CHAPTER 16

# Aerospace Neurology

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Listen to your patients. Listen and they will tell you what's wrong with them. And if you listen long enough, they will even tell you what will make them well.

*—Walter C. Alvarez*

A doctor who cannot take a good history and a patient who cannot give one are in danger of giving and receiving bad treatment.

*—Author Unknown*

The greatest mistake in the treatment of diseases is that there are physicians for the body and physicians for the soul, although the two cannot be separated.

*—Plato*

In the practice of medicine, the neurologist is called upon to answer the following questions (1):

1. Does the patient have neurologic disease?
2. If so, what is the localization of the lesion or lesions?
3. What is the pathophysiology of the process?
4. What is the preliminary differential diagnosis?

Utilizing the tools of the neurologic and medical history, the neurologic examination, ancillary studies, and one's education, training, and experience the neurologist arrives at a diagnosis. The aerospace medicine physician (evaluator) has the additional challenge of relating the neurologic condition to aviation safety and achieving an appropriate aeromedical disposition. Whether it is aviation medical examiner, flight surgeon, or regulator, the aerospace medicine physician shoulders the responsibility of a determination that may decide one's career in aviation or space. Considering the individual, and yet preserving aviation safety, is a never-ending challenge for the aerospace medicine physician. The evaluator has the dual responsibility of applying the standards, and also considering exceptions to the standards in allowing waivers from standards, while assuring aviation safety.

An important consideration in aeromedical disposition is the nature of the operation or the mission, as a condition might not be compromising in all aerospace operations. The evaluator must consider the condition in relation to space operations, potentially of long duration, military versus civil operations, single versus multicrew operations, and the nature of the operation. Demands within civil, private, commercial, and airline transport operations must be considered. For example, a history of migraine with certain characteristics might potentially compromise military operations where immediate worldwide deployment is possible, but the condition might be considered an acceptable risk for multicrew or private pilot operations.

## PRINCIPLES OF AEROSPACE NEUROLOGY

When a neurologic condition exists, the evaluator should consider the following:

1. Is the condition static? If so, what is the degree of functional incapacitation?
2. Is the condition progressive? If so, is the course predictable or unpredictable?
3. Can the condition be monitored successfully?
4. Can the condition result in sudden incapacitation?
5. Can the condition result in subtle incapacitation?

A pitfall in aeromedical disposition of aviators with neurologic disorders is making a major decision based on limited information. In neurologic diagnosis, the history is most often the richest source of information. The neurologic examination is often normal. Ancillary studies including laboratory studies, neuroimaging procedures, and sometimes sophisticated studies such as cardiac electrophysiological studies may also be normal. Often, the history is the sole means of diagnosis. One need only consider the migraineur, the epileptic with a normal electroencephalogram (EEG), the person with a transient ischemic attack (TIA) and no vascular bruit, or the victim of transient global amnesia (TGA) to grasp the importance of history.

The aerospace medicine physician is somewhat disadvantaged because evaluation is based on obtained medical records and history taken by others. Most often, the evaluator has no opportunity to interact with the individual or obtain one's own history. Yet efforts to obtain additional information when the history is inadequate often bear the most fruit. Observations of emergency services personnel, description of an event by a spouse or other observer, or comments from fellow aircrew may hold the key to diagnosis and appropriate aeromedical disposition. Diligent pursuit of a complete history is the evaluator's best guide to aeromedical disposition.

Another important consideration in neurologic diagnosis is the role of psychological factors. Symptoms that reflect true neurologic illnesses are often intertwined with complaints that have an emotional basis, and teasing out the respective contributions is important for the evaluator. Moreover, psychological influences often play an important role in a number of common disorders encountered by the neurologist. The influence of emotions in migraine, syncope, and chronic daily headache exemplifies this relationship.

This chapter does not address individuals in whom neurologic disease is absent. Rather, it addresses those who suffer from a neurologic condition, which may or may not compromise aviation safety, resulting in temporary or permanent disqualification or operational limitations.

The following pages will attempt to apply these principles to specific neurologic conditions encountered in aerospace medical certification.

## EPISODIC DISORDERS

Episodic neurologic disorders, including migraine, cluster headache, TGA, syncope, epilepsy, the single seizure, and vertigo, are of aeromedical significance because of the potential for sudden incapacitation. Some merit permanent disqualification, whereas others may be accommodated with treatment or operational limitations. Vertigo will be dealt with in Chapter 15. Although "central" vertigo may occur in association with brain stem disease [e.g., multiple sclerosis (MS) or ischemic vascular disease], most cases of paroxysmal vertigo represent peripheral vestibulopathies.

### Migraine

Migraine is common, with a prevalence of 17% in women and 6% in men. Common features of migraine include unilaterality (exclusively or predominantly one-sided), throbbing nature, nausea, vomiting, photophobia, phonophobia, and prostration. The migraine sufferer commonly prefers a dark, quiet room and relief may follow sleep. The headache may last hours to days and is commonly followed by a drained feeling and remnants of pain with head movement. Although migraine may be spontaneous, there are many precipitants including sleep deprivation, hunger, sun exposure, fatigue, menses or oral contraceptives, foodstuffs, alcohol, and emotional stress. Migraineurs tend to have perfectionistic and orderly personality traits, and family history is positive in 60% of cases. Migraine can appear at any age but commonly in adolescence, sometimes entering remission and appearing years later.

In common migraine, the headache begins without an antecedent aura. In classic migraine, an aura precedes the headache by 15 to 30 minutes. Visual auras are common with myriad descriptions including scintillating or sparkling lights, visual field defects such as hemianopia, colored or kaleidoscopic whorls or patterns, or patterns such as zigzag lightning or herringbone patterns. An important diagnostic feature is the "positive" nature of the visual aura, meaning the presence rather than the absence of light (ischemia characteristically is a "negative" visual phenomenon with absence of light). Nonvisual auras also occur, with symptoms such as marching face and hand numbness, or expressive speech difficulty.

A third variety of migraine is "migraine equivalent" (migraine variant, acephalgic migraine), in which a migraine aura occurs without developing a headache. Visual migraine equivalents are not uncommon beyond age 40(2), sometimes being mistaken for TIA due to cerebrovascular disease.

Rare forms of migraine include "complicated migraine," such as hemiplegic migraine accompanied by stroke, ophthalmoplegic migraine with oculomotor nerve palsy, and basilar migraine with ataxia and confusion.

Migraine may or may not be of aeromedical significance depending on its characteristics in a specific individual, and operational considerations (e.g., potential global military

deployment versus private pilot operations). To guide aeromedical disposition, the evaluator should consider a host of factors, including the following:

1. ***Prodrome*:** Some migraine sufferers will experience a prodrome of hours to a day or more, characterized by a sense of uneasiness, anxiety, apprehension, or general feeling of ill being. Recognition of prodrome may allow the aviator to avoid flying.
2. ***Precipitating factors*:** Many migraineurs will report specific precipitating factors, which, if avoided, may reduce migraine risk or preclude migraine altogether. These include emotional stress, multitask overload, sleep deprivation, fasting, foodstuffs and certain alcohols, menses, and other precipitants.
3. ***Migraine aura*:** Is the aura minor, or is there significant functional impairment? For example, slight perioral and unilateral fingertip paresthesiae may be inconsequential, as would a sliver of shimmery light in the far periphery of the visual field. Alternatively, a complete homonymous hemianopia or prominent aphasia would significantly compromise the individual.
4. ***Rapidity of onset*:** Some migraines develop rapidly, with vomiting and prostration occurring within 15 to 30 minutes of onset. Others develop slowly, perhaps beginning as an annoying discomfort over one eye, but not developing into a severe headache for hours. Onset during flight would allow corrective measures in this circumstance.
5. ***Frequency*:** Migraine-free intervals can vary widely from days to years or even decades. An individual experiencing several migraines per month would cause concern; a frequency of two per year would be far less worrisome.
6. ***Acute treatment measures*:** Aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen may be effective if taken early. These would be acceptable in an aviation environment. Triptans may be acceptable with timing limitations in relation to flight. Anticonvulsants, narcotic analgesics, and barbiturate-containing analgesics would be prohibitive.
7. ***Preventive treatment*:** Medications employed in migraine prophylaxis include $\beta$-blockers, calcium channel blockers, anticonvulsants, and antidepressants including tricyclic and selective serotonin reuptake inhibiting agents. $\beta$-Blockers and calcium channel blockers may be acceptable in aviation, whereas the others are prohibitive due to potential central nervous system effects.

Considering the prevalence of migraine, the diagnosis need not be disqualifying in most individuals. Individual consideration with attention to the features enumerated earlier may allow favorable aeromedical disposition depending on the aviation environment.

## Cluster Headache

True cluster headache, formerly known as *histamine headache* or *Horton's headache,* has very distinct clinical characteristics. The term *cluster* refers to a series of headaches lasting from weeks to months separated by symptom-free intervals of many months to several years or more. Each headache is identical for that individual. Clinical characteristics may include abrupt onset with intense pain peaking within a minute or two, unilateral location in or behind one eye, unilateral nasal stuffiness, drainage, eye redness, tearing, and perhaps a Horner syndrome (ptosis and pupillary constriction). Excruciating pain persists for 30 to 45 minutes followed by rapid resolution of symptoms. Headaches may occur precisely at the same time each day. After one or more headaches daily for a period, the cluster ends, affording welcome relief.

Cluster headache is treated with narcotic analgesics and other analgesics, lithium carbonate, and at times oxygen (a potent vasoconstrictor). Severe pain and analgesic requirements during a cluster are disqualifying, but long periods of remission usually allow certification once the cluster ends.

## Other Headache

Although not included in the episodic disorders, the most commonly occurring headache is chronic daily headache, formerly referred to as *tension headache*. This is a frequent (daily or nearly so) headache, often dull to moderate, nagging but not incapacitating, with resistance to treatment. It may be a component of a somatoform disorder, and in one study 46% of individuals with a primary complaint of chronic headache suffered from endogenous depression (3). The underlying condition and therapeutic agents utilized (narcotic- or barbiturate-containing analgesics, antidepressants, tranquilizers) ordinarily preclude aeromedical certification unless underlying issues are resolved.

## Transient Global Amnesia

TGA is a fascinating condition whose prime characteristic is severe anterograde and extensive retrograde amnesia. Initially described in 1954, TGA is a global amnesic state that resolves within 24 hours. Personal identity, level of consciousness, awareness, and ability to perform complex acts are well preserved, distinguishing TGA from confusional states. Strict diagnostic criteria include presence of a capable witness, clear anterograde amnesia, alert wakefulness, normal content of consciousness beyond memory, absence of focal symptoms and a normal neurologic examination, and resolution within 24 hours.

Although TGA has been reported from age 5 to 92 years, 90% of cases occur in the 50 to 80 range. Most attacks are 4 to 6 hours in duration, with retrograde amnesia ranging from hours to months and sometimes years, which upon recovery shrinks to a permanent retrograde gap of 1 hour.

Precipitating circumstances reported in TGA include cold water immersion, sexual intercourse, painful experiences, and medical procedures such as angiography on rare occasions. Association with physical exertion is present in 18%, emotional stress in 14% to 44%, and with migraine in 25% to 33% of cases.

At the onset of TGA there is disorientation for time and place, but preservation of personal identity. Repetitive asking of questions is a near universal feature. Preserved ability to perform complex acts such as operating an aircraft

or performing detailed carpenter work is a constant feature of TGA. Migraine-like headaches are associated with TGA in approximately 50% of patients.

Unilateral or bilateral medial temporal hypoperfusion has been demonstrated during TGA with magnetic resonance imaging (MRI) techniques, and experimentally, a slowly spreading cortical depression across the cerebral cortex has been shown. Interestingly, a similar mechanism of cortical spreading depression has been postulated in the aura of migraine.

Most individuals with TGA suffer a single episode, although recurrence rates of 3% annually over 5 years have been reported. Aeromedical disposition often depends on specific precipitating factors and often a period of symptom-free observation.

A monograph by Hodges (4) provides a comprehensive review and discussion of TGA.

## Syncope

The importance of history in neurologic diagnosis is clearly apparent when dealing with disorders of consciousness. Differentiating syncope from seizure (faint from fit) is a never-ending challenge for the aeromedical physician. An erroneous diagnosis has profound implications for the aviator. Up to one third of persons suffering syncope with convulsive accompaniments are incorrectly given a diagnosis of epilepsy.

The essence of syncope is loss of consciousness and postural tone due to global cerebral hypoperfusion followed by spontaneous recovery. In near syncope (presyncope), the process is incomplete (perhaps by a compensatory action such as sitting down), with partial preservation of consciousness.

Syncope is common, with a reported occurrence of 3+% in the Framingham Study. Approximately 75% of these individuals reported a single occurrence with a mean follow-up of 26 years. In a study of 3,000 healthy United States Air Force (USAF) personnel averaging 29 years of age, 2.7% reported syncope (5).

In the 1942 text *Fit to Fly, A Medical Handbook for Fliers,* coauthored by Grow and Armstrong, the following text appears: ''Low blood pressure occurs in 2.5% to 5% of the population and is probably more common in hot climates. Usually it indicates a person who is under par physically. They are usually underweight, show narrow, flat chests with poor expansion, and they commonly complain of lassitude, giddiness, vertigo, and a tendency to faint'' (6). There are no other references to syncope in the text.

Syncope occurs due to impaired homeostasis, the normal state of appropriate balance and regulation of cardiac output, circulating blood volume, and peripheral resistance provided by peripheral arterial smooth muscle. When one stands, 70% of circulating blood volume lies at or below the heart. Gravity pools 500 to 800 mL of blood in dependent vascular spaces in the lower extremities, with concomitant reduction in central venous pressure by 3 to 5 mm Hg and stroke volume by 50%. Resultant diminished baroreceptor stimulation leads to compensatory mechanisms including enhanced sympathetic and inhibited parasympathetic activity. Heart rate increases 10 to 25 beats per minute and sympathetic efferents to arterioles command an increase in peripheral resistance. Mean arterial blood pressure is preserved, assuring maintenance of homeostasis. Sudden pain, fear, and a host of other precipitants can momentarily defeat the delicate balance of homeostatic mechanisms, and syncope occurs.

The term *vasovagal syncope,* coined by Lewis in 1932, refers to dual mechanism of loss of peripheral vasoconstriction (collapse of peripheral resistance) and cardioinhibition (vagus-induced bradycardia). Terms appearing in contemporary literature including neurally mediated, neuroregulatory, and neurocardiogenic syncope are synonymous. Lewis recognized that loss of peripheral resistance was the predominant mechanism in most instances of syncope. The term *vasodepressor syncope* denotes hypotension without significant bradycardia, whereas *cardioinhibitory syncope* refers to vagally induced bradycardia as the predominant mechanism. This is a clinically important distinction.

The cardioinhibitory reflex can be powerful. Ventricular standstill and fibrillation have been reported with psychological stimuli. In contrast to vasodepressor syncope, cardiac syncope is sudden in onset. With asystole, presyncope occurs within several seconds and loss of consciousness within 6 to 8 seconds when upright. Injury and sudden death are attendant risks in malignant forms of cardioinhibitory syncope.

When evaluating syncope, the evaluator must ask first ''Is it syncope or something else?'' The following historical points aid accurate diagnosis:

1. ***Postural setting*:** Syncope characteristically occurs when upright, less often while seated, and rarely in recumbency. Seizures do not respect posture.
2. ***Length of prodrome*:** In vasodepressor (noncardiac) syncope, there is usually a lengthy prodrome of 2 to 5 minutes. Feelings of uneasiness, warmth, anxiety, and queasiness are common during the prodrome, along with a desire for cool air and ventilation. In contrast, seizure auras, if present, are usually brief.
3. ***Antecedent symptoms*:** Visual complaints including pale, yellow, white, bleached, darkened, or constricted vision (''tunnel vision'') denote retinal ischemia, indicating an extracerebral mechanism for the event. Respiratory antecedents might include yawning or deep breathing. Gastrointestinal (GI) symptoms include an empty, hollow, or unsettled sensation in the epigastrium. Anxiety, dry mouth, and clamminess in the forehead and hands are common. Giddiness and lightheadedness may occur as the systolic blood pressure approaches 70 mm Hg, but, unlike true vertigo, there is no element of rotation of the environment or the body.
4. ***Syncopal episode*:** Syncope is a brief event, lasting 10 to 15 seconds, with little or no confusion. It is a hypotonic rather than rigid event (''syncopal slump'') with pallor (white—loss of color, rather than blue). Respirations are shallow and often imperceptible. Return of consciousness is rapid, as is alertness. The embarrassed victim may

rise quickly only to repeat the episode. This feature is diagnostic of vasovagal syncope.

5. ***Convulsive accompaniments and urinary incontinence*:** In experimental syncope, the EEG background frequency slows, lowers in amplitude, and eventually becomes flat, devoid of activity, as syncope ensues. In 10% to 15% of fainters, brief myoclonic jerks of the face and hands, tonic posturing, or other brief seizure-like activity occurs. This phenomenon constitutes the *convulsive accompaniment* that may occur in syncope. This is *not* a seizure, which is characterized by excessive neuronal discharges rather than absence of cortical activity. This convulsive accompaniment rather reflects a state of functional decerebration. In addition, approximately 10% of fainters experience urinary incontinence, which, if coupled with convulsive accompaniments, may lead to an erroneous diagnosis of seizure or epilepsy in one third of cases.
6. ***The syncopal setting*:** The situation or the circumstances in which the event occurs is of utmost importance. Worry, emotional upset, medication, alcohol, physical exertion, dehydration, medical procedure, or other precipitants may be present.

The evaluator, having determined that syncope has indeed occurred, must attempt to determine the cause or mechanism if possible. Table 16-1 lists potential causes of syncope.

Fortunately 50% or more of syncope is benign and does not signify underlying disease. A careful history and physical examination may indicate the cause of syncope in 25% to 35% of fainters and in 75% of persons in whom a cause is found (7). Basic laboratory tests (complete blood count, chemistry panel) and 12-lead electrocardiogram (ECG) may provide an answer in 5% to 10% of patients. Further studies should be guided by the history and physical findings, and may direct one toward cardiac studies such as echocardiogram, Holter monitor, ambulatory event recording, or ultimately electrophysiological studies. Brain MRI and EEG studies are usually not helpful.

When initial studies do not provide an explanation, head-up tilt (HUT) table testing may be helpful in the evaluation of syncope. HUT may be positive in 50% of cases of syncope of unknown cause, supporting a vasovagal mechanism for the event. However, HUT without pharmacologic activation has a false-positive rate of approximately 10%, rising to 27% or more with pharmacologic activation (commonly nitroglycerine). False-positive studies have led to an incorrect diagnosis of syncope in individuals with clinical seizures. Other caveats involving HUT include nonstandard tilt angles, variable tilt duration, and lack of reproducibility in some studies. HUT is not recommended in the routine evaluation of syncope.

Aeromedical disposition in syncope can be favorable in most instances in which a benign mechanism, that is not likely to recur in flight, can be demonstrated. Satisfactory exclusion of serious causes of syncope can be accomplished with appropriate testing, and a period of symptom-free observation might provide further assurance.

**TABLE 16-1**

**Etiology of Syncope**

- Reflex-mediated vasomotor instability
  - Vasovagal (neurocardiogenic, neurally mediated, neuroregulatory) syncope: the common faint
  - Situational syncope (related to a particular circumstance)
    - Cough (tussive) syncope
    - Sneeze
    - Swallow
    - Defecation
    - Postmicturition syncope
    - Weight lifting
    - Exercise induced
    - Trumpet player
    - Mess trick
    - Valsalva
    - Medical procedure: physical examination (eye-oculovagal, ear, etc.), venipuncture, genitourinary or gastrointestinal instrumentation, etc.
    - Hot tub or shower
  - Orthostatic/dysautonomic
    - Primary autonomic dysfunction (autonomic neuropathy, CNS disorders)
  - Secondary autonomic dysfunction
    - Medications, alcohol
    - Prolonged illness, prolonged bedrest
    - Hypovolemia (blood loss, dehydration)
  - Impaired cardiac output
    - Obstructive disease: aortic stenosis, idiopathic hypertrophic subaortic stenosis, pulmonary stenosis
    - Pump failure: myocardial infarction, coronary artery disease, cardiomyopathy
  - Impaired cardiac rhythm
    - Bradycardias
    - Tachycardias
    - Mixed rhythm disturbances: sick sinus (brady/tachy) syndrome
  - Psychiatric disease
  - Miscellaneous
    - Carotid sinus syncope
    - Glossopharyngeal neuralgia
    - Anemia
- Unknown

Adapted from Benditt DG, Lurie KG, Adler SW, et al. Pathophysiology of vasovagal syncope, Table 1, 3; and Kapoor WN. Importance of neurocardiogenic causes in the etiology of syncope. Table 1, 56. In: Blann JJ, Benditt D, Sutton S, eds. *Neurally mediated syncope: pathophysiology, investigations and treatment*. The Bakken Research Center Series, Vol. 10. Armonk, NY: Futura, 1996; with permission. CNS, central nervous system.

## Seizure Disorder

Seizure disorder, convulsive disorder, and epilepsy are synonymous terms. A seizure is an abnormal, paroxysmal excessive discharge of cerebral neurons. Epilepsy is a chronic condition characterized by a tendency for recurrent (two or more), unprovoked seizures. The cumulative incidence

of epilepsy is between 1.3% and 3.1% by age 80, with high incidence peaks in those younger than 20 and older than 60 (11). Epilepsy is idiopathic in two thirds of patients.

Not all seizures represent epilepsy. All persons have a constitutional or genetically determined threshold for seizures, which if exceeded, leads to a clinical event. This threshold may fluctuate with time of day, hormonal influences, sleep deprivation, and other factors. *Acute symptomatic* seizures may occur with electrolyte disturbances (e.g., severe hypoglycemia or hyponatremia), infectious processes (e.g., pneumococcal meningitis with high-dose penicillin), and cardiac arrest with prolonged asystole and ensuing cerebral ischemia. Individuals with low-seizure threshold may experience seizures when exposed to medications (tricyclic antidepressants, bupropion, theophylline, and other medications). Additionally, some individuals with established epilepsy may achieve permanent remission (e.g., benign childhood epilepsy with centrotemporal spikes).

For aeromedical purposes, a simple classification for seizures is adequate; it is presented in Table 16-2. Seizures are generalized from the onset in approximately half the cases and of partial onset in the remainder. Whereas generalized seizures are accompanied by simultaneous appearance of abnormal discharges throughout the cerebral cortex at onset, as the name implies, partial seizures (focal seizures in older terminology) arise in a discrete area of the cerebral cortex. This is significant in that a partial seizure implies a focal lesion, which must be identified (scar, tumor, abscess, cavernous angioma, other).

In simple partial seizures, consciousness is preserved. Localized convulsive twitching of one hand might be caused from a lesion in the contralateral cerebral cortex. The individual remains alert, can carry on activity, and ordinarily suffers no after effects with cessation of the seizure.

In complex partial seizures, consciousness is impaired or even lost. Complex partial seizures are commonly preceded by an aura of myriad descriptions. *Déjà vu* experiences, an unpleasant smell (olfactory aura) or taste (gustatory aura), a forced thought, vivid visual memory, or feeling of detachment from one's self, may precede the seizure. The victim may engage in stereotyped movements such as repetitive lip-smacking, chewing movements, or hand or body movements such as fumbling with an object or rubbing a table. Awareness of surroundings is either compromised or lost, and one may or may not lose consciousness.

Any partial seizure may spread to adjacent areas of cortex and eventually to deep-seated midline structures that project to all areas of the cerebral cortex, culminating in a generalized tonic-clonic (grand mal) seizure. For example, a focal seizure beginning in one hand as described earlier may spread to the forearm, upper arm, face, and leg (jacksonian march described by Hughlings Jackson), followed by collapse and a grand mal seizure. This is a partial seizure with secondary generalization.

A generalized tonic-clonic seizure is announced by a tonic phase lasting 10 to 20 seconds, with brief flexion, then muscular rigidity with arms raised, abducted, partially flexed at the elbows, and externally rotated. Leg involvement is minor. Eyes remain open with upward deviation of the globes. Extension of the back and neck then follows, perhaps accompanied by an ''epileptic cry'' resulting from forced expiration through partially closed vocal cords. Arms and legs are extended, with apnea and cyanosis. The clonic phase then begins, which is in reality a rhythmic relaxation of tonic contractions. Clonic jerks become coarser and decline in frequency as relaxation phases lengthen. Tongue biting and urinary incontinence are common.

Grand mal seizures are characteristically followed by a postictal state, which often includes a deep, snoring sleep. Return of consciousness follows with a confused and often combative arousal phase, which gradually clears. Nausea, vomiting, and headaches are common. Violent muscular contractions leave the trunk and extremity muscles sore and tender, and shoulder dislocations or vertebral compression fractures may occur. The victim wants to sleep, and upon returning to wakefulness is amnesic for the event.

Petit mal (absence) seizures represent another variety of generalized epilepsy. Frequently appearing in childhood, petit mal seizures are characterized by brief lapse of awareness that may or may not be accompanied by myoclonic jerks and alterations of muscle tone. Brief loss of awareness, with repetitive eye flutter for 2 to 3 seconds, would be a representative example. The individual immediately resumes normal activity, and, if the spell is brief, may remain unaware of its occurrence.

As with syncope, a careful history is of utmost importance in the evaluation of one or more seizures. Description by an observer might be the most important ingredient in accurate diagnosis. Records from paramedics and ambulance personnel, and detailed emergency room records including physician evaluations and nursing notes, may provide important details in accurately defining the clinical event. Personal history, family history, medication, and social history including alcohol and substance misuse are clearly important.

Seizure evaluation, particularly in adults, must include brain MRI with and without gadolinium and a sleep-deprived wake and sleep EEG. Computed tomography (CT), even with contrast is insufficient because lesions such as mesial temporal sclerosis, hamartoma, or cavernous malformation

**TABLE 16-2**

**Basic Classification of Seizures**

1. Seizures that are generalized from the onset (e.g., idiopathic grand mal epilepsy, classic petit mal epilepsy)
2. Simple partial seizures with preservation of consciousness (e.g., focal motor seizure)
3. Complex partial seizures with alteration of consciousness (e.g., psychomotor seizure, temporal lobe automatism)
4. Partial seizures with secondary generalization (focal onset, progressing to generalized tonic-clonic seizure)

might be overlooked. Wake-only EEG recordings are not sufficient because activation of a potentially epileptiform discharge might occur only during sleep recording. Photic stimulation is employed to elicit reflex-induced seizures (photic epilepsy) in susceptible individuals. It is important to note that up to 40% of individuals with epilepsy have normal EEGs throughout their lives, again emphasizing the importance of history.

Clearly, a detailed evaluation is needed in the aeromedical disposition of persons with seizures or a question of seizures. A history of febrile seizures does not imply chronic seizure potential. Some persons with seizures achieve complete remission in adulthood, such as benign Rolandic epilepsy with centrotemporal spikes. Individuals with acute symptomatic seizures do not harbor chronic seizure potential. A thorough neurologic evaluation, at times coupled with a period of seizure-free and medication-free observation, may allow medical certification.

### The Single Seizure

A single unprovoked seizure does not constitute epilepsy unless it is followed by a second unprovoked event. An individual suffering a first-ever seizure should undergo a comprehensive general medical and neurologic evaluation.

Degree of recurrence risk following a single unprovoked seizure can be related to risk factors. A history of febrile seizures or seizure occurrence in a first-degree relative elevates the risk, as does a history of remote neurologic insult or previous acute symptomatic seizure. An abnormal neurologic examination or abnormal imaging study is associated with increased risk of recurrence. EEG abnormalities are also important. Specifically, epileptiform abnormalities are associated with a 60+% risk of recurrence, nonspecific slowing with a 30% to 40% risk, and with a normal EEG 10% to 25% risk (12,13).

Absent risk factors, recurrence risk is in the 26% to 33% range over 5 years (12), after which recurrence risk approximates that of the normal population. Most epileptologists elect not to treat individuals with a first-ever seizure and no risk factors because the majority would be treated unnecessarily. This is important for the aviator because a 5-year period of seizure-free and medication-free observation might allow consideration for aeromedical recertification.

Initial treatment with anticonvulsants delays the process. A second seizure during that period satisfies the criteria for epilepsy (two or more unprovoked seizures), and recurrence risk following a second seizure escalates to 73%.

## CEREBROVASCULAR DISEASE

Stroke is the third leading cause of death in the United States and a major contributor to disability. Approximately 700,000 strokes occur in the United States annually, of which 200,000 are recurrent strokes. Approximately 85% of strokes are ischemic, whereas the remaining are hemorrhagic.

### Ischemic Stroke

Ischemic stroke may be classified based on the presumed nature of focal brain injury and the type and localization of the vascular lesion (11). Major categories include large artery atherothrombotic infarction (extracranial, intracranial, or cardioembolic), small vessel disease, other causes (dissection, hypercoaguable states), and stroke of indeterminate cause.

Approximately 20% to 30% of strokes are cardioembolic. Large vessel disease is responsible in 15% to 20% of cases, 75% of which is extracranial in origin (carotid or vertebral arteries, aorta), the remainder arising from intracranial large vessels (intracranial portions of major arteries, basilar, anterior, middle, and posterior cerebral arteries and major branches). Small vessel disease (lacunar stroke) comprises approximately 20% stroke cases (12). Coagulation disorders account for 1% to 5% of cases of stroke, and stroke without demonstrable cause (cryptogenic stroke) occurs in a significant proportion of stroke victims.

The aeromedical physician must address the issue of stroke in terms of primary prevention, secondary prevention, assessment of degree of significant functional disability, and determination of recurrence risk.

Nonmodifiable risk factors for stroke include age (risk doubles in each decade for those older than 55 years), gender (males have higher risk than females), race (African Americans and Hispanics have higher risks than whites), and genetics (family history may increase risk).

Well-documented modifiable risk factors for stroke include prior TIA/stroke, hypertension, diabetes, tobacco use, dyslipidemia, cardiac disease, atrial fibrillation, and asymptomatic carotid stenosis. Additional factors not fully supported by rigorous science include alcohol and drug abuse, physical inactivity, impaired nutrition, hypercoaguable states, elevated homocysteine, hormone replacement therapy, and oral contraceptives.

Primary prevention of stroke involves vigorous attention to modifiable risk factors, which includes treatment of hypertension, physical exercise, addressing dyslipidemia with diet and/or medication, smoking cessation, avoiding excess alcohol ingestion, and detection and treatment of cardiac disease and significant asymptomatic carotid artery stenosis. Stringent diabetes management is important if the disease is present.

Secondary prevention following ischemic stroke involves identification and mitigation of modifiable risk factors (13). Hypertension contributes to a variety of ischemic stroke subtypes through atherosclerosis, small vessel lipohyalinosis, and cardiac impairment. Effective management of hypertension alone can reduce stroke incidence by as much as 70% (14). In the PROGRESS trial, a combination of perindopril and indapamide produced a 43% reduction in recurrent stroke risk without regard to initial blood pressure (15). The seventh report of the Joint National Committee on Prevention, *Detection, Evaluation, and Treatment of High Blood Pressure* (JNC-7) classifies blood pressure of less than 120/less than 80 as normal, 120–139/80–89 as prehypertension, 140–159/90–99 as hypertension stage I, and 160/100 or

greater as hypertension stage 2 (16). Lifestyle modifications including weight control, physical activity, and moderation of sodium intake are recommended for persons with prehypertension. Along with lifestyle modifications, guidelines recommend thiazide-type diuretics, perhaps combined with a single agent for stage I hypertension, and for stage II hypertension two-drug combination for most (thiazide-type diuretic along with an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, $\beta$-blocker, or calcium channel blocker).

Hyperlipidemia elevates stroke risk, particularly carotid artery–related strokes (17). American Stroke Association (ASA) guidelines recommend adopting National Cholesterol Education Program guidelines, which advise lifestyle modification, dietary changes, and medication for TIA or stroke patients with elevated cholesterol, comorbid cardiac disease, or evidence of atherosclerotic origin.

Diabetes is a clear risk factor for stroke, being present in 15% to 33% of ischemic stroke victims. Additionally, smoking is a highly significant independent risk factor for ischemic stroke. It is generally accepted that heavy alcohol consumption elevates stroke risk in all subtypes, with perhaps a protective effect in light to moderate drinkers, such as 1 to 2 ounces daily. Less well-documented evidence exists for obesity and physical inactivity.

ASA guidelines advocate carotid endarterectomy for symptomatic (TIA or stroke) patients with severe carotid stenosis (70%–99%), and in selected patients with 50% to 69% stenosis. Asymptomatic carotid stenosis is receiving increased attention along with treatment options. In unselected populations, 7% of men and 5% of women older than 65 years have greater than 50% carotid artery stenosis. The risk of stroke with greater than 60% stenosis is approximately 2% per year, with a myocardial infarction risk of approximately 5% per year (18). Treatment of asymptomatic carotid stenosis is controversial. Dodick et al. recommend consideration of carotid endarterectomy in patients with asymptomatic carotid artery stenosis only for medically stable patients with stenosis of 80% or greater who are expected to live for 5 years, and then only with surgeons who have a perioperative complication rate of less than 3% (19). Evidence-based guidelines for clinicians put forth by the American Academy of Neurology support these parameters for patients aged between 40 and 75 with 60% to 99% stenosis.

Atrial fibrillation is associated with significant risk of cardioembolic stroke. Trials have shown a relative risk reduction of 68% and an absolute reduction in annual stroke rate from 4.5% to 1.4% in patients treated with dose-adjusted warfarin.

Along with primary and secondary prevention strategies and assessment of residual neurologic deficit for functional significance, the evaluator must address recurrence risk for aeromedical disposition.

In terms of overall risk, up to 30% of persons suffering ischemic stroke will suffer recurrent stroke within 5 years (18). In the Northern Manhattan Stroke Study (NOMASS) involving a mixed ethnic cohort (40% black, 34% Hispanic, 26% white) older than age 39, stroke recurrence risk was 25% at 5 years (20). Survival was better with lacunar stroke. Dhamoon et al. reported an 18.3% risk of recurrent stroke over 5 years (mean age 69.7 and mean follow-up 4 years) (21). In the Perth Community Stroke Study reporting 10-year risk of first recurrent stroke, the recurrence risk was 43%, risk being highest within the first year and averaging 4% per year after the first year (22). Numbers were not large. Of 328 patients (69% with ischemic stroke), 30 persons suffered recurrent stroke in the first year, and 34 over the next 9 years. Predictors of recurrent stroke included increasing age, atrial fibrillation, high alcohol consumption, hemorrhagic stroke, and hypertension at the time of discharge. In a Spanish study (mean age 75.4 years), cumulative risk was 26% at 5 years, with age being the major predictor (23). In a British study, 5-year risk of recurrent stroke was 16.6% (24).

Recurrence risk varies with stroke subtype, an important consideration in aeromedical disposition. In a follow-up of at least 10 years of 178 patients with lacunar stroke, recurrent stroke occurred in 23.5% (annual risk of 2.4%) (25).

Stroke in the young warrants specific attention because recurrence risk may be lower compared to adults and etiology may vary. In a 5-year follow-up of 95 patients younger than 45 years, 4.7% suffered recurrent stroke (26). In the Baltimore-Washington Cooperative Young Stroke Study of 428 first strokes in persons aged 15 to 44, approximately 34.3% had stroke of indeterminate cause and another 18.7% had no probable cause but at least one possible cause (27). Identifiable causes included cardiac embolism (31.1%), hematologic/other causes (19.8%), nonatherosclerotic vasculopathy (11.3%), illicit drug use (9.4%), and migraine (1.4%). Large artery atherosclerotic disease accounted for only 3.8%. In a Spanish study of 272 young adults aged 15 to 45 with first-ever ischemic stroke, annual stroke recurrence rate was 3.6% during the first year, declining to 1.7% annually thereafter (28). In an Italian study of 60 patients aged 17 to 45 with TIA or ischemic stroke, recurrence rate was 7.4% over a mean span of 6.1 years (29).

Ischemic stroke of indeterminate cause (cryptogenic stroke) comprises a significant proportion of stroke (30%–40%) (30).

Medical information doubles within 10 years, and a MEDLINE search of cerebrovascular disorders from 1966 to 2004 generates more than 170,000 results (31). The evaluator seeking best evidence for aeromedical disposition in strokes must consider a large body of evidence outside his or her medical discipline. A principle of individual consideration utilizing best available evidence should be followed. Louis Caplan, Professor of Neurology at Harvard University who specializes in cerebrovascular disease, offered the following advice (personal communication, 2002):

> "My bias is and always has been that strokes are very heterogeneous and that the risk of recurrent strokes and seizures after stroke and cardiac risk varies with the etiology, nature, and location of the stroke in the individual. My advice would be to write no firm general rule, but to evaluate each individual case—preferably by a panel of individuals who specialize in stroke."

### Hemorrhagic Stroke

Intracerebral hemorrhage (bleeding into brain parenchyma from an arterial source) is associated with hypertension in 72% to 81% of cases (32). Sites of bleeding include pons, cerebellum, basal ganglia, and lobar (subcortical white matter). Death or severe disability is common, ordinarily precluding return to flying.

Nonhypertensive causes of intracerebral hemorrhage include vascular malformations such as subdural hematomas or arteriovenous malformations, amphetamine use, cerebral amyloid angiopathy, vasculitis, and hemorrhage into metastatic tumor. Malignant melanoma is the third most common metastatic lesion to the brain following breast and lung, and hemorrhage is common.

Prognosis following intracerebral hemorrhage is not uniformly poor, and good recovery may be achieved with identification and idealization of risk factors or surgery. Judicious treatment of hypertension might reduce recurrence risk to an acceptable level. Complete resection of a vascular malformation may be curative following intracerebral hemorrhage, but seizure risk must be addressed. Although most malformations present with hemorrhage, a significant proportion (32%) are associated with seizures (33). Seizures tend to be associated with large malformations involving the cerebral cortex. Although complete surgical resection may eliminate risk of hemorrhage, risk of seizures arising from the surrounding neuronal bed might remain and preclude certification.

### Intracranial Aneurysms

The most frequent cause of nontraumatic subarachnoid hemorrhage, accounting for 80% of cases, is a ruptured intracranial secular aneurysm (34). Prevalence of aneurysms greater than 3 mm in diameter has been reported in 4% of autopsies. Aneurysms commonly arise from major arteries at the base of the brain (circle of Willis) and are thought to arise from a combination of congenital defects in the muscular wall of the artery and degenerative changes injuring the internal elastic lamina. They involve the anterior circulation (anterior and middle cerebral artery distributions) in more than 80% of cases and are multiple in 31%. Mortality from ruptured aneurysms is 23%, and significant disability is present in more than 50% of survivors.

If an aneurysm is surgically isolated from the circulation and no others exist, the patient is cured. Conventional transfemoral cerebral angiography performed 3 to 12 months following surgery demonstrates cure. At times aneurysmal anatomy (e.g., fusiform or broad-necked aneurysm) precludes clipping, and noncurative procedures such as wrapping or use of glue are employed. Risk of bleeding, though perhaps lessened, remains.

The aeromedical evaluator's primary concern is residual neurologic impairment, which might include focal neurologic deficit or cognitive impairment. Careful neurologic evaluation is warranted, and an observation period of 1 year is commonly prescribed.

At times angiography does not demonstrate a source of bleeding despite multiple procedures. If an individual with idiopathic subarachnoid hemorrhage has no recurrence within 1 year, risk of further bleeding is acceptably low.

## TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) is a frequent cause of neurologic disability in the 20 to 55 age-group and is commonly encountered in aviators. The aeromedical evaluator is not concerned with acute management, but rather the possibility of persistent residual neurologic impairment. Essential ingredients in the evaluation of aviators with TBI include determination of the nature and severity of TBI.

Medical records will disclose the nature of TBI. Concussion is characterized by transient loss or alteration of consciousness (seconds to hours) caused by a blow to the head without evident tissue destruction. However, there may be microscopic injury, and petechial hemorrhage, axonal shearing with retraction bulbs, and edema may occur. Frank injury to brain parenchyma may occur through brain contusion, diffuse edema, laceration or penetration by a foreign object, and hemorrhage within the brain substance (intracerebral hematoma). Additionally, extraparenchymal bleeding (subdural or epidural hematoma) may cause cerebral injury through compression and herniation mechanisms.

Severity of TBI can be assessed utilizing the Glasgow Coma Scale (Table 16-3) and duration of posttraumatic amnesia (PTA) (Table 16-4). A Glasgow Coma score of 13 to 15

**TABLE 16-3**

**Glasgow Coma Scale**

| *Eye Opening* | *E* | *Best Verbal Response* | *V* | *Best Motor Response* | *M* |
|---|---|---|---|---|---|
| Spontaneous | 4 | Oriented and converses | 5 | Obeys commands | 6 |
| To voice command | 3 | Confused | 4 | Localizes to pain | 5 |
| To pain stimuli | 2 | Inappropriate words | 3 | Withdraws from pain | 4 |
| No response | 1 | Incomprehensible sounds | 2 | Decorticate (flexion) posturing | 3 |
| | | No sounds | 1 | Decerebrate (extension) posturing | 2 |
| | | | | No response | 1 |

E + V + M = 3 to 15.

**TABLE 16-4**

**Posttraumatic Amnesia (PTA)**

| | |
|---|---|
| Mild brain injury | 0–1 hr of PTA |
| Moderate brain injury | 1–24 hr of PTA |
| Severe brain injury | 1–7 d of PTA |
| Very severe brain injury | Beyond 7 d of PTA |

denotes mild TBI, a score of 9 to 12 moderate TBI, and below 3 to 8 severe TBI by these criteria. When Glasgow Coma score and duration of PTA are coupled with records documenting the clinical course during the acute recovery period, the evaluator can accurately determine the severity of TBI. A Glasgow Coma score below 9 and/or PTA greater than 24 hours should heighten concern for persistent neurologic impairment.

Sequelae of TBI include postconcussion syndrome, focal neurologic deficit, neuropsychological residual, and posttraumatic epilepsy (PTE).

### Postconcussion Syndrome

Postconcussion syndrome is a nonspecific constellation of symptoms that commonly follow minor or seemingly inconsequential head injury, perhaps without loss of consciousness. Symptoms include headache, irritability, inability to concentrate, inattention, insomnia, memory difficulty, and nonspecific dizziness. Neurologic examination and imaging studies are normal. In most individuals, symptoms are self limited, lasting days to weeks or at most 3 to 6 months. This syndrome ordinarily does not pose long-term implications for the aviator.

### Focal Neurologic Deficit

Focal neurologic deficit following TBI can take many forms, including cranial nerve palsies (olfactory nerve, optic nerve, nerves to extraocular muscles, facial nerve, acousticovestibular nerve, other), expressive aphasia, hemiparesis or other focal motor deficit, and ataxia. Most neurologic recovery occurs within 6 months, with further recovery occurring more slowly over a span of 2 to 3 years.

### Neuropsychological Residual

Accelerative and rotational forces can injure brain tissue exposed to irregular bony surfaces within the cranial vault. The frontal poles and orbitofrontal surfaces of the frontal lobes may suffer contusion injury, and the anterior temporal lobes are similarly susceptible.

The frontal lobes have to do with personality, behavior, and executive functions, whereas the temporal lobes are more related to intellect and memory. Frontal lobe injury may lead to behavioral changes including disinhibition, irritability, and impaired anger control with explosive outbursts. Alternatively, an individual might exhibit apathy, indifference, and depression. Impaired judgment, planning, reasoning, abstraction, and initiation of activity may reflect impaired executive functions. Perseveration (inability to change mental set) and inability to employ a problem-solving strategy are common. Deep white matter injury may cause impaired attention and concentration. Temporal lobe injury may lead to significant memory impairment, which is often a major sequela of TBI.

The aeromedical evaluator should remain mindful of the possibility of neuropsychological impairment in persons with moderate to severe TBI. If indicated by clinical evaluation and review of records, formal neuropsychological testing might be needed.

### Posttraumatic Epilepsy

A major aeromedical concern following TBI is risk of seizures. Whereas penetrating injuries involving dural laceration and violation of brain parenchyma confer a 20% to 40% risk of PTE, risk in closed head injury is approximately 5%. A history of febrile seizures, family history of seizures in a first-degree relative, cerebral contusion, and hematoma (epidural, subdural, intraparenchymal) are associated with increased risk for PTE.

An impact seizure, occurring as the name implies at the time of contact, ordinarily does not portend chronic seizure potential. Delayed seizures beginning weeks or months after TBI imply gliotic scar with risk of persistent seizure potential.

Risk of PTE increases with head injury severity (35), particularly with severe TBI. In this study by Annegers, 1-year risk with severe TBI was 6%, compared to less than 1% with mild to moderate TBI. Cerebral cortical contusion, cerebral hematoma, early seizures, loss of consciousness or PTA beyond 1 day, and depressed skull fracture are associated with increased seizure risk. The presence of subdural hematoma confers increased risk, as well as epidural hematoma to a lesser extent.

Iron compounds are important in animal models of epileptogenesis. Current thought reflects the hypothesis that PTE is an ''iron-driven'' phenomenon. The theory holds that extravasated red blood cells into neural tissue eventually leads to iron liberation from hemoglobin and formation of highly reactive free radical oxidants in the metabolism of iron, resulting in lipid peroxidation with injury to the cell membrane and cell organelles.

Approximately one third of individuals with PTE will have a first event within 3 months, 50% within 6 months, 75% within 1 year, and 90% within 2 years.

## NEOPLASMS

Intracranial neoplasms will be encountered in aviators. Presenting symptoms of tumors may include headaches, vomiting, seizures, cognitive changes, and focal neurologic symptoms such as hemiparesis or ataxia.

### Benign Neoplasms

Benign intracranial neoplasms can involve the dura, cranial nerves, or brain parenchyma (36). Extraparenchymal tumors

include meningioma, acoustic neuroma, neurofibroma, and pituitary adenoma. Benign parenchymal tumors include ependymoma, colloid cyst of the third ventricle (in reality a cyst), and choroid plexus papilloma. Symptoms usually arise from compression of neural structures rather than invasion. Some benign lesions cannot be safely removed for fear of compromising major or vital structures, giving rise to the term *malignant by position*. These may include tumors involving the clivus, the cavernous sinus, and craniopharyngiomas adherent to the floor of the third ventricle. Residual tumor may lead to recurrence.

Benign dura-based tumors or cranial nerve tumors lend themselves to complete resection, particularly if removed when small. These include meningiomas overlying the cerebral cortex, acoustic neuroma, trigeminal neurofibroma, and pituitary adenoma. Colloid cysts, choroid plexus papillomas, and pinealomas can often be totally removed.

### Malignant Neoplasms

Malignant intracranial neoplasms usually arise in brain parenchyma, are invasive, and have potential for rapid growth when of high grade. The gliomas (astrocytomas and oligodendrogliomas) are the most common malignant primary parenchymal tumors. The term *glioblastoma multiforme* refers to high-grade astrocytomas. Invasive features include finger-like projections of malignant cells that interdigitate with normal neural tissue. The surgeon can ''debulk'' the tumor, but cannot employ the principle of wide excision without compromising neurologic function.

Recurrence is the rule with gliomas, albeit possibly many years later when the tumor is of low grade. Surgical removal without recurrence is uncommon. There are exceptions, such as cystic astrocytoma of the cerebellum with mural nodule in children.

For aeromedical disposition, the evaluator must consider the nature (benign or malignant) and location of the tumor, the presenting signs, the nature and degree of residual deficit (motor, sensory, cognitive), potential for recurrence, and the possibility of seizures. As with resection of vascular malformations, complete tumor resection does not assure freedom from seizures, which may continue to arise from the altered neuronal bed of the lesion. Often a period of observation is employed. Despite apparent neurologic stability over a long period, even years, with low-grade gliomas, malignant parenchymal tumors characteristically recur, ordinarily barring medical certification.

## HEREDITARY, DEGENERATIVE, AND DEMYELINATING DISORDERS

Included here for discussion are several conditions that may be nonprogressive, intermittently active and cumulatively progressive, or follow a slowly progressive temporal profile. With appropriate monitoring, medical certification may be appropriate unless and until the condition compromises aviation safety.

### Familial and Essential Tremor

Essential tremor is the most common movement disorder with a reported prevalence of up to 5.6%. Familial tremor and essential tremor are the same, the only difference being the presence or absence of a family history of tremor. Autosomal dominant inheritance is present in 60% of cases (37). Although tremor may appear early in life, the mean age of onset is 35 to 45 years. Hand tremor is present in 94%, head tremor in 33%, voice tremor in 16%, and leg tremor in 12%. Slow worsening of tremor over many years is a characteristic feature.

Tremor is usually postural (voluntarily maintaining posture against gravity, such as arms outstretched) and with intention or use (directed voluntary movement toward a target). The tremor frequency is 8 to 12 Hz. Victims often describe difficulty in writing, balancing peas on a fork or soup on a spoon, carrying an empty cup on a saucer, using a screwdriver, or bringing a glass to the mouth. Rest tremor rarely occurs. Improvement with alcohol ingestion is commonly reported.

Essential/familial tremor may have aeromedical implications (e.g., difficulty targeting and manipulating small closely spaced cockpit switches). One of my patients, an airline captain, noted a vigorous shudder in his aircraft as he applied toe brakes after landing. He shut down the aircraft and had it towed to the gate, assuming a mechanical problem. Nothing was found, but recurrence on two other occasions led to identification of a foot tremor. Low-dose $\beta$-blocker treatment allowed him to complete his career.

Fortunately tremor causes little or no impairment in most individuals, progressing very slowly and perhaps not requiring treatment. If treatment is warranted, $\beta$-blockers are often highly effective. Primidone, an older anticonvulsant, is useful in pediatric dose ranges. However, primidone is a barbiturate derivative that can cause drowsiness, barring its use in the aviation environment. Gabapentin and benzodiazepines are also precluded because of potential central nervous system effects.

### Parkinson's Disease

Parkinson's disease is characterized by a classic triad of symptoms including tremor at rest, muscular rigidity, and slowness of movement (bradykinesia). Common clinical features include a slow-shuffling gait, freezing or gait arrest, a general attitude of flexion, impaired postural reflexes, diminished vocal volume, and paucity of facial expression (mask-like facies). These features are observed by the examiner, and neurologic examination usually discloses cogwheel rigidity and impaired rapidly alternating movements (foot tapping, finger wiggle, pronation–supination).

An individual may seek medical attention early in the course of the illness for purposes of identifying the condition, but with no desire or need for treatment. Aeromedical certification may be allowed with appropriate monitoring mechanisms for progression. When treatment is indicated, potential side effects of medication warrant consideration.

Anticholinergics, with their attendant risk of drowsiness and cognitive changes, were the only agents available for treatment until the advent of levodopa in the late 1960s. Levodopa remains the gold standard treatment, and many individuals function well with this agent, remaining relatively free of side effects. In later years, dopamine agonists, primarily pramipexole and ropinirole, came into favor as initial treatment, adding levodopa later if necessary. These agents were initially approved for use by the Federal Aviation Administration (FAA), but due to reports of excessive daytime sleepiness approval was withdrawn. Amantadine has been employed for treatment of tremor, and entacapone delays the breakdown of dopamine in individuals taking levodopa.

Some individuals with Parkinsonian symptoms exhibit evidence of a more widespread cerebral disturbance, giving rise to the term *Parkinson-plus* syndromes. Additional features may include dementia, impaired eye movements, ataxia, orthostatic hypotension, and dysautonomic manifestations. Multiple system atrophy and progressive supranuclear palsy are examples. The neurologist or movement disorder subspecialist differentiates these entities based on clinical features.

Early or mild Parkinson's disease causing little or no impairment need not preclude medical certification. Some medications, such as levodopa or amantadine, might be acceptable without significant side effects.

### Multiple Sclerosis

MS is a chronic disease affecting young- and middle-aged adults with slight female preponderance. The illness is characterized by multiple lesions of the nervous system, separated by space and by time. Lesions in MS consist of plaques, localized areas of inflammation, demyelination, and glial scarring involving the white matter of brain and spinal cord. Episodes of demyelination and remyelination account for the exacerbations and remissions commonly seen in MS.

The clinical course of MS may vary among individuals. In primary progressive MS, the disease follows a slowly progressive clinical course without interruption. In the more commonly encountered relapsing and remitting variety of MS, the characteristic exacerbations and remissions occur. Each exacerbation may incompletely resolve, resulting in cumulative neurologic deficit. In secondary progressive MS, a relapsing and remitting clinical course gives way to a slowly progressive decline in neurologic function in later years.

Clinical manifestations of MS can be highly variable depending on plaque distribution in brain and spinal cord. Unilateral optic neuritis is a common presenting sign of MS. Other symptoms might include diplopia, dysarthria, ataxia, motor or sensory symptoms, and bladder or bowel dysfunction. Approximately 14% of individuals with MS have mild or inconsequential neurologic deficit, giving rise to the term *benign MS*.

Acute exacerbations are commonly treated with intravenous corticosteroids, specifically methylprednisolone. Immunomodulatory therapy is employed in an effort to reduce the frequency and severity of exacerbations and slow the accumulation of neurologic deficit. Therapy consists of parenteral administration of an interferon preparation or glatirimer acetate. In individuals with significant progression despite steroids and immunomodulatory therapy, chemotherapeutic agents may be employed and agents that are prescribed include cyclophosphamide, azothioprine, methotrexate, and novantrone.

Aeromedical disposition may be favorable in some individuals with MS. Persons with "benign MS" may present no risk to aviation safety. Some with slowly progressive MS, and others with widely separated and relatively minor exacerbations without accumulation of significant neurologic deficit might warrant consideration. Others with significant functional disability, symptoms clearly related to aviation safety (e.g., vertigo, diplopia, cognitive change, etc.), or frequent severe exacerbations will not be candidates for medical certification.

## CAVEATS IN NEUROLOGIC AEROMEDICAL DISPOSITION

In neurologic diagnosis, a frequently occurring and vexing problem is the proper interpretation of ancillary studies. This is of utmost importance in aeromedical disposition because an inadequate or inaccurate history coupled with a misinterpreted laboratory study can erroneously hamper or end an aviation or space career. Interpretations that commonly confound neurologic diagnosis include those of HUT, EEG, and MRI studies.

### Head-Up Tilt Studies

As mentioned in the section **Syncope** in this chapter, HUT studies may aid the evaluation of unexplained syncope. Kapoor reported approximately 50% of patients with unexplained syncope have a positive response to passive tilt testing (38). In that study, two thirds of positive responses occurred with pharmacologic activation (isoproterenol) as opposed to passive tilt. However, a significant proportion of asymptomatic individuals may have a positive response. Kapoor and Brant reported a false-positive rate of 20% without pharmacologic evaluation and 31% with isoproterenol activation (39). Reproducibility is another issue. In a study involving 109 subjects undergoing HUT on 2 consecutive days, Brooks et al. reported a high degree of variability in responses to HUT, with frequent nonreproducibility of vasodepressor responses on the second day (40). Reproducible vasodepressor responses occurred in only 11 of 36 subjects (31%).

The aeromedical evaluator must be cautious in coupling a false-positive tilt table response with a nonsyncopal neurologic event, such as seizure. Such errors have occurred.

### Electroencephalogram

In the general population, there is a 10% to 15% incidence of minor nonspecific EEG abnormalities, and 2% to

3% of the population demonstrates moderate abnormalities (41). These changes may also occur in the presence of disease, and careful clinical judgment is necessary in determining their significance, if any. The aerospace medicine physician must be particularly cautious when attempting to couple reported EEG abnormalities with clinical events.

For example, a nonspecific EEG abnormality appearing in an individual with syncope accompanied by twitching and incontinence may lead to an erroneous diagnosis of epilepsy with its far reaching implications.

The aeromedical evaluator must keep in mind that individuals without seizures may demonstrate epileptiform abnormalities on EEG, whereas individuals with epilepsy (fits) may have persistently normal EEGs (spikes without fits and fits without spikes). Engel notes that 2% of the population demonstrates specific epileptiform abnormalities on EEG (42). This may lead to an inappropriate diagnosis of epilepsy.

It is well known that a significant proportion of individuals with epilepsy have a normal EEG (42–44). Studies in the literature report that 50% to 60% of routine EEGs (30-minute routine recordings without sleep deprivation), obtained after a seizure in patients later clearly diagnosed as having epilepsy, demonstrate epileptiform abnormalities (45). Activation techniques including hyperventilation, photic stimulation, sleep recording, and sleep-deprived recording may increase the yield. Interictal EEG abnormalities may be intermittent, and a 30-minute recording is a small sample of a 24-hour day. Serial EEG recordings may also increase yield, but little further yield is obtained after four recordings (46). It is important for the EEG interpreter to state that a normal EEG does not exclude the possibility of epilepsy, as well as mentioning sampling effect (47). In difficult cases, sustained video-EEG recording (days or more) can be accomplished in an epilepsy monitoring unit.

Lastly, there are known benign EEG patterns with epileptiform morphology that might be interpreted by less-experienced clinicians as being significant. Examples include 14 and 6 Hz positive spikes, small sharp spikes, 6 Hz spike and wave, and wicket spikes (47). These patterns can be seen in normal individuals.

## Magnetic Resonance Imaging

A frequently occurring finding in cerebral MRI is the presence of T2 hyper intense lesions, commonly referred to as *unidentified bright objects* (UBOs), or *nonspecific white matter hyperintensities* (WMHs). The reporting of these lesions may lead to diagnostic uncertainty for the aeromedical examiner (AME)/flight surgeon and have far reaching implications for the aviator or astronaut if interpreted wrongly. A fully trained and experienced neuroradiologist might report ''normal'' findings, whereas other interpreters might report concern for small vessel cerebrovascular disease (multi-infarct state) or demyelinating disease (MS).

In one study, UBOs were present in 5.3% of healthy individuals aged 16 to 65, but were less common in younger individuals (48). In another study, pathologic features of T2 silent WMHs in patients without neurologic signs or symptoms represented myelin pallor associated with vessels showing hypertensive and arteriosclerotic changes (49). Others feel the lesions represent dilated normally occurring perivascular (Virchow-Robin) spaces. UBOs occur with greater frequency in individuals with migraine (50).

The neurologic literature reflects considerable debate regarding the nature and significance of UBOs. The debate is also reflected in practice, as evidenced by variable interpretations among general radiologists, neuroradiologists, neurologists, and neurosurgeons. The aeromedical evaluator with less frequent exposure to MRI is further disadvantaged. One can only advise that the ability to distinguish between nonspecific WMHs (UBOs, WMHs) and disease-specific white matter lesions is an important consideration for the clinician. As in other ancillary studies, the test must be interpreted in the context of the patient and the clinical setting.

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