Cardiac Stress Testing

Introduction

Cardiovascular stress testing remains one of the most common diagnostic tests ordered by internists and family practitioners. Based on training, experience and availability, physicians have traditionally kept their stress testing options to a familiar minimum. However, during the past 10 years, an explosion of new and improved stress testing modalities have emerged, touting certain advantages over one another. Table I is a “short list” of the ones available in the Delaware Valley.
The proliferation of stress testing options has led to confusion among referring physicians and cardiologists alike. From this stress testing chaos, has emerged clinical guidelines and algorithms for the application of cardiovascular stress testing in certain patient populations. These guidelines\textsuperscript{1,2,3}, which the reader may independently review, have been developed together by the American Heart Association, the American College of Cardiology, the American Society of Nuclear Cardiology, the American Society of Echocardiography and the American College of Physicians. Several algorithms have emerged which are beyond the scope of this discussion. What follows is my algorithm, which is based in part on these guidelines, excerpts from the medical literature, test experience, test availability, cost and a term that I shall define later, “patient profiling.”

**Epidemiology of Coronary Artery Disease and Baye’s Theorem**

Stress testing is performed on patients for a variety of reasons. Table II lists some of the more common indications for the “inpatient setting”.

| Table II: Inpatient Indications |
|--------------------------------|--|
| • chest pain evaluation - no known CAD |
| • chest pain evaluation - known CAD |
| • pre non cardiac surgery |
| • post MI |
| • CHF/cardiomyopathy evaluation |
| • arrhythmia evaluation |
| • assess therapy for CAD |
| • assess HR (chronotropic competence) |
| • abnormal ECG |
Table III lists some common outpatient indications.

<table>
<thead>
<tr>
<th>Table III: Outpatient Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• chest pain (equivalent) evaluation</td>
</tr>
<tr>
<td>• <strong>Assess CAD risk (two or more risk factors)</strong>*</td>
</tr>
<tr>
<td>• pre non cardiac surgery</td>
</tr>
<tr>
<td>• post MI</td>
</tr>
<tr>
<td>• CHF/cardiomyopathy evaluation</td>
</tr>
<tr>
<td>• arrhythmia evaluation</td>
</tr>
<tr>
<td>• pre exercise program</td>
</tr>
<tr>
<td>• post cath assessment of ischemia</td>
</tr>
<tr>
<td>• abnormal ECG</td>
</tr>
<tr>
<td>• Eval re Critical AS</td>
</tr>
</tbody>
</table>

The evaluation of patients for coronary artery disease (CAD) represents the most common indication in both groups above. Therefore, let’s discuss stress testing in this context. Let’s also run through a practical approach to the evaluation of patients suspected of having CAD.

When patients present to us with symptoms that may be related to coronary artery disease, we consciously or unconsciously “size up” their probability of having CAD. This assessment is based on demographics, presence of cardiovascular risk factors, the history and physical and the ECG. This process is called determining the “pre test probability.” Sometimes our pretest probability of CAD is either very high or very low, and no further testing is needed to convince us of the diagnosis. Often, however, we find our pretest probability of CAD to “intermediate” or even close to a coin flip. Stress testing, therefore, moves us closer to or away from a diagnosis of CAD. If we know a particular stress testing modality’s probability of providing a “true” or “accurate” result (see below), we can multiply these probabilities to arrive at our “post test probability” that our patient has CAD. This process is called Baye’s Theorem. The particular mathematics involved in Baye’s Theorem (not shown here) is not important for an understanding of its clinical utility.

A practical corollary to Baye’s Theorem is that the post-test probability of CAD in a given population is dependent on the prevalence of CAD in the population studied. For example, inpatients have a much higher prevalence of CAD then outpatients. Therefore, for a given patient undergoing a cardiac stress test, the inpatient will have a higher posttest probability of CAD. Conversely, an outpatient with atypical chest pain and no risk factors will have a lower post test probability, even if the test is abnormal.

**Physiology of Stress Testing**
To best understand how each patient should be stressed, it is important to understand how stress testing effects normal physiology. Consider a patient with known coronary artery disease documented by cardiac catheterization. At rest this patient likely does not have symptoms. Therefore, to uncover CAD, one must upset the tenuous balance between myocardial supply (i.e. coronary blood flow) and myocardial demand. Stress testing increases the demand to evaluate supply side reserve. The determinates of supply and demand are shown in Figure 1.

![Coronary blood flow equation describing the determinates of supply and demand.](image)

Figure 1 Coronary blood flow equation describing the determinates of supply and demand.

On the demand side of this equation heart rate and blood pressure represent the easiest measurable targets for stress testing. One can easily design stress testing protocols around them (see exercise stress below). Contractility has become an alternative mechanism for stress testing (see dobutamine stress) in patients who cannot adequately exercise. The other parameters are not easily measured and are not used in stress testing.

The supply side of this equation is derived from the fact that coronary arteries are predominately perfused during diastole. The perfusion pressure is determined by the gradient between the diastolic blood pressure (DBP) and the mean right atrial pressure (RAP). During physical stress, this part of the equation is not all that important as diastolic blood pressure decreasing during aerobic exercise. Smooth muscle tone (SMT) also plays an important role in the supply of blood to the coronaries in that vasodilation (via neural or chemical effects) can significantly increase coronary blood flow. During treadmill stress, for example, one can see increases of 2 to 3 times normal coronary blood flow from the vasodilation induced by the byproducts of metabolism. The administration of potent coronary vasodilators (dipyridamole <Persantine® (Dupont)> and adenosine) can further dilate the coronary bed and increase coronary blood flow 5 to 6 times the resting value.

Now that we know how to alter the determinates of myocardial supply and demand for patients with CAD, how do we then measure the ischemia produced? As it turns out, of course, there are many ways to do this (see Figure 2).
Figure 2 portrays a plot of workload versus time for induced myocardial ischemia. This is may be more readily understood if one considers a “human laboratory experiment”, such as coronary angioplasty. Suppose we use our patient with known coronary artery disease. This patient has a known 90% obstruction in the left anterior descending coronary artery and agrees to undergo balloon angioplasty (i.e. PTCA). Suppose also that during this procedure, the patient agrees to an elaborate, multi-modality “ischemia” monitoring setup (the Dr. Lederman lab) that includes a 12 lead ECG, an echo machine, a nuclear medicine camera, a pulmonary artery (Swan-Gantz) catheter, and an intravascular (intracoronary) ultrasound (IVUS) catheter – angioplasty device (yes, these are commercially available). All of these devices are set up and calibrated before balloon inflation. The balloon is then fully inflated. Thallium\textsuperscript{201} (Mallinckrodt Medical) (or another radioisotope, see below) is then injected intravenously and all the devices for measuring ischemia are turned on. As in Figure 2, the first physiologic (? patho-physiologic) response is an abrupt cessation of coronary flow to the myocardium, distal to the site of balloon inflation, as measured by the IVUS catheter. This “flow heterogeneity” is also detected by the “gamma” nuclear camera and shows up as a “defect” in thallium perfusion. The pulmonary capillary wedge (PCW) pressure subsequently rises in concert with a change in doppler-derived diastolic dysfunction. Almost simultaneously, a decrease in myocardial wall thickening and motion (i.e. a new wall motion abnormality) appears on the real time echo screen. Shortly thereafter, the ECG reveals T and ST segment changes. Finally, the patient complains of chest discomfort and a small, but perceptible fall in blood pressure occurs. The balloon is released and these processes reverse. Admittedly, all these physiologic responses occur within a minute or two. However, this exercise portrays how myocardial ischemia may be measured by different modalities or “physiologic sensors”, if you will. What follows below is a more detailed description of the more clinical useful modalities as well as a discussion of their applicability and usefulness in different patient populations.
Types of Stress Testing

Table I listed all the available stress tests in the Delaware Valley that are used by physicians to diagnose CAD. From a practical standpoint, most physicians have become familiar with only a few based on their training, their experience and regional availability. However, this approach, though easy to implement, may be subjecting patients to an incomplete ischemia evaluation that, in turn, may lead to multiple tests that may be unnecessary, costly and sometimes dangerous.

To illustrate this concept, consider a patient who walks into your office complaining of chest pain. A baseline ECG reveals a left bundle branch block (LBBB). A thallium stress test is ordered. The thallium result suggests “septal ischemia”. A cardiac catheterization is recommended. The result is “angiographically normal coronary arteries.” Why? For the complete answer, see below (pharmacologic stress testing). Simply put, exercise thallium stress tests sometimes yield a result of “septal” and/or “anterior” ischemia, which with further testing, turns out to be a “false positive”. The initial choice of ordering a Persantine® thallium stress would have likely rendered a “normal” result and saved this patient the cost and risk of a cardiac cath. Thus it pays, to approach stress testing in a systematic and algorithmic fashion that utilizes your knowledge of stress test physiology and individual stress testing modalities.

I. Stress Electrocardiography (A.K.A. Stress ECG, GXT, EST, Graded Exercise Test, etc). Generically, Stress ECG is performed during exercise and pharmacologic stress testing. Because the latter is never used without a complementary imaging modality (i.e. dobutamine stress echo or Persantine® (Dupont) nuclear cardiac scintigraphy), we will assume that from now on Stress ECG refers to exercise stress testing.

There are basically two types of exercise stress testing in use today. One is the more familiar treadmill exercise stress testing. The other is bicycle exercise stress testing. Arm ergometry, which had been used in the past, has been replaced by pharmacologic stress testing (more sensitive and specific) for those who can’t exercise. It is more difficult to raise one’s heart rate with bicycle stress so treadmill testing is usually used.

There are basically three treadmill exercise protocols in clinical use today; the Bruce protocol (most common), the “modified Bruce protocol” and the Naughton protocol. The Bruce protocol is widely used, standardized and accepted by most as the “industry standard.” It consists of seven, three-minute stages (total of 21 minutes) and is designed to last about 5 to 8 minutes in most individuals. The modified Bruce protocol has two; three-minute “warm up” stages and then converts to a Bruce protocol at stage 3. It is used for immediate post myocardial infarction (MI) patients and patients with gait disturbances (i.e. elderly). The Naughton protocol has 2 minutes stages that rapidly accelerate the speed and incline. Its use is more a function of familiarity rather than a diagnostic advantage over the Bruce protocol. From now on please read “Bruce protocol” when I refer to exercise stress ECG, unless otherwise specifically stated.
Lots of cardiologists use a 2-minute Bruce because it’s faster..probably not better- I like the 3-min. Bruce. Should it be mentioned?
The exercise stress ECG provides a lot of clinical information regarding patients’ cardiovascular system and functional status (see Table IV).

In a normal individual, exercising on a treadmill leads to a gradual acceleration of heart rate and increase in blood pressure as a function of time (protocol stage). Systolic BP should increase 10 to 20 mm Hg per 3 minutes stage of a Bruce protocol. The diastolic BP usually falls slightly or stays the same. Oxygen extraction from the lungs quickly achieves a steady state until metabolic substrates are exhausted and energy production becomes “anaerobic” (A.K.A. the anaerobic threshold). Shortly thereafter, the patient has to stop exercising. The degree of stress achieved is reported in MET’s, or “metabolic equivalents.” One MET equals 3.5 cc O\textsubscript{2}/kg/min, or the basal amount of oxygen consumption needed to sustain life. Over 7 MET’s of work achieved is reported as New York Heart Association Functional Class I (no impairment); 5 to <7 MET’s; Class II (minimal functional impairment); 3-<5 NYHA Class III (moderate impairment); and <3, NYHA Class IV (severe impairment). Some labs report the “double product” (maximum heart rate achieved x maximum systolic BP achieved) as an indication of cardiovascular stress achieved, To have a “diagnostic” stress test the patient should attain 85% of their maximal predicted HR or attain a double product of 250 or greater (cross off the last 2 digits)-comes in handy when patients are stressed on rate control drugs. Mets are work equivalents. It’s a similar concept to the MET scale, but less disseminated. Usually, a patient will report angina at the same “double product”, so it may be a useful indicator of stress intensity and may used to guide response to therapy.

The electrocardiograph response to exercise stress testing is complex and beyond the scope of this discussion. However, ST segment depression is considered the hallmark of an ischemic response. A “line in the sand” is drawn at 1 mm, or more, horizontal or down-sloping ST depression in two or more leads of the standard 12 lead ECG. Up-

<table>
<thead>
<tr>
<th>Table IV Stress Test Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrocardiographic</td>
</tr>
<tr>
<td>• ST segment type/depression/elevation</td>
</tr>
<tr>
<td>• # leads showing ST changes</td>
</tr>
<tr>
<td>• duration of ST changes</td>
</tr>
<tr>
<td>• time to onset/duration ST segment changes</td>
</tr>
<tr>
<td>• exercise related arrhythmias</td>
</tr>
<tr>
<td>Hemodynamic</td>
</tr>
<tr>
<td>• maximum HR/BP/double-product</td>
</tr>
<tr>
<td>• heart rate response</td>
</tr>
<tr>
<td>• exertional hypotension</td>
</tr>
</tbody>
</table>

The electrocardiograph response to exercise stress testing is complex and beyond the scope of this discussion. However, ST segment depression is considered the hallmark of an ischemic response. A “line in the sand” is drawn at 1 mm, or more, horizontal or down-sloping ST depression in two or more leads of the standard 12 lead ECG. Up-
sloping ST segment depression requires **greater than 1.5 mm**. This seemingly arbitrary definition was derived from experiments using different “cut off” points to define an abnormal result that resulted in an acceptable sensitivity (the number of tests abnormal in a population with CAD) and **specificity** (the number of tests normal in the population without CAD).

The timing, **persistence** and degree of ST segment depression are important and prognostic in stress testing. **Earlier ST segment depression is usually indicative of more severe CAD (more obstruction and/or more vessels involved).** Similarly, **more lead involvement, and/or deeper (in millimeters) and/or persistent ST segment depression are usually indicative of more ischemic burden.** In contrast, **quick reversibility of these ST segment changes is usually associated with a false-positive result.** Sometimes, ST segment depression only occurs in recovery. This type of ST segment response is also indicative of ischemia and has a higher sensitivity for CAD.

Unfortunately, ST segment depression may occur in patients without CAD. There are several well-described situations when this may occur (see Table V). **Where is this table?** The most important of these scenarios to recognize is when patients have baseline ST segment abnormalities. **Also women with normal ECG?** In these situations, consideration needs to be given to complementary and adjunctive stress testing modalities (see below), in addition to the standard 12 lead ECG. As a general rule, when repolarization is abnormal (i.e. LVH with ST and T wave changes or “strain pattern”), or when repolarization occurs outside the natural conduction system (bundle branch block, WPW, paced rhythm, etc), complementary cardiac imaging is usually required (i.e. nuclear or echo). A notable exception is the right bundle branch block, in which case all the leads except for V1-V3 can be used to diagnose ST segment depression.

Finally, ST segment elevation may also occur during the stress electrocardiogram. It basically occurs during three scenarios. The first is in the leads that cover infarcted myocardium. In this instance, it is not necessarily abnormal. The second is in those ECG leads that have resting ST segment elevation. Lastly, it may occur in ECG leads that subend myocardium supplied by a critical stenosis and in which case coronary vasospasm is thought to occur. The particular situation is particularly ominous and identifies a patient at high risk for subsequent cardiac events.

II. **Myocardial Perfusion Imaging (MPI),** A.K.A. nuclear cardiac imaging, stress nuclear techniques, Stress Thallium®, SPECT Thallium®, Stress Myoview™, SPECT Thallium® Scintigraphy, etc). These techniques use intravenous radioactive pharmaceuticals that are administered during peak physical or pharmacologic stress and are imaged in the myocardium by an external “gamma camera”. These images are digitally recorded and manipulated to create a multidimensional depiction of the myocardium. Images can be viewed on a computer screen and qualitatively and quantitatively interpreted using comparative databases of normal subjects. Three isotopes are in common use today; $^{201}$thallous chloride (Thallium®, Mallinckrodt Medical), technetium $^{99m}$sestamibi (Cardiolite®, Dupont) and technetium $^{99m}$tetrofosmin (Myoview™, Amersham
Healthcare), Dupont). Although they are all effective methods to diagnose CAD, they differ in their clinical application and usefulness.

A. *Thallium*® *(Mallinckrodt Medical)* Stress Testing (*201* thallium scintigraphy): Thallium stress testing has been around for over 25 years and remains the most studied radioisotope for MPI. Its clinical use has produced reliable diagnostic and prognostic information. For example, you could tell your patient that the “normal” thallium stress test they just had carries with it a 0.8% likelihood of a major myocardial event (death, MI, etc) for the next year!

The radioisotope *201* thallous chloride is unique in that it is extracted from the blood stream by active transport by the Na⁺/K⁺ ATPase on the myocardial cell surface. This is important because this makes it an ideal radioisotope for myocardial viability studies. Stated another way, if the cells are not alive, they will not incorporate thallium and the image obtained will contain a relative thallium “defect”.

Here’s how it works. At peak stress (either exercise or pharmacologic), Thallium® *(Mallinckrodt Medical)* is injected intravenously and is quickly extracted by the myocardial cells (seconds). If there exists a significant (usually greater than 50%) coronary stenosis over an area of myocardium, a condition of decreased myocardial blood flow will exist, and most of the thallium injected would have taken the path of least resistance. Hence, this area will have a relative paucity of the radioisotope and a perfusion “defect” will show up on the stress image. This condition will only last for several minutes, after which the thallium will redistribute itself and the perfusion heterogeneity will approach equilibrium. According to the decay characteristics of thallium and the time frame it takes for ischemia to reverse, all living heart muscle will take on a similar appearance upon subsequent imaging several (3-4) hours later. This “rest” image represents basal blood flow characteristics of the myocardium at rest. Both these images are displayed “side-by-side” in three different axes for quantitative and qualitative comparison (figure 3).
A variety of pathophysiology conditions may therefore exist for thallium MPI. It is important to acquaint yourself with this terminology, which will ultimately appear in the report. The first thing that could occur is that a defect could appear on the stress image and then completely disappear or “reperfuse” (a.k.a. “fill in”, “redistribute”, etc). This is a condition of myocardial ischemia. The second thing that could occur is that the thallium defect could persist from stress to rest. This condition usually denotes myocardial infarction (a.k.a. “scar”). Of course, all things in life (as in imaging) are not quite that black and white. A spectrum of “in between” exists. For example, not uncommonly, a perfusion defect may have a significant “fixed” appearance with a rim of reversibility. This condition is commonly seen with a myocardial infarct with significant peri-infarct ischemia. Such a clinical scenario may occur if a patient had undergone reperfusion therapy with a thrombolytic or with PTCA, or if the infarct artery was well collateralized. Similarly, if a near equal amount of fixed and reversible thallium exists, than a mixed defect (out of a lack for a better word) will result. This situation may result from a mix of infarcted and ischemic myocardium (like peri-infarct) or from a high-grade coronary stenosis subtending viable myocardium, in which the thallium has not quite redistributed itself at the time of the resting image. These latter two clinical scenarios may be discerned by either waiting until the next day and re-image the patient or by re-injecting the patient with additional thallium before the rest image is performed. Re-injection protocols identify more viable myocardium and are therefore used more frequently.
We defined the prognostic utility of a normal stress thallium above. What are the harbingers, on thallium scintigraphy that bode a poor prognosis and identify high-risk patients for cardiac events? First, the number and extent of abnormalities (either ischemia or scar), logically predict future cardiac events. Second, enlargement of the LV cavity during stress only (called **transient ischemic dilatation** or **TID**), usually identifies a patient with extensive ischemia (and extensive CAD). Put another way, it takes a large amount of ischemic myocardium to affect wall motion enough to the extent that the left ventricle enlarges. Finally, similar to TID, a large enough quantity of ischemic myocardium may result in a fall in cardiac output and an elevated pulmonary capillary wedge pressure. This causes thallium to pool in the lungs, termed **lung uptake**. This simple parameter is one of the most important predictors of cardiovascular morbidity and mortality. **I think this is misleading. I agree that increased lung uptake is an important prognosticator for morbidity and mortality but it is not specific for ischemia. CM will have and frequently will improve at rest and severe COPD will have except it persists on both the post exercise and rest images. Most labs don’t do a rest lung uptake calculation unless you ask. Not sure how or if you want to address all of this—would rework if you want me to.**

A few words must be said about pharmacologic stress testing with thallium. Lung uptake is not so predictive in patients who have pharmacologically medicated stress thallium tests. All other parameters, such as location and amount of ischemia, TID, etc are. Also, it is common to combine some sort of physical exercise with dipyridamole (kicking legs, treadmill, handgrip). This is because dipyridamole induced vasodilatation, also results in increase flow to the splanchnic circulation (i.e. liver, spleen, gut) and increase radioisotope uptake in areas next to the heart. This can result in decreased “target-to-background ratio” and artifact formation. Exercise shunts blood away from the splanchnic circulation and improves image resolution. **Cool!—I do this but never knew why before.**

Though thallium is a useful diagnostic technique, it has some drawbacks. The radioisotope, $^{201}$thallous chloride, is a weak emitter or radiation, and therefore is subject to attenuation as it exits from the myocardium on its way to the imaging camera. Several anatomic structures, two in particular, have become recognizable “artifacts” on thallium scans. The first is the left breast, which may overlies the left ventricle in a non-uniform fashion. If the breast is large enough, or strategically located on the chest wall, it may create an anterior perfusion defect which is seen both stress and rest images. This perfusion artifact usually spares the apex, so the majority of these are recognizable from true anterior wall infarcts, which usually include the apex. The second is the muscular left hemi-diaphragm, which in part, lies right over the diaphragmatic (inferior) surface of the left ventricle. This soft tissue structure, more prominent in men, may create the appearance of inferior wall thinning or scar. To make matters worse, if the patient is hyperventilating after say a lengthy jaunt on the treadmill, the diaphragm may be into different positions between rest and stress. This may create the illusion of ischemia. This latter artifact, which is commonly recognized as such, is called diaphragmatic “creep” artifact.
The most feared problem with thallium albeit rare, is a “normal” test in a patient who turns out to have triple vessel CAD or left main disease with a high grade right coronary artery lesion. In these patients, **all areas of the myocardium are under-perfused and** the scans appear to have a uniform/homogeneous uptake of thallium. Fortunately, there may be other clues to this “false negative” scan, such as TID, **increased lung uptake**, hypotension with exercise, significant ST segment changes or a clinical history of angina that will lead you to suspect severe disease.

There are other exercise-induced artifacts that are not related to soft tissue attenuation. These mainly deal with altered electrical activation of the LV. For example, in the presence of a left bundle branch block (LBBB), a septal perfusion abnormality may occur with stress-induced increases in heart rate, which is not present during rest. This gives the appearance of septal ischemia. This occurs because septal perfusion is heavily dependent on the diastolic filling period in the presence of a LBBB. As HR increases, diastole shortens more than systole leading to relative hypoperfusion to the septum. This scenario can be obviated by the use of pharmacologic/vasodilatory stress techniques, even if the patient is able to exercise. A similar parallel can be drawn in patients who are pacemaker dependent. **A very important point that I frequently forget.**

B. **Cardiolite® (Dupont) and MyoviewTM (Amersham Healthcare) stress testing** will be discussed together as each has similar physical properties and performance characteristics for MPI. 99mtechnetium is a higher energy radioisotope than thallium (140 Kev vs. 83 Kev). This increase in energy is offset by a decrease in the time it stays in the body, so patient radiation is about the same. Higher energy also translates into better image quality and less soft tissue attenuation (i.e. artifacts from breast and diaphragm). Additionally, and perhaps most importantly, the higher energy of technetium allows the camera to get more image information per study. This additional information is then “gated” with the patients ECG cycle to produce high quality LV wall motion analysis and ejection fraction determination, similar to MUGA scanning. All this, of course, with the same amount of radiation to the patient. This addition of “function” to “physiology” is an attractive attribute of Cardiolite® (Dupont) and MyoviewTM (Amersham Healthcare) stress tests.

The two technetium labeled compounds that are available, technetium 99m-tetrofosmin (Myoview™, Amersham Healthcare) and technetium 99m-sestamibi (Cardiolite®, Dupont), differ little in their performance characteristics. Rather, their use in a particular lab is dependent on availability, price and familiarity. There is some evidence to suggest that Myoview™ (Amersham Healthcare) may be preferable to Cardiolite® (Dupont) because of decreased splanchnic uptake. **We use Myoview but my partner got because it’s cheaper- now we have a legitament clinical reason.** Like thallium, they enter the cardiomyocytes in proportion to the available coronary blood flow, under conditions of stress and rest. Unlike thallium, they diffuse into the myocardium via passive diffusion, rather than active transport. Because of this physiologic characteristic, technetium labeled compounds may not be as good as thallium in determining “viability”.

**The most feared problem with thallium albeit rare, is a “normal” test in a patient who turns out to have triple vessel CAD or left main disease with a high grade right coronary artery lesion. In these patients, **all areas of the myocardium are under-perfused and** the scans appear to have a uniform/homogeneous uptake of thallium. Fortunately, there may be other clues to this “false negative” scan, such as TID, **increased lung uptake**, hypotension with exercise, significant ST segment changes or a clinical history of angina that will lead you to suspect severe disease.**

*There are other exercise-induced artifacts that are not related to soft tissue attenuation. These mainly deal with altered electrical activation of the LV. For example, in the presence of a left bundle branch block (LBBB), a septal perfusion abnormality may occur with stress-induced increases in heart rate, which is not present during rest. This gives the appearance of septal ischemia. This occurs because septal perfusion is heavily dependent on the diastolic filling period in the presence of a LBBB. As HR increases, diastole shortens more than systole leading to relative hypoperfusion to the septum. This scenario can be obviated by the use of pharmacologic/vasodilatory stress techniques, even if the patient is able to exercise. A similar parallel can be drawn in patients who are pacemaker dependent. **A very important point that I frequently forget.**

B. **Cardiolite® (Dupont) and Myoview™ (Amersham Healthcare) stress testing** will be discussed together as each has similar physical properties and performance characteristics for MPI. 99mtechnetium is a higher energy radioisotope than thallium (140 Kev vs. 83 Kev). This increase in energy is offset by a decrease in the time it stays in the body, so patient radiation is about the same. Higher energy also translates into better image quality and less soft tissue attenuation (i.e. artifacts from breast and diaphragm). Additionally, and perhaps most importantly, the higher energy of technetium allows the camera to get more image information per study. This additional information is then “gated” with the patients ECG cycle to produce high quality LV wall motion analysis and ejection fraction determination, similar to MUGA scanning. All this, of course, with the same amount of radiation to the patient. This addition of “function” to “physiology” is an attractive attribute of Cardiolite® (Dupont) and Myoview™ (Amersham Healthcare) stress tests.

The two technetium labeled compounds that are available, technetium 99m-tetrofosmin (Myoview™, Amersham Healthcare) and technetium 99m-sestamibi (Cardiolite®, Dupont), differ little in their performance characteristics. Rather, their use in a particular lab is dependent on availability, price and familiarity. There is some evidence to suggest that Myoview™ (Amersham Healthcare) may be preferable to Cardiolite® (Dupont) because of decreased splanchnic uptake. **We use Myoview but my partner got because it’s cheaper- now we have a legitament clinical reason.** Like thallium, they enter the cardiomyocytes in proportion to the available coronary blood flow, under conditions of stress and rest. Unlike thallium, they diffuse into the myocardium via passive diffusion, rather than active transport. Because of this physiologic characteristic, technetium labeled compounds may not be as good as thallium in determining “viability.”*
Technetium labeled compounds are used in similar stress test scenarios as Thallium\textsuperscript{\textregistered}. The radioactivity kinetics and biologic properties, however, afford Cardiolite\textsuperscript{\textregistered} (Dupont) and Myoview\textsuperscript{TM} (Amersham Healthcare) more leeway in patient convenience and imaging flexibility. For example, a typical imaging protocol is the so-called “rest-stress” whereby the patient has their rest image first and then later performs a stress test, which is followed by the stress image. This cuts the total procedure time almost in half from 4 hours for Thallium\textsuperscript{\textregistered} to 1.5 to 2 hrs for Cardiolite\textsuperscript{\textregistered} (Dupont) and Myoview\textsuperscript{TM} (Amersham Healthcare).

So when do we order these scans? Well, because their prognostic value is similar to thallium, one can use them interchangeably in similar clinical situations. The higher energy characteristics and ability to evaluate wall motion, however, offer the most attractive exploitation of Cardiolite\textsuperscript{\textregistered} (Dupont) and Myoview\textsuperscript{TM} (Amersham Healthcare) in certain patients. For example, a woman with a large bust-line may pose a difficult imaging challenge because a large portion of the left ventricle lies behind the left breast, attenuating any radiation emanating from the heart. This may show up on the stress and rest scan as an anterior perfusion abnormality. With technetium based compounds, this occurs to a less extent. In addition, gated this patients study also allows the interpreter to see the anterior wall moving. This would likely not occur with an anterior infarct. Therefore, the interpreter can call this study “normal” rather than “cannot rule out anterior infarct vs. breast attenuation”. This also may hold true with obese patients in general, in whom the image quality is poor and prone to artifact. Finally, the inferior “diaphragmatic attenuation” (more common in men) can be identified as such with the use of wall motion analysis (i.e. an inferior wall MI will have abnormal wall motion).

III. Stress Echocardiography (SE, A.K.A. stress echo, dobutamine echo, etc). Stress echocardiography is a welcomed addition to the stress testing armamentarium. Although relatively new in terms of the historical significance, stress echo has emerged as a reliable modality for diagnosis and prognosis of CAD. Like MPI, stress echo can be performed as an adjunct to many forms of stress testing. The most popular forms of exercise include the bicycle (upright and supine) and the treadmill.

Recall that stress echo depends on the interpreter actually seeing wall motion abnormalities develop or change during stress as an indirect indicator of CAD. Transmural ischemia is usually required to elicit such a response in the form of decease LV wall thickening. These stress induced wall motion abnormalities (WMA) are often transient, so the technician must either image them while they occur or within 60 to 90 seconds after exercise ceases. This imaging is digitally stored for review later in a side-by-side comparison between rest and stress images, as shown in figure.
Myocardial ischemia is usually defined as a “normokinetic” wall of the LV at rest becoming hypo or akinetic during stress. There have evolved various shades of gray with this definition. For example a resting wall motion abnormality, such as hypokinetic inferior wall, that does not increase in motion or thickening with stress is sometime called abnormal (i.e. ischemia). Physical stress usually produces hyperkinesia in the normal individual and a decrease in LV cavity size that can be visually appreciated. When this doesn’t occur, some believe this also to represent an abnormal response. The most challenging scenario is when significant WMA’s exist (i.e. extensive MI). The interpreter must then evaluate whether this resting wall motion abnormality improves, worsens or stays the same with stress. These distinctions require good quality imaging and experience to sort out.

Like MPI, stress echo has its procedural and artifactual limitations. It is estimated that 5-20% of studies are technically unsuitable for interpretation. These patients are usually obese and/or have COPD. Stress echocardiography also requires a great deal of patient cooperation as WMA’s are transient and imaging must be completed within 60-90 seconds before WMA begin to resolve. Interpretation or: "scoring" of stress induced WMA requires a great deal of expertise, as this technique, unlike MPI, relies on qualitative interpretation. Finally, because of the subtleties mentioned above regarding the
appreciation of WMA, SE interpretation in the presence of significant resting wall motion abnormalities is challenging. Indeed, many authors recommend other forms of adjunctive stress testing modalities to look for ischemia and viability (like MPI) in the presence of multiple resting wall motion abnormalities or dilated cardiomyopathy.

Artifacts can occur in SE, even in the best quality images. The portions of the left ventricle near the avascular mitral valve plane (basal inferior wall and septum), may appear hypokinetic at rest and with stress, leading the interpreter to call this finding “abnormal”. Similarly, images not acquired in a similar fashion (as the heart changes position in the thorax during stress), between rest and stress can lead to false abnormal tests. Fortunately, with experience, these artifacts can be minimized.

A. Bicycle and treadmill stress echocardiography are the two most common forms of exercise echocardiography. The bicycle is used almost exclusively in some stress echo centers because it allows for simultaneous imaging during exercise and it eliminates the need of expeditious patient positioning for post exercise imaging. Supine and upright bicycle protocols have been used with similar results. However, bicycle stress, as mentioned above, may lead to sub maximal stress. Most labs now use treadmill exercise because of the familiarity with treadmill protocols and the degree of stress that it produces. It should be remembered, however, that with treadmill SE, unlike bicycle SE, the images first acquired are immediate “post” exercise, rather than “peak” exercise. Regardless of which exercise echo protocol is used, the advantage of SE is that results are immediately available to the patient.

B. Pharmacologic (dobutamine) stress echocardiography can also be performed in patients who are unable to be exercised. The inotrope dobutamine has become the most commonly employed agent though dipyridamole can be used. A new agent, Arbutamine is slowly becoming available as an improved agent, which elicits a more controlled heart rate response. Vasodilators, such as dipyridamole, can also be used and has been studied the most in Europe. Dobutamine echocardiography, however, is by far the most commonly used in this country.

Dobutamine echo is very labor intensive, and at present, is only performed in the hospital. Some patients require additional pharmacologic agents to augment their HR response during dobutamine stress testing, such as atropine. Initially, the testing physician uses low doses of the drug (5 µ/kg/min). The infusion is then increased at 3 minute intervals, until a peak dose of 40-50 µ/kg/min is reached or, until target heart rate is achieved, significant ST segment or wall motion abnormalities develop, or complications (such as arrhythmias) occur.

Patients who are not candidates for dobutamine stress echo include (but are not limited to); (I) patients who do not render an interpretable image (i.e. are “technically difficult”), (ii) patients who cannot stand lying on their left side with their left arm elevated for several minutes, (iii) patients in atrial fibrillation, (iv) patients who have a history of uncontrolled SVT or ventricular tachycardia, etc. In addition, because dobutamine stress echo uses
beta agonism to increase heart rate, drugs that blunt heart rate (i.e. beta blockers, some calcium channel blockers, etc), should be withheld (if possible) for 24 hours.

C. **Prognostic variables** of stress echocardiography are similar to myocardial perfusion imaging. Stress echocardiography has similar pathophysiologic correlates to other forms of stress testing. For example stress induced ischemia affects wall motion, created LV cavity dilation. When this is seen in SE, it has a similar multi-vessel CAD implication. Also, the number of wall motion abnormalities induced by SE, has a similar meaning to multiple perfusion abnormalities in MPI; that is, multivessel CAD. A unique diagnostic attribute of stress echocardiography is the development of mitral valvular insufficiency (i.e. “ischemic MR”), which is exceedingly difficult to diagnose clinically and requires a high index of suspicion. Also, other valvular and sub-valvular (IHSS) can be studied under exercise conditions and used to gage and predict therapeutic options.

Stress echocardiography is still a younger diagnostic modality than MPI. Therefore, many more prognostic studies have been done, testing the validity of MPI’s results. A normal stress echocardiogram, however, still carries an excellent prognosis (<1.5% major cardiac event in the first year – see above discussion for MPI). This number will likely approach that of MPI as more prognostic studies are completed and the technology improves. **Actually a normal ETT (by itself) after 8 min. is assoc with only a 1% CV event rate over 4 years (0.25%/year).**

**Choosing the Appropriate Stress Test**

We have discussed the many different patient, stressor, and ischemia detector (i.e. Thallium®) variables to consider before ordering a stress test. For most outpatients with normal ECG’s and who can exercise, regular treadmill testing remains the most appropriate choice. However, many patients require a more detailed “pre-test” evaluation so as to combine optimum diagnostic accuracy and cost effectiveness. Therefore, the ordering physician must ask several questions.

1. **Why am I ordering the stress test in the first place?** Tables II and III provide a starting point to answer this question. The most common reason still remains to rule out symptomatic or occult CAD. But there are other indications that are not so straightforward. For example, stressing a patient because they want to start an exercise program and you would like to gage their “physical fitness” and hemodynamic response to exercise. In the presence of a normal ECG at baseline, this patient would do very well with a regular stress test. Another scenario could be a school buss driver with cardiovascular risk factors and a regulatory agency (or your self) would like to assess his/her cardiovascular risk/event rate. This patient would likely benefit from a stress testing employing MPI or SE as a prognostic indicator. Additionally, suppose a patient had a myocardial infarction several weeks ago and received thrombolytic therapy. A pre discharge sub maximal thallium stress revealed only a small fixed scar. This patient wanted then to embark upon an exercise program. A MPI stress test would provide you with an assessment of the extent of residual ischemia (if any)
remained from reperfusion. SE may be an alternative here if the resting wall motion abnormality was small. There are many other examples.

2. Can the patient exercise? This perhaps is the most key question to ask before choosing a specific stress test. A poor exercise effort results in little increase in HR and BP and limited clinical and prognostic information. Pharmacologic stress testing in such a patient can provide significantly more information. How can we tell which patients cannot exercise? Obviously, those patients with significant orthopedic (i.e. arthritis), neurologic (i.e. s/p CVA) and vascular disease are intuitively ideal candidates for pharmacologic stress testing. Not so obvious are the elderly or patients who are more sedentary. These latter patients require an estimate of their aerobic capacity that can be ascertained by inquiring about their activity in daily life. For example, a patient who can’t walk across the room without getting significantly dyspneic likely would benefit from a form of pharmacologic stress. Similarly, an elderly patient who tells you that he/she can walk a half a mile a day at a decent pace without tiring represents a probable candidate for treadmill stress testing. Sometimes, in such a patient just described, it may be prudent to add a complimentary imaging modality, to increase the diagnostic accuracy of stress testing, if you have doubts about their aerobic capacity. Most very elderly patients (over 80) require pharmacologic stress.

3. Is the patient’s resting ECG normal? This question is critical, to avoid unnecessary patient time and expense. For example, mentioned above is the fact that patients who undergo exercise Thallium® stress testing, in the presence of a left bundle branch block, may develop a false positive result. The ordering physician, armed with the knowledge that patients with LBBB should be stressed with pharmacologic stress or stress echo, regardless of their ability to exercise, has the power to avoid such a mistake. Similarly, patients with other examples of abnormal conduction (i.e. WPW, ventricular paced rhythms) will benefit from pharmacologic stress or stress echo. Interestingly, patients with right bundle branch block do not have this problem. The rhythm is also important. Patients with atrial fibrillation, not uncommonly, have a steep rise in their HR with exercise. Therefore, unless one wants to gage their medical rate control, stressing with dipyridamole stress probably represents the most appropriate.

4. Does the patient’s body habitus pose specific problems to imaging? Whatever the body habitus, a patient who can exercise, and who has a normal ECG, should first undergo a regular stress. However, if the patient cannot exercise or who has an abnormal ECG, than body habitus considerations become important. Anything that comes between the heart and the image (air in hyperinflated lungs in a COPD patient, adipose tissue in an obese patient), has the potential to degrade image quality, regardless of the imaging modality. For Thallium® stress testing, obese patients or patients with barrel shaped chests, may have poor image quality. Technetium labeled compounds may offer an alternative in these patients. Echocardiography will also likely be of poor image quality, unless previous echocardiograms dictate otherwise.
COPD patients, who have significant reactive airways disease, cannot easily exercise or have dipyridamole because of the possibility of provoked brochospasm. In these patients, dobutamine echocardiography is the most appropriate. I think dobutamine tech. –better counts than thal.-poor echo in COPD.

5. Do patient symptoms matter in deciding the choice of stress testing? Most forms of stress testing will yield an accurate result, regardless of the symptoms. However, dyspnea, or suspected ischemic mitral insufficiency, may be best investigated with stress echocardiography.

6. Which tests are the most cost effective? Ideally, stress electrocardiography represents the least costly of all the stress modalities discussed. This test should be offered to patients with normal ECG’s that can exercise. However, because of the patient and ECG specific considerations mentioned above, complimentary imaging modalities must sometimes be used. When either MPI or echo can be used, and both are viewed as equally diagnostic/prognostic in the patient who you believe does not pose an imaging problem (see above), than SE wins on cost grounds alone. However, factor into this, your comfort level, availability and local expertise, and you may be swayed to one or the other.

**Stress Test Examples**

Let’s try out some real clinical decision making regarding the choice of the right stress test for the right patient. Please keep in mind that some of these examples and decisions may have several possible scenarios and in these cases, the choice is my opinion, rather than scientific dogma. I will try to highlight these where applicable.

1. **A 35 year old, premenopausal woman, with atypical chest pain and a normal ECG.**

   Given the low pre-test likelihood of CAD in this patient and a higher incidence of false positive stress test in woman, one could argue why bother stressing her at all. However, for whatever reason, the appropriate first choice of a stress test would be stress electrocardiography. A normal test still has significant predictive value.

2. **A 50 year old male with a history of a large anterior wall MI and known reduced left ventricular function (EF), who develops angina.**

   The choice here highlights several advantages of MPI. The first is that this patient is likely to have an abnormal resting ECG and needs some form of imaging modality. MPI represents a more appropriate choice because Thallium®, for example, can detect if there is significant “peri-infarct” ischemia and or ischemia anatomically distant from the infarct. If Thallium® is used, I wold suggest a “re-injection” protocol to maximize viability information. In addition, stress echo likely would find significant resting wall
motion abnormalities that the interpreter would have to subjectively interpret whether they improved or deteriorated with stress (difficult).

3. A 62-year-old woman with severe asthma, a barrel-shaped chest and a large bust size.

Nothing really works well in this situation. Firstly, this patient is unlikely to walk any significant distance on a treadmill, so pharmacologic stressing is needed. As far as the most appropriate “stressor”, dobutamine has an advantage in that it will not precipitate brochospasm. Secondly, patients with this body habitus are difficult to image with either MPI or SE. If there is an adequate echocardiographic “window” (even sub costal), dobutamine stress remains the most appropriate. I have stressed these patients with quiescent lung disease, with dipyridamole technetium compounds with some success as well. **Persantine could worsen the RAD-dobutamine myoview.**

4. A 55 year old male, who jogs regularly, with the following ECG.

![ECG Image]

This is a trick question. Patients with left bundle branch block have a high incidence of septal and, at times, anterior perfusion artifacts that resemble ischemic changes. Therefore, even though this patient can exercise to an adequate heart rate, one should still choose pharmacologic MPI (i.e. dipyridamole Thallium® or Tech). SE remains an alternative, but requires a keen eye to decipher septal wall motion changes.

4. A 40 year old, 349 lb. male with an intermediate probability of CAD.

I chose this weight because most treadmills have a warranty weight limit of 350 lbs., so he could still be stressed. Any way, any imaging modality is likely to have difficulty
with this patient’s body habitus. MPI with technetium based compounds, in my opinion and/or if the patient has a “technically limited” echo by history, is a good first choice. SE is likely not to render quality images in this patient.

5. **A 44 year old male runner with a history of WPW who has a normal baseline ECG.**

Because WPW may appear during the test, it is wise to perform this test with complimentary imaging. Either SE or MPI would be acceptable. **WPW-B simulates LBBB and may give you a false positive with exercise with MPI.**

6. **A 48-year-old commercial airline pilot with hypertension.**

Given the prognostic information needed here, a regular stress electrocardiogram may not suffice. Many airlines (and insurance companies) recommend MPI because of the amount of literature supporting its prognostic value. SE could also be used in this scenario.

7. **72- year-old woman with severe osteoarthitis.**

Pharmacologic stress (MPI with dipyridamole or dobutamine echo) is the best choice.

8. **65 year old male diabetic with a history of a severe dilated cardiomyopathy.**

SE would unlikely provide diagnostic or viability data given the severity of the resting wall motion abnormalities. MPI with exercise or stress, depending on the functional capacity of the patient, remains the best choice. **Could be a spot for Cardiopulmonary ETT-can also be done with MPI.**

**Frequently Asked Questions (FAQ’s)**

1. **Q. Which type of stress test should I order?**

A. The type of stress an individual should/can have is outlined in detail in the text (please see text and algorithm). Many (variables should be considered before choosing a specific stress testing modality (see text), including, but not limited to; gender, age, cerebrovascular or orthopedic disability, resting ECG, etc).

2. **Q. What instructions do I give my patients for a specific type of stress test?**

A. There are general and specific recommendations regarding pre stress test preparation. These can be obtained in written format from stress testing centers (i.e. our office @ 234-3332 or the hospital Cardiovascular Department, 267-0700, ext 3160). In general, patients should not eat, drink or smoke 2½ hours prior to
testing (NPO after midnight for pharmacologic stress testing – i.e. Persantine® (Dupont) and dobutamine). They should wear loose and comfortable clothing and footwear (preferable sneakers but no elevated heals). They should be emotionally incentivised to walk on the treadmill (if applicable) and to achieve their age specific target heart rate (“the more you walk, the more information we get about your heart”).

3. Q. Which medications do I stop prior to a stress test?

A. This is a very commonly asked and complex question. The simple, short answer is that it depends on the reason for doing the test. For example, if you have ordered the test to find out the extent of CAD/ischemia the patient may have, attempting to stop or decrease the anti-anginal medications may be desirable. Similarly, in a patient who has known CAD and you would like to test his new ant-ischemic drug regimen, then stress testing using all the patients’ usual medications is the way to go.

Caution! Anti-anginal medications cannot be just stopped in all patients. This may be dangerous to do if you have a patient who experienced recent unstable angina who was “stabilized” with aggressive medical management and now you would like to test this regimen. In such a patient, you would be wise to either postpone the test, cath the patient or perform the test on all the prescribed medications. It also follows that many patients who do not have recent unstable angina can have their medications adjusted. This may be accomplished, for example, by holding their medications the morning of the test.

Patients who are on medications that affect heart rate (beta-blockers and some calcium channel blockers) or the ECG response to exercise (i.e. digoxin or diuretics) should have their medications withdrawn at least 24 hours prior to exercise stress testing. If the patient has atrial fibrillation, it may have been wise to perform pharmacologic stress testing anyway unless you were testing the rate response characteristics of the medications in which case you would not have stopped them anyway. Patients should be told that they should report a change in symptoms or symptoms compatible with unstable angina if this strategy is to be recommended. Patients should also be appraised of what to do if they experience symptoms of acute coronary syndromes. Nitroglycerin should be prescribed (if not already done) and its use thoroughly explained to the patient.

4. Q. What does an “equivocal” stress test mean?

A. This term is used mostly with MPI. Given the nature of this technique, perfusion defects may occur that are so strange that one cannot tell if they are artifactual or real. If the stress electrocardiogram is normal, than one may be swayed into thinking the former, and visa-versa. However, often this imaging
5. **Q.** What do I do if the stress electrocardiogram was “inconclusive” or “indeterminate”?  

A. A stress test can be conclusively normal or abnormal depending on several factors. These include, but are not limited to, attainment of an 85% age predicted HR response, and the quality of the resting/exercise ECG or complimentary imaging. This conclusion usually applies only to a regular stress electrocardiogram (though imaging has its wimpy conclusions too, see question 4 above). If the patient has walked for 9 minutes and has an “inconclusive” heart rate response, that’s still better than if he went only for two minutes. **I agree-duration of exercise is probably the best prognosticator.**  

When this conclusion is encountered with an ETT the test should be repeated in conjunction with an imaging modality (MPI or echocardiography). Even if the repeat stress electrocardiogram is “inconclusive, the added information from the imaging modality will have clinical and prognostic value.  

6. **Q.** What does it mean that my patient had a “hypertensive” blood pressure response to exercise?  

A. Systolic blood pressure should rise 10 to 20 mm Hg each 3 minutes stage of a Bruce protocol. Diastolic pressure should fall or remain the same. Any other rise in BP outside these ranges qualifies as a “hypertensive” response. The most common occurrence, obviously, is in a patient with high blood pressure. If your patient does not have a clinical history of high blood pressure, they may be undiagnosed. This phenomenon also identifies a patient with a high predisposition for the development of high blood pressure and one should counsel your patients accordingly. If you patient regularly exercises to this intensity level, regardless of whether they have a diagnosis of hypertension, one should suggest a decrease in the intensity, or more aggressive treatment.  

7. **Q.** What does it mean that my patient had an abnormal ECG (ST segment) response but no symptoms of angina during the test?  

A. There are two possible answers to this. The first is that it represents a “false positive” test. There may be some clues that this is the case such as late onset and early offset ST segment changes, concurrent exercise induced hypertension, etc. Remember, the most common reason is that the patient has CAD and other complementary stress testing modalities may be needed. The second explanation is that your patient has “silent ischemia” (i.e. not uncommon in diabetic patients). Silent ischemia still identifies a patient with
CAD but may carry with it a slightly better prognosis that symptomatic ischemia.

8. **Q.** What significance is exercise induced or related ventricular ectopy?

   **A.** This has been a debated issue for quite some time. Patients who have any sort of ventricular ectopy are at a higher cardiovascular risk per given comparable risk factors, etc. If this ectopy was never clinical identified and was provoked with stress testing, than this patient is at a higher (slightly) cardiovascular event rate risk. This is especially true if the ectopy is ventricular tachycardia, which may or may not be related to CAD. Ventricular ectopy that is “overdriven” at higher heart rates may be more benign. **The prognosis of ventricular ectopy is determined by “the company that it keeps”** (i.e. What is the LV function like? What is the clinical status of the patient?)

9. **Q.** Should I be concerned if my patients have a fixed perfusion defect on MPI compatible with either breast attenuation or diaphragmatic attenuation artifact?

   **A.** Yes. Being compatible with an artifact does not rule out that such a fixed defect represents a tight coronary stenosis or a previous infarct. More robust adjunctive technologies (such as wall motion analysis and quantitative references) make it more likely that a given defect is artifactual. Often the interpreter will indicate this either directly (in the body of the report) or indirectly in the conclusion using suggested reporting formats (i.e. “probably normal”).

10. **Q.** What do I do if the stress test is positive?

    **A.** This seems like a silly question, but its not. The question can best be answered by including the pre test (clinical, physical and ECG) information, in the post test analysis. For example, if your pre test probability was low that your patient had CAD than you may want to confirm or refute the result with complementary testing (i.e. performing stress imaging, if the stress ECG was positive). Remember, the most common reason that the test is abnormal is because the patient has CAD!

    A positive result may also confirm your clinical suspicion that a particular patient has CAD/angina. You, and that patient, may also have decided on medical therapy only and serial stress tests (using the same modality) are providing prognostic and/or therapeutic information. A positive test may also confirm a clinically suspected diagnosis (CAD) in a patient in whom medical therapy is appropriate. In this patient, a search for non-cardiac diagnoses can now stop.
Certainly, something can be said for the degree of positivity, as was mentioned during the discussion of MPI and stress echo. Those patients with a “high risk” stress test should **be treated aggressively and have further investigation with cardiac catheterization and appropriate intervention (CABG/PTCA/stent)** as indicated. These treatment modalities can improve the patients’ quality and duration of life.

11. **Q.** How frequently should I order a stress test in a patient who has had an MI, CABG or PTCA?

**A.** The answer to this question is in evolution. If the patient is in, or qualifies for, cardiac rehab, then stress testing may be required by their insurance company/Medicare (yes, you read that right). Outside of this circumstance, I refer the reader to the document covering these topics. If it has been a recent MI then either stress testing in the hospital or, sub-acute, as an outpatient, may be needed (please see reference). If stress testing is to be done, complimentary imaging is advisable to garner the most information regarding viability, extent of CAD, prognosis, etc. MPI is my personal choice (i.e. Thallium® with re-injection), but stress echo may be appropriate, especially if the infarcted area is not too large and resting wall motion is acceptable for dynamic analysis.

The recommendations concerning CABG and PTCA are even more nebulous. (See reference) Two points should be made, however, regarding these two clinical scenarios. The first is symptoms. If the patient has symptoms suggestive of ischemia, then stress testing is indicated. The asymptomatic patient can be stressed if there is sufficient concern for silent ischemia (i.e. diabetic patient, aggressive or uncontrolled risk factors, PTCA(s) involving the proximal LAD or multivessel PTCA with a large area of myocardium at risk). Even the guidelines do not have a hard and fast answer, but that is my approach. The second point is the type of stress testing. Complimentary imaging (MPI or stress echo) is most useful since it provides the “extent” information needed to re-evaluate these patients for further invasive testing verses medical therapy.

12. **Q.** What should I do if the patient requests a stress test?

**A.** Patients not uncommonly approach physicians to request stress tests for a variety of reasons. In my experience, this usually follows a cardiovascular event (death, MI, CABG) of a family member or close friend. Sometimes, patients are savvy enough to request a stress test for an appropriate reason such as suspicious symptoms or desire to start and exercise program. The latter is recommended for patients over 40 years of age.

Physicians should counsel patients very carefully in this situation. Specifically, a thorough evaluation of a patients “pre test” probability should be performed.
In those patients who have a low pre test likelihood of CAD, patients should be counseled that an abnormal result might still mean that CAD is less likely and made lead to further, unnecessary testing (i.e. from a false positive result). If stress testing is appropriate, then all the rules and conditions we discussed certainly apply.

**References**


**CME Exam**

1. Which of the following variables is important in the choice of cardiac stress testing?
(a) the 12 lead ECG
(b) the history
(c) the physical examination
(d) the presence or absence of cardiovascular risk factors
(e) all of the above

2. Which of the following is not a determinate of myocardial oxygen consumption, or “demand”?

(a) heart rate
(b) blood pressure
(c) right atrial pressure
(d) contractility
(e) LV wall thickness

3. Exercise stress testing induces a higher increase in coronary blood flow than pharmacologic stress with dipyridamole (circle the best answer).

True False

4. All of the following are well recognized methods of detecting myocardial ischemia except…

(a) rise in pulmonary capillary wedge pressure
(b) T wave changes on a stress electrocardiogram
(c) flow heterogeneity measured by a perfusion abnormality on T
(d) Thallium stress test
(e) wall motion abnormality as detected by stress echocardiography
(f) ST segment changes on a stress electrocardiogram

4. Treadmill exercise provides a better aerobic stress on the cardiovascular system (circle one)

True False

5. A patient with a baseline 12 lead ECG showing a right bundle branch block always requires a complementary imaging modality (i.e. stress echo or MPI). Circle one.

True False

6. Which of the following is not a reason for a false positive stress electrocardiogram?

(a) patient is taking digoxin
(b) patient has baseline LVH with repolarization changes  
(c) patient has coronary artery disease  
(d) patient has a baseline left bundle branch block  
(e) a female patient with a low pretest possibility of CAD

7. Myocardial perfusion imaging using $^{201}$thallous chloride, is an important technique for detecting ischemia by observing changes in LV wall motion.

True  False

Please match the MPI terminology with the underlying pathophysiologic condition.

(a) reversible defect  
(b) fixed defect  
(c) mixed defect  
(d) transient ischemic dilation  
(e) abnormal lung uptake  
(f) peri-infarct ischemia  
(g) re-injection protocol

8. ___ a healed myocardial infarction

9. ___ multi-vessel or left main CAD

10. ___ elevated pulmonary capillary wedge pressure caused by a reduced EF or exercised induced left ventricular dysfunction

11. ___ a “border zone” or reversibility around a fixed defect

12. ___ a 90% lesion in a main coronary artery

13. ___ additional Thallium® given just before delayed (rest) imaging

14. ___ a post thrombolytic catheterization revealing a 75% lesion in a coronary artery supplying an area of myocardium which is half infarcted

Please match the MPI modality with the appropriate description

(a) $^{201}$thallous chloride (Thallium® (Mallinckrodt Medical))  
(b) 99mtechnetium sestamibi (Cardiolite® (Dupont))  
(c) 99mtechnetium tetrofosmin (Myoview)  
(d) all of the above  
(e) (b) and (c)  
(f) none of the above
15. ___ taken up by the myocardium by active transport via the Na+/K+ ATPase
16. ___ the preferred imaging agent to detect viability
17. ___ can be used with IV dipyridamole for pharmacologic stress testing
18. ___ is (are) radioactive
19. ___ is (are) the preferred agent(s) for use with very obese patients
20. ___ a “normal” test result with this (these) agent(s) confers a myocardial event rate of less than 0.8% in one year
21. ___ an abnormal result with this (these) agent(s) always signifies CAD

Match the following artifacts with the most appropriate statement.

(a) breast attenuation artifact
(b) diaphragmatic artifact
(c) diaphragmatic creep artifact
(d) all of the above
(e) none of the above

22. ___ is a more prominent artifact in men than in women
23. ___ is related to hyperventilation and seen in patients who exercise vigorously
24. ___ is a more prominent artifact in women than in men
25. ___ is (are) related to soft tissue attenuation of radioactivity
26. ___ can often be identified as an artifact by “gated” wall motion analysis with technetium labeled compounds
27. ___ is (are) related to a right bundle branch block

Match the MPI technique with the most appropriate statement

(a) exercise Thallium® stress test
(b) dipyridamole (Persantine®) Thallium® stress test
(c) exercise Myoview™/Cardiolite® stress test
(d) dipyridamole (Persantine®) Myoview™/Cardiolite® stress test
(e) all of the above
28. ___ patients must fast for a specified period of time before the test
29. ___ lung uptake of the radiopharmaceutical is an important prognostic marker
30. ___ should be preferentially used in patients with a left bundle branch block
31. ___ can be used to diagnose myocardial ischemia
32. ___ should be preferentially used in patients who are likely to have soft tissue attenuation artifacts
33. ___ is (are) able to give you wall motion analysis and ejection fraction information for the same amount of exposed radiation
34. ___ a normal stress test rules out the possibility of CAD
35. All of the following forms of stress echocardiography are in clinical practice except…
   (a) upright bicycle
   (b) treadmill
   (c) adenosine
   (d) dobutamine
   (e) arbutamine
   (f) none of the above

   Please match the stress echo technique with the appropriate clinical scenario

   (a) bicycle stress echo
   (b) treadmill stress echo
   (c) dobutamine stress echo
   (d) (a) and (c)
   (e) all of the above
   (f) none of the above

36. ___ this exercise modality is associated with the best HR/BP response
37. ___ this labor intensive modality is done only at Memorial Hospital
38. ___ is (are) acceptable forms of stressing a patient to evaluate chest pain
39. ___ of the three, may be the preferred method of stress echo in patients with asthma/COPD

40. ___ imaging may be performed during stress

41. ___ a normal test is associated with an excellent prognosis over the ensuing year

42. All of the following are contraindications for stress echocardiography except…
   (a) patients who have a history of technically poor quality echocardiographic images
   (b) left bundle branch block
   (c) patients with a history of atrial fibrillation with a rapid ventricular response
   (d) patients with a history of exercise induced ventricular tachycardia
   (e) patients who cannot lie on their left side and raise their left arm

43. Which of the following are potential limitations of stress echocardiography?
   (a) patients with significant resting wall motion abnormalities pose diagnostic challenges for detecting myocardial ischemia
   (b) imaging must be done within 60-90 seconds after exercise
   (c) 5-20% of studies are unsuitable for interpretation
   (d) falsely abnormal resting wall motion abnormalities may rarely occur near the avascular mitral valve plane
   (e) all of the above

44. Treadmill stress echocardiography may performed on patients with left bundle branch block.

   True     False

45. Results from a stress echocardiogram take several hours to generate.

   True     False

46. Beta-blockers (and other drugs that slow heart rate) should be withdrawn (under supervision of a physician) for a period of time before dobutamine stress echocardiography.

   True     False

Match the wall motion abnormality with the underlying suspected clinical process.

   (a) resting normal wall motion $\rightarrow$ hyperdynamic motion with stress
   (b) resting normal wall motion $\rightarrow$ hypo to akinetic motion with stress
   (c) resting hypokinesia to akinesia $\rightarrow$ remains hypo to akinetic with stress
(d) resting hypokinesia to akinesia $\Rightarrow$ becomes normo to hyperkinetic with dobutamine
(e) LV cavity normal size $\Rightarrow$ decreased cavity size
(f) LV cavity normal size $\Rightarrow$ increased cavity size

47. ___ exercise induced LV dysfunction
48. ___ myocardial ischemia
49. ___ myocardial infarction
50. ___ normal LV cavity response to exercise
51. ___ normal wall motion response to exercise
52. ___ an indication of viable myocardium

Match the most appropriate, cost-effective stress testing modality with clinical scenario (more than one may be correct)

(a) stress electrocardiogram
(b) Thallium® stress test
(c) Persantine® Thallium® stress test
(d) Myoview™ stress test with wall motion analysis
(e) Persantine® Myoview™ stress test with wall motion analysis
(f) stress echo with treadmill
(g) dobutamine stress echo

53. ___ a 36 year old male with a normal ECG
54. ___ a 72 year old female with a cane and a normal ECG
55. ___ a 42 year old male track star with a LBBB
56. ___ a 56 year old female with significant asthma
57. ___ a 45 year old morbidly obese male who can’t walk
58. ___ a 32 year old woman with resting ST-T wave changes
59. ___ a 44 year old male with a RBBB
60. ___ a 64 year woman with atrial fibrillation
61. ___ a 57 year old man with a pacemaker
62. ___ a 52 year old male with a history of a CABG

63. ___ a 45 year diabetic, female bus driver

Draft 1.5: August 23, 1999