CHAPTER 13

Clinical Aerospace Cardiovascular Medicine

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I was gratified to be able to answer promptly. I said, ''I don't know''.

—*Mark Twain*

Cardiovascular diseases (CVDs) will always be a major concern for aeromedical disposition and aircrew standards because they are a major health problem worldwide and a leading cause of mortality and morbidity in industrialized nations. Cardiac diagnoses are frequent causes of loss or restriction of licensure for all categories of civilian and military flying. Most requests for special issuance to fly with a cardiac disorder are for cases of coronary artery disease (CAD), including coronary revascularization (e.g., bypass surgery, stent). Cardiac dysrhythmias and valvular disorders are also common causes for medical review of flying eligibility.

Rapid advancements in cardiology present both challenges and benefits to aeromedical applications. This chapter can neither cover all cardiac diagnoses nor cover any in great detail. Topics of key aeromedical relevance will be discussed, including disposition of various electrocardiographic findings, CAD and CAD intervention, valvular disorders, and tachyarrhythmias. These discussions should also serve as an example of an aeromedical approach to other cardiac diagnoses.

A seven-step process for aeromedical decision making of cardiac diagnoses has been previously proposed and is briefly summarized and discussed as follows (1):

1. Establish a threshold of acceptable risk for aeromedically pertinent cardiac events. Annual event rates greater than threshold would be unacceptable for continued flying.
2. Select appropriate aeromedical events for the cardiac diagnosis under consideration.
3. Determine annual event rates for these selected events.
4. Address any special considerations, such as high $+G_z$ or single-pilot operations.
5. If continued flying is a consideration, a recertification policy must be formulated.
6. Other aeromedical endpoints not considered in the second step should be assessed.
7. And finally, consider the impact of medical therapy for the diagnosis being addressed.

In this process, aeromedical decisions are based on percent per year event rates at 1 to 3 years to address short-term safety and possibly at 5 to 10 years to address the longer-term likelihood of a continued aviation career. Data from aircrew populations and carefully selected populations from the clinical literature would be used. Within the selected threshold (e.g., 1% per year), sudden and complete incapacitation (sudden cardiac death, syncope) is of key importance but all events that may negatively affect proper performance of flying duties should be considered.

The earlier process and the following discussions of select cardiac disorders address applications to aviation, especially military and commercial aviation. This process applies readily to other special environments such as space flight while taking into consideration potentially different risk thresholds due to length of the space mission, isolation, and so on.

Aeromedical decision making may involve aircrew with symptomatic, clinical heart disease. For this, helpful clinical literature is usually available. However, aeromedical decision making must often consider aircrew with asymptomatic, subclinical disease for which helpful literature may be lacking or incomplete. And at times, a disease is not under consideration, but rather an abnormal test suggesting presence of disease [e.g., electrocardiogram (ECG) or graded exercise test]. The aeromedical issue then becomes estimating the risk of underlying heart disease and deciding to what extent this risk should prudently be pursued with further testing. These challenges are the bedrock of aerospace cardiology.

DISPOSITION OF ELECTROCARDIOGRAPHIC FINDINGS

A resting 12-lead ECG is required for routine surveillance of many aircrew positions but is somewhat of an enigma. Some ECG findings [e.g., left axis deviation (LAD), ST-T wave changes, and ventricular ectopy] are correlated with advancing age and an increased incidence of CAD and hypertension, and may have some predictive value. Yet, these same findings are often nonspecific, not reflective of underlying pathology, and often not evaluated in a clinical scenario. The aeromedical dilemma is to balance the pursuit of underlying disease against the unnecessary performance of tests, which themselves may prompt further testing.

When a minor ECG abnormality presents, comparison to prior tracings is often very helpful to determine aeromedical disposition. An ECG finding that has been present and stable for several years may not require evaluation, whereas an abrupt, new finding compared to prior ECG tracings may warrant thorough investigation. The diagnostic criteria for each of these findings are not discussed; rather the reader is referred to standard ECG textbooks.

Many ECG findings occur with such frequency and benignity that they may be considered normal variants, which do not require further evaluation. A list of suggested normal variants is in Table 13-1. This is not intended to be an all-inclusive list. Moreover certainly for individual cases, the aeromedical practitioner may choose to further evaluate any of these findings.

Conduction Disturbances

Right Bundle Branch Block

Incomplete right bundle branch block (RBBB) is a common ECG finding and is considered a normal variant (Table 13-1). Complete RBBB, reported in 0.2% to 0.4% of military aviators, has not been associated with increased risk of progressive conduction system disease or other cardiac problems in aviator populations (1,2). Echocardiography may be aeromedically prudent to exclude structural heart disease. If normal, unrestricted civilian and military flying duties may be allowed, including entry into military flying training. Periodic reassessment does not appear to be indicated.

TABLE 13-1

Normal Variant Electrocardiographic Findings

Sinus Bradycardia	Right Axis Deviation
Sinus tachycardia	Indeterminate axis
Sinus arrhythmia	Early repolarization ST segment elevation
Sinus pause of 3 s or less	Nonspecific interventricular conduction delay with QRS width <0.12 s
Ectopic atrial rhythm	Terminal conduction delay (wide S wave)
Wandering atrial pacemaker	Incomplete right bundle branch block
Junctional rhythm	RSR′ pattern in leads V1 and/or V2
Idioventricular rhythm	R wave taller than S wave in V1
First-degree atrioventricular (AV) block	Supraventricular or ventricular escape beats
Mobitz I (Wenckebach) AV block	Rare supraventricular or ventricular ectopy

Left Bundle Branch Block

Reported in 0.01% to 0.1% of military aviators, the prevalence of left bundle branch block (LBBB) increases with age as does the prevalence of CAD and hypertension. Rare in aviators aged 35 years or younger, LBBB became more common with advancing age older than 35 years (1,2). Aeromedical concerns are the association of LBBB with CAD and dilated cardiomyopathy. In the absence of underlying heart disease, LBBB does not present a significant risk for cardiac events, especially in the relatively young, healthy aviator population. Evaluation of underlying disease is required, but accuracy of exercise testing and nuclear myocardial perfusion imaging is limited by the LBBB itself. ECG ST-segment response during graded exercise testing is not interpretable in the presence of LBBB, and myocardial perfusion imaging is often abnormal in the anteroseptal region. Conventional coronary angiography remains the gold standard for definitely excluding underlying CAD, but is associated with inherent risks. Depending on the aircrew position, computed tomographic (CT) angiography might be considered to exclude most significant coronary lesions. However, approximately 25% of lesions may be incorrectly assessed by this method. Detection of coronary calcification should be as useful for screening as in other populations, although data are not available regarding its efficacy in LBBB. Detection of coronary calcification is discussed later in this chapter.

Experience with United States Air Force (USAF) aviators has revealed underlying CAD in approximately 10%, twice the estimated background incidence. Licensing authorities must consider whether initial assessment of LBBB should include invasive or noninvasive coronary angiography. For many years, the USAF has returned aviators with LBBB to unrestricted flying, if coronary angiography and noninvasive testing are normal. Periodic noninvasive reassessment is appropriate, especially if coronary angiography is not performed during initial evaluation. LBBB can be an early manifestation of dilated cardiomyopathy reinforcing the importance of regular follow-up.

Nonspecific Intraventricular Conduction Delay

Nonspecific intraventricular conduction delay (IVCD) is considered a normal variant in otherwise healthy subjects if the QRS interval is less than 120 ms. If the QRS interval is 120 ms or greater, the IVCD is considered abnormal but the risk of underlying disease and prognosis are unclear. Reported prevalence in military aviators is similar to RBBB. If underlying cardiac disease is present, cardiomegaly is often a feature. Evaluation with echocardiography and, at least in older aviators, graded exercise testing with nuclear or

echocardiographic stress imaging, should suffice to exclude underlying disease. In the absence of underlying cardiac disease, return to unrestricted flying duties appears indicated. Periodic reassessment may be appropriate.

Left Anterior and Posterior Hemiblock and Bifascicular Block

Prevalence of left anterior hemiblock (LAHB) and left posterior hemiblock (LPHB) has been reported to be 0.9% and 0.1%, respectively, in military aviators (1,2). ECG textbooks often indicate a significant likelihood of underlying cardiac disease, especially for LPHB. This has not been the case in the military aviator population; underlying cardiac disease is uncommon. Prognosis appears to be normal if no underlying cardiac disease is detected by noninvasive evaluation. Return to unrestricted flying duties may then be recommended without future reassessment.

These ECG findings do warrant investigation, especially if new compared to prior ECGs. Extent of evaluation may depend on the age of the individual and overall CAD risk profile. For the young, low-risk aviator (age 35 or younger), echocardiography may be sufficient. For the older or higher-risk aviator, echocardiography and graded exercise testing are recommended. In the absence of abnormal test results, periodic reassessment does not appear to be necessary.

The prevalence of bifascicular block (combination of RBBB and LAHB or LPHB) is not described for aircrew or other healthy populations. Studies of aviators with RBBB, however, have not shown any increased incidence of underlying disease for bifascicular block compared to RBBB with normal axis. Evaluation and disposition of bifascicular block should therefore be comparable to those of RBBB or of hemiblock alone.

Right and Left Axis Deviation

Axis deviations are not conduction disturbances but are discussed here because there is probably considerable overlap between them and the corresponding hemiblocks. Disposition of axis deviation is a common question for the aeromedical practitioner. Concern is whether axis deviation is a marker for underlying disease. Comparison with prior ECGs is helpful. Abrupt axis shifts might be more significant, whereas a gradual leftward axis shift often occurs with advancing age.

Right axis deviation (RAD) and left axis deviation (LAD) were reported in 0.07% and 0.9% of military aviators (1,2). Available reports in aviators do not indicate a concern for increased likelihood of cardiac disease or events. Echocardiography to exclude structural disease is reasonable. Graded exercise testing is a consideration for the older aviator with new-onset LAD. In the absence of underlying disease, unrestricted flying without future reassessment is recommended.

First-degree Atrioventricular Block

As an isolated finding, PR interval prolongation beyond 200 ms is benign in the relatively active, healthy aviator population. It has been reported in approximately 1% of healthy aviators and is felt to be due to increased resting vagal tone. Evaluation is unnecessary for mild PR prolongation. If the PR interval is markedly prolonged, but shortens to normal or near-normal duration during exercise and the ECG is otherwise normal, unrestricted flying duties are appropriate and future reevaluation is not indicated.

Second- and Third-degree Atrioventricular Block

Healthy, young subjects often demonstrate Mobitz I (Wenckebach) atrioventricular (AV) block on 24-hour ambulatory ECG, typically during sleep. Mobitz I AV block is a rare finding on routine 12-lead ECG, reported in only 0.004% of aviator ECGs (1), and is typically considered a normal variant due to enhanced vagal tone. Mobitz II AV block, reported in 0.003% of military aviator ECGs (1), is a risk for progression to advanced and third-degree AV block with possible hemodynamic symptoms and need for permanent pacing. Many specialists would consider even asymptomatic Mobitz II AV block an indication for permanent pacing. This finding should prompt removal from all flying duties.

Third-degree AV block was reported in 0.004% of military aviator ECGs (1), including both acquired and congenital forms. Acquired third-degree AV block should be disqualified from all flying duties due to the risk of bradycardia-related hemodynamic symptoms. Most specialists would consider symptomatic or asymptomatic acquired third-degree AV block an indication for permanent pacing. Congenital third-degree AV block is a more contentious issue. There is very little experience reported for this finding in military and commercial pilots, probably because it is considered disqualifying for initial flying training and licensure. Although these individuals usually do well clinically, an increased risk of sudden death has been reported. Certification for flying duties is not recommended.

Chamber Dilation and Hypertrophy

Atrial Abnormality

Right and left atrial abnormalities were reported in only 0.004% of military aviators (1,2). These ECG findings are nonspecific in the absence of symptoms or signs of underlying disease that is expected to cause atrial enlargement or hypertrophy. In the absence of such clinical evidence of disease or of other ECG changes, evaluation is unlikely to reveal pathology. Echocardiography will suffice for assessment and disposition should be determined by any underlying disease. More likely, echocardiography will be normal or may demonstrate only mild dilation of one or both atria without other abnormalities. This should be considered a normal variant, not requiring further assessment or any flying restriction.

Ventricular Hypertrophy

Right ventricular hypertrophy is an unusual ECG finding in an aviator population and is reflective of underlying disease. Echocardiography should be performed and further assessment and disposition guided by the findings.

Left ventricular hypertrophy (LVH) has repeatedly been shown to predict increased cardiac risk. This is especially true

if secondary ST-T wave changes are also present. Therefore, LVH voltage with associated ST-T wave changes should definitely be evaluated and appropriate medical and aeromedical disposition determined by the findings. Hypertension, aortic valve disease, and hypertrophic cardiomyopathy (HCM) would be considerations.

In the aviator population, LVH will more often be present as increased QRS voltage alone, without other ECG signs. Echocardiography will demonstrate whether LVH is truly present. If not present, no further assessment or future reassessment would seem warranted. If LVH is present, physiologic changes due to physical conditioning must be differentiated from a disease process. This is further discussed at the end of this ECG disposition section under **Athletic Heart versus Cardiac Pathology**.

Ectopy—Premature Supraventricular and Ventricular Contractions

Premature supraventricular contractions (PSVCs) include atrial and junctional premature beats. The prevalence of PSVC on ECG in military aviators is less than 1% (1). PSVCs are generally felt to be benign, even when frequent or paired (couplets) and not indicative of underlying disease. In USAF aviators, asymptomatic frequent and paired PSVCs have not been predictive of arrhythmic events or sustained supraventricular tachyarrhythmias (1). When very frequent and paired, PSVCs may be associated with mild symptoms. The aeromedical disposition would then be guided by the symptomatology.

Prevalence of premature ventricular contractions (PVCs) on ECG is also less than 1% in military aviators (1). Frequency and complexity of PVCs increase with advancing age, as does the prevalence of CAD and hypertension. Also, PVCs associated with some cardiac disorders are predictive of an increased risk of adverse cardiac events. Investigation for PVCs may therefore be more appropriate than for PSVCs. However, in USAF aviators, frequent and paired PVCs have not been predictive of sustained ventricular tachycardia (VT) or arrhythmic events, in the absence of underlying cardiac disease (3).

A single PSVC or PVC on an ECG may not warrant evaluation. It may be prudent to evaluate a single PVC in the older aviator and two or more ectopic beats regardless of age. Twenty-four hour ambulatory ECG will quantitate the frequency of isolated ectopy and will document any pairing or tachycardias. The frequency and complexity of ectopy should then guide further assessment (e.g., graded exercise test, echocardiography) as well as aeromedical disposition.

The USAF currently grades ectopy as a percentage of total beats on the 24-hour ambulatory recording. Rare and occasional ectopy (1% or less of total beats) is not further evaluated. Frequent ectopy (>1% up to 10% of total beats) is evaluated with echocardiography and graded exercise testing; one to ten pairs (couplets) per ambulatory recording is similarly evaluated. Very frequent ectopy (>10% of total beats) and frequent pairs (>10 pairs per ambulatory recording) are evaluated more thoroughly for underlying heart disease at a central facility. However, the significance of frequent ectopy and pairing is yet to be well defined.

Prolonged QT Interval

Prolonged QT interval may be due to primary congenital syndromes or acquired secondary to a wide variety of causes. Secondary causes must be excluded by careful history. The most common secondary cause is medication. Additional secondary causes include certain electrolyte imbalances (e.g., hypocalcemia), endocrine abnormalities, neurologic events, and nutritional deficiencies (e.g., associated with chronic alcohol abuse). Congenital long QT syndrome (LQTS) involves many genetically distinct mutations of cardiac ion channels that affect the action potential, causing susceptibility to VT. Currently, several genotypes are described. Inheritance is usually autosomal dominant, but with variable expression. Routine genetic testing for diagnosis is not yet available.

LQTS is essentially an ECG diagnosis. Other factors, primarily symptoms in the patient or relatives, are also helpful for diagnosis. QT interval varies with age, gender, and heart rate and is typically expressed as QTc (QT corrected for heart rate). Normal QTc is usually reported as 440 or less overall. For adult females, QTc greater than 460 is abnormal and QTc greater than 480 is essentially diagnostic. And for adult males, QTc greater than 450 is abnormal and QTc greater than 470 is essentially diagnostic. T-wave changes may also be present and characteristic for specific genotypes of LQTS. A patient may have only a borderline prolonged QTc or even, at times, a normal QTc and still have the LQTS syndrome.

Ambulatory ECG monitoring may demonstrate prolonged QTc and transient T-wave changes at different heart rates. The lethal arrhythmia is polymorphic VT (*torsade de pointes*), but short runs of VT are rarely documented on ambulatory monitoring. Exercise or startle often elicits the arrhythmia, yet it is rarely precipitated by exercise testing. Treadmill testing may help with the diagnosis—QT interval normally shortens during exercise and does not prolong during recovery. With at least some LQTS genotypes, QT interval may prolong significantly during the recovery phase. Electrophysiologic testing, signal-averaged ECG, and other sophisticated tests have not been helpful for diagnosing LQTS or predicting events.

A low-risk subset of LQTS includes subjects with LQTS by ECG and other studies, but no personal or family history of documented or suspected arrhythmic events. Annual event rate for sudden cardiac death or syncope is approximately 0.5% per year. Higher-risk subjects with a positive personal or family history of events have an approximately 5% per year risk of sudden death or syncope and 10% to 20% of first events are sudden death. Presumably, there is also a risk of presyncope and lightheadedness, although rates for these events are not well documented.

Symptoms are often provoked by exertion or startle situations. Other than recommending against competitive athletics, unrestricted activity is generally recommended for asymptomatic subjects, especially if on prophylactic

β-blocker therapy. Even symptomatic subjects, whose symptoms are controlled by β-blockers and who have a benign ambulatory ECG recording and treadmill, are generally not activity restricted except from competitive athletics. Aeromedical disposition of LQTS must consider the above risk of arrhythmic events and activity restrictions, particularly with the military aviator, for whom periodic physical fitness testing and other physical activity are often mandatory. These risks probably warrant disqualification from entry into initial flying training. If discovered in an older aviator, who has had no prior events and a negative family history, return to some restricted, low-performance flying duties may be a consideration. For pilots, this should include restriction to multipilot aircraft.

Possible Myocardial Ischemia and Infarction

ECG changes diagnostic for myocardial infarction (MI) should prompt removal from flying duties pending further diagnostic and prognostic evaluation, with disposition determined by the findings. A more common situation will be nondiagnostic changes suggesting a possible MI, such as small Q waves in the inferior limb leads or poor R-wave progression in the anterior precordial leads. Comparison with prior ECGs and repeat ECG with careful lead placement may be valuable. If further assessment is warranted, graded exercise testing alone is not adequate because it may be normal if there is no post-MI residual ischemia. More appropriate would be assessment for regional wall motion abnormalities by echocardiography or a perfusion defect by nuclear imaging. A more thorough evaluation would assess for both MI and residual ischemia either by exercise nuclear imaging or stress echocardiography.

Nonspecific ST-T wave changes can be a dilemma. They do have some predictive value for underlying disease, especially if new compared to prior tracings. However, they are also very nonspecific and the likelihood of significant disease in an otherwise healthy, active and asymptomatic aviator is low. Nonfasting condition can cause transient ST-T wave changes. If the changes persist on a repeat, fasting ECG and are new compared to prior tracings, then screening for CAD may be warranted for the older male aviator (e.g., age 35–45 years) and the postmenopausal female aviator. Younger males with high-risk profiles may also be considered for screening. Graded exercise testing is recommended.

Wolff-Parkinson-White Electrocardiographic Pattern

Wolff-Parkinson-White (WPW) ECG pattern is the classic ECG finding of short PR interval and delta wave without documented or suspected tachyarrhythmias. WPW syndrome is the ECG pattern plus tachyarrhythmia, especially supraventricular tachycardia (SVT). WPW ECG pattern is reported in approximately 1.5/1,000 in both the general population and military aviator populations. Risk of sudden death is 0.1% to 0.15% per year for all WPW subjects; low-risk subsets may be identifiable by electrophysiologic testing. The mechanism of sudden death is considered to be rapid SVT, which deteriorates into atrial fibrillation. If atrial fibrillation is conducted rapidly through the accessory pathway to the ventricle, ventricular fibrillation may ensue. The reported risk of SVT varies widely, but recent data from outpatient community populations and a military aviator population suggest a risk of 1% to 3% per year for at least 10 years after the initial diagnosis of the WPW ECG pattern.

Aeromedical disposition of WPW ECG pattern must consider the low risk of sudden death and the risk for SVT, especially for entry into initial flying training and for military aviation. Radiofrequency ablation will play an important role in some situations and is discussed with tachyarrhythmias in a later section.

Athletic Heart versus Cardiac Pathology

This topic is not exclusively ECG related, but often involves echocardiographic findings of mild dilation of one or more cardiac chambers or mild LVH. However, consideration is often precipitated by increased QRS voltage or other nonspecific ECG findings prompting the echocardiogram. In the absence of underlying pathology and any systolic or diastolic dysfunction, mild dilation or enlargement of one or more of the cardiac chambers is considered a normal physiologic variant, especially in a physically active, asymptomatic individual. No further assessment is recommended.

A common dilemma is mild, concentric LVH on echocardiogram, with or without accompanying LVH voltage on ECG, which may be physiologic hypertrophy or cardiac pathology. Two causes of LVH should be easily excluded or diagnosed. The echocardiogram itself should determine the presence or absence of aortic stenosis. Blood pressure checks should be performed for possible hypertension. If these two causes are excluded, the issue becomes physiologic variant due to physical conditioning versus HCM, an important distinction both medically and aeromedically. Most sources quote 11 mm as the upper limit of normal for left ventricular wall thickness. Left ventricular wall thickness is increased in competitive athletes compared to sedentary controls. Although this increase is usually within the normal range of wall thickness, it is often 12 to 13 mm but rarely exceeds 14 mm. Data from screening echocardiograms performed in military pilot applicants report wall thicknesses up to 12 mm in females and 13 mm in males (1).

In a physically active aviator without hypertension or aortic stenosis, mild, concentric left ventricular wall thickening of 12 to 13 mm may be considered a normal variant. Wall thickness of 14 mm or greater should be further evaluated. Serial echocardiography during abstinence from all exercise should differentiate physiology from disease. Physiologic hypertrophy will regress to normal wall thickness while HCM should not. The aviator must discontinue all aerobic and anaerobic exercise; merely reducing exercise will not cause regression of LVH. Regression is unlikely sooner than 4 weeks after exercise cessation. Continued flying, including high-G flying with straining maneuver, could be continued during this period of exercise cessation.

More than one monthly follow-up echocardiogram may be required. Once regression has been confirmed, the aviator may return to full exercise without requirement for future reassessment.

CORONARY ARTERY DISEASE

According to recent statistics published by the American Heart Association, CVDs, including stroke, CAD, and hypertension, continue to be the leading cause of death in the United States, accounting for more than 40% of all deaths (4). Atherosclerotic CAD is the leading cause of death in the industrialized world. Its importance as a concern for public health as well as aviation safety cannot be overstated. The World Health Organization projects that CVD will be the world's leading cause of morbidity and mortality by 2025.

CAD can present along a continuum from stable angina to unstable angina, MI, and sudden cardiac death. The first presentation of disease can often be sudden cardiac death or MI. Stable angina may be the presenting symptom in only 25% of men, with unstable angina, MI, and sudden death comprising most of the presentations. Any of these symptoms could lead to a decrement in performance or to a catastrophic, sudden incapacitating event. In fact, one half of those who die from an MI do so within 1 hour of symptom onset (5). Sudden cardiac death has been recognized in case reports and anecdotal experience as the cause of loss of life and aircraft in both military and commercial aviation.

Our understanding of the causes and treatment of heart disease has improved dramatically, with death rates from CVD dropping 20% over the last decade. Yet, it remains the major cause of death in industrialized countries. Atherosclerotic burden has been shown to occur at an early age, and clinical events are the late phase of the disease process. Opportunities aimed at prevention should therefore start early in the preclinical state of disease and the identification of those at highest risk must be sought. Cardiology knowledge continues to rapidly evolve with better understanding about the pathobiology of atherosclerosis, identification of novel risk factors, and technologic advances. The milieu in which we operate and the data that emerge lead to great debate on how to effectively screen for CAD, when to perform screening, how to treat, and the prognosis if disease is found. The role that new treatments and detection methods will play on future aeromedical decision making is unknown.

Coronary angiography has been the gold standard for defining the presence and extent of CAD and is properly thought of as a lumenogram. Lesion severity is then defined as percent narrowing of the lumen diameter. Clinically, minimal CAD is usually graded as maximum stenosis less than 50% and significant CAD as maximum stenosis 50% or greater; these definitions will be used in this discussion. However, it must be noted that some literature define significant CAD as maximum stenosis 70% or even 75% or greater. Angiography helps define plaque burden but tells little about composition of plaque. Interestingly, the lumen may appear normal or have only "luminal irregularities" by angiography, yet have significant atheroma within the arterial wall, as detected by intravascular ultrasonography. This has led to the understanding that early in the disease process, the adventitia expands and maintains a constant lumen despite minimal or even moderate plaque within the arterial wall.

Prevalence

In the United States, it is estimated that more than 10 million people currently have symptomatic CAD with an even greater number having asymptomatic disease. Estimated age-adjusted prevalence of CAD in adults aged 20 years or older is approximately 5.5% to 9.0%, depending on gender and race/ethnicity (4). Autopsy studies of young soldiers killed in war have shown evidence of atherosclerosis, with up to 10% having significant lesions. In 1981, a study from the United Kingdom reported similar prevalence of disease between military and commercial pilots who were killed in aircraft accidents. The prevalence of significant CAD in this study was 19% with a mean age of 32 years (1). A review of autopsy studies of commercial pilots showed an age dependency of severe disease prevalence, with 0.6% in pilots younger than 40 years and 7.4% in pilots aged 50 years or older (1). Data from the Royal Air Force reported the prevalence of significant disease by autopsy in private, commercial, and military aircrew as 7% below age 30, rising to 18% at age 30 to 49, and 43% at older than 50 years. Atherosclerosis detected by intravascular ultrasonography performed on donor hearts at the time of cardiac transplantation showed an even higher prevalence, being present in one of six teenagers, one of three aged 20 to 29, and one of two or 50% between the ages of 30 and 39 (6). Aeromedically, CAD is a leading cause of disqualification or denial of licensure in both civilian and military pilots. Aviators as a whole probably have less CAD than the general population but still have a prevalence of disease that warrants concern for detection and treatment.

Pathobiology

Acute coronary events are predominantly caused by plaque rupture or erosion, which is more common in intermediate than in high-grade stenoses. In several studies, one half or more of the sites where MI subsequently occurred had stenoses less than 50%. Although events can occur due to plaque rupture at sites of nonsignificant disease, so-called *vulnerable plaques*, stenoses less than 50% tend to be markers for more extensive disease and therefore poorer prognosis.

The atherosclerotic process is complex and not completely understood. Two initial processes that play important roles in the initiation of atherosclerosis include lipid accumulation and oxidation, along with endothelial dysfunction, caused by coronary risk factors. The initial lesion is a fatty streak, which mainly comprises lipid-laden macrophages. "Vulnerable plaques" are characteristically composed of lipid-rich macrophages with a thin fibrous cap and have less smooth muscle than more mature plaques.

A hallmark of plaque vulnerability is inflammatory cell infiltrates. No modality currently available accurately identifies the vulnerable plaque but this is an area of intense research. Two studies, the Pathobiological Determinants of Atherosclerosis of Youth (PDAY) and the Bogalusa Heart Study, have helped confirm that the process starts in childhood and that CAD prevalence and extent increase with age. In PDAY, all of the aortas and about half of the right coronary arteries in the youngest age-group (15–19 years) had atherosclerotic lesions (7).

Risk Factors

A constellation of risk factors for coronary disease, now termed *traditional or classic risk factors*, were clearly delineated in the Framingham Heart Study and include age, gender, family history of premature CAD, hypertension, smoking, hypercholesterolemia, diabetes mellitus, and LVH. The INTERHEART study identified nine risk factors that accounted for 90% of the risk for MI worldwide, which included smoking, raised ApoB/ApoA1 ratio, hypertension, abdominal obesity, psychosocial factors, lack of daily consumption of fruits and vegetables, daily alcohol consumption, and lack of physical activity (8). Risk factors are often synergistic, such as occurs in the metabolic syndrome.

Other "emerging" risk factors associated with increased risk include homocysteine, lipid fractions such as lipoprotein (a) and apolipoproteins A and B, inflammatory markers such as C-reactive protein (CRP), interleukin 6, and urine microalbumin. The precise role these emerging risk factors will have in screening and risk stratification is yet to be determined, but they may help to determine who should receive more aggressive risk-factor modification.

Although a detailed discussion of all risk factors is beyond the scope of this text, information about some specific risk factors is provided in the subsequent text.

Cigarette Smoking

The evidence linking cigarette smoking to CVD is based on observational studies. Cigarette smoking has been linked to 400,000 premature deaths in the United States annually. A 1989 report from the United States' Surgeon General presented data showing that smoking essentially doubled the incidence of CVD and increased CVD mortality by 50%. Nonsmokers exposed to second-hand smoke are also at a small, dose-related increased risk for coronary disease. Smoking accelerates the atherogenic process in both dose- and duration-dependent manners. Three smoking cessation trials in primary prevention populations demonstrated a 7% to 47% reduction in the rate of CAD events for those who stopped smoking. Smoking status should be a part of routine aviator evaluation. Appropriate counseling and smoking cessation programs should be made available.

Lipid Disorders

Lipoprotein content plays an important role in plaque development and disruption. Both genetic and environmental factors cause dyslipidemias. It is estimated that up to 90% of CAD patients have elevated low-density lipoprotein (LDL) cholesterol, with the majority having only modest elevation. High-density lipoprotein (HDL) cholesterol has an inverse relationship to CAD. In the Framingham Study, low-HDL cholesterol was a much stronger predictor of coronary risk than was increased LDL in subjects older than 50. The total cholesterol-to-HDL cholesterol ratio is the best discriminator between CAD cases and controls. In 1981, a retrospective analysis of USAF aviators examined total cholesterol-to-HDL cholesterol ratio in those who underwent coronary angiography for an abnormal treadmill test. A ratio greater than 6.0 was present in 88% of those with CAD compared to only 4% of those without CAD.

Lipoprotein subfractions may provide additional information about risk. Apolipoprotein B (ApoB) reflects total number of atherogenic lipoprotein particles (very LDL, intermediate-density LDL, LDL, and Lipoprotein[a]) and in some prospective studies it was found to be a better predictor of vascular events than LDL cholesterol. Increased ApoB and high triglyceride levels are more prevalent in patients with the metabolic syndrome and type 2 diabetes.

Lipoprotein (a) is an LDL particle in which ApoB is attached to the Apo(a) protein. Plasma levels of Lp(a) are determined by a single gene and hereditability is high. Lp(a) has been identified as a potent predictor of premature atherosclerosis in most prospective studies (9).

Metabolic Syndrome

The metabolic syndrome comprises a constellation of risk factors including abdominal obesity, dysglycemia, hypertension, and dyslipidemia (with low HDL cholesterol and elevated triglycerides). Diagnostic criteria have been developed by the National Cholesterol Education Panel Adult Treatment Panel III, the World Health Organization, and the International Diabetes Foundation. Of note, the different diagnostic criteria for abdominal obesity differ depending on racial background. The metabolic syndrome increases the risk for cardiovascular events significantly beyond that accounted for by the presence of the traditional risk factors (10) conferring an approximate twofold risk depending on the diagnostic criteria. The underlying mechanism appears to be related to insulin resistance. Risk for development of diabetes mellitus is also significantly increased in individuals with the metabolic syndrome.

Diabetes Mellitus

Diabetes mellitus is a common disorder and recent statistics show it to be increasing in prevalence. Diabetic patients are considered to be at high risk for coronary disease. Atherosclerosis accounts for 75% to 80% of all mortality in diabetic patients, with CAD as the leading culprit. Aggressive treatment of diabetic patients, and especially their other risk factors, is recommended. Military aircrew are usually excluded from aviation duties if diagnosed with diabetes requiring insulin or oral medications, which might cause hypoglycemia. In some jurisdictions, civilian aircrew with diabetes may be licensed for aviation duties. Such individuals

require more intensive screening for coronary disease. Further discussion of the approach to flying certification and diabetes, including insulin-dependent diabetes mellitus, may be found under the **Endocrine** section in Chapter 18 and the **Pilot Health and Aeromedical Certification** section in Chapter 11.

Obesity and Physical Activity

Physical inactivity is felt to increase the risk for coronary artery events about twofold. Quantifying the relationship between amount of physical activity and risk is often difficult. Many studies have shown that physical activity reduces the risk of CAD events, especially in men. The greatest cardiovascular risk reduction benefit is obtained when going from inactive to moderately active levels of physical activity, with less benefit going from moderate to extreme physical activity. Exercise improves hypertension control and leads to an elevation of HDL cholesterol. It has been estimated that running 10 mi/wk can increase HDL cholesterol by 25%. A linear relationship has been shown between body mass and mortality, although no study has specifically looked at the effect of weight loss and risk reduction. Typically, obesity is associated with other risk factors and these associations probably mediate its risk.

Family History

Although conventional risk factors explain much of the susceptibility to CAD, approximately 10% to 15% of individuals with CAD have no identifiable risk factors. Family studies in identical twins are consistent with premature CAD being strongly influenced by genetic factors (11). Among identical twins, premature cardiac death confers an eightfold increase in risk to the surviving male siblings and a 15-fold increase to female siblings. In the Framingham Offspring Study, parental cardiac disease led to an approximately twofold increase in risk (12).

Inflammatory Markers

Inflammation has been identified as a key element in the pathogenesis of atherosclerosis, and various markers of inflammation have been studied as indicators of atherosclerotic risk (13,14). These include inflammatory cytokines (e.g., interleukin-6), acute phase reactants such as CRP, with a high sensitivity assay-hs-CRP, and urinary microalbumin (e.g., creatinine-to-microalbumin ratio). Data from Women's Health Study and multiple other prospective studies have demonstrated hs-CRP as an independent predictor of cardiac events. The utilization of hs-CRP (and other markers of inflammation) in risk assessment remains somewhat controversial, but most data support the use of hs-CRP in further stratification of individuals assessed as intermediate risk through traditional risk factors.

Risk Assessment and Risk Stratification

As part of periodic medical screening or certification medical examinations, basic risk factor information should be assessed in military aircrew and civilian license holders to allow estimation of cardiovascular risk. Risk indices have been developed in North America (e.g., Framingham Heart Study), Europe (PROCAM study), and elsewhere, which utilize major risk factors to assess global cardiovascular risk. Risk engines are available on-line or in hard copy to calculate risk (http://www.nhlbi.nih.gov/guidelines/cholesterol/; http://www.chd-taskforce.com/).

Clinical guidelines generally stratify risk as low, intermediate, or high based on Framingham risk scores of less than 10%, 10% to 19%, and 20% or greater. Risk scores may be modulated upward with other risk factors, such as diabetes (high-risk equivalent), metabolic syndrome, or with a family history of early CAD. In intermediate-risk individuals, assessment of emerging risk factors including Lp(a), hs-CRP, ApoB, and urinary albumin/creatinine ratio may help further stratify risk as higher or lower.

Primary Prevention

Military flight surgeons and civilian aerospace medicine practitioners have dual roles, which include responsibilities for medical flight certification and opportunities for preventive medical intervention. In many cases, mandatory periodic medical screening or certification represents the only interface of aircrew with the medical system. Such opportunities should be leveraged to obtain a comprehensive cardiovascular risk assessment.

Risk stratification based on risk indices such as Framingham identifies individuals at increased global risk. Such assessments can be clinically useful for identifying aircrew at intermediate or high risk who warrant immediate attention and intervention. Risk assessments can also serve as a motivation to adhere to risk-reduction therapies.

An important point is that such indices serve as models for risk assessment, but they do have limitations. Many individuals at low or intermediate 10-year risk are at high risk in the long term due to the cumulative effects of a single risk factor, which can lead to premature CAD if left untreated. This means each major risk factor deserves intervention, regardless of short-term absolute risk. Furthermore, the risk indices do not take into account newer risk factors and may therefore indeed underestimate the risk of a given individual. Preventive efforts should target each major risk factor. The centerpiece of long-term risk reduction is modification of lifestyle habits with physical activity, weight control, smoking cessation, and proper diet.

Numerous clinical trials have demonstrated the efficacy of cholesterol lowering in primary and secondary prevention. Early trials such as West of Scotland Coronary Prevention Study (WOSCOPS) and Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) demonstrated clear efficacy in primary prevention with a 30% to 40% reduction in relative risk for nonfatal MI or coronary deaths. Other trials of secondary prevention in patients with established coronary disease, for example, Scandinavian Simvastatin Survival Study (4S), Cholesterol and Recurrent Events (CARE), and Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) demonstrated

the overwhelming benefit of lipid-modifying treatment in secondary prevention. When comparing primary and secondary trials, there was no significant difference in relative efficacy, only in absolute event rates (i.e., secondary prevention gives "more bang for the buck"). These trials support the role of aggressive lowering of LDL cholesterol in patients with documented CAD, along with aggressive lowering in patients with multiple risk factors or high-risk lipid profiles but without known disease. In recent secondary prevention trials (e.g., PROVE-IT), incremental benefit has been shown with intensive lipid lowering to LDL cholesterol targets less than or equal to 70 mg/dL.

All classes of lipid-lowering medications are in general compatible with flying duties. On initiation of treatment, a nonflying observation period of approximately 1 week is prudent to observe for idiosyncratic reactions. Statins and fenofibrates, particularly in combination, may cause myalgias or rarely, frank myositis. Concomitant use of antifungal drugs and macrolide antibiotics also increases the risk for myopathy. Patients should be cautioned to report any suspicious symptoms immediately, and creatinine kinase levels should be assessed if symptoms warrant. Statins and niacin may cause significant elevation of hepatic transaminases, and measurement of transaminase levels before and after initiating treatment is advised. A suggested protocol, currently used by the USAF, is to check hepatic transaminases before starting therapy, after 12 weeks of therapy, annually, and when clinically indicated. Creatine kinase could be obtained before therapy and when clinically indicated. In some jurisdictions [e.g., USAF, United States Navy (USN)], a waiver is required for certain classes of lipid-lowering medications, and some (e.g., niacin) are not allowed.

Guidelines for primary and secondary prevention have been published by several expert panels (15–17) and should be consulted for specific recommendations. A disturbing fact is that therapy is underutilized, with more than 80% not receiving therapy for secondary prevention and only 4% of primary prevention eligible patients receiving therapy (1,5). We in the medical profession are not adequately treating those who would benefit the most.

Screening for Coronary Artery Disease

The prevalence of asymptomatic CAD greatly exceeds that of established CAD. A major, often catastrophic event may be the initial presentation of coronary disease in up to half of previously asymptomatic individuals. Detection of asymptomatic CAD should facilitate initiation of more aggressive preventive measures to mitigate the risk of a major coronary event. Screening tests which detect asymptomatic CAD therefore have a dual role in prolonging and improving quality of life, and in reducing risk for occupational mishaps.

Screening tests for CAD are intended to detect flow-limiting, hemodynamically significant obstruction, or to detect the presence of coronary plaque. Tests for obstructive coronary lesions include exercise stress testing, stress nuclear perfusion imaging (NPI), and stress echocardiography. Techniques for plaque detection include tests for quantitative assessment of coronary artery calcium scores (CACS) utilizing electron beam computed tomography (EBCT), or multidetector computed tomography (MDCT). With the development of more sophisticated technology, with some limitations, CT contrast coronary angiography with MDCT provides information regarding both plaque burden and coronary lumenograms of a quality approaching conventional coronary angiography.

The utility of screening tests is related to the sensitivity and specificity of screening techniques, and to Bayes' theorem. Test sensitivity reflects the ability of a screening test to detect the disease when present. Specificity reflects the test ability to correctly identify the absence of disease. Bayes' theorem relates the post-test probability of the presence of disease to the prevalence in the population, or pretest probability. When the pretest probability is low, as is the overall prevalence of CAD in an aviator population, the post-test probability after a positive screening test remains low, with a low positive predictive value. Therefore, general screening of an aviator population with tests for obstructive coronary disease (stress testing, stress NPI, or stress echocardiography) is not recommended without prior risk stratification. Application of tools utilizing risk factor analysis (e.g. Framingham and other risk factors as discussed earlier) identifies individuals in whom the pretest probability is higher, and in whom secondary screening tests will have a greater utility. Individual aviation authorities must decide what level of pretest probability should trigger secondary screening testing. Generally, this is reserved for aviators identified as being at "high risk" based on risk factor analysis. However, the risk level identified for triggering secondary screening may relate not only to aviation safety but also to mission risk management, with a lower threshold, for example, in a long-duration space crewmember or a high-performance military aviator.

The choice of test for screening depends on availability, expertise, cost, and operating characteristics of the test (sensitivity, specificity). Tests with higher sensitivity will detect the disease more often when present, with fewer "false negatives." Higher specificity will be reflected in fewer "false-positive" results. An important consideration in determining aeromedical disposition is the prognostic value of a negative screening test. A recent meta-analysis indicated that in individuals with a normal exercise NPI or stress echocardiography study, event rates for MI or cardiac death were less than 0.6% per year over the following 3 years (18). USAF data comparing exercise treadmill, thallium NPI, and cardiac fluoroscopy showed event rates 0.5% per year or less over 5 years of follow-up for all three modalities.

Stress Testing

Exercise stress testing assesses for obstructive, flow-limiting coronary artery lesions and additionally provides information about blood pressure response, arrhythmias, and aerobic capacity. It has the advantage of being both safe and widely available. The sensitivity and specificity of exercise stress

testing for hemodynamically obstructive lesions is approximately 60% to 70%; therefore, application in a population with low-disease prevalence results in large numbers of false-positive results, requiring further investigation to clarify. Sensitivity and specificity may be lower in women.

Current recommendations by an expert committee are that exercise stress testing is a Class IIb indication (reflecting conflicting evidence or divergence of opinion) in asymptomatic men older than 45 years and for women older than 55 years involved in special occupations, such as aviation, in which impairment might affect public safety (19).

In an unselected military aviator population, the positive predictive value of an abnormal stress test for significant angiographic CAD was only 10%. Preselection by abnormal resting ECG doubled the positive predictive value to approximately 20% (1). A prospective study of treadmill testing in 25,927 apparently healthy, asymptomatic men with a mean age of 43 years showed that an abnormal treadmill test had an age-adjusted relative risk for CAD of 20. This increased sequentially as the number of risk factors increased (age-adjusted relative risk of 80 with three or more risk factors). They concluded that exercise testing was a worthwhile tool to predict future risk of CAD death, especially in those with more cardiac risk factors (20).

Nuclear Testing

NPI assesses the perfusion-dependent distribution of isotopes in the myocardium at rest and after stress. NPI with an isotope such as thallium or technetium improves the sensitivity and specificity of stress testing to approximately 85% to 90%. Stress may be induced either through exercise treadmill, cycle ergometry, or pharmacologically, as with dobutamine infusion. Because of the additional cost and radiation exposure involved, NPI is generally utilized in individuals with abnormal treadmill tests or baseline ECG abnormalities that preclude diagnostic ST changes (e.g., LBBB).

Multiple gated acquisition scans (MUGA) provide information about global ventricular function (measurement of ejection fraction) and segmental wall motion abnormalities, and may complement information provided by NPI studies.

Stress Echocardiography

Stress echocardiography assesses segmental and global myocardial contractility at rest and with stress. This is assessed by imaging the myocardium and endocardium. Stress may be accomplished with an exercise treadmill, supine bicycle exercise, or pharmacologically (e.g., dobutamine infusion). Sensitivity and specificity are similar to stress NPI (21). Limitations include technical difficulties in accurate imaging of all myocardial segments, which may be improved with injection of contrast agents that opacify the ventricles. Stress echocardiography may be particularly useful in women, avoiding radiation exposure while providing a more sensitive testing modality than stress testing, which has decreased sensitivity in women. Stress echocardiography may also be useful as a follow-on screen in individuals with positive stress tests.

Tests which Assess for Coronary Plaque

With the evolution of our understanding of the pathogenesis of CAD from the initial formation of atherosclerotic plaque, progressing slowly over time to flow-limiting obstructive lesions, the detection of early plaque lesions became appealing. The presence of calcium deposition in the coronary arteries almost always reflects the presence of coronary plaque, although earlier in evolution, plaque may not be calcified.

Coronary artery fluoroscopy (CAF) has been used since the 1960s and has been relatively accurate to predict the presence of anatomic atherosclerotic disease. CAF is a nonquantitative assessment for coronary calcium. In studies by the US Army and USAF, coronary calcium detected by CAF has been shown to have a higher positive and negative predictive value for obstructive coronary disease and coronary events than exercise stress testing or stress thallium, with a sensitivity and specificity of 70% to 75% (22,23).

Coronary artery calcium can be measured quantitatively by CT scanning techniques, which are coupled with ECG gating to overcome the problem of cardiac motion during acquisition. EBCT uses an electron sweep of stationary tungsten rings that generates rapid radiographic images. Multislice computed tomography or multidetector computed tomography (MSCT/MDCT) utilizes a gantry of multiple rapidly rotating CT scanners with rapid rotation (300–400 ms). Current generation MDCTs utilize up to 64 slices, with future generations already in development. EBCT and MDCT produce similar scores, except at very low score levels. Radiation exposure with MDCT is significantly greater than EBCT.

CACS results are quantitatively expressed in Agatston units. Normative data has been established in large data sets (24). Quantitative coronary calcium scores reflect overall plaque burden and have been demonstrated in both retrospective and prospective studies to provide incremental prognostic information for coronary events beyond that acquired from standard risk data. CACSs greater than 100 are considered to represent a threshold above which coronary events are more likely, with asensitivity, specificity, and odds ratio at 89%, 77%, and 25.8%, respectively (25). However, the presence of any coronary calcium reflects the presence of coronary plaque, and in conjunction with other risk factor data may guide the intensity of preventive measures (e.g., lipid-lowering targets) and further diagnostic evaluation.

Utilizing intravenous contrast, MDCT is capable of providing high-quality almost-instant noninvasive coronary angiography, with high diagnostic accuracy for the assessment of coronary artery stenoses and the identification and characterization of coronary plaques. Limitations include motion artifacts and heavily calcified coronary artery segments. MDCT coronary angiography technology is rapidly reaching a maturity level sufficient to provide accurate, noninvasive angiographic information in aviators in whom other noninvasive testing suggests the presence of coronary disease, or who are being assessed for possible return to aviation duties following revascularization or MI. An additional

feature of MDCT angiography is the capability of identifying noncalcified plaque, which may help guide the intensity of preventive intervention as well as coronary risk assessment.

Which test to use to further screen aviators in whom primary risk stratification triggers a requirement for secondary screening will depend on factors such as cost, availability, and the performance characteristics of the test. Exercise stress testing is widely available but has the lowest sensitivity and specificity, and will frequently produce false-positive results in a low-prevalence population. Stress echocardiography and NPI tests have a higher sensitivity and specificity, but are more expensive and are often reserved for further assessment of individuals with positive exercise stress tests. Assessment of CACSs by EBCT or MDCT is increasingly available, and provides the most sensitive and specific information about the presence of coronary plaque and related risk for coronary events. CT coronary angiography involves higher radiation dose exposure but provides definitive information about coronary plaque and lumen, and is best reserved for positive results with other testing modalities.

In the selection of crewmembers for long-duration space missions on the International Space Station (ISS), CACS screening is included in the primary screening process, along with traditional risk factor information and hs-CRP. Candidates with CACS greater than 100 or greater than the 90th age- and gender-matched percentile are required to undergo further testing which includes coronary angiography. The presence of angiographic coronary disease is disqualifying for long-duration mission assignment. CACSs are repeated every 5 years in ISS crewmembers.

Women and Coronary Artery Disease

Historically aviation as a whole, and especially military aviation, has been a male-dominated profession. Most aviation medicine literature therefore relates to the male aviator population, and especially the male pilot population, and may not be applicable to the growing female aviator population. This is particularly true for CAD. In the USAF, the number of female candidates screened for flying training has been approximately 10% since 1994. Much publicity is given to gender-specific problems, such as breast cancer and osteoporosis. However, as with men, CVD is the leading cause of mortality and morbidity in women. CVD is responsible for one third of all deaths of women worldwide, and half of all deaths of women older than 50 years in developing countries (26). The lifetime risk of developing CAD after age 40 is estimated as 49% for men and 32% for women (4). Several authors have expressed CAD as "an equal opportunity killer." The caveat is that CAD generally presents approximately 10 years later in women than in men.

Some research indicates that CAD is less aggressively pursued and treated in women than in men (a phenomenon described as the *Yentl syndrome*), and cardiovascular health in women is not improving as fast as that of men. However, the aeromedical emphasis in women, as in men, is on risk assessment of known or suspected CAD as it relates to safe continuation of flying duties.

Clinically, CAD often presents differently in women than men. Women have smaller coronary arteries and less collateral circulation than men, which may lead to an increase in ischemia, particularly during exertion or stress. Framingham data indicate that 69% of women initially present with unstable angina compared with 30% of men. Atypical prodromal symptoms in women include fatigue; difficulty breathing, shortness of breath and dyspnea; neck and jaw pain; palpitations; cough; nausea and vomiting; and indigestion.

Although the same cardiac risk factors generally apply to women as they do to men, there appear to be some gender differences with respect to risk factors. Smoking rates are higher in men. The prevalence of obesity and associated insulin resistance is higher in women and they tend to be less physically active than men. Before menopause, women have better risk profiles than men, with lower blood pressures and LDL cholesterol levels and higher HDL cholesterol levels. Some of these differences are thought to be mediated through sex hormones and, following menopause, risk profiles of men and women become more similar.

Risk factor modification works for both women and men. Recent statin trials have clearly demonstrated that the benefits of lipid modification apply to women as well as men, for both primary and secondary prevention of CAD. After menopause, the risk for CAD rises sharply in women. Hormone replacement therapy, once thought to be protective, was shown in the Women's Health Study to increase cardiovascular risk. Although many beneficial effects on risk factors and CAD markers have been demonstrated, the rate of CVD is not decreasing in women as well as it is in men. However, the standard efforts of smoking cessation, weight control, regular exercise, detection and control of diabetes and hypertension, and management of dyslipidemia are clearly effective for women. Nonpharmacologic and pharmacologic risk factor modification should be aggressively pursued in aviators of both genders.

The screening tests discussed earlier were mostly related to male subject populations; good data on female populations, especially female aviators, is still lacking. ECG response on treadmill testing is reportedly less reliable in women, resulting primarily in more false-positive tests, a problem especially of concern for aeromedical issues. Myocardial perfusion imaging with thallium or other agents is more accurate than treadmill alone, although false defects due to breast attenuation are a problem. Stress echocardiography is reportedly more accurate and cost effective for CAD screening and evaluation of chest pain syndromes in women. The overall prognostic value of coronary plaque load assessed by CT coronary artery calcium scoring does not appear to be affected by gender, but coronary calcium scores are lower in premenopausal women than age-matched men and gender-specific normative data should be used when assessing risk.

These influences of gender on risk factors and primary prevention, the application of secondary screening technologies, and the potential atypical symptomatic presentations

must be considered by the aeromedical practitioner and by licensing authorities when evaluating female aviators for suspected or known CAD. Further discussion may be found under the section **Women's Health Issues** in Chapter 22.

Natural History and Aeromedical Disposition

CAD is typically a progressive disease in two respects; established lesions become more stenotic and new lesions develop. The true natural history of CAD is unknown because most patients with diagnosed CAD are on medical therapy and/or have had coronary revascularization. In general, cardiovascular risk factors related to the incidence of CAD also contribute to the prognosis after an event. Aggressive secondary prevention is therefore extremely important, both clinically and aeromedically. Natural history data on aviators with CAD is sparse. Compared to the general population, aviator groups are generally healthier, with fewer risk factors, and are often asymptomatic. Aeromedical decisions regarding CAD are usually based on data from clinical populations, which may or may not apply well to aviators. Also, the state of knowledge in the clinical realm of diagnosing and treating disease is rapidly evolving. Aspirin use, better treatment of hypertension, and aggressive therapy for lipid abnormalities, especially with statins, may significantly alter the statistics from which current opinion is rendered.

Despite its imperfect assessment of disease extent, coronary angiography does predict intermediate and long-term outcomes. Several studies have shown that the extent of anatomic CAD is a strong predictor of survival and other clinical events. Current recommendations of many aviation regulatory agencies consider this and allow varying degrees of CAD to maintain licensure, although often restricted. Civilian and military aviation policies regarding return to flight duties involve very different missions, including combat and high-performance flight for the military. If certain degrees of CAD are allowed to return to some categories of flying, policies should also place a greater emphasis on secondary prevention.

Several groups have performed long-term follow-up of apparently healthy civilian populations and patients with normal coronary arteries by angiography, reporting annual cardiac event rates of 0.0% to 0.65% per year over 10 years (1). A review of apparently healthy USAF aviators showed a 5-year annual cardiac event rate that increased progressively with age, but only up to approximately 0.15% per year for the oldest age-group of 45 to 54 years (27). These ''normal'' cardiac event rates may be compared to those for minimal and significant CAD for the purpose of aeromedical decision making.

Minimal Coronary Artery Disease

Long-term studies of minimal CAD (maximum angiographic lesion <50%) report annual cardiac event rates of approximately 1.5% to 3.0% per year over approximately 10 years of follow-up. Moreover, event rates increased progressively with increasing severity of nonsignificant disease. In these studies, the cohort of patients typically had a chest pain syndrome that ultimately led to coronary angiography. In contrast, USAF experience with approximately 250 asymptomatic military aviators with minimal CAD showed an event rate of approximately 0.5% per year over 10 years of follow-up. In the Coronary Artery Surgery Study (CASS) registry, a subset of 6,758 patients had no significant coronary stenoses. In this subset, 4,463 had normal coronary angiography, 1,368 had at least one minimal (30%–50%) lesion, and 927 had at least one moderate (50%–70%) lesion. In CASS, significant CAD was defined as maximum lesion greater than 70%. Survival at 12 years was 91%, 86%, and 79% for normal coronary angiography, minimal lesions, and moderate lesions, respectively (28).

Given the low event rate in their aviators with minimal CAD, the USAF has for years allowed such members to continue to fly, restricted to low-performance, multipilot aircraft, if they are asymptomatic and have had no prior cardiac events. The effects of high $+G_z$ forces on minimal lesions are unknown and most high-performance aircraft are single seat. Plaque rupture of even minimal lesions and asymptomatic progression to significant CAD are additional concerns. Return to multipilot commercial flying and general aviation is also recommended. Periodic noninvasive evaluation is recommended, annually for military aviators. The rate of progression of minimal CAD to significant CAD is unknown. Pending more reliable noninvasive methods to detect asymptomatic progression and better data in aviator populations with minimal CAD, periodic repeat coronary angiography (3- to 5-year intervals) is a consideration, depending on extent of disease, stability of noninvasive testing, control of modifiable risk factors, and type of flying duties.

Significant Coronary Artery Disease

In the CASS registry, overall 4-year survival rates for medically treated patients with zero-, one-, two-, and three-vessel significant CAD were 97%, 92%, 84%, and 68%, respectively, and 12-year survival rates were 88%, 74%, 59%, and 40%, respectively. Again, CASS defined significant CAD as a lesion stenosis equal to 70% or more. Angiographic extent of disease was the most important variable in determining 4- and 12-year survival rates. Another powerful predictor of survival was the status of left ventricular function (28). Reported annual mortality rates for all categories of significant CAD combined are approximately 3.0% to 4.0% per year. In some of these studies, as with CASS, maximum stenosis of 70%, rather than 50%, was the criteria for significant disease. The USAF compared cardiac event rates in a subset of 92 military aviators with minimal to moderate CAD (maximum lesion 40%, $n = 38$, versus maximum lesion 50%, $n = 54$). For the 40% group, the annual cardiac event rate was approximately 0.5% per year at both 5- and 10-year mean follow-up, with no cardiac deaths. For the 50% group, the annual cardiac event rate was approximately 3.0% per year at 5 years and 2.5% per year at 10 years, with one cardiac death. In most studies, event rates are also correlated with the number of

arteries involved, whether the left main coronary artery is involved, and the status of left ventricular function.

One of the most compelling aeromedical concerns is disease progression, especially development of new significant lesions (≥50% stenosis) in artery segments that previously appeared normal by angiography. The Medicine, Angioplasty, or Surgery Study (MASS) was a prospective trial of patients with symptomatic single-vessel (left anterior descending artery) significant CAD who were randomized to medical treatment, angioplasty, or surgical bypass with an internal mammary artery graft. Development of new significant lesions occurred in 30% to 35% of patients at 2 years, regardless of treatment group (1,29). At 5 years, new significant lesions appeared in approximately 60%, 50%, and 45% of those treated medically, by angioplasty and by surgery, respectively. And in the medically treated group, the annual cardiac event rate was 4.8% per year at 5 years (29).

Without revascularization (e.g., angioplasty, stent, bypass surgery), return to flying is generally not recommended for significant CAD (maximum stenosis ≥50%). Return to restricted civilian or military aviation might be considered for single-vessel moderate disease (maximum lesion 50%–70%) with limited minimal disease at other sites. The aviator should be asymptomatic, without evidence of ischemia in the distribution of the significant lesion, and off antianginal medications. Overall, left ventricular function should be normal without regional wall motion abnormalities. In USAF experience, military aviators meeting these criteria had average annual event rates of approximately 1.0% per year. Annual noninvasive reevaluation is recommended. Repeat coronary angiography at 3- to 5-year intervals is a consideration. Further discussion of civilian issues may be found in Chapter 11.

Percutaneous Coronary Intervention

The standard treatment of CAD has been medical, surgical bypass, and percutaneous coronary interventions (PCIs), aimed at secondary prevention of events and relief of symptoms. PCI is the current term for nonsurgical, catheter-based coronary revascularization, such as angioplasty and stents. Coronary revascularization, surgical or PCI, has typically been disqualifying for military aviation duties. However, commercial aviation licensing agencies often allow return to flying duties for select lower-risk individuals after successful revascularization procedures.

A number of percutaneous modalities have emerged since the late 1970s when percutaneous transluminal coronary angioplasty (PTCA) was first used. PCI includes PTCA, directional atherectomy, rotational atherectomy, laser-guided procedures, and coronary artery stents. The specific indications of each procedure will not be discussed. With the advent of PCI, the mortality and MI could be reduced. For most patients with one- or two-vessel CAD, multiple trials have repeatedly shown no significant benefit regarding survival or MI for PCI compared to medical therapy.

The main problem with PCI has been short-term restenosis at the treated site, typically occurring within 3 to 6 months after PCI. Restenosis occurs in approximately one third of all angioplasties, when defined as return of symptoms, and may be as high as one half when defined angiographically. Restenosis rate is reduced to 10% to 20% or less with the use of coronary stents, especially drug-eluting stents. Prediction of subsequent cardiac events based on the degree of restenosis has been difficult.

Another major problem is that native vessel disease is often present in other locations and may progress or lead to acute clinical events due to plaque rupture. Also, PCI of moderate disease may lead to a more severe stenosis with a significant incidence of restenosis and worse clinical outcome. Studies of asymptomatic patients treated with PTCA have shown no significant change in exercise tolerance and no significant reduction of future symptoms, revascularization, MI, or cardiac death. Performing PCI on asymptomatic aviators only for occupational purposes and without standard clinical indications may not be advisable.

Recent PTCA and stent trials report annual cardiac event rates (cardiac death or nonfatal MI) of approximately 1% to 2% per year for successful/uncomplicated PCI of one-vessel and most two-vessel diseases (1). Annual cardiac event rates are approximately doubled if angina and repeat revascularization are added. For the PTCA arm of the MASS trial, the annual event rate at 5 years of follow-up was approximately 8% per year; for cardiac death or nonfatal MI it was slightly above 2% per year. However, most repeat revascularizations were performed for unstable angina (29). Much of this literature involves PTCA. In more recent stent trials in low-risk patient subsets, event rates have been in the range of 1% to 3% per year, some even less than 1% per year.

Return to restricted flight duties in multipilot, low $+G_z$ aircraft may be acceptable for select pilots who have undergone PCI of a native vessel, who have no significant restenosis, no evidence of reversible ischemia, and preserved left ventricular function. Initial assessment should be at least 6 months after PCI. Coronary angiography is recommended as part of the initial evaluation if return to flying is being considered for commercial or military aviation. Noninvasive reevaluation should be performed at least annually. Periodic repeat coronary angiography at 3- to 5-year intervals is again a consideration.

Coronary Artery Bypass Surgery

Coronary artery bypass grafting (CABG) is very effective treatment for reducing the symptoms of angina. And, in select groups such as three-vessel disease, it has significant mortality benefit. However, the disease process is still present after CABG, with progression of native vessel disease along with disease development in the grafts, primarily in saphenous vein grafts, which have a reported annual failure rate of approximately 3% per year. This emphasizes the point that CABG is only palliative, not curative. Graft patency is significantly improved, as is survival, with the use of the internal mammary artery as a graft conduit. Risk factors that

lead to CAD, especially lipids and smoking, significantly affect outcome after CABG. Subjects considered for CABG for established clinical indications will usually have significant two- or three-vessel disease and many will have had previous MI or reduced left ventricular function. Graft occlusion and progression of native disease are the primary concerns.

Annual event rates in the first few years post-CABG generally exceed 2% per year. For low-risk groups post-CABG, annual event rates for only cardiac death or nonfatal MI are approximately 1% to 2% per year, compared to 5% per year or greater for moderate- to high-risk groups. Adding other endpoints, such as angina and repeat revascularization, approximately doubles the annual event rates to 3% to 4% per year for low-risk groups. Select low-risk groups may have annual event rates as low as 0.5% to 1.0% per year for cardiac death or nonfatal MI (1). For the surgical arm of the MASS trial, annual event rate at 5 years was 1.7% per year; all events were fatal or nonfatal MI (29).

As with PCI, return to civilian flying has been allowed by licensing authorities for years. Return to restricted flight duties in multipilot, low $+G_z$ aircraft may be acceptable for select military aviators post-CABG. As with PCI, there should be preserved left ventricular function and no evidence of reversible ischemia off cardioactive medications. Initial assessment should be at least 3 to 6 months after CABG. Coronary angiography is recommended as part of the initial evaluation if return to flying is being considered for commercial or military aviation. All grafts should be patent and all significant lesions should be grafted (complete revascularization). Noninvasive reevaluation should be performed at least annually. Periodic repeat coronary angiography is again a consideration. Civilian aeromedical certification issues are covered in Chapter 11.

Myocardial Infarction

The mortality rate associated with CAD has declined but the number of acute MIs has remained relatively constant. Prognosis is complex depending primarily on the status of left ventricular function and severity of underlying CAD. Aeromedical disposition post MI is affected by these factors and several others, such as revascularization post MI, patent versus occluded infarct-related artery, success of secondary preventive efforts, and residual ischemia. Presence of a prior MI increases the event rate for all significant CAD groups, with or without revascularization. Recommended post-MI medications must also be considered. Most guidelines recommend statin, β-blocker and angiotensin-converting enzyme (ACE) inhibitor therapy post MI unless specifically contraindicated. Any consideration of return to flying post MI must be tailored to the individual clinical scenario and the type of aviation.

HYPERTENSION

Hypertension is an established and important risk factor for CVD, especially stroke and CAD, contributing to increased mortality in men and women of all ages and ethnic groups. It also leads to other significant complications such as peripheral vascular disease, end-stage renal disease, and heart failure. Numerous studies have documented a continuous relationship between the level of blood pressure and risk, for both systolic and diastolic pressure. Like CAD, hypertension is a complex disease modified by both genetic and environmental determinants. Most hypertensives are classified as essential, meaning that no definable pathologic process is apparent as the etiology. Hypertension has generally been defined as a blood pressure greater than 140/90 mm Hg.

Classification and Evaluation of Hypertension

The classification of hypertension has changed with increased understanding of the risk of high blood pressure along a continuum. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) offers excellent background information as well as recommendations for classification, risk stratification, and therapy. As most hypertensive subjects are asymptomatic, blood pressure should be recorded on each health care encounter. Diagnosis of hypertension should take into account at least three blood pressure readings taken on different days.

JNC 7 continues to define hypertension as systolic pressure greater than or equal to 140 mm Hg, diastolic pressure greater than or equal to 90 mm Hg, or requirement for chronic medication to control blood pressure. A new category, prehypertension, is 120–139/80–89 mm Hg and normal or optimal blood pressure is less than 120/80 mm Hg. Lifestyle modifications are recommended for prehypertension. Control of treated hypertension is generally defined as less than 140/90 mm Hg. Lower thresholds for medication and lower treatment target levels are recommended for higher-risk patient groups as well as for those with additional risk factors, target organ effects, or diagnosed CVDs.

After diagnosing hypertension, routine evaluation should include medical history, physical examination, and routine laboratory tests. History should focus on duration of disease, symptoms, current medications, lifestyle habits, and comorbid conditions. Physical examination should focus on other areas of vascular disease—bruits, pulses, S4 on cardiac auscultation, and hypertensive retinal changes, as well as changes suggestive of secondary hypertension (e.g., renal artery stenosis, endocrine causes for hypertension etc.). Laboratory tests should include serum electrolytes, complete blood count (CBC), lipid profile, fasting glucose, and creatinine. ECG should be performed, looking for signs of LVH or manifestations of CAD.

White Coat Hypertension

Blood pressures may be elevated in the physician's office, then appear normal on subsequent checks, a condition often called *white coat hypertension*. Many investigators have addressed

the significance of white coat hypertension. This is still debated as studies have emerged on both sides of this issue. Data indicate that true hypertension is worse than white coat hypertension regarding clinical course and end-organ damage. However, white coat hypertensives are at greater risk than normotensives. This entity must not be considered just a normal variant. It might more appropriately be considered labile hypertension or prehypertension. Lifestyle modifications should be instituted, although pharmacologic therapy may not yet be indicated.

Aeromedical Disposition and Summary

Hypertension itself does not carry the risk of sudden incapacitation. The obvious concern for the aviator community is its risk for stroke and heart disease, which can be suddenly incapacitating. Exposure to the high $+G_z$ environment has not been shown to pose a risk for developing hypertension. Failure to diagnose and treat hypertension appropriately in the interest of a flying career does the aviator a disservice. JNC VII guidelines are well recognized and accepted; they are also readily adapted to aeromedical policies and disposition. Current USAF policy allows continued flying duties if blood pressure is controlled nonpharmacoligically or by approved medications to less than 140/90 mm Hg and there is no evidence of end-organ damage. For initial blood pressure greater than 140/90 but less than 160/100, a 6-month trial of nonpharmacologic therapy (lifestyle modifications) is allowed, with the aviator remaining on flying duties. Currently approved medications for USAF aviators are thiazides and lisinopril. Aviators started on medical therapy should have an initial grounding period, usually approximately 1 week, to observe for idiosyncratic reaction or other untoward side effects.

STRUCTURAL HEART DISEASE: VALVULAR AND CONGENITAL

The detection of significant structural heart disease in trained aircrew, either valvular or congenital, commonly leads to assignment of an operational flying restriction with a requirement for regular cardiac assessment for any change or progression. In some cases, it leads to permanent grounding. Aeromedical concerns with respect to structural heart disease include the potential for sudden incapacitation due to arrhythmias, thromboembolic events, or other complications such as subacute bacterial endocarditis (SBE). For many years, the American Heart Association has published guidelines for SBE prophylaxis in cooperation with appropriate professional societies from the dental, infectious diseases, and pediatric communities.

In early 2007, the American Heart Association published new SBE guidelines that are dramatically different from past recommendations. SBE prophylaxis was recommended only for specified high-risk groups, particularly for dental procedures, respiratory tract procedures, and procedures on infected skin, skin structures, or musculoskeletal tissue. Prophylaxis was no longer recommended for gastrointestinal or genitourinary procedures. Conditions commonly seen by most aerospace medicine practitioners were not included in the list of high-risk conditions. Such common conditions no longer recommended for SBE prophylaxis included, but are not limited to, mitral valve prolapse (MVP), bicuspid aortic valve (BAV), mitral or aortic regurgitation with normal valve, and uncorrected small defects of the atrial and ventricular septum. The high-risk group was limited to prosthetic cardiac valves, previous SBE, select congenital heart conditions, and cardiac transplant patients with valvulopathy. As the medical community reacts and responds to these very significant changes, aerospace medicine practitioners, licensing authorities, and aircrew standards groups are advised to consult their own cardiology and infectious disease consultants for specific occupational guidance.

Additional operational concerns include impairment of cardiac output under high $+G_z$ with loss of consciousness, worsening of the valvular problem through repetitive $+G_z$ exposure, or the hypothetical potential for type II decompression sickness (DCS) through right-to-left shunts. Developments in operative and percutaneous treatments of structural heart disease have raised further operational concerns over the suitability and durability of these repairs in the hostile aviation environment. This has resulted in additional challenges for aviators with repaired structural heart disease as well as the organizations and aeromedical physicians who are charged with their care.

Echocardiographic Screening in Aircrew

For military and other flying training programs, screening for structural cardiac disease may reduce the problem of congenital and acquired valvular heart disease in trained aircrew. Over the last decade, some air forces have incorporated echocardiographic screening into their aircrew medical selection programs (30). Echocardiographic screening programs for aircrew applicants are ideally managed by providing centralized screening at a single or at most a very limited number of locations, supervised by a cardiologist knowledgeable about the aeromedical implications of structural cardiac anomalies. Application of high-quality echocardiographic techniques by certified, well-trained technicians, with consistent interpretation using well-defined criteria such as those of the American Society for Echocardiography is most important. Screening echocardiography can detect structural heart disease including valvular disorders and congenital heart disease, as well as disorders of the myocardium such as cardiomyopathies or segmental wall motion abnormalities.

Utilizing screening echocardiography, the incidence of disqualifying findings in candidates was found to be 7.8% in Canadian Forces aircrew (31). The most common disqualifying echocardiographic finding was MVP (4.5%), followed by aortic regurgitation through normal valves (1.3%) and BAV with or without regurgitation (0.9%). Later studies in USAF pilot candidates revealed a disqualification

rate of only 1.5% (1), the difference mainly reflecting a lower incidence of MVP as a result of more stringent criteria for echocardiographic diagnosis of MVP. A review of 299 Canadian Forces pilot candidates screened in 1999 and 2000 showed a disqualification rate of 2.6% for echocardiographic findings, with an incidence of MVP of only 1.3% (Gray GW, 2006).

Recent investigations into the utility of echocardiographic screening programs have called into question their overall effectiveness. In an analysis of 20,208 USAF pilot applicants, the initial disqualification rate was 1.45% ($n = 294$). The most common abnormalities were BAV with or without mild aortic insufficiency (AI) (0.76%), mild AI with a trileaflet aortic valve (0.25%), and MVP (0.29%). Over a 12-year period of data collection, however, waiver standards were gradually changed so that the earlier diagnoses, while still disqualifying, were ''waiverable'' for entry into pilot training. Therefore, after applying current waiver standards to the entire cohort, it was found that only nine screening examinations yielded a diagnosis which was disqualifying and ineligible for waiver, a rate of only 0.045% (32). The utility of echocardiography screening is therefore seen to be tied to aeromedical waiver policy, and should be tailored by each aircrew training organization appropriately.

Echocardiography can also play an important role in the evaluation of trained aircrew with valvular heart disease for determining medical fitness for continued flying status or licensing medical certification. Echocardiography has been effectively utilized to assess the question as to whether repeated exposure to sustained G-forces has an effect on cardiac structure or function. In a multinational study of North Atlantic Treaty Organization (NATO) military aircrew, which compared echocardiographic findings in 289 experienced and actively flying high-performance pilots with 254 pilots of non–high-performance aircraft, there were no significant differences found in cardiac structure or function (33).

Clinical Examination for Structural Heart Disease

Particular attention should be paid to the cardiac examination in both trained aircrew and aircrew candidates, in whom clinical signs of congenital and early-acquired valvular disease may be very subtle. Murmurs and extra sounds may vary considerably with end-diastolic volumes and may be heard in one position but not another. Physicians examining aircrew should incorporate into their physical examination a routine of cardiac auscultation designed to elicit signs of structural heart disease. Auscultation should be done in a series of positions beginning with the individual seated, progressing to supine, then in the left lateral decubitus position, and then standing. This should be followed by auscultation in the crouch or squat position, followed by standing. Finally, if any suspicious findings are elicited, further auscultation may be done through and after a Valsalva maneuver, with dynamic exercise such as handgrip, or after inhalation of amyl nitrite. By incorporating such a protocol into the clinical examination routine, physicians will maximize the sensitivity of the physical examination for detecting structural cardiac disease.

In the generally healthy and fit aircrew population, physiologic flow murmurs are common, and are characterized by their generally soft quality (grade 1-2 out of 6), and midsystolic timing. Such innocent flow murmurs generally disappear on standing. Right-sided murmurs generally increase with inspiration and left-sided murmurs with expiration. Typical systolic physiologic flow murmurs do not require further assessment. The following auscultatory findings should be considered sufficient indication for echocardiographic assessment: new murmur, prominent midsystolic murmurs, grade 3 or greater; holosystolic and mid-through-late systolic murmurs; systolic murmurs which increase on standing, or after Valsalva; and all diastolic murmurs. The finding of extra cardiac sounds such as an ejection click, apical nonejection click, or fixed split second sound should also trigger an echocardiographic examination for an underlying structural heart substrate.

VALVULAR HEART DISEASE

Aortic Stenosis

Valvular aortic stenosis (AS) occurs as a consequence of a congenital BAV, rheumatic fever, or as a result of degenerative valve disease. The latter occurs in older adults and is unlikely to be an aeromedical issue. Although not unknown, rheumatic heart disease is uncommon in industrialized countries, so the most common substrate for aortic stenosis in aviators is a BAV.

Valvular AS is suspected clinically by the presence of a crescendo–decrescendo systolic murmur heard in the upper right sternal area, with radiation to the carotids and down the left sternal border to the cardiac apex, where it may be best heard. Severe AS may not produce appreciable murmurs, but at that stage clinical symptoms are generally established. There may be an ejection systolic click, and a fourth heart sound reflecting developing LVH. The ECG may show evidence of LVH and strain, and the chest x-ray may show cardiac enlargement with left ventricular prominence.

Regardless of etiology, the natural history of AS is one of gradual progression over years, during which the individual is asymptomatic. The outflow obstruction caused by valvular AS results in left ventricular pressure overload and consequent hypertrophy. With progression of AS, the pressure overload leads to left ventricular diastolic and later systolic dysfunction with left ventricular dilatation. The onset of symptoms, which include dyspnea, angina, and syncope, indicates progression to moderate or severe stenosis with significant potential for acute incapacitation.

From an aeromedical standpoint, AS should be detected well before the onset of symptoms through clinical and ECG findings on periodic medical examinations. A two-dimensional (2-D) echocardiogram and Doppler study will elucidate aortic valve morphology and left ventricular

size, wall thickness, and function. Occasionally, cardiac catheterization may be necessary if the echocardiographic study is inadequate or concurrent definition of the coronary arteries is required.

The prognosis and hence the aeromedical disposition depends on the degree of stenosis, which is classified as *mild, moderate,* or *severe*. Classification systems have been developed based on valve area, pressure gradient, and maximum flow velocity. Using valve area, published guidelines grade aortic stenosis as mild with valve area greater than 1.5 cm^2, moderate for valve areas 1.1 to 1.5 cm^2, and severe when the valve area is less than or equal to 1.0 cm^2. Using mean pressure gradient, stenosis is graded as mild for mean gradients less than or equal to 20 mm Hg, moderate for gradients 21 to 39 mm Hg, and severe for gradients greater than or equal to 40 mm Hg. Maximum flow velocity is a newer parameter with less data available related to outcome.

On the basis of mean pressure gradient, athletes with mild AS are considered fit for all competitive activities. For mild-to-moderate AS, competition is restricted to low-to-moderate intensity isometric and aerobic activities. Individuals with severe AS or moderate AS with symptoms are advised against participation in all competitive sports.

Suggested aeromedical recommendations combine valve area and mean pressure gradient, as shown in Table 13-2. The aeromedical concerns for AS relate to the occurrence of clinical events (syncope, angina, and sudden death), and the limitation of cardiac output through the fixed obstruction, a significant concern for aerobatic and military high-performance flying.

Aircrew with mild AS are considered fit for unrestricted flying but require periodic echocardiographic follow-up. Actual experience with mild AS and high-performance flight is scant and as yet unreported. Mild AS may progress or may remain static for many years. For aeromedical purposes, assessment of the rate of progression requires an annual echocardiogram for at least several years to assess serial change in the severity of stenosis and left ventricular parameters. Fortunately, up to half the number of individuals with mild AS may remain stable over many years and in such cases the periodicity of serial echocardiography may be extended to biannual. The average rate of progression is approximately 0.12 cm^2/yr, but unfortunately it is not possible to predict the rate of progression in any particular individual.

TABLE 13-2

Classification of Aortic Stenosis

Grade of Aortic Stenosis	*Valve Area (cm^2)*	*Mean Gradient (mm Hg)*
Mild	>1.5	≤20
Mild-to-moderate	1.1–1.5	≤20
Moderate	1.1–1.5	21–39
Severe	≤1.0	≥40

The event rate increases as stenosis progresses from mild to moderate. Asymptomatic moderate AS has an event rate of approximately 5% per year. If symptoms are present, the event rate is at least 10% per year. Therefore, individuals with moderate AS are unfit for military flying duties. For mild-to-moderate asymptomatic AS, consideration may be given to restricted low-performance flying operations. Patients with severe AS are candidates for valve replacement and are unfit for military flying. Although the incidence of sudden death, even with severe AS, is likely less than 1% per year, licensing agencies considering medical certification of aviators with moderate or severe AS should consider the potential for other events, including angina and syncope, which may occur in emergency situations with high levels of adrenergic stimulation. Carefully supervised exercise or pharmacologic (e.g., dobutamine) stress testing may help identify individuals with stress-induced symptoms despite a negative medical history, or conversely, patients with a low cardiac output and only mild-to-moderate AS.

Aortic Regurgitation

Aortic regurgitation (AR) develops as a result of aortic valve disease, either idiopathic or secondary to BAV, rheumatic heart disease, endocarditis, or degenerative disease with sclerosis and calcification of the valve. It may also develop as a result of aortic root dilatation related to hypertension, aortitis, or connective tissue disease. In the aircrew population, BAV and idiopathic regurgitation through a trileaflet valve are most common.

The hemodynamic effects of chronic AR are due to volume overload, with gradual enlargement and hypertrophy of the left ventricle. Symptoms develop only late in the process as left ventricular systolic function declines and left ventricular failure develops. Initial symptoms are unexpected shortness of breath on exertion, reduced exercise tolerance, and general fatigue, and later, as left ventricular failure ensues, orthopnea and paroxysmal nocturnal dyspnea. Angina may develop in the absence of coronary disease due to hypertrophy-driven increased oxygen demand with reduced coronary perfusion.

Rarely, acute AR may develop as a result of endocarditis or aortic dissection. Such a sudden volume overload may be poorly tolerated with resultant pulmonary congestion and edema, and low-flow state with shock and sudden death possible outcomes. This is a medical and surgical emergency.

The classical clinical finding in AR is a high-pitched decrescendo diastolic murmur heard along the sternal border (left side for aortic valve disease, right side for aortic root disease). This murmur is easily missed, especially with mild AR. Often more prominent is a short ejection systolic murmur radiating up the carotids from flow turbulence due to the increased stroke volume. Auscultation of such a systolic murmur should prompt careful examination for an AR diastolic murmur, which may be enhanced by listening with a breath-hold at end-expiration in the seated position with the individual leaning forward or during a squat. When the AR jet is directed across the anterior mitral valve leaflet

thereby preventing full opening, auscultation may reveal a rumbling diastolic murmur at the apex due to functional mitral stenosis (Austin-Flint murmur). Other clinical signs include awide pulse pressure, and rapid decay of the pulse pressure.

The diagnosis and quantification of severity are best assessed through echocardiography and Doppler studies. The 2-D echocardiogram will provide information on left ventricular size and function. AR is graded as trace, mild, moderate, or severe based on several qualitative and semiquantitative measures on color flow imaging, Doppler-derived pressure decay half-times, and flow reversal in the descending thoracic aorta. Pressure halftimes greater than 600 m/s are consistent with trace or mild AR, 500 to 600 m/s with mild AR, 200 to 500 m/s with moderate AR, and less than 200 m/s with severe AR. Other investigations used to quantify the severity and hemodynamic consequences of chronic AR include aortography, rest and exercise radionuclide ventriculography, and magnetic resonance imaging (MRI).

As left ventricular volume increases, treatment with vasodilators, such as hydralazine and nifedipine, have been shown to delay the requirement for valve replacement and improve operative results, and are currently recommended therapy for even asymptomatic patients with severe AR and left ventricular dilatation. ACE inhibitors have similar hemodynamic effects and are more often prescribed, although results of the outcomes are not as well demonstrated. Valve replacement is indicated as symptoms worsen, or in asymptomatic individuals with failing left ventricular systolic function (ejection fractions <25%) or severe dilatation (end-systolic or end-diastolic dimension >55 or 75 mm, respectively).

From an aeromedical standpoint, chronic AR is unlikely to cause acute incapacitation, and aeromedical concerns relate to issues of selection into flying training, medications used to treat AR in later stages, and possible aggravation of AR by stresses encountered in high-performance flying.

With regard to selection, individuals with moderate or severe AR are likely to progress to require valve replacement and are not good candidates for entry into flying training, especially military. While slight or even mild regurgitation through the mitral, tricuspid, and pulmonic valves is not an uncommon finding on routine screening echocardiograms, trace AR is a rarer finding, and mild AR is very uncommon. An analysis of 52 military aviators with BAV and mild AR revealed that only 15% progressed to moderate AR over a 3.5 year follow-up (mean age at baseline 47 years, follow-up range 0.5 to 14.5 years) (34). Therefore, the available information suggests that mild or less AR is unlikely to progress, and therefore may be acceptable for selection into military pilot training. However, variability in valve morphology (tricuspid versus bicuspid, degree of thickening and/or calcification) may accelerate or slow AR progression compared to published rates. Individuals with these findings may present an increased risk for training investment resources (1).

The possible hemodynamic effects on AR of repeated exposure to radial accelerative forces and countermeasures are unknown, but the repetitive cycling of preload and afterload could theoretically aggravate both aortic root dilatation and aortic regurgitation. The echocardiographic study, which addressed the question of possible adverse cardiac effects of repeated exposure to high sustained $+G_z$ in NATO aircrew, found no cases of AR in the cohort of 289 high-performance pilots, while four cases were noted in the control group of 254 non–high-performance pilots (33). A small USAF study followed 16 high-performance pilots and a control group of 16 low-performance pilots for a mean of 5 years. Severity of AR increased in five low-performance pilots but in only one high-performance pilot, and left ventricular function and dimensions remained stable in both groups (1).

Current aeromedical recommendations are that individuals with mild AR are fit for unrestricted flying duties. Aircrew with moderate AR should be restricted from high-performance aircraft. Aviators with severe AR and normal LV dimensions and systolic function may likewise be fit for low-performance restricted flying, but as LV dilatation occurs such individuals should receive vasodilator therapy as standard of care and may then be considered unfit for military flying duties. Alternatively, because sudden events are not an issue, severe AI might be considered acceptable for continued low-performance flying until the aviator meets published guidelines criteria for valve surgery. The decision as to civilian medical certification and licensing will depend on the policy of the licensing agency regarding vasodilator therapy. All aircrew with AR beyond trace should be followed up with echocardiographic and Doppler study at 1- to 3-year intervals.

Mitral Regurgitation

Mitral regurgitation (MR) can develop due to abnormalities in the mitral leaflets or supporting structures including the annulus, chordae tendineae, and papillary muscles. Rupture of a major chorda tendinea or papillary muscle most commonly occurs in the setting of ischemic heart disease and causes acute, often severe MR. This is a medical emergency with sudden rise in left atrial and pulmonary vascular pressures leading to pulmonary congestion and edema and often atrial fibrillation.

The most common cause of progression of chronic MR to moderate or severe degrees is myxomatous mitral valve disease with MVP. Other causes include dilated cardiomyopathy, endocarditis, and rheumatic heart disease. Chronic MR causes volume overload of the left ventricle, which dilates to maintain stroke volume. Left atrial enlargement develops to compensate for increased volume and pressure. Eventually, progressive left ventricular dilatation leads to contractile impairment and heart failure. Atrial fibrillation may develop with progressive left atrial enlargement, predisposing to thromboembolic events.

Early symptoms of MR include easy fatigability and unexpected dyspnea on exertion. Progression leads to heart failure symptoms with orthopnea, paroxysmal nocturnal

dyspnea, and edema. Physical findings are an apical systolic murmur radiating laterally to the axilla. Posteriorly directed jets may be heard over the back. With myxomatous disease, a variable midsystolic click of MVP may be heard preceding the murmur. As MR progresses in severity, the duration of the murmur may extend through systole. Paradoxically, severe MR may have little to no murmur, even on careful auscultation. In late stages of disease, the first heart sound may be muffled, and a third heart sound often develops.

Repetitive exposure to high sustained $+G_z$ with related protective countermeasures that increase afterload might be expected to aggravate the severity of MR, but there is little data to address this concern. The NATO aircrew echocardiographic study (33), which addressed the question of possible adverse cardiac effects of repeated exposure to high sustained $+G_z$, found no cases of abnormal (as opposed to physiologic) MR. Albery (35) reported no change in MR in 18 centrifuge subjects each exposed to more than 45 minutes of cumulative $+G_z$ exposure greater than or equal to 2 G. Although MR was not specifically monitored, a longitudinal study of six female centrifuge subjects showed no change in left atrial dimension after approximately 100 exposures of 3 minutes to high $+G_z$ (up to 9 G) over 7 months. This is considered to be approximately equivalent to a 3-year G-dose in typical F-16 pilots (36).

Aeromedical disposition of MR must take into consideration both the underlying cause and hemodynamic effects. Evaluation should include an echocardiographic and Doppler study to assess the degree of regurgitation as well as cardiac structure and function. Transesophageal echocardiography (TEE) provides a sensitive assessment for MR and may be required for individuals with technically unsatisfactory transthoracic echocardiograms. Exercise stress testing will provide information on exercise tolerance and helps assess for exercise-induced arrhythmias. Stress echocardiography or exercise radionuclide ventriculography may be helpful to assess the left ventricular response to exercise.

Trace or even mild MR is a common finding on routine echocardiographic Doppler studies in aircrew candidates (1,31). In the presence of a structurally normal heart, including the mitral valve apparatus, this is considered to be a physiologically normal variant. The available evidence suggests that physiologic MR is not aggravated by even high-performance flying, and such individuals are fit for training and unrestricted flying and licensing.

Progressive MR leading to moderate-to-severe and severe regurgitation is an abnormal finding. While G-exposure apparently does not affect physiologic MR, there is no data available on moderate or severe MR and such individuals may be restricted from high-performance flying, particularly when there is evidence of chamber dilatation or left ventricular dysfunction. Continued non–high-performance flying and civilian licensing are reasonable with annual review, provided there are no symptoms, sinus rhythm is maintained, the left atrium is not markedly enlarged ($<$50 mm) and left ventricular function is normal or near normal.

Mitral Stenosis

Mitral stenosis is most commonly acquired as result of rheumatic fever or as a complication of systemic lupus erythematodes. It may remain asymptomatic for many years, and may be discovered in candidates for training or licensing with an unknown or undisclosed rheumatic fever history—only approximately 50% of patients with isolated mitral stenosis recall a history of rheumatic fever. Careful clinical examination should detect the characteristic opening snap and low-pitched diastolic rumble heard best with auscultation in the left lateral decubitus position at the apex with the bell of the stethoscope. The first sound may be accentuated. ECG may show evidence of left atrial enlargement, with biphasic P waves in V1 being the earliest sign, and widened, notched inferior P waves evolving as enlargement progresses. The chest x-ray may show left atrial enlargement, pulmonary congestion, and mitral calcification.

Mitral stenosis restricts transmitral forward diastolic flow, which is maintained by elevating left atrial pressure, leading to progressive left atrial enlargement. Symptoms typically develop in the third and fourth decade as forward flow is progressively restricted and pulmonary venous and capillary pressures rise, with unexpected dyspnea on exertion and easy fatigability as the earliest symptoms. Left atrial enlargement predisposes to atrial fibrillation, which occurs in 30% to 40% of patients with symptomatic mitral stenosis.

Doppler echocardiography is the test of choice to establish the diagnosis and assess the severity of mitral stenosis. Valve morphology and planimetered opening valve area, left atrial and ventricular dimensions, and left ventricular function are assessed on the 2-D study. And, valve area can be further calculated by measuring the pressure gradient with Doppler.

Interventions to relieve mitral stenosis include percutaneous balloon valvuloplasty, surgical commissurotomy, and valve replacement. Balloon valvuloplasty is the initial intervention of choice. For patients not suitable for valvuloplasty, such as with significant concurrent MR, surgical commissurotomy provides equivalent short- and medium-term results. Both procedures are palliative, though, with stenosis gradually recurring, and approximately 5% to 10% of patients requiring a repeat procedure within 5 years.

Rheumatic mitral stenosis is a progressive disease and is disqualifying for candidates for military aviator training. Applicants for civilian licensing require careful assessment but may be suitable provided the individual is asymptomatic and the degree of stenosis is mild (valve area $>2.5\ cm^2$), sinus rhythm is maintained, left ventricular function is normal, and the left atrium is not markedly enlarged ($<$50 mm).

Tricuspid Valve Disease

Trace and mild tricuspid regurgitation are very common findings, detected on more than half of screening echocardiograms in military pilot candidates (1,31). Even moderate tricuspid regurgitation is not unusual, and should be considered physiologic and not a disqualification for aircrew selection or training, in the absence of secondary causes. Isolated severe tricuspid regurgitation is rare, but may be

caused by rheumatic disease, tricuspid valve prolapse, endocarditis, trauma, carcinoid, or secondary to right ventricular dilatation due to pulmonary or cardiac causes. The clinical findings are a long or pansystolic murmur at the lower left or right sternal border that increases with inspiration. Prominent V waves are typically observed in the jugular venous pulse, and in severe cases, pulsatile hepatomegaly.

Echocardiography confirms the diagnosis and assesses the severity and cause. Aeromedical disposition will depend on the underlying cause as well as the severity of regurgitation. Isolated moderate-to-severe or severe regurgitation, for example due to trauma or prolapse, with normal right ventricular function may be suitable for low-performance restricted military flying or civilian licensing with regular periodic echocardiographic and clinical assessment.

Tricuspid stenosis occurs in 5% to 10% of patients with rheumatic mitral stenosis. The rheumatic tricuspid valve is usually both stenotic and regurgitant. The involvement of multiple cardiac valves is a disqualification for military aviator selection and would likely be for commercial civilian licensing.

Pulmonary Valve Disorders

Right ventricular outflow obstruction can be infundibular, supravalvular, or due to valvular pulmonic stenosis (PS). Infundibular stenosis is almost always associated with a ventricular septal defect. Valvular PS is generally congenital and mild in severity when diagnosed in adults. The characteristic physical finding is a systolic crescendo–decrescendo murmur heard best along the left upper sternal border, accentuated by inspiration, which radiates to the left infraclavicular area. There may be an ejection click, which is better heard during expiration. The diagnosis is confirmed by echocardiography, which shows a conical or dome-like fusion of the pulmonary valve cusps. In most cases, the severity can be graded by Doppler flow assessment of velocities, although occasionally right heart catheterization may be necessary. Mild PS (peak gradient <30 mm Hg) generally carries a good prognosis and such individuals are considered medically fit for military aviator selection and training, and for civilian licensing, with periodic assessment for the unusual situation of progression. Moderate or severe PS results in right ventricular hypertrophy and is more likely to be progressive, resulting in symptoms such as undue exertional dyspnea due to limitation of cardiac output. Moderate to severe PS is treated with balloon valvulotomy with good long-term outcomes. Individuals with moderate or severe PS are unfit for military aircrew selection, but may be fit for civilian licensing if asymptomatic, with good exercise tolerance on exercise stress testing. Aviators who are postvalvulotomy may be acceptable for continued civilian licensing or military flying duties, provided there is a good hemodynamic result and no significant residua or complications.

Trace and mild degrees of pulmonary regurgitation (PR) are common findings on screening echocardiograms and may be viewed as physiologic normal variants. Progression is rare and such individuals are considered medically fit for military aircrew selection and civilian licensing. Moderate and severe PR are rare but require case-by-case judgment for aeromedical disposition, based on the severity of PR, symptoms, and hemodynamic effects such as right ventricular dilation and tricuspid regurgitation.

Valve Replacement or Repair

Valve replacement or repair may be required for progressive or acute regurgitation, endocarditis, or stenosis, generally involving the aortic or mitral valves. Criteria for valve replacement and management of such patients have been well established. Although improving hemodynamics, valvular surgery carries the potential for long-term complications with event rates often unacceptable for continued flying. Replacement valves may be mechanical or bioprosthetic, either heterografts (xenografts) derived from animal tissue (bovine, porcine) or homografts derived from human sources. Complications include gradual or sudden valve failure requiring reoperation, endocarditis, thrombosis, thromboembolism, and arrhythmias. Mechanical valves require life-long warfarin anticoagulation with attendant risk of significant bleeding, which must be factored into the risk assessment for aeromedical disposition. The event rate for complications related to mechanical valves and required anticoagulation may exceed 5% per year and is generally not compatible with continued flying status (37). Heterograft valves do not require anticoagulation, but are more likely to gradually deteriorate and to require replacement. The overall complication rate for standard bioprosthetic valves also exceeds 5% per year (38). Mechanical and heterograft bioprosthetic valves are considered disqualifying for military flying, and with complication rates exceeding 5% per year, do not meet the generally accepted 1% rule for commercial licensing. Newer stentless bioprosthetic valves have improved hemodynamics, although the thromboembolism rate remains approximately 1% per year, and valve degeneration requiring replacement is approximately 2% per year.

More promising from an aeromedical standpoint are human homograft valve replacements. These procedures involve placement of an allograft valve, which is antibiotic-sterilized and preserved by cryotherapy. The Ross procedure involves replacement of a diseased aortic valve with a pulmonary autograft, the pulmonic valve then being replaced by an aortic allograft. For younger patients, autografts tend to have a better long-term survival. As for other bioprosthetic valves anticoagulation is not required. The long-term outcome is generally better for homografts than heterografts, although the incidence for both valve-related complications is approximately 2% to 4% per year. However, aeromedically worrisome complications such as acute valve failure are extremely rare, and in selected patients with excellent surgical outcomes and a return to normal or near normal hemodynamics, consideration may be given to flying duties in multicrew operations.

The USAF currently has five aviators with replaced aortic valves on flight duties, nearly all with aortic homografts (Strader, JR, 2007). All but one have been restricted

to multipilot, low-performance operations. Recently, however, the USAF returned to unrestricted flying duties—the first high- performance pilot with an aortic valve replacement (39). In this case, a novel porcine ''whole root'' heterograft was used, which restored normal hemodynamics of the left ventricular outflow tract, aortic valve, and aortic root as a whole (40). These types of investigational approaches to aortic valve replacement are promising from an aeromedical viewpoint, in that they appear to preserve normal hemodynamics with reasonable durability and low-event rates. As with all aviators with valve surgery, however, these must be evaluated on a case-by-case basis.

Mitral valve replacement carries complication rates similar to that for aortic valve replacement. The need for anticoagulation is even greater with mechanical and bioprosthetic mitral valve replacement due to lower flow rates across the valve and an increased likelihood for thrombus formation. Therefore, mitral valve replacement generally necessitates warfarin anticoagulation and in general is a contradiction to aviation duties. However, surgical repair rather than replacement of regurgitant mitral valves has resulted in lower postoperative complication rates and improved long-term prognosis. Repairs of degenerative, myxomatous, or flail mitral valve leaflets usually involve resection of the diseased leaflet with surgical repair of the remaining sections. Mitral valve repairs may often be combined with ring annuloplasty to attempt to normalize mitral annular geometry and reapproximate the mitral leaflet cusps, particularly if the preoperative condition was associated with severe MR. With an excellent surgical outcome, improvement in hemodynamics, normal or near-normal valve and myocardial function, maintenance of sinus rhythm, and good exercise tolerance, consideration may be given to a return to restricted multicrew operations after mitral valve repair. The USAF currently has eight aircrew with repaired mitral valves on restricted flight duties (Kruyer, WB, 2007).

When an aviator is faced with the need for valve surgery, knowledge of the restrictions and associated risks and benefits of the various surgical options can assist in medical decision making. Therefore, close collaboration between the surgical consultant, aviator, and aerospace medicine specialist is recommended. Most aviators choose to avoid valve replacements requiring Coumadin if possible, due to the associated event rates and aviation restrictions inherent with mechanical valves. Counseling on the expected outcomes of alternative valve replacements (e.g., aortic homografts) or repairs (e.g., mitral) and rates of long-term complications such as the risk for eventual reoperation is crucial before any operative decision.

Aeromedical management of aviators who are on any type of flight duties with repaired or replaced cardiac valves requires serial studies to assess for continued competence of the surgical repair and lack of associated complications. This can largely be achieved with serial echocardiography to assess for valve function, continued anatomic alignment, left ventricular function, valvular hemodynamics, and degree of residual regurgitation or stenosis, if any. Stress echocardiography can be useful to assess valve function under physiological stress, and can be achieved with either exercise (treadmill or supine bicycle ergometry) or pharmacologically (dobutamine infusion). For aviators with aortic valve replacements, it is important to know if the coronary arteries were reimplanted along with the valve replacement, as this would necessitate periodic screening for coronary artery stenosis at the reanastomosis. Finally, incorporating 24-hour ambulatory ECG monitoring into a periodic evaluation allows for assessment of any associated arrhythmias, although the appearance of valve surgery–related arrhythmias late after operative repair is rare.

CONGENITAL HEART DISEASE

Congenital heart disease may present aeromedically in candidates or license applicants with known repaired congenital defects, with undiagnosed defects detected clinically or on echocardiographic screening, or in aircrew following training or licensing.

Bicuspid Aortic Valve

BAV is the second most common form of adult hereditocongenital heart disease after MVP. The incidence in the adult population based on necropsy studies is 1% to 2% (41), but on screening echocardiograms in aircrew candidates, the incidence was found to be only 0.5% to 0.9% (1,31). The lower incidence in military pilot candidates may represent a selection bias because applicants must first pass screening medical examinations.

Clinically, BAV may be suspected by the presence of systolic ejection clicks. These are high-pitched sounds occurring concurrent with or immediately following the first heart sound and are best heard with the diaphragm in the aortic area just to the right of the upper sternum or at the apex. There may be an associated aortic outflow murmur due to flow turbulence without stenosis, or murmurs related to aortic stenosis or regurgitation, which occur as complications. Auscultatory findings in BAV are not consistent, and in many individuals BAV is asymptomatic and clinically silent before the onset of complications. 2-D echocardiography provides a sensitive and specific tool for diagnosis of BAV and for serial follow-up for developing complications.

Complications of BAV include endocarditis, aortic stenosis, aortic regurgitation, and ascending aortic aneurysm formation with or without aortic dissection. Most of the available natural history data is based on necropsy studies with attendant selection bias, with a paucity of data based on echocardiographically diagnosed, normally functioning BAVs. Complications of BAV are age related, with endocarditis and critical aortic stenosis most common in childhood and early adult life, then aortic regurgitation and aortic dissection more common in early to middle adult age.

The BAV is a substrate for endocarditis with estimates as high as 30% based on selected case series, although the true incidence is likely much less (41). BAV incurs about a ninefold increase in the relative risk of aortic dissection, which is usually preceded by aortic root dilatation, often associated with hypertension. Aortic root enlargement is a common finding in BAVs, and occurs as often in normally functional BAVs as in those complicated by stenosis or insufficiency. With the decline in rheumatic fever, BAV is the most common substrate for development of aortic stenosis, which tends to develop slowly and progressively over time with the development of sclerosis in the second and third decade and calcification thereafter. The average aortic valve gradient increases concurrently by 18 mm Hg per decade. Aortic regurgitation in BAVs may occur in isolation, or as a consequence of endocarditis or aortic root dilatation. Conversely, aortic regurgitation may cause aortic root dilatation. Aortic regurgitation tends to occur at a younger age than aortic stenosis, affecting aircrew during their flying career.

From an aeromedical standpoint, BAV is primarily of concern because of the potential for complications. Over a lifetime, serious complications occur in at least one third of individuals born with BAV (41). Of these complications, only aortic dissection is likely to present as sudden incapacitation, although aortic regurgitation may develop suddenly in an infected valve. In an analysis of 52 active duty USAF aviators with BAV (mean age 47 years), baseline trace or mild AI and AS were common (60% to 70% of the cohort). Over an average of 3.5 years of follow-up, progression to mild or moderate AR or AS was relatively common, occurring in more than half the subjects. However, progression to severe disease was rare (34). Therefore, while it is true that many individuals with BAV ultimately progress to requiring surgical intervention, most of these will not happen until after a military aviation career is complete. This may be a larger issue for civilian aviation authorities because age restrictions on civilian licensing would allow continued duties for many of the individuals who will ultimately progress to needing medical or surgical intervention.

From a licensing or retention standpoint, individuals with normally functioning BAVs are fit for unrestricted flying. Annual clinical assessment and periodic echocardiographic follow-up (e.g., every 2 to 3 years) should be performed to assess for developing complications. It is a risk assessment decision whether or not to admit into military flying training applicants with BAV. Most such individuals are likely to be able to complete their projected career, but a policy decision that admits individuals with BAV must accept a degree of attrition of trained aircrew due to later complications. Aircrew admitted into training with BAV will require periodic echocardiography to assess for developing complications, and will require antibiotic prophylaxis for dental and surgical procedures. The impact of the stresses of military flying such as G-forces and G-protection life support equipment and maneuvers on the progression of BAV complications such as aortic root dilation, dissection, and aortic regurgitation is unknown. A recent publication, however, found that repeated exposure to $+G_z$ stress over a follow-up of 12 years in high-performance pilots did not accelerate progression of BAV compared to low-performance pilots, suggesting that the presence of a BAV in and of itself should not be automatically disqualifying for aviator duties (42).

Mitral Valve Prolapse

MVP occurs when the leaflets of the mitral valve extend beyond the plane of mitral annulus into the left atrial cavity during ventricular systole. This is a common congenital valvular abnormality, with prevalence in the general population of 2% to 4% (1,24). The prevalence of MVP in most aviation cohorts has been reported as ranging from 0.2 to 1.0% (1,32), probably reflecting a selection bias due to flight-commissioning physicals. The diagnosis of MVP is usually made on 2-D echocardiography and the definition has been standardized to require prolapse of at least 2 mm beyond the annular plane in the parasternal long-axis view. M-mode findings or displacement of the posterior leaflets on apical views may provide supportive evidence. MVP may be suspected clinically when a midsystolic click is heard on auscultation. The click varies in timing with changes in left ventricular volume, moving later in systole as volume increases. Therefore, a true midsystolic click can be differentiated from other sounds by maneuvers on physical examination designed to alter left ventricular volume conditions (squat, Valsalva strain, and release phase). A brief late systolic murmur often, but not always, follows the midsystolic click. These auscultatory findings may be transient and dissimilar on different days, reflecting differing autonomic tone, hydration, volume status, and other factors.

Morphologically, MVP is often associated with other structural abnormalities of the mitral chordae and subvalvular apparatus. There are commonly histological abnormalities of the collagen matrix of the leaflets themselves, which predispose over time to the development of mitral leaflet thickening and myxomatous degeneration due to glycoprotein deposition, usually at sites of chordal insertion. The chordae undergo similar destructive changes with elongation and thinning (the anatomic substrate for chordal rupture). The posterior leaflet is most often involved (67%), with isolated involvement of the anterior leaflet infrequent (10%), and both in approximately 25%.

The major functional concern arising from MVP is the degree of any associated MR. As the valve deteriorates over time, MR may progress from being absent or only trivial early in the disease to severe MR requiring surgical correction. In the late stages, a sudden increase in the degree of MR may occur as diseased chordae may rupture and flail leaflets result. Although the timeline for progression of disease typically is in decades, young flight crew and pilot applicants with MVP and any degree of MR pose operational and selection questions to most aviation organizations and authorities regarding the risk for progression to severe disease. Additional concerns with MVP include the risk of infective endocarditis (IE), which appears to be related to

the degree of structural valve abnormality. The presence of a click alone confers no increased risk for IE. However, the incidence of IE has been as high as 6% to 8% in patients with MVP and regurgitant murmurs. In case-controlled studies, the overall relative risk is approximately five times normal (43). The current consensus recommendation from the American Heart Association for endocarditis prophylaxis is that antibiotics are not recommended for most individuals with MVP.

Cerebral transient ischemic attacks and stroke have been attributed to MVP. There are multiple confounding factors, however, including prothrombotic coagulation disorders, other cardiac substrates such as patent foramen ovale (PFO), atrial septal defect (ASD), or left atrial enlargement with atrial fibrillation. However, both the absolute and relative attributable risks are extremely low, and in persons younger than 45 years, the Framingham investigators found no evidence linking MVP with stroke (1).

Although the absolute risk for clinical complications is low, because of the increased relative risk for complications including endocarditis, thromboembolic events, progressive MR, and arrhythmias, particularly in the high sustained $+G_Z$ environment, MVP has been considered disqualifying for selection in pilot training by most NATO air forces (30). The USAF policy regarding MVP changed in 2004, when pilot applicants with MVP and mild or less associated MR were allowed waivers for initial pilot training. When discovered in a trained aircrew, the policy is generally to allow continuation of flying duties, including high performance flying, but with regular surveillance for complications. This should include an echocardiographic/Doppler study, treadmill test, and 24-hour ambulatory ECG monitoring. For duties involving high sustained $+G_z$, a monitored centrifuge evaluation for arrhythmias may be considered; however, this was found to be unproductive in a review of approximately 400 USAF aviators with MVP. While potentially incapacitating endpoints occur infrequently when MVP is discovered in trained aircrew, the overall rate of disqualifying endpoints was found to be 1.4% per year in a retrospective study of USAF aircrew (1).

Defects of the Atrial Septum

Defects in interatrial septal development may result in an ASD, atrial septal aneurysm (ASA), or PFO. There are three types of ASD—ostium secundum, ostium primum, and sinoseptal defects. Ostium secundum ASDs are a result of abnormal development of the septum primum with failure to cover the fossa ovalis. This is the most common type of ASD, representing approximately 75% of all ASDs. Inadequate development of the endocardial cushion with failure to close the ostium primum results in an ostium primum ASD. Because the anterior leaflet of the mitral valve also develops from the endocardial cushion, ostium primum defects are almost always associated with a cleft anterior mitral leaflet. Such defects are most commonly seen in Down syndrome. Ostium primum defects constitute approximately 15% of ASDs. Sinoseptal defects are the least common, representing only 10% or less of all ASDs. Sinoseptal defects result from abnormal embryologic evolution of the sinus venosus and sinus valves. The most common is the sinus venosus ASD, which is located near the inflow of the superior vena cava and is usually associated with anomalous pulmonary venous return from part or all of the right lung, either directly into the right atrium, or into to the superior vena cava.

Under normal circumstances, ASDs allow flow from the left to right atrium with resultant right-sided volume overload and enlargement of the right atrium and ventricle. The hemodynamic consequences depend on the size of the ASD. With transient reversals of interatrial pressure as may occur with straining, coughing, Valsalva, anti-G straining maneuvers, or positive pressure breathing, flow may be reversed and ASDs could hypothetically serve as a conduit for embolic material, whether clot or venous gas bubbles.

The development of symptoms or complications from ASDs depends on the magnitude of the shunt. ASDs with shunts greater than a 1.5 pulmonary-to-systemic flow ratio generally produce significant right ventricular volume overload with resultant symptoms, including easy fatigue, dyspnea, especially on exertion, and arrhythmias, especially atrial fibrillation. Undetected, ASDs may go on to cause pulmonary hypertension with reversal of the shunt (Eisenmenger syndrome). In aircrew, who by nature of their job undergo frequent periodic medical screening, ASDs are most likely to be detected while still asymptomatic, during clinical examination, ECG or chest x-ray, or on an echocardiogram. Even after closure of an ASD, patients are at increased risk for atrial arrhythmias, especially atrial fibrillation, particularly if pulmonary artery pressures have been elevated.

ASDs typically have a fixed split second heart sound which lacks variability with respiration, and a right ventricular systolic outflow murmur (a midsystolic murmur heard best along the upper left sternal border). Careful auscultation may reveal an early diastolic rumble reflecting the volume overload flow across the tricuspid valve, heard best just to the right of the lower sternum. The ECG may show a mild right ventricular conduction delay (RSR′ in V1/V2), and a frontal axis greater than 90 degrees. The chest x-ray may show prominent main and branch pulmonary arteries, and right ventricular enlargement.

TTE is usually the procedure of choice for demonstrating and assessing an ASD. Flow across the septum can be demonstrated with color Doppler, and right atrial and ventricular chamber sizes can be determined. Pulmonary to systemic blood flow ratio can be quantified using Doppler techniques.

Closure of ASDs may be performed by direct surgical repair, or more recently by transcatheter devices. These involve the deployment of an occlusion device from a femoral venous approach. The devices work best in patients with centrally located secundum defects. Closure is indicated clinically for ASDs with pulmonic-to-systemic flow ratios greater than 1.5 and right ventricular enlargement, and for improvement of symptoms.

Aeromedical disposition of ASDs depends on the type of ASD and the magnitude of any associated shunt. The aeromedical concerns would be the potential for right-to-left shunting of blood clots or venous gas emboli. Hemodynamically insignificant ASDs are of no aeromedical consequence and may be considered for entry into flying training or for continued unrestricted flying. Prognosis after successful and uncomplicated closure of significant secundum ASD is normal if repair is performed for candidates younger than 25 years. Prognosis is significantly reduced for repairs performed after age 25, due to late occurrence of atrial fibrillation, stroke, and right heart failure. Successful ASD repairs performed earlier than age 25 are candidates for flying training and unrestricted flying if there is no residual shunt and cardiac structures and functions are normal. Repairs performed after age 25 should be considered on a case-by-case basis and followed more carefully. Prognosis for repaired sinus venosus ASD is similar to that of secundum ASD and may be treated similarly (1). Prognosis after repair of other ASDs is often not as favorable as for secundum ASD. These should be considered on a case-by-case basis. Again, repair at an early age offers the best outcomes. Specifically, repaired ostium primum ASD may experience concerning late events, such as significant mitral or tricuspid regurgitation, atrial fibrillation, and conduction defects (1).

Patent Foramen Ovale

Persistent patency of the foramen ovale into adult life is relatively common, and is normally of no hemodynamic consequence. The incidence of PFOs in autopsy series is approximately 25%, decreasing with age from 34% in the first three decades to 25% in the fourth to eighth decades. The average foramen size increases with age, with an overall average of 4.9 mm (44).

Clinical examination cannot detect PFOs. TEE with color flow or contrast injection is considered the "gold standard" for PFO detection, with close to 100% sensitivity for detection of PFOs compared to autopsy. Howver, TEE is an invasive and unpleasant procedure not without risk. TTE shows good specificity when compared to TEE, but suffers from lack of sensitivity, which is reported as less than 50%. This may be improved by the use of contrast agents, such as saline bubble infusion, together with a concurrent provocative maneuver such as a Valsalva strain, but TTE is still less than satisfactory as a stand-alone screening tool. ASAs and Chiari networks are associated with an increased prevalence of PFOs, and the presence of either on a TTE should intensify the search for a PFO.

The pressure difference between left and right atrium is usually small, approximately 5 mm Hg, and provocative maneuvers such as a Valsalva or anti-G strain may transiently reverse the pressure after release of the strain. Contrast imaging, for example, with a saline bubble infusion agitated in a double syringe system and injected to reach the right atrium just as the strain is released, increases the sensitivity for detection of a right to left shunt. Using contrast injection increases the sensitivity of TTE or TEE for detecting a PFO. Inferior vena caval flow, which courses along the atrial septum, may divert superior vena caval flow away from the septum, resulting in false-negative contrast infusions injected from the arm.

Because of the frequent occurrence of PFO and the low risk of events, most licensing agencies would consider asymptomatic, incidentally discovered PFOs to be acceptable for selection into flying training and for unrestricted flying duties. The aeromedical concerns relate to the hypothetical potential for PFOs as right-to-left conduits for blood clots, causing stroke, or for venous gas emboli resulting from altitude decompression, with resulting central nervous system DCS.

Cerebrovascular accidents (CVAs) (stroke or transient ischemic event) are uncommon in the aviator population but in this generally younger population, a PFO might serve as a substrate for embolic CVA. The incidence of PFO is particularly high (>50%) in cases of cryptogenic stroke where no other cause is identifiable. Careful screening for a right to left shunt including a PFO should be included in the evaluation of any aviator suffering an unexplained cerebrovascular event. Detection of a PFO as a substrate for such an event may allow consideration for a return to flying duties if there are no neurologic sequelae of aeromedical significance, and with successful closure of the PFO.

Most information regarding the increased risk for type II DCS with PFO is derived from diving studies. Although similar, in that decompression is involved in both, altitude and diving exposures are physiologically not equivalent and data from diving is neither directly applicable nor directly transferable to altitude DCS scenarios.

Retrospective analysis of diving data has demonstrated an increased relative (2–3 times) risk for type II DCS, particularly with early involvement of the brain, in divers with PFO, although the absolute risk remains low. MRI studies of sports divers have demonstrated significantly more ischemic brain lesions [(the white matter lesions that have been described in this context are unfortunately not very specific and are often the equivalent of "leucoaraiosis" = "white matter lesion" that are seen in many of our general patients) and association is not equal to causation] in divers with and without PFO compared to control subjects, but the divers with PFOs had a 4.5 fold increase in DCS events, and twice as many ischemic brain lesions than divers without PFO (45). On the basis of such information, it would seem prudent to screen aircrew who develop type II DCS during or following altitude decompression for any right to left shunt including a PFO.

Treatment of individuals with a PFO and CVA or DCS event remains controversial. While transvenous placement of PFO closure devices is an increasingly mature technique with excellent results, closure of a PFO in individuals who have suffered a CVA or DCS event necessarily implies that the PFO is believed to have been causal. However, the assumption of causality in individuals with a PFO and CVA or DCS is highly uncertain. The clinical literature is heterogeneous with respect to investigations addressing

causality of PFOs in CVA and DCS. Previous prospective and retrospective studies of high quality have often reached incongruent conclusions regarding causality of PFO in cryptogenic stroke and DCS; therefore, the clinical and aeromedical disposition of individuals who have suffered from these events must by nature be highly individualized. The finding of a PFO in any given individual alone is insufficient to imply causality given the high incidence of PFOs in the overall population. Therefore, decisions regarding PFO closure and/or resumption of aeromedical duties are best made on case-by-case basis. Until a clearer picture of the causal relationship emerges, a ''one-size fits all'' aeromedical policy could result in unnecessary treatment procedures or suboptimal aeromedical disposition.

Atrial Septal Aneurysms

ASAs are not detectable on clinical examination and are usually discovered incidentally on echocardiography carried out for aeromedical screening purposes, or as part of a cardiac investigation. An ASA is defined on echocardiography by protrusion of the atrial septum greater than or equal to 15 mm beyond the plane of the interatrial septum or phasic excursion of the septum greater than or equal to 15 mm total amplitude during the cardiorespiratory cycle, with the diameter of the base of the aneurysmal portion measuring greater than or equal to 15 mm. The prevalence of ASAs in the general population is approximately 2%. They are frequently associated with a PFO, and both may act as a substrate for thromboembolic stroke (46).

From an aeromedical standpoint, while both PFO and ASA carry an increased relative risk for thromboembolic stroke, the absolute risk remains low. Because of the low absolute associated risk, ASAs should not be a disqualification for unrestricted licensing. With respect to medical selection for flying training, the issue is similar to BAV and involves a policy decision with respect to the risk assessment of investment of training dollars.

For aviators who do have a thromboembolic event and are found to have an ASA or PFO, and provided there is complete neurologic recovery, repair of the aneurysm or closure of the PFO surgically or with a transcatheter device may eliminate or minimize the risk for a recurrent event and allow a return to flying.

Ventricular Septal Defect

Because of the prominent auscultatory finding of a harsh pansystolic murmur along the left sternal border, previously undiagnosed ventricular septal defects (VSDs) are unlikely to present in trained aircrew. Small, hemodynamically insignificant VSDs present no increased risk from an aeromedical standpoint, and such individuals are medically fit for military pilot training and civilian licensing. Large hemodynamically significant VSDs create a significant left-to-right shunt with the development of pulmonary hypertension and pulmonary occlusive vascular disease. Such defects are generally surgically closed in early childhood, but later prognosis depends on the age at which repair occurred as well as pulmonary vascular complications. Repair before age 2 results in a good long-term prognosis, and such individuals are generally acceptable for military pilot selection and civilian licensing. Candidates for aircrew selection or licensing with VSDs repaired after age 2 require case-by-case assessment for pulmonary vascular resistance and pressures, and assessment for arrhythmias and conduction disturbances.

Patent Ductus Arteriosus

Likewise, a patent ductus arteriosus (PDA) is an unlikely finding in candidates for aircrew training or licensing because of the prominent continuous murmur heard best in the second left intercostal space, reflecting the continuous flow across the left-to-right shunt. Significant PDAs are almost always closed in childhood with surgical ligation through thoracotomy. Individuals with successfully repaired PDAs are acceptable for military aircrew training and civilian licensing. Evaluation should include assessment for any residual shunt, normal right ventricular function, and normal pulmonary vascular resistance and pressures.

Coarctation of the Aorta

Coarctation of the aorta is usually diagnosed in childhood, but may not be discovered until adulthood. The localized narrowing in the aortic arch usually occurs just distal to the left subclavian artery, resulting in a pressure differential between upper and lower extremities. Associated disorders include BAV, aneurysm of the aorta proximal or just distal to the coarctation, and cerebrovascular aneurysms. The diagnosis should be suspected with the finding of elevated blood pressures in the arms, and diminished pulses and blood pressures in the legs. Coarctations are generally discovered and repaired in childhood, but even after repair the aorta remains abnormal with risk of aneurysm, dissection, and rupture. Long-term prognosis is related to age of repair, with the best outcome for correction under age 9 (1). Because of the continuing risk even after surgery, individuals with repaired coarctations are considered unfit for military pilot training. Medical certification for licensing is predicated on the age of correction and outcome. Evaluation should include assessment for hypertension at rest and with exercise, and evaluation of left ventricular structure and function with echocardiography or nuclear imaging. The prognosis of insignificant coarctations with gradients less than 20 mm Hg is not well defined, and such individuals are likely acceptable for medical certification.

Hypertrophic Cardiomyopathy

Estimated prevalence of HCM is 0.02% to 0.2%. Screening echocardiograms performed in more than 20,000 USAF pilot candidates have revealed no cases of HCM. Spontaneous cases are common but approximately 50% are inherited in an autosomal dominant pattern with variable penetrance and clinical expression. HCM may be classified as obstructive or nonobstructive; only approximately 25% have a dynamic obstruction across the left ventricular outflow tract. The

presence and severity of left ventricular outflow tract obstruction are not related to sudden death or to symptoms. Most patients are asymptomatic or mildly symptomatic, but symptoms can be severe and are often exertion related. Although most sudden deaths occur at rest or with mild exertion, approximately one third occur during or just after vigorous activity.

Annual mortality rates of 1% per year or less are reported in various community populations and asymptomatic subjects. Sudden death is most common in younger subjects but may occur in middle age, even without prior symptoms. Markers for sudden death include young age at diagnosis, syncope, family member with HCM and sudden death, some genetic markers, severe hypertrophy, and nonsustained VT. Progression to dilated cardiomyopathy occurs in 10% to 15% and atrial fibrillation in another 10%.

Nonsustained VT on ambulatory monitoring, hypotension during graded exercise test, and a history of syncope may predict mortality greater than 1% per year. Absence of these factors predicts a mortality risk less than 1% per year. Nonfatal events such as presyncope, lightheadedness, chest pain, and dyspnea increase the aeromedically pertinent event rate to greater than 1% per year, on the order of 5% per year.

Military, commercial, and aerobatic flying are not recommended. Generally, private aviation might be considered for asymptomatic low-risk subjects. Annual 24- to 48-hour ambulatory monitoring, graded exercise testing, and echocardiography are recommended. Published guidelines for competitive athletes similarly recommend against participation except for select low-intensity sports, regardless of age, gender, symptom status, presence/absence of outflow obstruction, or treatment.

TACHYARRHYTHMIAS AND RADIOFREQUENCY ABLATION

Tachyarrhythmias are a significant aeromedical concern because of their sudden, often unpredictable onset and possible hemodynamic symptoms that might impair flying performance. Medications to suppress tachyarrhythmias were previously the primary therapeutic option and such therapy has its own clinical and aeromedical concerns. Perfect control is often unattainable and should not be assumed—the possibility of the tachyarrhythmia "breaking through" the medication must always be considered. And medications may have concerning side effects, especially the proarrhythmic effect of many antiarrhythmic medications. Radiofrequency ablation offers a curative approach for many tachyarrhythmias with return to restricted or even unrestricted flying duties for aviators who previously may have been permanently disqualified.

For purpose of this discussion, tachyarrhythmias will be defined as three or more consecutive ectopic supraventricular or ventricular beats at a rate of 100 beats/minute or faster.

Supraventricular Tachyarrhythmias

Atrioventricular Node Reentrant Tachycardia

This is the most common type of SVT, comprising approximately 60% of all instances of SVT. Dual or multiple pathways within the AV node create a micro reentrant circuit within the AV node. Most electrophysiologists consider that once an initial episode has occurred, atrioventricular node reentrant tachcardia (AVNRT) will recur throughout a patient's lifetime. Electrophysiology literature reports recurrence rates as high as 70% within a few months. However, such data are from tertiary center experience and likely suffer from referral bias. Recent experience regarding all SVT mechanisms from community-based studies and a military aviator population suggest recurrence rates of 10% per year or less after an initial episode of sustained SVT (1).

Atrioventricular Reentrant Tachycardia

This second most common type of SVT comprises approximately 30% of cases. Atrioventricular reentrant tachycardia (AVRT) involves a macro reentrant circuit involving an accessory pathway or bypass tract. WPW is the most common such condition. Usually, the direction of propagation of SVT is antegrade down the AV node pathway and retrograde up the accessory pathway, yielding a narrow QRS complex SVT. In occasional patients, the direction of SVT propagation is reversed, antegrade down the accessory pathway and retrograde up the AV node pathway, yielding a wide QRS complex SVT that may easily be mistaken for VT.

Other Supraventricular Tachycardias

Uncommon mechanisms comprise the remaining 10% of SVT cases, including automatic atrial tachycardia, intra-atrial reentrant tachycardia, and sinus node reentrant tachycardia.

Aeromedical Disposition of Supraventricular Tachycardia

The aeromedical concern is the risk of recurrent sustained episodes of SVT and possible symptoms that may incapacitate the aviator or otherwise adversely affect flying performance. SVT with associated hemodynamic symptoms (e.g., syncope, presyncope, lightheadedness) should be disqualifying for flying duties. Multiple episodes of sustained SVT, even without hemodynamic symptoms, should also probably be disqualifying because of the likelihood of future episodes and unreliability of medical control. If waiver is considered for medically controlled SVT, the most likely candidates for such clearance are digitalis preparations, β-blockers, and calcium channel antagonists. Cure of the SVT by radiofrequency ablation (discussed in the subsequent text) may also be eligible for waiver.

The aeromedical disposition of a single sustained episode of SVT without hemodynamic or other significant symptoms is more flexible. With possible recurrence rates of 10% or less per year, return to some categories of flying duties may be feasible, even in the absence of medical therapy. The USAF has returned such aviators to unrestricted flying duties for many years without incident (1).

Aeromedical Disposition of Atrial Flutter and Atrial Fibrillation

Atrial flutter is often associated with atrial fibrillation but may occur as an isolated rhythm disturbance. It presents unique considerations. In an otherwise healthy and unmedicated individual, the atrial rate is approximately 300 beats/minute and AV conduction is often 2:1, yielding a ventricular rate of 150 beats/minute. And 1:1 conduction, with a ventricular rate of 300 beats/minute, is quite possible, especially in young subjects. Although this may be tolerated well, such rates are certainly concerning. Medical therapy is required to increase the AV block ratio and thereby control ventricular rate. Because of the possibility of rapid ventricular rates, licensing authorities may consider atrial flutter disqualifying for flying duties. However, select cases that are well controlled by medication may be considered acceptable for private aviation.

Atrial fibrillation may occur as a consequence of underlying cardiac pathology, especially valvular disease. In such cases, aeromedical disposition should be determined by the underlying process, as discussed elsewhere in this chapter. Lone atrial fibrillation is considered here—atrial fibrillation in the absence of demonstrable underlying cardiac disease. Within the definition of lone atrial fibrillation, most authors also exclude hypertension and age older than 60 years. Lone atrial fibrillation may present as one of three distinct entities: a single, isolated episode of atrial fibrillation; recurrent paroxysms of atrial fibrillation; or persistent, chronic atrial fibrillation.

Single episodes often have an identifiable precipitating cause, such as acute abuse of alcohol and/or other stimulants (holiday heart syndrome). Single episodes are also frequently self-limited and convert spontaneously to normal sinus rhythm. Paroxysmal and chronic lone atrial fibrillation are often asymptomatic in otherwise healthy subjects, although inadequate cardiac output response to stress and reduced exercise tolerance may be present. Risk of stroke in lone atrial fibrillation is typically less than 1% per year, negating the need for warfarin anticoagulation. As with atrial flutter, medication is often indicated for ventricular rate control for paroxysmal or chronic atrial fibrillation. Even if the ventricular rate is not accelerated under resting conditions, it typically accelerates quickly and excessively with exertion or stress. Again, digitalis preparations, β- blockers and calcium channel antagonists are aeromedically most acceptable. Other medications have unacceptable side effects, including proarrhythmia.

A single episode of atrial fibrillation without associated hemodynamic symptoms may be acceptable for return to flying duties, including unrestricted military flying, after an observation period of a few months and exclusion of underlying cardiac disease. Paroxysmal or chronic lone atrial fibrillation may be acceptable for military and civilian flying duties if asymptomatic with good exercise tolerance and good control of ventricular rate, including graded exercise testing. Restriction to low-performance aircraft is recommended; both atrial fibrillation itself and rate controlling medications may reduce $+G_z$ tolerance. Ablation of atrial fibrillation, discussed later, offers possible return to high-performance flying. Reassessment at 1- to 3-year intervals is appropriate.

Ventricular Tachycardia

Mention of VT usually elicits a strong visceral response in clinical and aeromedical practitioners. Most clinical and literature experience deals with sustained or hemodynamically symptomatic VT. Here, the aeromedical disposition seems obvious—removal from all categories of flying. More often, the aeromedical dilemma will involve the disposition of nonsustained runs of VT without hemodynamic symptoms.

When associated with some cardiac diseases, such as CAD or cardiomyopathy, the presence of nonsustained VT carries additive risk for adverse cardiac events. In the presence of other, ''unrelated'' cardiac disorders, there appears to be no increased risk from nonsustained VT. These entities should be treated aeromedically like idiopathic nonsustained VT. When there is no underlying cardiac disease, the arrhythmia is termed *idiopathic VT*. Cardiac literature suggests, and most cardiologists would advise, that idiopathic nonsustained VT is benign. However, most literature on idiopathic nonsustained VT considers sudden cardiac death as the only primary endpoint. Many articles do not address the issue of syncope and even fewer address the occurrence of presyncope, lightheadedness, dyspnea, and other hemodynamic symptoms. These consequences are certainly of aeromedical concern.

Another consideration is the frequency and duration of nonsustained VT episodes. Cardiac literature does support a benign prognosis for infrequent episodes of short-duration VT (a few beats to several beats duration). Prognosis is not well-defined for frequent episodes or episodes longer than four to ten beats' duration. Recent USAF experience reflects these data (1,3). In 103 military aviators with asymptomatic idiopathic nonsustained VT, the annual event rate for sudden cardiac death, syncope, presyncope, or sustained VT was less than 0.5% per year during a mean follow-up of approximately 10 years. However, the majority had VT runs of only three beats' duration and only one VT episode per 24-hour ambulatory ECG recording. Only 10% had more than four episodes of nonsustained VT per 24-hour ambulatory recording and only 3% had VT episodes longer than ten beats duration. On the basis of this data, USAF guidelines recommend no more than four episodes per 24-hour ambulatory ECG recording and duration of 11 beats or less for return to unrestricted flying.

Aeromedical Disposition of Ventricular Tachycardia

Noninvasive evaluation is required to exclude underlying cardiac pathology, especially CAD and cardiomyopathy. A minimum of graded exercise testing, echocardiography, 24-hour ambulatory ECG recording, and examination for coronary artery calcification are recommended. Exercise radionuclide imaging or stress echocardiography are a consideration, especially in older male aviators, postmenopausal female aviators, or other higher-risk situations. Consideration of

coronary angiography should be guided by noninvasive test results.

Disqualification from all categories of flying is recommended for sustained VT and any duration VT with associated hemodynamic symptoms. If nonsustained VT is asymptomatic but associated with an underlying disease that increases risk, such as cardiomyopathy or CAD, disqualification may be appropriate, particularly for military aviation and commercial flying.

The risk of frequent or long-duration runs of nonsustained idiopathic VT is not clear. A prudent policy for nonsustained idiopathic VT should limit the number and duration of episodes. Published recommendations for competitive athletics recommend return to full athletic competition for episodes with duration of approximately 10 beats or less. Recommendations regarding acceptable frequency of episodes are usually lacking. Current USAF guidelines recommend no more than four episodes per 24-hour ambulatory ECG recording and duration of 11 beats or less for return to unrestricted flying.

Radiofrequency Ablation of Tachyarrhythmias

Atrioventricular Node Reentrant Tachycardia and Atrioventricular Reentrant Tachycardia

Ablation success rates for these two SVT mechanisms are similar and well reported. In experienced laboratories, the immediate success rate is 95% or greater; repeat ablation for initial failures is also 95% or more successful. Cure is therefore possible for nearly all cases. Recurrence of a functional reentrant circuit after apparent immediate success is 5% or less. Most clinical recurrences appear within 2 to 4 months of ablation and late recurrences are reportedly unusual. Clinically, recurrence is typically defined as recurrence of SVT or return of the WPW ECG pattern (for that disorder). The complication rate is low, but includes the possibility of complete heart block and subsequent requirement for permanent cardiac pacing. This risk is inherent to ablation performed on or near the anterior surface of the AV node. Regarding AVRT, approximately 5% to 10% of accessory pathways are located in this dangerous area; risk of complete heart block for such cases is 5% to 10%. Ablation of AVNRT is typically performed on the posterior surface of the AV node; risk of complete heart block at this location is approximately1%.

Return to unrestricted flying duties is considered for successful, uncomplicated ablation. A nonflying observation period of 3 to 4 months is appropriate to get beyond the window of most clinical recurrences. The appropriate documentation of successful ablation is an important aeromedical decision. Initial USAF policy required follow-up electrophysiologic testing no sooner than 3 months after ablation. Results were consistently negative, so this requirement was eliminated. Current USAF policy requires only a nonflying observation period of 4 months with no arrhythmia symptoms, no SVT, and normal ECG. Ambulatory ECG recording and graded exercise testing may be performed; in the USAF experience they were also nonproductive. Follow-up electrophysiologic testing should be considered for SVT with associated significant hemodynamic symptoms.

Other Supraventricular Tachycardias

As stated previously, these are unusual tachyarrhythmias that are primarily automatic atrial tachycardias. There is less-reported literature experience for ablation of these compared to AVNRT and AVRT, especially with long-term follow-up. However, reported outcomes for ablation of these rhythm disturbances are similar to those for AVNRT and AVRT. Aeromedical disposition should probably be patterned from policies for ablation of AVNRT and AVRT and considered on a case-by-case basis.

Atrial Flutter

Atrial flutter is a reentrant tachyarrhythmia with the reentry circuit located near the tricuspid valve. As such, it is quite amenable to ablation. Success rates are 95% or better with no significant complications. Aeromedical considerations are similar to those of AVNRT and AVRT given in the preceding text, plus post–ablation atrial fibrillation, reported in 20% to 30%. A patient may therefore have successful ablation for atrial flutter only to experience paroxysmal or chronic atrial fibrillation. This is more likely if atrial fibrillation was present before flutter ablation. Aeromedical disposition must then consider this additional complicating feature. Return to unrestricted flying duties is a consideration, after an observation period of approximately 6 months.

Atrial Fibrillation

Specific procedures for atrial fibrillation ablation are continuously under development and refinement. Success rates are procedure dependent and range 60% to 90% off all antiarrhythmic medications. Recurrence rates as high as 25% are reported, again mostly within 3 to 6 months (1). Late recurrence is more likely than for ablation of SVT mechanisms. An observation period of 4 to 6 months is recommended, with return to unrestricted flying if noninvasive testing is unremarkable. Graded exercise testing, 24-hour ambulatory monitoring, and echocardiography are recommended. In recent years, the USAF has returned several aviators to unrestricted flying after ablation of paroxysmal or chronic atrial fibrillation, with no reported problems or incidents to date.

Ventricular Tachycardia

A discussion of the disposition of radiofrequency ablation of VT is more difficult than for ablation of the various types of SVT. On the one hand, one might consider aeromedical disposition to be easy and simple, a disqualification for all flying duties. On the other hand, cardiologists who perform ablation may advise that the procedure is curative for idiopathic VT and therefore no risk for aviation. VT that has required ablation and is associated with underlying cardiac substrate, such as CAD or cardiomyopathy, should

be disqualified for all classes of flying. The underlying disease substrate frequently gives rise to multiple foci of VT; in such cases ablation may only be palliative or an adjunct to other therapy, such as antiarrhythmic medications and implantable defibrillators. And the underlying disease itself may well be disqualifying.

Consideration of return to any flying duties should be limited to ablation of idiopathic VT. And here exists a paradox. VT ablation is likely to be clinically recommended for sustained or nonsustained VT, especially if frequent, symptomatic, or resistant to medical therapy. Although stating that ablation may be curative for idiopathic VT, some published guidelines recommend that ablation is contraindicated for asymptomatic, nonsustained idiopathic VT. In other words, the more serious and symptomatic cases present for consideration of return to flying duties after ablation.

The scenario is more complicated than for SVT ablations, with less reported experience and long-term follow-up. Also, electrophysiologic testing is less reliable to document a cure than for SVT ablations. And in the literature, ''cure'' of VT by ablation may mean only no recurrence of spontaneous or ECG-documented sustained VT and absence of hemodynamic symptoms. Episodes of nonsustained VT may persist and ''cure'' may mean that the rhythm is now controlled on antiarrhythmic medications. In other words, ''cure'' may not mean complete eradication of the VT and absence of any medications.

There are several mechanisms for VT. The most common mechanism and location for idiopathic VT may also be the most benign and most amenable to ablative ''cure''—right ventricular outflow tract (RVOT) VT. This procedure holds promise for future aeromedical disposition, pending further information regarding long-term success and outcomes. In the interim, waiver for restricted flying may be considered on a case-by-case basis. If so, a longer observation period of 6 to 12 months is recommended, with thorough noninvasive evaluation and annual reassessment.

PERICARDITIS AND MYOCARDITIS

Pericarditis

In the aviator population, pericarditis will usually be viral or idiopathic, presumed viral. The aeromedical disposition of other etiologies (e.g., bacteria, tuberculosis, cancer, autoimmune disorders) should be on the basis of prognosis of the underlying disease and is not further considered. The acute phase of viral/idiopathic pericarditis usually follows a viral illness within a few weeks, and is characterized by fever, other constitutional symptoms, chest discomfort, pericardial friction rub, and serial ST-T wave ECG changes. This typically lasts 2 to 6 weeks, after which the course is typically benign. An aviator should be relieved of flight duties during the acute phase.

After the acute phase has resolved, the primary aeromedical concerns are recurrent pericardial pain and supraventricular arrhythmias. Late pericardial effusion, with or without tamponade, and development of chronic constrictive pericarditis are unusual. Approximately one fourth of patients reportedly develop recurrent chest pain within a few months of or even up to a year following the acute illness. Recurrent symptoms usually respond to nonsteroidal anti-inflammatory agents or colchicine; rarely steroids may be required. There is no helpful data regarding the likelihood of supraventricular arrhythmias, although they are known to occur.

To avoid complications, such as recurrent chest pain, recurrent pericardial effusion, and arrhythmias, a prudent aeromedical policy would include a time of nonflying observation after the acute phase, including a period of time after discontinuation of medications. Observation for 2 to 3 months after resolution of symptoms and at least 1month after discontinuation of anti-inflammatory medication should be sufficient for most cases. At that time, evaluation with echocardiography and ambulatory monitoring is recommended.

Graded exercise testing might be considered to exclude exertion-induced arrhythmias or to document normal exercise tolerance, but is not routinely recommended. It is unlikely to be helpful if there have been no arrhythmias by clinical presentation or ambulatory monitoring and no evidence of associated myocarditis. Additionally, the ST-T wave changes of pericarditis may require weeks to months to resolve and may cause secondary ST depression during graded exercise testing, adding unnecessary confusion to the case.

Late complications are unusual and unlikely in the absence of symptoms or signs; routine reassessment is therefore not required for uncomplicated viral/idiopathic cases. After clinical resolution, the specified observation period and acceptable findings on follow-up examination, return to unrestricted flying duties can be recommended.

Myocarditis

In the aviator population, myocarditis is also most often caused by a viral infection, but the possible consequences may be much more significant. The spectrum of presentation ranges from undetected, subclinical infection to rapidly progressive and fatal congestive heart failure. Myocarditis and pericarditis share common viral etiologies and myocarditis may often accompany or complicate pericarditis. Viral myocarditis is probably more common than clinically diagnosed; many cases of idiopathic-dilated cardiomyopathy are very likely the end result of undiagnosed viral myocarditis.

Viral myocarditis may cause dilation of cardiac chambers, ventricular systolic dysfunction, heart failure, arrhythmias, and conduction disturbances. Although recovery is typically complete, dilated cardiomyopathy may be the end result, appearing either during the acute phase or as a delayed effect after a latent, asymptomatic period.

Aeromedical disposition should require resolution of symptoms and recovery of cardiac chamber sizes and function to normal or near normal. A nonflying period of

observation is recommended; most sources would probably suggest 6 months. Subsequent aeromedical assessment should test for cardiac recovery, functional capacity, and arrhythmias. This would include echocardiography, 24-hour ambulatory ECG monitoring, and graded exercise testing with either stress echocardiography to assess ventricular function at peak stress. Return to unrestricted flying duties may be recommended if recovery is documented—good functional capacity, normal or near normal cardiac chamber sizes and function, and no significant arrhythmias. Because dilated cardiomyopathy may appear late, periodic reassessment is also recommended.

SUMMARY

Within the aerospace medicine community, we aeromedical practitioners often express our mission as "to keep them flying—safely." Our necessarily conservative approach often gains us a much different reputation in the view of the aviator and our clinical colleagues. Ours is a unique medical practice with less of the intrinsic reward inherent to clinical medicine. Requiring solid safety and outcomes data, we are generally limited to well-validated, established resources rather than the most recent medication, the latest test, or the hottest new procedure. However, it is a unique medical environment and aerospace cardiology is only one of its many fascinating aspects.

In this chapter, we have been able to only briefly discuss some of the more important issues regarding cardiac disorders and aeromedical decision making. It would have been very difficult, even impossible, to give the reader irrefutable data supporting ironclad aeromedical dispositions for all cardiac diagnoses. With such a broad spectrum of civilian and military aviation categories, different opinions and philosophies, and so on, aerospace medicine truly demonstrates that medical practice is as much an art as it is a science. Rather we sought to illustrate an aeromedical decision-making process that can be applied to most, if not all, diagnoses, ranging from common cardiac disorders to one-of-a-kind cases. Select an event rate threshold, define appropriate aeromedical events, determine annual event rates, consider special situations (e.g., high $+G_z$), formulate a recertification policy, consider the impact of other endpoints and therapy and . . . KEEP′ EM FLYING—SAFELY.

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