a prime example. Acute and sustained glucocorticoid release also can precipitate changes in peripheral and central immune signaling, resulting in cytokine profiles that may be deleterious for functional recovery in the face of neurologic challenge.²³

Accumulation of risk is another concept that plays a pivotal role in the life-course model of chronic diseases. Allostasis is defined as the ability to achieve stability through change. The price of this accommodation to stress has been defined as the allostatic load. It follows that acute stress (the "fight, flight, or freeze" response) and chronic stress resulting from the cumulative load of minor day-to-day stresses can add to the allostatic load and have long-term consequences. Subacute stress is defined as an accumulation of stressful life events over a duration of months and includes emotional factors, such as hostility and anger, as well as affective disorders such as major depression and anxiety disorders. Chronic stressors include factors, such as low social support, work stress, marital stress, and caregiver strain, and present as feelings of fatigue, lack of energy, irritability, and demoralization.

The link between chronic psychologic distress and adverse behavior, such as overeating, may be centrally mediated. Normally, glucocorticoids help end acute stress responses by exerting negative feedback on the HPA axis. The combination of chronic stress and high glucocorticoid levels seems to stimulate a preferential desire to ingest sweet and fatty foods, presumably by affecting dopaminergic transmission in areas of the brain associated with motivation and reward.¹⁷

Brain areas associated with reward are linked with those that sense physical pain. Chronic pain can cause depression, and depression can increase pain. Most individuals who have depression also present with physical symptoms. Studies using functional magnetic resonance imaging (fMRI) have shown that social rejection lights up brain areas that are also key regions in the response to physical pain. The area of the anterior cingulate cortex that is activated by visceral pain also is activated in cases of social rejection.

Disturbances of neurologic function can result in behavioral disturbances that mimic disturbances of mental function in psychiatric disorders. *Delusions*, or fixed false beliefs, have been reported in a great variety of

Box 28-2

RAPID-EYE-MOVEMENT (REM) SLEEP BEHAVIOR DISORDER AND RELATED BRAINSTEM STRUCTURES

- Substantia nigra (midbrain-dopaminergic)
- Locus caeruleus (brainstem-noradrenergic)
- Pedunculopontine nucleus (pons-cerebellum)
- Dorsal vagus nucleus
- Dorsal raphe nucleus (involved in serotonin pathways)
- Gigantocellular reticular nucleus (control of arousal)

Modified from Gagnon JF. Rapid-eye-movement sleep behaviour disorder and neurodegenerative diseases. *Neurol* 5(5): 424-432, 2006.

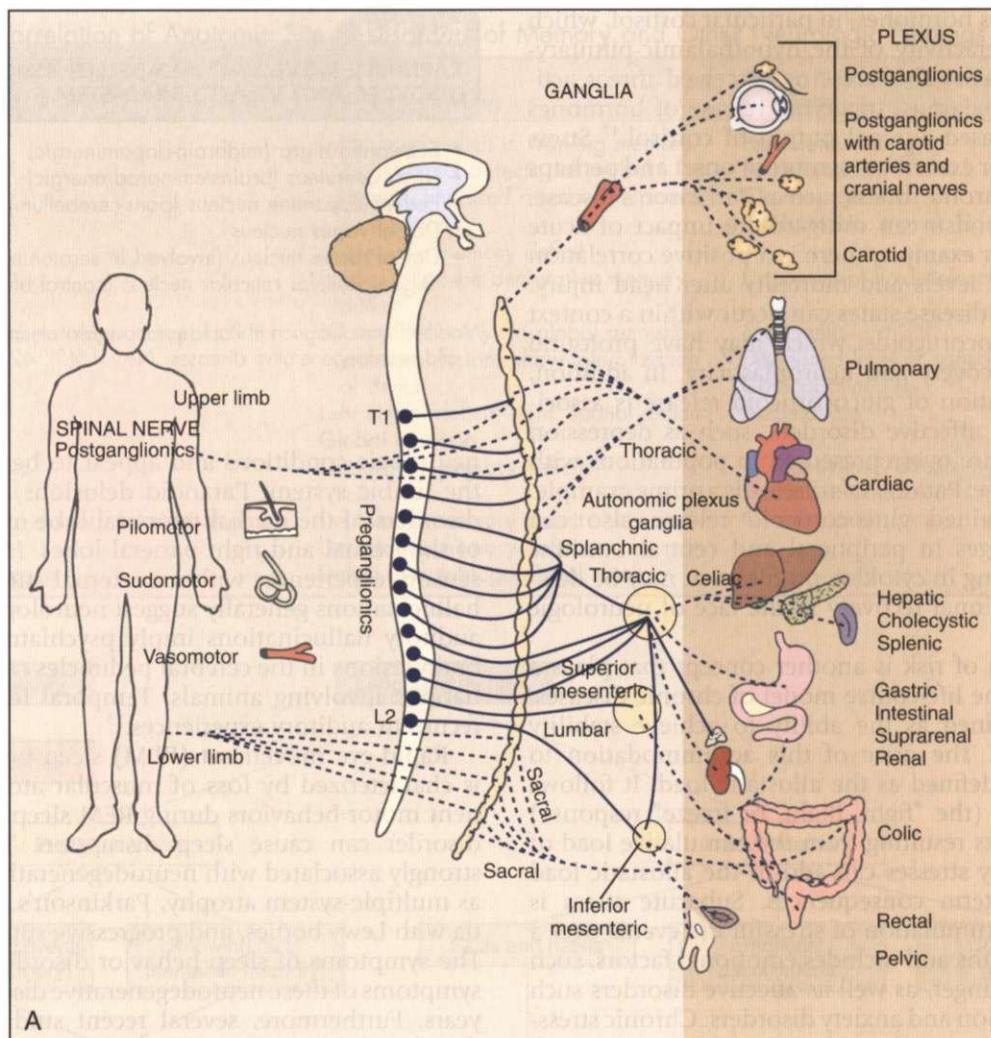
neurologic conditions and appear to be associated with the limbic system. Paranoid delusions are common in disorders of the medial temporal lobe or a combination of the frontal and right parietal lobes. *Hallucinations* are sensory experiences without external stimulation. Visual hallucinations generally suggest neurologic involvement; auditory hallucinations imply psychiatric disease. Midbrain lesions in the cerebral peduncles can cause hallucinations involving animals. Temporal lesions can cause recurrent auditory experiences.¹³

Rapid-eye movement (REM) sleep behavior disorder is characterized by loss of muscular atonia and prominent motor behaviors during REM sleep. Sleep behavior disorder can cause sleep disruption. The disorder is strongly associated with neurodegenerative diseases such as multiple-system atrophy, Parkinson's disease, dementia with Lewy bodies, and progressive supranuclear palsy. The symptoms of sleep behavior disorder precede other symptoms of these neurodegenerative disorders by several years. Furthermore, several recent studies have shown that sleep behavior disorder is associated with abnormalities of electroencephalographic (EEG) activity; cerebral blood flow; and cognitive, perceptual, and autonomic functions. Sleep behavior disorder might be a stage in the development of neurodegenerative disorder. Box 28-2 includes the areas of the brain that play a role in sleep behavior.¹⁸

Lesions of the hemispheres or lobes may cause loss of the functions that each hemisphere controls. Because diseases and damage caused by trauma will often affect one area of the brain, the associated syndromes for the main areas of the brain are described.³³

Autonomic Nervous System

The term *autonomic nervous system* was introduced to describe the system of nerves that controls the unstriated tissue, the cardiac muscle, and the glandular tissue of mammals involved in the control of autonomic function. The autonomic CNS neurons are located at many levels from the cerebral cortex to the spinal cord. Efferent autonomic pathways are organized in two major outflows: the sympathetic and parasympathetic. Finally, the enteric nervous system, which is considered a separate and independent division of the autonomic nervous system, is located in the walls of the gut. The schematic diagram of the autonomic nervous system is seen in Fig. 28-18.

**Figure 28-18**

Sympathetic (A) and parasympathetic (B) divisions of the autonomic nervous system: efferent systems. (From Levy MN, Koeppen BM: *Berne and Levy principles of physiology*, ed 4, St. Louis, 2006, Mosby.)

Neurons in the cerebral cortex, basal forebrain, hypothalamus, midbrain, pons, and medulla participate in autonomic control. The central autonomic network integrates visceral, humoral, and environmental information to produce coordinated autonomic, neuroendocrine, and behavioral responses to external or internal stimuli. A coordinated response is generated through interconnections among the amygdala and the neocortex, forebrain, hypothalamus, and autonomic and somatic motor nuclei of the brainstem. The insular and medial prefrontal cortices (paralimbic areas) and nuclei of the amygdala are the higher centers involved in the processing of visceral information and the initiation of integrated autonomic responses. The central nucleus of the amygdala projects to the hypothalamus, periaqueductal gray (PAG), and autonomic nuclei of the brainstem to integrate autonomic, endocrine, and motor responses to emotionally relevant stimuli.

The hypothalamus integrates the autonomic and endocrine responses that are critical for homeostasis. The PAG matter of the midbrain is the site of integrated autonomic, behavioral, and antinociceptive stress responses.

It is organized into separate columns that control specific patterns of response to stress. The lateral PAG mediates sympathoexcitation, opioid-independent analgesia, and motor responses consistent with the fight-or-flight reaction. The ventrolateral PAG produces sympathoinhibition, opioid-dependent analgesia, and motor inhibition.

Neurons in the medulla are critical for the control of cardiovascular, respiratory, and gastrointestinal functions. The medullary nucleus of the solitary tract is the first relay station for the arterial baroreceptors and chemoreceptors, as well as cardiopulmonary and gastrointestinal afferents.

Preganglionic sympathetic neurons are organized into different functional units that control blood flow to the skin and muscles, secretion of sweat glands, skin hair follicles, systemic blood flow, as well as the function of viscera. Selectivity is refined by the release of different neurotransmitters. Acetylcholine is the neurotransmitter of the sympathetic and parasympathetic preganglionic neurons. The main postganglionic sympathetic neurotransmitter is norepinephrine.

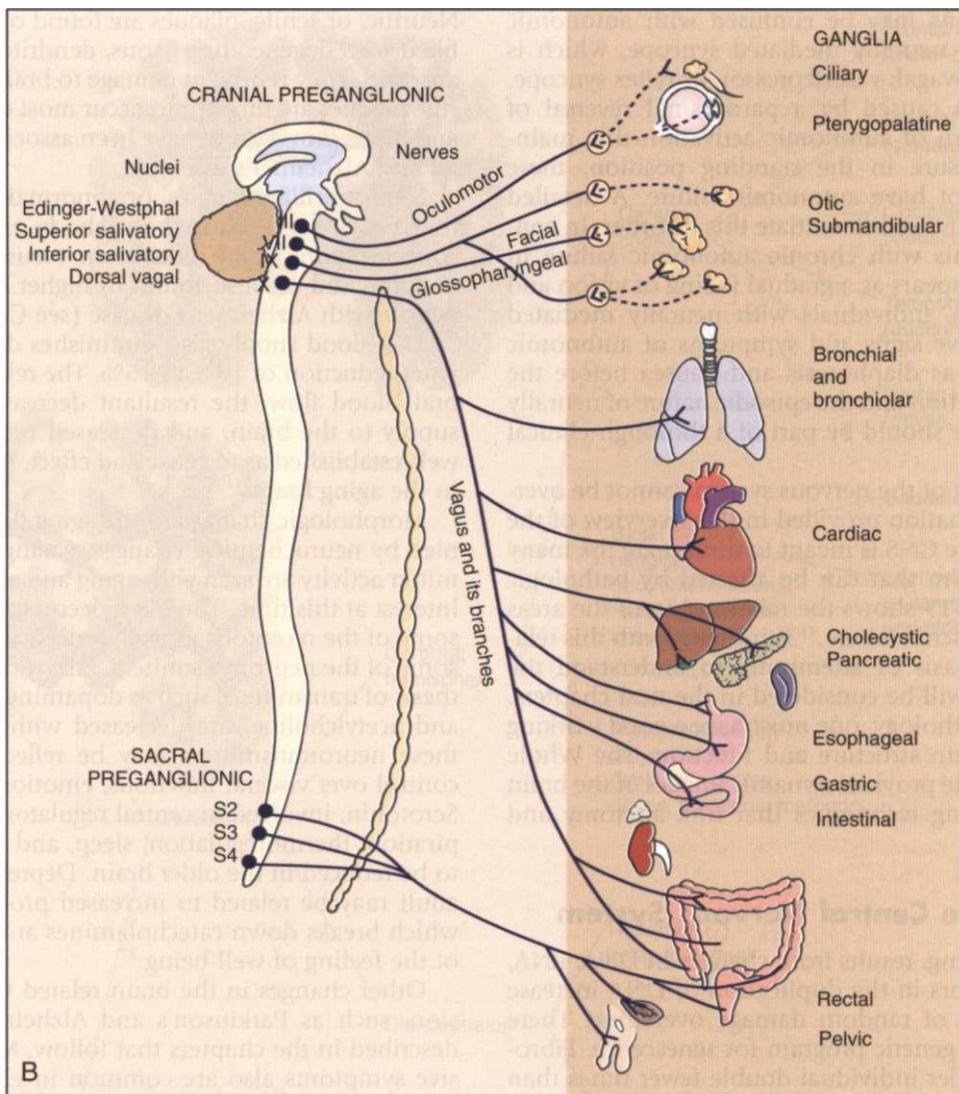


Figure 28-18, cont'd

See legend on previous page.

Visceral afferents transmit conscious sensations (e.g., gut distention and cardiac ischemia) and unconscious visceral sensations (e.g., blood pressure and chemical composition of the blood). Their most important function is to initiate autonomic reflexes at the local, ganglion, spinal, and supraspinal levels. Visceral sensation is carried primarily by the spinothalamic and spinoreticular pathways, which transmit visceral pain and sexual sensations. Brainstem visceral afferents are carried by the vagus and glossopharyngeal nerves. Brainstem visceral afferents are important in complex automatic motor acts such as swallowing, vomiting, and coughing.²¹

Traumatic spinal cord injury, particularly injury above the T5 level, is associated with severe and disabling cardiovascular, gastrointestinal, bladder, and sexual dysfunction. These individuals have both supine and orthostatic hypotension and are at risk of developing bradycardia and cardiac arrest during tracheal suction or other maneuvers that activate the vagovagal reflexes.

Pure autonomic failure with no other neurologic deficits is rare. More often, autonomic failure occurs in combination with other neurologic disorders, such as Parkinson's disease, and multiple system atrophy. In these individuals, it is important for the examiner to inquire about abnormalities in gait, changes in facial expression, the presence of dysarthria, difficulty in swallowing, and balance problems. Autonomic failure also occurs in individuals with some peripheral neuropathies such as those associated with diabetes. Because autonomic failure may be caused by lesions at different levels of the nervous system, a history of secondary trauma, cerebrovascular disease, tumors, infections, or demyelinating diseases should be established. Additionally, because the most frequent type of autonomic dysfunction encountered in medical practice is pharmacologic, there should be a thorough review of medication use, especially antihypertensive and psychotropic drugs.

Some conditions may be confused with autonomic failure, including neurally mediated syncope, which is referred to as vasovagal, vasodepressor, or reflex syncope. This condition is caused by a paroxysmal reversal of the normal pattern of autonomic activation that maintains blood pressure in the standing position; these individuals do not have autonomic failure. A detailed history is important to differentiate this disorder. In contrast to individuals with chronic autonomic failure in whom syncope appears as a gradual fading of vision and loss of awareness, individuals with neurally mediated syncope often have signs and symptoms of autonomic overactivity such as diaphoresis and nausea before the event. This distinction and the episodic nature of neurally mediated syncope should be part of a thorough clinical history.

The complexity of the nervous system cannot be overstated. The information provided in this overview of the components of the CNS is meant to illuminate the many facets of the system that can be affected by pathologic processes. Fig. 28-19 shows the relationship of the areas that have been described here.⁴¹ Familiarity with this relationship is the basis of attempting to understand the pathologies that will be considered in the next chapters. To understand pathology, one must have a good working knowledge of brain structure and function. The Whole Brain Atlas web site provides dynamic images of the brain integrating imaging techniques that link anatomy and pathology.⁶⁶

Aging and the Central Nervous System

Senescence, or aging, results from changes in DNA, RNA, and proteins. Errors in the duplication of DNA increase with age because of random damage over time. There may be a specific genetic program for senescence. Fibroblasts from an older individual double fewer times than those of an embryo.

Age-related reduction in adult brain weight represents loss of brain tissue. There is highly selective atrophy of brain tissue in the aging CNS. It is not clear how much of the change represents actual loss of nerve cells, since the changes in vascular tissue and glial cells may represent some of the loss. Simple loss of cells is common. Nerve cell shrinking, causing possible changes in functional efficiency, may be a more important effect of old age than cell loss. Nerve conduction velocity decreases with age in both the motor and sensory systems. By the eighth decade there is an average loss of 15% of the velocity in the myelinated fibers.³²

The inner structure of the nerve cell changes with aging. The presence of lipofuscin, or wear and tear pigment, a pigmented lipid found in the cytoplasm, may interfere with normal cell function via pressure on the cell nucleus. The pigmented nuclei of the brainstem catecholaminergic neurotransmitter accumulates with age. Damage to an axon close to the neuronal cell body results in changes in the area of the cell body and is referred to as an axonal reaction. The mechanism and relationship to dysfunction are still not clearly understood. The deposition of amyloid- β protein creating plaques in the cerebral cortex is found in many but not all older people.

Neuritic, or senile, plaques are found outside the neuron filled with degenerating axons, dendrites, astrocytes, and amyloid. They represent damage to brain tissue. The neuritic plaques are thought to occur most often in the cortex and hippocampus and have been associated with dementia and Alzheimer's disease.¹⁴

Neurofibrillary tangles, or abnormal neurologic fibers that displace and distort the cell body, are found in higher concentrations in the older brain. Neurofibrillary tangles and amyloid are also found in higher concentrations in people with Alzheimer's disease (see Chapter 31).

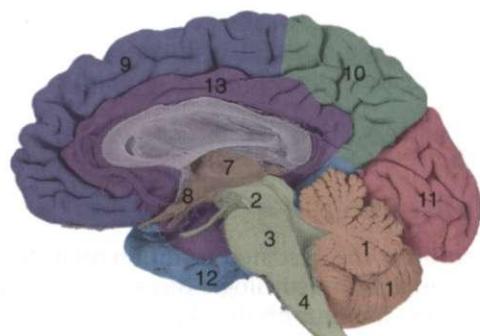
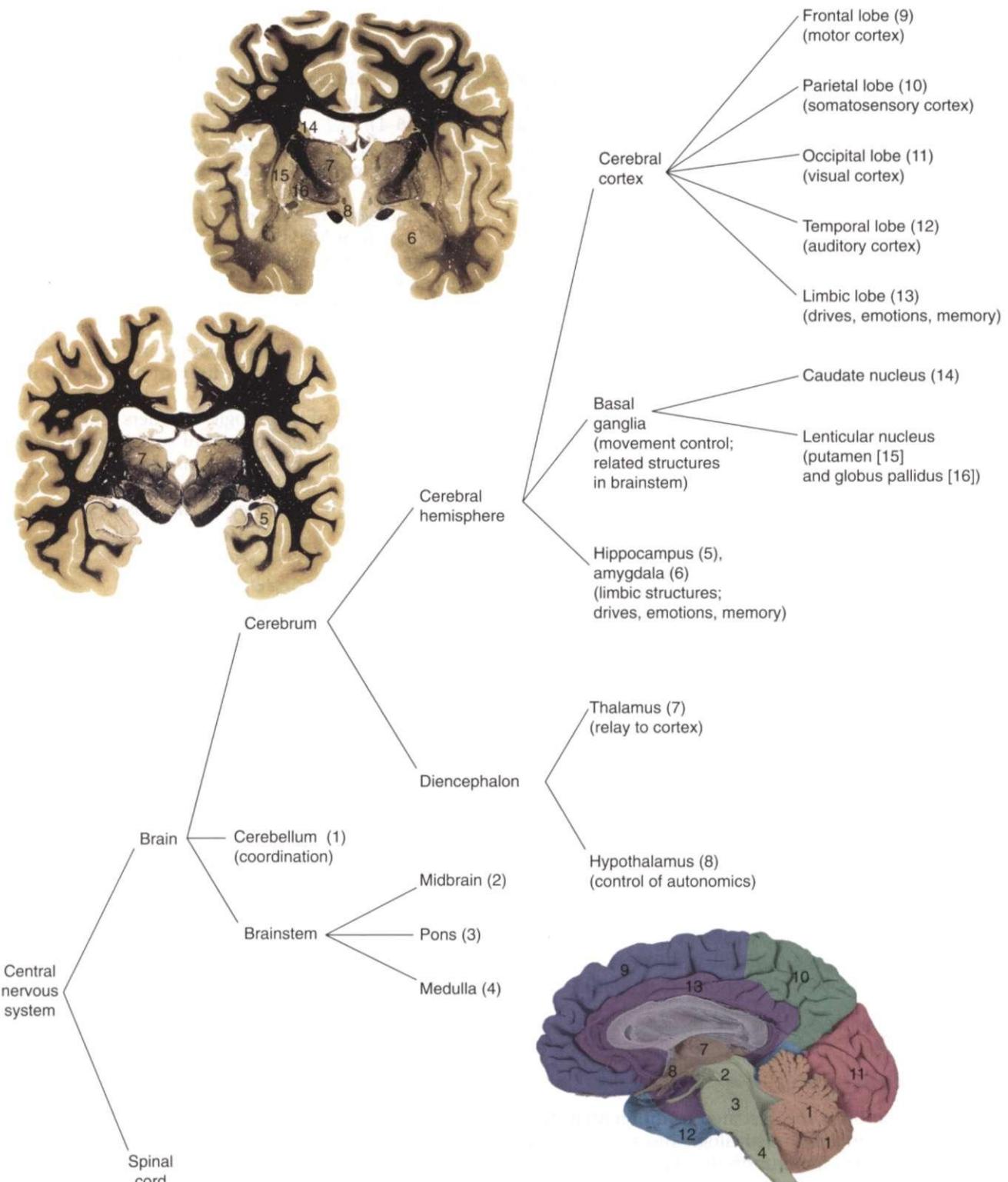
The blood supply also diminishes during aging, with a net reduction of 10% to 15%. The relationship of cerebral blood flow, the resultant decrease in the glucose supply to the brain, and decreased metabolism are not well-established as to cause and effect. All three are noted in the aging brain.⁴⁴

Morphologic changes in the aging brain are accompanied by neurochemical changes. Changes in neurotransmitter activity are seen with aging and are an area of great interest at this time. There is a decrease in the number of some of the receptors, as well as decreases in synthesis of some of the neurotransmitters. Enzymes involved in synthesis of transmitters, such as dopamine, norepinephrine, and acetylcholine, are decreased with age. Changes in these neurotransmitters may be reflected in decreased control over visceral functions, emotions, and attention. Serotonin, involved in central regulatory activities of respiration, thermoregulation, sleep, and memory, appears to be reduced in the older brain. Depression in the older adult may be related to increased production of MAO, which breaks down catecholamines and results in a loss of the feeling of well-being.²⁷

Other changes in the brain related to neurotransmission, such as Parkinson's and Alzheimer's disease, are described in the chapters that follow. Mood and depressive symptoms also are common in elderly individuals who are ill and are associated with increased morbidity and mortality. There is a relationship between inflammatory cytokines and depressive disorders. Age-associated alterations in immunity are apparent in the innate immune cells of the brain. There is an elevated inflammatory profile in the aging brain consisting of an increased population of reactive glia. A potential consequence of a reactive glial cell population in the brain is an exaggerated inflammatory response to innate immune activation. Even in the absence of detectable disease, the glia population undergoes an age-related transformation that creates a more sensitive brain environment.

An amplified and prolonged inflammatory response in the aged brain promotes protracted behavioral and cognitive impairments and the behavioral consequences of illness and infection in the elderly, if prolonged, can have deleterious effects on mental health. There is an increased prevalence of delirium in elderly individuals who present to the emergency department as a result of infections unrelated to the CNS. Viral or bacterial pneumonia in the aged frequently presents clinically as delirium, even in the absence of classic pneumonia symptoms.²⁰

The central mechanisms that are involved in the control of balance do not appear to change excessively with age but are more likely to be affected by degenerative

**Figure 28-19**

Overview of the subdivisions of the central nervous system (CNS). [From Nolte J: *The human brain: an introduction to its functional anatomy*, ed 5, St Louis, 2002, Mosby.]

neurologic diseases such as Parkinson's or Alzheimer's disease. Age-related changes in the peripheral vestibular system include hair cell receptors that begin to decrease at the age of 30 years, and by 55 to 60 years, there is a loss of the vestibular receptor ganglion cells. The myelinated nerve cells of the vestibular system show up to a 40% loss. Partial loss of vestibular function in the older population can lead to complaints of dizziness, with less ability of the nervous system to accommodate the loss compared with younger persons.

In addition to vestibular losses, there is concomitant loss of other sensory inputs relating to balance and mobility: vision and somatosensation. Maintaining equilibrium, or balance, requires a multimodal system integrating vestibular, visual, and somatosensory signals. The integration of these signals in the CNS coordinates multiple output responses: eye movement, postural correction, motor skill, and conscious awareness of spatial orientation. There are longer response latencies and delayed reaction times. Vision changes include loss of acuity, decreased peripheral fields, and loss of depth perception. The loss of input from this combination is slow, with compensation developing through the years.¹¹ Eventually a loss of functional reserve, or redundant function, that is normally present in virtually all physiologic systems is seen with aging. There is an apparent decrease in the ability to integrate conflicting sensory information to determine appropriate postural responses. Changes occur as well in motor output that may contribute to the loss of balance and mobility.¹⁰ Although the response patterns are the same in young and old people, with responses being activated in the stretched ankle muscle and radiating up to the thigh, in some older people, this response is disrupted with the proximal muscles being activated before the distal muscles. In the older person, there appears to be more co-contraction of muscles around the ankle as a result of perturbation.⁵³

Neurologic disease is more prevalent in older persons, as is the risk of neurologic sequelae as a result of intracranial hemorrhage, subdural hematoma, and neoplasms. Awareness of the signs and symptoms of these disorders is essential. The therapist may be the person able to identify a disease or the potential for a disorder that may manifest during a treatment session.

DIAGNOSIS

Clinical Localization

Clinical localization is the first step to differential diagnosis for an individual with neurologic disease. Coupling the time course of the illness with the clinical localization is the essence of neurology. The history of the onset and nature of the symptoms is critical to establish the diagnosis related to the neurologic disorder. In many cases, based on the history and symptoms, the clinician is able to generate a hypothesis regarding the site in the nervous system that has been affected and the nature of the lesion. A complete history of the nature of the symptoms is also critical to determining which diagnostic tools will provide the most accurate differential diagnosis and best determine the cause.

The examination of the client with neurologic dysfunction often begins with mental status changes. Alterations of consciousness and disturbances of higher brain function give the clinician clues about the nature of the disease process and the location of damage within the brain⁵⁹ (Table 28-4).

Motor and sensory changes will also reflect the type, level, and extent of damage to the system in the case of both disease and trauma. Understanding the typical motor and sensory changes associated with a particular disease or disorder leads the evaluation. For example, knowing that ALS involves both upper and lower motor signs may help the clinician when this otherwise perplexing condition presents in the clinic. Understanding the functional deficits related to each condition can also lead the clinician to a diagnosis. Gait disorders are often representative of the level or location of damage within the nervous system.

The diagnosis of neurologic disorders remains a clinical specialty, although the use of sophisticated imaging and measurement of neural function have provided insight into the pathologic state of the nervous system. The following are examples of diagnostic test currently performed.

Computed Tomography

Computed tomography (CT) scans allow a snapshot of the CNS, and damage within tissue can be identified. Disorders affecting blood flow, multiple sclerosis, neoplasm, and infection can be identified with these scans. CT is an excellent study to evaluate for acute intracranial hemorrhage, particularly in the subarachnoid space. Active bleeding may be detected in either epidural or subdural hemorrhages as a relative lucency, which is commonly referred to as the "swirl sign." Edema from excitotoxic damage associated with infarct or diffuse anoxia can be seen representing intracellular fluid, and vasogenic edema is the abnormal accumulation of extracellular fluid in the white matter that looks like fingers following the white matter tracts. Evaluation of ventricular size can be done by CT. Enlargement of the temporal horns out of proportion to the lateral ventricular bodies is helpful in recognizing early hydrocephalus. CT can be helpful to follow ventricular size after shunting.

CT is very useful for detecting intracranial calcifications such as those seen in congenital infections, vascular lesions, and metabolic disease. The location and distribution of calcifications is helpful in differentiating these various causes. The identification of calcification in a neoplasm aids in differential diagnosis.²¹

Magnetic Resonance Imaging

MRI signal patterns are recognizable with common diseases such as cerebral edema, neoplasm, abscess, infarcts, or demyelinating processes. MRI is the study of choice to evaluate all lesions in the brain and spine. CT, however, is more sensitive than MRI for the evaluation of calcifications, subtle fractures, and remains pivotal in the diagnosis of acute subarachnoid hemorrhage. Additionally, MRI cannot be performed in individuals who have

Table 28-4 Useful Studies in the Evaluation of Disorder of Level of Consciousness

| Syndrome | Neuroimaging | Electrophysiology | Fluid and Tissue Analysis | Neuropsychologic Tests |
|--|--|--|---|--|
| Bilateral cortical dysfunction; confusion and delirium | Usually normal; may show atrophy; rarely bilateral chronic subdural hematoma or evidence of herpes simplex encephalitis; dural enhancement in meningitis, especially neoplastic meningitis | Diffuse slowing; often, FIRDA; in herpes simplex encephalitis, PLEDS | Blood or urine analyses may reveal etiology; CSF may show evidence of infection or neoplastic cells | In mild cases, difficulty with attention (e.g., trailmaking tests); in more severe cases, formal testing is not possible |
| Diencephalic dysfunction | Lesion(s) in or displacing of diencephalon; also displays mass displacing the diencephalon | Usually, diffuse slowing; rarely, FIRDA; in displacement syndromes, effect of the mass producing displacement (e.g., focal delta activity, loss of faster rhythms) | Usually not helpful | Usually not obtained |
| Midbrain dysfunction | Lesion(s) in the midbrain or displacing it | Usually, diffuse slowing; alpha coma; evoked response testing may demonstrate failure of conduction above the lesion EEG: usually normal; evoked responses usually normal | Rarely, platelet or coagulation abnormalities | Usually not performed |
| Pontine dysfunction | Lesion(s) producing syndrome; thrombosis of basilar artery | EEG: usually normal; evoked responses usually normal | Rarely, platelet or coagulation | Usually not performed |
| Medullary dysfunction | Lesion(s) producing dysfunction | EEG: normal; brainstem auditory and somatosensory evoked responses may show conduction abnormalities | Rarely, platelet or coagulation abnormalities | Usually not performed |
| Herniation syndromes | Lesion(s) producing herniation; appearance of perimesencephalic cistern | Findings related to etiology | Findings related to etiology | Usually not performed |
| Locked-in syndrome | Infarction of basis pontis | EEG and evoked potential studies: normal | Findings related to etiology | Usually not performed |
| Death by brain criteria | Absence of intracranial blood flow above the foramen magnum | EEG: electrocerebral silence; evoked potential studies may show peripheral components (e.g., wave I of brainstem auditory evoked response) but no central conduction | Absence of hypnotic drugs | Not done |
| Psychogenic unresponsiveness | Normal | Normal | Normal | Helpful after patient "awakens" |

From Koenigsberg RA, Faro SH, Hershey BL, et al: Neuroimaging. In Goetz CG: *Textbook of clinical neurology*, ed 2, Philadelphia, 2003, WB Saunders.

FIRDA, Frontally predominant intermittent rhythmic delta activity; PLEDS, periodic lateralized epileptiform activity; CSF, cerebrospinal fluid; EEG, electroencephalogram.

intraorbital foreign bodies, pacemakers, or non-MRI-compatible implants, such as artificial heart valves, vascular clips, cochlear implants, or ventilators. The use of MRI is the modality of choice for detecting congenital malformations. Infection of the spine is better evaluated by MRI.

Functional Magnetic Resonance Imaging

fMRI is based on blood oxygenation level-dependent (BOLD) imaging of the brain and provides functional data of cerebral activation during any given task (e.g.,

motor, visual, or cognitive). This method allows for a quantitative nonclinical method for assessing changes in cerebral function as related to cerebral activities (i.e., performance of physical or cognitive tasks). The BOLD fMRI technique allows for detection of minute changes in cerebral oxygenation. fMRI studies of various pathways of the brain, including the language, memory, and visual pathways, will enhance our ability to connect activity to changes in the brain. For example, frontal and lateral three-dimensional (3D) fMRI renderings show functional activity in the occipital lobe secondary to a visual stimulus.

Positron Emission Tomography

Positron emission tomography (PET) and single-photon emission CT (SPECT) scanning can show cellular activity via regional blood flow in the brain and are now used to monitor changes in the brain with functional activity. Both techniques can be used to depict the regional density of a number of neurotransmitters, allowing researchers to better understand the role of different parts of the brain during activity.

Electroencephalography

Cerebral ischemia produces neuronal dysfunction, leading to slowing of frequencies or reduced amplitude in the EEG tracing. These changes may be generalized (global ischemia) or regional (focal ischemia). The depth of ischemia is associated with the severity of EEG changes. EEG cannot assess the whole cerebral cortex, however, and is less reliable at assessing subcortical structures.

Brainstem Auditory Evoked Potentials

Potentials generated in the auditory nerve and in different regions of the auditory pathways in the brainstem can be recorded. The attention of the subject is not required. Because the brainstem auditory evoked potential (BAEP) is of very low voltage, between 1000 and 2000 responses are generally recorded so that the BAEP can be extracted by averaging from the background noise. Wave III probably arises in the region of the superior olive, whereas waves IV and V arise in the midbrain and inferior colliculus. Waves VI and VII are of uncertain origin and little clinical utility because of their inconsistency in normal subjects. The most consistent components are waves I, III, and V, and it is to these that attention is directed when BAEPs are evaluated for clinical purposes.

The BAEP is an important means of evaluating function of the cranial nerve VIII and the central auditory pathways in the brainstem. In infants, young children, and adults who are unable to cooperate for behavioral testing, BAEPs can be used to evaluate hearing. The wave V component of the response is generated by auditory stimuli that are too weak to generate other components. The BAEP is also useful in assessing the integrity of the brainstem. The presence of normal BAEPs in comatose individuals suggests either that the coma is due to bihemispheric disease or that it relates to metabolic or toxic factors; abnormal BAEPs in this context imply brainstem pathology and a poorer prognosis than otherwise. When coma is due to brainstem pathology, the BAEP findings help in localizing the lesion.

BAEPs have been used to detect subclinical brainstem pathology in individuals with suspected multiple sclerosis. However, the yield in this circumstance is less than with the visual or somatosensory evoked potentials, possibly because the auditory pathway is relatively short or is more likely to be spared. Cerebral ischemia results in delay in the arrival of or reduction in amplitude of evoked responses.²¹

Transcranial Doppler Ultrasonography

Transcranial Doppler ultrasonography uniquely measures local blood flow velocity in the proximal portions of large intracranial arteries. Hemodynamic compromise is inferred when there is reduction in mean flow velocities or when there is slow flow acceleration. In addition, transcranial Doppler ultrasonography can detect cerebral microembolic signals, reflecting the presence of gaseous or particulate matter in the cerebral artery. Solid, fat, gas, or air materials in flowing blood are larger and of different composition and, thus, have different acoustic impedance than surrounding red blood cells. Thus the Doppler ultrasound beam is both reflected and scattered at the interface between the embolus and blood, resulting in an increased intensity of the received Doppler signal. A completely accurate and reliable characterization of embolus size and composition, however, is not yet possible with current technology.

Near-Infrared Spectroscopy

In brain tissue, the venous oxygen saturation predominates (70% to 80%), and cerebral oximetry relies on this fact. Near-infrared spectroscopy (NIRS) uses light optical spectroscopy in the near-infrared range to evaluate brain oxygen saturation by measuring regional cerebral venous oxygen saturation. Table 28-5 describes the use of various imaging techniques correlated to anatomic site.

TREATMENT

Treatment is based on an understanding of the level and type of neuronal dysfunction. Treatment of neurologic disorders has been a frustrating science in the past, but with better understanding of the cellular processes and changes related to disease, treatment holds more promise.

Methods to Control Central Nervous System Damage

Damage or disease of the nervous system often results in changes in the production and uptake of neurotransmitters. Many important drugs that alter nervous system function act by selective interaction with neurotransmitter receptors. Drugs that act at synapses either enhance or block the action of these neurotransmitters. Most neurotransmitters with a prominent role in brain function produce very brief receptor-mediated actions at specific groups of synapses. A few neurotransmitters are more prolonged and act more widely throughout the extracellular space. The combined action of both a briefly acting and a more enduring neurotransmitter produces a modulation of postsynaptic neuronal activity. Pharmacologic strategies are currently aimed at modulation of neurotransmitter synthesis, release, reuptake, and degradation.²⁵ Some drugs mediate inhibition of neurotransmitter release by acting at presynaptic receptors. Opiates are one group of drugs that act by the inhibition of neurotransmitter release. Drugs used to control excessive tone in

Table 28-5 Neuroimaging Applications in Diagnosis and Therapy

| Technique | Diffuse or Multifocal Cerebral | Focal Cerebral | Subcortical | Brainstem | Spinal Cord |
|-----------------|--------------------------------|----------------------|----------------------|----------------------|----------------------|
| Plain film | Neoplasm | Neoplasm | Not useful | Not useful | Trauma |
| | Metabolic | | | | Neoplasm |
| | Congenital | | | | Degenerative |
| CT | Hemorrhage | Hemorrhage | Hemorrhage | Hemorrhage | Hemorrhage |
| | Calcification | Calcification | Calcification | Calcification | Calcification |
| | Infarct | Infarct | Infarct | Infarct | Neoplasm |
| | Neoplasm | Neoplasm | Neoplasm | Neoplasm | Inflammation |
| | Inflammation | Inflammation | Inflammation | Inflammation | |
| | Vascular | Vascular | Vascular | Vascular | |
| | Neoplasm | Neoplasm | Neoplasm | Neoplasm | Neoplasm |
| | Inflammation | Inflammation | Inflammation | Inflammatory | Inflammatory |
| | Hemorrhage | Hemorrhage | Hemorrhage | Hemorrhage | Hemorrhage |
| | Vascular | Vascular | Vascular | Vascular | Vascular |
| MR | White matter disease | White matter disease | White matter disease | White matter disease | White matter disease |
| | Congenital | Congenital | Infarct | Infarct | Infarct |
| | Infarct | Infarct | | | |
| | Not useful | Not useful | Not useful | Not useful | Degenerative |
| | | | | | Neoplasm |
| | | | | | Hematoma |
| | | | | | Inflammatory |
| | | | | | Vascular |
| | | | | | Congenital |
| | | | | | AVM |
| Angiography | Mass effect | AVM tumor | AVM tumor | AVM tumor | AVM |
| | Vasculopathy | Aneurysm | Aneurysm | Aneurysm | |
| | Atherosclerosis | Atherosclerosis | Atherosclerosis | Atherosclerosis | |
| | Hemorrhage | Hemorrhage | Hemorrhage | Congenital | Congenital |
| | Neonatal | Neonatal | Neonatal | Neoplasm | Neoplasm |
| | Congenital | Congenital | Congenital | | |
| | Neoplasm | Neoplasm | Neoplasm | | |
| | Infection | Infection | Infection | | |
| | Vascular | Vascular | Vascular | | |
| | Vascular | Vascular | | | |
| Ultrasonography | Neoplasm | Neoplasm | | | |
| | Infection | Infection | | | |
| | Degenerative | Degenerative | | | |
| | Trauma | Trauma | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| PET-SPECT | Vascular | Vascular | Vascular | Not useful | Not useful |
| | Neoplasm | Neoplasm | Neoplasm | | |
| | Infection | Infection | Infection | | |
| | Degenerative | Degenerative | Degenerative | | |
| | Trauma | Trauma | Trauma | | |
| | | | | | |
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From Koenigsberg RA, Faro SH, Hershey BL, et al: Neuroimaging. In Goetz CG: *Textbook of clinical neurology*, ed 2, Philadelphia, 2003, WB Saunders. AVM, Arteriovenous malformation; PET-SPECT, positron emission tomography-single-photon emission computed tomography.

specific muscle groups often work by inhibiting neurotransmitter release. Anesthetic drugs modify the actions of neurotransmitter receptors by changing the membranes of cells on or within which the receptors are located.

Drug therapy can stimulate neurotransmitter release. Drugs aimed at maintaining neurotransmitter activity in the synaptic cleft can be useful in neuromuscular junction diseases. Another way to regulate the level of neurotransmitters is to influence the rate of chemical degradation. Drugs can inhibit the breakdown of certain elements that may be broken down by natural processes such as oxidation. One action of these drugs is to prolong the efficacy of released neurotransmitters by inhibiting their degradation.⁶¹ An example of this process is the regulation dopamine. Dopamine activity can be increased by four mechanisms:

- Increased synthesis
- Increased release
- Prolongation of neurotransmitter activity
- Direct receptor stimulation

Synthesis of the neurotransmitter can be increased by giving dopa because it is the product beyond the rate-limiting enzyme and there is ordinarily an abundant amount of aromatic amino acid decarboxylase in the CNS. When dopa is combined with a peripherally active decarboxylase inhibitor, more dopa is delivered across the blood-brain barrier and can be used to synthesize central dopamine. Drugs, such as cocaine, amphetamine, and methylphenidate, can increase release.

The normal metabolism of dopamine involves reuptake of dopamine into the presynaptic cell, with subsequent metabolism by two enzymes, MAO and COMT. Prolongation of dopamine activity can be effected by blocking reuptake or altering enzyme activity. Amantadine and possibly some tricyclic antidepressant medications operate on the dopaminergic system through blockade of reuptake. MAO inhibitors and COMT inhibitors for human use also increase dopaminergic activity. Finally, direct activation of the dopamine receptors on the striatal cell can be induced by agonists like bromocriptine,

pergolide, and other drugs. Importantly, orally administered dopamine itself has no place in altering the CNS dopamine levels, because, being a positively charged molecule, it cannot cross the blood-brain barrier.²¹

Other drugs protect the cell membrane in the presence of toxins that act on the membrane such as the toxic effects of the free radicals produced in brain tissue after hypoxia, ischemia, and seizures. Damage to the neuron occurs when the free radical is allowed to penetrate the membrane.⁴⁵ The best defense is to prevent penetrance. Antioxidant therapies are being examined for a variety of neurodegenerative disorders and the sequelae of stroke and spinal cord injury. It is believed that the toxicity of glutamate can be blocked by various antioxidants. Vitamin E, a free radical scavenger, is an antioxidant that has been tested widely. However, it does not pass easily through the blood-brain barrier, and as a fat-soluble vitamin, it can be toxic in large doses. Estrogen can work as an antioxidant through intrinsic neurotrophic activities. Ongoing studies are looking at the natural substances noted above as well as manufactured substances that will provide antioxidant or free radical scavenging. There is great hope that substances that will slow down the destruction related to oxidative stress will prove to be curative for progressive diseases of the CNS, as well as other degenerative processes associated with connective tissue, neoplasm, and aging.⁷ Specific drugs used for primary neurologic disorders are described in the next chapters.

Exciting new advancements in the field of molecular genetics have begun to identify novel candidate genes that may be involved in many inherited or acquired neurologic disorders. The basic principle of gene therapy is to transfer exogenous genes into specific cell types within the human body to correct a pathologic disorder. Currently, gene therapies are based on simple nucleic acid sequences or derived from unique viruses. Researchers have attempted to use the power of viruses to essentially hijack cells for gene expression of appropriate therapeutic molecules.

Stem cells are unspecialized living cells that have the capacity to renew themselves for long periods of time through cell division. Under certain physiologic or experimental conditions, they can be induced to become cells with special functions such as the beating cells of the heart muscle or the insulin-producing cells of the pancreas. *Embryonic stem cells* are derived from embryos that develop from eggs that have been fertilized in vitro and then donated for research purposes with the informed consent of the donors. The embryos from which human embryonic stem cells are derived are typically 4 or 5 days old and consist of a hollow microscopic collection of cells called the *blastocyst*. An *adult stem cell* is an undifferentiated cell found among differentiated cells in a tissue or organ. The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. Some researchers now use the term *somatic stem cell* instead of adult stem cell. Unlike embryonic stem cells, which are defined by their origin, the origin of adult stem cells in mature tissues is unknown. A single adult stem cell could have the ability generate a line of genetically identical cells, or *clones*.²

There is evidence for the impact of immune system dysfunction in these diseases despite the blood-brain barrier protection of the CNS from the direct effects of autoimmune responses. Identification of immune system elements is leading researchers toward an understanding of the role of the immune system in diseases such as multiple sclerosis, ALS, Parkinson's disease, and Alzheimer's disease.

Use of catheters to deliver drugs directly into the cerebrospinal fluid or brain tissue has enhanced the ability to deliver drugs that act directly on the neuron. Although the catheters have been made more sophisticated and can deliver the drugs in measured doses, complications of administration and uneven levels of absorption continue to be limiting factors.

Treatment of Nonneuronal Dysfunction

Many drugs used to treat neurologic disorders influence nonneuronal tissue, including cerebral blood vessels and glia. Cerebral edema can increase the permeability of the blood-brain barrier, causing an increase in fluid within the brain. The resulting compression of brain tissue can be life-threatening. Drugs, such as mannitol, that control cerebral edema, or drugs that provide diuresis can help preserve neuronal function. In demyelinating disease, antiinflammatory and immunosuppressive drugs are used to preserve the function of the glial cells that produce the myelin sheath.

For some of the viruses that invade the CNS there is replication of cells in nonneuronal tissue. Use of drugs that inhibit RNA or DNA synthesis can prevent viral replication without disrupting neuronal integrity. Acyclovir, used in the treatment of herpes encephalitis, is an example of this type of drug.

In infants and children, there is an altered drug metabolism that should be considered whenever administering drugs that act on the nervous system. Concomitant illness and fever will further alter drug metabolism. An immature blood-brain barrier can also affect the absorption of drugs into brain tissue. When anticonvulsants are administered, close monitoring of blood levels is necessary.

PROGNOSIS

Prognosis is the keystone to management of neurologic disorders because it links diagnosis to outcomes and identifies need for treatment. Prognostic studies can also identify if available treatment is ineffective. In addition, these studies can indicate which diseases have an important impact on function or disability.³⁴

Disability resulting from neurologic disease and trauma can be extensive, and care of these clients often requires use of limited resources: time and money. With the tremendous advances made in the emergent medical care of trauma victims and people with significant neurologic disease, the number of people living with neurologic disorder is increasing at a steady rate.⁶

Permanent or progressive impairments can be demoralizing to clients and their families. Clients must reorganize their perspectives in order to learn alternative ways

of regaining as much control as possible over life activities. Success builds a sense of efficacy, and failure undermines self-worth. Tackling challenges in successive attainable steps will lead to further competencies in associated tasks. When individuals see others with similar disabilities perform successfully, they may have increased confidence in their own abilities. The persuasion of health care providers and caregivers can boost effort but must be realistic. Perceived self-efficacy can influence the course of health outcomes and functional status. The prognosis for an individual should consider both the social and cognitive status of the individual in relationship to the diagnosis.⁴

The economic evaluation of health care reflects the complexity of the disease treatment process and the value of health effects. Policy makers are demanding information about the economic outcomes of diseases and their treatments. Research methodologies oriented toward cost-of-illness and cost-benefit analysis have emerged. Clinicians should be involved in this analysis to maintain perspective, especially in catastrophic and degenerative processes.³⁰

Several chronic neurologic disease states, such as Alzheimer's disease, are associated with elevated secretion of stress hormones such as Cortisol. Stress also can trigger or exacerbate symptom onset and perhaps progression of chronic illness such as Parkinson's disease. Stress hormones also can mitigate the impact of acute neurotrauma; for example, there is a positive correlation between **Cortisol** levels and mortality after head injury. Thus neurologic disease states can occur within a context of elevated glucocorticoids, which may have profound influences on recovery and neuroplasticity. In addition, abnormal regulation of glucocorticoid release is associated with many affective disorders, such as depression and PTSD, that are overrepresented in populations with neurologic disease. Release of glucocorticoids, however, also can occur in anticipation of adverse events, which is a mechanism particularly relevant to neurologists and psychoneuroimmunologists. Anticipatory release of glucocorticoids occurs in the absence of a frank physical stimulus, keyed by memories or instinctual predispositions.

Measures of health-related quality of life address the impact of health on physical, social, and psychologic aspects of life. The particular scale may address issues related to a specific population or may be sensitive to a clinical intervention. The therapist should be familiar with the measurement tools typically used during intervention for a condition or disease. As much as possible, these tools are described in the appropriate chapter in this section.⁶

Physiologic Basis for the Recovery of Function

After injury to the nervous system, there are changes in the structure and function of the neurons. In some instances the changes can lead to further damage, whereas other changes facilitate recovery.

Diaschisis, or neural shock, occurs when there is injury to a nerve and disruption of the neural pathway that

extends a distance from the site of injury. When the neurons distal to the injury regain function, which may be soon after the injury, partial function may return.

Injury may be secondary to either swelling of the axon or edema in the surrounding tissue that blocks *synaptic activity* in the injured neurons, as well as that in the surrounding area. With reduction of the edema, function may return. This is the reason that medications that reduce edema are often given in the context of diffuse brain swelling.

When there is a loss of presynaptic function in one area, the postsynaptic target cells for that area may become more sensitive to neurotransmitters that are now produced in lower concentrations. The compensatory mechanism is known as *demyelination supersensitivity*. *Regenerative synaptogenesis* occurs when injured axons begin sprouting. *Collateral sprouting* is the process of neighboring axons sprouting to connect with sites that were previously innervated by the injured axon.

Suppression of a response to a stimulus is considered habituation, whereas sensitization is an increased response to a stimulus, usually related to noxious stimuli or pain. Adaptation is the ability to modify a motor response based on changes in the sensory environment or input received.

Long-term potentiation occurs when a weak input and a strong input arrive at a dendrite at the same time. The weak stimulus is enhanced by the strong stimulus. With repeated activation of combined stimuli, there is an increase in the presynaptic transmitter associated with the stimulus. After the long-term potentiation has been established, the weak input will elicit a stronger response than it had initially.³¹

The characteristics of a lesion will have a profound effect on recovery from a brain injury. Small lesions of the brainstem may in fact be as devastating as large lesions of the cerebral cortex. Cerebellar damage can affect both learning and memory of movements. Lesions that occur gradually appear to cause less disruption of function than lesions that occur all at once such as with strokes. Advanced age will adversely affect the return of function. Studies show that a person's prior level of activity and environment will affect the rate and extent of recovery. An enriched environment will positively affect recovery when it is available either before the insult or during the recovery period.

Redistribution of cortical mapping is seen after a lesion in the brain.⁶ These changes may involve unmasking of previously nonfunctional synaptic connections from adjacent areas, or the ability of the neighboring inputs may take over. It is clear that both sensory and motor maps in the cortex are constantly changing according to input from the environment. In addition, the brain appears to increase use of ipsilateral pathways after a lesion that affects one side of the brain.

Recovery of function by strict definition is the return to original processes for an activity. When alternative processes are used to complete the task, it is considered compensation. Neural modifiability may be seen as a change in the organization of connections among neurons and is often referred to as plasticity. Some of the recovery after CNS damage is considered spontaneous. Forced

recovery is the result of specific interventions that create change in the neural structure.⁵³ Constraint-induced training makes use of this action.

Physiologic studies suggest that motor relearning and recovery of function may be accomplished through the same neural mechanisms and reflect the plasticity of the brain. Learning alters our capability to perform the appropriate motor act by changing both the effectiveness of the neural pathways used and the anatomic connections.

Learning involves storage of memory and can occur in all parts of the brain with both parallel and hierarchic processing. The area of representation within the brain becomes specialized for both inputs and outputs. Areas of the brain used during the early phase of learning movement are different from those used once a skill is learned. Initially, more areas of the brain are active, since skill develops both the number of neurons firing and location of activity change. The use of sensory input is increased in the early stages of learning. The prefrontal areas are also more active in the learning phase and become less active during automatic movements.⁵ The stimuli repeatedly excite cortical neuron populations, and the neurons progressively grow in numbers. Repetition will lead to greater specificity, and the responses become stronger. With skill acquisition, sensory feedback appears to be less critical.

Control of learning comes from many areas of the CNS working together. The area involved may depend on a number of variables associated with the type of learning taking place and is influenced by the environment. The cortex is involved in learning through sensorimotor integration. It is postulated that there are widely distributed groups of neurons acting as a cortical engram, composed of multiple functional groupings. Thus, when an activity is repeated and stored in memory, the engrams are available to trigger groups of cells that fire synchronously during movement. The engrams appear to influence the precision, speed, and accuracy of movement.³¹

The limbic system is critical to the learning phase because it generates need-directed motor activity and communicates the intent to the rest of the brain. The limbic system is a critical part of the neural representation necessary for memory that includes the cortex and thalamus.

The cerebellum appears to be active during procedural learning. A possible mechanism is through the influence of the climbing fibers on the mossy fibers with eventual change in the output fibers, the Purkinje fibers.⁵⁸ The lateral cerebellum affects cognition through its relationship to the frontal areas active during cognitive processes.⁴⁶

The basal ganglia appear to be highly involved in the cognitive aspects of motor behavior although the level of contribution remains unclear. Habit formation appears to be associated with functions of the basal ganglia, and the control of internally generated movement here appears to be a part of the motor learning continuum.³¹

SPECIAL IMPLICATIONS FOR THE THERAPIST

28-1

Motor Learning Strategies

PREFERRED PRACTICE PATTERNS

5A: Primary Prevention/Risk Reduction for Loss of Balance and Falling

5D: Impaired Motor Function and Sensory Integrity Associated with Nonprogressive Disorders of the Central Nervous System—Acquired in Adolescence or Adulthood

5E: Impaired Motor Function and Sensory Integrity Associated with Progressive Disorders of the Central Nervous System

5H: Impaired Motor Function, Peripheral Nerve Integrity, and Sensory Integrity Associated with Nonprogressive Disorders of the Spinal Cord

5I: Impaired Arousal, Range of Motion, and Motor Control Associated with Coma, Near Coma, or Vegetative State

During the examination and evaluation of disability the therapist should recognize the impairments that contribute to abnormal motor control. Force production, speed of motion, coordination of movement, and cognition are often affected in neurologic disorders. Identification and modification of environments that can alter responses should be made early in the management process. Difficulty with bowel and bladder control can affect progress with recovery and should be managed with either physical or medical means. Treatment of nonneural tissue changes secondary to weakness or changes in tone should be addressed in the intervention. Substitution devices, assistive devices, and environmental changes should be considered when it is clear that the client will not recover from specific impairments. Reintegration into social and personal roles is of prime importance to the client with neurologic dysfunction. Functional status is the critical outcome marker, and physical therapists are able to positively influence outcomes in this area.

The recovery of function after CNS injury involves the reacquisition of complex tasks. Inherent in the recovery of function that has been lost secondary to a neurologic insult is the process of motor relearning, which can be defined as the process of acquisition or modification of movement.^{11,53} Clients with a neurologic deficit must learn appropriate strategies to move through the environment. Motor learning is a modification of behavior by experience. Memory is the retention of these modifications, therefore memory plays a critical role in motor learning.³¹

Theories underlying the relationship of motor control, motor learning, memory, and recovery of function are varied, and research continues toward increasing our understanding of that relationship.^{12,40,50,53} Various types of motor learning are recognized today and incorporated into the programs established for individuals with brain injury.

Two forms of associative learning based on an association between two different stimuli are classical and operant conditioning. *Classical conditioning* is a form of learning in which a conditioned stimulus produces a greater response by association with a strong