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AGARD

ADVISORY GROUP FOR AEROSPACE RESEARCH & DEVELOPMENT

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AGARD REPORT No.758

Short Course on Cardiopulmonary Aspects of Aerospace Medicine

NORTH ATLANTIC TREATY ORGANIZATION

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ADVISORY GROUP FOR AEROSPACE RESEARCH AND DEVELOPMENT

(ORGANISATION DU TRAITE DE L'ATLANTIQUE NORD)

AGARD Report No.758

SHORT COURSE ON CARDIOPULMONARY ASPECTS OF AEROSPACE MEDICINE

The material in this report has been prepared under the sponsorship of the Aerospace Medical Panel of AGARD and was presented as a Short Course at Fürstenfeldbruck, Federal Republic of Germany from 18 to 20 May 1987, at Athens, Greece from 21 to 23 May 1987, at Copenhagen, Denmark from 9 to 11 June 1987 and at Eskisehir, Turkey from 15 to 17 June 1987.

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14. Abstract

This Short Course is 21 hours in length of which 8 hours involves direct audience participation. The Course content is based upon the available data in asymptomatic aviator populations. The major thrust of the Course is directed toward aeromedical decision making based upon actual data from groups of aviators. Major clinical aerospace medical problems such as arrhythmias, coronary disease, valvular disease, hypertension, bronchiopulmonary disease and risk factors are addressed.

As major emphasis is placed on decision making, the classical technique of case presentation and discussion is employed. Early in the Course, the lecturers present the data and its interpretation with the aeromedical disposition supplied by the Course attendees. This case method is felt to be essential since aeromedical disposition will vary among different countries even for identical data. The varying viewpoints regarding aeromedical disposition is believed to be an educational stimulus both for Course attendees and lecturers. Later in the Course, attendees are presented only raw data from which they will derive both diagnosis and discussion.

One shortcoming of most medical courses is inadequate time for physicians and other health professionals to actually discuss interesting cases in-depth, in the presence of experienced aerospace medical specialists. A wealth of interesting cases needs to be shared. On the final day of the Course, attendees are asked to prepare in advance their most difficult and perplexing aeromedical cases for presentation and discussion.

PREFACE

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CONTENTS

CARDIOPULMONARY ASPECTS OF AEROSPACE MEDICINE

A SHORT COURSE SPONSORED BY THE
AEROSPACE MEDICAL PANEL OF AGARD

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COURSE SCHEDULE AND CONTENT

DAY NO. 1

DAY NO. 2

AEROMEDICAL EVALUATION AND DISPOSITION OF ELECTROCARDIOGRAPHIC ABNORMALITIES

by
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INTRODUCTION

In this section, electrocardiographic abnormalities in aviators will be discussed regarding their aeromedical significance, evaluation and disposition. Standard textbooks discuss the significance of electrocardiographic abnormalities based on studies of clinical populations. The United States Air Force School of Aerospace Medicine (USAFSAM) criteria are derived primarily from the observation of electrocardiographic findings in its own healthy aviator population and the natural history of abnormal findings in that same population. The USAF Central Electrocardiographic Library was established in 1957 to serve as a repository of all electrocardiograms on Air Force aviators, to perform analysis on the collected electrocardiographic data and to provide consultation to the Medical Corps and Surgeon General on electrocardiographic problems. The Library currently has approximately 1.4 million electrocardiograms of past and present active duty Air Force aviators on file. This central repository allows a very important serial followup comparison of electrocardiograms on aviators. A serial change on an electrocardiogram over time may be much more significant than a nonspecific finding on an isolated tracing. Past review of all initial electrocardiograms in the Library has revealed that 83% are normal and 17% are abnormal[1]. Ten percent of the normal electrocardiograms have been classified as normal variants[1]. The major normal variants and abnormalities are discussed.

Sinus Bradycardia

Standard textbooks define sinus bradycardia as a sinus rhythm with a heart rate less than 60 beats per minute[2]. As a group, aviators are relatively young and healthy with good physical conditioning. Sinus bradycardia has therefore been defined aeromedically as less than 50 beats per minute. This avoids the logistic problem of screening large numbers of healthy, young aviators with resting heart rates of 50 to 60 beats per minute on an electrocardiogram. Sinus bradycardia often occurs in the elderly and also in healthy young, athletic individuals. It is a frequent finding in the military aviator, occurring in 9.4% of all aviators and in 11.4% of those under the age of 30[3]. However, one cannot presume safely that sinus bradycardia is due to conditioning; an exercise history and comparison to old tracings are very important. Sinus bradycardia as a serial change may be a pathologic finding, especially in a nonexerciser, and suggests the presence of sinus node dysfunction. A USAFSAM study of 88 individuals with new sinus bradycardia revealed that 20% rarely exercised and 40% had an inadequate heart rate response to intravenous atropine[3].

The evaluation of sinus bradycardia includes comparison to old tracings and recording of an exercise history. If the sinus bradycardia is a new finding and is not accounted for by the individual's exercise program, then treadmill stress testing and ambulatory electrocardiographic recordings should be performed. If the heart rate response to exercise and daily activities is inadequate, then 0.02 mg/kg intravenous atropine should be administered. An appropriate response to atropine is a doubling of the heart rate or an increase of the heart rate to greater than 100 beats per minute. If the response is abnormal, then electrophysiologic testing to assess the function of the sinus node should be considered. Sinus bradycardia which responds appropriately to activity or atropine is a normal variant and acceptable for flying training and all classes of flying duties. Sinus bradycardia due to sinus node dysfunction is disqualifying for both flying training and all classes of flying duties.

Sinus Tachycardia

Sinus tachycardia is classically and aeromedically defined as a sinus rhythm with a heart rate greater than 100 beats per minute[2]. An analysis of over 100,000 initial electrocardiograms by Hiss and Lamb[4] revealed sinus tachycardia in aviators to be most frequent in the 16 to 24-year old group. They felt that the decreasing incidence of sinus tachycardia during routine flight examinations with age was related to decreased apprehension regarding the physical examination. Sinus tachycardia may also be related to the use of tobacco products, alcohol, caffeinated beverages and over-the-counter cold preparations. Repeat determinations of heart rate should be performed in a relaxed setting and off all such cardiac stimulants. If the sinus tachycardia is persistent, an evaluation should be performed to exclude hyperadrenergic states hyperthyroidism, and other underlying causes of sinus tachycardia. Sinus tachycardia as a normal, physiologic finding is acceptable for flying training and duties, but sinus tachycardia due to an underlying metabolic or disease process is disqualifying due to the underlying problem.

First Degree Atrioventricular Block

First degree atrioventricular (AV) block is classically defined as a PR interval greater than 0.20 second during sinus rhythm with every sinus P wave conducted to the ventricles and a constant PR interval[2]. Using this classic criteria, Hiss and Lamb[4] found an incidence of first degree AV block on initial electrocardiograms of 0.7%. Because the PR interval lengthens with decreasing heart rate and sinus bradycardia is a frequent, normal variant finding in aviators, first degree AV block has been more recently defined aeromedically as a PR interval greater than or equal to 0.22 second. It is a frequent, normal variant finding in the aviator population in association with sinus bradycardia and increased resting vagal tone due to physical conditioning. Other situations associated with first degree AV block include age (without evidence of other disease), myocarditis, myocardial infarction, digitalis effect, acute rheumatic fever, therapy with quinidine or procainamide, hyperkalemia and uremia.

The aeromedical evaluation of first degree AV block includes assessment of the individual's exercise

program and assessment by electrocardiography of the response of the PR interval to an increased heart rate. This may be done by recording an electrocardiogram following brief running in place or by other maneuvers, such as treadmill stress testing, hyperventilation, orthostasis or intravenous atropine. Increasing the heart rate to approximately 100 beats per minute is satisfactory for this assessment. If the PR interval shortens and becomes normal with an increased heart rate, the first degree AV block is then considered a normal variant due probably to a high degree of resting vagal tone. If it does not shorten and become normal, it is disqualifying for flying duties and flying training, unless and until further studies are performed to evaluate the possibility of underlying conduction system disease.

Second Degree Atrioventricular Block

Mobitz I second degree AV block or Wenckebach phenomenon occurs within the AV node. The PR interval of successive beats progressively lengthens until a P wave fails to conduct to the ventricle. The next P wave after the nonconducted beat has a shorter PR interval due to recovery of conduction in the AV node during the pause. The cycle of progressive PR interval prolongation then repeats itself. This is a nonspecific finding with a wide variety of etiologies including infections, digitalis effect, treatment with quinidine or procainamide, uremia, electrolyte disturbances, and inferior myocardial infarction. Mobitz I second degree AV block occurring at rest or during sleep, along with sinus bradycardia is also a normal variant due to a high degree of resting vagal tone in healthy, especially athletic, individuals. It is not surprising, therefore, to find Wenckebach in healthy aviators, particularly on a 24-hour ambulatory electrocardiographic recording. If no underlying process exists and examination reveals a normal, active and healthy individual, then treadmill stress testing and ambulatory electrocardiographic recording should be performed. If no other conduction system disturbances are noted, heart rate response to exercise and activity is normal, and the Mobitz I second degree AV block resolves with increased heart rates, then it may be considered a normal variant. As such it is acceptable for flying training and all classes of flying duties.

Mobitz II is an infranodal lesion which is frequently associated with bundle branch block, especially the combination of right bundle branch block and left anterior hemiblock. During sinus rhythm there is periodically a nonconducted P wave without previous progressive prolongation of the PR interval. The PR interval in the conducted beats is constant. Mobitz Type II is often a precursor of third degree AV block and an indication of significant conduction system disease. Its presence may often be heralded by such hemodynamic symptoms as dizziness, syncope or the precipitation of congestive heart failure. Permanent pacemaker implantation is often indicated. Because of the significant risk of incapacitating hemodynamic symptoms, this entity is disqualifying for all flying duties and flying training.

Third Degree Atrioventricular Block

In third degree AV block antegrade conduction between the atria and ventricles is completely blocked, and the atria and ventricles are activated independently. This may occur as a congenital finding in the absence of other underlying cardiac disease, but when diagnosed in an adult it is usually associated with underlying organic heart disease. Since syncrony of atrial and ventricular contraction is lost, the individual has decreased cardiac output and a decreased heart rate response to activity resulting in decreased exercise tolerance and predilection for dizziness and loss of consciousness. Possible etiologies include the toxic effects of various medications such as digitalis, myocardial infarction, myocarditis, coronary artery disease, chronic degenerative changes in the conduction system, infectious processes and electrolyte disturbances. It is disqualifying for flying training and all classes of flying duties, due to its obvious significant aeromedical hazard.

Axis Deviation

Electrocardiographic criteria for right and left axis deviation vary between different sources. Left axis deviation has been described as more negative than 0° in the frontal plane by some authors and as more negative than -30° by others. Right axis deviation has been described as an axis in the frontal plane of greater than a value ranging from 90° to 120°. At USAFSAM right axis deviation is defined as a mean QRS axis of 120° or more in the frontal plane and left axis deviation is defined as a mean QRS axis equal to or more negative than -30° in the frontal plane.

Hiss and Lamb[4] describe right axis deviation in 0.1% of initial electrocardiograms. The incidence was highest in young individuals aged 15 to 29 years. Isolated right axis deviation in a healthy young individual represents a persistent juvenile pattern, a normal variant. In individuals over 45 years of age, right axis deviation as an initial finding occurred only in those with known heart or pulmonary disease. A routine flight physical examination includes a history, physical, screening blood work, routine electrocardiography and routine pulmonary function tests. Right axis deviation as an initial finding with a normal flight physical examination is considered a normal variant and therefore is acceptable for flying training and flying duties. Right axis deviation occurring as a serial change requires repeat electrocardiography, ensuring that the patient is supine and that all leads are properly positioned. If the right axis deviation is still present, echocardiography and consultation with an internist or cardiologist are required. If underlying cardiac or pulmonary disease are diagnosed, then the aeromedical disposition will be determined by the underlying disease process. If no evidence of underlying cardiac or pulmonary disease is found, then the right axis deviation is acceptable for flying training and continued flying duties.

Left axis deviation may be related to conduction system disease, myocardial disease, coronary artery disease or obesity. A noninvasive evaluation is required for left axis deviation presenting as an initial finding or a serial change. Besides the routine flight physical examination, treadmill stress testing, echocardiography, and consultation with an internist or cardiologist is required. If no underlying disease process is discovered, left axis deviation is acceptable for flying training or continued flying duties.

Right Bundle Branch Block

Right bundle branch block (RBBB)is defined as a QRS interval of 0.12 second or wider with a wide S

wave in the lateral limb and precordial leads and a wide R or R' wave in V_1[2]. Possible sites of the conduction delay include the His bundle, the right bundle branch, or the distal Purkinje fibers. According to Hiss and Lamb[4], 0.18% of initial electrocardiograms show complete right bundle branch block with an equal incidence in all age groups. Acquired RBBB discovered on serial electrocardiography is present in approximately 0.6% of all aviators with a gradual increased incidence with age[3]. Complete RBBB is disqualifying for entry into flying training, but may be waiverable as a new, serial finding in a trained aviator. In the past the discovery of complete RBBB in a trained aviator has required a complete noninvasive evaluation at USAFSAM plus left heart catheterization and electrophysiologic studies to exclude the presence of underlying coronary artery disease, cardiomyopathy and other conduction system disease. Previous studies performed and reported at USAFSAM showed the RBBB to be intact with the block located distally at the level of the Purkinje fibers beyond the moderator band[5]. Progressive conduction system disease was felt to therefore be unlikely and in fact, only one of 394 patients evaluated developed third degree AV block in a followup of over ten years[6]. RBBB was also found not to be a marker for either coronary artery disease or cardiomyopathy[7]. Therefore, RBBB block may now be waivered for all classes of flying duties if a noninvasive evaluation at USAFSAM is normal. The aviator with waivered simple RBBB returns for USAFSAM followup evaluation every three years. Cardiac catheterization and electrophysiologic studies are only indicated for abnormal noninvasive tests and RBBB complicated by hemiblock or other evidence of further conduction system disease, such as first or second degree AV block.

Of the 394 patients initially studied at the School of Aerospace Medicine, 372 had complete evaluation including electrophysiologic studies. Ninety-four percent had no disease, 3% had coronary artery disease, 2% had hypertensive cardiac disease and 1% had other abnormalities including abnormal His bundle studies. Greater than ten years of followup was obtained in 95% of the subjects. Six percent ultimately developed coronary artery disease or hypertension and less than 1% suffered cardiac death[6].

Studies such as this demonstrate the extreme importance of a central location for evaluating asymptomatic abnormalities in aviators. Data collection and analysis on RBBB subjects allowed a significant evolution in the aeromedical disposition of acquired RBBB. Initially, RBBB was considered disqualifying for flying duties. A study group was established that allowed RBBB to be waivered for continued flying duties if a full evaluation, including cardiac catheterization and electrophysiologic studies, was normal. Now it has been demonstrated that a normal noninvasive evaluation is sufficient to establish the safety of continued flying duties in a subject with acquired RBBB. This process has ultimately saved many thousands of dollars in training expenses and many years of flying experience and has eliminated the necessity for unnecessary invasive procedures.

Left Bundle Branch Block

Left bundle branch block (LBBB) has a QRS interval equal to or greater than 0.12 second with a broad and sometimes notched monophasic R wave and loss of septal Q waves in the lateral leads and a wide QS complex in the anterior precordial leads[2]. Of over 122,000 initial electrocardiograms analyzed by Hiss and Lamb[4], only 17 demonstrated LBBB. None of these subjects were less than 25 years old and it was a rare finding in subjects less than 35 years old. This occurrence of LBBB in the slightly older aviator population parallels the increasing incidence with age of coronary artery disease and hypertension and underscores the greater aeromedical concern regarding LBBB compared to RBBB. Acquired LBBB is disqualifying for entry into pilot training but may be waiverable for continued flying duties when discovered as a serial change in a trained aviator. In studies performed at USAFSAM, 77 LBBB subjects underwent noninvasive evaluation plus cardiac catheterization and a subset of 33 of those subjects also had electrophysiologic studies. Sixty-three subjects (82%) had no coronary artery disease, 3 subjects (4%) had minimal coronary artery disease and 11 subjects (14%) had significant coronary artery disease. Of the 63 subjects without coronary artery disease, 53 remained asymptomatic and unchanged on followup evaluations. Two of the 63 subjects had cardiomyopathy diagnosed during their initial evaluation and three later developed cardiomyopathy. Four others experienced cardiac events, including one subject that required a permanent pacemaker. One subject suffered a noncardiac death. Of the five subjects who had or later developed cardiomyopathy associated with their LBBB, three remained asymptomatic during the followup period, one died of congestive heart failure and one died suddenly. Twenty-eight (85%) of the electrophysiologic studies revealed no other conduction system abnormalities, while five (15%) did display other conduction system abnormalities, usually prolongation of conduction time from the His bundle to the ventricles. All of the subjects with a normal electrophysiologic study remained asymptomatic during followup. Two of the five abnormal electrophysiologic studies occurred in individuals with associated cardiomyopathy. It has also been observed at USAFSAM that an increased incidence of abnormal thallium scintigraphy occurs in subjects with complete LBBB and normal coronary arteries at catheterization. With the observation that cardiomyopathy has developed in several of these subjects, this raises the question of a more diffuse process which affects both the myocardium and the conduction tissue.

In summary, studies in the LBBB subjects have demonstrated an 18% incidence of some degree of measurable coronary artery disease, a 6.5% incidence of initial or later development of cardiomyopathy, and a 15% incidence of further conduction system abnormalities on electrophysiologic testing. Because of these considerations, all acquired LBBB in aviators is referred to USAFSAM for a complete noninvasive and invasive evaluation. Noninvasive evaluation includes exercise stress testing, echocardiography, ambulatory electrocardiographic monitoring, rest and stress thallium scintigraphy, and rest and stress radionuclide angiography. Radionuclide angiography is extremely important to follow these subjects for the development or progression of cardiomyopathy. Invasive evaluation includes left heart catheterization to define the coronary anatomy and assess resting left ventricular function and electrophysiologic studies to assess the integrity of the rest of the conduction system. If the evaluation reveals simple LBBB without any complicating features, waiver for all classes of continued flying duties is granted with followup evaluations performed at USAFSAM at three year intervals.

Supraventricular and Ventricular Ectopy

Aeromedical concern regarding supraventricular and ventricular ectopy is a very difficult subject. On the one hand, ectopy is very common in normal individuals without underlying heart disease and does not

seem to predispose to more complex arrhythmias. These individuals should not have their flying career compromised and should be identified with a minimum of testing. On the other hand, ectopy may be the sole indicator of underlying organic heart disease and may also be a precursor/substrate for more complex tachyarrhythmias. These individuals should be identified and carefully evaluated and, in most instances, disqualified from flying duties. However, our current technology and knowledge from the literature limit our ability to differentiate these two groups. Also, standard cardiology literature regarding the significance and threat of various types of ectopy may not apply to the unique stresses and hazards of flight, particularly high performance flight. The major aeromedical concern regarding ectopy is the potential for incapacitating tachyarrhythmias during flight. According to Hiss and Lamb[4], supraventricular premature beats (SVPB) occur in 0.6% of initial electrocardiograms and ventricular premature beats (VPB) occur in 0.8% of initial electrocardiograms. SVPBs and VPBs occur with approximately equal frequency in the under 40 age group, but VPBs are more common in the older age group. After an initial normal electrocardiogram, the prevalence of SVPBs on followup electrocardiograms is constant but the prevalence of VPBs progressively increases with age up to 40, then plateaus at 26% of aviators over the age of 40[1]. This increased prevalence of VPBs with age parallels the increased frequency with age of hypertension, coronary artery disease and cardiomyopathy. This observation highlights the concern about tachyarrhythmias in aviators. Certainly tachyarrhythmias may cause incapacitating hemodynamic symptoms, but they also may be well tolerated in an otherwise healthy subject. However, a tachyarrhythmia may precipitate angina pectoris or other ischemic syndromes when occurring in an individual with unsuspected, subclinical, coronary artery disease. At the present time supraventricular or ventricular pairs, multiform VPBs and frequent ectopy with bigeminy, trigeminy or quadrigeminy are disqualifying for entry into flying training. Frequent ectopy may be waiverable for flying training if a thorough evaluation reveals no tachyarrhythmia or underlying organic heart disease. All of these classes of ectopy may be waiverable in a trained aviator depending upon the results of a thorough evaluation.

SVPBs are very common in apparently healthy populations with an incidence of up to 50% reported in some series. They may be related to ingestion of stimulants, such as tobacco products, caffeine or alcohol. They constitute a substrate for significant tachyarrhythmias such as supraventricular tachycardia, atrial fibrillation, and atrial flutter. SVPBs occurring on a routine electrocardiogram warrant a careful history and physical examination and 24-hour ambulatory electrocardiographic monitoring. The history should include careful questioning regarding the use of arrhythmogenic food substances and medications, including over-the-counter preparations. Treadmill stress testing, echocardiography and thyroid function testing may be performed if clinically indicated. Frequent SVPBs and SVPB pairs in a trained aviator are waiverable for all classes of flying duty if the evaluation reveals no evidence of tachyarrhythmias or underlying organic heart disease. Supraventricular pairs must be evaluated noninvasively at USAFSAM; frequent isolated supraventricular ectopy may be evaluated locally with the results forwarded to USAFSAM for review and inclusion in the aviator's files in the USAF Central Electrocardiographic Library.

VPBs have also been reported in up to 50% of apparently normal subjects, but the likelihood of underlying disease increases as the frequency of VPBs increases. VPBs may occur in association with cardiomyopathy, coronary artery disease, hypertension or abnormal metabolic states and, like SVPBs, may be precipitated or aggravated by arrhythmogenic food substances and medications. VPBs usually do not herald underlying cardiac disease or future development of ventricular tachycardia. Ventricular ectopy on a routine electrocardiogram warrants a careful history and physical examination and a 24-hour ambulatory electrocardiographic recording. Frequent, isolated ventricular ectopy may be evaluated locally with echocardiography and treadmill stress testing with the results referred to USAFSAM for review and filing. Ventricular pairing and multiformity require a complete noninvasive evaluation at USAFSAM. If evaluation demonstrates no evidence of underlying organic heart disease or ventricular tachycardia, waiver for continued flying duties for frequent ventricular ectopy, ventricular multiformity, and ventricular pairing may be granted.

Supraventricular or ventricular ectopy occurring during stress has been shown to be a very poor predictor of underlying organic heart disease. The frequency, complexity, QRS configuration, and time of appearance of stress ectopy have no predictive value for future tachyarrhythmias or underlying heart disease. The evaluation and disposition of stress ectopy is identical to that for ectopy occurring at rest.

USAFSAM reevaluations for ectopy are performed every two or three years.

Supraventricular Tachyarrhythmia

Supraventricular tachyarrhythmia is defined as three or more supraventricular beats in a row at a rate greater than or equal to 100 beats per minute. This includes atrial tachycardia, junctional tachycardia, undifferentiated supraventricular tachycardia, atrial fibrillation and flutter, and multifocal atrial tachycardia. A history of even a single episode of supraventricular tachyarrhythmia is disqualifying for entry into flying training. Recurrent nonsustained or sustained supraventricular tachyarrhythmia is disqualifying for all classes of flying duties. A single episode of nonsustained or sustained supraventricular tachyarrhythmia occurring in a trained aviator is potentially waiverable depending on the results of a complete USAFSAM evaluation. Atrial flutter is the only supraventricular tachyarrhythmia that is not waiverable; the risk of one-to-one atrioventricular conduction with resultant excessive ventricular rates is considered too great for waiver consideration. During a rapid supraventricular tachyarrhythmia, decreased diastolic filling of the heart may lead to decreased cardiac output with resultant dizziness or loss of consciousness, even in otherwise normal subjects. With unsuspected coexisting subclinical coronary artery disease, the tachyarrhythmia may precipitate such ischemic events as angina, myocardial infarction, ventricular tachycardia, ventricular fibrillation, congestive heart failure or cardiovascular collapse. The most frequent and favorable supraventricular tachyarrhythmia in aviators is the "holiday heart syndrome". This usually occurs as atrial fibrillation and is related to a combination of fatigue, lack of sleep, hunger, anxiety, and over-ingestion of caffeine, alcohol, or tobacco. Usually this tachyarrhythmia is self-limited and does not recur if the aviator avoids such circumstances.

Until 1973 all types of supraventricular tachyarrhythmia were considered disqualifying for all flying duties. In 1973 a study group was begun to identify the proper evaluation of supraventricular tachy-

arrhythmia and identify which subsets may be considered safe for continued flying duties. Recurrent supraventricular tachyarrhythmia, defined as two or more episodes, is still considered disqualifying for all classes of flying duties and waiver is not recommended. If an aviator has a single episode of supraventricular tachyarrhythmia without any hemodynamic symptoms, he is disqualified from flying duties and is observed for six months. During this time thyroid function tests are performed and three Holter monitors are obtained to rule out recurrent supraventricular tachyarrhythmia. If these studies are normal, then a complete evaluation at USAFSAM is performed. Previously, electrophysiologic testing was required for all such supraventricular arrhythmias, preceded by left heart catheterization if the aviator was over age 35 or had significant coronary artery disease risk factors. A recent review was conducted of 85 electrophysiologic studies performed to evaluate supraventricular tachyarrhythmia. None of them disclosed evidence of sick sinus syndrome or an unsuspected bypass tract. Induction of supraventricular tachyarrhythmia with rapid atrial pacing or programmed atrial stimulation occurred only in some individuals being evaluated for sustained supraventricular tachyarrhythmia; the electrophysiologic studies were always normal in individuals being evaluated for nonsustained supraventricular tachyarrhythmia. Consequently, electrophysiologic testing is now performed only to evaluate single episodes of sustained supraventricular tachyarrhythmia. Left heart catheterization to define the coronary artery anatomy is still performed as part of the evaluation if the individual is greater than age 35 or has significant coronary artery disease risk factors. The risk of supraventricular tachycardia occurring in combination with underlying coronary artery disease is considered too great to rely only on current noninvasive procedures to rule out coronary artery disease in this subset of aviators at risk. Nineteen percent of supraventricular tachyarrhythmia referrals have been disqualified due to coronary artery disease discovered at cardiac catheterization. A combination of supraventricular tachyarrhythmia and any degree of measurable coronary artery disease is disqualifying for flying duties and waiver is not recommended.

A single episode of sustained or nonsustained supraventricular tachyarrhythmia is waiverable for all classes of flying duties if (1) The USAFSAM noninvasive evaluation is normal; (2) left heart catheterization, if indicated, reveals normal coronary arteries and (3) electrophysiologic study, if indicated, is normal. Noninvasive reevaluation at USAFSAM is performed at two to three year intervals.

Ventricular Tachycardia

Ventricular tachycardia is three or more premature ventricular beats in a row at a rate greater than or equal to 100 beats per minute[1]. During the period 1965 through 1978, ventricular tachycardia occurred during 0.5% of treadmills performed at USAFSAM[8]. In 1978 a retrospective eight year study was performed of 45 aviators with exercise induced ventricular tachycardia[8]. Ten (22%) later developed cardiac events including angina, myocardial infarction, and three deaths. The three deaths were in individuals with amyloidosis, myocardial infarction and mitral valve prolapse. Twenty of the 45 subjects had undergone left heart catheterization demonstrating normal coronary arteries in 16 and coronary artery disease in four. None of the subjects with normal coronary arteries had any cardiac events whereas all four of the subjects with documented coronary artery disease had events. The longest episode of ventricular tachycardia was seven beats. Warning arrhythmias occurred in 29 of the 45 subjects with exercise induced ventricular tachycardia, but occurred with equal frequency in the two subgroups with and without subsequent cardiac events. Analysis of the data revealed no discriminators between the subsequent cardiac event group versus the nonevent group except the status of coronary artery disease at cardiac catheterization. Potential discriminators that were examined included length of ventricular tachycardia, number of episodes of ventricular tachycardia, rate of ventricular tachycardia, configuration of the QRS complex, heart rate at onset of ventricular tachycardia, presence of ST segment abnormalities during the stress test and warning arrhythmias. Other noninvasive tests such as 24 hour ambulatory electrocardiographic monitoring and echocardiography also failed to discriminate between the event and nonevent groups. The exercise induced ventricular tachycardia was nonsustained, with the longest run being seven beats, and typically occurred as an isolated event during late exercise or early recovery with a heart rate greater than 150 beats per minute. Most of the subjects did not have a substrate of frequent PVCs on their preexercise electrocardiogram or their 24 hour ambulatory electrocardiographic recording.

Ventricular tachycardia remains disqualifying for entry into flying training. However, based on the above data, a single episode of ventricular tachycardia may be waiverable in a trained aviator after a complete evaluation at USAFSAM. It must be an isolated episode of monomorphic ventricular tachycardia of less than or equal to seven beats. A complete noninvasive evaluation must reveal no evidence of underlying cardiac pathology, including coronary artery disease, cardiomyopathy, and valvular disease. Cardiac catheterization is required for waiver consideration and there must be no measurable coronary artery lesions. If all these criteria are met, the aviator is recommended a waiver for flying duties restricted to tankers/transports/bombers. Noninvasive reevaluation at USAFSAM is required at one year intervals to continue the waiver. This policy was established in 1978 to apply only to exercise induced ventricular tachycardia. Since that time 12 out of 31 aviators evaluated have been waivered for restricted flying duties. In 1981 this policy with the identical criteria and evaluation was extended to include ventricular tachycardia occurring at rest. Since that time 8 of 28 aviators evaluated have been waivered for restricted flying duties. To this date, none of these aviators waivered for restricted flying duties has suffered a cardiac event.

Atrial Abnormalities

Atrial enlargement or hypertrophy diagnosed from a routine electrocardiogram is better described as atrial abnormality because correlation with atrial size and pressures is not good. The aeromedical criteria for left and right atrial abnormalities are identical to that of standard cardiology textbooks[1]. Left atrial abnormality criteria include (1) Wide (3 mm or more) and notched P waves in leads I, II and aVL, and (2) a negative component of the P wave in leads V1 or V2 measuring 1 mm or more in depth and width. Right atrial abnormality criteria including (1) Peaked and tall (3 mm or more) P waves in leads II, III and aVF, and (2) less commonly a positive component of the P wave in lead V1 or V2 of 2 mm or more. When right or left atrial abnormalities are discovered as a serial or initial finding on routine electrocardiography, a consultation with an internist or cardiologist and echocardiography are recommended to rule out the presence of underlying organic heart disease. If this evaluation is normal, then the electrocardio-

graphic finding is considered a normal variant and waiver is not necessary for continued unrestricted flying duties. In our experience with the aviator population, a common underlying organic cause for left atrial abnormality is early hypertensive disease and may occur prior to the standard QRST changes suggestive of ventricular hypertrophy.

Left Ventricular Hypertrophy

Standard electrocardiographic criteria for left ventricular hypertrophy are well established in the cardiology literature and include a variety of voltage criteria plus left axis deviation, the delayed intrinsicoid interval and secondary lateral and inferior T wave changes. Voltage criteria for left ventricular hypertrophy in the absence of other supporting electrocardiographic findings is a very nonspecific discovery and includes a large number of normal individuals without ventricular hypertrophy. Based on prior experience at the USAF Central Electrocardiographic Library, the following criteria have been utilized for screening electrocardiograms: The sum of the S wave in V_1 or V_2 plus the R wave in V_5 or V_6 greater than 55 mm in individuals under age 35 and greater than 45 mm in individuals age 35 or older. If a trained aviator exceeds these voltage criteria or meets standard voltage and secondary criteria for left ventricular hypertrophy, M-mode and two-dimensional echocardiography should be performed. If good quality studies are obtained and rule out the presence of left ventricular hypertrophy, then further evaluation and waiver consideration are not necessary. If the echocardiograms show definite or suspected left ventricular hypertrophy, then the aviator is disqualified for further flying duties pending a USAFSAM evaluation. If that evaluation reveals underlying hypertensive or cardiac disease as a cause for left ventricular hypertrophy, the aviator is permanently disqualified from all flying duties. Such secondary left ventricular hypertrophy implies hemodynamic significance of the underlying disease process. If no underlying disease process is found to explain the left ventricular hypertrophy, then the individual is considered to have either athletic heart syndrome or a concentric type of hypertrophic cardiomyopathy. A history of the aviators exercise program becomes extremely important at this point. Frequent, regular exercise, particularly isometric exercise, may cause compensatory left ventricular hypertrophy. This is considered a normal physiologic variant and regresses quickly with discontinuation of the exercise. An aviator with unexplained left ventricular hypertrophy and a reasonable exercise program is therefore disqualified from flying duties and advised to discontinue or severely restrict his exercise. Repeat echocardiography is performed his local base three months later and reviewed at USAFSAM. If it shows regression or resolution of the left ventricular hypertrophy, the aviator returns to USAFSAM. If followup studies at USAFSAM confirm resolution of his left ventricular hypertrophy, he is considered to have an athletic heart syndrome and is returned to unrestricted flying duties. He may also resume any exercise program that he desires. If the left ventricular hypertrophy does not resolve during this observation period, the aviator is considered to have hypertrophic cardiomyopathy and is permanently disqualified from all flying duties.

If an applicant for flying training has a suspicion of left ventricular hypertrophy on his screening electrocardiogram, he must obtain a similar evaluation through civilian medical sources. In other words, the burden of proof is upon the applicant to exclude left ventricular hypertrophy and to demonstrate his medical acceptance for flying training.

Right Ventricular Hypertrophy

Right ventricular hypertrophy is also an electrocardiographic diagnosis associated with a lack of specificity, especially if there are no repolarization changes. Aeromedical criteria are identical to that of classic cardiology textbooks. Increased anterior forces are seen in right ventricular hypertrophy, posterior wall infarction, nonspecific conduction disturbances and as an unexplained phenomenon in the absence of apparent underlying disease. When right ventricular hypertrophy is discovered as a serial change in a trained aviator, a clinical evaluation including echocardiography is necessary similar to that of left ventricular hypertrophy. If right ventricular hypertrophy is found, it is disqualifying for all flying duties and a complete evaluation is warranted. The School of Aerospace Medicine has not encountered a case of right ventricular hypertrophy without an underlying cardiac or pulmonary cause.

Nonspecific ST Segment and T Wave Changes

Hiss and Lamb[4] reported that 1.2% of initial electrocardiograms in aviators demonstrated nonspecific T wave changes; they did not address the incidence of nonspecific ST segment changes. After a normal initial electrocardiogram, the prevalence of nonspecific ST and T wave changes in aviators increases with age to 32% by age 50-54 years[3]. In an asymptomatic, healthy population serial nonspecific ST and T wave changes are the most significant and underscore the importance of a central repository such as the USAF Central Electrocardiographic Library. Such serial changes double the predictive value of a screening treadmill exercise test for coronary artery disease[3]. If a routine resting electrocardiogram shows nonspecific ST segment or T wave changes, a repeat fasting supine electrocardiogram should be performed. Lamb[9] reported on 226 individuals with nonspecific T wave changes and in one-half of the subjects the T waves became normal with a repeat fasting electrocardiogram. If a second repeat electrocardiogram was performed after loading with 100 grams of glucose, the nonspecific T wave changes reappeared. Nonspecific changes may occur with the nonfasting state, standing, respiratory variation, obesity, hyperventilation and anxiety. They have also been reported due to vagatonia[10] and may therefore normalize with exercise or atropine. If repeat electrocardiography does not demonstrate lability of the ST segment/T wave changes, then a maximum treadmill stress test should be performed at the local base and the original tracings referred to the USAF Central Electrocardiographic Library. If the treadmill test is normal, then the evaluation is terminated and no further action taken. If the treadmill test is abnormal in any way (usually borderline or abnormal ST segment response), then the aviator is disqualified from flying duties and referred to USAFSAM for a complete evaluation to exclude the presence of coronary artery or other organic heart disease.

Q Waves

Abnormal Q waves are 0.04 second or greater in duration with a depth equal to or greater than 1/4th to

1/3rd of the height of the accompanying R wave. Definitely abnormal Q waves suggest the presence of a prior myocardial infarction, particularly when occurring as a new finding, and require further evaluation to definitely exclude or make the diagnosis of myocardial infarction. Myocardial infarction is permanently disqualifying for all classes of flying duties, because of a known risk for future cardiac events. Non-diagnostic Q waves are of lesser amplitude and duration and may be a normal variant. If they are not a new finding compared to old electrocardiograms, then they are considered a normal variant and no further evaluation is necessary. Q waves are commonly found in the inferior leads, particularly lead III. If new nondiagnostic Q waves occur inferiorly, repeat electrocardiography during inspiration and expiration may demonstrate them to be a labile, respiratory event. No further evaluation is necessary for this finding. If they are persistent then further evaluation is warranted including treadmill stress testing, echocardiography, and possible vectorcardiography if available. If this local evaluation does not resolve the question of possible myocardial damage by review at the USAF Central Electrocardiographic Library, then a full USAFSAM evaluation is warranted. Q waves or poor R wave progression in the anterior precordial leads suggest possible anterior wall damage and require a repeat fasting electrocardiogram and precordial map. For a precordial map, the standard precordial leads are recorded one and two interspaces below the standard position. If the precordial map reveals normal anterior forces, then the poor R wave progression is considered to be a normal variant and no further evaluation is needed. If anterior forces still appear to be decreased, then the aviator should be disqualified for flying duties pending a full evaluation at USAFSAM to exclude a previous anterior myocardial infarction. Possible myocardial infarction appearing on a routine electrocardiogram again highlights the importance of the Central Electrocardiographic Library so that annual electrocardiograms may be compared to previous tracings to see if abnormalities represent a new serial change or a stable old finding.

Short PR Syndromes

The Wolff-Parkinson-White (WPW) electrocardiographic pattern is a short PR interval (usually less than or equal to 0.10 second), a delta wave and wide QRS complex. All individuals with the WPW electrocardiographic pattern, who also have tachyarrhythmias, have the WPW syndrome by definition. The electrocardiographic pattern implies the presence of a bypass tract and the predisposition for, but not the presence of, tachyarrhythmias. It has been estimated that 0.15 to 0.2% of the general population have the electrocardiographic pattern. What percentage develop tachyarrhythmias is unknown; many people with only the electrocardiographic pattern never have routine electrocardiography and are therefore never diagnosed. Also, the pattern may be present only intermittently and may not be seen on routine electrocardiography.

The WPW syndrome is disqualifying for flying training and all classes of flying duties. The WPW electrocardiographic pattern is a cause for rejection for pilot training due to the risk of future disqualification from flying duties because of the development of tachyarrhythmias. However, a new WPW electrocardiographic pattern in a fully trained aviator requires evaluation at USAFSAM and is potentially waiverable if there are no tachyarrhythmias or other disqualifying cardiac defects. When the WPW pattern is discovered in a fully trained aviator, we generally have a number of years of experience with this individual demonstrating no problems with tachyarrhythmias in the flight environment. Therefore, electrophysiologic studies are not performed on these individuals; it is not necessary to demonstrate the presence of the bypass tract and artificial induction of a tachyarrhythmia in this situation would not change the recommendation for a waiver. If the trained aviator with a WPW pattern flies high performance aircraft, he must undergo a monitored centrifuge evaluation as part of his assessment at USAFSAM. Re-evaluation is performed at USAFSAM at two to three year intervals.

WPW is not a predictor of future coronary artery disease, but the tachyarrhythmias may occur at any age, including later in life when coronary artery disease may also be developing. A tachyarrhythmia occurring in an individual with unsuspected, subclinical coronary artery disease may precipitate such ischemic events as angina pectoris, myocardial infarction, cardiovascular collapse, ventricular tachycardia or fibrillation and syncope. Also, the ST segment response to treadmill stress testing becomes uninterpretable in many of those with the WPW pattern. The physician then loses the use of this tool as a screening test for developing coronary artery disease. Electrophysiologic testing in flying training applicants with the WPW electrocardiographic pattern might identify a subset of subjects that would be acceptable trainees. However, because of the above further considerations, the WPW pattern continues to be disqualifying for entry into flying training.

The Lown-Ganong-Levine syndrome is characterized by a short PR interval and normal QRS complex, without a delta wave, associated with paroxysmal tachyarrhythmias. This syndrome is disqualifying for flying training and all classes of flying duties. In the absence of tachyarrhythmias there are no characteristic electrocardiographic features of this syndrome other than the short PR interval. However, many normal individuals will have a short PR interval as a normal variant. Therefore the diagnosis is only made when associated with tachyarrhythmias. An evaluation is not routinely performed on aviators with just a short PR interval and normal QRS complex. However, a constant PR interval of less than 0.10 second and the presence of P waves of definite sinus origin is less likely to be a normal variant and more likely to represent the presence of an underlying bypass tract. In such a case, evaluation and surveillance should probably be considered.

Summary

Electrocardiographic abnormalities in asymptomatic individuals often merely raise the possibility of an underlying, aeromedically significant problem. Natural history followup studies are necessary to determine the significance of most electrocardiographic findings in the aviator population. Such studies have already contributed significantly to our knowledge and experience at USAFSAM and have allowed a large number of aviators to be safely returned to flying duties. In the USAF, aviators have routine electrocardiography performed upon entry into flying training and every other year (beginning at age 35) as part of their routine flight physical examination. Filing of these electrocardiograms in the Central Electrocardiographic Library greatly facilitates the consistent application of these discussed standards and allows the extremely important observation for serial changes.

REFERENCES

1. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia, Lea and Febiger, 434-444, 1985.

2. Chung, E.: Electrocardiography: Practical Applications with Vectorial Principles, Hagerstown, MD, Harper and Row, Publishers. Inc. 1974.

3. Hickman, J.R., Jr.: Disposition of Electrocardiographic Abnormalities in Aviators. Advisory Group for Aerospace Research and Development (NATO), Report No. 681-11-1 to 11-13, National Technical Information Service, Springfield, VA, 1980.

4. Hiss, R. and Lamb, L.. Electrocardiographic Findings in 122,043 Individuals. Circ 25:947-961, June 1962.

5. Albert, B.: Right Ventricular Conduction Times in Asymptomatic Isolated Right Bundle Branch Block. (Abstract) AJC 41(1):385, February 1978.

6. Rotman, M. and Triebwasser, J.: A Clinical and Followup Study of Right and Left Bundle Branch Block. Circ 51:477-484, March 1975.

7. Massing, G. and Lancaster, M.: Clinical Significance of Acquired Right Bundle Branch Block in 59 Patients Without Overt Cardiac Disease. Aerospace Medicine 40:967-971, September 1969.

8. Alpert, B.: The Prognosis of Exercise-Induced Ventricular Tachycardia in Asymptomatic Patients. Circ 58(4)II:238, 1978.

9. Lamb, L.: The First International Symposium on Cardiology In Aviation. Brooks Air Force Base, TX, School of Aerospace Medicine, November 1985, 329-346.

10. Iglesias, R.: T Wave Inversion of the Electrocardiogram in Healthy Individuals with Vagotonia. Aerospace Medicine 39:318-320, March 69.

NONINVASIVE METHODS FOR THE DETECTION OF CORONARY ARTERY DISEASE IN AVIATORS - A STRATIFIED BAYESIAN APPROACH

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The detection of asymptomatic coronary artery disease is a major goal of most aeromedical services, especially those which utilize high-performance aircraft. Unfortunately, the pursuit of silent coronary artery disease with contemporary noninvasive diagnostic methods has been disappointing. This lecture will discuss the epidemiological principles which underlie this rather poor performance of contemporary diagnostic tools in a population where coronary arterydisease is of low prevalence. The underlying statistical problem is best explained by an analysis of Bayes' theorem, which applies conditional probability analysis to diagnostic tests which are not perfect. The predictive power of a positive diagnostic test is very heavily dependent upon the prevalence of the disease in the population being tested.

Unlike sensitivity and specificity, which are independent of disease prevalence, predictive value is strongly influenced by stratification of the test population into subsets with a high pretest probability of disease. This lecture will discuss strategies to improve the poor performance of contemporary noninvasive tools in the testing of otherwise healthy individuals. The USAFSAM Risk Index will be offered as a theoretical, but unvalidated, stratification tool.

The detection of coronary artery disease in the asymptomatic aircrew member is a difficult problem because contemporary diagnostic tools which were derived for a "sick" clinical population must be applied in a healthy population which has not been stratified by the presence of symptoms. As we shall demonstrate in this discussion, the performance of contemporary diagnostic tests in a population with a low prevalence of the disease in question is suboptimal.

Before discussing methods for the detection of asymptomatic coronary artery disease, it is important to ask this rhetorical question: "Is there a mandate to identify asymptomatic anatomic coronary artery disease?" I ask this question because aeromedical services must be very clear as to whether they are dedicated to the pursuit of silent coronary disease. This question must be pondered at some length before embarking on a program for the detection of asymptomatic coronary disease, because if one answers "yes," an entire series of new questions unfolds later on. These later questions involve expenditure of medical resources, the use of diagnostic tools which are not completely risk free, and the necessity to decide where to set aeromedical thresholds for the disease process. If the answer to this question is "no," and there are some who feel that the diagnosis of asymptomatic coronary artery disease is not a valid aeromedical goal, then one can await the disease process to declare itself by symptoms. Coronary artery disease may present as acute myocardial infarction, angina pectoris, ischemic arrhythmias and conduction disturbances, or may persist as silent ischemia. A great deal of epidemiological information revolves around the observation that angina pectoris may actually be a minority presentation of the disease, and that more than half of all cases of silent coronary artery disease will present with a catastrophe. Of course, ischemic arrhythmias or angina pectoris may be quite incapacitating, so there is really no desirable aeromedical presentation for silent coronary artery disease. If one feels that a mandate to pursue silent disease exists, we must now examine how we have pursued this disease in the past. One assumes that we have all been in pursuit of silent coronary artery disease, since we have been regularly doing electrocardiograms, occasional stress tests, and recurrent evaluation of other risk factors. In the United States Air Force, we believe that our prevalence of serious silent coronary artery disease is approximately 5%. In the U.S. Air Force, as in most healthy populations, the leading cause of death in our aviators is due to trauma. However, if a USAF aviator dies a medical death while on active duty, the cause will be coronary artery disease 70% of the time. The autopsy series of battle casualties from the Korean War and the Vietnam War have underscored the observation that coronary artery disease is not a disease of old men, but has its beginnings early in life, with significant numbers of young men in the second and third decades having hemodynamically significant lesions. The advent of the new generation of high-performance fighter aircraft, which are placing unprecedented stress on the cardiovascular system, has placed a major premium on the discovery of coronary artery disease while it is still in a mild to moderate pathologic state. In the U.S. Air Force, as in most other NATO air forces, the view has been taken that aerospace safety and the ethical imperatives of occupational medicine require the pursuit of asymptomatic coronary artery disease.

Let us now turn to a listing of the contemporary tools available for the pursuit of asymptomatic coronary artery disease. As you can see from this listing in Figure 1, there is no category for "marked value." Why is this so? We are all aware that the

Essentially No Value	Limited Value
History	Resting ECG
Physical examination	Exercise electrocardiography
Holter monitor	Exercise myocardial scintigraphy
Echocardiography	Exercise radionuclide ventriculography
	Cardiac fluoroscopy

Figure 1. Contemporary tools available for the pursuit of asymptomatic coronary artery disease.

treadmill in a "sick patient" population has a very strong correlation with angiographic coronary artery disease. In fact, the current diagnostic tools to assess reversible ischemia function rather well in a clinical population, but unfortunately function rather poorly in a healthy population where the disease is sparse (Fig. 2)

*Predictive Values for 50% Angiographic Coronary Lesions

	Clinical Population	Aviators
Treadmill	>80%	35%
Thallium	80%-90%	<50%
MUGA	>80%	<25%

$$\text{*Predictive value} = \frac{\text{True positives}}{\text{Total positives}}$$

Figure 2. What happens to conventional diagnostic techniques when applied in a healthy population?

The predictive value of a diagnostic test is the percentage of positive results which are true positives. The sensitivity of a diagnostic test is the percent of positive results in patients with the disease. Sensitivity is a measure of a test's ability to identify those with the disease process. Specificity is the percent of negative results among those who do not have the disease. Specificity is a measure of the test's ability to correctly label those without the disease. These epidemiological terms are noted in Figure 3.

		Disease		
		Yes	No	
Test	+	TP	FP	TP+FP
	-	FN	TN	FN+TN
		TP+FN	FP+TN	TP+FP+FN+TN

Predictive value (risk) if test positive = TP/(TP+FP)

Sensitivity = TP/(TP+FN)

Specificity = TN/(FP+TN)

Predictive value = Percent of positive tests which are "true" positives

Sensitivity = Percent of "true" positives among all subjects with disease
How good is the test in identifying those with disease?

Specificity = Percent of "true" negatives among all subjects free of disease
How good is the test in identifying the "innocent?"

TP = True Positive
FP = False Positive
TN = True Negative
FN = False Negative

Figure 3. Measures related to a test's performance

Sensitivity and specificity are attributes of the diagnostic test and are independent of the prevalence of the disease in the population tested. However, the predictive value of a diagnostic test is not an immutable property of the test, but is highly dependent upon the prevalence of the disease in the population tested. It is extremely important for those who are involved in the testing of apparently healthy subjects to understand this principle, because the major problems encountered in screening for silent coronary artery disease are due to this phenomenon. Let us examine the performance of a diagnostic test with a sensitivity of 60% and a specificity of 90% in a population of 10,000 subjects with a 50% disease prevalence (Fig. 4). A test

		Disease: Yes	Disease: No	
Test	+	6,000 (TP)	1,000 (FP)	7,000
	-	4,000 (FN)	9,000 (TN)	13,000
		10,000	10,000	20,000

$$\text{Predictive value of positive test} = \frac{TP}{TP+FP} = \frac{6,000}{7,000} = 85.7\%$$

Figure 4. Performance of a test with 60% sensitivity and 90% specificity in 20,000 people with 50% prevalence of disease

sensitivity of 60% would correctly label 3,000 of the 5,000 with disease as true positives, with 2,000 remaining as false negatives. A 90% specificity would correctly identify 4,500 of the true negatives, leaving 500 false positives. Under these conditions, the predictive value of an abnormal test, the ratio of true positives to all positive tests, is 85.7%. One would consider this excellent performance of the diagnostic test. Let us assume that we are referring to a treadmill test. If one now takes the very same technicians, physicians, electronics and treadmill apparatus, and moves all this from the hospital to the flight surgeon's office, what happens to the predictive value? Unlike the hospital population, the prevalence of disease in the aviator population is 5%. The performance of the diagnostic test under such circumstances is portrayed in Figure 5. A 60% sensitivity would correctly label 300 of the diseased subjects as true positives and 200 as false negatives. A 90% specificity would identify 8,550 of the nondiseased as true negatives, leaving 950 false positives. Even though this diagnostic test has done a superb job of identifying those without disease, the total number of subjects without the disease is so large that the very modest false positive rate in the "innocent" grossly outnumbers the small number of true positives. Even though the false positive rate is quite modest, the enormous number of candidates to be false positives produces a very low predictive value of the diagnostic test. This is the essential problem in the pursuit of any disease in a healthy population. The Bayesian Theorem applies conditional probability analysis to diagnostic tests which are

		Disease: Yes	Disease: No	
Test	+	600 (TP)	1,900 (FP)	2,500
	-	400 (FN)	17,100 (TN)	17,500
		1,000	19,000	20,000

$$\text{Predictive value of positive test} = \frac{TP}{TP+FP} = \frac{600}{2,500} = 24\%$$

Figure 5. Performance of a test with 60% sensitivity and 90% specificity in 20,000 people with 5% prevalence of disease

not perfect. In practice, this means that the predictive value of a diagnostic test is very heavily dependent upon the prevalence of disease in the population tested. Let us now turn to a demonstration of the Bayesian problem in real life. Figure 6 demonstrates the U.S. Air Force's experience with attempts to detect coronary artery disease in the asymptomatic male. If one performs a treadmill test on an unselected male population who have normal electrocardiograms, and then performs angiography upon those with

ECG SCREENING STUDIES

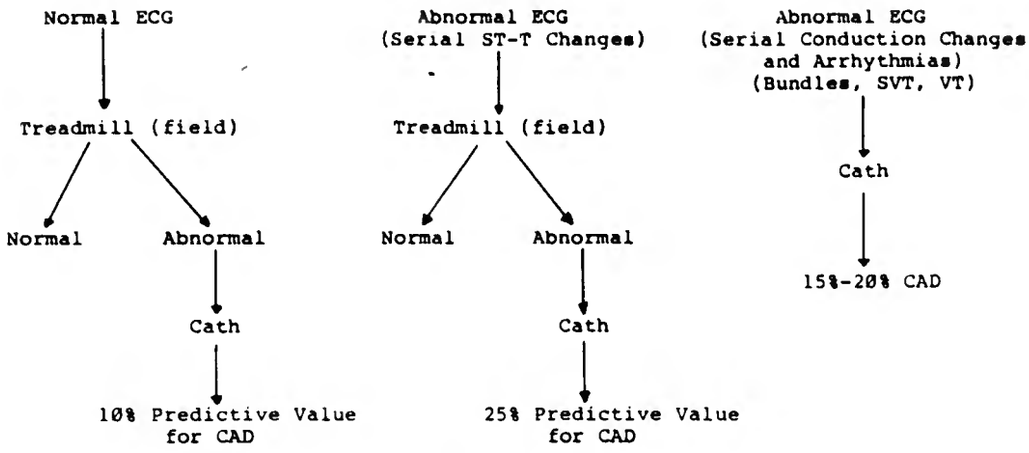

Figure 6. USAFSAM CAD* experience based on angiographic data (1969-1984) (*50% coronary lesions)

abnormal tests, the resultant predictive value is only 10%. If one performs the treadmill test only on those with nonspecific ST and T wave serial changes on the annual electrocardiogram, the predictive value of the exercise test increases to 25%. The predictive value of electrocardiographic changes which require angiography in and of themselves (left bundle branch block, ventricular tachycardia and some cases of supraventricular tachycardia) ranges from 15% to 20%. Given these rather poor predictive values of commonly used diagnostic tools, how does one solve the poor predictive value of diagnostic tests in a low-prevalence population? One may view noninvasive tests, as well as coronary risk factors, in one of two ways, either to predict future events or to attempt to predict the presence of silent disease today. One may use them as epidemiological tools to predict a future clinical end-point. Such prediction has utility, but in aerospace medicine, it is far more important to know who has angiographic disease today, rather than who will develop a cardiovascular end-point seven years from now.

The other role of these tests is to attempt to apply them as angiographic predictors. The epidemiologic use of the treadmill is well founded. A major epidemiological study from the U.S. Air Force revealed that an abnormal treadmill test, when compared to a normal treadmill test, had a risk ratio of 14:1 for coronary events over the ensuing 6.6 years (1). While the treadmill test has a poor predictive value for angiographic disease when applied in an unstratified fashion, the risk ratio of 14-fold cannot be ignored. For this reason, the U.S. Air Force, as well as many other air forces, requires angiography for an abnormal treadmill test. Thallium scintigraphy has a sensitivity and specificity of approximately 90% in a clinical population. However, sensitivity and specificity would need to exceed 95% in order to reach a 50% predictive value of a positive test in a population where the disease was 5% prevalent. In a similar fashion, multiple gated acquisition scans, using a combination of ejection fraction and wall motion information, reveal very similar limitations in predictive value in a healthy population (see Figure 7).

*Predictive Values for 50% Angiographic Coronary Lesions

	Clinical Population	Aviators
Treadmill	>80%	35%
Thallium	80%-90%	<50%
MUGA	>80%	<25%

$$\text{*Predictive value} = \frac{\text{True positives}}{\text{Total positives}}$$

Figure 7. Predictive values of common cardiovascular tools in clinical subjects and in aviators.

In the U.S. Air Force, one could sum up our previous efforts to identify asymptomatic coronary artery disease as follows:

1. Only a relatively small amount of coronary disease has been identified in comparison to that which truly exists. This finding is largely because the resting electrocardiogram is normal in most cases of asymptomatic coronary artery disease which we see.

2. From a study of the Bayesian aspects of the problem, it becomes obvious that most of our diagnostic energies have been expended on those with little probability of having coronary artery disease.

3. The end result of the above factors is that almost 75% of the cardiac catheterizations have been in those without coronary artery disease.

The U.S. Air Force has been performing angiography in air force aviators since 1968 and we have never experienced a myocardial infarction, a cerebrovascular accident, a catheterization-related death, or a major vascular accident. The complication rate for cardiac catheterization in strong, vigorous, relatively young, healthy males is approximately 0.05%. Cardiac catheterizations can be performed with great safety on aircrew members, but we must continually try to refine our indications for cardiac catheterizations for occupational reasons. The nonspecificity of our noninvasive cardiovascular tests means that the great bulk of the diagnostic risk, radiation exposure, grounding from flying for a period of time, and the attendant emotional stress falls upon the shoulders of those free of coronary artery disease. A high rate of false positive tests also imposes a significant manpower and materiel burden on the aeromedical system. However, one must always choose high sensitivity over high specificity. Unfortunately, any modification of our contemporary noninvasive tools which increases specificity is usually accompanied by a corresponding decrease in sensitivity. Sensitivity must always be favored over specificity in aerospace medicine. Still, we feel that we have learned a great deal about the pursuit of asymptomatic coronary artery disease, and we should be able to decrease the number of normal cardiac catheterizations considerably. In terms of cardiac catheterizations, the problem is not that of an unacceptable complication rate. The complications have been extremely low. The problem is that many of the cardiac catheterizations are being performed on the wrong subjects. While the many disadvantages of performing cardiac catheterizations on those without disease have been outlined above, it must also follow that one will be detecting very little real disease if most of one's time and effort are expended on those who are free of the disease.

STRATEGIES FOR THE DETECTION OF ASYMPTOMATIC CORONARY ARTERY DISEASE IN AVIATORS

Briefly, the following strategies have yielded no useful information in the pursuit of asymptomatic disease: 1) echocardiography, both rest and exercise; however, we are continuing to study the potential of exercise echocardiography; 2) systolic time intervals; and 3) Holter monitoring (the occurrence of ST segment elevation, frequently reported in a clinical population as a manifestation of silent ischemia, has been extremely uncommon in our aviators with asymptomatic coronary artery disease. The coronary artery disease in the asymptomatic state is largely discovered by exertional testing which magnifies the supply/demand imbalance. Thus, it is not really surprising that Holter monitoring has not been very revealing). We have also tested a number of strategies in an attempt to improve the predictive value of our noninvasive cardiovascular tests. We have subjected the scalar electrocardiogram to intensive computer analysis. We have also looked at the treadmill with in-depth computer analysis. Neither of these strategies has significantly altered the basic problem. We have also attempted to look at combinations of all data available within the conventional treadmill test (2), but multivariant treadmill analysis has made little impact on the false positive problem. The predictive value of the ST response at varying degrees of maximal ST depression, the predictive value of the ST response at varying degrees of maximal ST depression during the first nine minutes of exercise, the predictive value of the ST response at times of onset of ischemia and the predictive value of the ST response at varying percentages of the maximal predicted heart rates have all been analyzed in depth in the treadmills of aviators who went to angiography. One can sum up the results of these treadmill strategies by stating that one has no difficulty in coming up with treadmill information which is highly specific, but the tradeoffs result in very unacceptable sensitivity. The same is true for any combinations of high sensitivity, producing lowered specificity. For example, we could change our criterion for abnormality of the treadmill test from 0.1 millivolt of ST segment depression to 0.2 millivolts. This would result in an increased predictive value of the test and would certainly be more specific, but clearly less sensitive. Let us now review the tradeoffs between loss of specificity versus loss of sensitivity.

LOSS OF SPECIFICITY

1. Leads to further testing.
2. Expensive and time-consuming.
3. Imposes some risk on subjects free of disease.

LOSS OF SENSITIVITY

1. Disease goes undetected.
2. Unacceptable in dangerous occupations.

It now becomes clear that modification of our contemporary diagnostic tools does not seem to be the solution to the Bayesian dilemma. Modification of the test does not seem to be necessary, since the test functions quite well where disease density is relatively high. Our problem, then, becomes one of changing a low-prevalence situation into a high-prevalence situation. The true answer to the Bayesian dilemma lies in performing the test on the right people and avoiding the testing of the wrong people. In those populations where the pretest probability of disease is high, we can make the Bayesian aspect of the problem work for us, rather than against us. How does one condense a very large population where the disease is quite sparse into a much smaller population where the disease is quite abundant? To pursue this problem, we must turn to classical coronary risk factors which have served us well in the prediction of future events. Can we use classical risk factors to help us predict the presence of angiographic disease at this moment? Figure 8 reveals the Framingham Risk Equation. One can

$$\text{Risk} = \frac{1}{1 + e^{-bx}}$$

$$BX = B_0 + B_1 \text{ Age} + B_2 \text{ Age}^2 + B_3 \text{ Age x Total Cholesterol} + B_4 \text{ Total Cholesterol} +$$

$$B_5 \text{ SBP} + B_6 \text{ Smoke} + B_7 \text{ LVH on ECG} + B_8 \text{ DM}$$

Note: The equation was derived prior to clinical availability of HDL determinations (1979).

Figure 8. Framingham Risk Equation - predicts events

instantly note that age enters into the equation three times, once as a squared function. One also notes that cholesterol enters into the equation twice. Thus, the bulk of the risk information is contained in age and blood lipids. At USAFSAM, we used a modification of the Framingham equation to evaluate a large series of aviators who went to angiography, dividing them into 10 deciles of risk, the lowest risk for coronary disease residing in the first decile and the highest risks residing in the tenth decile. As one can see from Figure 9, we did 48 cardiac catheterizations in the first decile of risk to find only one case of disease. The Framingham equation would have predicted five cases, but it must be borne in mind that the Framingham equation was derived to predict future events. Even accepting this limitation of the Framingham equation, one can see that, in the fifth decile of risk, we performed 48 cardiac catheterizations to find 11 cases of

Decile of Risk	No. of Caths	Expected Cases*	Observed Cases*
1	48	5	1
2	47	7.4	4
3	48	10.1	6
4	47	12.4	10
5	48	14.7	11
6	48	16.7	16
7	47	18.7	12
8	48	23.1	19
9	47	27.2	26
10	48	33.3	35

*for 50% lesions

Figure 9. USAFSAM modification of Framingham Risk Equation

(Modification derived prior to clinical availability of HDL determinations)

disease, and in the tenth decile of risk, we performed 48 cardiac catheterizations to find 35 cases of disease. A summary of the results of the USAFSAM modified Framingham Risk Equation is contained in Figure 10. In the first five deciles of risk, we performed 238 cardiac catheterizations, to find only 32 cases of disease. In the last five deciles of risk, we performed 238 catheterizations, to find 108 cases of disease. In

First 5 deciles:	32 cases CAD/238 Caths
Last 5 deciles:	108 cases CAD/233 Caths
Highest decile:	35 cases CAD/48 Caths (72%)

Figure 10. Summary of USAFSAM modified Framingham Risk Equation

the highest decile of risk, we found disease in 72% of the subjects. Thus, it should become quite clear that we can select a segment of the population in whom an abnormal, noninvasive test should have very high predictive value. One does not even have to use a sophisticated regression equation to gain significant stratification of coronary risk. Figure 11 demonstrates the rather impressive performance of a simple analysis of the number of cardinal risk factors present in an aviator with an abnormal treadmill test. In these 255 asymptomatic aviators, the overall predictive value of the exercise test was only 25%. However, it can be readily seen from this table that 25% predictive value defines the population rather poorly, since there is clearly a hierarchy of predictive

N = 255 asymptomatic aviators cathed for abnormal treadmills

Overall predictive value = 25% (65/255) for >50% lesions

Number of risk factors	Predictive value of treadmill
0	9%
1	20%
2	27%
3	39%
≥4	64%

Risks analyzed

Cholesterol ≥240 mg%

Abnormal GTT

Smoking (≥20 cigarettes per day)

Hypertension

Positive family history (first-degree relative <65 years)

Figure 11. USAFSAM use of cardinal risk factors to predict angiographic CAD

values among all of these essentially identical subjects. For those with no risk factors, the predictive value of the treadmill was only 9%. However, for those with four or more risk factors, the predictive value of the exercise test was 64%. Thus, it becomes clear that, by simply using the ordinal number of risk factors, one should be able to identify a population of aviators in whom a positive exercise test is much more likely to represent a true positive. One may also conclude from these data that it is probably incorrect to state that any test has a given predictive value for an asymptomatic population, since there are individuals within the group of such widely varying risk for the disease. This is rather unlike a clinical population, wherein symptoms of angina tend to produce a population at catheterization which is very homogeneous in terms of risk factors, thereby producing a group of rather high uniform pretest probability of disease. Thus, a single predictive value of a diagnostic test in a high-prevalence population is far more scientifically accurate than the same statement applied to a group of healthy individuals. In order to look further at these cardinal risk factors, we shall introduce a new epidemiological term, the Likelihood Ratio.

The Likelihood Ratio is the ratio of the true positive to the false positive rate. The Likelihood Ratio defines the effectiveness of a single diagnostic test criterion when isolated from other observations. A ratio of <1 indicates no association between the tested variable and the disease state. A ratio of >1 indicates a predictor which makes an independent contribution to the diagnosis of the disease state. Figure 12 indicates a series of Likelihood Ratios for individual risk factors in aviators who went to cardiac catheterization, defining a case of coronary disease as one 50% lesion in a major vessel. As expected, the highest Likelihood Ratio for angiographic disease was in those aviators with three or more cardinal risk factors.

Cholesterol >240 mg%	-	1.75
Smoker	-	1.30
Family history	-	1.20
Glucose intolerance	-	2.70
Hypertension	-	1.50
≥2 risk factors	-	3.65
≥3 risk factors	-	5.66

Figure 12. Likelihood Ratios for cardinal risk factors in aviators undergoing catheterization for abnormal treadmill (Coronary disease defined as a 50% luminal narrowing)

USEFULNESS OF HDL CHOLESTEROL IN THE PREDICTION OF ASYMPTOMATIC CORONARY DISEASE

It is now well established that the level and type of circulating lipoprotein concentrations are related to the extent and severity of arteriosclerotic heart disease at angiography. This concept has been proven in multiple clinical studies and has likewise been documented in a population of healthy aviators undergoing cardiac catheterization at USAFSAM (3). At USAFSAM, the predictive value of an abnormal exercise test in an aviator with a cholesterol/HDL cholesterol ratio of equal to or greater than 6.0 exceeds 70% for significant coronary artery disease. The mean age of aviators proceeding to cardiac catheterization at USAFSAM is 40±5 years. Clearly, a cholesterol/HDL cholesterol ratio of 6.0 has greater angiographic impact at age 45 than when discovered at age 25. Just as in the Framingham equation, we must combine our risk information with the very potent risk of advancing age. While the concept may be quite obvious, it must be emphasized that the search for asymptomatic coronary artery disease should be strongly influenced by age. At USAFSAM, only 5% of those cardiac catheterizations which have been performed under age 30 have yielded coronary artery disease. In the 30-34 age group, the yield was 20%; in the 35-39 age group, the yield was 25%; in the 40-44 age group, it was 41%; in the 45-49 age group, it was 48%; and in the over-50 age group, it was 56%. If one analyzes the last 350 cases of coronary artery disease (of any degree stenosis) at USAFSAM, one finds that 334 of the 350 cases were found in aviators of age 35 or older. Of the last 350 cases of disease, 237 were significant coronary disease, with lesions of at least 50% stenosis. Of these 237 cases, 229 were discovered in aviators age 35 or older. Thus, if we are to go into the aviator population and search for asymptomatic coronary artery disease, we will waste much time and resources searching for cases in individuals who are under age 35. While this observation may seem quite elementary, very few aeromedical services have stratified the use of noninvasive testing based upon age and other cardinal risk factors.

THE USAFSAM RISK INDEX

The USAFSAM Risk Index (Figure 13) is a dimensionless number which expresses the risk of angiographic coronary artery disease if one goes to catheterization while asymptomatic as a result of a noninvasive test. Unlike other risk scores, which predict future events, the USAFSAM Risk Index is intended to be an angiographic predictor. The primary purpose of the risk index is to identify those aviators who need second-order testing such as treadmill exercise tests. Since the score does represent graduated coronary risk, we expect that it will also be of benefit in identifying those who are at risk of developing atherosclerosis, as well as having atherosclerosis. We hope that it will be of benefit in identifying those who need risk intervention. This risk index

$$I = Age^2 \left(\frac{Chol-HDL}{HDL} \right)$$

Derivation based upon angiographic data

Based upon easily verified risk factors

Uses readily available "care" data

Has not been prospectively validated

Figure 13. The USAFSAM Risk Index

was derived retrospectively, based upon angiographic data from USAF aviators. It is based upon easily verified risk factor information and has the advantage of using continuous, rather than noncontinuous, information. This index is currently being prospectively validated, whereby we are actually choosing aviators for treadmill exercise testing based upon their coronary risk as assessed by the USAFSAM Risk Index. This index has not yet been put into operational use in the U.S. Air Force and we would advise our colleagues to withhold any application of this index until we have finished a validation of several years. This index was specifically derived from a population aged 40±5 years, who have a largely North American diet and lifestyle, and who are USAF pilots. In addition to these special conditions, the index was specifically derived only to aid in the identification of asymptomatic coronary artery disease. The USAFSAM Risk Index may not be applicable to other populations. It is also disturbing to some aeromedical specialists to note that the index contains only age, cholesterol and HDL cholesterol. We were also somewhat surprised at this finding, but the addition of hypertension, glucose intolerance, family history, and cigarette smoking did not add statistically significant information to the Risk Index. There are plausible explanations for this result. In the U.S. Air Force, we have almost no untreated hypertension because of intensive disease surveillance. Thus, the population curve for hypertensive morbidity is truncated in our aviators well before the morbidity and mortality curve starts to rise. USAF aviators with hypertension who do not respond to thiazide diuretics are removed from flying status. Thus, the derivation of the USAFSAM Risk Index did not include hypertensives who were either uncontrolled or had experienced end-organ damage, since they do not remain on flying status. We have very few pilots with chemical diabetes on active duty in the U.S. Air Force. Family history would have been of greater benefit in this equation if the population of subjects had been older. A premature family history of coronary artery disease (a coronary event in a first-degree relative under age 65) may not have yet occurred in an aviator age 40 whose parents are still in their early sixties. Family history is also notoriously inaccurate and also suffers from the disadvantage of entering the equation as a dichotomous (noncontinuous) variable. The incorrect recording of family history, which enters any regression equation as a "yes" or "no" answer, causes a major perturbation in the equation when misassigned. The effect of smoking tends to be mediated by the potentiation of lipid risks, since HDL cholesterol is lowered by smoking. Further, the period of exposure is also a function of age. In summary, greater than 90% of the risk information for angiographic disease was contained in the three factors of age, cholesterol and HDL cholesterol. Figure 14 represents retrospective information regarding the performance of the USAFSAM Risk Index in those with abnormal exercise tests. For those at very low coronary risk (index <5,000), the predictive value of the exercise test was only 5.7%. However, the predictive value of the exercise test climbed steadily with increasing index until a predictive value of 75% was reached in those with an index equal to or greater than 12,000. It must be emphasized that the predictive value of 75% is the predictive value of an abnormal exercise test in a population with an index of at least 12,000. It does not mean that, if one has an index of 12,000, one has a 75% chance of having coronary artery

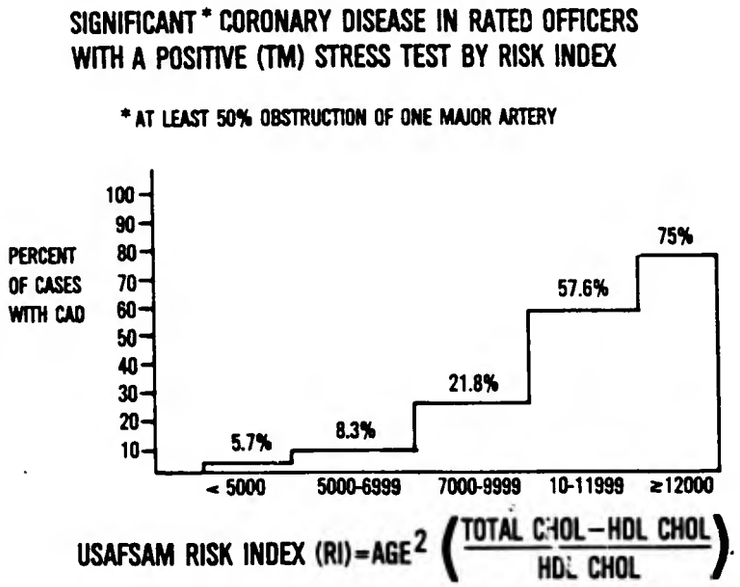

Figure 14. Significant* coronary disease in rated officers with a positive treadmill stress test by risk index

disease. Figure 15 represents the evaluation protocol currently being used by the U.S. Air Force to validate our Risk Index. For those with indices less than 5,000, no actions are contemplated. For those with indices between 5,000 and 7,000, risk-reduction counseling will be given. For those with indices from 7,000 to 10,000, the local electrocardiogram, when compared at USAFSAM with all previous tracings, will be the determining factor. Serial changes on the annual electrocardiogram for those in this risk group will result in a treadmill test. Those with abnormal treadmill tests will be refered to USAFSAM for further evaluation. For those with indices of 10,000 to 12,000, a treadmill test will be performed at the local base. Abnormal treadmill tests will be referred to USAFSAM. For those with indices of greater than 12,000, a direct USAFSAM evaluation will result. We feel that a direct USAFSAM referral for an index of 12,000 or greater is necessary because treadmill false negative rates have their

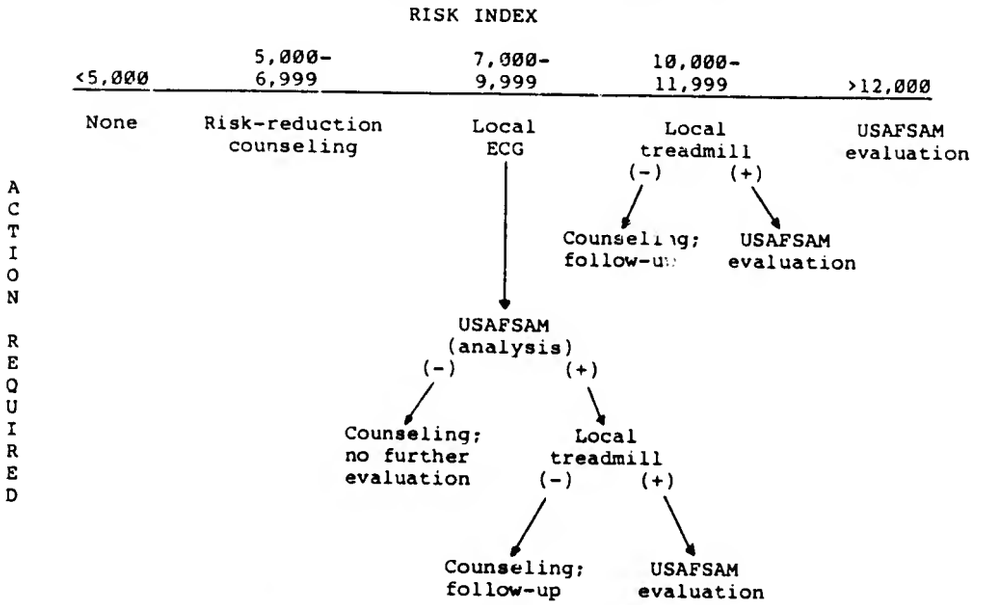

Figure 15. Evaluation protocol by risk index

greatest aeromedical impact when high-grade disease is missed. False negatives may occur due to collateralized high-grade obstructions, or high-grade "balanced" disease may yield a falsely negative thallium scan. Just as false positive tests are a problem where the disease is very sparsely populated, false negative tests become the problem at the other end of the spectrum, where there are indeed a great many candidates to be false negatives. For this reason, those with indices of over 12,000 will receive treadmill exercise testing, a thallium scintigram, a gated blood pool study, and cardiac fluoroscopy. Only 1% of our USAF aviators have risk indices of 12,000 or greater; 1.3% of our aviators are between 10,000 and 12,000, and only 8.1% are between 7,000 and 10,000. Approximately 90% of all USAF aviators have risk indices of under 7,000. In the U.S. Air Force, we anticipate that the index will prove to have great utility in solving the Bayesian dilemma. We anticipate that more angiographic disease will be identified and that more cases of ominous anatomy will be represented in those who are identified. We anticipate that our resources will be focused on the higher-risk populations, thereby eliminating the large number of nonproductive evaluations in the large low-risk population. We also anticipate that, over time, disease discovery will shift to more mild to moderate cases, as it becomes more difficult for aviators with unfavorable lipids to escape detection until the fifth decade. We fully expect that the thresholds for various types of testing will need to be changed once we have more experience following the validation. The USAFSAM Risk Index represents the culmination of a number of goals in risk stratification for the U.S. Air Force. We wish to enhance predictive value of our noninvasive tests by increasing the pretest probability of disease. We wish to avoid second-order tests in aviators with no risks for the disease. We wish to minimize grounding for workups which are ultimately unrevealing. We also wish to increase the ratio of significant high-grade disease cases which are discovered. Ultimately, once the cases of serious high-grade anatomy are markedly decreased by risk stratification, we hope that the majority of disease which we discover will be in the mild to moderate range. In reality, the aeromedical mission is not being performed well if most of the disease which we discover is high-grade disease, because aviators with serious coronary obstructions will have been involved in operational flying. Our goal is to discover the disease early, when it exists in a mild obstructive state, well before the aeromedical risk becomes gre

BIBLIOGRAPHY

1. Froelicher VF, Thomas MM, Pillow C, Lancaster MC. Epidemiologic study of asymptomatic men screened by maximal treadmill testing for latent coronary artery disease. Am J Cardiol, vol 34, 1974, p. 770.

2. Hopkirk JAC, Uhl GS, Hickman JR, Fischer J. Discriminant value of clinical and exercise variables in detecting significant coronary artery disease in asymptomatic men. J Am Coll Cardiol, vol 3, 1984, pp. 887-894.

3. Uhl GS, Troxler RG, Hickman JR, Clark JD. Relation between high density lipoprotein cholesterol and coronary artery disease in asymptomatic men. Am J Cardiol, vol 48, 1981, pp. 903-910.

VALVULAR AND CONGENITAL HEART DISEASE IN THE AVIATOR

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Many valvular and congenital heart lesions can have major impact in the aviation environment. In the flying population, such lesions are typically asymptomatic and may be subtle enough that their presence can be detected only by very careful physical or laboratory examination. Thus, valvular or congenital cardiac disease is often found in a flier in whom there is a great deal of time, effort, and monetary investment. The loss of such an individual from flying status should thus be avoided if at all possible. As in all aeromedical decisions, these considerations must be weighed against the likelihood of significant impairment while performing aviation duties resulting either directly or indirectly from the cardiac lesion of concern. With these conflicting considerations in mind, the following is a discussion of regulations and medical aspects of specific valvular and congenital problems as approached by the USAF School of Aerospace Medicine.

Bacterial Endocarditis

Bacterial endocarditis is considered first since this disease is of great medical and aeromedical significance. This problem is a consideration in the majority of lesions to be considered later.

Although endocarditis has a low incidence, this catastrophic complication of structural heart disease should be assiduously avoided. In the clinical setting, endocarditis is a subendothelial infection with inflammation of the endocardial surfaces, and most often affects one or more of the cardiac valves. Vegetations which result from intense inflammation typically consist of fibrin and platelet deposits which form microthrombi. These thrombi often contain clusters of bacteria located either on or near the endocardial surface. Intense microscopic inflammatory changes are common, and consist of monocytes, lymphocytes, and histiocytes with rare polymorphonuclear leukocytes. The lesions are destructive to the valve surface, probably from the massive immune and inflammatory response.

In a clinical context, endocarditis is classified as acute or subacute depending on the organism causing the infection. The illness is acute when infection is caused by Staphylococcus aureus, Neisseria species (gonorrhea or meningitidis), Hemophilus influenza, and the Streptococci pneumonia and pyogenes. Conversely, subacute bacterial endocarditis results from infection by Streptococcus viridans or Staphylococcus epidermidis. This differentiation is more important than name alone, because clinical course, complications, and prognosis are related to the acute versus subacute differentiation.

Endocarditis most frequently results from transient bacteremias. It is worthwhile recalling that in bacteremia, organisms are present, but not actively replicating , while in septicemia the reproduction of organisms is actively ongoing. Bacteremias most often result from mechanical disturbances in body areas harboring organisms naturally such as the upper and lower gastrointestinal tract (mouth, large and small bowel), upper airway, skin, and external genital areas. For example, alpha streptococcal bacteremia resulting from tooth extraction occurs in up to 85 percent of all procedures performed. The actual time during which organisms can be cultured from the blood stream is short, averaging five to fifteen minutes after the procedure. However this short time can result in endocardial infection in susceptible individuals. Dental cleaning, tooth brushing, the use of dental floss, chewing hard objects, and the use of fluid oral irrigation devices have all been documented to result in transient bacteremias. Non-oral upper airway manipulations which can result in bacteremia include bronchoscopy and nasal surgery. Normal intestinal flora have been detected in the bloodstream following barium enema, colonoscopy, proctoscopy, and gastroscopy. Normal urinary flora bacteremia has resulted from cystoscopy even when the urine cultured from such a procedure was sterile. Finally, mild external infections of the skin as occur in acne can also result in bacteremia and

endocarditis.

Individuals with flow abnormalities within the heart are clearly at a higher risk of endocarditis. Lesions most frequently resulting in endocarditis are insufficient and stenotic valves, hypertrophic cardiomyopathy (IHSS), mitral valve prolapse, and the Marfan syndrome (rarely) even without mitral valve prolapse. Congenital cardiac defects associated with a higher risk of endocarditis are ventricular septal defects, patent ductus arteriosus and the Tetralogy of Fallot syndrome. Secundum atrial septal defects do not represent a significant risk of disease, and endocarditis prophylaxis is not currently recommended. As a general rule, lesions which result in a high pressure blood jet, or are a communication between a high and low pressure chamber put a patient at risk of endocarditis.

The signs, symptoms, and findings in endocarditis vary widely. Symptoms are generally non-specific, with generalized lassitude predominating. Fever is seen most frequently in endocarditis. Associated with fever are cardiac murmurs (but not always), anemia, and pallor of the mucous membranes. There are five classical findings in endocarditis. Petechiae and subungual "splinter" hemorrhages probably represent visible microemboli to dermal tissue. Osler nodes are tender, small, raised, red lesions and are found on the pads of the fingers and toes, and on the soles of the feet. Janeway lesions are painless, small red lesions which are irregular and flat, and occur on the palms and soles in subacute infective endocarditis. Clubbing of the fingers and/or toes also occurs. Roth spots are whitish "cotton wool" exudates seen in the eye grounds. Finally, splenomegaly is a frequent physical finding.

The laboratory examination in endocarditis is typified by an elevated erythrocyte sedimentation rate and anemia in the early stages. The leukocyte count in most cases is normal but usually exhibits a distinct leftward shift. The urine is usually normal, although proteinuria can be an early indication of endocarditis. If hematuria is seen, it usually occurs later and suggests secondary glomerulonephritis, interstitial nephritis, or renal infarction. Blood cultures should be drawn if there is any suspicion of endocarditis, especially in an individual who is known to be at risk of disease and has unexplained but definite laboratory abnormalities. Echocardiography should also be performed if endocarditis is suspected. The echocardiographic signs of endocarditis consist of valvular vegetations and endocardial thickening. The absence of these echocardiographic signs by no means implies that endocarditis is not present, because the sensitivity of echocardiography for detecting endocarditis is estimated at roughly 55%.

The management of endocarditis is best left to the specialist. Currently, duration of antibiotic therapy is controversial, but is generally two to six weeks of parenteral antibiotics. Valve replacement is sometimes required, usually due to refractory congestive heart failure, emboli, unresponsiveness to antibiotics, and relapse within 3 months of therapy. Overall prognosis is good in these days of potent antibiotics, but mortality still occurs. The overall five year survival ranges from 45 to 90 percent depending on the individual. Younger individuals have a better prognosis.

Important for the flight surgeon is the issue of prevention through antibiotic prophylaxis. The most recent (December 1984) guidelines for the prevention of bacterial endocarditis by the American Heart Association recommend the following.

Endocarditis Prophylaxis is recommended for:

- Mitral Valve Prolapse
- "Most" congenital malformations
- Prosthetic heart valves
- Rheumatic and other acquired valvular dysfunction
- Hypertrophic Cardiomyopathy (IHSS)
- History of Bacterial Endocarditis

Endocarditis Prophylaxis is not recommended for:

- Isolated secundum atrial septal defect
- Secundum atrial septal defect repaired without a patch six or more months earlier
- Patent ductus arteriosus ligated and divided six or more months earlier
- postoperative coronary bypass surgery

Procedures for which endocarditis prophylaxis is indicated:

- All dental procedures likely to induce gingival bleeding

- Tonsillectomy and/or adenoidectomy
- surgical procedures or biopsy involving respiratory mucosa
- bronchoscopy
- Incision and drainage of infected tissue
- Genitourinary and gastrointestinal procedures

US Air Force Regulations
Valvular and Congenital Heart Disease

U.S. Air Force Regulation 160-43 (para 4-18 and 5-20) states that for enlistment and commissioning purposes all organic disorders of the heart are disqualifying, including those improved by surgery. For U.S. Air Force entrance into flying training, a history of cardiac surgery or any significant congenital anomaly is disqualifying. Specific lesions will now be discussed with regard to diagnosis, prognosis, and waiver recommendation policy.

Specific Regulations

Valvular and congenital heart disease are of concern to the flight surgeon because of the potential for and association with arrhythmias, myocardial ischemia, heart failure, abnormal hemodynamics, embolic phenomena, and endocarditis. Aeromedical evaluation in the individual suspected of having a valvular or congenital lesion should at minimum undergo physical examination by an experienced cardiac specialist and have a complete echocardiographic examination including M-Mode, Two dimensional, and Doppler studies where possible. Other studies which may be indicated include exercise stress testing, 24 hour electrocardiographic monitoring, Thallium-201 scintigraphy, gated radionuclide blood studies, cardiac catheterization and centrifuge stress testing. These examinations are for both diagnostic and functional evaluation.

In general, waivers in the U.S. Air Force are restricted to rated individuals. While some valvular and congenital anomalies are waiverable, most lesions requiring cardiac surgery are permanently disqualifying. Those lesions which are waiverable must fulfill the criteria of having no hemodynamic significance, having no significant arrthymias (Supraventricular/Ventricular tachycardias), having no additional conditions such as coronary artery disease, and requiring no medication for the condition aside from endocarditis prophylaxis. Table I lists waiverable lesions and Table II lists non-waiverable lesions.

Some congenital heart defects may be waivered, but this is contingent upon the nature and severity of the lesion and how the lesion was corrected. It also depends on the natural course of the lesion, its associated symptoms, arrhythmias, and integrity of the conduction system. Those congenital lesions waiverable by the U.S. Air Force are listed in Table III.

SPECIFIC CONDITIONS

Mitral Valve Stenosis

Aeromedical: Mitral Stenosis is permanently disqualifying, even in mild cases. This is due in part to the potential for pulmonary hypertension, the potential for hypoxia-induced pulmonary vasoconstriction, and the propensity for arrhythmias and emboli.

Etiology: Mitral stenosis most frequently results from Rheumatic fever, but may more rarely be congenital. Frequently there is coexistent mitral valve insufficiency. Isolated rheumatic mitral valve disease is virtually nonexistent, i.e. if the diagnosis of rheumatic mitral valve disease is made, the aortic valve is almost certainly affected as well. It is rarely associated with Atrial Septal Defect (Lutembacher's syndrome). Left Atrial myxoma can sometimes mimic mitral stenosis.

Clinical: Clinical manifestations are usually present when the disease has significant hemodynamic effects. Symptoms include dyspnea, fatigue, hemoptysis, and anginal chest pain (in about 15% of patients). Some cases present with embolic events. Atrial fibrillation is a common finding in advanced cases.

Physical findings: In advanced cases there are prominent "a" waves of the jugular venous pulse, a palpable right ventricular heave along the left sternal border, and sometimes a characteristic ruborous or flushed facial appearance. Auscultation demonstrates a loud S1 (if the leaflets are still pliable), a narrowly split S2, and an opening snap which follows S2. The opening snap is late and should not be confused with the splitting of S2. The longer the delay between S2 and the opening snap, the less severe the stenosis is likely to be. The classical murmur is a low pitched, blowing diastolic "rumble" which usually has a pre-systolic accentuation.

Laboratory: Echocardiography is the best way to noninvasively assess mitral stenosis. Severity can be assessed with doppler echocardiography.

Mitral Valve Insufficiency

Aeromedical: This condition is waiverable. However the patient should

1) be asymptomatic with normal exercise tolerance

2) have disease of no other valve

3) have no dilation of the left ventricle or atrium

4) have no left ventricular dysfunction

5) have no significant arrhythmias

The valvular insufficiency must not be due to ruptured chordae tendineae. Thus, most patients with mitral insufficiency are those with mitral valve prolapse. A centrifuge stress test may be helpful for assessing the potential for arrhythmias. Yearly examination is indicated, with periodic subspecialty followup every 2-3 years. Endocarditis prophylaxis is essential.

Etiology: As noted above, most aeromedical mitral insufficency results from mitral valve prolapse. Marfan's syndrome has rarely caused isolated mitral insufficiency. Most other causes of isolated insufficiency such as mitral ring dilation or calcification, and left ventricular dilation are disqualifying for other reasons. Ischemic papillary muscle dysfunction causes mitral insufficiency, but coronary artery disease severe enough to cause this dysfunction would almost certainly result in disqualification.

Clinical: Mild mitral insufficiency is generally asymptomatic. Dyspnea, fatigue, and exhaustion are related to low cardiac output. Atrial fibrillation is present in advanced cases. Chest pain is rare, but not necessarily due to coronary artery disease.

Physical findings: These may be separated into those which identify mitral insufficiency and those which quantify its severity. The identifying features are a soft first sound, and a blowing, pansystolic murmur heard best at the apex and which is transmitted to the axilla. Those signs which quantitate the severity of mitral stenosis as more severe are a third heart sound, wide splitting of S2, and an increase in the pulmonic component of S2. If an S3 is heard, the left ventricle can fill rapidly; thus significant mitral stenosis may effectively be ruled out.

Laboratory: Echocardiography detects the presence and estimates the severity of insufficiency, especially with doppler examination where the spatial extent of the insufficient jet can be mapped. Cardiac Catheterization can also determine the severity.

Aortic Valve Stenosis

Aeromedical: Mild Aortic stenosis is waiverable if certain conditions are fulfilled. Cardiac catheterization for aeromedical purposes is frequently necessary to adequately evaluate the hemodyanmic significance of disease. A centrifuge stress test will determine the potential for arrhythmias. In addition, for waiver to be recommended the following must be true. The aviator should

1) have no more than 20 mmHg peak valve gradient

2) be asymptomatic

3) have no associated or additional cardiac problems

4) have no evidence of left ventricular hypertrophy or cardiac dysfunction.

Patients with aortic stenosis should have frequent followup and receive SBE prophylaxis. The advent of doppler echocardiography allows noninvasive determination of the aortic valve gradient so that progression may be followed.

Etiology: In the military flying population, aortic stenosis typically results from congenital defects, most commonly bicuspid aortic valves which spontaneously stenose. Bicuspid aortic valve occurs in roughly 1% - 2% of the general population. Unicuspid aortic valve also occurs and causes eventual stenosis. Calcific aortic stenosis in young adulthood is typically rheumatic, although congenital valve defects may occasionally calcify at rapid rates.

Clinical: Aortic stenosis is most commonly recognized in the young patient by murmur, or following a syncopal episode. Syncope can be due to arrhythmia (bradycardia or tachycardia), can occur with exertion, and can be fatal. Rarely, congestive heart failure is the presenting complaint. Angina pectoris can also be the presenting complaint and does not necessarily imply significant coronary artery disease. Angina pectoris, syncope, or cardiac failure are ominous prognostic signs in the aortic stenosis patient, and the individual should be promptly referred for surgical consideration.

Physical findings: In moderate and severe stenosis, the arterial pulse has a slow upstroke, and is delayed. Frequently the left ventricle is hyperdynamic at the apex and can be easily palpated. The classical murmur has a harsh ejection quality, is heard at both upper sternal borders, and is transmitted to the neck and head. If the valve is still pliable, an ejection sound (an ejection "click") is heard following S1, especially in bicuspid valves. These ejection sounds are high frequency, and remain present even with heavy pressure of the stethoscope diaphragm against the chest, which makes the diaphragm into a higher frequency filter. This simple maneuver can be used to differentiate a fourth heart sound (S4) from an ejection click.

Laboratory: Echocardiography provides excellent evaluation of aortic stenosis with the valve easily visualized in most cases. Determination of the number of cusps is usually possible. Doppler echocardiography, when properly performed, gives accurate estimation of transvalvular gradient and cardiac output. Cardiac catheterization may be needed if there is a question of coronary artery disease, or if the echocardiographic study is indeterminate.

Aortic Valve Insufficiency

Aeromedical: Aortic insufficiency is a categorically waiverable condition (the aviator is limited to flying tanker, transport, or bomber aircraft) if the disease is not severe. High performance aircraft and the associated high G environment leads to greatly increased afterload on the heart. This increased diastolic pressure might accelerate the leaking valve's detrimental effects on the ventricle. For waiver recommendation, the patient should

1) be asymptomatic

2) have a left ventricular end diastolic pressure less than 14 mmHg

3) have angiographic insufficiency less than 2+

4) have a regurgitant fraction less than 25%

5) have no associated aortic root disease or other cardiac disease

6) have no significant arrhythmias

These patients should have close followup and receive SBE prophylaxis as well.

Etiology: As in the case of aortic stenosis, the most frequent cause of aortic insufficiency in the flying population is the bicuspid aortic valve. Other less common causes can be the Marfan's syndrome, bacterial endocarditis, collagen vascular disease, and ruptured cusps.

Clinical: Aortic Insufficiency is most commonly recognized in the flying population when a diastolic murmur is heard. Mild disease is rarely symptomatic, and the condition remains silent for many years. It eventually becomes symptomatic when the heart is enlarged, with correspondingly large regurgitant fractions. Symptoms are dyspnea and fatigue. Once heart failure has occurred, the prognosis is not as good. Tachycardias which are detrimental in other valvular heart disease may actually improve the hemodynamics in aortic insufficiency since the diastolic period of filling is shorter; there is thus less time for leakage to occur.

Physical findings: Severity of disease can be judged clinically with the blood pressure cuff. Severe disease leads to lowering of the diastolic pressure, and if the diastolic pressure is 75 mmHg or more, the disease cannot be severe. The lowest diastolic pressures typically achieved are in the 30 to 40 mmHg range because the left ventricular pressure rises to this level in severe disease. The finding of diastolic pressures in the 50 mmHg range suggests severe aortic insufficiency. The venous pulsations of the neck are normal, and in significant disease there are visible capillary pulsations in the fingernails. The arterial pulse collapses with a sudden deceleration perceived with the fingers (the "waterhammer" pulse), and the ventricle is hyperdynamic. The murmur of aortic insufficiency is high-pitched, blowing, and diastolic. It is usually heard best along the left sternal border. Sometimes the murmur is heard along the right sternal border, and in either case if the patient is told to empty his lungs as completely as possible and then lean far forward, the murmur can be better heard. Careful listening may also detect the so-called Austin-Flint murmur which is soft, diastolic, and heard at the apex. It mimics the murmur of mitral stenosis except that no opening snap is heard and there is no accentuation of the first heart sound. This murmur comes from the jet of insufficient aortic blood partially closing the mitral valve in diastole yielding turbulence of the inflowing mitral blood.

Laboratory: Echocardiography is the mainstay of noninvasive evaluation, and frequently detects a bicuspid aortic valve. Doppler echocardiography reliably establishes the presence of aortic insufficiency. Quantitation of insufficiency is more difficult, but can be done with color flow doppler technology.

Tricuspid Valve Disease (stenosis/insufficiency)

Aeromedical: Tricuspid valve disease, whether insufficiency or stenosis, is disqualifying without waiver. In the aviation environment, hypoxic pulmonary vasoconstriction and resulting pulmonary hypertension will aggrevate the detrimental hemodynamics of tricuspid insufficiency.

Etiology: Tricuspid valve disease may be functional or organic. For example, functional tricuspid insufficiency may result from atrial arrhythmias or in association with conditions causing pulmonary hypertension (pulmonary artery pressures above 45/20 mmHg). Organic, structural tricuspid valve disease occurs as a result of rheumatic fever, and myxoma of the right atrium, Ebstein's anomaly and in tricuspid valve prolapse. Tricuspid valve prolapse occurs in roughly 20 % of patients with mitral valve prolapse.

Tricuspid stenosis is always organic, and rare. It is usually seen in conjunction with the carcinoid syndrome and in rheumatic heart disease. When it occurs as a result of rheumatic heart disease, the mitral valve is virtually always involved.

Clinical: The effect of tricuspid valve disease is usually to unload the lungs of blood, at the cost of overloading the venous system with that blood. There is thus little dyspnea, and significant edema peripherally in severe disease. Blunt chest trauma can rupture a tricuspid papillary muscle, and years later result in clinical problems. Taking a history of previous trauma is thus essential.

Physical findings: In tricuspid stenosis, the venous pulsations in the neck have a slow descent. There is a low pitched rumbling diastolic murmur heard usually at the lower left sternal border which increases with inspiration. Most right heart murmurs increase with inspiration because right heart blood flow increases when a breath is taken due to the lowering of intra- thoracic pressure. In tricuspid insufficiency, the "v" waves of the neck vein pulsation are increased. In severe cases, the liver may pulsate. There is also a pansystolic murmur which increases with inspiration heard at the lower left sternal border.

Laboratory: Echocardiography and doppler studies can usually document and quantify the degree of tricuspid valve disease. This newer technology has found clinically silent tricuspid valve insufficiency in a majority of healthy young individuals. Observation of hepatic vein flow is useful for quantifying the severity of the insufficiency and in the "normal" aviation population this is usually mild.

Pulmonary Valve Disease

Aeromedical: Pulmonary Valve Insufficiency is disqualifying without waiver. Pulmonary Valve stenosis is waiverable if the aviator

1) is asymptomatic

2) has normal cardiac function

3) has no significant associated arrhythmias

4) has normal cardiac conduction

5) has no other cardiac abnormalities

6) has a pulmonary valve gradient of less than 20 mmHg

Careful followup, and SBE prophylaxis is highly recommended.

Etiology: Pulmonary valve stenosis is usually congenital. Unlike the aortic valve, the pulmonary valve is rarely bicuspid. Stenosis most often is from hypoplasia of the valve ring itself.

Pulmonary valve insufficiency is commonly functional secondary to pulmonary hypertension. Marfan's syndrome and bacterial endocarditis are other causes.

Clinical: Pulmonic stenosis is not progressive as is aortic stenosis. Mild pulmonic stenosis carries a low risk of hemodynamic difficulty, and a normal, asymptomatic life is the rule. Pulmonic stenosis can be part of the congenital Tetralogy of Fallot syndrome (pulmonic stenosis, ventricular septal defect, right ventricular hypertrophy, and overriding aorta), or it may be isolated.

Pulmonary valve insufficiency can also be tolerated chronically, except that it is usually secondary to pulmonary hypertension which is frequently progressive.

Physical findings: In pulmonic stenosis there is an increased "a" wave in the neck vein pulsations. There is a palpable right ventricular lift, an ejection click, and P2 is late and diminished. The typical pulmonic stenosis murmur is ejection in nature, harsh, louder with inspiration and heard best at the left second or third interspaces near the sternum. The murmur of pulmonic insufficiency is sometimes called the Graham-Steell murmur (usually secondary to pulmonary hypertension). This murmur is high-pitched, blowing, decrescendo in nature and begins immediately following P2. It is heard best in the left parasternal area of the second to fourth intercostal spaces. It resembles the murmur of aortic insufficiency, but may be differentiated by association with an accentuated P2 or a fused S2. It usually increases with inspiration, changes

little after amyl nitrite administration, and is diminished with Valsalva maneuver.

Laboratory: Echocardiography is both sensitive and specific for detection of pulmonic valve disease when the doppler examination is included.

Hypertrophic Cardiomyopathy (HCM, HOCM, IHSS)

Aeromedical: This interesting cardiac condition is permanently disqualifying for all classes of flying duty. The reason is the association with syncope and sudden death in affected individuals. Syncope may be either hemodynamic or arrhythmic. Roughly 22% of all afflicted patients are asymptomatic, and over half have no functional limitation to everyday life.

Etiology: The etiology is unknown. The disease has had a vast array of names, but most seem to reflect the disproportionate septal thickening seen in the commonest form. It is hereditary as autosomal dominant, so diagnosis mandates prompt examination of family members. The left ventricle of an affected patient is hyperdynamic. The mitral valve sometimes exhibits a characteristic systolic anterior motion which is usually associated with an intraventricular pressure gradient. Controversy has raged over the significance of the intraventricular gradient, and whether this represents an obstruction to outflow by the septum and mitral valve or is a result of rapid, forceful ventricular contraction.

Clinical: This condition is most commonly a disease of young adults (average age at presentation is 26 years). Dyspnea is the most frequent complaint of those individuals who are symptomatic. Other symptoms are angina pectoris, fatigue, and loss of consciousness, especially with exertion. In the aeromedical population, the disease is most often found by routine electrocardiography because of the characteristic electrocardiogram. In other patients there is evidence only of left ventricular hypertrophy. The flight surgeon who is caring for a patient with left ventricular hypertrophy presumed secondary to hypertension should also consider this disease entity (or a variant) if the hypertrophy does not respond to adequate blood pressure management.

Physical findings: A rapid "a" wave is sometimes seen in the neck vein contour. The arterial pulse has a characteristic rapid rise (in contrast to aortic stenosis where the rise is slow), and is frequently bifid in nature. Classically, the murmur is harsh with an ejection quality and is heard best low on the precordium. The murmur is increased by Valsalva maneuver since the left ventricular volume is decreased and the gradient increases. If the examiner is fortunate enough to hear a ventricular extrasystolic beat, the sinus beat following this one greatly exaggerates the murmur. Amyl nitrate also exaggerates the murmur since the ventricular volume is smaller (more venous pooling). Mitral insufficiency is commonly associated with this condition, and this murmur can frequently be heard.

Laboratory: Echocardiography has probably become the definitive diagnostic method for this entity. A ratio of septal thickness:posterior wall thickness of 1.3 or greater with enhanced ventricular contraction and appropriate physical findings is considered diagnostic. Systolic anterior motion of the mitral valve can usually be easily demonstrated when present.

Atrial Septal Defect

Aeromedical: Secundum atrial septal defect, if repaired, is a waiverable condition after a mandatory six month waiting period postoperatively. It is frequently recommended that cardiac catheterization be repeated in the postoperative period to insure effectiveness of surgery and proper intracardiac pressures. There are two other less common types of atrial septal defect, primum defects (low, near the atrioventricular junction) and sinus venosus defects (high, near the entrance of the pulmonary veins). These defects are not waiverable because of associated anomalies.

Etiology: The etiology of this defect is uniformly congenital. The variants are as noted above.

Clinical: Typically small lesions are silent into early adulthood and not associated with significant symptoms. In larger defects, symptoms will usually develop by age 40, and present as dyspnea on exertion, congestive heart failure, and symptoms

related to supraventricular arrhythmias (tachycardia, atrial fibrillation) which are associated. It is important to detect and correct this problem early so that permanent damage to the lung vasculature does not result from the chronic right heart volume overload state. Pulmonary hypertension can result, but rarely occurs before age 20 in individuals at sea level. This problem can occur earlier in people living at higher altitudes.

Physical findings: The typical patient with atrial septal defect is usually gracile and sometimes has a prominent left chest since the right ventricle presses the left chest wall outward. The venous pressure is normal in the asymptomatic patient. The right heart is palpable on the precordium. There is sometimes a systolic murmur in the pulmonic area, soft, and due to increased right heart flow. If there is a large left to right heart flow, there is a diastolic flow murmur originating from flow through the tricuspid valve (not from flow through the defect). The second heart sound has a wide and fixed split, because the right heart has a larger volume to expel with each heartbeat and thus takes longer.

Laboratory: Echocardiography when combined with doppler methods can demonstrate most defects of clinical significance. Electrocardiography sometimes shows complete or incomplete right bundle branch block, and/or an rSr' pattern in precordial lead V1. The chest X-Ray shows right atrial and right ventricular enlargement in proportion to the increased stroke volume. The central pulmonary arteries are enlarged proportionately to flow through them and the degree of pulmonary hypertension, if present. The degree of vascularity on X-ray is inversely proportional to the degree of pulmonary vascular disease.

Ventricular Septal Defect (VSD)

Aeromedical: Ventricular septal defect is analogous in many ways to atrial septal defect in regard to aeromedical status and disposition. Repair of the small VSD is required for waiver, and a mandatory waiting period of six months postoperatively should be observed. During this period, cardiac catheterization or careful echocardiographic/doppler examination should be performed. Endocarditis prophylaxis is mandatory.

Etiology: Etiology is virtually always congenital in the aviator, and other causes such as ischemic necrosis are obviously disqualifying for other reasons.

Clinical: The physiology of VSD is quite different from that of ASD, since the communication is between a high pressure (left ventricle) and lower pressure (right ventricle) chamber. Clinically, sizes may be seen from only a few millimeters to patients in which virtually the entire septum is absent. The symptomatology is related to defect size, and most of the aeromedical patients will be asymptomatic. The natural history is related to the state of the pulmonary vasculature, and whether damage is done because of high pressure and volume overload. Operation for medical reasons should definitely precede development of this dreadful complication. Aeromedically, most patients will be discovered because of the murmur, and operation can be undertaken without problem.

Physical findings: Large defects at birth result in poor development, so that such a situation is unlikely to appear in the aviator. Chest deformities are common with large defects in the form of a bulging sternum. Either or both ventricles may be felt on palpation. If there is left to right flow through the defect (as should be the case in the aeromedical context), auscultation reveals a harsh pansystolic murmur loudest in the lower left sternal area with radiation over the entire precordium. The murmur is louder in smaller defects, because a jet is formed, and these are the so-called "maladie de Roger" lesions.

Laboratory: Echocardiography can visualize larger defects, and doppler techniques can detect both large and small defects with high sensitivity and specificity. The x-ray is usually normal, especially with small defects.

Helpful Auscultatory Hints

Organic murmurs are:

* Diastolic, pansystolic, or continous
* Loud
* Associated with other cardiac abnormalities

Innocent Murmurs are:

* NOT associated with abnormal S2 splitting
* NOT diastolic
* NOT pansystolic
* NOT loudest in the aortic area
* NOT loud
* NOT found to radiate widely

Types of Innocent murmurs:

Completely Innocent:

* Cervical venous hum
* Supraclavicular arterial bruit
* Mammary souffle
* Still's vibratory murmur
* Pulmonary systolic ejection murmur

Relatively Innocent:

* Early systolic murmurs
* Pulmonary flow murmurs with high output

Table I
Cardiac Lesions waiverable in the U.S. Air Force

Minimal Aortic Valve Stenosis
Mild Aortic Valve Insufficiency
Isolated Mitral Valve Insufficiency
Mild Congenital Pulmonic Valve Stenosis

Table II
Cardiac Lesions which are not waiverable under any circumstance

Mitral Valve Stenosis
Mitral Valve Insufficiency secondary
to ruptured chordal apparatus, or
ischemic papillary muscle dysfunction.
Significant Tricuspid Valve Disease
Pulmonary valve insufficiency secondary
to pulmonary hypertension

Table III
Waiverable congenital heart lesions

Discrete Subvalvular/Supravalvular Aortic Stenosis
Ostium Secundum Atrial Septal Defect
Coarctation of the Aorta (mild)
Patent Ductus Arteriosus
Ventricular Septal Defect (small)

Aortic Stenosis

Aortic Insufficiency

Mitral Stenosis

Mitral Insufficiency

Hypertrophic Cardiomyopathy

Ventricular Septal Defect

AEROMEDICAL ASPECTS OF MITRAL VALVE PROLAPSE

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Mitral valve prolapse (MVP) continues to be a major aeromedical problem. Current issues revolve around diagnostic criteria, aeromedical thresholds for disqualification and the lack of definitive natural history studies upon which to base aeromedical decisions. Currently, there are no existing natural history studies of incidentally discovered mitral valve prolapse in the asymptomatic male. USAFSAM is currently following over 300 mitral valve prolapse subjects on a recurrent basis in order to determine this natural history. The comparison of this natural history group with age-matched controls should be completed in approximately 1988. Preliminary data offered in this report enumerate the most common grounding causes of mitral valve prolapse in the first 202 aviators with prolapse in the study. A suggested scheme for clinical evaluation, aeromedical disposition of MVP and suggested aeromedical diagnostic criteria are offered.

Prevalence of Mitral Valve Prolapse

Mitral valve prolapse in the general population ranges from a prevalence of 4.6% to 21%, depending upon the study quoted. Figure 1 lists the sources of these estimates (1, 2, 3, 4, 5, 6). This rather wide range is explained by population selection factors and variance in diagnostic criteria. The most widely quoted prevalence figure is 6-7%, using combined auscultatory and echocardiographic criteria in a mixed male/female population. Among the last 14,128 aviators evaluated at USAFSAM, the prevalence of mitral valve prolapse was 2.3%. This lower-than-expected prevalence of mitral valve prolapse in military aviators may be explained in part by: 1) there are practically no women in the denominator, and MVP is more common in females; 2) some auscultatory screening had been performed before entry into flying training, and subjects diagnosed with MVP do not usually enter flying training; 3) some USAFSAM subjects who received highly specified evaluations (e.g., ophthalmology) may not have been studied with echocardiography. Also, echocardiography was not generally available until 1971-72; and 4) the prevalence figure for mitral valve prolapse in a referral population such as USAFSAM includes a significant number of mitral valve prolapse subjects referred because of that diagnosis, which would tend to push prevalence higher rather than lower. However, because mitral valve prolapse was diagnosed with relative infrequency prior to the early 1970s, overall prevalence figures are severely affected by increasing diagnostic sensitivity after 1972. Without an echocardiographic survey of applicants for undergraduate pilot training, rather than selectees, it is impossible to know the true prevalence of mitral valve prolapse in a training population. The prevalence of mitral valve prolapse in undergraduate pilot training selectees, who have already received an auscultatory examination is also unknown in the US Air Force. Dr Gray will later present some echocardiographic screening statistics for the Canadian Air Force.

Devereux, et al., Circ 1976	6%
Brown, et al., Circ 1975	4.6%
Progacci, et al., NEJM 1976	6.3%
Warth, et al., Circ 1983	13%
Sasaki, et al., Jap. Cardiography 1982	11%
Leatham, A., et al., AHJ 1980	21%

Figure 1 - Reported MVP Prevalence from the Medical Literature

Diagnostic Criteria

The issue of prevalence bears upon diagnostic criteria. The major issue is whether or not some degree of mitral valve prolapse (some degree of mitral valve protrusion into the left atrium during systole) might not be "normal." One does not readily accept the idea of collapse of the mitral valve under "normal" hemodynamic conditions, or that failure of the mitral leaflets to coapt with even minimal retrograde regurgitation is "normal." Unfortunately, the relative infrequency of such findings in "healthy persons" has been a barrier to effective echocardiographic diagnostic criteria. Quantitative

criteria for mitral valve prolapse from angiography have been published, with the only asymptomatic series coming from USAFSAM (7). The criteria were quite specific, but less sensitive. A 20% prevalence of acoustically silent mitral valve prolapse (detected angiographically) places a strong reliance on echocardiography, even in the face of somewhat nebulous echocardiographic diagnostic criteria. This diagnostic dilemma was highlighted in one published series by Abassi (8), who reported diagnostic sensitivities for combined M-mode, two-dimensional echocardiogram and Doppler from a low of 50% alone with M-mode to a high of 93% using all three modalities, with the midsystolic click serving as the "gold standard." These data are displayed in Figure 2. It must be recognized that no matter which diagnostic criteria one employs, there will be gray zone cases. A suggested list of criteria which may be useful in the aeromedical setting are those designed at USAFSAM. The USAFSAM diagnostic criteria (Figure 3), published from USAFSAM in 1980 (9), require anatomic confirmation, either by echocardiogram or angiography, or confirmation of a midsystolic click by two competent auscultators in order to label a case as definite MVP, rather than possible or probable MVP. This differentiation is important since findings which may be associated with mitral valve prolapse such as supraventricular tachycardia and ventricular tachycardia (which are waiverable for some categories of flying in and of themselves) may become the drivers for angiography since they are not considered waiverable in the face of mitral valve prolapse. If there are no disqualifying mitral valve prolapse subsets, it is not essential that the distinction between possible and probable prolapse be made, since the aeromedical disposition and follow-up are unaffected.

Auscultatory MVP	125
M-Mode MVP	62 (50%)
2D - Echo	85 (68%)
Doppler	90 (72%)
M and 2D	96 (77%)
M and D	111 (89%)
M, 2D and D	116 (93%)

Legend: 2D = two-dimensional
D = Doppler
M = M-Mode Echo

From Abassi, et al., JACC, Dec 83

Figure 2 - Performance of Echo/Doppler Studies in Auscultatory MVP

	Left Ventricular Cineangiogram		M-Mode Echocardiogram		Auscultation
Definite	Posterior mitral leaflet herniation > 10 mm into left atrium	OR	Mid-late systolic posterior "buckling" > 2 mm from C-D line	OR	Midsystolic click documented by 2 observers
Probable			Holosystolic posterior mitral motion	AND	Non-ejection click and/or late systolic murmur
Possible			Holosystolic posterior mitral motion	OR	Isolated non-ejection click

Modified from Engel and Hickman, 1980

Figure 3 - Recommended USAFSAM Aeromedical Diagnostic Criteria for MVP in Aviators

At USAFSAM, we still recommend bacterial endocarditis prophylaxis for those with possible or probable mitral valve prolapse. Mid to late systolic buckling is the most specific M-mode finding for MVP, while holosystolic motion or flattening is suggestive of MVP but not diagnostic. The two-dimensional echocardiogram has provided even better

anatomic definition, and good quality two-dimensional echocardiograms detect many patterns of mitral motion behind the annular plane. Specific criteria for the additional information supplied by Doppler have not been established at USAFSAM, but this diagnostic tool may provide a very sensitive method of detecting the minimal mitral regurgitation often associated with the prolapsing mitral valve. At USAFSAM, we resort only to angiography in mitral valve prolapse when the diagnosis is equivocal and arrhythmias are present which are permanently disqualifying in the face of mitral valve prolapse. Under these conditions, we recommend left anterior oblique and right anterior oblique ventriculograms. In most cases of mitral valve prolapse in aviators, there are no disqualifying subsets of MVP, and the differentiation between definite, possible, and probable mitral valve prolapse is not critical. Only when the diagnosis is absolutely critical to the aeromedical disposition is angiography necessary.

Aeromedical Concerns in Mitral Valve Prolapse

Many associated phenomena have been reported to occur with mitral valve prolapse which are not compatible with flying. The major aeromedical concerns are outlined in Figure 4. Figure 5 outlines a composite estimate of the complication rate for mitral valve prolapse patients in a clinical population. It should be noted that the overall complication rate is an estimated 12-15%. However, these studies were performed on patients who reported to physicians because of complaints. The true prevalence of mitral valve prolapse complications in asymptomatic individuals will not be known until a large cohort of aviators with incidentally discovered asymptomatic mitral valve prolapse are followed in a long-term epidemiological study. Currently, at USAFSAM, a natural history

1. Incapacitating chest pain
2. Significant ventricular and atrial arrhythmias
3. Significant mitral regurgitation
4. Endocarditis
5. Embolic phenomena
   - A. Retinal
   - B. Cerebral hemispheres
   - C. Brainstem
6. Sudden death
   - A. Arrhythmic
   - B. Conduction disturbances

Figure 4 - Aeromedical Concerns in MVP

Ventricular Arrhythmias	50%
Atrial Arrhythmias	60%
Endocarditis	3%
Ruptured Chordae	Unknown
Sudden Death	Unknown
Overall Complication Rate	12-15%

Figure 5 - Estimated MVP Risks (Composite Average) from Multiple Clinical Series

study has been underway for a number of years. In 202 consecutive cases of mitral valve prolapse evaluated serially with a full noninvasive and clinical evaluation, 75 aviators were disqualified because of findings associated with mitral valve prolapse. Of these 75 disqualifications, 11 occurred in those who were undergoing aviation training, 51 occurred in actively flying pilots or navigators, and 13 occurred in aircrew other than pilots and navigators. The causes for disqualification of these aviators with mitral valve prolapse are enumerated in Figure 6. As one can see, the overwhelming majority of these disqualifications were due to arrhythmias. Figure 7 reveals the distribution of the disqualifying arrhythmias. There were actually 32 disqualifying arrhythmias in 31

MVP with arrhythmias	31
MVP with other medical	21
MVP and associated cardiac disease	7
MVP with conduction defects	6
MVP with coronary disease	5
MVP with chest pain	2
MVP only (flying training subsets)	2
Other (non-medical)	1

N = 75

Figure 6 - Causes for MVP Disqualification in 75 Cases at USAFSAM (202 MVPs)

Ventricular Ectopy (Holter)	9
Stress Arrhythmias (TM)	6
Ventricular Tachycardia	6
Supraventricular Tachycardia	11

N = 32

Figure 7 - Distribution of MVP Disqualifications for Arrhythmias at USAFSAM

aviators, since one aviator had both complex ventricular and atrial arrhythmias. Figure 8 describes the 11 disqualifying supraventricular tachycardias. Reentrant supraventricular tachycardias were the most common. Figure 9 lists the six associated conduction disturbances. Figure 10 enumerates the seven cases of mitral valve prolapse associated with other cardiac diseases. One aviator was disqualified for significant mitral regurgitation with progressive left atrial enlargement. Two others were disqualified for disease of the aortic root, one of which was associated with significant aortic insufficiency. Two other cases of valvular aortic insufficiency were associated with myxomatosis degeneration of the aortic valve. One case of clear-cut Marfan's syndrome was noted. In summary, 37% of our mitral valve prolapse subjects were disqualified at a mean follow-up period of approximately five years. While this disqualification rate is quite high, the disqualifications were largely based upon our concept of what should be disqualifying, such as asymptomatic significant rhythm disturbances, rather than symptomatic or incapacitating events. However, one must set aeromedical thresholds for disqualification which are dependent upon recurrent testing rather than clinical symptomatic endpoints. These 202 cases dealt solely with abnormalities which were discovered during recurrent clinical examinations at USAFSAM. Three other subjects were disqualified because of symptomatic histories, all three of which were related to the central nervous system. One aviator suffered a major hemispheric stroke because of a cerebral embolus, another suffered a retinal embolus, and a third experienced a retinal embolus, but acephalgic migraine could not be totally ruled out in the latter case. Prior to the advent of the long-term mitral valve prolapse study group, one aviator with mitral valve

Reentrant SVT	7
Multifocal Atrial Tachycardia	1
Atrial Fibrillation	3

N = 11

Figure 8 - Distribution of MVP Disqualifications for Supraventricular Tachycardia at USAFSAM

1. Right Bundle Branch Block and Left Anterior Hemiblock
2. Incomplete Right Bundle Branch Block and Left Anterior Hemiblock
3. Mobitz I AV Block
4. Mobitz II AV Block
5. Wolff-Parkinson-White EKG Finding
6. Marked Sinus Bradycardia

Figure 9 - Conduction Disturbances in MVP

1.	Significant Mitral Regurgitation	(1)
2.	Aortic Root Disease/AI	(1)
3.	Marfan's Syndrome	(1)
4.	Aortic Insufficiency	(2)
5.	Rheumatic Heart Disease	(1)
6.	Aortic Root Disease/No AI	(1)

N = 7

AI = Aortic Insufficiency

Figure 10 - Other Disqualifying Cardiac Conditions in MVP Subjects

prolapse and a previous episode of exercise-induced ventricular tachycardia died suddenly during follow-up. The issue of the prevalence of central nervous system events in mitral valve prolapse, such as stroke, may be pursued in two ways. One may study a population of mitral valve prolapse subjects and evaluate the prospective incidence of cerebral events (which is the method currently being employed at USAFSAM) or alternatively one may study in retrospect the frequency of central nervous system events in a young population to determine if mitral valve prolapse is overrepresented. The Mayo Clinic Study (10) is a prospective study of 1,138 patients with mitral valve prolapse, of whom 40 suffered subsequent cerebrovascular accidents. Twenty-six of these 40 had no identifiable cause for their strokes. Ten of the 26 had definite evidence of an embolic phenomenon. Two-thirds of these patients were women and one-third were men. They were all greater than 20 years of age with a mean age of 48 years. The prevalence of stroke in the 22-44 year age group was 3%. Despite the female predominance of mitral valve prolapse subjects, the complication of stroke was more prevalent in males. Overall, the prevalence rate for cerebral infarction was 4-5 times greater than the expected population rate. Other studies have approached the problem by looking at the prevalence of mitral valve prolapse in groups of young patients with unexplained cerebral events. As can be seen from Figure 11, mitral valve prolapse is grossly overrepresented in a population of young people with unexplained cerebral ischemic events (11, 12, 13, 14, 15).

STUDY	N	MEAN AGE	% MVP PTS.	MVP CONTROLS
BARNETT	36	$\leq$ 45	61%	7% (P < .001)
BENSAID	20	< 40	20%	
HART	15	$\leq$ 40	47%	
DEBONO	40	58	15%	4%
SCHARF	47	< 45	28%	8.4%

Figure 11 - Unexplained Cerebral Ischemic Events in Younger Subjects (Extracted partially from Hart, R. and Easton, D., Mitral Valve Prolapse and Cerebral Infarction, Stroke July-August, 1982, 13: 429-430 [Editorial])

Obviously, strokes are so uncommon in the aviator population that the construction of an adequate comparison group is difficult. However, we can make some estimate based on young adults in North America. The prevalence of cerebrovascular accidents in young adults under age 40 is only 3 per 100,000 subjects per year, or 1 stroke per 33,0000 persons per year. If one considers that one-third of the strokes in young people in North America are secondary to mitral valve prolapse, the risk of cerebrovascular accident in mitral valve prolapse is approximately 1 in 6,000 per year. Mitral valve prolapse precipitating a stroke is rare, but prolapse has emerged as the leading cause of strokes in young people in North America. The rather gross excess prevalence of asymptomatic cardiac arrhythmias in an aviator population, which spans the age group in which prolapse is the most common cause of stroke, is rather worrisome.

Aeromedical Evaluation of the Aviator with Mitral Valve Prolapse

Figure 12 lists the suggested workup of mitral valve prolapse. The treadmill test is recommended largely to detect exercise-induced arrhythmias. A significant number of abnormal ST segment responses will be detected if one performs a treadmill exercise tolerance test on asymptomatic mitral valve prolapse subjects. At USAFSAM, only 7% of our aviators have an abnormal treadmill test when subjected to exercise testing in an unselected fashion. However, 28% of all mitral valve prolapse aviator subjects will have an abnormal ST segment response (16). We also noted that the mitral valve prolapse

subjects revealed vasoregulatory changes with standing and hyperventilation far more often than non-MVP aviators. In fact, a rather characteristic pattern of the abnormal exercise test emerged in the MVP subjects. There were usually postural changes during pre-exercise, ST segment depression usually less than 2 mm occurred during early to mid exercise, and the ST segment response frequently normalized during peak exercise and recovery. The ST abnormalities may reappear during late exercise. This particular pattern was noted to occur in 58% of our prolapse subjects with abnormal treadmill tests, and in only 2% of other subjects with coronary disease or "false-positive" treadmill tests. Mitral valve prolapse should be suspected in aviators with abnormal stress

1. Thorough Clinical History & Physical
2. M-Mode and 2-D Echocardiogram
3. Doppler/Echocardiogram if Available
4. Treadmill Test for Arrhythmia Detection
5. 24-hour Holter Monitor
6. Centrifuge For Fighter Pilots
7. Catheterization in Cases with Equivocal Noninvasive Findings and Serious Arrhythmias
8. Periodic Re-examination at 1- to 3-year Intervals

Figure 12 - Suggested Aeromedical Evaluation of MVP Subjects

tests and vasoregulatory abnormalities. Because of the frequency of the abnormal exercise tests in aviators, we recommend that those aviators 35 years of age and under be exempted from cardiac catheterization to elucidate the abnormal ST segment response if they have no significant risk factors for coronary artery disease. A thallium scintigram may not be of much assistance in resolving the etiology of the abnormal ST segment response in mitral valve prolapse subjects, since abnormal thallium scintigrams are also quite common in mitral valve prolapse. Aviators who are flying high-performance aircraft should at some point undergo centrifuge testing in order to evaluate the response of this entity to $+G_z$ acceleration. Cardiac catheterization will only be required in those cases in which the diagnosis is equivocal, and other disqualifying features mandate a definitive diagnosis of mitral valve prolapse. We also strongly urge a periodic noninvasive evaluation until the natural history data regarding asymptomatic MVP subjects becomes available in the future. Currently at USAFSAM, the mitral valve prolapse disqualifications seem to be distributed rather equally between the first, second, third and fourth evaluations. This is somewhat disconcerting, since it implies that the aeromedical prognosis cannot be assumed from a single initially normal evaluation. Figure 13 enumerates the disposition of aviators with mitral valve prolapse. In the USAF, as in many air forces throughout the world, mitral valve prolapse is not acceptable for flying training. However, aviators who are found to have mitral valve prolapse after

1. Not Qualified to Enter Aviation Training
2. Waiverable in Rated Aviators if:
   - No Significant Chest Pain
   - No Prolonged QT Interval
   - No History of Endocarditis
   - No Significant Mitral Regurgitation
   - No Aortic Root or Aortic Valve Disease
   - No Other Associated Cardiac Abnormality
   - No Conduction Disturbance Except RBBB and First-Degree AV Block (Which Normalizes with Exercise)
   - No Left Atrial or Left Ventricular Enlargement
   - No Complex Arrhythmias
     - Supraventricular Tachycardia
     - Ventricular Tachycardia
     - Multifocal Atrial Tachycardia
     - Ventricular Pairing on Holter (Acceptable on Exercise Testing)

Figure 13 - Aeromedical Disposition of Mitral Valve Prolapse

they are trained to fly may be waived for flying under certain guidelines. Obviously, many aviators with mitral valve prolapse enter flying training with the prolapsing valve undetected on routine clinical examination. This raises the issue of whether or not applicants for aviation training should receive echocardiography. This subject was discussed at considerable length at a recent AGARD symposium (17, 18). Dr Gray of the Canadian Air Force will next present some preliminary data regarding echocardiographic

screening of aviation applicants. There appears to be emerging a general consensus that echocardiography is needed for aviation applicants, both for the discovery of subclinical disorders such as mitral valve prolapse, as well as to serve as a baseline study of resting cardiac function and structure. Such a baseline study may become invaluable later in the aviator's career to serially assess possible acquired cardiac abnormalities (19).

References

1. Devereaux RB, Perloff JK, Reichek N, Josephson ME. Mitral valve prolapse. Circulation 54, 1976, 3-14.

2. Brown OR, Kloster FE, Demots H. Incidence of mitral valve prolapse in the asymptomatic individual. Circulation 51-52 (suppl II), 1975, II-77 (abstract).

3. Procacci PM, Savran SV, Schreiter SL, Bryson AL. Prevalence of clinical mitral valve prolapse in 1169 young women. N Engl J Med 294, 1976, 1086-8.

4. Warth DC, King ME, Cohen J. Prevalence of mitral valve prolapse in a normal pediatric population assessed by cross-sectional echocardiography. Circulation 68 (suppl III), 1983, III-111 (abstract).

5. Sasaki H. Orawas, Handa S. Two-dimensional echocardiographic diagnosis of mitral valve prolapse syndrome in presumably healthy young students. Jap Cardiography 12, 1982, 23-31.

6. Leatham A, Brigden W. Mild mitral regurgitation and the mitral prolapse fiasco. Am Heart J 99, 1980, 659-664.

7. Engel PJ, Hickman JR, Cowley MJ. Angiographic diagnosis of posterior mitral valve leaflet prolapse. J Am Coll Cardiol 3, April 1984, 1085-91.

8. Abassi AS, Decristofaro D, Anabtawi J, Irwin L. Mitral valve prolapse: comparative value of M-mode, two-dimensional and Doppler echocardiography. J Am Coll Cardiol 2, December 1983, 1219-23.

9. Engel PJ and Hickman JR. Mitral valve prolapse -- a review. Aviation Space and Environmental Medicine 51, Mar 80, 273-286.

10. Sandok BA and Giuliani E. Cerebral ischemic events in patients with mitral valve prolapse, Stroke 13, July-August 1982, 448-450.

11. Barnett H, Boughner D, Taylor W, Cooper P, Kostuk M, Nichol P. Further evidence relating mitral valve prolapse to cerebral ischemic events. N Engl J Med, 302, January 17, 1980, 139-144.

12. Bensaid J, Cuisinier Y, Renaudin D. Accident vasculaires cerebraux ischemiques: role etiogique du prolapus valvulaire mitral. Nouv Presse, Med 9, 1980, 1716.

13. Hart RG, Miller VT, Coull BM, Yatsu FM. Cerebral infarction in young adults (Unpublished data).

14. DeBono DP, Warlow CP. Potential sources of embolism in patients with presumed transient cerebral or retinal ischemia. Lancet 1, 1981, 343-345.

15. Scharf RE, Hennerici M, Bcuschke V. Cerebral ischemia in young patients: is it associated with mitral valve prolapse and abnormal platelet activity in vivo? Stroke 13, 1982, 454-458.

16. Engel PJ, Alpert BL and Hickman JR. The nature and prevalence of the abnormal exercise electrocardiogram in mitral valve prolapse. Am Heart J 98(6), 1979, 716-724.

17. Hickman JR, McGranahan GM, Paull RM, DeHart RM. Cardiovascular standards for selection and retention of high performance pilots in the USAF: perspectives for the next decade. AGARD (NATO), Conference Proceedings No. 396, December 1985, 31-1 - 31-7.

18. Gray GW. Canadian Forces approach to aircraft medical selection. AGARD (NATO), Conference Proceedings No. 396, December 1985, 29-1 - 29-6.

19. Ille H, Didier A, Allegrioni N, Maurel C. Selection et surveillance medicales des pilotes de mirage 2000: apport de l'echocardiographie. AGARD (NATO) Conference Proceedings No. 396, December 1985, 32-1 - 32-13.

CASE D.H.

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D.H. is a 42-year-old colonel, fighter pilot, who was admitted to the hospital for an episode of chest pain which was strongly suggestive of angina pectoris. His risk for coronary artery disease included a cholesterol of 229 mg% and an HDL cholesterol of 34 mg% (ratio of 6.7). His father sustained a myocardial infarction at age 55 and underwent coronary artery bypass surgery. Evaluation revealed an abnormal treadmill test with 4 mm of ST segment depression in the precordial leads, associated with chest pain in late exercise. A thallium scintigram revealed significant perfusion defects in the anterior wall. Coronary angiography revealed a 90% proximal left anterior descending lesion, a 90% lesion of the first diagonal and a 70% lesion of the proximal right coronary artery. The left anterior descending coronary artery filled retrograde from a right ventricular branch which was itself narrowed by 90%.

D.H. was initially managed medically following beta blockade with resting heart rates in the range of 50 beats/min. A treadmill test with a heart rate of 135 beats/min revealed 5 mm of ST segment depression. He ultimately underwent coronary artery bypass surgery with a sequential graft placed side-to-side to the left anterior descending and end-to-side to the first diagonal. A second graft was placed to the mid right coronary artery. He made an excellent recovery and was asymptomatic thereafter.

1. What is your aeromedical disposition?

2. If you choose to place this aviator back on flying status, what follow-up studies would you perform, and at what intervals?

3. If you choose to place this aviator back on flying status, what is your threshold for subsequent disqualification? For repeat angiography?

This aviator received an excellent result from coronary artery bypass surgery with no recurrence of angina at age 49, almost seven years after the initial onset of angina. His maximal treadmill exercise test and thallium scintigram are currently normal.

Discussion:

Although this aviator received excellent clinical results from coronary artery bypass surgery, he was not certified for any category of flying in the USAF. Coronary artery bypass grafting precludes a return to flying in the military environment, regardless of the clinical or anatomical results. In the United States, the Federal Aviation Administration was directed by the National Transportation Safety Board to medically certify civilian pilots after bypass surgery in a number of instances between 1978-1982. In May 1982, the federal aviation regulations were amended to more closely restrict certification for coronary artery disease which either had been clinically significant, symptomatic or had required treatment. Most specialists in aerospace medicine consider coronary artery bypass surgery to be a palliative procedure. Bypass grafting does not solve the problem of the underlying disease, since the disease substrate remains unchanged. The disease may progress to involve the distal native circulation, the insertion of the graft at the native vessel or the graft itself. The annual graft occlusion rate is approximately 3% per graft, meaning that an individual with two grafts has a 6% per annum occlusion rate, and one with three grafts would have approximately a 9% per annum occlusion rate. Coronary artery disease is a very capricious and unpredictable disease, and it is difficult to formulate a satisfying aeromedical policy for close surveillance of aviators who have been bypassed. If such precise estimates of needed surveillance could be brought to bear on coronary artery bypass patients, clinicians would certainly utilize such strategies in the general population, since coronary artery bypass patients are subject to a continuing array of coronary artery disease complications. If cardiologists were able to deploy their diagnostic tools with the predictive accuracy which is desired, we would certainly do so for all of our patients, not just aviators. In this regard, technological prowess, intended to preclude suddenly incapacitating events, has been perhaps overstated. Our bypass patients, with regular and careful follow-up, still experience complications such as graft occlusion with considerable regularity. Is it reasonable to believe that we can accomplish for our aviators what we cannot accomplish for our other patients? In the view of many aviation cardiologists, coronary artery disease of more than minimal degree remains incompatible with aviation safety.

CASE REPORT JP

by
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HISTORY:

JP was a 42 year old KC-135 command pilot with 3600 total flying hours. When he was 37 years old, a mid systolic click was first auscultated during a routine annual flight physical examination and a followup local echocardiogram demonstrated mitral valve prolapse. A USAF School of Aerospace Medicine (USAFSAM) evaluation was performed in September 1981. At that time he was completely asymptomatic, specifically denying chest discomfort, palpitations, dizziness or syncope. Family history was negative for history of heart murmur, history of sudden death, cardiac disease, diabetes mellitus and hypertension. He smoked 5 or less cigars per day for 17 years. Alcohol intake consisted of 4-5 beers, 2-3 glasses of wine and 1 mixed drink per week. Previously he had drunk 5-10 cups of caffeinated coffee per day, but decreased to 1 cup per day when his mitral valve prolapse was diagnosed. He did not follow any regular exercise program or any particular diet. Physical examination at that time demonstrated multiple mid systolic to late systolic clicks but no murmur. Routine resting electrocardiogram was normal. M-mode and two-dimensional echocardiography demonstrated a redundant anterior mitral valve leaflet which clearly prolapsed. He underwent treadmill stress testing with a good exercise time and double product with normal ST segment response and rare uniform premature ventricular and rare premature atrial beats. Seventeen hours of ambulatory electrocardiographic monitoring demonstrated 5-10 per hour uniform premature ventricular beats. Thallium scintigraphy, routine urinalysis and routine screening blood work were normal. In the absence of symptoms, evidence of complicating factors of mitral valve prolapse, or other disqualifying defects, a waiver for unrestricted flying duties was recommended and later granted. Reevaluation in two years at USAFSAM was originally requested. However, his case was reviewed two years later and his waiver extended for three more years. He then returned to USAFSAM for his first reevaluation five years after his original diagnosis. He was again completely asymptomatic. Since his original evaluation he had discontinued use of all tobacco products and eliminated alcohol intake. However, he had increased his caffeine ingestion to six cups of coffee per day. He had also begun an exercise program, jogging 2.5 kilometers per day, two days per week.

PHYSICAL EXAMINATION:

Height 189 cm, weight 86 Kg, blood pressure 102/60 mmHg right arm sitting, and 104/60 mmHg left arm sitting, pulse 60 beats per minute and regular. There was no thyromegaly or adenopathy. Lungs were clear to auscultation and percussion. Carotid and peripheral pulses were normal without bruits. Jugular venous pulsations were normal and there was no jugular venous distention. Chest palpation was normal without thrills or lifts. Apical impulse was of normal quality and non-displaced. S_1 and S_2 were normal. There were two mid systolic clicks and a grade 1-2/6 late systolic murmur at the left lower sternal border and apex. The clicks and murmur moved closer to S_1 with Valsalva, sitting and standing and moved further from S_1 in the supine position.

LABORATORY EVALUATION:

Routine urinalysis and screening blood work were normal. Total cholesterol was 218 mg% and HDL cholesterol was 68 mg%, yielding a ratio of 3.2. This was minimally improved from his initial evaluation. Chest and KUB radiographs were normal and coronary artery fluoroscopy was negative for calcification in the coronary arteries. Seventeen hours of ambulatory electrocardiographic monitoring demonstrated occasional uniform premature ventricular beats and rare premature atrial beats. M-mode and two-dimensional echocardiography demonstrated a redundant, prolapsing anterior mitral valve leaflet and were otherwise normal. Routine electrocardiogram was normal and unchanged from his prior tracing. He performed 15 minutes of a modified Balke treadmill protocol with a good exercise effort and good double product. ST segment response was again normal. During exercise he had rare isolated premature atrial beats and rare isolated uniform premature ventricular beats. At approximately two and minute of recovery he had 13 beats of supraventricular tachycardia at a rate over 200 beats per minute; this was initiated by a premature atrial beat. He was asymptomatic during the short run of tachyarrhythmia. Thallium rest and exercise scintigraphy were again normal.

DISPOSITION:

JP was disqualified for flying duties because of mitral valve prolapse complicated by supraventricular tachycardia. Because of this combination, waiver for flying duties was not recommended.

QUESTIONS:

1. What is your aeromedical disposition of this case?

2. If you recommend waiver for flying duties, would you recommend unlimited aircraft or restricted to tankers-transports-bombers?

3. What followup surveillance would you recommend - what studies and at what intervals?

4. What would be your threshold for disqualification in the future if you decide to waiver this individual for flying status now?

5. Do you recommend any therapy for the supraventricular tachycardia?

6. What are the aeromedical concerns in mitral valve prolapse?

DISCUSSION:

The aeromedical implications of mitral valve prolapse have been discussed earlier in the course booklet and in a didactic presentation. Items of aeromedical concern are incapacitating chest discomfort, significant supraventricular and ventricular arrhythmias, development of significant mitral regurgitation, infective endocarditis, embolic phenomena, and sudden death. Because of all these considerations, mitral valve prolapse is disqualifying for entry into flying training in the United States Air Force without waiver recommendation. A trained aviator with newly diagnosed mitral valve prolapse may be granted a waiver for unlimited flying duties in the absence of any of these complicating factors or any other disqualifying cardiac or noncardiac defects. United States Air Force standards and policies regarding mitral valve prolapse, particularly for flying training applicants, are currently undergoing intensive study and consideration. Transient visual field defects, loss of consciousness, significant stress arrhythmias, ventricular tachycardia and ventricular premature beat pairing are significantly over-represented in the mitral valve prolapse population followed at USAFSAM. Mitral valve prolapse with any of these complicating factors is disqualifying for all flying duties without waiver recommendation.

Aviators with mitral valve prolapse who receive a waiver for continued flying duties are reevaluated at USAFSAM at two to three year intervals for the development or appearance of any of the above complicating factors. Continued surveillance throughout their active flying career is necessary, as any of these complicating factors may occur at any time during their life. This is well-illustrated by the case of JP who had no complicating factors on his initial evaluation, but demonstrated supraventricular tachycardia during treadmill stress testing five years later. A complete noninvasive cardiovascular evaluation is performed to screen for these complicating factors of mitral valve prolapse and to also evaluate the aviator for the development of other cardiac defects, particularly coronary artery disease. The most important studies for surveillance for mitral valve prolapse include history, physical examination, ambulatory electrocardiographic recording, echocardiography, and treadmill stress testing.

Medical therapy for his supraventricular tachycardia was not recommended because it was an isolated, nonsustained and asymptomatic event. He was advised to avoid possible arrhythmogenic substances, such as alcohol, tobacco, caffeine, chocolate and over-the-counter cold medications.

REFERENCES:

1. Braunwald, E.: Heart Disease: A Textbook of Cardiovascular Medicine, 2nd Edition. Philadelphia, W.B. Saunders Company, 1984, 1089-1095.

2. Rubinstein, E.: Scientific American Medicine. New York, Scientific American Inc., 1986, XI:7.

3. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia, Lea and Febiger, 1985, 444-447.

CASE PRESENTATION
(CASE SR)

SUPRAVENTRICULAR TACHYCARDIA

Dr. G.W. Gray

LCol SR is a 41 year old tactical fighter pilot on active flying duty. Shortly after awakening one morning, as he was rising from bed, he noticed that he felt slightly lightheaded, and that his heart seemed to be racing. The lightheaded sensation was very transient, lasting well under a minute, but the sensation of a racing heart continued throughout breakfast and while he was driving to the flight line. Wisely, he checked with the Flight Surgeon, who noted that his pulse was rapid and irregularly irregular. An electrocardiogram confirmed the diagnosis of atrial fibrillation, with a ventricular response averaging about 110 beats per minute. There were no ST nor T wave changes at that time. He was admitted to hospital, and within a couple of hours, prior to any pharmacologic or other intervention, he reverted to normal sinus rhythym. He was aware of his palpitations suddenly disappearing, and had no lightheadedness at that time.

For the few days prior to the episode of atrial fibrillation, he had felt somewhat unwell, and thought he might have a cold or flu-like illness. One of his eyes felt gritty and he felt some achiness in his body. In addition, the two weeks prior to the episode had been particularly hectic, with an overseas trip, and a busy NATO flying exercise. During this period, he had been smoking more, and drinking more coffee and alcohol than was his usual custom.

On examination following reversion to sinus rhythm, he appeared healthy and apart from mild nasal and pharyngeal congestion and a slight conjunctivitis. His temperature was 37.5° Celsius, and his pulse 70 and regular. The arterial pulse, volume and contour were normal. There was no cyanosis, clubbing nor jugular venous distension. His blood pressure was 110/80 mm Hg. The thyroid gland was not enlarged, and there were no clinical signs of hyperthyroidism. The heart was not clinically enlarged, and the heart sounds were normal. There were no clicks, and no third nor fourth sounds. There was a soft Grade 1/6 midsystolic murmur best heard along the lower left sternal border at the apex, with little radiation. The lungs were clear. All peripheral pulses were palpable and strong.

He was kept in hospital under observation for nine days. Routine screening for myocardial infaraction including daily electrocardiograms and cardiac enzymes were all normal. The resting electrocardiograms were quite normal in all respects. The chest x-ray was normal.

During the first few days in hospital he continued to have symptoms of mild coryza. After nine days, he was discharged home, feeling quite healthy. The following day, he returned to see the Flight Surgeon about returning to flying duties.

Do you think LCol RS can be safely returned to flying duties? What further investigations, if any, do you feel are indicated or required? (Please list any further tests you think he should have before reading on).

Supraventricular tachycardia may cause sudden incapacitation, and even in healthy individuals, rapid tachycardias may cause a fall in cardiac output and presyncopal symptoms. Tolerance to G would certainly be impaired. SVT may also precipitate coronary insufficiency in individuals with latent coronary artery disease. Before consideration can be given to returning an aviator to flying duties following an episode of SVT, the individual must be investigated for structural cardiac abnormalities, endocrine and metabolic predisposing causes for SVT, asymptomatic coronary artery disease, and predisposition towards an arrhythmia recurrence.

An M-mode and 2D echocardiogram were done which showed normal ventricular wall motion, and normal cardiac structure. The cardiac wall and chamber dimensions were all normal. An exercise stress test was done on a treadmill, and he worked through to his maximum heart rate without evidence of ST or T wave changes. There were a few ventricular extrasystoles during recovery, but no other arrhythmias were observed. Thallium images were normal, with no evidence of either a fixed or reversible perfusion defect. A rest and excersie MUGA scan showed normal contractility with an ejection fraction at rest of 55% which increased to 70% with exercise.

A 24 hour ambulatory electrocardiogram showed normal sinus rhythm throughout, with only a very occasional ventricular and atrial extrasystole. Hematologic and biochemical screening tests were normal. His thyroid function was normal. Serum electrolytes were normal. Acute viral titers showed a mildly elevated titer to a Coxsackie virus B.

With this further information, what is your aeromedical disposition? When can he return to full flying duties as a tactical fighter pilot? Do you think that yet additional studies should be performed? If so, please list them below.

Other possible studies that might be contemplated include coronary angiography and left ventriculography to fully exclude coronary artery disease, and electrophysiologic studies to rule out concealed bypass tracts, to detect abnormal refractory period, and to document unstable hemodynamics if the arrhythmia is induced during the study. Centrifuge exposure to plus G_z with ECG monitoring might also be considered.

LCol RS had a centrifuge study and had a normal relaxed and straining G tolerance with only rare atrial extrasystoles during the recovery phase. He was in fact grounded initially while investigations were being carried out and then (about 2 months after the episode), was returned to dual flying only for a further 6 months of observation. He had no further symptoms, and it was assumed that the episode may have been related to a minor degree of myo-or pericarditis associated with a Coxsackie infection. He was subsequently returned to full flying duties.

Reference

1. Hickman, JR. Disposition of Electrocardiographic Abnormalities in Aviators. AGARD Report 681:11-1 to 11-13, 1980.

CASE R.S.

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R.S. is a 35-year-old aviator whose annual electrocardiogram revealed a newly acquired complete left bundle branch block. He was totally asymptomatic from a cardiovascular standpoint. He had experienced no episodes of weakness, syncope or near syncope. He was a lifelong nonsmoker and jogged 25 miles per week. There was a strong family history of adult-onset diabetes mellitus. His father died of a cerebrovascular accident at age 44. His mother was diabetic at age 70, and his maternal grandfather died of a myocardial infarction at age 55. The physical examination was within normal limits except for a paradoxical second heart sound. Routine screening laboratory data revealed normal blood sugars, a cholesterol of 196 mg% and an HDL cholesterol of 52 mg%. The electrocardiogram revealed a complete left bundle branch block. Echocardiography revealed only a septal paradox. Exercise testing revealed no arrhythmias and normal exercise tolerance. The ST segment was uninterpretable because of the left bundle branch block. A 17-hour Holter monitor revealed no evidence of AV block or arrhythmia. A thallium scintigram was abnormal with septal reperfusion.

1. What is your aeromedical disposition?

2. What is known of acquired left bundle branch block in asymptomatic males?

3. What studies do you feel are needed to make a final aeromedical disposition in this case?

This aviator underwent coronary arteriography and left ventriculography, both of which were normal. An electrophysiologic study was likewise normal with an H/ interval of 52 msec and an HQ of 65 msec. The HV interval ranged from 55-65 msec during atrial pacing. The HV was also normal during programmed atrial stimulation. This aviator was returned to unlimited flying status.

Discussion of Case R.S.

Left bundle branch block occurs in approximately 2 aviators per 1,000 under the age of 50. Right bundle branch block occurs in approximately 6 aviators per 1,000 below age 50. USAFSAM now has a lengthy experience with acquired asymptomatic left bundle branch block in otherwise healthy males. Seventy-three percent of all asymptomatic acquired left bundles in USAF aviators have had no evidence of underlying organic heart disease on initial evaluation and during extensive follow-up. Twenty-two percent were found to have coronary artery disease, and 5% were disqualified due to other causes. Only one aviator in over 300 subjects followed long-term developed complete heart block. The abnormal thallium scintigram, especially septal reperfusion, is quite common in individuals with left bundle branch block, even in the absence of coronary artery disease. The presence of abnormal thallium scintigrams in aviators with left bundle branch block and normal coronary arteriograms suggests that the basic defect in such asymptomatic subjects may be a process that is not confined to the conduction system but may stem from a common process effecting both myocardium and specialized conduction tissue. All available data indicate that aviators with left bundle branch block, in the absence of organic heart disease, may be returned safely to flying status.

CASE PRESENTATION
(CASE RB)

RIGHT BUNDLE BRANCH BLOCK

Dr. G.W. Gray

Captain RB is a 37 year old Air Force aviator who has always enjoyed excellent health. His electrocardiogram done at the time of initial aircrew selection at the age of 17 showed an incomplete form of right bundle branch block, and this has been a consistent finding on his aircrew ECG's throughout his career. The PR interval over this 20 year span has also been consistent at 0.16 seconds.

This year his aircrew electrocardiogram is changed, now showing a complete right bundle branch block with a PR interval of .16 seonds, and a QRS duration of 0.12 seconds.

He has had no symptoms of a cardiovascular disturbance. Specifically, he has had no symptoms of syncope or presyncope, and his tolerance to G has not noticeably changed. He has had no chest discomfort even with extreme exertion, and no claudication. He keeps himself fit by jogging in the summer, and in the winter by playing ice hockey.

He is a non-smoker, and has not had documented high blood pressure in the past. Total cholesterol levels have been normal. He has had several episodes of gout and is currently taking 300 mg per day of allopurinol. There is no family history of heart disease except in later life (8th decade).

On examination, he is moderately overweight at 90 kg for his height of 180 cm. His blood pressure is 120/70 mmHg. His resting pulse is 70 beats per minute and is regular, and the arterial pulse volume and contour are normal. The fundi appear normal. The venous waves in the neck are normal. The apex beat is normally situated, and is of normal contour. There are no clicks, extra heart sounds, or murmurs on ausculation. The second heart sound is widely split but closes with expiration. All peripheral pulses are normal. The lungs are clear on percussion and auscultation.

What are your recommendations regarding additional investigations for this aviator with newly acquired right bundle branch block? (please list) Can he continue to fly with this change in his electrocardiogram?

An exercise stress test is carried out to maximum perceived exertion. He has a high estimated maximum oxygen uptake. He achieves a maximum heart rate of 180 beats per minute. The PR interval remains constant, as does the conduction pattern. There are no ST nor T wave changes, and no arrhythmias develop. An exercise thallium study is also carried out, and there is no evidence of a fixed or reversible perfusion defect. A 24 hour ambulatory electrocardiogram shows no arrhythmias or ectopic activity.

With this additional information, can he now be returned to full flying duties? If not, what additional information do you require?

Acquired right bundle branch block in otherwise healthy individuals develops at a distol site in the right bundle and is not of itself a harbinger of more serious types of conduction disturbance nor of coronary artery disease. Given a normal non-invasive cardiovascular evaluation such as Captain RB has had, aviators with acquired RBBB as the sole abnormality can safely be returned to unrestricted flying duties. In the presence of other type of conduction disturbance e.g. first or seond degree AV block, additional investigations such as electrophysiologic studies will be required.

REFERENCES

1. Rotman, M., and Triebwasser, J.H. A clinical and follow-up study of right and left bundle branch block. Circulation 51: 477, 1975.

2. Lancaster, M.C., Schecter, E. and Massing, G.K. Acquired complete right bundle branch block without overt cardiac disease: Clinical and hemodynamic study of 37 patients. Am. J. Cardiol. 30: 32, 1972.

CASE N.S.

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N.S. is a 42-year-old fighter pilot, evaluated because of nonspecific serial ST-T wave changes on the annual electrocardiogram. A treadmill test performed in follow-up of these changes was abnormal due to 1 mm of ST segment depression during the ninth to eleventh minutes of exercise. He remained entirely asymptomatic, and there was no history of chest pain, shortness of breath, orthopnea, palpitations, syncope or edema. All other noninvasive studies, including an echocardiogram, Holter monitor, chest x-ray, apexcardiogram and phonocardiogram were within normal limits. An exercise thallium study was within normal limits. The exercise tracing, performed in conjunction with this second stress test, revealed 2 mm of ST segment depression in the precordial leads. Cardiac catheterization was undertaken for aeromedical indications, revealing a discrete 75% proximal left anterior descending coronary artery lesion, as well as a mildly hypokinetic anterior wall. A MUGA study revealed an appropriate rise in the ejection fraction with very mild wall motion abnormalities of the anterior wall.

What is your aeromedical disposition of this significant coronary lesion?

Are there any therapeutic interventions which could conceivably return this aviator to flying status, in your opinion?

This aviator underwent a second cardiac catheterization, in anticipation of performing a balloon angioplasty on the 75% lesion. Upon crossing the left anterior descending stenosis, only a 20 mm gradient was found. A 4 mm balloon was inflated to a maximal pressure of 6 atmospheres. The resulting stenosis was 30% with a translesion gradient of 6 mm. Repeat coronary arteriograms performed six months after the coronary angioplasty revealed that the lesion had remained at 30%. The aviator had been maintained on Verapamil, 360 mg per day, and aspirin during the six months following the angioplasty, in order to prevent coronary artery spasm at the site of the angioplasty. On a trial basis, this aviator, along with two other aviators, received waivers for nonhigh-performance flying following coronary angioplasty of a discrete, asymptomatic lesion.

What concerns do you have about the granting of a waiver for flying following coronary angioplasty?

Would you have qualified this aviator with only a 6 mm gradient across the lesion for high-performance flying?

Discussion:

Between 1980 and 1982, the USAF granted nonhigh-performance flying waivers for especially selected cases of single-vessel coronary artery disease which had been successfully dilated with angioplasty. Following six months of observation, and a repeat cardiac catheterization confirming the patency of the angioplasty, such cases were suitable for flying waivers as cases of minimal coronary artery disease. Prior to 1976, no cases of coronary artery disease of any degree had been returned to flying status by the USAF Surgeon General. Since 1976, we have returned cases of asymptomatic minimal coronary artery disease to nonhigh-performance flying if the subjects were asymptomatic, no lesion was greater than 30% and the sum of lesions was not greater than 50%. Under this category of minimal coronary artery disease, successful angioplasty was included for aeromedical purposes.

In the USAF, we discontinued waivers for coronary balloon angioplasty in 1982. The three individuals who were returned to flying remained well and had no recurrence of the lesion. The discontinuation of coronary angioplasty for aviators with mild to moderate disease was based upon: 1) the relatively high recurrence rate of 30% in six months, although recurrence was not observed in our three aviators. The performance of coronary angioplasty in an asymptomatic individual for solely occupational reasons must weigh the risks of the procedure against recurrence of the lesion, or worsening of the lesion; and 2) observations in several clinical centers, including those of Dr Andreas Gruntzig, inventor of coronary angioplasty, revealed that recurrence of stenosis in lesions which were 50% or less prior to angioplasty often resulted in stenoses which were worse than the original lesion. These observations have lead many cardiologists to refrain from performing balloon angioplasty on mild to moderate lesions.

The USAF is closely observing advances in coronary angioscopy as well as laser angioplasty. Perhaps a combination of these techniques will still allow for remedial management of asymptomatic lesions in aviators in the future. Currently, civil aviation authorities in the US will certify cases of balloon dilatation if functional testing (treadmill and thallium) are normal.

CASE R.C.

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R.C. is a fighter pilot who underwent a treadmill test at age 40 at his local base because of an elevated coronary risk (persistent cholesterol/HDL cholesterol ratios of 6.7-7.0). The treadmill exercise tolerance test was abnormal with 1-2 mm of ST segment depression in leads X and CM5. A thallium perfusion scan was normal as were all other noninvasive tests. A second treadmill test performed with a thallium scintigram was also abnormal. Coronary angiography revealed a discrete 20% lesion of the proximal left anterior descending coronary artery and a 10% narrowing of the first circumflex marginal branch. This aviator had been asymptomatic and was a nonsmoker without a history of hypertension. There was no family history of premature coronary events.

1. What is your aeromedical disposition?

2. If you wished to consider a special flying waiver, what conditions do you wish to attach to this aviator's certification to fly?

3. How do you view the significance of an abnormal treadmill test (or any abnormal noninvasive test) in an aviator with minimal coronary artery disease who is being considered for continued flying status?

4. If you choose to return this aviator to fly, what specific tests and at what specific intervals do you require?

5. When would you perform repeat angiography for aeromedical purposes?

6. What would be your threshold for removal of this aviator from flying status in the future?

This aviator underwent repeat cardiac catheterization at age 43 with no significant angiographic progression noted. There had been no deterioration of his noninvasive testing. At age 46, six years after the initial catheterization and three years after the second catheterization, the thallium perfusion scan remained normal and the treadmill test revealed 2.5 mm of ST segment depression in the precordial leads. A repeat cardiac catheterization was performed at six years, revealing progression of the proximal LAD lesion to 40%, with the occurrence of two additional lesions of 30% and 40% in the mid LAD. The circumflex marginal lesion was now a 30% obstruction. This aviator was allowed to fly in the USAF in nonhigh-performance aircraft for six years following the discovery of minimal coronary artery disease. He was disqualified from all categories of flying following the third cardiac catheterization at age 46.

Discussion:

If one performs noninvasive studies on significant numbers of aviators, one will discover an appreciable amount of minimal coronary artery disease. We believe that much of the minimal disease is unrelated to the abnormal noninvasive tests for which cardiac catheterization was performed. However, the two-dimensional information from a coronary arteriogram may be misleading in terms of the hemodynamic consequences of lesions which look identical (in cases of almost identical lesion anatomy, translesion gradients prior to angioplasty have revealed marked differences in gradient). As lesions progress beyond 30%, the probability that the coronary lesion is the cause of the abnormal noninvasive tests increases. Prior to 1976 in the USAF, any degree of coronary artery disease, except intimal roughening, was disqualifying for flying status. Bruschke, from the Cleveland Clinic, reported that patients with lesions equal to or less than 30% had a five-year mortality of less than 2%, which was less than the mortality for the general population of similar age who had not had their coronary anatomy defined by angiography. It must be emphasized that the majority of such cases underwent cardiac catheterization because of chest pain. Unfortunately, there was no apparently healthy, asymptomatic population similar to aviators who had undergone coronary angiography and had received serial follow-up evaluations, including serial angiography. To address this problem, the USAF created the Minimal Coronary Artery Disease Study Group in 1976, returning aviators to flying status with no single angiographic lesion greater than 30% and no aggregate of lesions greater than 50%. Aviators returned to flying under such conditions were returned only to tankers, bombers and transport. In order to qualify for the Minimal Coronary Artery Disease Study Group, minimal disease criteria must be satisfied and the aviator must be willing to undergo intensive risk factor modification, extensive annual noninvasive evaluation at USAFSAM and a repeat cardiac catheterization at speci-

fied intervals. Aviators were excluded from the Minimal Coronary Artery Disease Study Group if any lesion was greater than 30% or the sum of lesions was greater than 50% or if there was any left main coronary artery disease, symptoms suggestive of ischemia, suspected myocardial damage, any significant arrhythmia, valvular heart disease including mitral valve prolapse, any evidence of left ventricular dysfunction, diabetes mellitus, hypertension unresponsive to diet or thiazide therapy, significant conduction defects or recent left anterior or posterior hemiblock or preexcitation. The entry criteria were also contingent upon a willingness to undergo serial follow-up catheterizations. A repeat cardiac catheterization was mandatory within three years of the initial diagnosis. A decision to perform a repeat catheterization at less than three years was dependent upon deterioration of noninvasive testing. Aviators initially selected for flying under these conditions could be subsequently disqualified, after entry, if any of the conditions which were disqualifying for initial entry occurred or because of refusal to undergo annual cardiac catheterization or failure to attempt risk factor modification. In the first 326 aviators with gradeable angiographic disease at USAFSAM (any lesion greater than 10% narrowing), 90 aviators had minimal coronary artery disease, 31 had intermediate coronary disease with lesions between 30-50% and 205 had significant coronary disease with at least one lesion narrowed by 50% or more. Of the 90 aviators who had minimal coronary artery disease at angiography, 61 met the study group criteria and 29 were determined ineligible. Of the 61 eligibles, 48 remained on flying status with 32 currently flying. Sixteen retired while still on flying status; thirteen were subsequently disqualified for flying duties. Eighteen aviators underwent repeat cardiac catheterizations; thirteen of these were study group members still on flying status, of whom ten aviators continued to meet the angiographic criteria for minimal coronary disease. Three of the thirteen progressed to significant coronary artery disease.

One hundred percent follow-up was obtained on the total 90 aviators with angiographic minimal coronary artery disease. Only 6 of the 90 aviators with minimal disease had coronary events (angina, infarction or sudden death). In the six aviators with events, the average time from the initial cardiac catheterization to the coronary event was 7.7 years. The earliest event was 5.8 years. The expected event rate, based upon the Framingham formula, was not different from age-matched controls. It is the opinion at USAFSAM, based on our follow-up experience of individuals with minimal disease, that such individuals may be returned to nonhigh-performance flying status without an increased risk of sudden incapacitation or death. If stringent annual noninvasive examinations are performed and cardiac catheterization is performed at a minimum of three-year intervals, a strong case can be made for the maintenance of categorical flying for minimal coronary artery disease subjects.

PULMONARY PHYSIOLOGY AND PULMONARY FUNCTION TESTING IN AEROSPACE MEDICINE

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Respiratory diseases may have serious consequences in the aviation environment, ranging from life threatening incapacitation (e.g. tension pneumothorax), through to aggravation of hypoxia, acceleration atelectasis and perhaps lowered G tolerance in individuals with relatively minor degrees of pulmonary dysfunction caused by subtle degrees of small airways disease.

This presentation will review some concepts of respiratory physiology which are of particular relevance in the aviation environment, and discuss current methods of pulmonary function testing which can be applied to detect asymptomatic disease in screening aircrew.

Aviation Medical Problems Caused or Aggravated by Pulmonary Disease

Pneumothorax

Hypoxia

Acceleration Atelectasis

Aeroembolism

HYPOXIA CAUSED BY AVIATION - INDUCED PULMONARY DYSFUNCTION

Respiratory disease and dysfunction aggravate aviation-related hypoxic hypoxia, mainly by interfering with gas exchange through ventilation/perfusion mismatch. Oxygen delivery to the tissues is a function of three variables, namely cardiac output (or regional blood flow), hemoglobin concentration, and hemoglobin saturation with oxygen. Advanced respiratory disease may interfere with cardiac output, but in aircrew, pulmonary dysfunction compromises oxygen delivery by interfering with gas exchange and hence hemoglobin saturation.

It might be helpful to briefly review the "oxygen cascade", following oxygen tensions from atmosphere through to tissue, to clarify the mechanisms by which respiratory diseases contribute to hypoxia.

Figure I is a diagrammatic representation of oxygen tensions at each step in the "cascade" from atmosphere to tissues. Pulmonary dysfunction can act at two stages to decrease arterial and hence tissue oxygen tensions, first, by reducing alveolar ventilation, and secondly, by interfering with gas exchange. Although global alveolar hypoventilation resulting from a variety of neurologic and neuromuscular disease states may cause hypoxia in a clinical setting, this is a rare and unusual cause of hypoxia in aviators. Distortion of chest wall/diaphragm mechanics by influences such as respiratory straining manoevers, positive pressure breathing, positive pressure breathing jerkins and abdominal bladders in anti-G garments, and abdominal and chest wall distortion during HSG potentially could cause alveolar hypoventilation, but this has not been documented. Aviation stressors cause hypoxia primarily by interfering with ventilation and perfusion matching.

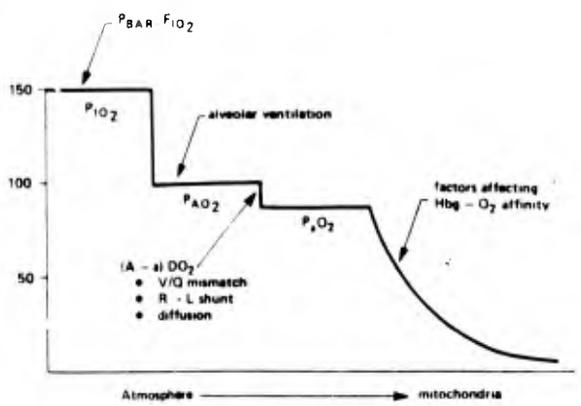


FIGURE 1

VENTILATION-PERFUSION MATCHING AND GAS EXCHANGE IN AVIATION

While right to left shunts and diffusion limitation can affect gas exchange and reduce arterial oxygen saturation, in aviation these two factors rarely play a significant role in causing hypoxia. Ventilation-perfusion matching on the other hand is markedly sensitive to gravitational forces and to pressure breathing and hence is frequently subject to distortion in the military aviation environment. Minor degrees of airway dysfunction which may be of no consequence in a normal clinical setting may become significant when combined with acceleration forces and positive pressure breathing. Glaister has extensively studied the effects of acceleration on pulmonary function, and has written excellent reviews on the subject (1,8).

Figure 2 shows the normal distribution of ventilation and perfusion in the upright lung in a one G environment, and the resulting ventilation-perfusion ratios. There is a gradient for both ventilation and for perfusion from top to bottom of the lung, with the bases being both better ventilated and better perfused than the apices. Both these gradients are a result of the effect of gravity. Ideal matching of ventilation and perfusion occurs in only a small region of the lung. Above this, ventilation exceeds perfusion, and the excess ventilation contributes to alveolar dead space. Below the ideally matched region, perfusion exceeds ventilation, and contributes to venous admixture and hence arterial hypoxia.

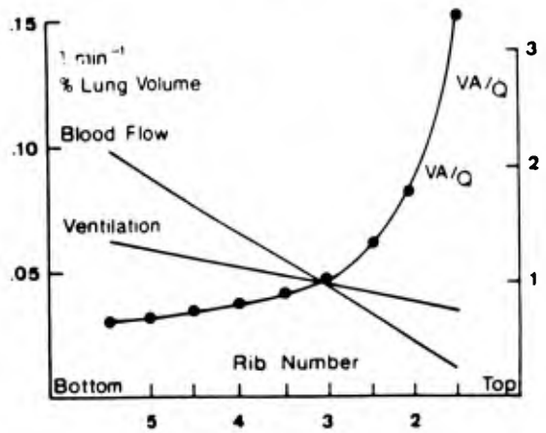


FIGURE 2 (from West)

Distribution of Ventilation

In the case of ventilation, the weight of the lung within the thorax creates a gradient for pleural pressure, with the pleural pressure being significantly more negative (about 10 cm H_2O) at the lung apex than at the base. The effect of this pleural pressure gradient is that different parts of the lung operate on different parts of the pressure-volume curve, as indicated in Figure 3, with the bases undergoing a significantly greater volume change for a given pressure change, under normal tidal breathing conditions.

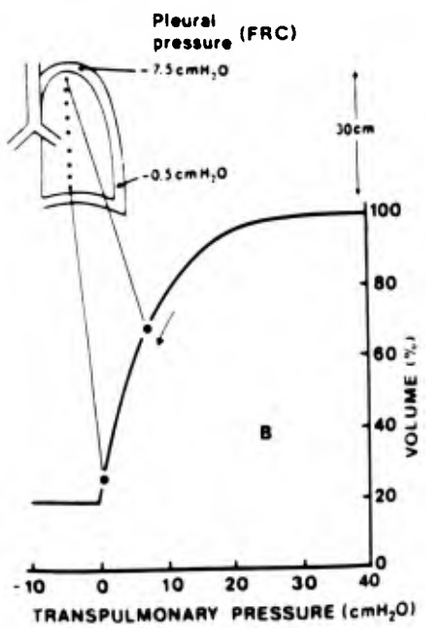


FIGURE 3 (from West)

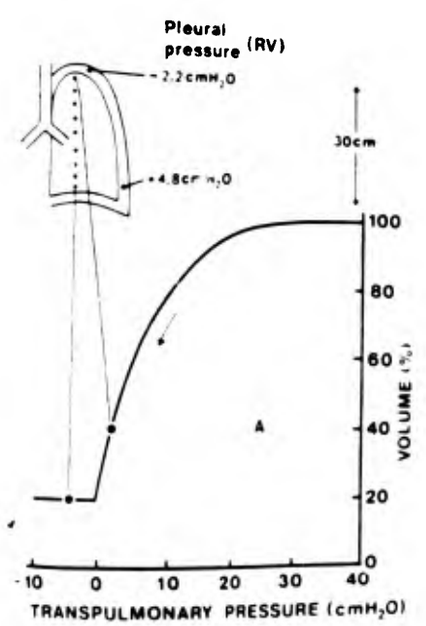
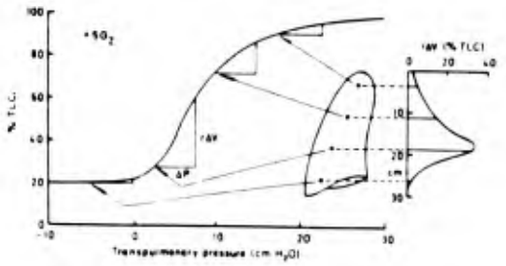


FIGURE 4 (from West)

At low lung volumes, with higher transpulmonary pressures, the lung bases operate on the bottom of the pressure-volume curve, and in fact the most dependent airways are closed. Breathing with small tidal volumes at low lung volumes (near residual volume) results in inspired gas going almost exclusively to lung apices, as indicated in Figure 4. Increased "+Gz" forces may cause a similar circumstance by altering the pleural pressure gradient, and as shown in Figure 5, at higher levels of G, ventilation is mainly distributed to the hilar areas with the lung bases being very poorly ventilated.



Transpulmonary pressures at four levels within a 30-cm tall lung of specific gravity 0.25 are indicated on the lung's pressure-volume curve for an acceleration of +5G. The regional volume changes (ΔV) which would follow a uniform increase in transpulmonary pressure of 5 cm H_2O are indicated and plotted on the inset diagram.

FIGURE 5 (from Glaister)

Distribution of Perfusion

In the pulmonary circulation, because of its low pressures (compared with systemic), a similar gravitational pressure gradient is created, with the base of the lung being much better perfused than the apex. John West (2,3) described a model which relates alveolar pressure, pulmonary arterial pressure, and pulmonary venous pressure in four distinct "zones" from lung apex to base. Since this model has some relevance when considering the combined effects of gravitational forces with positive pressure breathing, let's examine it in some detail (Figure 6).

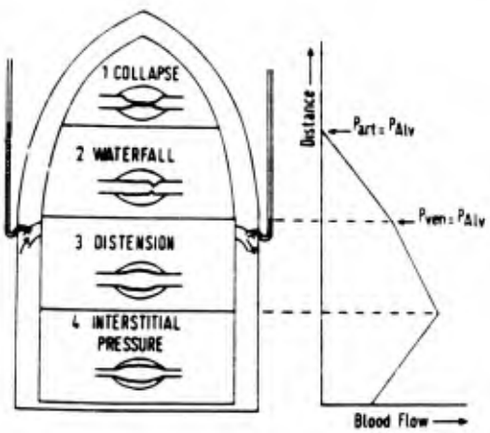


FIGURE 6
(from West)

In zone I, at the apex, alveolar pressure exceeds both pulmonary venous and pulmonary arterial pressure, and there is very little blood flow. In zone II, moving down the lung towards the hilum, gravitational forces increase arterial pressure which now is greater than alveolar pressure, although this is still higher than pulmonary venous pressure. In zone II, flow is determined by the gradient between arterial and alveolar pressures, (as in a Starling resistor) and hence flow increases rapidly down the zone as arterial pressure increases. In zone III, both pulmonary arterial and venous pressures exceed alveolar pressure, and flow is determined by the normal arterial-venous pressure difference.

In the most dependent lung zones, a region of decreased flow is often seen, known as zone IV. The decreased flow in this region can not be explained solely on the basis of arterial, alveolar and arterial pressures. It is postulated that the decreased flow is due to an increase in the vascular resistance of extra-alveolar vessels.

Consider the potential impact of increased gravitational forces, and of positive pressure breathing on the distribution of blood flow as predicted by this model. Increasing "+Gz" forces reduce pulmonary arterial pressure through zone I and II, and hence flow in these areas decreases and is redirected through zone III. Figure 7 (from Glaister) shows the effect of +Gz acceleration on the distribution of perfusion down the lung.

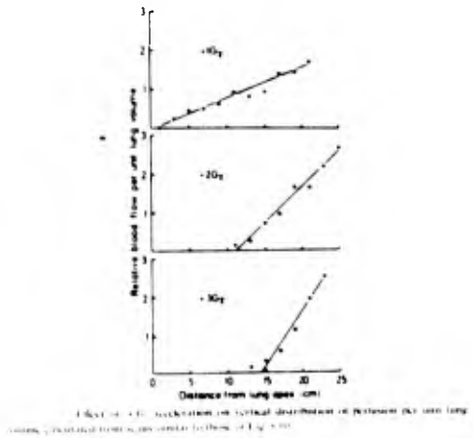


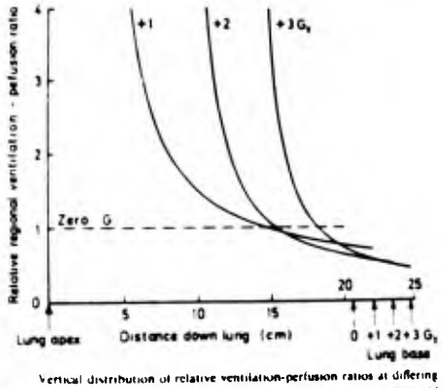
FIGURE 7 (from Glaister)

Whinnery (4) has beautifully demonstrated the effects of acceleration on pulmonary blood flow in miniature swine at levels of G varying from -4Gz to +8Gz confirming the extending previous observations by Glaister (5) and Bryan (6).

Positive pressure breathing, which increases alveolar pressure, has a similar effect on blood flow, pushing zones I and II further down the lung, and redirecting blood flow to lung bases.

The Effect of Increased Gravitational Forces on Gas Exchange

Since with increasing gravitational forces blood flow is redirected increasingly to lung bases, while at the same time ventilation is directed away from lung bases, ventilation and perfusion become increasingly mismatched, as shown in Figure 8. Increasing amounts of venous admixture develop in lung bases, where V/Q ratios drop to exceedingly low values as +Gz increases, and this produces increasing levels of arterial desaturation. The contribution to reduced G tolerance of this hypoxia caused by pulmonary dysfunction has not been precisely documented, but clearly this mechanism may play a significant role.



Vertical distribution of relative ventilation-perfusion ratios at differing levels of +G acceleration. The prediction for weightlessness was obtained by extrapolating blood flow per unit volume and ventilation per unit volume data back to zero G. (From Glaister, 1967a.)

FIGURE 8 (from Glaister)

ACCELERATION ATELECTASIS

Acceleration atelectasis occurs in aviators who breathe high inspired oxygen concentrations while exposed to high sustained G. Because of the increase in transpulmonary pressure caused by the increased +Gz, airway closure occurs in dependent lung zones. If the gas trapped peripheral to the closed airways has a high oxygen concentration, rapid absorption occurs and atelectasis develops. Inspired oxygen concentrations greater than 70% can result in aeroatelectasis (7). Symptoms include chest pain, coughing episodes that are difficult to suppress, and difficulty taking a deep breath.

Understanding the physiology of acceleration atelectasis involves a grasp of why airways close and remain closed at HSG. Airway closure can be measured by means of a single-breath inert gas washout, such as the nitrogen washout curve (Figure 9).

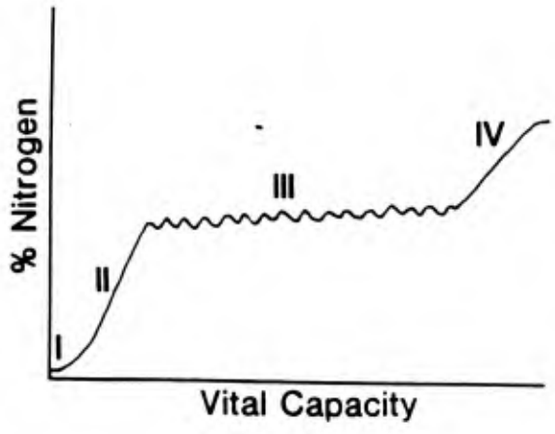


FIGURE 9

In this test, expired nitrogen concentration is monitored along with volume as the subject breathes out after a vital capacity inspiration of pure oxygen. Near the end of the expiration, there is a sudden sharp rise in nitrogen concentration as the airways in the dependent parts of the lung close. The remaining gas expired after the dependent airways close comes from upper lung zones which are more rich in nitrogen, because in this region which is less well ventilated than lower zones, the residual nitrogen is less diluted by the inspired pure oxygen. The volume under the terminal nitrogen rise is called the "closing volume".

Glaister (8) has measured closing volumes in subjects exposed to acceleration on the centrifuge, and has demonstrated that closing volume increases with increasing +Gz, so that above +3Gz, closing volume exceeds functional residual capacity and eventually inspiratory reserve volume. In this situation, dependent airways remain closed throughout the tidal breathing range and atelectasis can develop within a few seconds in subjects breathing pure oxygen.

Acceleration atelectasis is a potentially serious problem in the high sustained G environment, causing symptoms that are at the very least distracting while also causing a further perturbation to an already badly distorted gas exchange system, contributing further to hypoxia, desaturation, and impaired G tolerance.

Closing volume increases with age, in smokers, and in other persons with small airways disease, and such individuals must be at increased risk of acceleration atelectasis. Screening for small airways disease is discussed in the next section.

PULMONARY FUNCTION SCREENING IN AIRCREW

Ideal gas exchange occurs only in alveoli where ventilation and perfusion are appropriately matched. Even in the normal lung under basal conditions such circumstances occur only in a very limited region. We have had some discussion as to how the stresses of acceleration can greatly interfere with ventilation and perfusion distribution and hence with gas exchange, and can produce hypoxia which can reduce tolerance to G.

Perturbations of lung function caused by disease, even if asymptomatic, can further complicate the situation. Individuals with small airway dysfunction from whatever the cause will, potentially at least, be more hypoxic for any given G exposure and hence have a lower G tolerance, will be more susceptible to acceleration atelectasis and its associated problems, and even in those flying environments where acceleration is not a consideration, will tend to be more hypoxic in a situation of reduced inspired oxygen tension.

With these considerations in mind, it makes a good deal of sense to screen potential military aircrew candidates, especially those slated for fighter operations, for asymptomatic small airways disease. The problem lies in identifying which tests of airway function, if any, have sufficient sensitivity and specificity to be applied to detect airflow limitation, either persistent or variable, in an asymptomatic population.

Pulmonary Function Tests for Small Airways Disease

1. Measurement of total airways resistance.

2. Forces expiratory curves
   a. Volume-time curves
   b. Flow-volume curves

3. Single-breath nitrogen washout curves. (SBNT)

4. Measurement of lung volumes.

5. Stimulation tests of airway reactivity.

Total Airways Resistance

This measured as the ratio of the pressure drop between mouth and alveoli divided by the flow rate. It is generally measured using a body plethysmograph, and a two-stage panting technique with a flow-interruptor. The advantage of the method is that it measures resistance at normal flow rates, and over the tidal volume range. The main drawback is that the method measures the total airways resistance, and in normal persons, most of this is due to resistance in the larger central airways. Small peripheral airways of less than 3mm diameter, which are the site for early small airways disease, contribute less than 25% to total airways resistance in normals, and as a result small airways disease must be far advanced before it significantly affects total airways resistance. This, then is not a suitable method for detecting early, asymptomatic small airways disease.

Forced Expiratory Curves

Forced expirations may be analysed either as changes in volume versus time (volume-time curves), or as a plot of flow rate against volume (flow-volume curves), as illustrated in Figure 10.

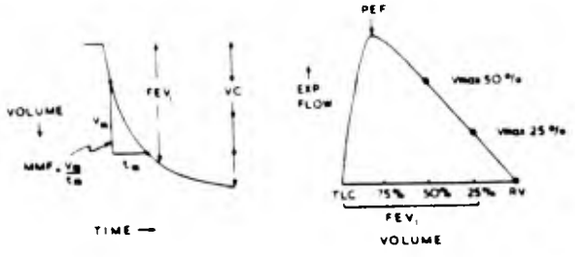


FIGURE 10

Forced expirations may themselves affect bronchial muscle tone, and so these manoevers may induce changes in the very parameters they are trying to measure. However, they are widely used clinically, and are relatively easy to perform. Common parameters derived from the volume-time curve include the FEV_1, or forced expiratory volume in one second, the MMFR, or maximum mid-expiratory flow rate, and the ratio of FEV_1 to the total forced vital capacity or FVC. Commonly derived measurements from the flow-volume curve are the peak expiratory flow (PEF), the flow rate when 50% of the forced vital capacity has been expired ($Vmax_{50}$), or when three quarters of the volume has been expired (termed $Vmax_{25}$, because 25% of the FVC remains to be expired).

A modification of the flow-volume curve has been to compare maximum flows when breathing air or an 80% helium 20% oxygen mixture. (Figure 11). Since flow in small peripheral airways is mainly laminar, and laminar flow is not dependent on gas density, while flow in more central airways tends to be turbulent and so affected by gas density, subjects in whom the predominance of total airways resistance comes from small peripheral airways will not show a significant change in flow rates when breathing helium-oxygen. Subjects with normal airways, in whom most of total airways resistance is central, have considerable increased expiratory flow rates with heliox, when compared with air. An increase of at least 20% in the $Vmax_{50}$ occurs in normals.

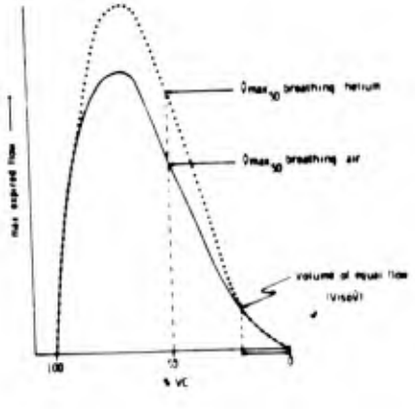


FIGURE 11

Single-breath Nitrogen Washout Test (SBNT)

This test has already been briefly described in the discussion on acceleration atelectasis (see Figure 9). Expired nitrogen concentration measured after a vital capacity inspiration of 100% oxygen shows four distinct phases. In Phase I, which is very small, nitrogen concentration is almost zero, representing pure oxygen coming from large central conducting airways (dead-space). In Phase II there is a rapid rise in nitrogen concentration as alveolar gas mixes with dead space gas. Phase III represents alveolar gas and in normal subjects has a slight upward slope. As residual volume is approached, the airways in dependent lung zones close, and the final expired volume comes from upper lung zones relatively rich in nitrogen, with a consequent rapid rise in nitrogen concentration. The volume of this final expirate is called Phase IV, or the "closing volume". Total lung capacity and residual volume can be derived from this curve by measuring the area under the curve and applying the alveolar dilution principle. The sum of residual volume and closing volume is termed "closing capacity".

The test is simple, easy to perform, and is widely used as a test of early small airways disease.

Measurement of Static Lung Volumes

While lung volumes can be measured fairly easily with a variety of techniques and do indeed show changes in advanced small airways disease, the problem is that the measurement of lung volumes is not a sufficiently sensitive technique to detect early small airways disease.

Frequency Dependence of Compliance

This test measures lung compliance at different breathing frequencies, and is a sensitive measure of early airways disease. However, accurate measurement requires the subject to pass an esophageal balloon to accurately measure intrathoracic pressures, so while the method is applicable in a research setting, it can not be applied in the widespread screening of aircrew.

Tests of Airway Sensitivity

Airway sensitivity can be measured by means of inhalation provocation tests, in which the subject inhales in gradually increasing doses a known respiratory irritant such as histamine or methacholine. Cold air is also used, as are specific allergens or occupational irritants in specific applications, but the most commonly used and standardized tests are the methacholine and histamine challenge tests. Precise methods and standards for these tests have been published (9). Methacholine is somewhat preferable to histamine in that the side-effects are less pronounced, but in general, both tests are safe, reproducible, and easy to perform. These tests are particularly helpful in the assessment of airway sensitivity in aircrew candidates by providing an objective measurement in applicants who have a history of asthma or significant atopy in childhood, and who may tend to downplay recent symptomatology.

In a standard methacholine challenge test, the subject breathes increasing concentrations of methacholine delivered through a nebulizer with a known fixed output. Each concentration is breathed for 2 minutes, and the subject then performs an FEV_1. This is compared with baseline values, and a positive response is considered to be a drop of 20% or greater in FEV_1. The concentration of methacholine required to produce this 20% fall in FEV_1 is called the PC_{20}. Values below 4.0 mg/ml indicate increased airway sensitivity, and below 8.0 mg/ml are suggestive.

Assessment of Tests of Small Airway Function

The sensitivity and specificity of various tests of small airway function have been addressed in a number of studies. Cosio et al (10) compared histopathologic findings at lung biopsy with pulmonary function results and found that the comparison of flows from air and heliox flow volume curves provided the most sensitive means of detecting small airways disease based on flow volume manoevers. MMFR, FEV_1/FVC ratios, and $Vmax_{50}$ became abnormal as more severe grades of small airways disease were noted histopathologically. The single breath nitrogen test was found to be comparable in sensitivity to the air/heliox flow volume curves.

Berend et al (11) studied the reproducibility of histopathologic measurements of small airways disease, and compared antomic findings with functional tests. Air/heliox flow volume curves were not assessed. They found that the $Vmax_{50}$ and the MMFR correlated best with their Total Pathologic Score, but that the SBNT was the best at predicting inflammation, and indeed the highest correlation between structure and function was between the SBNT and the inflammation scores. Abnormalities in the SBNT have been shown to reverse after smoking cessation (12) which might be explained by a reversibility of tobacco-induced inflammation and bronchiolitis.

Dosman (13) used the FEV_1/FVC ratio as to establish a reference diagnosis, and studied the specificity and sensitivity of the SBNT. He found the specificity of the CV/VC ratio to be about 93%, with a sensitivity of 37%, while the slope of phase III showed a sensitivity of 65% with a specificity of 75-80%.

In summary, there are a number of tests of small airway function which have been shown to predict small airways disease, hopefully at a stage at which at least some of the changes (e.g. inflammation) are still reversible. None of these tests combine a high degree of specificity and sensitivity, and it seems best at present to use a battery of tests including the SBNT, and maximum expiratory flow-volume curves on air and heliox, to detect early asymptomatic small airways disease.

REFERENCES

1. Glaister, .D.H. Effects of Acceleration. In "Regional Differences in the Lung", edited by J.B. West, Academic Press, 1977, Chapter 8, pp 323 - 379.

2. West J.B., Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. J. Appl. Phsiol. 19, 713 - 724, 1964.

3. Hughes, J.M.B., Glazier, J.B., Maloney, J.E., and West, J.B. Effect of extra-alveolar vessels on distribution of blood flow in the dog lung. J. Appl. Physiol. 25, 701 - 712, 1968.

4. Wninnery, J.E. Acceleration effects on pulmonary blood flow distribution using perfusion scintigraphy. Aviat. Space Environ. Med. 51, 485 - 491, 1980.

5. Glaister, D.J. Regional ventilation and perfusion in the lung during positive acceleration measured with 133Xe. J. Physiol. (London) 177, 73 -74P, 1965.

6. Bryan, A.C., McNamara, W.D., Simpson, J., and Wagner, H.N. Effect of acceleration on the distribution of pulmonary blood flow. J. Appl. Physiol. 20, 1129 - 32, 1965.

7. Hastill, M.S., Tacker, W.A., Balldin, U.I., and Burton, R.R. Influence of inspired oxygen concentration on acceleration atelectasis. Aviat. Space Environ. Med 57, 432 - 437, 1986.

8. Glaister, D.H. The Effects of Gravity and Acceleration on the Lung. AGARDoGRAPH No 133, 1970.

9. Hargreave, F.E., Dolovich, J., and Boulet, L.P. Inhalation provocation tests. Sem. in Resp. Physiol. 4, 224 - 235, 1983.

10. Cosio, M., Ghezzo, H. Hogg J.C., Corbin R., Loveland, M., Dosman, J., Macklem, P.T. The relations between structural changes in small airways and pulmonary function tests. New Eng. J. Med. 298, 1277 - 1281, 1978.

11. Berend, N., Wright, J.C., Thurlbeck, W.M., Marlin, G.E., Woolcock, A.J. Small airways disease, reproducibility of measurements and correlation with lung function. Chest, 79. 263 - 269, 1979.

12. McCarthy, D.S., Craig, D.B., Cherniak, R.M. Effect of modification of the smoking habit on lung function. Am. Rev. Resp. Dis. 114. 103 - 113, 1976.

13. Dosman, J.D., Cotton, D.J. Interpretation of tests of early lung dysfunction. Chest 79. 261 - 263, 1981.

AEROMEDICAL DISPOSITION OF PULMONARY SARCOIDOSIS, CHRONIC OBSTRUCTIVE LUNG DISEASE, REACTIVE AIRWAY DISEASE AND SPONTANEOUS PNEUMOTHORAX

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SUMMARY

Four respiratory diseases are described in relation to aviation medicine. Each is discussed in the context of flying safety, operational efficiency, and problems of treatment. Guidelines are offered for decisions on management and disposal of aircrew candidates and of trained aircrew who give a history of one of these diseases or who develop the disease during their flying career.

INTRODUCTION

The four diseases of the title are all important causes of restrictions or disqualification amongst aviators. None are as common as the acute bacterial and viral respiratory infections such as bronchitis and pneumonia, but none of the four are rare. Their diagnosis, treatment, follow-up and appropriate aeromedical disposition are important to the flight surgeon and other specialists concerned with aircrew health.

The significance of these four diseases for aviation medicine will be dealt with under three headings. The first is sudden or insidious incapacitation, which would directly threaten flight safety by impairment of the aircrewman's mental or physical efficiency. The second is operational efficiency, which covers all aspects of the aircrewman's performance over a period of time, including his ability to respond appropriately to all the varying demands of the flying environment including emergencies. For military aircrew this must include consideration of high cabin altitudes, the greater likelihood of sudden decompression, pressure breathing, high G-forces, the stresses of aerial combat possibly with injury, emergency ejection, evasion, captivity, escape and survival, demands which are unknown or exceptionally unusual in civil flying. Thirdly, treatment (drugs or surgery) which requires continued co-operation by the patient, administration by appropriate specialists, and constant monitoring for unwanted effects which are likely themselves to be hazards to flight safety. The effects of some drug treatments preclude flying duties during their administration; even with drugs considered safe for aviators, a period of grounding during their initial administration, in case of unforseen or idiosyncratic adverse reactions, is almost always advisable.

The standards described will in general be appropriate for single-seat operations in high-performance aircraft. Some relaxation may be possible for pilots of transport or tanker aircraft, or for navigators, engineers and other flight-deck crew. Waiver policy will be more liberal with cabin crew. In almost every instance, somewhat less stringent standards will apply to civil aircrew than to their military counterparts.

SARCOIDOSIS

Sarcoidosis is a chronic granulomatous disease of unknown aetiology. Many systems may be involved, but the commonest form appears to affect the respiratory system alone. Often this form is symptomless and is detected by a routine chest xray showing bilateral hilar lymph-node enlargement, sometimes with bilateral pulmonary shadowing, typically in the upper zones [1]. Such patients may however have cough, mucoid sputum or wheeze, and a few have some systemic upset, eg malaise, fever or weight loss. Erythema nodosum, sometimes with large-joint arthritis, is the only common accompanying clinical manifestation.

This type of pulmonary sarcoidosis has a good prognosis: at least 80% of those affected show complete and sustained resolution of all features of the disorder within two to five years [2, 3]. It is the only form of the disease commonly seen in aircrew; amongst healthy young men, the prospects of spontaneous permanent cure may be even better than that indicated above, particularly if there is no pulmonary parenchymal shadowing.

The main hazard of sarcoidosis is inapparent involvement of other systems, especially the central nervous system or the heart [4]. It is believed that a small number of those even with apparently benign pulmonary hilar disease may have involvement of the heart [1, 5]. Cardiac sarcoidosis has an ominous reputation. It is present in 13-20% of those dying of sarcoidosis [1, 6]. In post-mortem studies of patients with known cardiac sarcoidosis, sudden death has occurred in up to two thirds [1, 7] and congestive cardiac failure has been present in a further quarter. Sudden death may be the presenting feature of sarcoid heart disease[8]. Electrocardiographic abnormalities include bundle-branch blocks, various degress of A-V dissociation, types of ectopic activity and paroxysmal arrhythmias [1, 9]. These features may appear many years after the initial illness. Post-mortems, even on those with no cardiac symptoms, may disclose granulomata of the cardiac conduction system [4]. Extensive granulomatous disease, causing a dilated heart with cardiac failure, is less common.

The potential risk to flying safety of cardiac sarcoidosis is obvious[10]. In-flight episodes of paroxysmal tachyarrhythmias, complete heart block with Stokes-Adams attacks or cardiac arrest would be likely to lead to disaster. More insidious incapacity would arise from gradual cardiac decompensation.

For these reasons any aircrewman with suspected sarcoidosis, whether asymptomatic or not, should be grounded immediately pending specialist evaluation [11]. A diagnosis can usually be confidently made as a result of a typical clinical picture, the presence of non-caseating granulomata on tissue histology (eg bronchial or lymph-node biopsy) or a positive Kveim test. Appropriate tests should exclude other granulomatous diseases.

Most such aircrew will have disease apparently confined to the hilar and paratracheal nodes. All, however, will require detailed investigation to exclude disease of other systems, notably the cardiovascular system. This further investigation will often be delayed until there is marked improvement or complete resolution of the intra-thoracic lymphadenopathy. The cardiac work-up will include echocardiography, 24-hour ECG tape monitoring, a maximal exercise test, and radio isotope cardiac imaging, usually a thallium [5] and a MUGA scan. All these investigations must be normal before the patient is proclaimed free of cardiac sarcoidosis. A few patients will require invasive study with physiological testing of the A-V conduction system. Unfortunately, because of the patchy distribution of the sarcoid, cardiac biopsy is quite often unhelpful [12].

Aeromedical Disposition

a. Because of the risk of silent cardiac involvement, applicants for flying training who give a history of sarcoidosis should be rejected. To avoid injustice, every effort must be made to determine that the diagnosis was established beyond doubt. Candidates for training as aircrew other than pilots might be licensed provided the disease was exclusively pulmonary and had remitted completely several years before. Even so, an employer might have reservations about such a candidate.

b. Trained aircrew who develop sarcoidosis should be grounded and investigated as indicated above. Uncomplicated pulmonary sarcoidosis which remits completely according to clinical, radiological, pulmonary function and haematological criteria, and in whom cardiac sarcoidosis has been excluded, are considered for return to flying duties, usually not less than a year after the onset of their illness. Restrictions (eg as or with co-pilot) are customary for a year, and after that, specialist follow-up for several years is usual, though flying may be unrestricted.

Disease of other systems (neurological, ocular, dermatological, bone) generally has a less good prognosis and often requires drug treatment (v.i). Such individuals will rarely regain an unrestricted flying category, and may face permanent grounding.

Treatment with systemic corticosteroids is reserved for those with more severe, or progressive, or complicated sarcoidosis. The benefits of steroid treatment are unfortunately doubtful. Steroids involve hazards (peptic ulceration, diabetes mellitus, hypertension and neuropsychiatric sequelae) particularly important for aviation safety. For all these reasons, an aviator who requires steroid treatment for sarcoidosis will rarely be granted a waiver for return to flying duties.

Multi-crew operations, particularly in civil airline or commercial operations, may allow a more liberal disposition, eg for asymptomatic chronic sarcoid lymphadenopathy, or with stable minor pulmonary shadowing or skin sarcoidosis. A private pilot's licence may be renewed under similar circumstances; evidence of cardiac sarcoidosis should, however, preclude return to any form of flying where incapacity might prejudice aircraft safety.

CHRONIC OBSTRUCTIVE LUNG DISEASE (C.O.L.D)

Chronic bronchitis and emphysema are included in this rubric. Chronic bronchitis causes a persistent cough due to over-production of mucoid sputum; if present on most days for at least three months during two or more consecutive years, the diagnosis is established. Many factors may contribute to the development of chronic bronchitis, but in western society the most important factor by far is cigarette smoking [13]. Chronic bronchitics are prone to recurrent respiratory infection. Ventilatory function deteriorates more rapidly than the normal secular decline, and the deficit is usually "fixed"; stopping smoking, especially in the early stages, may delay the functional deterioration. Effort dyspnoea, abnormal blood gases and secondary cardiac damage are late features of the disease.

Emphysema is a pathological diagnosis meaning an increase in the size of the air spaces distal to the terminal bronchioles [14]. However, its existence may be strongly suspected from clinical features such as increasing effort dyspnoea (cough, if present, is usually non-productive), a fixed barrel-shaped chest with generalised decrease in air entry and absent hepatic and cardiac dullness to percussion, with a chest xray showing generalised increase in pulmonary trans-radiancy with flattened diaphragms and narrowed mediastinum. Spirometry shows a combined restrictive-obstructive pattern, little affected by bronchodilators. Emphysema, like bronchitis, is strongly associated with cigarette smoking. Individuals with the inherited biochemical defect of alpha-one-antitrypsin deficiency are strongly predisposed to emphysema. Smokers with this deficiency do particularly badly.

Aircrew with C.O.L.D may present with symptoms but more often are detected as a result of routine ventilatory function tests. Bronchospasm (asthma) can be virtually excluded by the fixed nature of the abnormality. Clinical, radiological and possibly blood gas or gas transfer studies should complete the evaluation. Management will concentrate on stopping all smoking for life, treatment of inter-current infections, regular monitoring and general health measures (weight reduction, exercise training).

Disposition of aircrew with C.O.L.D should be along the following lines.

Applicants for flying training with an established diagnosis of C.O.L.D should be refused. The same is probably true of asymptomatic individuals who are known to have alpha-one-antitrypsin deficiency. In the author's view, cigarette smokers should not be recruited for flying duties, certainly not for military flying. However, no licensing authority is known to have adopted this restriction, although some airlines will not recruit cigarette smokers.

Trained aircrew with C.O.L.D, often asymptomatic or with minimal symptoms, require assessment and long-term follow-up but may usually be safely returned to flying duties. Stopping smoking much improves their chances of completing a full career. Hypoxia will rarely be an increased risk. However, cockpit fumes or smoke may precipitate disabling symptoms, and a few patients with C.O.L.D have paroxysmal cough, sometimes proceeding to cough syncope, even with apparently mild disease. Evidence of deterioration, clinical or laboratory, and particularly development of blood gas abnormalities, either at rest or easily provoked by exercise, are likely to require restrictions or even grounding.

A few patients with emphysema may have one or more bullae, evident as pulmonary translucencies with hair-line circular margins on chest xray, 1 cm or more in diameter. These commonly do not connect with an airway and therefore expand and may rupture during ascent to altitude, causing pneumothorax, surgical emphysema or even air embolism. Presence of bullae is usually a bar to unrestricted military flying; for any kind of flying, a test chamber ride to the anticipated maximum cabin altitude is the minimum prerequisite to flying. A single bulla may be excised surgically to improve prospects of return to full flying duties [11].

Treatment of C.O.L.D, apart from cessation of smoking, is rather ineffectual and involves drugs (beta-adrenergic receptor stimulants, methylxanthines, steroids) which may pose threats to flying safety. Aircrew who require long-term drug treatment for C.O.L.D are unlikely to receive a waiver for flying duties; occasionally a civil licence might be granted, eg a private pilot's licence for fairly mild C.O.L.D treated with a salbutamol inhaler. Intercurrent infections require grounding for appropriate (eg antibiotic) treatment but have long-term implications only if frequent or severe.

REACTIVE AIRWAY DISEASE

Asthma and bronchospasm are terms used almost synonymously. Asthma is defined as a disorder characterised by obstruction of the intrapulmonary airways, such obstruction varying widely in short periods of time. At times, in mild asthmatics, airflow may be repeatedly normal, and even exceptional methods (eg exercise in cold atmospheres) may fail to induce detectable obstruction during a remission. The condition is a syndrome rather than a disease, being a condition of bronchial hyper-reactivity to a wide variety of stimuli. It is common - the prevalence is 2-5% in the USA and the UK. Most asthma in children and young adults is "atopic" - based on a familial alteration in immune responsiveness and characterised by development of bronchial hyper-reactivity to a variety of external agents [15]. Recognition of the true nature of wheezing attacks ("recurrent bronchitis") in babies and young children is often delayed or missed completely. Thus some cases of "adult onset asthma" are in fact cases of missed atopic bronchospasm. Other cases of adult onset asthma ("intrinsic asthma") have no demonstrable allergic basis and carry a worse prognosis than atopic asthma. Allergy to a single agent, as in some industrial asthma cases, is rather unusual; their recognition is important as they are some of the few cases where removal of the provoking agent may produce a "cure".

The prognosis of childhood asthma is now known to be less good than was generally believed. 40% have continued fairly mild attacks, and 10% have more severe disease throughout life. About 50% appear to remit completely, usually during adolescence, but about half of these relapse in later life, and such relapsers are then much more prone to recurrent or persistent bronchospasm. Thus, in all, nearly three quarters of childhood asthmatics can expect to suffer attacks of bronchospasm during adult life. Sometimes a relapse may be abrupt and severe.

The disorder has important aeromedical implications. Its course and severity are unpredictable; an acute attack may be suddenly disabling and even fatal. It is affected by many of the stresses of the aviation environment; thermal stress, fumes and smoke, pressure breathing, emotional stress, exertion and probably G-forces.

A history of asthma in an applicant for flying training should for these reasons result in rejection for military flying. Applicants for civil flying with a remote history of mild wheezing in childhood may be accepted, especially for a private pilot's licence, but are at increased risk of disability. Few will be acceptable for professional flying.

Development of wheezing in a trained pilot requires detailed evaluation [16]. Those with highly reactive airways demonstrated by exercise or histamine challenge are at high risk of disabling symptoms and should usually be grounded. Less severe disease, easily controlled by permissible medications (v.i) may be acceptable for return to flying duties but will be restricted from fast jet flying and will usually fly only "as or with co-pilot". They require indefinite specialist follow-up. Other flight deck aircrew may receive waivers on a similar basis. However mild the disease may apparently be, acute severe attacks are possible; immersion, cold climate operations, fumes and smoke, escape and evasion are all likely to be more hazardous in asthmatics.

Treatment of asthma in aircrew is restricted to inhaled cromoglycate ("Intal") and inhaled corticosteroids [3]. Oral beta-2 agonist stimulants (eg salbutamol, terbutaline) have metabolic and cardiac effects which make them hazardous for aviators. Inhaled, these drugs may still cause muscle tremor, and should not be used within four hours of flying. Indeed, an aviator with symptoms sufficiently marked to need such treatment should probably not fly. The methylxanthines (eg theophylline) have a high incidence of side-effects; toxicity is likely because of their critical therapeutic ratio. They should not be prescribed for aircrew.

Aircrew whose disorder appears perfectly controlled by permissible medication over a prolonged period may be considered for a return to single-seat operations. Such a decision calls for expert advice. Where the remission appears dependant on continued treatment, the difficulty in ensuring life-long compliance in asymptomatic aircrew should not be under-estimated.

SPONTANEOUS PNEUMOTHORAX

Spontaneous pneumothorax occurs when there is escape of air from the lung into the pleural space, with consequent partial or complete collapse of the lung. Usually no precipitating cause is evident. Simultaneous bilateral pneumothoraces may occur and are particularly dangerous. In any case, a person who has suffered a spontaneous pneumothorax on one side is more liable than a normal individual to have a spontaneous pneumothorax on the other side. Spontaneous pneumothorax is very prone to recurrence; at least 30% will recur after an initial episode, 50% after a second, and 80% after a third [17]. Recurrence is usually early, within 12 months of the last episode.

A tension pneumothorax occurs when the leak of air into the pleural space is progressive, a "one way flow" being caused by a flap-valve action of the visceral pleural breach. As positive pressure develops in the pleural space, the mediastinum is displaced with compression of the other lung; acute cardio-respiratory embarrassment develops, with potentially fatal consequences. Other complications of spontaneous pneumothorax include chronicity (broncho-pleural fistula), pleural haemorrhage (haemothorax) which may be persistent and exsanguinating, and serous effusion.

The cause is usually a sub-pleural apical bleb or bulla which ruptures through the visceral pleura. For some reason this is commonest in young men, usually with a tall lean body build. Other, more serious underlying lung pathology, such as pulmonary tuberculosis or tumour, is very uncommon.

Spontaneous pneumothorax may rarely be asymptomatic; a small leak may be detected on a routine chest xray. More often the diagnosis is missed because the significance of the symptoms is not appreciated and physical signs are subtle or absent. Most patients suffer pain, which may be incapacitating, and dyspnoea in proportion to the size of the leak. Complications listed above are likely to be prostrating.

The aeromedical implications of spontaneous pneumothorax are very important and have recently been exhaustively reviewed [18]. Recruits with a history of spontaneous pneumothorax should in general be rejected, for fear of relapse. However, a remote history of a single episode (more than two years before) might be acceptable as by that stage, recurrence is much less likely. A history of satisfactory surgical treatment (parietal pleurectomy) with normal subsequent respiratory function is acceptable.

A trained aviator who develops a spontaneous pneumothorax should be grounded pending assessment and surgical treatment. This is because of the special aeromedical hazards of the disorder; even where the leak seals spontaneously, the pleural air-space will expand with altitude. Pain and dyspnoea may be incapacitating. Although one might expect the conditions of high performance flying (high G-forces, rapidly varying cabin pressure, pressure breathing) to predispose to spontaneous pneumothorax, its development in the air seems in fact to be rarely recorded [17, 19, 20]; occurrence during rapid decompression in an altitude chamber may be commoner [18]. However, the potential hazards are so great that the risk of early return to flying duties following a spontaneous pneumothorax is unacceptably high.

Following investigation, most aviators will be suitably treated by surgery (thoracotomy, oversewing of apical pleural blebs, and parietal pleurectomy [21]). This apparently severe procedure causes surprisingly little immediate upset and no long-term decrement in respiratory function. Where pleural blebs are known to be present on the opposite side, surgery may have to be bilateral; indeed, some authorities [18] propose this as the minimal procedure. However, most air forces accept the unilateral operation where the opposite lung appears normal on xray. Following convalescence and rehabilitation the aviator may resume full flying duties, usually 3 months post-operatively. The apparently lesser procedure of "medical" pleurodesis causes as much if not more morbidity as pleurectomy and is followed by a high recurrence rate [22]. For this reason pleurodesis is no longer an acceptable form of treatment.

REFERENCES

1. Pettyjohn F S, Spoor D H and Buckendorf W A. Sarcoid and the heart - an aeromedical risk. Aviat Space Environ Med 48 (10): 955-958, 1977.

2. Hillerdal G, Nou E, Osterman K and Schmekel B. Sarcoidosis: Epidemiology and prognosis. Am Rev Respir Dis 130: 29-32, 1984.

3. Hopkirk J A C in: Textbook of Aviation Medicine (Butterworth). In press.

4. Silverman K J, Hutchins G M and Bulkley B H. Cardiac sarcoid: a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. Circulation 58 (6): 1204-1211, 1978.

5. Kinney E L, Jackson G L, Reeves W C, Zelis R and Beers E. Thallium-scan myocardial defects and echocardiographic abnormalities in patients with sarcoidosis without clinical cardiac dysfunction. Am J Med 68: 497-503, 1980.

6. Longcope W and Freiman D. A small study of sarcoidosis based on combined investigations of 160 cases including 30 autopsies from Johns Hopkins Hospital and Massachusetts General Hospital. Medicine 31: 1, 1952.

7. Porter G H. Sarcoid heart disease. N Engl J Med 263: 1360, 1960.

8. Fleming H A. Sarcoid heart disease: a review and an appeal. Thorax 35(9): 641-643, 1980.

9. Fleming H A. Sarcoid heart disease. Br [illegible] Heart Journal 36(1): 54-68, 1974.

10. Hill I R. Sarcoidosis: a review of some features of importance in aviation medicine. Aviat Space Environ Med 48: 95 -954, 1977.

11. Hopkirk J A C. The management of common respirator diseases in aviation medicine. British J Aviat Med 2: 10-15, 1984

12. Ratner S J, Fenoglio J J and Urse P C. Utility of endomyocardial biopsy in the diagnosis of cardiac sarcoidosis. Chest 90(4): 528-533, 1986.

13. Hale K A, Ewing S L, Gosnel B A and Niewohner D E. Lung disease in long-term cigarette smokers with and without chronic airflow obstruction. Am Rev Respir Dis 130: 716-721, 1984.

14. Thurlbeck W M. A pathologist's approach to chronic bronchitis and emphysema. In: Fishman A P ed. Update, pulmonary diseases and disorders. New York. McGraw-Hill, 1982: 137.

15. Burrows B. The natural history of asthma, chronic bronchitis and emphysema. Medicine International 3rd Series: 35, 1422-1425, 1986.

16. Hopkirk J A C. The natural history of asthma: aeromedical implications. Aviat Space Environ Med 55: 419-421, 1984.

17. Cran I R and Rumball C A. Survey of spontaneous pneumothoraces in the Royal Air Force. Thorax 22: 462-465, 1967.

18. Voge V M and Anthracite R. Spontaneous pneumothorax in the USAF aircrew population: a retrospective study. Aviat Space Environ Med 57: 939-49, 1986.

19. Rayman R B. Sudden incapacitation in flight 1 Jan 1966 - 30 Nov 1971. Aerosp Med 44: 953-955, 1973.

20. Fuchs H S. Idiopathic spontaneous pneumothorax and flying. Aerosp Med 38: 1283-1285, 1967.

21. Askew A. Parietal pleurectomy for recurrent pneumothorax. British J Surgery 63: 203-205, 1976.

22. Hopkirk J A C, Pullen M J and Fraser J R. Pleurodesis: the results of treatment of spontaneous pneumothorax in the Royal Air Force. Aviat Space Environ Med 54: 158-160, 1983.

CASE D.L. (by Dr Hull) Air Force Navigator Age 28 years

Painful heels	3 weeks
Swollen ankles	2 weeks
Tender red lumps both shins	1 week
Poor appetite, weight loss of 3 Kg	2 weeks

Non-smoker. Systems enquiry - no other complaints.

Physical examination:

Afebrile
Bruising of heels
Tender red lumps both shins - lesions up to 4 cms wide
Bilateral ankle oedema
Passive ankle movement - painful at extremes
General examination - normal

Q1 What is the condition affecting his lower limbs?

Q2 What further investigations do you require?

The condition of the lower limbs is erythema nodosum. D.L. probably has mild arthritis of the large joints related to the rash.

Pulmonary tuberculosis is now a rare cause of E.nodosum in the West, but streptococcal infections, drug reactions and inflammatory bowel disease are quite likely. D.L. showed no such cause, but a chest xray showed hilar lymphadenopathy.

Sarcoidosis is much the likeliest diagnosis, though pulmonary tuberculosis could present in this fashion.

Intradermal tuberculin test - negative
Sputa - no AAFB seen
Tomography - confirmed hilar node enlargement
Xrays of bones and joints normal
Hb 11.5G, ESR 75 mm in 1 h. TWBC 5,600. N.diff. Haematocrit 36.7, MCH 27.4, MCV 87
Film: RBC's normocytic, normochromic
Blood biochemistry including liver function tests - normal (alpha-2 globulins slightly increased)
Vital capacity 4.4L; FEV1 3.9L = 88% = normal
Scalene node biopsy - no evidence of sarcoidosis
Kveim test - positive.

Q3 Has the diagnosis of sarcoidosis been established?

Q4 What further tests should be done?

Q5 All symptoms and signs had disappeared by the time his Kveim test was ready, 6 weeks after injection.

What is your decision on his return to flying duties?

(Further questions regarding Case D.L. on next page.)

3 months after his initial illness he completed the following tests.

Full clinical examination
Resting 12-lead ECG
Cross-sectional (2-D) echocardiograph
Maximal treadmill test
MUGA study
Thallium study

All were normal.

6 months after his initial illness he was reviewed; clinical examination,
FBC, ESR
Blood biochemistry
Pulmonary function tests
Chest xray
Resting and exercise ECG's

were all normal.

Q6 a. May he now return to flying duties?

b. Should flying be restricted to any type of aircraft?

Q7 What follow-up should be arranged?

Q8 Do you consider the prognosis to be

very good?
fair?
rather poor, with relapse likely within 5 years?
other?

CASE PRESENTATION
(CASE CPD)

CHRONIC OBSTRUCTIVE LUNG DISEASE

Dr. G.W. Gray

Major CPD is a 40 year old fighter pilot who is reported to have a 4 centimeter bulla in his left lower lobe on a routine chest x-ray done as part of his annual aircrew medical examination.

12 years previously, he developed chest discomfort and dyspnea while flying ACM in a Saber. On return to base he was noted to have some abnormal densities in his left lower lobe on chest x-ray, and was told he had a collapsed lung. He was felt at the time to have a viral pneumonitis. The x-ray changes resolved over a few days, and he was returned to flying duties. 3 years later, he suffered a traumatic left hemothorax in motor vehicle accident, with fractures of his 3rd through 7th left ribs. 500 milliliters of bloody fluid were drained by thoracentesis.

In the intervening years, he felt quite well, and continued to fly. He started smoking cigarettes as a teenager, and continues to smoke about 40 cigarettes per day. He has a mild morning cough on most days, with a small amount of whitish phlegm. There is no family history of lung disease. He has a reasonable exercise tolerance on annual testing, although he does not do any regular exercise. He does admit to feeling unexpectedly short of breath if he has to do strenuous physical activity, especially outside in cold air, although he does not describe any frank wheezing.

On physical examination, he is a tall, lanky man. His blood pressure is 120/75 mm Hg with about 5 mm Hg of pulsus paradoxis. There is no clubbing, and no cyanosis. The trachea is midline, and the external chest configuration appears normal. There is 3 inches of chest expansion. There is good air entry in all lung zones on auscultation, with only a few fine crackles in the left lower lung posteriorly. The heart sounds are normal, with no murmurs. The liver and spleen are not palpable.

Based on the information available to you at this point, what further investigations would you request?

Major CPD's repeat chest x-ray with magnification views of the left lower lobe, and tomograms show some post-inflammatory changes at the left base with one margin resembling a bulla, but there is no clear bulla observed, and no vascular displacement to suggest an air containing cyst.

His hemoblobin level is 176 g/L with a hematocrit of 49%. His alpha-1 antitrypsin levels are normal.

Pulmonary function tests show the following results:

	Result	Percent Predicted	Post-Bronchodilator
FVC (L)	5.8	120	5.8
FEV_1 (L/S)	3.9	101	4.1
FEV_1/FVC (%)	68%	76	70%
MMFR (L/S)	2.5	64	2.6
V_{50} (L/S)	2.3	46	2 3
V_{75} (L/S)	0.9	38	1.1
TLC (L)	7.37	105	7.52
FRC (L)	3.90	101	3.92
RV (L)	2.1	90	2.2
DL_{CO} (ml/min/mmHg)	16.6	85	

A methacholine challenge test was done, and Major CPD reacted with a 20% fall in his FEV_1 at a concentration of 4.0 mg/ml (this result indicates a borderline or slightly increased airway sensitivity).

What is your interpretation of these tests? What are the aeromedical implications? Are there any additional studies you would recommend?

Major CPD then underwent a low oxygen study, in which arterial blood gases were monitored while breathing room air, and then while breathing a gas mixture containing 13.6% oxygen, remainder oxygen, equivalent to breathing ambient air at 10,000 feet.

The results were interpreted as indicating an excessive ventilation/perfusion imbalance on room air, because of the high alveolar to arterial oxygen gradient (24 mmHg), and an abnormally reduced arterial oxygen tension while breathing the hypoxic gas mixture (his arterial oxygen tension fell to 37 mmHg).

What are your recommendations to Major CPD? What are your recommendations regarding aeromedical disposition?

Major CPD is grounded, and takes your advice and stops smoking. At the same time, he begins a regular exercise program, with daily 30 minute jogs and some isometric exercises. After two years, he feels much better, and no longer notices any unusual dyspnea, even when exercising strenuously in cool weather. He requests a review of his flying status.

On clinical examination, he appears fit and healthy. Clinical examination of the chest is quite normal.

A repeat chest x-ray continues to show the patchy scarring in the left base, but otherwise is normal. Repeat pulmonary function tests are done, with the following results:

	PREBRONCHODILATOR			POSTBRONCHODILATOR	
	Predicted	Observed	% Pred	Observed	%Prebronch
TLC (L)	6.8	7.9	116	7.7	97
FRC (L)	3.8	3.6	95	3.5	97
VC (L)	4.6	5.8	126	5.8	100
RV (L)	2.2	2.1	95	1.9	90
RV/TLC %	32.6	27.0	83	25.1	93
FVC (L/S)	4.6	5.8	126	5.8	100
FEV_1 (L)	3.5	4.0	114	4.1	103
FEV_1/FVC %	76	69	90	71	103
V50 (L/S)	4.6	3.4	74	3.4	100
V25 (L/S)	2.3	1.1	48	1.1	100
DCO (ml/min/mmHg)	38.2	33.3	87		

He is exposed to simulated altitude in an altitude chamber, with non-invasive monitoring of his oxygen saturation with an ear oximeter. The results are:

Altitude	Saturation
Ground	97%
5,000 feet	96%
10,000 feet	94%
12,000 feet	90%
15,000 feet	81%

A repeat methacholine challenge test shows a PC_{20} of 12 mg/ml, suggesting less airway reactivity than on his previous test, and now essentially normal. A SBNT shows a normal closing volume and closing capacity for his age, and the slope of the alveolar plateau is normal.

What are your aeromedical recommendations at this time?

Small airways disease with airflow limitation can interfere with aircrew performance in a number of ways. Because of impaired gas exchange, a mild reduction in inspired oxygen tension may result in significant hypoxia. Early airway closure (as indicated by a SBNT) may predispose to acceleration atelectasis. Ventilation-perfusion mismatching by increased G forces may be significantly aggravated by small airways disease, and lead to a reduced G tolerance.

Fortunately, at least some of the functional changes induced by cigarette smoking are at least partially reversible, including flow limitation and airway sensitivity, as Major CPD demonstrates. This reversibility is felt to be due to a resolution of the inflammatory bronchiolitis caused by cigarette smoke.

Two years after stopping smoking, with the demonstration of relatively normal pulmonary function, Major CPD was returned to full flying duties.

Explanation of Abbreviations:

FVC	Forced Vital Capacity (liters)
TLC	Total Lung Capacity (liters)
FRC	Functional Residual Capacity (liters)
RV	Residual Volume (liters)
FEV_1	Forced Expiratory Volume in 1 second (liters)
MMFR	Maximum mid-expiratory flow rate (liters per second)
V50	Flow rate at 50% of a Forced Vital Capacity (liters per second)
V75	Flow rate when 75% of an FVC has been expired (liters per second)
DL_{CO}	Single-breath diffusing capacity for carbon monoxide (milliliters per minute per millimter of mercury)

REFERENCE

1. McCarthy, D.S., Craig, D.B., and Cherniak, R.M. Effect of modification of smoking habit on lung function. Am. Rev. Resp. Dis. 14: 103-113, 1976.

CASE L.H. (by Dr Hull) Age 27 years

Helicopter pilot (search and rescue)

Complaint: Recurrent summer upper respiratory and chest symptoms for 3 years.

Past health: No illness. Nothing similar. No eczema.

Family health: A sister has hay fever.

3 years ago, in July, acute onset of clear nasal discharge, nasal irritation and itching eyes.

After 3 days, cough, wheeze and scanty yellow sputum.
Not severely affected - able to continue his flying duties.
All symptoms remitted completely after 3 weeks, but recurred each July.

On examination: (January). Completely normal.

Chest xray - normal
ECG - normal
Hb 14.5 G, TWBC 5.4, total eosinophils 0.2 (= 4%)
Skin testing - sensitive to B2 grasses only; negative to aspergillus fumigatus.
Spirometry: FVC 5.5L; FEV1 4.5 = 82%
but FEV1 5.0 = 91% after bronchodilator
PFR 600 L/min with no diurnal variation
Exercise test - No alteration in peak flow, vital capacity or FEV1.

Q1 What is your diagnosis?

Q2 How would you manage him?

He was returned to flying duties with instructions to take topical cromoglycate for his ocular, nasal and respiratory symptoms, at the first sign of any recurrence of symptoms.

In July he became aware of a recurrence which however was fully controlled by Rynacrom, Opticrom, and Intal inhaler.

A diagnosis was made of mild hay fever and bronchospasm based on a familial atopic tendency.

A medical board made him A3 - unfit high performance aircraft, fit to fly only as or with co-pilot.

Q3 After 3 more seasons, his short-term treatment every July continues to give complete control of all his symptoms. Objective assessment during treatment confirms normal respiratory function with no diurnal swing in PFR.

May his flying restrictions be eased? If so, in what way?

Age 34

CASE H.B. (by Dr Hull)

Civilian commercial pilot's licence.

Life-long non-smoker.
Family - no respiratory disease.

Age 26 On an escalator in a Cardiff store.

Acute severe left-sided chest pain; stabbing quality, with dyspnoea.
Collapsed.
Emergency hospital admission.

Small left-sided spontaneous pneumothorax.
Re-expanded without intervention.
Chest xray - probable bilateral basal emphysema.
VQ scan - washout delayed bilaterally but left worse than right.
Heterozygous for alpha-one antitrypsin deficiency - actual blood level only slightly reduced.

Returned to flying duties.
Ascent to altitude regularly caused recurrence of left lower chest pain, less severe but similar quality to initial episode. Would fly with left hand "splinting" his chest.

Age 27 Left thoracotomy.
Left lower lobe anterior basal segment was diffusely emphysematous and over-expanded. It was resected, and parietal pleurectomy accomplished.

After 3 months - return to flying duties Well for 2 years.

Age 29 Developed similar pain on <u>right</u>, felt only during flying, usually on ascent.

Age 30 Reassessed. Sound thoracotomy scar. Physically normal.

Age 34 Reviewed. No symptoms for 4 years. Physically normal.
Chest xray: pleural shadowing left base with reduced vessel markings.
Lung function: Spirometry normal. DLCO, KCO - normal.
CAT scan. Bulla left base with bullous emphysema almost up to carina. Minor bullous emphysema right base also.
Ventilation scan. Gas trapping left base consistent with large emphysematous bulla.

Q1 Will you allow H.B. to continue professional flying duties?

If not, why not?

<u>Specialist Aeromedical Advice</u> at this stage was permanent grounding, on the basis of bilateral disease with a history of bilateral symptoms, despite later subjective remission for nearly 4 years.

H.B. appeals against this decision on the grounds of absence of symptoms, and after obtaining advice of another chest specialist who told him he was fit to fly.

Q2 How would you answer to H.B's appeal?

Can further investigation help your decision? If so, what?

HYPERTENSION IN THE AVIATOR

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SUMMARY

Systemic hypertension is one of the most commonly encountered medical problems for both the general medical practitioner and the specialist in aerospace medicine. Its frequent occurrence, its contribution to the risk of cardiovascular events, and problems with early detection and compliance with therapy all make hypertension a health problem of significant concern. It is clear from the literature that therapy for moderate and severe hypertension significantly reduces morbidity and mortality. However, much study and debate has occurred regarding the benefit of therapy of mild hypertension. The appropriateness of therapy for mild hypertension is discussed here, based on a review of several major studies from the world literature. Detri-mental effects of thiazide diuretics have been reported recently, prompting interest in the use of smaller doses of thiazide diuretics as well as interest in the use of other agents as first line therapeutic choices. Current United States Air Force policies regarding the treatment of hypertension in aviators is discussed, as well as considerations that must be addressed in the study of new medications for use in the aviator population.

Hypertension is one of the most commonly encountered diseases in both general clinical medicine and aerospace medicine. Twenty per cent of the United States adult population has hypertension, representing over sixty million people. Hypertension is one of the most significant risk factors for coronary artery disease and a leading cause of congestive heart failure, cerebrovascular accidents, and renal failure. In spite of a health problem of such magnitude, its detection and therapy have often been neglected by both the physician and the patient for several reasons. Patients are asymptomatic until end organ complications have occurred and they are subjected to life-long therapy. Detection of the disease is not as much a problem presently due to widespread education of the general population and physicians. According to 1984 estimates, 50 - 55% of the United States hypertensive population are aware of their diagnosis and 30 to 35% are on therapy.

Actuarial studies clearly show that the morbidity and mortality of hypertension increase steadily with increasing systolic and/or diastolic blood pressure without any clear cut-off level. The definition of hypertension is somewhat arbitrary and varies between different sources but most attempt to identify a level of blood pressure associated with a 50% increase in mortality. The 1984 report of the Joint National Committee defines a blood pressure greater than or equal to 140/90 mmHg as hypertensive[1]. The same level is used for U. S. Air Force and U. S. Army aviation standards. The relative merits of home blood pressure recordings versus 24-hour ambulatory blood pressure recordings versus multiple office blood pressure recordings in the diagnosis of hypertension will not be discussed. The use of phase 4 sounds versus phase 5 sounds for recording diastolic blood pressure will also not be discussed. All authorities agree that an average or predominance of multiple blood pressure determinations must be elevated to make a diagnosis of hypertension. Twice-a-day determinations over a three to five day period are most commonly used in the U.S. Air Force when hypertension is suspected.

Hypertension demands our utmost concern because it affects a large number of patients, it clearly increases morbidity and mortality, and therapy has been shown to be effective in reducing its morbidity and mortality. However, its detection and therapy in clinical, preventive and aviation medicine continue to be less than satisfactory. Because of the potentially adverse effect of the diagnosis of hyper-tension on an aviator's career, it is often not diagnosed or done so only belatedly. We must honestly diagnose and treat hypertension in aviators because of the long-term morbidity and mortality considerations and because of possible complications that may lead to sudden incapacitation during flight. Total mortality, cardiovascular mortality, congestive heart failure, renal failure, retinopathy and left ventricular hypertrophy are all clearly complications of hypertensive disease. Sudden, incapacitating, complications of hypertension --such as myocardial infarction, cerebrovascular accident, transient ischemic attacks, aortic dissection, and ischemic discomfort and arrhythmias -- pose particular aeromedical risks. We must realize that an aviator who is not treated for hypertension during his active flying career may return to the health system years later with myocardial infarction, stroke, congestive heart failure, renal failure, etc., and be forced to retire prematurely from the entire working environment.

The world literature is clear that treatment of moderate and severe hypertension is effective in decreasing the associated morbidity and mortality. Controversy has surrounded the treatment of mild hypertension, especially the stepped care approach with diuretics as the first line of therapy. One problem with this issue is that various reports define mild hypertension differently. Diastolic blood pressures of 90 to 104 mmHg, less than or equal to 100 mmHg, and 90 to 94 mmHg are all subgroups that have been separated from the data of large clinical trials. A statistical hazard exists in this case, if the original protocol did not define the subgroups in their methods. The 1984 report of the Joint National Committee[1] defines mild diastolic hypertension as 90 to 104 mmHg. Both the Joint National Committee and the United States National Hypertension Education Program recommend treatment for diastolic blood pressures greater than 90 mmHg based on their review of the available literature. The bulk of evidence from several studies shows a benefit from treatment of mild hypertension (90-104 mmHg diastolic) in decreasing the incidence of cerebrovascular events, congestive heart failure, aortic dissection and left ventricular hypertrophy. Some studies further suggest that the progression from mild to moderate and severe hypertension is also decreased. Some studies also show a decreased total mortality. However, less evidence exists for decreased coronary artery disease morbidity and mortality. A brief review of the major studies in the literature should prove beneficial.

Hypertension Detection and Followup Program[2]

Over 10,900 patients, aged 30 to 69, with initial diastolic blood pressures of 90 to 104 mmHg were followed for five years. Comparison of an aggressive or stepped care approach versus usual or routine care therapy was performed. No placebo or untreated control group was used. Total mortality in the stepped care group was decreased 21% compared to the routine care group and cardiovascular mortality was decreased 26%. The authors estimated that 70% of the hypertensive population and 60% of the excess mortality occur in this group of mildly hypertensive patients.

The Oslo Study[3]

In this study, 785 males without evidence of target organ complications, aged 40 to 49, with initial diastolic blood pressures 90 to 109 mmHg were followed for five years. Subjects were placed in either a treatment or no treatment group. No significant difference was found between the two groups in cardiovascular morbidity, cardiovascular mortality or total mortality. The subgroup with an initial diastolic blood pressure greater than or equal to 100 mmHg did demonstrate significantly fewer cardiovascular events with therapy. Cerebrovascular events, fatal abdominal aortic aneurysms, left ventricular hypertrophy and congestive heart failure occurred only in the untreated control group.

The Australian Study[4]

Over 3,000 men and women, aged 30 to 69, without target organ damage were followed for four years. Initial diastolic blood pressures ranged from 95 to 109 mmHg. Subjects were placed in a treatment versus placebo control group. The treatment group had significantly fewer total and cardiovascular deaths and fewer cerebrovascular events. However, no significant difference was found in the incidence of coronary artery disease events.

Medical Research Council[5]

Over 17,000 men and women, aged 35 to 64, were followed for five and one-half years. Initial diastolic blood pressure ranged from 90 to 109 mmHg. Beta blocker therapy and diuretic therapy were compared to a placebo control group. The treatment groups had significantly fewer total cardiovascular events, but no decrease in total mortality. Significantly fewer cerebrovascular accidents occurred in the treatment groups but the incidence of coronary events was not significantly changed.

Veterans' Administration Study[6]

Three hundred-eighty men with an initial diastolic blood pressure of 90 to 114 mmHg were randomized to treatment versus placebo control groups who were followed for three years. There was a 75% risk reduction in the subgroup with diastolic blood pressures ranging from 104 to 114 mmHg and a 35% risk reduction in the subgroup with diastolic blood pressures ranging from 90 to 104 mmHg. The incidence of cerebrovascular accidents, congestive heart failure, renal failure and accelerated hypertension was significantly reduced in the treatment group. No significant difference was found in the incidence of coronary artery disease complications.

United States Public Health Service Study[7]

In a treatment vs placebo control study, 389 patients, aged 21 to 55, were followed seven to ten years. Initial diastolic blood pressures ranged from 90 to 115 mmHg. The treatment group had a significantly lower incidence of left ventricular hypertrophy, cardiomegaly, cerebrovascular accidents and retinopathy. No significant difference existed between the two groups in total mortality or in the incidence of coronary artery disease events.

Multiple Risk Factor Intervention Trial[8]

Over 12,000 subjects at increased risk for coronary artery disease were followed for seven years. Ages ranged from 35 to 57 years and the subjects were placed in either a stepped care or usual care group. No significant difference was found between the two groups in total or coronary artery disease mortality. Coronary artery disease mortality was decreased in male subjects with normal blood pressures or elevated blood pressures with a normal electrocardiogram. Coronary artery disease mortality was increased in male subjects with hypertension and an abnormal electrocardiogram.

Coronary artery disease events and mortality were not decreased in these large studies. However, the incidence and mortality of other cardiovascular events was significantly decreased. The conclusions regarding coronary artery disease events and mortality may not be completely valid. In some of these studies an aggressive or stepped care therapy approach was compared to a routine or usual care therapy approach rather than to an untreated or placebo control group. Some studies did compare a treatment group to an untreated or placebo control group; however, the control group was still treated in the sense that those subjects were under frequent medical surveillance and often received nonmedical interventions, such as dietary and exercise counseling. The relatively young age of the subjects and the short followup periods may also have affected the results. Many practitioners may feel that the significant reduction in nonatherosclerotic events and mortality precludes longer followup studies to settle the issues of whether treatment of mild hypertension reduces atherosclerotic events and mortality.

The literature clearly favors treatment of mild hypertension. However, the equivocal effect of therapy on the incidence of coronary artery disease events and mortality is disturbing. All of these studies used a diuretic as the first line therapeutic agent. Thiazide diuretics, with or without triamterene, are the only medications a USAF aviator may take for hypertension and continue flying duties. The U. S. Army also allows prazosin and captopril for antihypertensive use in its aviators. Other countries allow other medications, including beta blockers, especially in non high performance aircraft. Estimates indicate that 25% of aviators with mild hypertension can be controlled with nonpharmacologic methods, such as weight reduction, sodium reduction, decreased dietary fat, behavioral modification and discontinuation of tobacco products and alcohol. According to further estimates, 50% can be controlled with thiazide diuretics and

the above nonpharmacologic methods. The failure of diuretics and nonpharmacologic methods to control up to 50% of the hypertensive aviator population and the question of a possible increased coronary artery disease risk due to diuretic therapy in mild hypertensive subjects, together raise the issue of alternative drugs for the aviator with hypertension. Testing of other medications requires an extensive evaluation, especially if their use is considered in aviators flying high performance aircraft. Such an evaluation includes the effect of the drug on mental and physical performance, orthostatic stress response, $+G_z$ acceleration tolerance, exercise tolerance, the response to hypoxia and decreased barometric pressure, cardiac rhythm stability, psychomotor function, blood volume changes and metabolic homeostasis. Masking of the signs and symptoms of developing coronary artery disease by nondiuretic antihypertensive medications must also be a concern.

Diuretics reduce serum potassium in 10 to 30% of patients, thus causing a risk of increased ectopy, especially when combined with cardiac ischemic events. Coronary artery disease remains the most common cause of death in hypertensive patients. Other concerning effects of diuretic therapy include decreased glucose tolerance and adverse effects on lipid profiles. Data from the Framingham studies have shown that diuretic therapy for hypertension increases total cholesterol 10 to 20 mg%, neutralizing the risk reduction effect of decreasing blood pressure. Thiazide diuretics have been reported to increase total cholesterol, triglycerides, LDL cholesterol and uric acid. Beta blockers increase total cholesterol and triglycerides and decrease HDL cholesterol. In a cross-over randomized trial of mildly hypertensive patients treated with thiazide diuretics, Grimm[9] reported a 6% increase in total cholesterol, 17% increase in triglycerides, and significant increases in LDLand VLDL cholesterol. No significant change occurred in HDL cholesterol levels. Lipid profile changes induced by thiazide diuretics were corrected with dietary modifications. Because of the cancelling effects of lowering blood pressure but increasing total and LDL cholesterol, the authors predicted no change in the five year and twenty year risk of developing coronary artery disease. All of these considerations suggest that diuretic therapy for mild hypertension may cancel the coronary artery disease protective effects of lowering blood pressure but still preserve the protection from other cardiovascular events and mortality.

As we see, hypertension poses a threat for long-term morbidity and mortality both medically and aeromedically. Treatment of hypertension, including mild hypertension, decreases this risk. Diuretics may not be the best first line agents for mild hypertension because of their effects on lipid profiles and other factors; but newer agents will have to be carefully and extensively evaluated prior to their use in the military aviator population, especially those flying high performance aircraft. The aerospace medicine specialist will ultimately best serve his aviators by a timely diagnosis and appropriate therapy of their hypertension, even though this care may adversely affect their flying status.

REFERENCES:

1. The 1984 Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. NIH Publication No. 84-1088, Sep 84. Arch IM 144:1045-1057, May 84.

2. Hypertension Detection and Followup Program Cooperative Group: Five Year Findings of the Hypertension Detection and Followup Program: I. Reduction in Mortality of Persons with High Blood Pressure, Including Mild Hypertension. JAMA 242:2562-2571, 7 Dec 79.

3. Helgeland, A.: Treatment of Mild Hypertension: A Five Year Controlled Drug Trial. The Oslo Study. Am J Med 69:725-732, Nov 80.

4. The Management Committee: The Australian Therapeutic Trial in Mild Hypertension. Lancet 1:1261-1267, 14 Jun 80.

5. Medical Research Council Working Party: Medical Research Council Trial of Treatment of Mild Hypertension: Principle Results. Br Med J 291:97-104, 13 Jul 85.

6. Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of Treatment on Morbidity in Hypertension. II. Results in Patients with Diastolic Blood Pressures Averaging 90 to 114 mmHg. JAMA 213(7): 1143-1152, 17 Aug 70.

7. Smith, W. with the United States Public Health Service Hospitals Cooperative Study Group: Treatment of Mild Hypertension: Results of a Ten Year Intervention Trial. Circ Research 40(5) Suppl 1, I-98-105, May 77.

8. Multiple Risk Factor Intervention Trial Research Group: Multiple Risk Factor Intervention Trial: Risk Factor Changes and Mortality Results. JAMA 248: 1465-1477, 24 Sep 82.

9. Grimm, R.: Effect of Thiazide Diuretics on Plasma Lipids and Lipoproteins in Mildly Hypertensive Patients. Annals 94:7-11, Jan 81.

GENERAL REFERENCES:

1. Rubenstein, E.: Scientific American Medicine. New York, Scientific American, Inc., 1986, pages VII:1-29.

2. Frohlich, E.: Practical Management of Hypertension. Current Problems in Cardiology. Vol X, No. 7, Jul 85.

3. Kaplan, N.: New Approaches to the Treatment of Mild Hypertension. AJC 51: 621-627, 24 Feb 83.

4. Kaplan, N.: When to Treat: The Dilemma of Mild Hypertension. AHJ 101(6):867-870, Jun 81.

5. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia, Lea and Febiger, 1985, 431-434.

CORONARY RISK FACTORS IN AEROSPACE MEDICINE

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Coronary risk factors may be used in the aeromedical setting to identify aviators who are at high risk for the development of coronary artery disease and are, therefore, at a higher risk for sudden incapacitation. Coronary risks may be used to identify those aviators who need additional testing in an attempt to discover asymptomatic coronary artery disease. Coronary risk factor analysis should also be applied to the entire aviator population in order to identify those aviators who need routine or intensive risk factor modification. Certain lipid patterns, especially familial hyperlipidemia patterns, may be used to identify younger trainees who do not represent a good long-term training investment because of the high risk of subsequent development of coronary artery disease.

Coronary artery disease is a major military public health problem, representing a significant cost in death and disability for the Air Forces of the NATO allies. Coronary artery disease has a bearing on readiness, and it must be viewed as a major risk from the standpoint of aviation safety. Coronary artery disease is not a disease of "old men," but rather it must be looked upon as a disease which has its genesis relatively early in life. In the United States, 29% of all deaths between the ages of 35 and 44 years of age are due to cardiovascular disease (1). The rather striking occurrence of coronary artery disease in relatively young men was noted in US battle casualty autopsies. In 300 autopsies from the Korean War, mean age of 22.1 years in 200 cases, some degree of atherosclerosis was discovered on gross inspection in 77% of the cases. At least one 50% narrowing was noted in 15% of the subjects, and one or more total occlusions noted in 5% (2). In 105 battle casualty autopsies from the Vietnam War, mean age 22 years, postmortem angiography and dissection demonstrated evidence of atherosclerosis in 45%. Five percent had gross evidence of severe atherosclerosis (3), although postmortem angiography, with its inherent limitations, was unable to confirm significant narrowing. Nevertheless, the amount of atherosclerotic substrate in this young population was striking. Thus, it has become apparent that coronary artery disease is in some respects almost a pediatric disease. It is, therefore, not inappropriate to discuss coronary artery disease in the context of a relatively young population. In the United States Air Force, approximately 500 personnel throughout the Air Force will experience significant disability or death because of coronary artery disease each year. The annual cost directly attributable to coronary artery disease is approximately $70 million per year in lost work time, medical treatment and premature disability. Premature coronary artery disease has a definite bearing on readiness, because coronary artery disease is a continual risk for sudden incapacitation or impaired performance. The bearing on aerospace safety has never been more marked than during the advent of the new high-performance fighters with rapid rates of $+G_z$ acceleration, coupled with sustained $+G_z$. Thirty percent of our rated force in the USAF is equal to or greater than 35 years of age. We have 2,000 aviators equal to or greater than 40 years of age. If a United States Air Force aviator dies of a medical cause of death while on active duty, over 70% of these deaths will be due to cardiovascular disease. Of course, the leading causes of death in any population which is predominantly under the age of 40 will be traumatic. However, coronary artery disease is the leading cause of nontraumatic death in our aviators. We are all well aware that coronary artery disease presents as a catastrophe in most circumstances, and less than one-half of patients are fortunate enough to present with angina. Because sudden death or myocardial infarction is such a frequent manifestation, coronary artery disease prevention becomes the only reasonable strategy.

Figure 1 defines those conditions which describe a risk factor. These criteria for the definition of a risk factor are rather stringent. Only those coronary risk factors which meet these criteria will be discussed during this paper.

* Increased frequency or higher level of a factor in those with evidence of the disease

* Over time, increased incidence of the risk factor is associated with increased occurrence of the disease

* Evidence that reduction in risk leads to reduction in disease

* Relationship to disease is independent of other risk factors

* A scientifically acceptable explanation exists for the causal relationship to disease

Figure 1 - Definition of a Risk Factor

Serum Cholesterol

The habitual consumption of saturated fats and cholesterol is strongly correlated with the mean serum cholesterol on a population basis (4, 5). Further, the mean serum cholesterol levels in a population are strongly correlated with the prevalence of coronary artery disease (6, 7). This latter association has been repeatedly demonstrated in both natural history studies as well as coronary angiographic studies. There have also been multiple high quality studies which have demonstrated that a decrease in the serum cholesterol on a population basis is associated with a decrease in coronary risk (8, 9, 10). While there are those who still dispute the apparently strong causal relationship between serum cholesterol and coronary artery disease, it is difficult to be nihilistic about this relationship in the face of rather compelling literature studies. However, it is perhaps even more difficult to minimize the relationship between blood fats and coronary events in a population at high occupational risk for sudden incapacitation. Given the rather impressive array of epidemiological data available, it is difficult from an occupational medicine standpoint to withhold our coronary prevention efforts because some very small degree of doubt may be harbored about the "diet-heart theory." The information available to us in the world's literature clearly seems strong enough to pursue an active coronary artery disease prevention program.

Coronary Risk and HDL Cholesterol

High density lipoprotein (HDL), which is 90% apoprotein by weight, is a protein detergent molecule capable of solubilizing phospholipids and cholesterol in large quantities. One gram of HDL apoprotein can dissolve 2.5 grams of phospholipid. The role of HDL in lipid transport appears to result in a net removal of cholesterol from tissues as well as the "acceptance" of cholesterol during very low density lipoprotein metabolism. HDL appears to favor the transport of cholesterol from the arterial wall. Angiographic correlative studies, both in symptomatic and asymptomatic populations, have documented that the level and type of circulating lipoprotein concentrations are related to the extent and severity of atherosclerotic heart disease at angiography (11, 12). In the Framingham study, HDL cholesterol was the best discriminator in separating arteriosclerotic heart disease from healthy subjects over 50 years of age (13). As HDL levels became elevated, a strong negative correlation between HDL cholesterol and coronary disease became evident, and this relationship persisted even after the adjustment of the relative risk of atherosclerosis for other major risk factors. The protective effect of HDL has been well documented in a USAFSAM arteriographic study of aviators (14). The ratio of cholesterol to HDL was the strongest contemporary expression of coronary risk, with a level of 6.0 representing the beginning of an elevated risk. HDL has only been determined regularly in most laboratories since the late 1970s, and long-term epidemiological studies confirming the value of raising the HDL have not yet been completed. However, HDL may be elevated by restriction of total calories from dietary fat, aerobic exercise and modest alcohol intake. Alcohol is believed to induce higher levels of high density lipoprotein because of an increased very low density lipoprotein flux (triglyceride carrying lipoproteins) resulting in an increased HDL concentration. Figure 2 displays the distribution of total serum cholesterol levels in USAF personnel (both flying and nonflying personnel). These studies were performed on a study population of 41,822 males and 2,547 females. In the United States, we consider cholesterols greater than 260 mg% to be seriously elevated, while we consider below 200 mg% to be optimal.

TOTAL CHOLESTEROL IN MG%

	≤200	200-249	250-299	≥300
MALES	56%	32%	9.5%	2.5%
(N = 41,822)				
FEMALES	71%	23%	4.5%	1.5%
(N = 2,547)				

Figure 2 - Distribution of Total Cholesterol Levels in USAF Personnel

Figure 3 reveals the distribution of cholesterol to HDL ratios in USAF personnel, a population including both flying and nonflying personnel. Approximately 22% of our male Air Force members have cholesterol to HDL ratios of 6.0 or greater and are considered at increased risk. Seven percent of our female personnel have ratios of 6.0 or greater.

RATIO OF CHOL/HDL

	4.5 OR LESS	4.6-5.9	6.0 OR GREATER
MALES	51%	27.5%	21.5%
(N = 39,066)			
FEMALES	78%	15%	7%
(N = 2,435)			

Figure 3 - Distribution of Cholesterol/HDL Ratios in USAF Personnel

Figure 4 displays the distribution of the highest risks in the USAF, defined as a serum cholesterol of equal to or greater than 300 mg% or a cholesterol to HDL ratio of equal to or greater than 6.0. One can see a steady increase in the number of individuals at high risk with advancing age among our male Air Force members. Twenty-eight percent fell into the highest risk category at age 46-50. Figure 5 outlines the recommendations of the American Heart Association for a prudent diet. The USAF has adopted these dietary goals of the American Heart Association.

AGE BY 5-YEAR GROUPS

	<25	26-30	31-35	36-40	41-45	46-50	>50
MALES	7.7	11.6	17.9	21.5	26.0	28.2	26.6
(N = 41,593)							
FEMALES	5.5	7.0	10.1	7.9	**	**	**
(N = 2,532)							

* When total cholesterol 235-300 mg%
** Small sample size

Figure 4 - USAF Personnel "At Risk" with Total Cholesterol ≥ 300 mg% or Ratio ≥ 6.0*

* Only 30-34% of total daily calories from fat
* Limit dietary cholesterol to 300 mg daily
* Only 10% of total daily calories from saturated or polyunsaturated fatty acids

Figure 5 - American Heart Association Prudent Diet

Obesity

It has been difficult to attribute a stand-alone, isolated risk to obesity, but numerous investigators believe that obesity is an independent risk factor. However, the primary risk effects of obesity revolve around the effect of obesity on other primary coronary risks. The Framingham Study demonstrated that for each 10% increase in body weight, there was a 6.5 mmHg increase in systolic blood pressure, a 12.5 mg% increase in serum cholesterol and slight increases in blood sugar and uric acid. In the Framingham Study, subjects who were 30% or more overweight had an increased incidence of sudden death and angina. The effects of increased body weight were about one-half as severe in women as in men for the same increase in body weight above the optimal. Figure 6 reveals that 2.8% of our USAF personnel are obese, either failing to meet our USAF height and weight standards or exceeding the body fat standard of 24% for males and 32% for females. Of those identified, 82.5% were in active intervention programs to lose weight.

SAMPLE SIZE	OBESE*	% ENROLLED IN INTERVENTION
44,167	2.8%	82.5%

* Fails to meet height/weight standards or % body fat standard exceeded (Males-24%, Females-32%)

Figure 6 - Obesity in the USAF

Blood Pressure

It is well established that hypertension accelerates atherosclerosis and potentiates other coronary risks. Of course, hypertension also has adverse primary effects on the blood vessels of the brain, heart and kidneys. In the Framingham Study, both the excess mortality and morbidity associated with hypertension were directly related to the height of the blood pressure. Blood pressure has emerged as a no threshold phenomenon with increasing risks for increasing blood pressure, even within the accepted "normal" range. In the Framingham Study, for each 10 mmHg increment in blood pressure throughout the entire range, there was a 30% increase in cardiovascular risk, with no discernible critical blood pressure. The Framingham Study also revealed that random blood pressure readings have meaning. In the USAF, we have almost no untreated hypertension, because blood pressures are taken during flight physicals, periodic physicals of nonflying personnel, at sick call and even at the dental clinic. The very aggressive detection and management of hypertension has been a very successful chapter in military medicine.

Cigarette Smoking

From the Framingham Study, moderate cigarette smoking (20 cigarettes per day) doubled the risk associated with other coronary risk factors. There was even an increased coronary risk for men who smoked 10 cigarettes per day. The risk of sudden death in the Framingham Study was also increased for individuals with coronary disease who continued to smoke. The rate of coronary events after enrolling in the Framingham Study was halved for men who stopped smoking. Figure 7 outlines the percent of smokers in USAF personnel. These percentages are very similar to those of the civilian population in North America and closely parallel those of most developed societies.

	SMOKERS*	SMOKERS IN INTERVENTION CLINICS
MALES	29%	64%
FEMALES	28%	72%

* $\geq$ 1/2 pack of cigarettes per day or regular smoker/inhaler of pipes or cigars

Figure 7 - Smoking in USAF Personnel

The Exercise Hypothesis

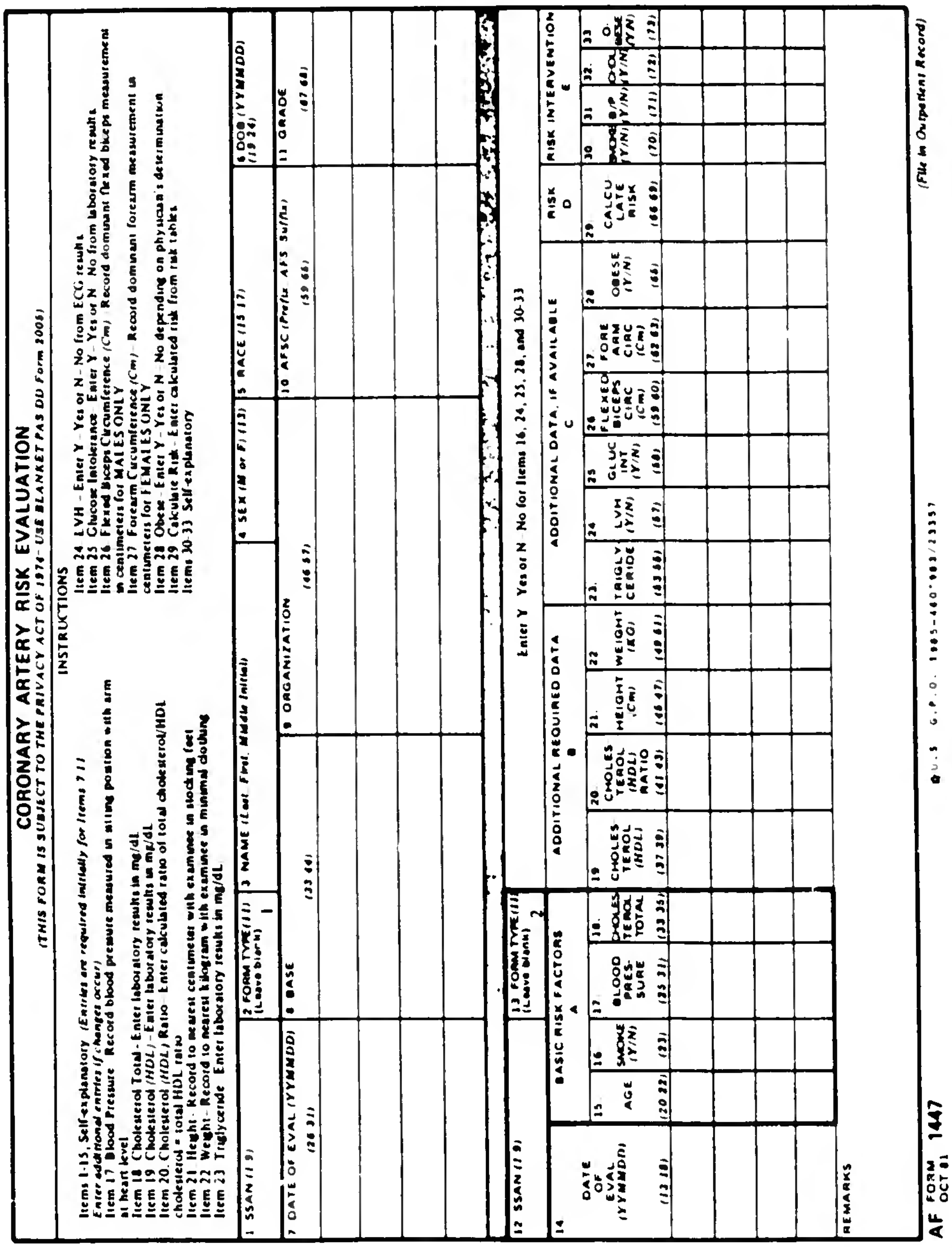
Before discussing an intervention program for military aviators, it is necessary to briefly touch upon the controversy regarding the possible protective effects of regular exercise against coronary heart disease in man. Regular exercise is known to improve cardiac efficiency by reducing the heart rate and blood pressure. Maximal oxygen extraction is improved in those who exercise regularly. Regular exercise reduces some blood fats (cholesterol) and raises other blood fats (high density lipoprotein). Regular exercise may reduce depression and anxiety, if the pursuit of exercise does not become an unhealthy fetish. Exercise improves musculoskeletal efficiency and fosters the aerobic capacity which is required in many military occupations. It is also established that very few regular exercisers smoke, and most regular exercisers will not pursue an unhealthy diet. However, the question of whether exercise exerts any protective coronary effect has not been completely settled as of this date. Associations between exercise and coronary disease were noted in London transport workers (15), Iowa farmers (16), British civil servants (17), in the Seattle Heart Watch Study (18) and in the Framingham Study (19). There have been several studies which have failed to document any effect of exercise on coronary prevention, but most of these studies had some epidemiological faults. The best studies to date with well-controlled, nonexercise variables were the San Francisco Longshoreman Study (20) and the Harvard Alumni Study (21). In the San Francisco Study, 3,263 males were enrolled in a 16-year study. In those whose occupations required aerobic expenditure as opposed to those who lead sedentary occupations, the coronary event rate for each 10,000-work-years was 5.6 versus 15.7. This threefold increase in coronary events among sedentary workers, with all other nonexercise variables controlled, is a compelling study. The most recent study, and perhaps the most conclusive, was that of 16,936 male Harvard alumni who were followed up from 16-50 years after enrollment at Harvard. The lowest coronary event rates were in those who ran 20-29 miles per week. However, increasing degrees of coronary artery disease prevention were noted with increasing levels of exercise, even beginning with those who only walked regularly. Perhaps one of the primary mediating factors of exercise on coronary artery disease prevention is that of exercise-induced elevation of HDL. Exercise appears to increase triglyceride extraction from chylomicrons, leading to increased lipoprotein lipase activity and resulting in elevated HDL levels. Studies in athletes have documented increases in HDL levels, well correlated with increases in maximal oxygen extraction. In 1987, the weight of the evidence supports the view that persons who exercise regularly have a lower risk of coronary heart disease.

Coronary Artery Disease Prevention for Aviators

Studies in Oslo, Norway (22); North Karelia, Finland (23); the Leiden Intervention Trial (24); and the Ireland-Boston Diet-Heart Study (25) strongly support the thesis that primary risk factor intervention will reduce coronary mortality and morbidity. In the USAF, the Surgeon General of the Air Force formulated a program called the "CARE" program, the abbreviation for the Coronary Artery Risk Evaluation program. This program of the USAF Surgeon General was started in Jan 82 and involves every active duty person in the USAF. A CARE assessment begins with every periodic physical examination at or after age 25 and each five years thereafter. Surveillance for aviators begins with every complete flying physical and each two years thereafter. The flight surgeon's office has primary responsibility for the CARE program, both for flying and nonflying personnel. While coronary risks are evaluated periodically based upon physical examinations, any Air Force member who is found to be at elevated risk is placed into a risk factor intervention program. For those found to be at increased risk, the coronary artery risk evaluation surveillance is performed annually. Figures 2, 3, 4, 6 and 7 represent preliminary risk analyses of a cohort of CARE evaluations. (These data were prepared by Rufus M. Dehart, BG, USAF, MC, and Chief Master Sergeant Billy Holmes.) Figure 8 is a sample copy of the USAF Form 1447, which is the primary record-keeping form for our risk intervention program. The CARE program is based upon the assignment of relative risk for the individual, based upon a modified Framingham risk. Group counseling in risk reduction is used whenever possible, emphasizing weight loss, dietary counseling, smoking cessation, life style counseling and graduated exercise programs. The CARE program is based upon a prior research coronary artery disease prevention program in the USAF entitled the HEART program (Health Evaluation and Risk Tabulation). This research program utilized a cost-benefit model, which was designed by the Department of Industrial Engineering at Purdue University. In 1978, this model was chosen "model of the year" by the Society of Industrial Engineers in the United States. This cost-benefit model utilized calculations based upon the most conservative risk reduction benefit assumptions and utilized actual cost. An analysis of return on investment revealed that after ten years in the USAF, $1.00 spent on coronary prevention would return $3.58. Our goals in coronary artery disease prevention in the USAF are: 1) to access the degree of coronary risks in all USAF personnel; 2) to conduct intensive intervention programs and recurrence surveillance for each member declared "at risk"; and 3) to utilize the CARE data to identify those aviators who need second order testing.

The USAFSAM Risk Index

Details regarding the USAFSAM Risk Index were discussed earlier in this lecture series. The goal of the risk index was to identify those aviators who needed second order testing. This use of a stratified risk equation, based upon angiographic data, would eliminate large numbers of unproductive workups in those with little risk of



CORONARY ARTERY RISK EVALUATION

(THIS FORM IS SUBJECT TO THE PRIVACY ACT OF 1974 - USE BLANKET PAS DD Form 2005)

INSTRUCTIONS

Items 1-15, Self-explanatory *(Entries are required initially for Items 7-11. Enter additional entries if changes occur)*
Item 17 Blood Pressure - Record blood pressure measured in sitting position with arm at heart level
Item 18 Cholesterol Total - Enter laboratory results in mg/dL
Item 19 Cholesterol *(HDL)* - Enter laboratory results in mg/dL
Item 20. Cholesterol *(HDL)* Ratio - Enter calculated ratio of total cholesterol/HDL cholesterol = total HDL ratio
Item 21 Height - Record to nearest centimeter with examinee in stocking feet
Item 22 Weight - Record to nearest kilogram with examinee in minimal clothing
Item 23 Triglyceride - Enter laboratory results in mg/dL
Item 24 LVH - Enter Y - Yes or N - No from ECG results
Item 25 Glucose Intolerance - Enter Y - Yes or N - No from laboratory results
Item 26 Flexed Biceps Circumference *(Cm)* - Record dominant flexed biceps measurement in centimeters for MALES ONLY
Item 27 Forearm Circumference *(Cm)* - Record dominant forearm measurement in centimeters for FEMALES ONLY
Item 28 Obese - Enter Y - Yes or N - No depending on physician's determination
Item 29 Calculate Risk - Enter calculated risk from risk tables
Items 30-33 Self-explanatory

1 SSAN *(1-9)*	2 FORM TYPE *(11)* (Leave blank) 1	3 NAME *(Last, First, Middle Initial)*	4 SEX *(M or F) (13)*	5 RACE *(15-17)*	6 DOB *(YYMMDD) (19-24)*

7 DATE OF EVAL *(YYMMDD)* *(26-31)*	8 BASE *(33-44)*	9 ORGANIZATION *(46-57)*	10 AFSC *(Prefix, AFS, Suffix)* *(59-66)*	11 GRADE *(67-68)*

12 SSAN *(1-9)*	13 FORM TYPE *(11)* (Leave blank) 2	Enter Y - Yes or N - No for Items 16, 24, 25, 28, and 30-33

14	BASIC RISK FACTORS A				ADDITIONAL REQUIRED DATA B				ADDITIONAL DATA, IF AVAILABLE C						RISK D	RISK INTERVENTION E			
DATE OF EVAL *(YYMMDD)* *(13-18)*	15 AGE *(20-22)*	16 SMOKE *(Y/N)* *(23)*	17 BLOOD PRES-SURE *(25-31)*	18 CHOLES-TEROL TOTAL *(33-35)*	19 CHOLES-TEROL *(HDL)* *(37-39)*	20 CHOLES-TEROL *(HDL)* RATIO *(41-43)*	21 HEIGHT *(Cm)* *(45-47)*	22 WEIGHT *(KG)* *(49-51)*	23 TRIGLY-CERIDE *(53-55)*	24 LVH *(Y/N)* *(57)*	25 GLUC INT *(Y/N)* *(58)*	26 FLEXED BICEPS CIRC *(Cm)* *(59-60)*	27 FORE ARM CIRC *(Cm)* *(62-63)*	28 OBESE *(Y/N)* *(66)*	29 CALCU-LATE RISK *(66-69)*	30 SMOKE *(Y/N)* *(70)*	31 B/P *(Y/N)* *(71)*	32 CHOL *(Y/N)* *(72)*	33 OBESE *(Y/N)* *(73)*

REMARKS

AF FORM 1447 OCT 81 — U.S. G.P.O. 1985-460-983/23357 — *(File in Outpatient Record)*

Figure 8 - Coronary Artery Risk Evaluation Form
(By permission of the USAF Surgeon General)

either having or developing coronary artery disease. Figure 9 demonstrates the distribution of the USAFSAM Risk Index (I = age^2 [CHOL - HDL/HDL]) in active duty pilots and navigators. These 1,046 pilots and navigators were the aviator subset of the 11,673 members of the HEART data base. Only about 2% of our Air Force aviators have a risk index of 10,000 or greater. Only slightly more than 10% of our military aviators have risk indices of 7,000 or greater. The majority of our coronary discovery strategy should revolve around these 10%. Over 80% of our USAF aviators have coronary risk indices below 5,000, and approximately 90% have risk indices of under 7,000. The use of cardinal risk factors to stratify aviators for second order noninvasive testing is the newest use of coronary risk factors in the USAF. This concept is currently undergoing field testing in one of our fighter commands and is not yet in general operational use in the USAF.

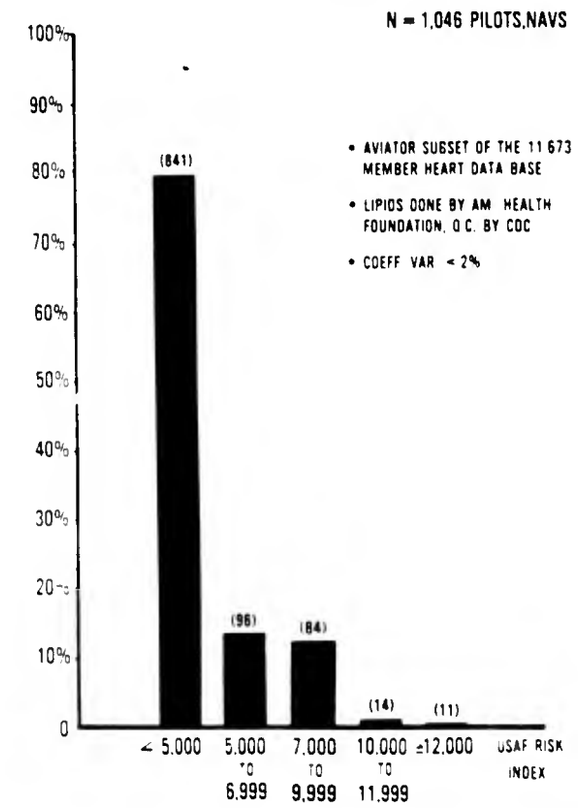


Figure 9 - Distribution of Risk Indices in USAF Aviators

A final use of coronary risk factors in aerospace medicine is that of establishing lipid selection criteria for aviation training. Familial hyperlipidemias are disqualifying for all flying training in the USAF. Any applicant for flying training whose serum cholesterol exceeds 230 mg% will have a repeat cholesterol as well as an HDL determination made after a 14-hour fast. Any repeated and confirmed serum cholesterol in excess of 230 mg% with one or more of the following criteria present is disqualifying from flying training: 1) HDL cholesterol equal to or less than 15% of total cholesterol; 2) total cholesterol greater than 300 mg%; 3) xanthelasma or xanthomas; and 4) a documented family history of coronary heart disease (documented occurrence of angina, myocardial infarction or sudden death in a first-degree relative under age 60).

References

1. National Center for Health Statistics, US Public Health Service, Department of Health, Education and Welfare.

2. Enos WF, Holmes RH, Berger J. Coronary disease among United States soldiers killed in action in Korea. JAMA 152, 1953, 1090.

3. McNammara JJ, Malot MA, Stremple JF and Cutting RT. Coronary artery disease in combat casualties in Vietnam. JAMA 216, 1971, 1185.

4. Sirtori CR, Gatti E, Mantero O, Conti F, Agradi E, Tremoli E, Sirtori M, Fraterrigo L, Tavazzi L, Kritchevsky D. Clinical experience with the soybean protein diet in the treatment of hypercholesterolemia. Am J Clin Nutr 32(8), Aug 79, 1645-58.

5. Gustafsson IB, Vessby B, Boberg J, Karlstrom B, Lithen H. Effects of lipid-lowering diets on patients with hyperlipoproteinemia. J Amer Dietetic Association 80(5), May 82, 426-32.

6. Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: the Framingham study. Am J Cardiol, 38(1), July 76, 46-51.

7. Stamler J. Lifestyles, major risk factors, proof and public policy. Circulation, 58(1), July 80, 3-19.

8. Turpeinen O. Effect of cholesterol-lowering diet on mortality from coronary heart disease and other causes. Circulation 59(1), Jan 79, 1-7.

9. The Lipid Research Clinic's coronary primary prevention trial results, I. Reduction in incidence of coronary heart disease. JAMA 251(3), Jan 20, 1984, 351-364.

10. The Lipid Research Clinic's coronary primary prevention trial results, II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA 251(3), Jan 20, 1984, 365-374.

11. Brensike JF, Levy RI, Kelsey SF, Passamani ER, Richardson JM, Loh IK, Stone NJ, Aldrich RF, Battaglini JW, Moridrity DJ. Effects of therapy with cholestyramine on progression of coronary arteriosclerosis: results of the NHLBI type II coronary intervention study. Circulation 69(2), Feb 84, 313-24.

12. Kuo PT, Hayasek, Kostis JB, Moreyra AE. Use of combined diet and Cholestipol in long-term (7-7.5 years) treatment of patients with type II hyperlipoproteinemia. Circulation 59(2), Feb 79, 199-211.

13. Gordon T, Castelli WP, Hjortlund MC, Kannel WB, Dawber TR. Predicting coronary heart disease in middle-aged and older persons: the Framingham study. JAMA 238, 1977, 497-9.

14. Uhl GS, Troxler RG, Hickman JR, Clark JD. Relation between high density lipoprotein cholesterol and coronary artery disease in asymptomatic men. Am J Cardiol 43, 1981, 903-910.

15. Morris JN, Heady JA, Raffle PAB, Roberts CG, Parks JW. Coronary heart disease and physical activity of work. Lancet II, 1953, 1053-57.

16. Pomrehn PR, Wallace RB, Burmeister LF. Ischemic heart disease mortality in Iowa farmers. The influence of lifestyle. JAMA 248, 1982, 1073-1076.

17. Morris JN, Everitt MG, Pollard R, Chave SPW, Semmence AM. Vigorous exercise in leisure-time: protection against coronary heart disease. Lancet II, 1980, 1207-1210.

18. Bruce RA, DeRouen TA, Hossack KF, Blake B, Hofer V. Value of maximal exercise tests in risk assessment of primary coronary heart disease events in healthy men. AM J Cardiol 46, 1980, 371-378.

19. Kannel WB, Jorcie P. Some health benefits of physical activity: the Framingham study. Arch Intern Med 139, 1979, 857-861.

20. Brand RJ, Paffenbarger RS, Sholtz RI, Kampert JB. Work activity and fatal heart attack studied by multiple logistic risk analysis. Am J Epidemiol 110, 1979, 52-62.

21. Paffenbarger RS, Hyde RT, Wing AL, Hsieh C. Physical activity, all-cause mortality, and longevity of college alumni. N Engl J Med, 314, 1986, 605-614.

22. Hjerman I, Holme I, Velve Byre K, Leren P. Effect of diet and smoking intervention on the incidence of coronary heart disease. Lancet II, 1981, 1303-1310.

23. Salonen JT, Puska P, Mustaniemi H. Changes in morbidity and mortality during comprehensive coumming programme to control cardiovascular diseases during 1972-77 in North Karelia. Br Med J, 1979, 1178-1183.

24. Arntzenius AC, Krcmhout D, Barth J, Reiber JHC, Bruschke A, Buis B, Van Gent C, Kemgen-Voogd N, Strikwerda S, Van der Velde E. Diet, lipoproteins, and the progression of coronary atherosclerosis: the Leiden intervention trial. N Engl J Med, 312, 1985, 805-811.

25. Kushi L, Lew RA, Stare FJ, Ellison CR, Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulchahy R, Kevaney J. Diet and 20-year mortality from coronary heart disease: the Ireland-Boston diet-heart study. N Engl J Med 312, 1985, 811-818.

CASE REPORT JC

by
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Brooks Air Force Base, Texas 78235-5301

HISTORY:

JC was a 39 year old white male, a senior pilot with 2700 total flying hours and 1300 hours in his most recent aircraft, the C-130. On 3 Dec 85 he took a business trip to Alabama. Just prior to departing he had the onset of a flu-like illness with fever, headache, diarrhea, nausea, sore throat, myalgias and malaise. This symptom complex lasted for approximately 5 days. He awoke about 0200 hours on 8 Dec 85 with a mild mid sternal chest burning and aching discomfort. He went back to sleep and awoke again at 0630 hours, his usual time, with the chest discomfort still present. During the morning the chest discomfort continued and increased in intensity somewhat with radiation to the left shoulder. He went to the local flight surgeon's office and was referred via ambulance to the emergency room for evaluation and admission. He denied any positional or respiratory component to the chest discomfort or any prior similar episodes. On examination in the emergency room, neck was supple without thyromegaly or adenopathy. Lungs were clear to auscultation and percussion. Carotid and peripheral pulses were normal without bruits. Jugular venous pulsations were normal without distention. Chest palpation was normal. Heart sounds were soft and S_2 was physiologically split. At the left lower sternal border there was a grade 2/6 mid systolic and a grade 2/6 pre systolic scratchy, superficial sound which increased during expiration and sitting. Resting 12-lead electrocardiogram obtained in the emergency room is shown in Figure 1. Sublingual nitroglycerin times two was given without effect on the chest discomfort. Four milligrams of IV morphine sulfate was given with a significant decrease in the chest discomfort. He was admitted to the coronary care unit for observation and to rule out a myocardial infarction. In the coronary care unit an M-mode echocardiograph showed good left ventricular wall motion, normal left ventricular wall thickness, normal chamber sizes and normal valves. There was a small clear space posterior to the left ventricular free wall. The chest discomfort was treated overnight with IV morphine sulfate and sublingual nitroglycerin with variable response. The discomfort was still present the next morning, 9 Dec 85; and the routine electrocardiogram of that morning is shown in Figure 2. Creatine kinase levels were elevated to approximately three times the upper limits of normal with a significant increase in the MB fraction compatible with myocardial damage. Cardiac catheterization was performed the morning after admission because of the continuation of pain and the electrocardiographic and enzyme findings. Resting hemodynamics were normal except for an elevated left ventricular end diastolic pressure of 22 mmHg. The left ventriculogram was interpreted as showing a small area of high anterolateral wall mild hypokinesis with no mitral regurgitation. Coronary arteries were interpreted as normal. For the rest of that day, JC was treated with oral Indomethacin and intravenous morphine sulfate, and complete resolution of his symptoms resulted. The morphine sulfate was discontinued 10 Dec 85 and the oral Indomethacin was continued for one week. On 13 Dec 85, five days after admission, a resting radionuclide angiogram was normal with a resting ejection fraction of 55%. Followup M-mode and two-dimensional echocardiography on 13 Dec 85 was unchanged from the previous report, except that the posterior clear space behind the left ventricular free wall had resolved. A treadmill stress test was performed on 5 Jan 86. He performed 14-1/2 minutes of a Bruce protocol reaching a heart rate of 162 beats per minute and a blood pressure of 188/78 mmHg. ST segments remained at baseline and there were no arrhythmias. Based on the interpretation of the chest discomfort, the left ventriculogram at cardiac catheterization, the enzyme findings, and the electrocardiographic changes, JC was told that he had normal coronary arteries but had suffered a small myocardial infarction. He was then disqualified from further flying duties.

He presented to the USAF School of Aerospace Medicine (USAFSAM) in May 86 for his initial evaluation for the above described illness. At that time he was completely asymptomatic, denying any further episodes or any prior episodes of the above chest discomfort, dyspnea on exertion, paroxysmal nocturnal dyspnea, peripheral edema, decreased exercise tolerance, palpitations, dizziness or syncope. Family history was noncontributory, except for his father dying at age 73 of a myocardial infarction, but with no prior cardiac history. JC's only ingestion of tobacco products was smoking three cigars per week for the three years prior to this illness. He drank four to five mixed drinks per week and two cups of caffeinated beverage per day. He ran three to four kilometers per day, three days per week, and also regularly used an ergometer and lifted weights.

PHYSICAL EXAMINATION:

Height 172 cm, weight 74 Kg, blood pressure 120/75 mmHg right arm sitting and 118/70 mmHg left arm sitting, pulse 64 beats per minute and regular. Neck was supple without thyromegaly or adenopathy. Lungs were clear to auscultation and percussion. Carotid and peripheral pulses were normal without bruits. Jugular venous pulsations were normal without distention. Chest palpation was normal. Apical impulse was nondisplaced and of normal character. S_1 and S_2 were normal. There were no systolic or diastolic sounds except a grade 1/6 early systolic short crescendo/decrescendo murmur along the left sternal border which decreased with inspiration, Valsalva, sitting and standing.

LABORATORY DATA:

Routine urinalysis and screening blood work were normal. The total cholesterol was 221 mg% and HDL cholesterol was 35 mg%, yielding a ratio of 6.3. Triglycerides were 120 mg%. Routine resting 12-lead electrocardiogram is shown in Figure 3. He performed 14 minutes on a modified Balke treadmill stress test protocol, reaching a maximum heart rate of 156 beats per minute and a blood pressure of 196/78 mmHg. ST segments remained at baseline and there was one premature complex with a narrow QRS configuration 2 minutes into the recovery phase. Seventeen hours of Holter monitoring demonstrated rare isolated premature ectopy with a narrow QRS configuration. Thallium rest and stress scintigraphy did not demonstrate any perfusion, reperfusion or washout defects. Rest and exercise radionuclide angiography demonstrated a normal sized left ventricle with normal wall motion at rest and throughout exercise and a resting ejection fraction of

62%, rising progressively during exercise to 71%. The cardiac catheterization films were reviewed, and were interpreted as demonstrating normal coronary arteries without any evidence of atherosclerotic disease and a normal left ventriculogram.

QUESTIONS:

1. What is your diagnosis?

2. What are your aeromedical concerns and what data are needed to make an aeromedical disposition?

3. What is your aeromedical disposition? Should JC be disqualified from further flying duties, should he return to flying duties in either an unlimited capacity or be restricted to tanker-transport-bomber aircraft?

4. If you return JC to flying duties, how often will you reevaluate him and what studies will be most useful for future surveillance? What is your threshold for disqualification in the future?

Refer to the next three pages for Figures 1, 2 and 3 of case report JC.

Turn to page A-1 for the diagnosis and discussion of Case JC.

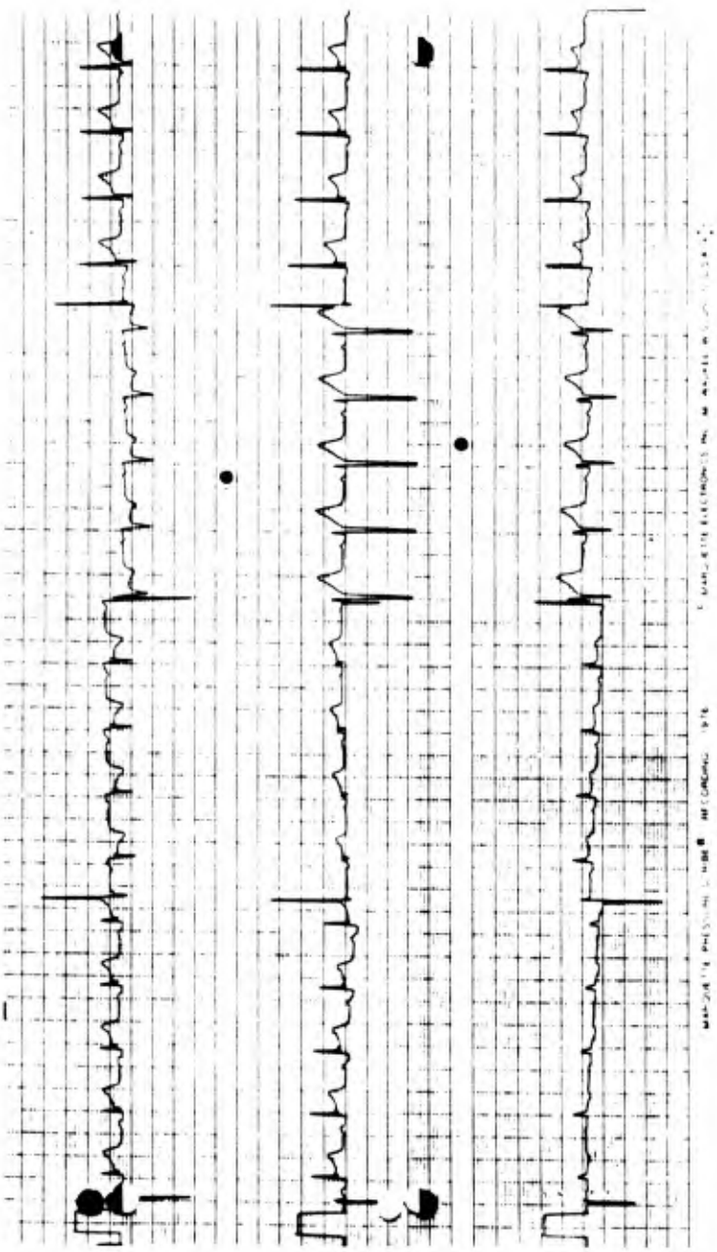

Figure 1

Case Report JC

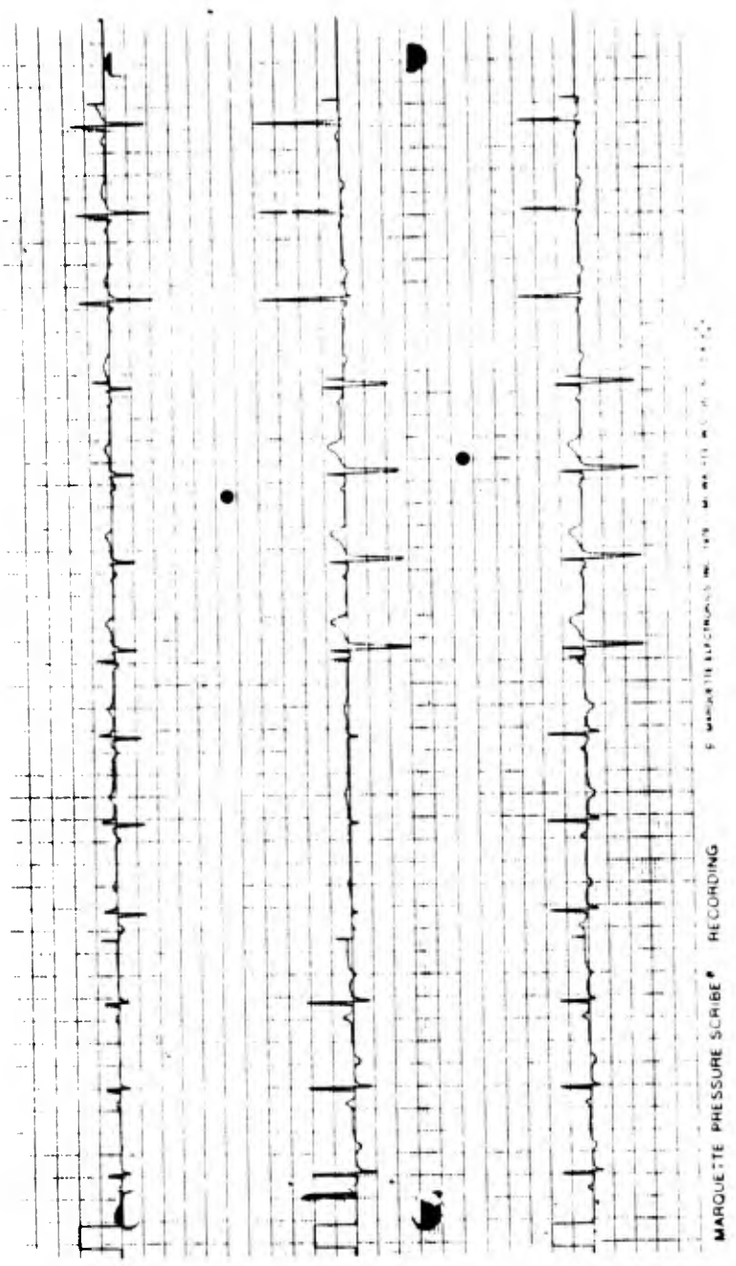

Figure 2

Case Report JC

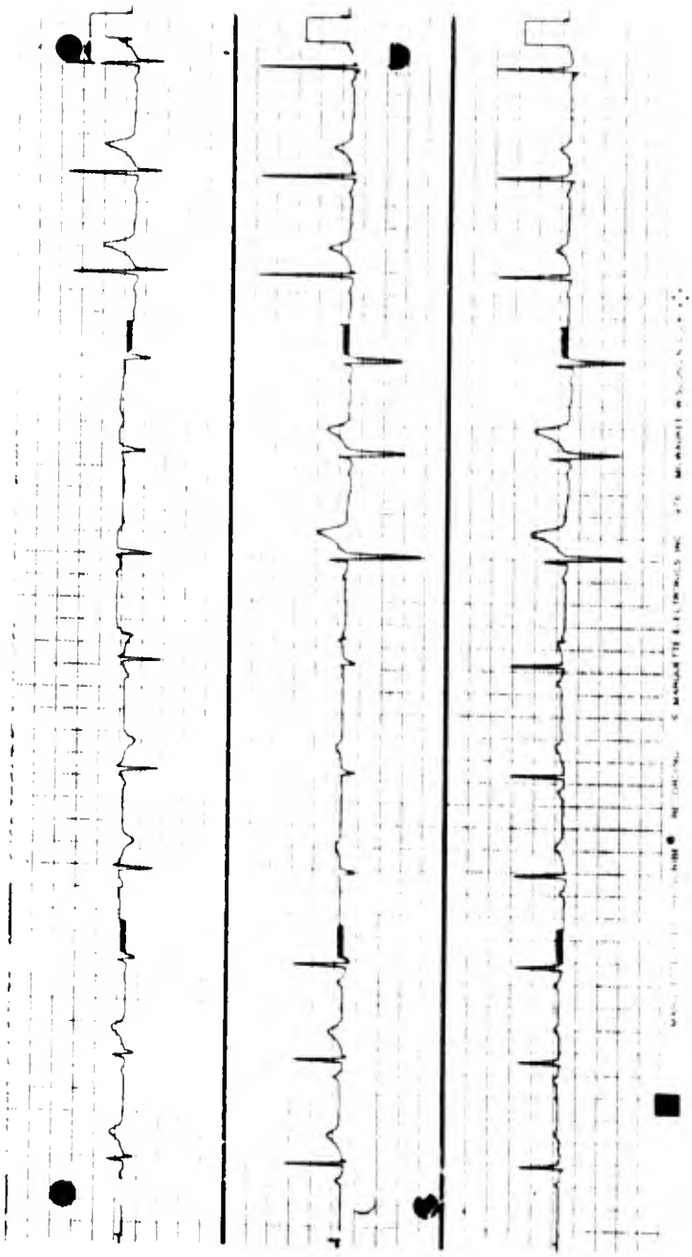

Figure 3

Case Report JC

CASE K.P.H.

James R. Hickman, Jr., Col, USAF, MC, SFS
Chief, Clinical Sciences Division
United States Air Force School of Aerospace Medicine
Brooks Air Force Base, Texas 78235-5301

K.P.H. is a 36-year-old fighter pilot who was referred for evaluation of palpitations, occurring during $+G_z$ acceleration of greater than $+3G_z$. He had experienced no symptoms at +1G. No syncope, visual disturbances or other neurological symptoms were noted. "Lightheadedness" occurred briefly during one episode. The episodes usually lasted only a few seconds.

The past medical history revealed a cardiac murmur discovered shortly after graduation from pilot training.

Physical Examination:

His height was 74 inches, weight 150 pounds, blood pressure 120/80 mmHg and heart rate was 76 beats/min and regular. The cardiac examination revealed a grade II/VI aortic ejection murmur, radiating into both carotids, right greater than left. The murmur was also audible in the suprasternal notch, where a slight thrill could be palpated. The murmur did not change significantly with postural changes.

Laboratory Studies:

The PA chest film revealed mild thoracic scoliosis. The ECG revealed borderline right axis deviation. A vectorcardiogram revealed only nonspecific findings. On Holter monitoring for 24 hours, ventricular premature beats occurred up to 150/hour or 5/min. Frequent episodes of ventricular pairing were noted. The M-mode echocardiogram revealed diastolic eccentricity of the aortic valve and a suggestion of holosystolic posterior mitral bowing. Treadmill testing was normal except for two episodes of ventricular pairing at peak exercise, as well as frequent atrial premature beats. The carotid pulse tracing and apexcardiogram were normal. A phonocardiogram demonstrated probable mid-systolic click. No ejection clicks were noted.

What is your tentative diagnosis?

What further studies do you feel are needed to make an aeromedical disposition?

This aviator was reexamined following the inhalation of amyl nitrite, but no additional information was gained. A centrifuge study revealed relatively low G tolerance. A five-beat run of a wide QRS tachycardia, preceded by paired ventricular premature beats, occurred during the straining phase of the gradual onset G run. This arrhythmia is depicted in Figure 1.

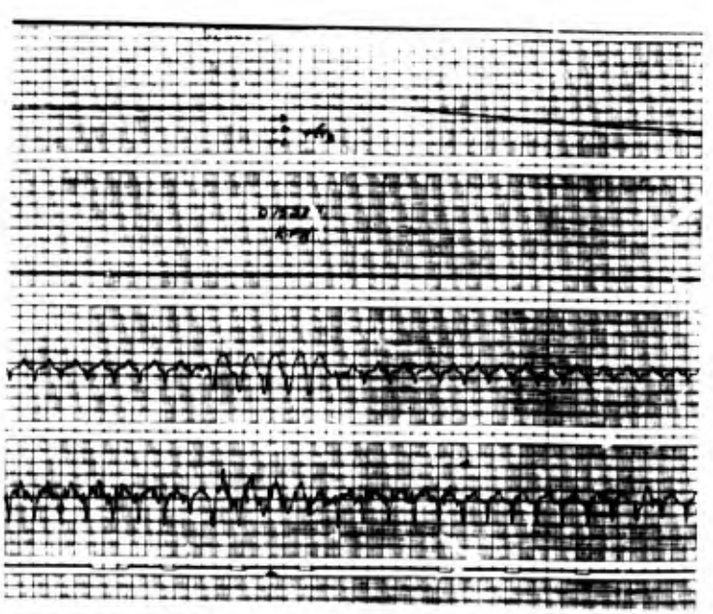

Figure 1 - Centrifuge Rhythm Strip of K.P.H.

What is the arrhythmia?

What is your aeromedical disposition at this point?

The aviator then underwent a left heart catheterization with right and left anterior oblique ventriculograms as well as an aortic root injection. Figures 2 and 3 demonstrate the ventriculograms.

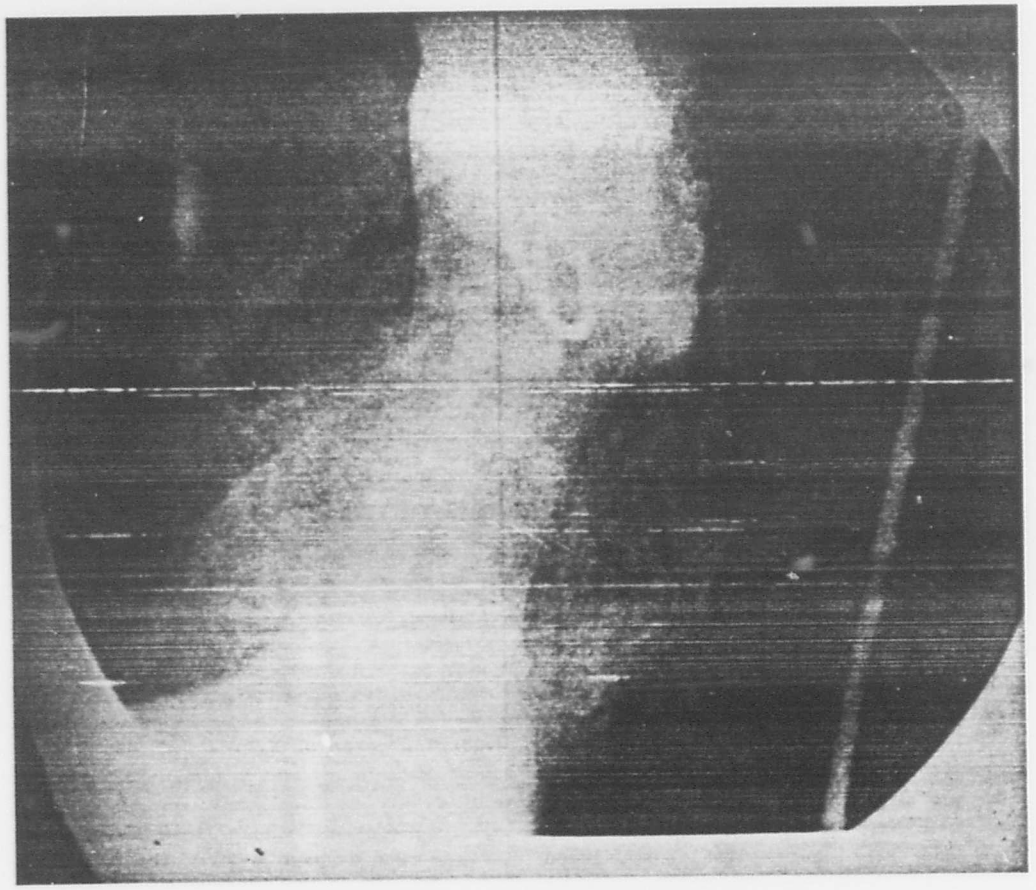

Figure 2 - Left anterior oblique ventriculogram of K.P.H.

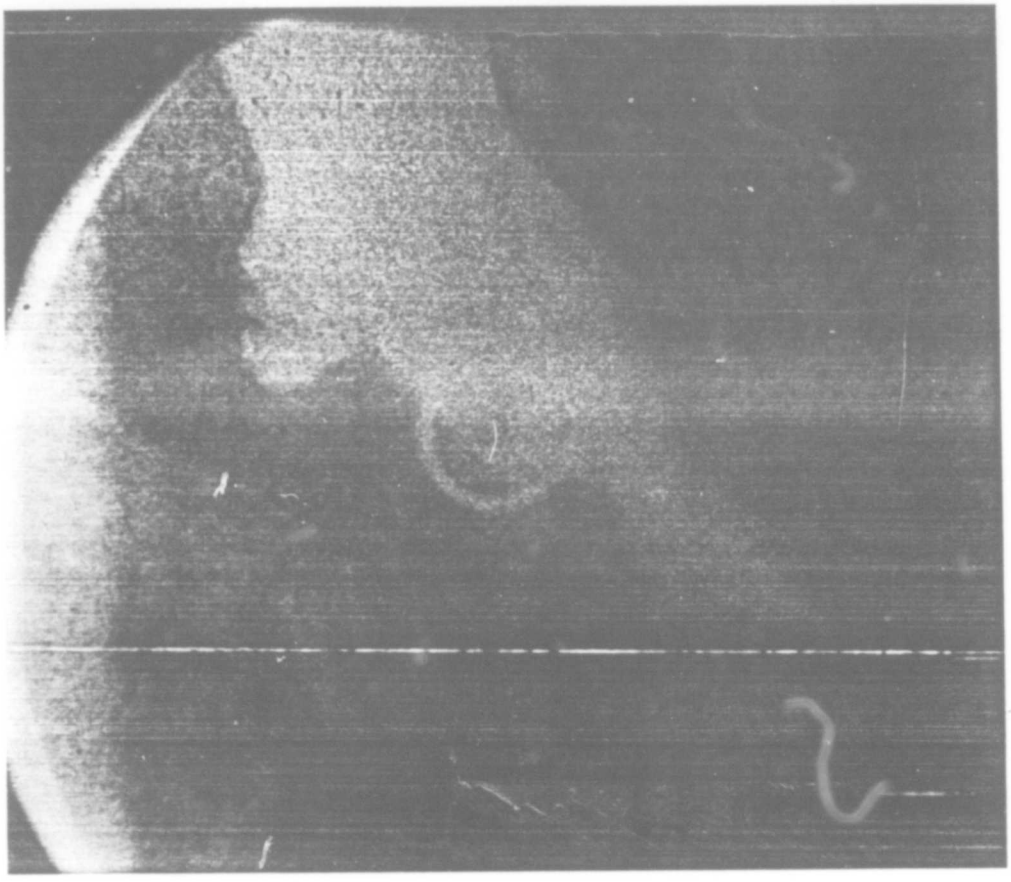

Figure 3 - Right anterior oblique ventriculogram of K.P.H.

What is your final cardiovascular diagnosis?

What is your final aeromedical disposition? Please turn to page A-2 for the case discussion.

CASE REPORT WS

by
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Brooks Air Force Base, Texas 78235-530

HISTORY:

WS was a 40 year old white male, an active duty USAF Command Pilot with 2200 total flying hours and 1000 hours in the F-15, his current aircraft. In Oct 83 a routine electrocardiogram performed during a flight physical examination showed prominent voltage in the precordial leads and inferolateral T wave inversion and ST segment depression. These changes had been present on several previous electrocardiograms, but the ST - T wave changes were slowly progressive. A treadmill stress test was performed locally to evaluate this electrocardiogram and demonstrated, during exercise, 2.5 mm of ST segment depression beyond the baseline changes. Due to these findings, a USAF School of Aerospace Medicine (USAFSAM) evaluation was requested and was performed in Jan 84. He denied any cardiac symptoms, specifically denying chest discomfort, palpitations, dizziness, loss of consciousness, dyspnea on exertion, pedal edema, paroxysmal nocturnal dyspnea, and decreased exercise tolerance. His father died at age 50 with a myocardial infarction and his mother was 61 years old and alive and well. There was no other family history of cardiac defects, sudden death, hypertension or diabetes. He smoked two packs of cigarettes per day for 21 years and was still smoking at the time of his evaluation. He drank one mixed alcoholic drink per day and no caffeine. He did not have any regular exercise program other than playing 18 holes of golf once per week.

PHYSICAL EXAMINATION:

Height 173 cm, weight 85 Kg, blood pressure 112/80 mmHg in the left arm sitting and 114/76 mmHg in the right arm sitting, pulse 60 beats per minute and regular. Neck was supple without thyromegaly or adenopathy. Lungs were clear to auscultation and percussion. Carotid and peripheral pulses were normal without bruits or radiated murmurs. Chest palpation revealed a forceful, nondisplaced apical impulse; the apical impulse was double with a presystolic and a systolic component. S_1 and S_2 were normal. There was a loud S_4 at the apex and left lower sternal border. There was no ejection click, non-ejection click, S_3 or diastolic murmur. A grade 2/6 harsh systolic crescendo/decrescendo murmur was heard at the apex and left lower sternal border which radiated to the base and increased with Valsalva and standing. Physical examination was otherwise unremarkable.

LABORATORY DATA:

Routine resting 12-lead electrocardiogram is shown in Figure 1. Figure 2 is an M-mode echocardiographic view at the level of the aorta, aortic valve and left atrium. Figure 3 is an M-mode echocardiographic view at the level of the left ventricle and mitral valve. Two-dimensional echocardiography demonstrated normal chamber sizes, a hypercontractile left ventricle, an intraventricular septal thickness in diastole of 20 mm and a left ventricular wall thickness in diastole of 13 mm. Valvular structures appeared normal except for anterior motion of the mitral valve apparatus during systole. WS performed 9 min and 49 sec of a modified Balke treadmill protocol, reaching a maximum heart rate of 155 beats per minute and a maximum blood pressure of 180/80 mmHg. There was 2.7 mm of ST segment depression from the baseline in the inferolateral leads beginning at 9 minutes of exercise. He denied any symptoms during exercise and there were no arrhythmias. Thallium rest and stress scintigraphy demonstrated no perfusion, reperfusion or wash out abnormalities. Rest and exercise radionuclide angiography demonstrated a normal left ventricular size, no focal wall motion abnormalities, and an ejection fraction of 80% at rest, rising to 88% at maximum stress. Ambulatory electrocardiographic monitoring demonstrated 2 isolated premature atrial beats, 2 uniform, isolated premature ventricular beats and 4 beats of supraventricular tachycardia at a rate of 150 beats per minute. Cardiac catheterization was ultimately performed and demonstrated near obliteration of the left ventricular cavity during systole, a resting ejection fraction of 77%, increased left ventricular wall thickness, normal coronary arteries, and no resting left ventricular - aortic pressure gradient.

QUESTIONS:

1. What is your diagnosis?

2. What are your aeromedical concerns and what is your disposition?

3. If you return WS to flying duties, what is your threshold for disqualification in the future?

4. How frequently would you follow WS and what procedures would be most important for long-term surveillance?

Turn to page A-3 for the diagnosis and discussion of Case WS

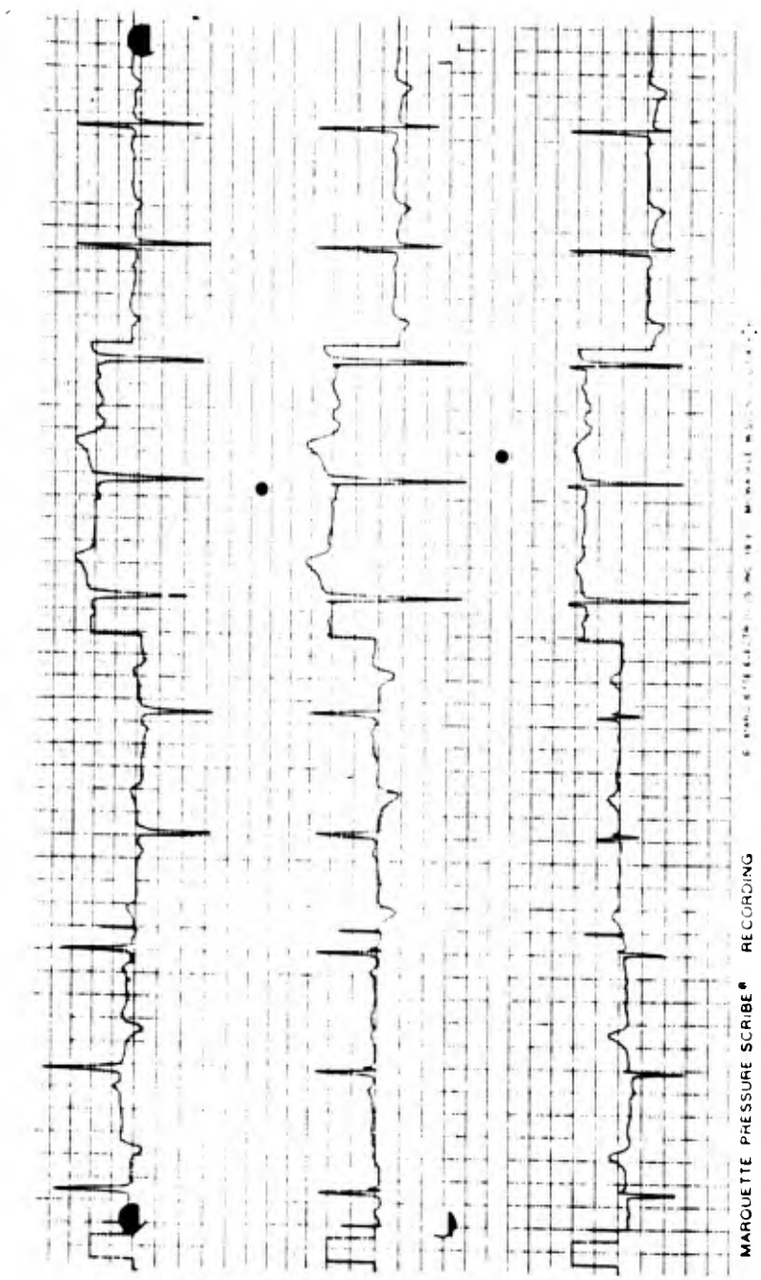


Figure 1

Case Report WS

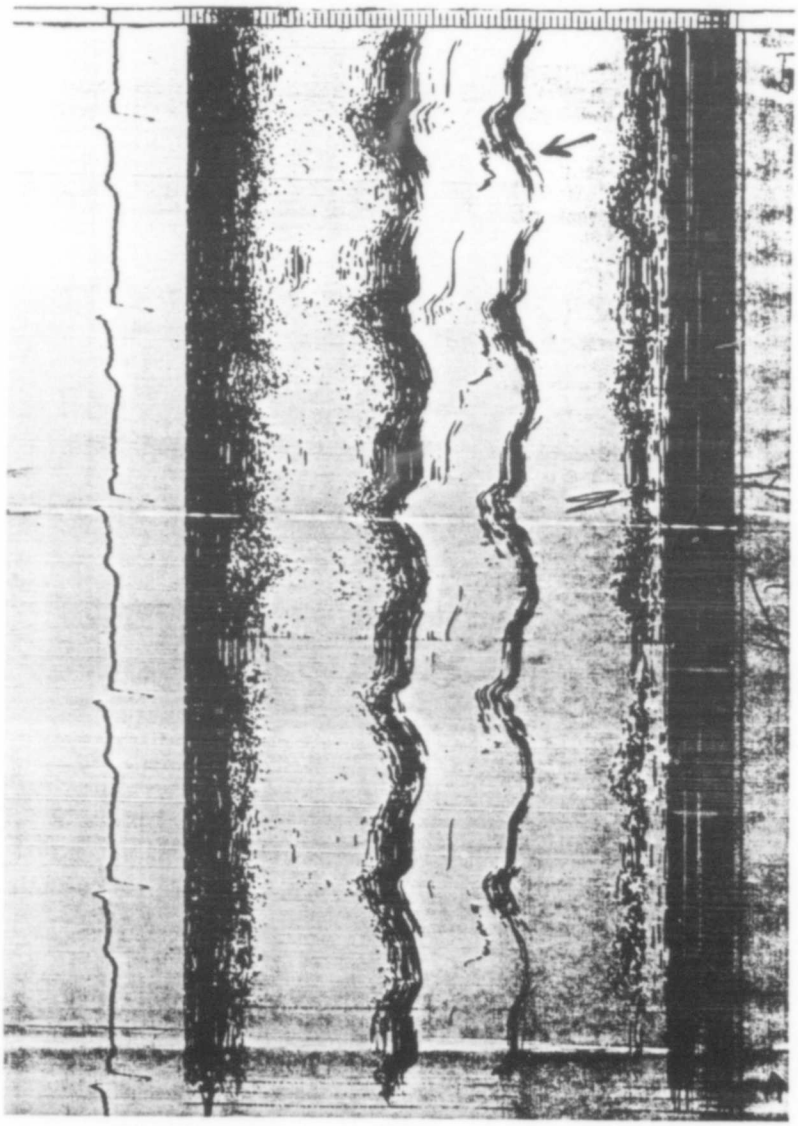


Figure 2

Case Report WS

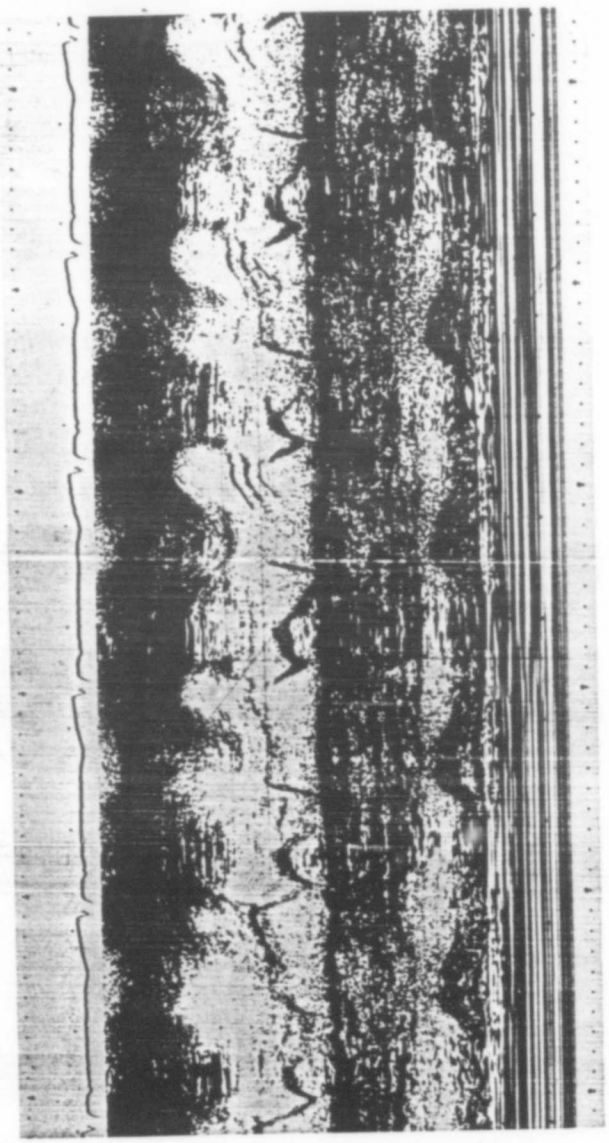


Figure 3

Case Report WS

CASE REPORT JF

by
William B. Kruyer, Lt Col, USAF, MC, FS
USAF School of Aerospace Medicine
Brooks Air Force Base, Texas 78235-5301

HISTORY:

JF was a 23 year old white male, an active duty U.S. Air Force A7 pilot trainee assigned with an Air National Guard Unit in Arizona. In May 1985 during a routine physical examination by the Air National Guard Flight Surgeon, systolic and diastolic murmurs were auscultated. He was referred to the flight surgeon's office at Davis-Monthan AFB where these murmurs were again heard. At that time his electrocardiogram showed normal sinus rhythm with a rate of 70 beats per minute and an RSR' pattern in lead V_1; this was unchanged from an electrocardiogram of August 1982. Radiographic cardiac series with barium swallow was normal. JF was subsequently referred to the USAF School of Aerospace Medicine (USAFSAM) for evaluation in June 1985.

At USAFSAM JF denied any cardiac symptoms, specifically denying any chest discomfort compatible with angina pectoris, decreased exercise tolerance, palpitations, dizziness or syncope. He had two routine physical examinations in August 1982 and February 1985 with no mention of any systolic or diastolic murmurs. In April 1985 he had an accident while riding a bicycle. While avoiding collision with an automobile, his bicycle hit the curb and he was thrown from the bicycle, landing against a signpost with significant force. The signpost struck him across the lower thoracic and upper lumbar regions of his back. He was hospitalized for several days and found to have fractures of the right transverse processes of L_1 thru L_3 and microhematuria with a normal intravenous pyelogram. He subsequently recovered without sequelae from this accident. No murmurs were noted during that hospitalization however. One month later, murmurs were auscultated on a routine examination. His family history was noncontributory except for a father, aged 49, who took an unspecified cardiac medication for some type of rhythm disturbance. JF was a nonsmoker. He drank four beers per week and consumed no caffeine. He had a regular exercise program consisting of lifting weights one to one and one-half hours per day, three days per week and jogging three to four kilometers per day, three to four days per week.

PHYSICAL EXAMINATION:

Height 182 cm, weight 78 Kg, blood pressure 120/60/0 mmHg in both arms sitting, pulse 52 and regular. Physical examination was normal except for the cardiac exam. Carotid and peripheral pulses were hyperdynamic. A transmitted systolic murmur was heard over both carotids. Jugular venous pulsations were normal and there was no jugular venous distention. Palpation of the chest revealed a right ventricular tap and a nondisplaced, but somewhat sustained apical impulse. S_1 was decreased in intensity and S_2 was normal with normal physiologic splitting. During systole, a grade 2/6 early peaking crescendo/decrescendo murmur began after S_1 and ended prior to S_2. Also, an early systolic click was heard, at the base, which did not change appreciably with maneuvers or respiration. During diastole a grade 3/6 holodiastolic decrescendo blowing murmur was heard, along the left sternal border and at the apex, which began immediately with S_2. At the apex there was also a grade 1/6 low pitched rumbling murmur which lasted approximately 2/3s of diastole. A soft S_3 was also appreciated at the apex and left lower sternal border.

LABORATORY DATA:

Routine urinalysis and screening blood work were normal. Total cholesterol was 162 mg% and HDL cholesterol was 58 mg%, yielding a ratio of 2.8. Resting electrocardiogram (Fig. 1) demonstrates prominent voltage, $S_1S_2S_3$ pattern, and an RSR' in V_1. This was not significantly changed from prior tracings. He performed 22 minutes on a modified Balke treadmill protocol, reaching a heart rate of 189 beats per minute and a blood pressure of 195/70 mmHg. ST segment response remained at baseline and there were no arrhythmias. Seventeen hours of Holter monitoring demonstrated four uniform premature ventricular beats and 18 isolated premature atrial beats. Figure 2, an M-mode echocardiographic view of the left ventricle at the level of the mitral valve, demonstrates coarse fluttering of the mitral valve leaflets during diastole. Left ventricular size appears to be upper normal limits to mildly enlarged. At the appropriate view for measurements, the M-mode echocardiogram demonstrated a left ventricular internal dimension during diastole of 59 mm. Figure 3, an M-mode echocardiographic view at the level of the aortic valve and left atrium, demonstrates eccentric closure of the aortic valve during systole. Thallium scintigraphy was not performed during this evaluation. Rest and exercise MUGA scanning demonstrated a left ventricle at the upper limits of normal size, normal left ventricular wall motion, and resting ejection fraction of 61% rising progressively to 68% at peak exercise. Right and left cardiac catheterization was performed. Right and left sided hemodynamics were normal. Mean pulmonary capillary wedge pressure was 8 mmHg. Left ventricular end diastolic pressure was 11 mmHg at rest and 14 mmHg following angiography. There was no resting pressure gradient across the aortic valve. Coronary arteries were large and free of any atherosclerotic lesions. Left ventricular angiography demonstrated normal wall motion and no regurgitation of dye into the left atrium. Calculated ejection fraction was 71%. Aortic root injection demonstrated a normal aortic root and two aortic valve leaflets. During aortic root injection, there was immediate opacification of the left ventricle of a density equal to or slightly greater than that of the aortic root. Clearing of dye from the left ventricle paralleled clearing of dye from the aortic root.

QUESTIONS:

1. What is your diagnosis?

2. What are your aeromedical concerns and what is your aeromedical disposition?

3. If you return JF to flying duties, what is your threshold for disqualification in the future?

4. How frequently would you follow JF and at what intervals?

5. What test or tests would be most useful for surveillance of this case?

Refer to the next three pages for Figures 1, 2, and 3 of case report JF.

Turn to page A-4 for the diagnosis and discussion of case JF.

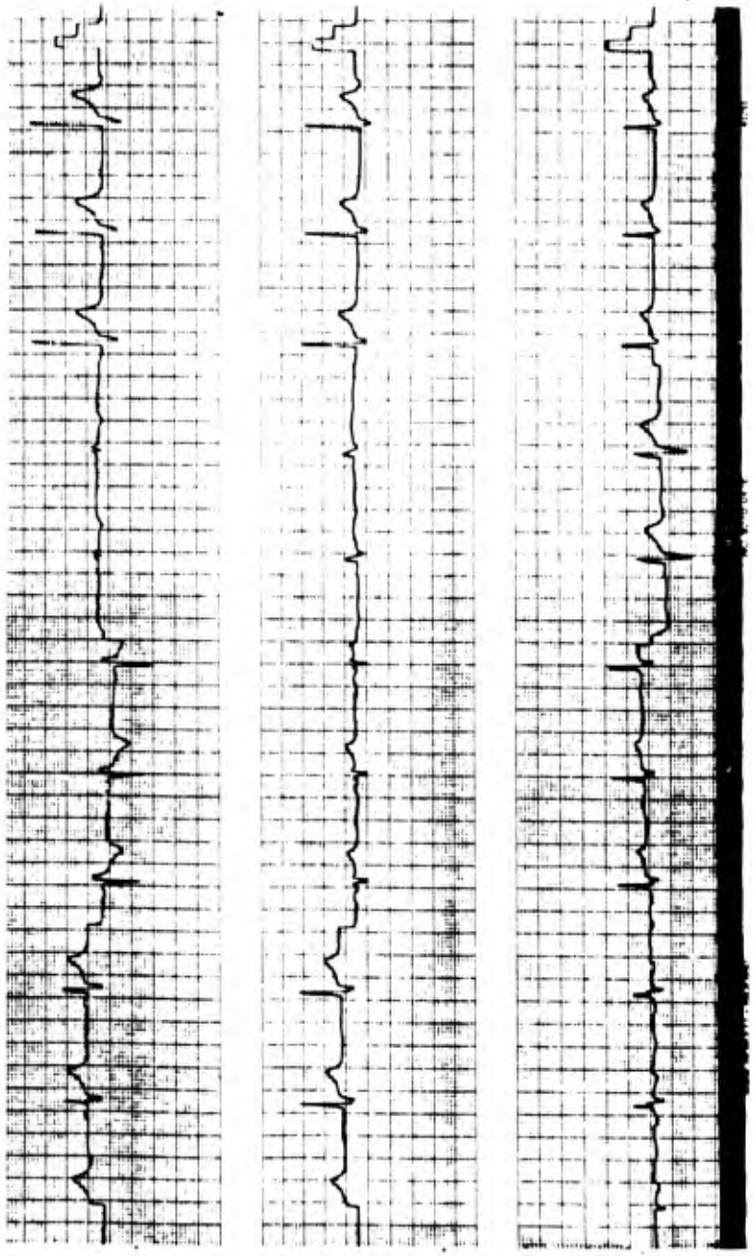


Figure 1

Case Report JF

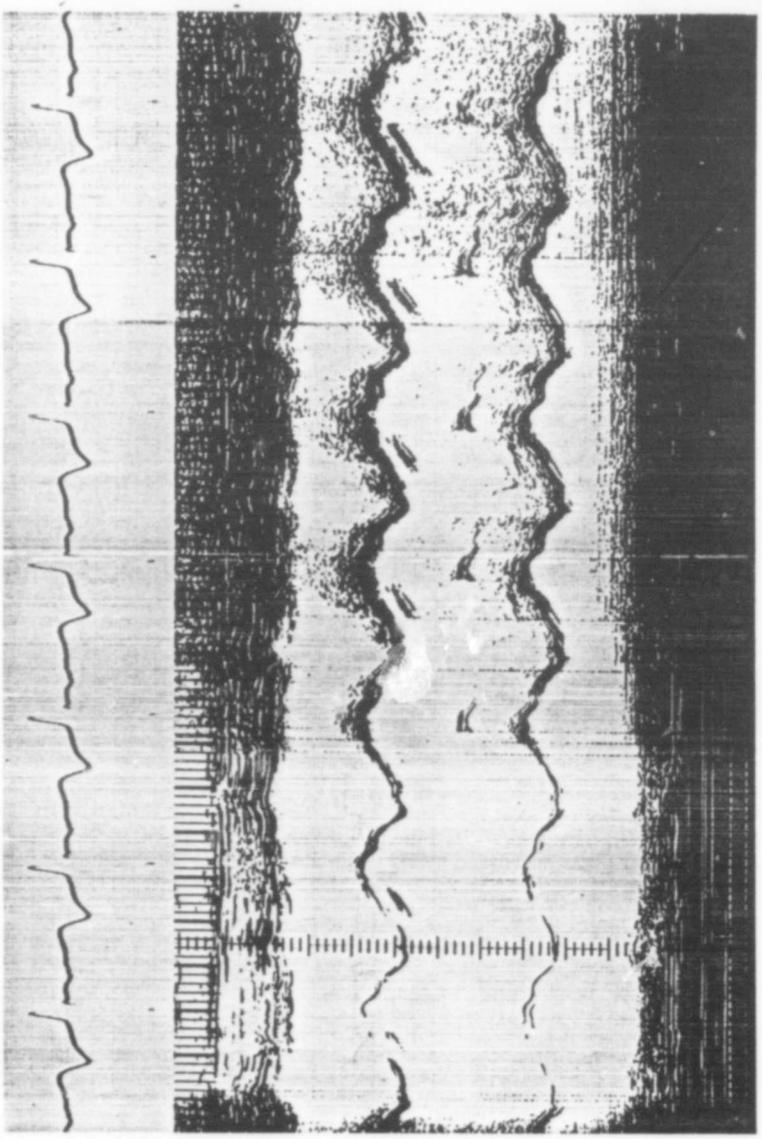


Figure 2

Case Report JF

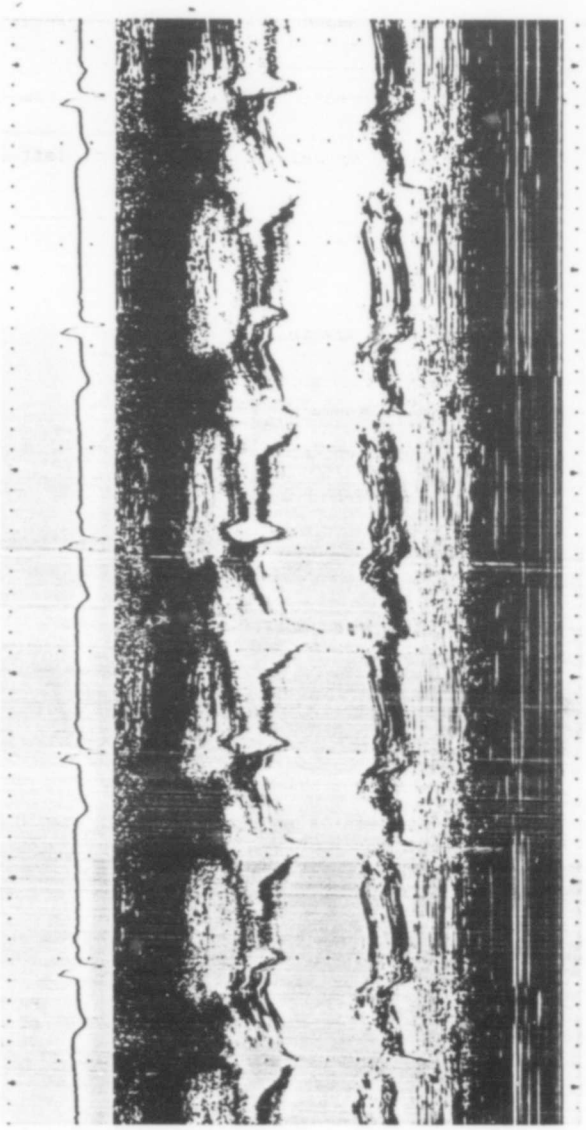


Figure 3

Case Report JF

CASE R.N. (by Dr Hull) Male Pilot dob 1940

No symptoms.
No family history of chest disease and no known contact with chest disease.
1975 Routine chest xray. Opacity left apex. Not investigated.
Nov 1978 Routine chest xray. Opacity still present. Possibly a little larger.
July 1979 Routine chest xray (release medical examination). "Fibro-nodular" left apical shadowing still present - ? cavitated.
Tomography - cavitation confirmed.

August 1979 Clinical assessment. Asymptomatic. Weight steady. Smokes 15 cigarettes daily (since early adult life). Physical examination normal.

Investigations: Chest xray unchanged vs July 1979. Cavity in left apical shadowing.

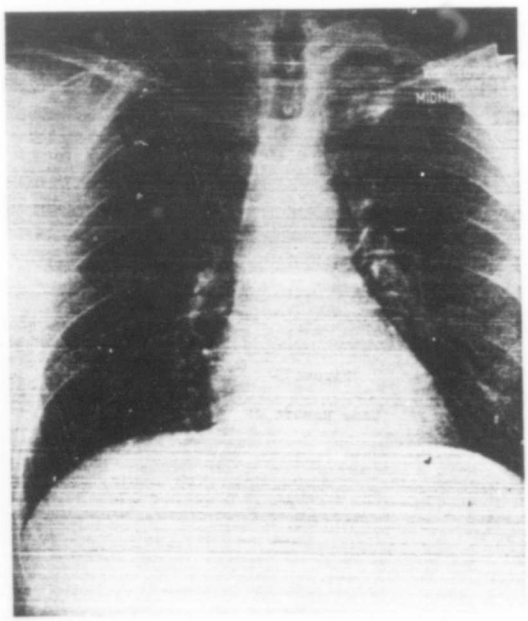
Haematology:
Hb 15.2
TWBC 10,300. P 67% E 3% B 1% L 23% M 6%
ESR 12 mms in first hour
Blood film normal
Serum Na^+ 142 mmol/l
K^+ 3.9 mmol/l
Creatinine 109 micro mol/l
Alkaline Phosphatase 327 1U/L
SGOT 24 1U/L
SGPT 42 1U/L

9 Aug 79 Bronchoscopy (GA). Normal.

Q1 List possible diagnoses, in order of probability

Q2 What further tests should be carried out?

Please pass to page A-6 for further details and discussion of case R.N.



PA chest radiograph of Case R.N. (8 Aug 79)

CARDIOPULMONARY SCREENING FOR HIGH-PERFORMANCE FLYING: SELECTION AND RETENTION ISSUES

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The performance characteristics of the new generation fighters place new demands on the human side of the man-machine interface, and necessitate a fresh look at the medical screening requirements for current and future aircrew. Such reassessment of aircrew medical screening is certainly not a new topic, occuring on a cyclic basis with the introduction of each new generation of tactical military aircraft. Adaptations and alterations in screening tests for those who fly the new generation fighters was addressed at a 1979 USAF Workshop on "Pilot Selection and Flying Physical Standards for the 1980's" (1). Most of the recommendations from that Workshop are still valid, but the time constants for implementation of medical recommendations are often long. A recent AGARD Conference (2) also addressed medical selection and screening issues for fighter aircrew.

Since the approach taken to achieve tactical air superiority by the United States and other NATO nations has been to develop and introduce fighter aircraft of the highest achievable quality, as opposed to building large numbers of less sophisticated aircraft, this policy decision must be reflected in the medical selection of the men who will fly these machines, and the ongoing medical screening of those who already are.

Aircrew candidates must now be screened using the most modern medical technology for diseases or disorders that are almost certainly to be asymptomatic, and are probably not detectable by standard clinical examination, and in addition, for diseases that exist only as a future possibility. In the aircrew candidate cardiopulmonary screening must be designed to identify structural cardiac abnormalities and cardiac arrhythmias that may be a problem in the high +Gz environment. Individuals with a high potential for developing coronary artery disease must be identified and screened out. Screening must be included for pulmonary disorders or dysfunction which may compromise human effectiveness in rapid onset high G (ROHG), and high sustained G (HSG) fighter operations.

Amongst experienced pilots, the incidence of coronary artery disease increases with age, and because of the potential for acute incapacitation, the major thrust of cardiovascular screening in this group must be to identify individuals with significant disease while it is still asymptomatic. Small airways disease increases with age as the lungs get older and lose some of their elasticity, (and all too often are ravaged by cigarette smoke). Although the effect of small airways disease on tolerance to HSG and ROHG has not as yet been defined, it seems prudent to screen for advancing disease. A question which begs as yet to be answered is whether or not repeated exposure to HSG over long periods of time may cause structural cardiac abnormalities, and if so, up to what point these changes are reversible.

SCREENING TESTS AND SELECTION STANDARDS IN AIRCREW CANDIDATES

What are we screening for?

1. Structural cardiac abnormalities

   - congenital heart lesions
   - aortic stenosis and insufficiency
   - mitral valve disease, including mitral valve prolapse
   - hypertrophic cardiomyopathy

2. Conduction defects

   - left bundle branch block
   - 2° AV block, Mobitz type II
   - complete heart block
   - AV bypass tracts, WPW pattern

3. Complex arrhythmias

   - ventricular tachycardia
   - supraventricular tachycardia

4. Coronary risk factors

   - total and HDL cholesterol
   - tobacco smoking
   - family history of early coronary disease
   - hypertension

5. Small airways disease

6. Reactive airways disease

What are the tools available?

1. Standard clinical evaluation

This remains the most important part of the overall evaluation, both in terms of an accurate, incisive history, and careful and thorough physical evaluation. However, aircrew candidates are not always ready to divulge medical information, and clincal examination may not detect the problems for which we are screening.

2. Scalar electrocardiograph

The standard 12 lead ECG is still a cost-effective and manpower efficient means of screening. New techniques being evaluated with more extensive multiple lead placements may yield even more information (3).

3. Exercise stress testing

The exercise stress test may be used to detect cardiac arrhythmias, to detect coronary artery disease, to evaluate cardiopulmonary fitness, and to assess bronchial reactivity to exercise.

Amongst the population of young aircrew candidates in whom the prevalence of ischemic heart disease is very low, the exercise electrocardiograph, because of its lack of specificity, has no place as a general screening tool for coronary artery disease.

The exercise ECG is a helpful adjunct in the evaluation of arrhythmias detected by other means. However, the significance of arrhythmias including ventricular tachycardia associated with high levels of exercise in persons with otherwise normal cardiovascular assessments is not clear and no standards exist for such findings.

Maximum oxygen uptake can be measured directly during exercise or estimated from nomograms which relate heart rate to energy expenditure. There is now substantial evidence demonstrating an inverse relation between very high levels of aerobic fitness and tolerance to G. However, there is no justification for routine exercise testing to evaluate cardiovascular fitness in aircrew candidates.

In candidates with a history of possible exercise induced asthma, the exercise assessment of bronchial reactivity may provide useful information.

4. Ambulatory electrocardiograph

The Holter monitor is a valuable tool in evaluating candidates with suspected arrhythmias. It is, however, a labour intensive investigation for both technician and physician. In addition, apparently worrisome degrees of ectopy and AV conduction disturbances may be observed in apparently normal individuals, and the significance of such findings is unknown, since no standards exist.

5. Echocardiograph

Combined two-demensional and M mode echocardiography provides direct visualization of cardiac structure and is the best currently available non-invasive tool for assessing cardiac anatomy. A certain amount of information about cardiac function can also be derived. Recent technical additions to the echo include colour Doppler monitoring which gives an accurate and sensitive evaluation of forward and regurgitant flows.

Various reports have recommended that the echocardiograph be included in the cardiac screening of at least HPF, if not all aircrew (1,2).

The Canadian Forces recently conducted a study of echocardiographic findings in 677 pilot and navigator candidates. These applicants had already undergone standard clinical and electrocardiographic screening at a Recruiting Center. During further aircrew medical screening at the Central Medical Board at DCIEM, M-mode and 2D echocardiographs were performed. 6.6% of candidates had echocardiographic evidence of mitral valve prolapse and of these, only 18% were clinically suspected. One ventricular septal defect (clinically suspected), and two biscuspid aortic valves were also found. The echocardiograph was confirmed as a useful tool in screening aircrew candidates for clinically unsuspected structural cardiac anomalies with aeromedical implications in the high G environment.

6. Coronary risk

Although the prevalence of coronary artery disease is very low in the population of young aircrew recruits, amongst experienced aircrew it is the largest single cause of cardiovascular morbidity. With the clear epidemiologic linking of certain factors such as lipid abnormalities and cigarette smoking to the later development of ischemic heart disease, it seems prudent to screen aircrew recruits for such risk factors and to reject individuals at apparently high risk from flight training. The problem with this approach is that epidemiologic statistics apply only to groups and not to individuals, and in the current atmosphere of Human Rights concerns, it is increasingly difficult to substantiate the application of such statistical probabilities as selection standards to apply to any particular candidate. An alternate approach is still to screen for apparently high risk individuals, and then to carefully follow them with regular non-invasive screening for the possible development of coronary artery disease. The approach taken, i.e. strict selection standards, or careful ongoing screening, depends to some extent as to which approach can be

6. Cont'd

instituted in the particular NATO country. Colonel Hickman's presentation covers the application of risk factor analysis.

7. Pulmonary function tests

The question of the relationship, if any, between small airways tolerance to +Gz has yet to be resolved, but based on current knowledge of the effect of accelerative forces on pulmonary function it would seem prudent to screen candidates for tactical fighter operations to ensure normal pulmonary function, and in particular, small airways function. Because of the exponential increase in cross sectional airways diameter as airways generations increase, small airways disease can be far advanced before it significantly contributes to an overall increase in resistance. However, several tests have been shown to be sensitive enough to detect small airways disease at an early stage. These were described in the presentation on Pulmonary Function, and include maximum expiratory flow volume curves on air and helium-oxygen, and the single-breath nitrogen washout curve. It is recommended that these two screening tests by applied to all candidates for tactical fighter operations.

8. Airway challenge tests

Individuals with a history of reactive airways disease during childhood, or with continuing significant symptoms of upper airway atopy during adolescence and early adult years may have quite normal pulmonary function most of the time, yet develop wheezing and significant small airway dysfunction given certain stimuli. Breathing cold air, and particularly heavy exertion in cold air, or a mild respiratory infection may trigger small airways reactivity. Aircrew candidates at times may conceal or minimize such symptoms even when directly questioned.

Because of the potential impact of small airways dysfunction on aircrew performance in the HSG environment, individuals in whom there is the slightest suspicion of increased airways sensitivity should be screened with an airways challenge test. This should include any person with a history of wheezing episodes in the past, or with a history of continuing significant upper airway atopic symptoms. The various challenge tests were described in the presentation on Pulmonary Function.

CARDIOVASCULAR SCREENING RECOMMENDED FOR AIRCREW CANDIDATES

ALL CANDIDATES	FOR SPECIFIC INDICATIONS
Thorough clinical examination	Exercise stress testing
Resting electrocardiograph	Ambulatory ECG
Echocardiograph/M-mode + 2D	Echo with Doppler
Coronary risk evaluation	Airway challenge testing
Pulmonary Function Tests Flow-volume curves on air and heliox + SBNT	
Chest x-ray	

SCREENING EXPERIENCED AIRCREW

In experienced aircrew, the emphasis shifts to the detection of cardiopulmonary abnormalities which develop with age. The most critical of these because of the potential for acute incapacitation is coronary artery disease. Sudden death is the first symptom in up to 30% of new coronary events in persons with previously unsuspected coronary artery disease. The prevalence of asymptomatic CAD increases with age, and is in the range of 5 to 10% in the 35 - 45 age range. Because of the low predictive value of the exercise electrocardiographic stress test in a population with such a low prevalence of disease, it is not of help as a general screening tool. Efforts must be aimed at identifying individuals at increased risk through analysis of risk factors, and then applying additional screening tests which may include an exercise ECG, exercise thallium scintigraphy, and gated nuclear angiogram with rest and exercise.

Small airways disease increases with age as a result of a normal decrease in the lung's elastic recoil, together with an increasing cumulative dose of exposure to a variety of environmental irritants, including cigarette smoke inhaled either actively or passively. Closing volume increases with age beyond adolescence, and increasing degrees of airway closure during HSG may reduce G tolerance. By using sensitive tests of small airway function, small airways disease may be detected at a relatively early stage when flow obstruction is at least to some degree reversible, e.g. by smoking cessation.

SCREENING TESTS RECOMMENDED FOR EXPERIENCED AIRCREW

ALL AIRCREW	FOR SPECIFIC INDICATIONS
Thorough clinical examination	Exercise stress test
Cardiovascular risk assessment	Exercise thallium test
Electrocardiograph*	MUGA scan
Chest x-ray*	Ambulatory ECG
Pulmonary Function Tests* Flow-volume curves on air and heliox + SBNT	Echocardiograph
(*Biannually before age 40 annually beyond age 40)	

CURRENT ISSUES IN SELECTION AND RETENTION

Tobacco Smoking

The contribution of tobacco smoking to the risk of ischemic heart disease and small airways disease is no longer controversial. We carefully screen both our aircrew candidates and experienced pilots for cardiovascular risk, refusing applicants with even mild but definite hypertension, yet accepting those who smoke. The evidence is in, and has been for some time, linking cigarette smoking to ischemic heart disease, and to small airways disease, both of which are of major concern in the military aviation environment. Even passive cigarette smoke inhalation is being incriminated as a cause of respiratory disease in non-smokers. On the flight decks of multicrew aircraft, in standby quarters, in messes and other military institutions non-smoking aircrew are exposed to second hand smoke. Yet for a variety of reasons, cigarette smoking, although discouraged, is not banned in serving aircrew, and candidates continue to be selected who smoke. It is time to stop.

Effects of Repetitive HSG on the Heart and Lungs

High sustained G can produce cardiac arrhythmias, and in animals at very high G, has been shown to produce myocardial damage. There have been some reports linking HSG to right ventricular hypertrophy (4). The fact is that the long term effects on the cardiovascular system and lungs of repetitive exposure to HSG is unknown.

Exposure to HSG requires the application of respiratory manoeuvers such as the LI and MI, which may raise mean intrathoracic pressure, and hence mean pulmonary artery pressure, by more than 60 mmHg. Repetitive, frequent application of such pressures may be sufficient to produce pulmonary damage, and to cause right ventricular hypertrophy, if not other cardiac changes.

A longitudinal study of cardiac and pulmonary changes in tactical fighter aircrew is needed to clarify these questions. Such a study would be best carried out by a cooperative effort amongst NATO nations. Important issues include whether or not there are cardiac changes from HSG, and if there are, up to what point they are reversible.

Minimal Coronary Artery Disease and Coronary Angioplasty

By carefully screening experienced aircrew for asymptomatic coronary artery disease, individuals will be found who have minor degrees of disease, or who may have a single lesion amenable to coronary angioplasty. Whether or not aviators with minimal degrees of coronary artery disease may return to flying duties is still controversial, as is the question of criteria of what constitutes "minimal disease", since even low grade lesions can occlude suddenly with a plaque rupture. Coronary angioplasty is increasing in popularity, and aircrew with single proximal lesions successfully dilated are requesting return to flying status. The rate of restenosis after coronary angioplasty is high, however, and whether such individuals could be safely waivered is also a matter of controversy. If such aviators are to return to flying duties, they might better be redirected to multicrew cockpits than return to tactical fighter operations.

REFERENCES

1. Proceedings of the USAF Multidisciplinary Workshop on Pilot Selection and Flying Physical Standards the 1980's. Bonfili, H.F., and DeHart, R.M., eds. Office of the Surgeon General, Aerospace Medical Consultants Division, Air Force Medical Service Center, Brooks Air Force Base Texas, 3-5 April, 1979.

2. Medical Selection and Physiologic Training of Future Fighter Aircrew. AGARD Conference Proceedings No. 396, 1985.

3. Selvester, R.J., and Solomon, J.C. Optimal ECG electrode sites and criteria for detection of asymptomatic coronary artery disease at rest and with exercise. USAFSAM-TR-85-47, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas, 1985.

4. Ille, H., Didier A., Allegrini, N., and Maurel, C. Selection et surveillance medicales des pilotes de Mirage 2000: Apport de l'echocardiographie. AGARD-CP-396, 32, 1985.

CASE PRESENTATION
(CASE CD)

ABNORMAL LIPIDS IN AN AIRCREW CANDIDATE

Dr. G.W. Gray

Mr. CD is an 18 year old man applying for military pilot training. He appears fit and healthy. He exercises regularly, jogging 4 to 6 kilometers at least three times per week, and he plays soccer twice a week. He has never had any symptoms suggestive of cardiovascular disease. He smokes about twenty cigarettes per day.

His father had a myocardial infarction at age 47, and is still living at age 55, following coronary artery bypass surgery at age 53. His father's younger brother (paternal uncle) has just recently had a myocardial infarction at age 49. Both were cigarette smokers, were overweight, and mildly hypertensive.

On clinical examination, Mr. CD appears to be fit and healthy, and is not overweight. His blood pressure is 140/90 in each arm, seated, and his pulse 72 and regular. There are no xanthomas nor xanthelasma. Clinical examination of the cardiovascular system is entirely normal.

His resting electrocardiogram shows large amplitude QRS complexes suggestive of left ventricular hypertrophy, but the T waves and ST segments are entirely normal. The echocardiogram is normal, as is the chest x-ray.

His fasting cholesterol level is 240 mg/dl (6.20 mmol/L), and the triglycerides are 125 mg/dl (1.25 g/L).

Does Mr. CD meet your medical selection standards for pilot selection? Do you require any additional information to help with the decision?

His plasma lipids are repeated, after a definite 14 hour fast. The plasma is clear. His repeat total cholesterol is 245 mg/dl (6.33 mmol/L), with an HDL (high density lipoprotein) cholesterol of 36 mg/dl (0.93 mmol/L). The repeat triglycerides are 115 mg/dl.

Do you now have sufficient information to accept or reject this candidate with your current medical selection standards? If not, what additional information do you require?

A further repeat of his fasting plasma lipid levels, sent to another laboratory, gives the following results: total cholesterol 240 mg/dl (6.20 mmol/L), HDL cholesterol 44 mg/dl (1.14 mmol/L), triglycerides 105 mg/dl, LDL cholesterol (calculated) 155 mg/dl (4.00 mmol/L). His thyroid function indices are normal, as are his screening tests of hepatic and renal function.

Review of his dietary patterns indicate that he has a relatively low intake of dietary cholesterol, having been so advised by his father's physician. He avoids eggs, red meats and dairy products, but does not pay particular attention to dietary fat other than avoiding these sources of cholesterol.

Do you think an exercise stress test would be likely to provide useful information in this young man?

The exercise stress test shows an excellent level of cardiovascular fitness, based on the estimated maximum oxygen uptake. There are no arrhythmias. There is some upsloping ST segment depression in leads V4-V6 during the latter stages of exercise, which are less than 1 millimeter by 80 msec after the S wave.

Would Mr. CD now meet your medical selection standards? At what level would you place his risk for developing coronary artery disease over the course of his flying career? If he is acceptable for selection, what recommendations would you have for monitoring him through his career? What recommendations would you have for him now in terms of diet and lifestyle modification?

REFERENCES

1. The Lipid Research Clinics Program Epidemiology Committee: Plasma lipid distributions in selected North American populations: the Lipid Research Clinics Program Prevalence Study, Circulation 60: 427, 1979.

2. A symposium: laboratory lipid values. Am. J. Cardiol 56: 18, 1985.

3. National Institutes of Health Consensus Development Conference: Lowering blood cholesterol to prevent heart disease. JAMA 253: 080, 1985.

CASE REPORT BV

by
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Brooks Air Force Base, Texas 78235-5301

HISTORY:

BV, a 21 year old white male, was a senior cadet at the U.S. Air Force Academy. During a routine physical examination for commissioning and flying training, a grade 1-2/6 systolic ejection murmur was heard along the left sternal border and he was referred to the Air Force Academy cardiologist for evaluation. He denied any prior history of a heart murmur or rheumatic fever. A murmur was not noted on his entrance physical examination for the Air Force Academy. He was asymptomatic, specifically denying any chest discomfort, palpitations, dizzy spells, loss of consciousness, nocturnal dyspnea, pedal edema or decreased exercise tolerance. The family history was negative for cardiac disease, heart murmur, diabetes mellitus or hypertension. He was a nonsmoker and did not drink alcoholic beverages. He drank 2-3 cups of caffeinated coffee and 2-3 servings of caffeinated soft drinks per day. He participated in squadron intramural athletics twice a week and jogged for one hour three times a week. He was administered penicillin therapy for streptococcal pharyngitis three years ago and had a generalized rash.

PHYSICAL EXAMINATION:

Height 178 cm, weight 76.5 Kg, blood pressure 124/72 mmHg left arm sitting, and 128/74 mmHg right arm sitting, pulse 56 beats per minutes and regular. There was no thyromegaly. Lungs were clear to auscultation and percussion. Carotid pulses had a normal volume and contour with a soft transmitted murmur bilaterally. There was no jugular venous distention and jugular venous pulsations were normal. Peripheral pulses were normal with no brachial-femoral lag. Precordial palpation was normal. S_1 was split and S_2 was normal with physiologic splitting and a normal intensity P_2. A grade 2/6 early peaking systolic ejection murmur was heard at the base with radiation to the carotid arteries and along the left sternal border. The murmur was preceded, at the base, by a loud ejection click which did not vary with respiration. The murmur increased during expiration in the supine position and decreased with Valsalva and sitting. No gallops, rubs or diastolic murmurs were heard. The rest of the physical examination was normal.

This examination is typical of a bicuspid aortic valve with minimal or no aortic stenosis and no aortic insufficiency.

LABORATORY DATA:

Resting electrocardiogram showed normal sinus rhythm and prominent voltage in the precordial leads without ST-T wave changes. Chest radiograph was normal. M-mode echocardiography demonstrated normal chamber sizes, normal left ventricular function and normal valves, except for an eccentric aortic valve closure. Two-dimensional echocardiography demonstrated normal chamber sizes and wall motion and normal valvular structures except for a bicuspid, somewhat thickened aortic valve. Doppler echocardiography demonstrated no evidence of aortic insufficiency. Maximal treadmill exercise testing was normal and a 24-hour ambulatory electrocardiographic recording demonstrated normal sinus rhythm, sinus bradycardia and 13 isolated atrial premature beats.

DISPOSITION:

A waiver request was submitted for flying training and was not granted.

QUESTIONS:

1. Would you accept this candidate for flying training?

2. If yes, would you train him for all aircraft or only tankers-transports-bombers?

3. What are the short and long term aeromedical concerns relating to the natural history of bicuspid aortic valves?

4. If you accept him for flying training, what do you recommend for surveillance - what studies and how often?

5. What is your recommendation regarding infective endocarditis prophylaxis?

DISCUSSION:

By current U.S. Air Force standards all congenital heart disease is disqualifying for entry into flying training. Bicuspid aortic valve would not be waivered for entry into flying training. However, waiver would be possible in a trained aviator in the absence of hemodynamically significant aortic stenosis or insufficiency, other associated cardiac disease, or any history of infective endocarditis. If aortic stenosis were present, its severity might have to be definitively assessed by a cardiac catheterization.

Bicuspid aortic valve is one of the most common congenital cardiac defects, occurring in 1-2% of the general population. It is the most common cause of aortic stenosis. The valve has two leaflets rather than three; one leaflet is larger than the other and contains a raphe at its midpoint. Eccentricity of the valve orifice results. This valve may remain functionally normal throughout life, but may also become thickened, fibrotic, calcified and later stenotic. By age 45, 50% of bicuspid aortic valves have some degree of stenosis. Aortic valvular insufficiency is also a common complication, presenting usually in the third or fourth decade. Twenty percent of cases of bicuspid aortic valve have some associated cardiac anomaly, usually coarctation of the aorta or valvular pulmonic stenosis.

Aeromedical concerns regarding bicuspid aortic valve, therefore, involve the indefinite risk of infective endocarditis and the risk of development during the aviator's active flying career of significant aortic stenosis or aortic insufficiency which might be disqualifying for further flying duties. Further discussion regarding the disposition of valvular abnormalities in aviators was presented in the didactic presentations on Day 1.

An aviator flying with a waiver for bicuspid aortic valve would be re-evaluated at the School of Aerospace Medicine, usually every three years. The most important procedures would be history, physical examination and echo-cardiography. However, a reevaluation includes complete noninvasive cardiac testing to search also for the presence or development of other cardiac con-ditions, such as dysrhythmia and coronary artery disease. If aortic insufficiency developed, rest and exercise radionuclide angiography would also be an important surveillance tool.

Active duty U.S. Air Force personnel undergo annual dental examination and cleaning, so the risk of infective endocarditis is an important concern. Bicuspid aortic valve with complicating insufficiency is particularly susceptible, even if the insufficiency is hemodynamically insignificant. Infective endocarditis prophylaxis is recommended for all cases of bicuspid aortic valve. This particular individual would require prophylaxis with a non-penicillin antibiotic because of his prior allergic reaction.

REFERENCES:

1. Braunwald, E.: Heart Disease: A Textbook of Cardiovascular Medicine, 2nd Edition. Philadelphia, W.B. Saunders Co., 1984, 1095-1114.

2. Rubenstein, E.: Scientific American Medicine. New York, Scientific American Inc., 1986, XI:1-4.

3. Hurst, J.: The Heart, 5th Edition. New York, McGraw-Hill Inc., 1982, 285-287, 729-731.

4. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia: Lea and Febiger, 1985, 447-452.

CASE PRESENTATION
(CASE WP)

WOLFF-PARKINSON-WHITE PATTERN

* Dr. G.W. Gray

Officer Cadet WP is a 22 year old Military College student who has been previously screened and selected for pilot training and now goes for his annual aircrew medical examination. He is in excellent condition with a high level of cardiovascular fitness. His last electrocardiogram was done at the time of initial aircrew selection four years before and showed left axis deviation (-30°) and two ventricular extrasystoles on the mounted tracing. His electrocardiogram now shows a Wolff-Parkinson-White conduction pattern, type A. He has been very active in sports and is Captain of the College soccer team. He is unaware of having had any symptoms of irregular or unexpected rapid heart action, and he has not had any episodes of lightheadedness or presyncope. He has completed primary flying school, with 13 hours dual and 7 hours solo in a single engine light aircraft.

Can Officer Cadet WP proceed with advanced flying training, for which he is now scheduled? Yes/No/Maybe (please circle your decision)

If you selected No, what are your reasons for refusing this dedicated young man further flying training?

If you selected Yes, please justify your reasons for sending a young man with WPW pattern (with the potential for serious tachyarrhythmias) into flying training?

If you selected Maybe, what further information would you like to help you with your decision?

Officer Cadet WP is referred for evaluation by a cardiologist. Clinical evaluation was entirely normal at the time of the evaluation. The resting ECG showed the WPW pattern. A treadmill exercise test was performed to a target maximum heart rate of 175 beats per minute. Bypass tract conduction ceased once the heart rate reached the range of 160 beats per minute, and resumed in a 2:1 and then a 1:1 fashion as the heart rate slowed in the recovery period. A 24 hour ambulatory electrocardiogram showed varying periods of WPW bypass tract conduction interspersed with normal conduction. Occassional, infrequent unifocal ventricular extrasystoles were noted, but no other arrhythmias were observed. A 2D and M-mode echocardiogram were normal.

Do you think that you can now recommend OCdt WP for flying training? Do you require any additional information? If so, what?

Officer Cadet WP returns to the cardiologist for a "non-invasive" electrophysiologic study utilizing an esophageal electrode positioned behind the left atrium in order to perform atrial pacing. The cardiologist finds that the refractory properties of the bypass tract are long, (greater than 300 msec), and he concludes that there is virtually no risk of atrial fibrillation with rapid conduction across the bypass tract. In addition, he introduces a variety of premature atrial stimuli and is unable to induce paroxysmal atrial tachycardia (PAT). He concludes that it is most unlikely that Officer Cadet WP is prone to developing PAT, and suggests that he is fit for military flying training.

Are you now satisfied that Officer Cadet WP is fit? Are there any unanswered questions or undefined risks? Are yet further studies required?

Although the method of stimulation via the esophageal electrode allows the cardiac electrophysiologist to define the refractory properties of the bypass tract, a full cardiac electrophysiologic study is required to fully define the potential for arrhythmias e.g. in some patients PAT will develop only following ventricular stimulation.

In inexperienced aircrew candidates, such intensive investigation are generally not indicated. However, some highly motivated candidates may undergo such investigations privately, and present themselves for aircrew selection. If it has been clarified through an invasive electrophysiologic study that they have no increased potential for tachyarrhythmias, they might possibly be considered for aircrew training. Arguments against accepting individuals with WPW pattern who have had satisfactory electrophysiological studies include the uninterpretability of the ST segment response to exercise in the presence of WPW conduction, thus making this test useless for future screening for ischemic heart disease.

Experienced aircrew who have an intermittently conducting accessory bypass tract may not be discovered until after they are fully trained. In this case, electrophysiologic studies should be undertaken to define the potential for tachyarrhythmias, if they are to be allowed to continue with unrestricted flying in tactical fighter operations.

CASE P.D. (by Dr Hull) Age 21 years

Student pilot

Age 11 Wheezing attacks ? bronchitis
Continued to age 16 and ceased spontaneously
Occurred mainly during summer months
Treated with salbutamol ("Ventolin") tablets only as required
Never hospitalised
No hay fever or eczema
"Allergic" to cats - watering eyes
Non-smoker.

Family history: No asthma, eczema or hay fever.

Q1 Would you accept the diagnosis of bronchitis in childhood?

Age 19 Enlisted for Air Force pilot training

Age 21 During flying training he had 2 attacks of acute asthma - no obvious cause.

Second attack - peak flow rate (PFR) 130 L/min

Good response to bronchodilators.

Following second attack, grounded and referred for investigation.

On examination: Looked well.
Chest - mild generalised high-pitched wheezing.
CVS and general examination normal.
FBC Hb 15.2
TWBC 7.2 - Eosinophils 1.0 = 14%
Sputum - Eosinophils ++. Sterile.
Skin tests - sensitive to a wide range of common antigens.
Chest xray - normal.

Pulmoanry function tests:
FVC 5.5, FEV1 2.7 = 49%. After bronchodilator, 5.6 and 3.7 = 66%
PFR - On admission 340 L/min with diurnal swing of up to 200 L.
After treatment, 580 L/min with swing of 100 L.

Treatment. Bronchodilators and short course of oral prednisolone.
Good response (v.s.).

Continued on full doses of inhaled beta-agonists. Respiratory function declined again when oral steroids stopped.

"Becotide" inhaler (2 puffs qds) and terbutaline inhaler (ditto) stablised PFR at 580 L/min.
Asymptomatic for several weeks after discharge, whilst on this regime.

Q2 Should he be returned to flying training?

If yes, what should be his further treatment and follow-up?

If no, why not?

APPENDIX

Discussion of cases presented in Section 11 as "unknowns" with diagnosis and disposition to have been supplied by the course attendees.

Discussion of Case Report JC

Based on a review of all the information and the evaluation at USAFSAM, JC was diagnosed as having myopericarditis, probably viral. Viral titers were not drawn during his initial illness and his evaluation at USAFSAM revealed no evidence of underlying metabolic, autoimmune, neoplastic or other causes. The physical examination acutely described a typical, two-component pericardial friction rub and his symptoms responded quickly to Indomethacin but not to nitroglycerin. His electrocardiograms show a typical evolutionary pattern of pericarditis with initial diffuse ST elevation, followed by return of the ST segments to baseline, followed by T wave inversion, followed by return of the T waves to normal. T wave inversion may persist indefinitely or may return to normal over a variable length of time. His pain pattern was atypical for pericarditis in that no positional or respiratory component was appreciated. Also, myocardial infarction may be complicated by pericarditis. His enzymes were elevated compatible with myocardial damage, but this occurs in myocarditis as well as myocardial infarction. Resting radionuclide angiography and two-dimensional echocardiography obtained during his acute illness failed to demonstrate any focal wall motion abnormalities consistent with myocardial infarction. His cardiac catheterization films were reviewed at USAFSAM and were felt to be normal with normal coronary arteries and a normal left ventriculogram; we disagreed with the local interpretation of the left ventriculogram. Also, followup studies obtained at USAFSAM failed to demonstrate any focal wall motion abnormalities. If he indeed had a small myocardial infraction, one would have to postulate an embolic event, small vessel disease, or coronary spasm. Small vessel coronary artery disease does not really explain this particular clinical presentation although it is a cause of anginal chest pain in the presence of normal m or epicardial coronary arteries. The diagnosis of small vessel coronary artery disease is difficult to postulate, however, in the absence of exercise-induced wall motion abnormalities on a stress radionuclide angiogram. An embolic phenomenon and coronary spasm are also very unlikely and the clinical picture is best explained as an episode of viral myopericarditis.

Viral myocarditis usually occurs two to four weeks after the flu-like illness, but may occur earlier; it usually resolves in a few weeks. It is usually subclinical, but may be fulminant and fatal during the acute phase. In various autopsy studies, 4 to 10% of routine postmortem examinations disclose evidence of clinically unrecognized myocarditis. Some patients may seem to recover completely only to have the illness recur or to develop congestive cardiomyopathy years later.

Viral pericarditis also occurs soon after a flu-like illness but 30 to 40% will recur at least once in the next several weeks. This probably represents an immunologic response to the initial event. Coxsackie and Echoviruses are the most likely agents to cause viral myopericarditis. A small percentage may also progress to chronic constrictive pericarditis.

The aeromedical concerns following a single case of myopericarditis are ventricular and atrial arrhythmias which may be associated with both pericarditis and myocarditis, progression to congestive cardiomyopathy and recurrence of the myocarditis or pericarditis. After six months observation for recurrence and evidence for underlying etiologies, a USAFSAM evaluation is performed. If no arrhythmias are found, left ventricular function is normal, and no evidence exists of constriction or other cardiac defects, a waiver for unrestricted flying duties may be recommended. Because of the concern for future complications, particularly the development of constrictive pericarditis or congestive cardiomyopathy, followup evaluations at USAFSAM are performed at one to three year intervals.

The most important procedures for long-term surveillance, other than history and physical examination, are echocardiography and radionuclide angiography to assess for left ventricular wall motion and function and ambulatory electrocardiographic monitoring and treadmill stress testing to assess for arrhythmias.

JC had a normal evaluation and was returned to unlimited flying duties with followup scheduled in one year at USAFSAM.

REFERENCES:

1. Braunwald, E.: Heart Disease: A Textbook of Cardiovascular Medicine, 2nd Edition. Philadelphia, W.B. Saunders Company, 1984, 1432-1436, 1474-1478, 1497-1498.

2. Hurst, J.: The Heart, 5th Edition. New York, McGraw-Hill, Inc., 1982, 1278-1299, 1372-1380.

3. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia, Lea and Febiger, 1985, 455-456.

4. Rubenstein, E.: Scientific American Medicine. New York, Scientific American, Inc., 1986, XIII:1-2.

Discussion of Case K.P.H.

This aviator had evidence of significant ventricular arrhythmias. In most aeromedical services, both military and civilian, the primary question regarding such rhythm disturbances is: "Is there evidence of underlying organic heart disease, i.e., is there anatomic evidence of organic heart disease?" In this case, the aviator had complex ventricular ectopy on Holter and treadmill, culminating in ventricular tachycardia on centrifuge testing. Ventricular tachycardia, in the presence of mitral valve prolapse, is not considered to be an acceptable arrhythmia by most aeromedical services. Ventricular tachycardia, in the absence of structural heart disease, is acceptable in the USAF and FAA (civilian) certification authorities. In the USAF, asymptomatic exercise-induced ventricular tachycardia is waiverable only for nonhigh-performance flying. Most observers do not view a bicuspid aortic valve as an arrhythmogenic lesion. However, in this case, there is a clear question of mitral valve prolapse. If MVP can be ruled out, this aviator may be considered for a tanker-bomber-transport waiver. When the entire disposition hinges on the presence or absence of mitral valve prolapse, angiography is a valid aeromedical tool. In this case, the ventriculogram revealed acoustically silent mitral valve prolapse with posterior leaflet prolapse and minimal mitral regurgitation. Ventricular tachycardia and mitral valve prolapse are an unacceptable combination for any category of flying. The aortic root injection revealed no aortic insufficiency, but it confirmed the presence of a bicuspid aortic valve. There was no gradient across the aortic valve. In cases of mitral valve prolapse in aviators, any suspicion of aortic valve disease or aortic root disease must be vigorously pursued to preclude the presence of a common myxomatous process involving the mitral valve, aortic valve and/or aortic root. In the great majority of cases, aortic valve disease in the healthy male is usually a congenitally bicuspid valve, an abnormality not associated etiologically with mitral valve prolapse. Angiography is rarely needed to make the diagnosis of mitral valve prolapse, but it must be undertaken in some cases when a definitive diagnosis of prolapse is necessary.

Discussion of Case Report WS

WS has a fairly typical presentation of nonobstructive hypertrophic cardiomyopathy (HCM). Physical examination features of HCM include a harsh systolic ejection murmur heard best at the apex and left lower sternal border which, unlike a functional outflow murmur, increases with Valsalva and standing. Apical impulse is often forceful due to the ventricular hypertrophy. The apical impulse may also be double if there is a palpable S_4 or even triple in obstructive HCM. Carotid pulsations are brisk and, in the case of obstructive HCM, are typically bisferiens. A loud S_4 due to the noncompliant, hypertrophied left ventricle is also typical. Routine electrocardiography demonstrates voltage changes of left ventricular hypertrophy and left ventricular strain pattern ST/T wave changes. Echocardiographic features of hypertrophic cardiomyopathy include abnormal systolic motion or early closure of the aortic valve, left ventricular hypertrophy in a variety of patterns, a narrow left ventricular outflow tract in the case of obstructive HCM, systolic anterior motion of the anterior mitral valve structure, a small and hypercontractile left ventricular cavity, and decreased septal motion and septal thickening during systole.

WS had many of these typical features. He had a typical systolic ejection murmur and a loud and palpable S_4 on physical examination. His electrocardiogram demonstrates left ventricular hypertrophy with a left ventricular strain pattern. Echocardiography demonstrates abnormal systolic motion of the aortic valve, left ventricular hypertrophy with asymmetric septal hypertrophy, decreased septal motion and thickening, and systolic anterior motion of the mitral valve. Echocardiography, radionuclide angiography and cardiac catheterization all demonstrated a normal size, but hypercontractile, left ventricle. WS did not have all the classic features of hypertrophic cardiomyopathy because he did not have a resting left ventricular - aortic pressure gradient. At catheterization he had no gradient at rest or exercise but had a 100 mmHg gradient provoked with Isuprel infusion.

Hypertrophic cardiomyopathy is disqualifying for all flying duties without waiver recommendation because of its known predilliction for sudden death, supraventricular and ventricular arrhythmias, chest pain which may be incapacitating, dyspnea and syncope.

Supraventricular and ventricular arrhythmias are reported in approximatley one-half of all patients with HCM; 20% will demonstrate ventricular tachycardia during prolonged ambulatory electrocardiographic monitoring. Atrial fibrillation may occur in as many as 5 to 10% of HCM patients. Atrial systole plays a major role in maintaining left ventricular filling and therefore cardiac output in HCM because of the hypertrophied, noncompliant state of the left ventricle. Loss of atrial systole during atrial fibrillation may, therefore, precipitate sudden congestive heart failure or even collapse. Often the symptoms and arrhythmias are precipitated by exercise, so stress testing may be of significant use to disclose arrhythmias not present at rest. The arrhythmias, symptoms and incidence of sudden death do not correlate with the presence or degree of the obstruction. Young patients, patients with little or no resting gradient and patients presenting with HCM symptoms at a young age appear to be at particular risk of sudden death. The subgroup of HCM patients with a positive family history of sudden death are at a particularly high risk of sudden death. HCM is the most common autopsy diagnosis of young athletes experiencing sudden death. Experience in the literature reports an average 5% per year mortality rate from HCM and a 10% incidence of infective endocarditis. Infective endocarditis prophylaxis is recommended.

HCM is often transmitted as an autosomal dominant trait, so screening echocardiography of first degree relatives of an HCM patient is extremely important. Screening physical examination is inadequate as 50% of first degree relatives of HCM patients will have asymmetric septal hypertrophy or concentric hypertrophy on echocardiography in the absence of symptoms and with a normal physical examination.

WS was disqualified from all flying duties and was counseled to have his first degree relatives screened by physical examination and echocardiography. USAFSAM reevaluation was performed in Sep 86. He remained asymptomatic and his physical examination and noninvasive testing were essentially unchanged from his original evaluation.

REFERENCES:

1. Braunwald, E.: Heart Disease: A Textbook of Cardiovascular Medicine, 2nd Edition. Philadelphia, W.B. Saunders Company, 1984, 1409-1422.

2. Rubenstein, E.: Scientific American Medicine. New York, Scientific American Inc., 1986, XIV:9-18.

3. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia, Lea and Febiger, 1985, 456-457.

4. Hurst, J.: The Heart, 5th Edition. New York, McGraw-Hill, Inc., 1982, 1309-1323

Discussion of Case Report JF

JF has aortic insufficiency. His physical examination demonstrates a systolic aortic flow murmur due to the increased volume of flow, a holodiastolic aortic insufficiency murmur, an S_3 and Austin-Flint murmur. An Austin-Flint murmur is the low pitched, rumbling diastolic murmur of relative mitral stenosis due to partial closure of the anterior mitral leaflet by the aortic insufficiency stream. His hyperdynamic pulses and sustained apical impulse are a reflection of the hyperdynamic state of his volume loaded left ventricle. His pulse pressure is also increased. He also has an aortic ejection click, due probably to a bicuspid aortic valve. Electrocardiography is unremarkable and performance on a treadmill stress test is excellent. His M-mode echocardiogram (Figure 2) shows an eccentric aortic valve closure which suggests the presence of a bicuspid aortic valve. Two-dimensional echocardiography confirmed this diagnosis. M-mode echocardiography in Figure 3 shows coarse diastolic fluttering of the mitral valve leaflets; this is due to the flow of blood regurgitating from the aortic root back into the left ventricle during diastole and is a typical finding with aortic valve insufficiency. Cardiac catheterization demonstrated significant aortic insufficiency graded as 4+, but normal resting hemodynamics. JF therefore has angiographic and physical examination evidence of significant aortic insufficiency but with no symptoms, and excellent exercise capacity and mild left ventricular enlargement. The sudden appearance of significant aortic insufficiency in this individual, after several normal examinations, and no history compatible with infective endocarditis, raises the possibility of aortic insufficiency due to the trauma occurring with his bicycle accident one month earlier. However, he does also have a bicuspid aortic valve which is frequently a cause of aortic insufficiency.

Isolated aortic insufficiency is usually due to a bicuspid aortic valve; rheumatic heart disease is a very unusual cause of aortic insufficiency without involvement of other valves, particularly the mitral valve. Infection, trauma and diseases of the aortic root are other potential causes of aortic insufficiency. Aortic insufficiency results in a volume load on the left ventricle with secondary left ventricular dilitation and proportionate left ventricular hypertrophy, resulting in increased left ventricular wall stress. Ventricular ejection is rapid and stroke volume increases to compensate for the regurgitant volume and increase in wall stress. Peripheral resistence and the duration of diastole significantly affect the amount of aortic regurgitation.

Minimal aortic insufficiency may have a normal physical examination, except for a diastolic decrescendo murmur along the left sternal border and base which is increased during held expiration, leaning forward and handgrip. Moderate to severe aortic insufficiency has hyperdynamic pulses, rapid and possibly bisferiens carotid pulsations, hyperdynamic apical impulse, and a longer, holodiastolic murmur at the base and left sternal border which may radiate to the apex. Frequently there is an ejection click if there is underlying bicuspid aortic valve. An aortic systolic flow murmur is frequently present due to the increased outflow volume. An apical diastolic rumble of relative mitral stenosis, an Austin-Flint murmur, may be present.

Depending on the severity and chronicity of the aortic insufficiency, chest radiograph may be normal or may show left atrial and left ventricular enlargement. Electrocardiography may demonstrate changes consistent with left ventricular hypertrophy. M-mode and two-dimensional echocardiography are useful to demonstrate signs of aortic insufficiency, such as diastolic fluttering of the mitral valve leaflet, and to assess chamber sizes and resting left ventricular function and ejection fraction. Rest and exercise radionuclide angiography is an important tool to assess myocardial reserve as reflected by the ejection fraction response to exercise. Cardiac cathterization may be indicated to diagnose the presence and/or severity of aortic insufficiency as well as its cause.

Aortic insufficiency may be aggravated by frequent $+G_Z$ exposure. Also $+G_Z$ forces affect the perfusion column in aortic insufficiency, lowering $+G_Z$ tolerance. Coronary artery blood flow is also affected in aortic insufficiency due to decreased diastolic filling and the increased left ventricular mass. Myocardial ischemia with all its potential risks including angina pectoris, arrhythmia and syncope may occur even with normal epicardial coronary arteries.

Aortic insufficiency is acceptable for continued flying duties in a trained aviator if it is hemodynamically insignificant and asymptomatic and no other cardiac defects are present. It is acceptable only for tanker-transport-bomber aircraft due to the concern regarding the effect of repeated $+G_Z$ exposure on the severity of aortic insufficiency. It is not acceptable for entry into initial flying training. In aviators the subclinical, asymptomatic phase of acrtic insufficiency usually extends through an entire active flying career. There must be no left ventricular hypertrophy and noninvasive evaluation should disclose mild to moderate aortic insufficiency. If cardiac catheterization is performed, the aortic insufficiency should be graded as less than or equal to 2+ and the regurgitant fraction should be less than or equal to 25%. In the case of JF, aortic insufficiency was graded as 4+ and the regurgitant fraction was 35%. Exercise capacity should be normal with no significant exercise induced arrhythmias. The primary surveillance tools are echocardiography and radionuclide angiography; echocardiography is used primarily to follow chamber size, particularly left ventricular size, and exercise radionuclide angiography is used to follow the ejection fraction response to exercise. Progressive left ventricular enlargement and an abnormal ejection fraction response to exercise are grounds for disqualification from flying duties and are also grounds for consideration for valvular replacement. Aviators with aortic insufficiency are reevaluated at USAFSAM at one to two year intervals.

During his initial evaluation at USAFSAM, JF was disqualified for flying duties due to the severity of his aortic insufficiency, even in the absence of symptoms. He returned for followup evaluation in October 1986 with essentially no changes in his history, physical examination, or noninvasive evaluation. Upon medical advice, he had discontinued all weight-lifting. However, he switched to tri-athletics at a competition level. Due to concern regarding the effects of excessive, competitive exercise on his aortic insufficiency and left ventricular function, he was advised to discontinue all exercises with a significant isometric component, including cycling, and to decrease his aerobic exercise to a more non competitive level.

REFERENCES:

1. Braunwald, E.: Heart Disease: A Textbook of Cardiovascular Medicine, 2nd Edition. Philadelphia, W.B. Saunders Company, 1984, 1105-1114.

2. Hurst, J.: The Heart, 5th Edition. New York, McGraw-Hill, Inc., 1982, 874-887.

3. DeHart, R.: Fundamentals of Aerospace Medicine, 1st Edition. Philadelphia, Lea and Febiger, 1985, 447-452.

4. Rubenstein, E.: Scientific American Medicine. New York, Scientific American, Inc., 1986, XI:1-6.

5. Sixteenth Bethesda Conference: Cardiovascular Abnormalities in the Athlete. Recommendations Regarding Eligibility for Competition. JACC, 6:1189-1232, December 85.

Part II Intradermal skin testing (Mantoux 1 : 10,000) was strongly positive.
Sputum - direct - numerous acid and alcohol-fast bacilli - culture - M. tuberculosis resistant to streptomycin, sensitive to all other drugs tested.

Q3 What treatment will you prescribe?

For how long?

Q4 May R.N. return to flying duties? If so, when?

Treatment was started with the following drugs on 12 Aug 1979:

"Rimactazid 300" tabs 2 per d. (Rifampicin 300 mg + Isoniazid 150 mg)
Ethambutol 1.2 G per d
Pyrazinamide 1.0 G x 2 per d
"Limited bed rest" for 3 weeks.

14 Sep 79 Repeat sputum tests now show no AAFB
Liver function tests normal (carried out every 2 weeks during treatment).

5 Oct 79 Discharged on unchanged drug treatment.

4 Nov 79 Readmitted. Well. Some morning cough and sputum.
Xrays - considerable improvement; less shadowing, cavity smaller.
FBC normal. Film NAD.
TWBC 7,500
Liver function tests remain normal
Pyrazinamide) both stopped
Ethambutol)
Rimactazid 300 tabs 2 per d continued on discharge.

3 Dec 79 Readmitted. Continued well.
Chest xray, tomography - no change vs 4 Nov 79 apart from reduction in cavity size to 0.5 cm
FBC normal
LFT's normal
Sputum - AAFB - negative
FVC 5.15; FEV1 3.8 = 73%

Q5 How long should drug treatment be continued?

Q6 A cavity is still present after 4 months' treatment. Should surgery be considered?

10 Dec 79 Closure of the cavity under medical treatment was judged unlikely
Left thoracotomy and segmental resection carried out
Uneventful recovery
Operation specimen - culture positive for M. tuberculosis.

21 Jan 80 Well.
CXR satisfactory. FBC, ESR normal
Spirometry: FVC 4.4L; FEV1 3.5L = 80%

Q7 How long should drug treatment be continued?

Q8 When may he return to flying duties?

Q9a If he returns to flying duties, what restrictions are appropriate?

(Discussion of R.N. continued on next page)

Q9b When, if ever, may these be relaxed?

Discussion. Active pulmonary tuberculosis in adult westerners of the professional classes is now extremely unusual. In trained aircrew it is now so rare that there is pressure to abolish routine chest radiography altogether.

R.N. illustrates advantages and hazards of routine chest radiography. His lesion was discovered but the radiologist considered and reported it as inactive, healed tuberculosis. Action was delayed even when there was increase in the shadowing. Clearly, any abnormality in a chest xray of an aviator requires clinical as well as radiological assessment.

Clinical evaluation led to diagnosis and drug treatment. The first few weeks of treatment were given in hospital, with "semi-bed rest". Such conditions make compliance probable, and facilitate early recognition and assessment of drug side-effects, but in fact modern drug treatment is as effective in ambulant out-patients as in in-patients, and bed rest is required only for seriously ill cases.

Multiple drug treatment remains essential. Streptomycin and P.A.S. have been largely abandoned on grounds of toxicity, except as drugs of last resort, for pulmonary TB. The drugs used in R.N's case all have serious potential side-effects although he experienced none of these. The potential risks are sufficient to preclude flying duties whilst taking combined drug therapy, even were the underlying lung disease mild enough to allow this. In general, the only antituberculous drug compatible with flying duties is Isoniazid.

After 4 months of drug treatment R.N. was well, was sputum-negative for AAFB, and his xray showed improvement. However, a small (0.5 mm) thick-walled cavity remained. In itself this was unlikely to constitute an aeromedical hazard; almost certainly it communicated with a bronchus or bronchiole, and even if not, at this size and surrounded by a dense chronic fibrotic reaction, the likelihood of problems from expansion at altitude is remote.

However, resection was advised on clinical grounds. The specimen contained viable tubercle bacilli. It is suggested that some bacilli may persist in densely fibrotic lesions even after a full course of modern drug treatment. Traditionally, persistence of a cavity is regarded as unsafe for the same reason. In retrospect, the decision to submit R.N. to surgery appears well justified.

Return to flying after a thoracotomy and partial lobe resection depends on full recovery and a period of 3 months observation on the ground is usual. An altitude chamber ride might be requested but is rarely considered essential.

R.N's return to flying was delayed until he had completed a further 5 months of drug treatment (v.s). A total of 9 months treatment with modern drugs is now known to confer near 100% cure where compliance has been good.

R.N. was asymptomatic at the end of his drug treatment, his chest radiograph remained normal (post-thoracotomy) and he was re-licensed for full flying duties. Thereafter he had occasional (6-monthly, then annual) review, though this may be unnecessary with modern treatment.

Conclusion. R.N's case illustrates the following principles:

1. Any abnormality on the chest radiograph of an aviator should be promptly and fully evaluated. Radiological criteria of "activity" or otherwise in any lesion are unreliable.

2. Though rare, pulmonary tuberculosis still occurs in the military and aviation community.

3. The outlook for cure with modern drugs is excellent, but surgery may still be required in some cases.

4. Nine months' grounding is necessary for completion of drug treatment. Thereafter, a good outcome is compatible with return to full flying duties.

5. Unless disease, and hence pulmonary surgery, is extensive, a return to full flying duties 3 months after thoracotomy is likely, providing no other contra-indications exist.

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As major emphasis is placed on decision making, the classical technique of case presentation and discussion is employed. Early in the Course, the lecturers present the data and its interpretation with the aeromedical disposition supplied by the Course attendees. This case method is felt to be essential since aeromedical disposition will vary among different countries even for identical data. The varying viewpoints regarding aeromedical disposition is believed to be an educational stimulus both for Course attendees and lecturers. Later in the Course, attendees are presented only raw data from which they will derive both diagnosis and discussion.

One shortcoming of most medical courses is inadequate time for physicians and other health professionals to actually discuss interesting cases in-depth, in the presence of experienced aerospace medical specialists. A wealth of interesting cases needs to be shared. On the final day of the Course, attendees are asked to prepare in advance their most difficult and perplexing aeromedical cases for presentation and discussion.

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