Neurologic Disorders

EPILEPSY

Epilepsy is a term that refers to a group of disorders characterized by chronic recurrent, paroxysmal changes in neurologic function (seizures), altered consciousness, or involuntary movements caused by abnormal and spontaneous electrical activity in the brain. Seizures may be convulsive (i.e., accompanied by motor manifestations) or may occur with other changes in neurologic function (i.e., sensory, cognitive, and emotional). In the past, much confusion surrounded the nature and classification of epilepsy, but recent efforts have enhanced our understanding of these disorders. Today, epilepsy denotes a group of chronic conditions whose major manifestation is the occurrence of epileptic seizures. Seizures are characterized by discrete episodes that tend to be recurrent and are often unprovoked, in which movement, sensation, behavior, perception, and consciousness are disturbed. Symptoms are produced by excessive temporary neuronal discharging, which results from intracranial or extracranial causes.

Incidence and Prevalence

Approximately 10% of the population will have at least one epileptic seizure in a lifetime, and 2% to 4% will have recurrent seizures at some time during their lives. The overall incidence of seizures is 0.5%. Seizures are most common during childhood, with as many as 4% of children having at least one seizure during the first 15 years of life. Most children outgrow the disorder. About 4 in 1000 children do not outgrow the disorder and require medical care. Seizures also are common in the elderly, with an estimated annual incidence of 134 per 100,000.

Etiology

The cause of epilepsy is idiopathic in more than half of all patients. Vascular (cerebrovascular disease) and developmental abnormalities (cavernous malformation), intracranial neoplasms (gliomas), and head trauma are causative in about 35% of adult cases. Other common causes include hypoglycemia, drug withdrawal, infection, and febrile illness (e.g., meningitis, encephalitis). Seizures occur with genetic conditions such as Down syndrome, tuberous sclerosis, and neurofi bromatosis and are associated with several genetic abnormalities that result in neuronal channel

dysfunction. Seizures sometimes can be evoked by specific stimuli. Approximately 1 of 15 patients reports that seizures occurred after exposure to fl ickering lights, monotonous sounds, music, or a loud noise.

CLINICAL PRESENTATION

Signs and Symptoms

The clinical manifestations of generalized tonic-clonic convulsions (grand mal seizure) are classic. An aura (a momentary sensory alteration that produces an unusual smell or visual disturbance) precedes the convulsion in one third of patients. Irritability is another premonitory signal. After the aura warning, the patient emits a sudden "epileptic cry" (caused by spasm of the diaphragmatic muscles) and immediately loses consciousness. The tonic phase consists of generalized muscle rigidity, pupil dilation, eyes rolling upward or to the side, and loss of consciousness. Breathing may stop because of spasm of respiratory muscles. This is followed by clonic activity that consists of uncoordinated beating movements of the limbs and head, forcible jaw closing, and head rocking. Urinary incontinence is common, but fecal incontinence is rare. The seizure (ictus) usually does not last longer than 90 seconds; then, movement ceases, muscles relax, and a gradual return to consciousness occurs, which is accompanied by stupor, headache, confusion, and mental dulling. Several hours of rest or sleep may be needed for the patient to fully regain cognitive and physical abilities.

Laboratory Findings

The diagnosis of epilepsy generally is based on the history of seizures and an abnormal electroencephalogram (EEG). Seizures produce characteristic spike and sharp wave patterns on EEG. Serial recordings of sleep deprivation that can induce seizures may help to establish the diagnosis. Other diagnostic procedures that are useful for ruling out other causes of seizures include computed axial tomography (CT), magnetic resonance imaging (MRI), single-photon emission computed tomography (SPECT), lumbar puncture, serum chemistry profiles, and toxicology screening.

MEDICAL MANAGEMENT

The medical management of epilepsy usually is based on long-term drug therapy. Phenytoin (Dilantin), carbamazepine (Tegretol), and valproic acid are considered first-line treatments. Several other drugs are available for control of generalized tonic-clonic seizures

TABLE 27-1
Anticonvulsants Used in the Management of Generalized Tonic-Clonic (Grand Mal) Seizures

Generic Name	Trade Name	Mechanism of Action	Dental Considerations
DRUGS OF CHOICE			
Phenytoin*	Dilantin	Blocks sodium channels	Gingival hyperplasia, increased incidence of microbial infection, delayed healing, gingival bleeding (leukopenia), osteoporosis, Stevens-Johnson syndrome
Carbamazepine*	Tegretol	Blocks sodium channels	Xerostomia, microbial infection, delayed healing, ataxia, gingival bleeding (leukopenia and thrombocytopenia), ataxia, osteoporosis, Stevens-Johnson syndrome. Drug interactions: Propoxyphene, erythromycin
Valproic acid*	Depakene, Depakote	γ-Aminobutyric acid (GABA) augmentation and N-methyl-d-aspartate (NMDA) receptor	Excessive bleeding and petechiae, decreased platelet aggregation, increased incidence of microbial infection, delayed healing, drowsiness, gingival bleeding (leukopenia and thrombocytopenia), hepatotoxicity. Drug interactions: Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs)
Lamotrigine*	Lamictal	Blocks sodium and calcium channels, reduces glutamate	Ataxia, may require help getting into and out of the dental chair, risk for developing Stevens-Johnson syndrome
ALTERNATIVES			
Clonazepam*	Klonopin	Augments inhibitory GABAergic system	Drug interactions: Central nervous system (CNS) depressants
Ethosuximide	Zarontin	Blocks sodium and calcium channels	Risk for developing Stevens-Johnson syndrome, blood dyscracias
Felbamate	Felbatol	Blocks sodium channels, reduces glutamate	Risks for aplastic anemia, Stevens-Johnson syndrome
Gabapentin	Neurontin	Modulates calcium channel; augments GABAergic system	Dizziness
Oxcarbazepine	Trileptal	Blocks sodium channels	Liver enzyme induction but less than carbamazepine
Phenobarbital*	Luminal	Blocks calcium channel; augments inhibitory GABAergic system	Sedation, liver enzyme induction. Drug interaction: CNS depressants
Primidone*	Mysoline	Blocks calcium channel; augments inhibitory GABAergic system	Ataxia, vertigo—increased risk of falls
Topiramate	Topemax	Blocks sodium channel; augments inhibitory GABAergic system	Impaired cognition
Vigabatrin	Sabril	Augments inhibitory GABAergic system	Drug interactions: CNS depressants

*Preexisting liver disease can exacerbate adverse effects associated with antiepileptics. Drugs of choice for absence (petit mal) seizures: Ethosuximide (Zarontin), valproate, lamotrigine, or clonazepam. Drugs of choice for status epilepticus: Lorazepam 4 to 8 mg, or diazepam 10 mg, intravenously.

DENTAL MANAGEMENT

Medical Considerations

The first step in the management of an epileptic dental patient is identification. This is best accomplished by the medical history and by discussion with the patient or family members. Once a patient with epilepsy has been identified, the dental practitioner must learn as much as possible about the seizure history, including the type of seizures, age at onset, cause (if known), current and regular use of medications, frequency of physician visits, degree of seizure control, frequency of seizures, date of last seizure, and any known precipitating factors. In addition, a history of previous injuries associated with seizures and their treatment may be helpful. Fortunately, most epileptic patients are able to attain good control of their seizures with anticonvulsant drugs and are therefore able to receive normal routine dental care. In some instances, however, the history may reveal a degree of seizure activity that suggests noncompliance or a severe seizure disorder that does not respond to anticonvulsants. For these patients, a consultation with the physician is advised before dental treatment is rendered. A patient with poorly controlled disease may require additional anticonvulsant or sedative medication, as directed by the physician. Patients who take anticonvulsants may suffer from the toxic effects of these drugs, and the dentist should be aware of their manifestations. In addition to the more common adverse effects, allergy may be seen occasionally as a rash, erythema multiforme, or worse (Stevens-Johnson syndrome). Phenytoin, carbamazepine, and valproic acid can cause bone marrow suppression, leukopenia, and thrombocytopenia, resulting in an increased incidence of microbial infection, delayed healing, and gingival and postoperative bleeding.Valproic acid can decrease platelet aggregation, leading to spontaneous hemorrhage and petechiae.Propoxyphene and erythromycin should not be administered to patients who are taking carbamazepine because of interference with metabolism of carbamazepine, which could lead to toxic levels of the anticonvulsant drug. Aspirin and nonsteroidal anti-infl ammatory drugs (NSAIDs) should not be administered to patients who are taking valproic acid because they can further decrease platelet aggregation, leading to hemorrhagic episodes. No contraindication has been

identified to the use of local anesthetics in proper amounts in these patients. Patients who have a VNS device implanted in their chest do not need antibiotic prophylaxis before undergoing invasive dental procedures.

Seizure Management. In spite of appropriate preventive measures taken by the dentist and by the patient, the possibility always exists that an epileptic patient may have a generalized tonic-clonic convulsion in the dental office. The dentist and staff should anticipate this occurrence and be prepared for it. Preventive measures include knowing the patient's history, scheduling the patient at a time within a few hours of taking the anticonvulsant medication, using a mouth prop, removing dentures, and discussing with the patient the urgency of mentioning anaura as soon as it is sensed. The clinician also should be aware that irritability is often a symptom of impending seizure. If sufficient time in the premonitory stage occurs, 0.5 to 2 mg of lorazepam can be given sublingually, or 2 to 10 mg diazepam can be given intravenously. If the patient has a seizure while in the dental chair, the primary task of management is to protect the patient and try to prevent injury. No attempt should be made to move the patient to the floor. Instead, the instruments and instrument tray should be cleared from the area, and the chair should be placed in a supported supine position. The patient's airway should be maintained patent. No attempt should be made to restrain or hold the patient down. Passive restraint should be used only to prevent injury that may result when the patient hits nearby objects or falls out of the chair. If a mouth prop (e.g., a padded tongue blade between the teeth to prevent tongue biting) is used, it should be inserted at the beginning of the dental procedure. Trying to insert a mouth prop is not advised during the seizure, because doing so may damage the patient's teeth or oral soft tissue and may be nearly an impossible task. An exception would occur if the patient senses a pending seizure and can cooperate. Seizures generally do not last longer than a few minutes. Afterward, the patient may fall into a deep sleep from which he or she cannot be aroused. Oxygen (100%), maintenance of a patent airway, and mouth suction should be provided during this phase. Alternatively, the patient can be turned to the side to control the airway and to minimize aspiration of secretions. Within a few minutes, the patient gradually regains consciousness but may be confused, disoriented, and embarrassed. Headache is a prominent feature during this period. If the patient does not respond

within a few minutes, the seizure may be associated with low serum glucose, and delivery of glucose may be needed. No further dental treatment should be attempted after generalized tonic-clonic seizures, although examination for sustained injuries (e.g., lacerations, fractures) should be performed. In the event of avulsed or fractured teeth or a fractured appliance, an attempt should be made to locate the tooth or fragments to rule out aspiration. A chest radiograph may be required to locate a missing fragment or tooth. In the event that a seizure becomes prolonged (status epilepticus) or is repeated, intravenous lorazepam (0.05- 0.1 mg/kg) 4 to 8 mg, or 10 mg diazepam, is generally effective in controlling it. Lorazepam is preferred by many experts because it is more effi cacious and lasts longer than diazepam. Oxygen and respiratory support should be provided because respiratory function may become depressed. If the seizure lasts longer than 15 minutes, the following should be provided: intravenous access, repeat lorazepam dosing, fosphenytoin administration, and activation of the emergency medical system (EMS)

BOX 27-2

Dental Management of the Epileptic Patient

1. Identification of patient by history
   a. Type of seizure
   b. Age at time of onset
   c. Cause of seizures (if known)
   d. Medications
   e. Frequency of physician visits (name and phone number)
   f. Degree of seizure control
   g. Frequency of seizures
   h. Date of last seizure
   i. Known precipitating factors
   j. History of seizure-related injuries
2. Provision of normal care: Well-controlled seizures pose no management problems
3. If questionable history or poorly controlled seizures, consultation with physician before dental treatment—may require modification of medications
4. Attention to adverse effects of anticonvulsants; these include:
   a. Drowsiness
   b. Slow mentation
   c. Dizziness
   d. Ataxia
   e. Gastrointestinal upset
   f. Allergic signs (rash, erythema multiforme)
5. Possibility of bleeding tendency in patients taking valproic acid (Depakene) or carbamazepine (Tegretol) as the result of platelet interference—Pretreatment platelet function analyzer (PFA)-100; if grossly abnormal, consultation with physician
6. Management of grand mal seizure
   a. Possible placement of a ligated mouth prop at the beginning of the procedure
   b. Chair back in supported supine position
7. Management of the seizure
   a. Clear the area
   b. Turn the patient to the side (to avoid aspiration)
   c. Do not attempt to use a padded tongue blade
   d. Passively restrain
8. After the seizure
   a. Examine for traumatic injuries
   b. Discontinue treatment, arrange for patient transport

Figure 27-1. Dental chair in the supine position with the back supported by the operator's or by the assistant's stool.

Treatment Planning Considerations

Because gingival overgrowth is associated with phenytoin administration, every effort should be made to maintain a patient at an optimal level of oral hygiene. This may require frequent visits for monitoring of progress. If significant gingival overgrowth exists, surgical reduction will be necessary. However, this must be accompanied by an increased awareness of oral hygiene needs and a positive commitment by the patient to maintain oral cleanliness. A missing tooth or teeth should be replaced if possible to

prevent the tongue from being caught in the edentulous space during a seizure (as commonly happens). Generally, a fixed prosthesis or implant is preferable to a removable one. (The removable prosthesis becomes dislodged more easily.) For fixed prostheses, all-metal units should be considered when possible to minimize the chance of fracture. When placing anterior castings, the dentist may wish to consider using three quarter crowns or retentive nonporcelain facings. Removable prostheses are, nevertheless, sometimes constructed for epileptic patients. Metallic palates and bases are preferable to all-acrylic ones. If acrylic is used, it should be reinforced with wire mesh.

Oral Complications and Manifestations

The most significant oral complication seen in epileptic patients is gingival overgrowth, which is associated with phenytoin and rarely with valproic acid and vigabatrin. The incidence of phenytoin-induced gingival overgrowth in epileptic patients ranges from 0% to 100%, with an average rate of approximately 42%.20 A greater tendency to develop gingival overgrowth occurs in youngsters than in adults. The anterior labial surfaces of the maxillary and mandibular gingivae are most commonly and severely affected. Meticulous oral hygiene is important for preventing and signifi cantly decreasing its severity. Good home care must always be combined with the removal of irritants, such as overhanging restorations and calculus. Frequently, enlarged tissues interfere with function or appearance, and surgical reduction may become necessary. Traumatic injuries such as broken teeth, tongue lacerations, and lip scars also are common in patients who experience generalized tonic-clonic seizures. Stomatitis, erythema multiforme, and Stevens-Johnson syndrome are rare adverse effects associated with the use of phenytoin, valproic acid, lamotrigine, phenobarbital, and carbamazepine. These complications are more common during the fi rst 8 weeks of treatment.

STROKE

Stroke is a generic term that is used to refer to a cerebrovascular accident—a serious and often fatal neurologic event caused by sudden interruption of oxygenated blood to the brain. This in turn results in focal necrosis of brain tissue and possibly death. Even if a stroke is not fatal, the survivor often is to

some degree debilitated in motor function, speech, or mentation. The scope and gravity of stroke are reflected in the fact that stroke is the leading cause of serious, long-term disability in the United States; 5% of the population older than 65 years of age has had one stroke.

EPIDEMIOLOGY

Incidence and Prevalence

Although the incidence of stroke has declined, it remains one of the most signifi cant health problems in the United States. Each year in the United States, about 700,000 people experience new or recurrent stroke.This translates to the occurrence of one stroke about every minute, and 75% of persons survive their stroke. Approximately 4.5 million persons living in 2001 had survived a stroke. Risk is associated with race; African Americans are at 38% greater risk of first stroke than are whitesStroke is the third leading cause of death (behind heart disease and cancer) in the United States, with 275,000 Americans dying of stroke annually.

Etiology

Stroke is caused by the interruption of blood supply and oxygen to the brain as a result of ischemia or hemorrhage. The most common type is ischemic stroke induced by thrombosis (60% to 80% of cases) of a cerebral vessel. Ischemic stroke can also result from occlusion of a cerebral blood vessel by distant emboli. Hemorrhage causes about 15% of all strokes and has a 1-year mortality greater than 60%. Cerebrovascular disease is the primary factor associated with stroke. Atherosclerosis and cardiac pathosis (myocardial infarction, atrial fi brillation) increase the risk of thrombolic and embolic strokes, whereas hypertension is the most important risk factor for intracerebral hemorrhagic stroke. Approximately 10% of persons who have had a myocardial infarction will have a stroke within 6 years. Additional factors that increase the risk for stroke include the occurrence of transient ischemic attacks, a previous stroke, high dietary fat, obesity and elevated blood lipid levels, physical inactivity, uncontrolled hypertension, cardiac abnormalities, diabetes mellitus, elevated homocysteine levels, elevated hematocrit, elevated antiphospholipid antibodies, heavy tobacco smoking, increasing age (risk doubles each decade after 65 years), and periodontal disease.Increased risk for hemorrhagic stroke also occurs with use of phenylpropanolamine, an alpha-adrenergic agonist. This has led to an order

from the U.S. Food and Drug Administration that phenylpropanolamine must be removed from over-thecounter cold remedies and weight loss aids. Intake of fruits and vegetables and moderate levels of exercise have a protective effect against stroke.

CLINICAL PRESENTATION

Signs and Symptoms

Familiarity with the warning signs and symptoms and the phases of stroke can lead to appropriate action that may be lifesaving. Four events associated with stroke are

(1) the transient ischemic attack (TIA),

(2) reversible ischemic neurologic defi cit (RIND),

(3) stroke-in-evolution, and

(4) the completed stroke.

These events are defined principally by their duration. A TIA is a "mini" stroke that is caused by a temporary disturbance in blood supply to a localized area of the brain. A TIA often causes numbness of the face, arm, or leg on one side of the body (hemiplegia), weakness, tingling, numbness, or speech disturbances that usually last less than 10 minutes. Most commonly, a major stroke is preceded by one or two TIAs within several days of the fi rst attack. A RIND is a neurologic deficit that is similar to a TIA but does not clear within 24 hours; eventual recovery occurs. Stroke-in-evolution is a neurologic condition that is caused by occlusion or hemorrhage of a cerebral artery in which the deficit has been present for several hours and continues to worsen during a period of observation. Signs of stroke include hemiplegia, temporary loss of speech or trouble in speaking or understanding speech, temporary dimness or loss of vision, particularly in one eye (may be confused with migraine), unexplained dizziness, unsteadiness, or a sudden fall. Clinical manifestations that remain after a stroke vary in accordance with the site and size of residual brain defi cits; these include language disorders, hemiplegia, and paresis, a form of paralysis that is associated with loss of sensory function and memory and weakened motor power. Of note, in most patients with stroke, the intellect remains intact; however, large, left-sided stroke has been associated with cognitive decline.

BOX 27-3

Differences Between Right-Sided Brain Damage and Left-Sided Brain Damage

Right-Sided Brain Damage	Left-Sided Brain Damage
• Paralyzed left side	• Paralyzed right side
• Spatial/perceptual deficits	• Language and speech problems
• Thought impaired	• Decreased auditory memory (cannot remember long instructions)
• Quick, impulsive behavior	• Slow, cautious, disorganized behavior
• Patient cannot use mirror	• Memory deficits—language based
• Difficulty performing tasks (toothbrushing)	• Patients anxious
• Memory deficits	
• Neglect of left side	

Laboratory Findings

Patients suspected of having had a stroke usually receive a variety of laboratory and diagnostic imaging tests to rule out conditions that can produce neurologic alterations, such as diabetes mellitus, uremia, abscess, tumor, acute alcoholism, drug poisoning, and extradural hemorrhage. Laboratory tests often include urinalysis, blood sugar level, complete blood count, erythrocyte sedimentation rate, serologic tests for syphilis, blood cholesterol and lipid levels, chest radiographs, and electrocardiogram. Various abnormalities may be disclosed by these test results, depending on the type and severity of stroke and its causative factors. A lumbar puncture also may be ordered by the physician in an effort to check for blood or protein in the cerebrospinal fl uid (CSF) and for altered CSF pressure that would be suggestive of subarachnoid hemorrhage.Doppler blood fl ow, EEG, cerebral angiography, CT, and MRI, including diffusion and perfusion studies of the brain, are important for determining the extent and location of arterial injury.

MEDICAL MANAGEMENT

Prevention

The fi rst aspect of stroke management is prevention. This is accomplished by identifying risk factors in individuals (e.g., hypertension, diabetes, atherosclerosis, cigarette smoking) and attempting to reduce or eliminate as many of these as possible. Blood pressure lowering, antiplatelet therapy, and statin therapy are primary stroke prevention methods. Carotid endarterectomy is a secondary stroke prevention method. The benefi t of lowering blood pressure is evident in the fact that a reduction of systolic blood pressure by 10 mm Hg is associated with a one-third reduction in risk for stroke. Aspirin, ticlopidine, and extended-release dipyridamole are accepted preventive therapies for ischemic stroke in patients who have experienced TIAs, or who have had a stroke. Aspirin dosed at 81 to 325 mg daily reduces the risk of stroke by about 25% in this at-risk population. Similarly, statin therapy reduces risk by about 20%. Also, surgical intervention through endarterectomy reduces the risk by about 1% per year, such that one stroke is prevented for every 20 patients who undergo surgery over a 5-year period.

Stroke Treatment

If an individual has a stroke, treatment is generally threefold. The immediate task is to sustain life during the period immediately after the stroke. This is done by means of life support measures and transport to a hospital. The second task involves emergency efforts to prevent further thrombosis or hemorrhage, and to attempt to lyse the clot in cases of thrombosis or embolism. Thrombolysis and improved neurologic outcomes have been achieved with intravenous recombinant tissue-type plasminogen activator (rt-PA) and intra-arterial prourokinase. Of the two, intravenous administration of rt-PA within 3 hours of ischemic stroke onset is the only approved therapy in the United States. After the initial period, efforts to stabilize the patient continue with anticoagulant medications such as heparin, coumarin, aspirin, and dipyridamole combined with aspirin (Aggrenox) in cases of thrombosis or embolism. Heparin is administered intravenously during acute episodes, whereas coumarin, dipyridamole, aspirin, subcutaneous low molecular weight heparin, or platelet receptor antagonists (clopidogrel, abciximab, ticlopidine) are employed for prolonged

periods to reduce risk of thrombosis (e.g., deep vein thrombosis). Corticosteroids may be used acutely after a stroke to reduce the cerebral edema that accompanies cerebral infarction. This can markedly lessen complications. Surgical intervention may be indicated for removal of a superfi cial hematoma or management of a vascular obstruction. The latter usually is accomplished by thromboendarterectomy or by bypass grafts in the neck or thorax. Valium, Dilantin, and other anticonvulsants are prescribed in the management of seizures that may accompany the postoperative course of stroke. If the patient survives, the third and fi nal task consists of institution of preventive therapy, administration of medications that reduce the risk of another stroke (statins and antihypertensive drugs), and initiation of rehabilitation. Rehabilitation generally is accomplished by intense physical, occupational, and speech therapy (if indicated). Although marked improvement is common, many patients are left with some degree of permanent deficit.

DENTAL MANAGEMENT

Medical Considerations

Some primary tasks of the dentist include stroke prevention and identifi cation of the stroke-prone individual. Patients with a history or clinical evidence of hypertension, congestive heart failure, diabetes mellitus, previous stroke or TIA, and advancing age are predisposed to stroke, as well as to myocardial infarction. As these factors increase, so does the level of risk The dentist should assess patient risk, encourage individuals to seek medical care, and eliminate or control all possible risk factors. Assessment of risk aids in the decision-making process regarding the timing and type of dental care to be provided. For example, a patient who has had a stroke or TIA is at greater risk for having another than a person who has not had one. In fact, up to one third of strokes recur within 1 month of the initial event, and risk remains elevated for at least 6 months. These individuals therefore should be approached with a degree of caution, and deferral of treatment is advised for 6 months. Although risk decreases after 6 months, it continues to be present; 14% of those who survive a stroke or TIA have a recurrence within 1 year. In addition, patients who experience a TIA or RIND are unstable and should not undergo elective dental care. Medical consultation and referral to a physician are mandatory. A patient who takes coumarin or

antiplatelet drugs is at risk for abnormal bleeding . The status of coumarin anticoagulation is monitored by assessment of the international normalized ratio (INR). An INR level of 3.5 or less is acceptable for performance of most invasive and noninvasive dental procedures. If the INR is greater than 3.5 and oral surgery is planned, significant bleeding may occur, and the physician should be consulted for a decrease in dosage of the anticoagulant. In these cases, a reduction in dose of the anticoagulant is recommended over interruption of anticoagulation therapy because the risk for significant adverse outcomes is minimized by this approach. Also, metronidazole and tetracycline may increase the INR by inhibiting the metabolism of Coumadin; therefore, concurrent use of these drugs may have to be avoided.
The effects of aspirin and dipyridamole on platelet aggregation are monitored by the platelet function analyzer (PFA)-100. Abnormal results should be discussed with the physician. Postoperative pain should be managed with acetaminophen-containing products. Management of stroke-prone patients or patients with a history of stroke includes the use of short, midmorning appointments that are as stress free as possible. Assisted transfer to the dental chair may be needed. Do not overestimate the patient's abilities, especially because some stroke patients may be able to verbalize but do not realize the extent of paresis that is present. Dental care providers should move slowly around the patient and should speak clearly while facing the patient with the mask off.
Blood pressure should be monitored to ensure good control. Pain control is important. Nitrous oxide–oxygen may be given if good oxygenation is maintained at all times. A pulse oximeter should be used to ensure that oxygenation is adequate. A local anesthetic with 1 : 100,000 or 1 : 200,000 epinephrine may be used in judicious amounts ($\leq$ 4 mL). Gingival retraction cord impregnated with epinephrine should not be used. A patient who develops signs or symptoms of a stroke in the dental offi ce should be provided oxygen, and the EMS should be activated. Transport to a medical facility should not be delayed (minutes count when one is treating patients with acute stroke). For ischemic stroke, thrombolytic agents should be administered within 3hours if they are to be maximally effective in reestablishing arterial flow; the earlier subjects receive these agents, the better is the outcome. The phrase "time is brain" emphasizes the immediacy

of the situation. Finally, the dental staff should remember that patients who have had a stroke have feelings of grief, loss, and depression and should be treated with compassion. Treatment Planning Modifi cations Technical modifications may be required for patients with residual physical defi cits who have difficulty practice adequate oral hygiene. For these patients, extensive bridgework is not a good choice. However, fi xed prostheses may be more desirable than removable ones because of diffi culties associated with daily placement and removal. Individualized treatment plans are important. All restorations should be placed with ease of cleansability in mind. Hygiene is often facilitated by an electric toothbrush, a large-handled toothbrush, or a water irrigation device. Flossing aids should be prescribed, and loved ones and personal care providers should be instructed on how and when these services should be provided. Frequent professional prophylaxis and the provision of topical fluoride and chlorhexidine are advisable.

Oral Complications and Manifestations

A stroke-in-evolution may become apparent through slurred speech, a weak palate, or diffi culty swallowing. After a stroke, loss or diffi culty in speech, unilateral paralysis of the orofacial musculature, and loss of sensory stimuli of oral tissues may occur. The tongue may be fl accid, with multiple folds, and may deviate on extrusion. Dysphagia is common, along with diffi culty in managing liquids and solids. Patients with right-sided brain damage may neglect the left side. Thus, food and debris may accumulate around teeth, beneath the tongue, or in alveolar folds. Patients may need to learn to clean teeth or dentures with only one hand, or they may require assistance to maintain oral hygiene; otherwise, caries, periodontal disease, and halitosis occur commonly. Calcified atherosclerotic plaques have been demonstrated in the carotid arteries of elderly and diabetic patients on panoramic films This radiographic feature indicates a risk for stroke and warrants referral to the patient's physician for evaluation. Also of note, severe periodontal bone loss is associated with carotid artery plaques and increased risk for stroke. However, the exact causative relationship between periodontal disease and stroke remains to be defined .Although periodontal treatment can reduce serum inflammatory markers potentially involved in stroke, evidence that

periodontal therapy reduces the risk for stroke is lacking

BOX 27-4

Dental Management of the Patient With Stroke

1. Identify risk factors.
   a. Hypertension*
   b. Congestive heart failure*
   c. Diabetes mellitus*
   d. TIA or previous stroke*
   e. Increasing age ≥75 years*
   f. Elevated blood cholesterol or lipid levels
   g. Coronary atherosclerosis
   h. Cigarette smoking
   i. *Note:* Risk of stroke increases by a factor of 1.5 for each condition above indicated by*. Thus, having multiple risk factors listed above greatly increases the risk of a stroke.[48]
2. Encourage control of risk factors (referral to physician, if appropriate).
3. Obtain thorough history of stroke.
   a. Note date of event, current status, medical therapy, and any residual disabilities.
   b. Provide only urgent dental care during first 6 months after a stroke, TIA, or RIND.
   c. Avoid elective care in patients who have had recent TIAs or RINDs.
   d. Determine risk for bleeding problems in patients taking anticoagulant drugs, and minimize perioperative bleeding.
      (1) Aspirin ± dipyridamole (Aggrenox), clopidogrel (Plavix), abciximab (ReoPro), or ticlopidine (Ticlid); obtain pretreatment PFA-100.
      (2) Coumarin—Pretreatment INR ≤3.5. Higher levels require consultation with physician to reduce dose.
      (3) Heparin (IV)—Use palliative emergency dental care only, or 6 to 12 hours before surgery, discontinue heparin and start another anticoagulant (e.g., coumadin) with physician's approval. Then, restart heparin after clot forms (6 h later). Heparin (subcutaneous, low molecular weight)—generally, no changes required.
      (4) Use measures that minimize hemorrhage (atraumatic surgery, pressure, gelfoam, suturing), as needed.
      (5) Have available nonadrenergic hemostatic agents and devices (stents, electrocautery).
4. Schedule short, stress-free, midmorning appointments. Provide N_2O-O_2 inhalation as needed.
5. Monitor blood pressure and oxygen saturation.
6. Use minimum amount of anesthetic containing vasoconstrictor.
7. Avoid epinephrine in retraction cord.
8. Recognize signs and symptoms of a stroke, provide emergency care, and activate emergency medical support system.
9. A prior stroke may require assistance for patient transfer to the chair, effective oral evacuation and airway management, and rigorous oral hygiene measures delivered by a health care provider.

INR, International normalized ratio; IV, intravenous; PFA, platelet function analyzer; RIND, reversible ischemic neurologic deficits; TIA, transient ischemic attack.

PARKINSON'S DISEASE

Parkinson's disease, fi rst described by James Parkinson in 1817, is a progressive neurodegenerative disorder of neurons that produce dopamine. Loss of these neurons results in characteristic motor disturbances (resting tremor, muscular rigidity, bradykinesia, postural instability). Dopaminergic neurons are found in the nigrostriatal pathway of the brain. Approximately 80% of the dopamine in these neurons must be depleted before symptoms of the disease arise. This disease is chronic and progressive.

EPIDEMIOLOGY

Incidence and Prevalence

Parkinson's disease is a common disease of the central nervous system (CNS) that affects about 1 million Americans, or 1 in 300 persons. Each year, this disease is diagnosed in 50,000 individuals. About 1% of the population older than 50 years of age and 2.5% of the population over age 70 have the disease. Given the aging phenomenon in the United States, a threefold to fourfold increase in Parkinson's disease frequency is predicted over the next 50years. Parkinson's disease has a peak age of onset between 55 and 66 years, but a particular form of the disease can strike teenagers. Men are affected slightly more often than women, and no racial predilection exists. An average dental practice of 2000 adult patients is predicted to include about 6 patients who have Parkinson's disease.

Etiology

Parkinson's disease is caused by death and depletion of dopaminergic neurons, which are manufactured in the substantia nigra and released in the caudate nucleus and putamen (the nigrostriatal pathway). Although the cause of Parkinson's disease remains unknown, many factors have been identified that are associated with development of the disease. Genetic mutations (such as mutations in the alpha-synuclein gene or the Parkin gene, which contributes to protein degradation) contribute to less than 10% of cases. Other causes include stroke, brain tumor, and head injury (e.g., boxing) that damage cells in the nigrostriatal pathway. Exposure to manganese (in miners and welders), mercury, carbon disulfi de, certain agricultural herbicides (rotenone), and street heroin contaminated with a meperidine analog (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) can be neurotoxic and give rise to Parkinson's disease symptoms. Also, neuroleptic drugs (phenothiazines,

butyrophenones) may cause Parkinson symptoms and rigidity. Pathophysiology and Complications Parkinson's disease is thought to be caused by environmental and genetic factors that trigger failure in proteasome-mediated protein turnover in susceptible neurons, resulting in accumulation of toxic proteins. This leads to degeneration and loss of pigmented neurons primarily of the substantia nigra and destructive lesions in the circuitry to the limbic system, motor system, and centers that regulate autonomic functions. Damaged neurons display neuronal cytoskeleton changes, including eosinophilic intraneuronal inclusion bodies (called Lewy bodies) and Lewy neurites in their neuronal processes.Inclusion bodies contain compacted aggregates of presynaptic protein alpha-synuclein. The course of the disease is complicated by degeneration of other regions in the brain such as the cholinergic nucleus basalis, which can result in depression.

CLINICAL PRESENTATION

Signs and Symptoms

Parkinson's disease results in resting tremor (that is attenuated during activity), muscle rigidity, slow movement (bradykinesia, shuffl ing gait), and facial impassiveness (mask of Parkinson's disease) . The tremor, which is rhythmic and fi ne and is best seen in the extremity at rest, produces a "pill-rolling rest tremor" and handwriting changes. Cogwheel-type rigidity (decreased arm swing with walking and foot dragging), stooped posture, unsteadiness, imbalance (gait instability), and falls also are common features. In addition, pain, (musculoskeletal, sensory [burning, numbness, tingling], or akathisia—subjective feeling of restlessness—restless leg syndrome), orthostatic hypotension, and bowel and bladder dysfunction occur in approximately 50% of patients. Cognitive impairment of memory and concentration occurs to varying degrees, depending on the extent of destruction of the cortical–basal ganglia–thalamic neural loops. Mood disturbances (depression, dysthymia, apathy, anxiety), insomnia, and fatigue occur in approximately 40% of patients; dementia occurs in approximately 25% of patients. Psychosis, related to dopaminergic medications, occurs in approximately 20% of patients.

Laboratory Findings

Because no diagnostic test is available to detect Parkinson's disease, the diagnosis requires a thorough history, clinical examination, and specifi c

tests and images to rule out diseases that can produce similar symptoms, such as Wilson's disease, arteriosclerotic pseudoparkinsonism, multiple stem atrophy, and progressive supranuclear palsy.

MEDICAL MANAGEMENT

Therapy is begun with the goal of increasing dopamine levels in the brain. Because no optimal drug treatment is available for Parkinson's disease, each person is treated on an individual basis with a variety of drugs. Drug therapy generally is not initiated until lifestyle impairment such as slowness or imbalance occurs. Drug selection is based on anticipated adverse effects and complications and is initiated at the lowest effective dose. The mainstay of treatment for advanced Parkinson's disease is carbidopa/levodopa (Sinemet), an immediate precursor of the neurotransmitter dopamine. Its use is generally reserved for later in the course of the disease because its activity wanes after about 5 to 10 years, and when given over the long term, it produces complicating adverse effects (dyskinesia—involuntary rapid, flowing movements of limbs, trunk, or head). Management of progressive disease requires a careful balance between the benefi cial effects of Sinemet or controlled-release levodopa (Sinemet CR) and the use of adjunct medications such as (1) dopamine agonists and (2) catechol-Omethyltransferase (COMT) inhibitors (entacapone) used to diminish motor fl uctuations, as well as (3) serotonin reuptake inhibitors used to manage depression and (4) acetylcholinesterase inhibitors given for dementia. Dosage adjustments are required when dyskinesias, immobility, psychosis, or other adverse effects occur. Physical therapy is important for providing patients with safe methods for rising from a chair, walking around a room, traversing stairs, and combating immobility and contractures. If symptoms progress despite drug therapy, surgery involving replacement of dopamine neurons by grafting of fetal nerve tissue appears to be an encouraging alternative for those with advanced Parkinson's disease. Newer modalities are focusing on halting neuronal loss with the use of antioxidants, or introducing (injecting) trophic factors through lentiviral delivery of a gene that encodes glial cell line–derived neurotrophic factor. Deep brain stimulation of subthalamic nuclei, thalamotomy, or pallidotomy
is reserved for advanced disease and severe disabling or intractable tremor.

DENTAL MANAGEMENT

Medical Considerations

The dentist who manages adult patients plays an important role in recognizing the features of Parkinson's disease and making a referral to a physician for thorough evaluation of patients who exhibit features of the disease. Once the diagnosis has been made, concerns in dental management are twofold: (1) minimizing the adverse outcomes of muscle rigidity and tremor, and (2) avoiding drug interactions. Because the muscular defect and tremor can contribute to poor oral hygiene, the dentist should assess patients' ability to cleanse their dentition by demonstration. If a patient is unable to provide adequate home care, alternative solutions should be provided, such as the introduction of the Collis curve toothbrush, mechanical toothbrushes, assisted brushing, or chlorhexidine rinses. Although no adverse interactions have been reported between COMT inhibitors (tolcapone [Tasmar]; entacapone [Comtan]) and epinephrine at dosages typically used in dentistry, they can potentially interact, and it is advisable to limit the dose of epinephrine to 2 carpules containing 1:100,000 epinephrine (36 μg) in patients who take COMT inhibitors. Erythromycin should not be given to patients who take the dopamine agonist, pramipexole (Mirapex). The clinician should be aware that antiparkinsonian drugs can be CNS depressants, and a dentally prescribed sedative may have an additive effect.

TABLE 27-2
Drugs Used in the Management of Parkinson's Disease

Class and Drug	Reason Used	Adverse Effects	Dental Consideration
ANTICHOLINERGIC	Blocks the effect of another brain neurotransmitter (acetylcholine) to rebalance its levels with dopamine		
Trihexyphenidyl HCl (Artane) Benztropine mesylate (Cogentin)		Sedation, urinary retention, constipation	Dry mouth
DOPAMINE PRECURSOR	Provides a drug that is metabolized into dopamine (dopamine replacement)		
Levodopa Carbidopa/levodopa (Sinemet CR, Madopar CR)		Dyskinesia, fatigue, headache, anxiety, confusion, insomnia, orthostatic hypotension	If choreiform movements, dyskinesias, or tremors present, may require sedation techniques to perform dentistry; caution when getting up from the dental chair
DOPAMINE AGONIST	Mimics the action of dopamine		
Bromocriptine mesylate (Parlodel)*		Dopaminergic effects: Psychosis (hallucinations, delusions), orthostatic hypotension, dyskinesia, nausea	Caution when getting up from the dental chair
Pramipexole (Mirapex) Ropinirole HCl (Requip)			Mirapex adversely interacts with erythromycin
CATECHOL-O-METHYLTRANSFERASE (COMT) INHIBITOR	Used along with levodopa. This medication blocks an enzyme (COMT), to prevent levodopa breakdown in the intestine, thus allowing more of levodopa to reach the brain		
Tolcapone (Tasmar)* Entacapone (Comtan)		Potentiate levodopa effects: Dyskinesia, psychosis, or orthostatic hypotension; nausea and diarrhea, abnormal taste	Caution with use of vasoconstrictors. Monitor vital signs during and after administration of first capsule; limit dose to 2 capsules containing 1:100,000 epinephrine (36 µg) or less, depending on vital signs and patient response; aspirate to avoid intravascular injection
MONOAMINE OXIDASE B INHIBITOR	Prevents metabolism of dopamine within the brain		
Selegiline		Dizziness, orthostatic hypotension, nausea	Select adrenergic agents (i.e., amphetamine, pseudoephedrine, and tyramine) may cause increased pressor response. However, this does not appear to occur with epinephrine or levonordefrin
NEUROTRANSMITTER INHIBITOR	Has anticholinergic properties that enhance dopamine transmission		
Amantadine		Sedation, urinary retention, peripheral edema, nausea, constipation, confusion	

*May cause significant hepatic toxicity.
†Also has adverse vasoconstrictive properties.

Orthostatic hypotension and rigidity are common in patients who have Parkinson's disease. Orthostatic hypotension is an adverse effect associated with COMT inhibitors. To reduce the likelihood of a fall from the dental chair, the patient should be assisted to and from the chair. At the end of the appointment, the chair should be inclined slowly to allow for reequilibration. Treatment Planning Modifi cations The treatment plan for the patient with Parkinson's disease may require modifi cation based on the patient's ability to cleanse the oral cavity. When communicating the treatment plan and other advice, the dentist should directly face the patient. This provides effective communication with a person who has the potential for cognitive impairment. Patients should receive dental care during the time of day at which their medication has maximum effect (generally, 2 to 3 hours after taking it). The presence of tremors or choreiform movements may dictate that the dentist use soft arm restraints or sedation procedures. Oral Complications and Manifestations Parkinson's disease is associated with staring, excess salivation and drooling, and decreased frequency of blinking and swallowing. Muscle rigidity makes repetitive muscle movement and maintenance of good oral hygiene difficult. In contrast, the drugs used to manage the disease (anticholinergics, dopaminergics, amantadine, and Ldopa) often result in xerostomia, nausea, and tardive dyskinesia. Dental recall visits should be more frequent for this population, and specifi c measures (specialized toothbrushes—e.g., Collis curve toothbrush, mechanical brushes) should be devised to maintain adequate oral hygiene. If the patient is experiencing xerostomia, then dysphagia and poor denture retention are likely. Salivary substitutes are benefi cial in alleviating symptoms. Topical fluoride should be considered for use in dentate patients with xerostomia to prevent root caries. Personal care providers should be educated about their role in assisting and maintaining the oral hygiene of these patients.

Suggestive Reading

James W Little, Craig S Miller, Nelson L Rhodus. Dental management of medically compromised patient, 9th edition, Elsevier, 2018