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Thallium 201 Scintigraphy

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The radioactive isotope thallium 201 behaves physiologically as a potassium analog, and when injected intravenously accumulates rapidly within the cells of many organs. Uptake of the isotope reflects both regional perfusion and sodium-potassium pump activity. The radionuclide emits 80 keV x-rays which are suitable for scintillation camera imaging.

The main clinical application of ^{201}Tl scintigraphy has been in myocardial imaging. Abnormal uptake of the isotope results in a cold spot on the myocardial image. In patients with coronary artery disease, the differentiation of ischemic and infarcted myocardium is made by comparing images obtained after injecting the radionuclide at the peak of a maximal exercise test with those obtained after injection at rest. Abnormalities due to ischemia usually are seen only on the stress image whereas fixed defects in both rest and stress studies usually indicate areas of infarction or scarring. Some investigators believe that redistribution images obtained four to six hours after stress injection (without administering further ^{201}Tl) give the same information as a separate rest study. The sensitivity of stress imaging for detecting significant coronary disease is of the order of 80 percent to 95 percent, though computer processing of the images may be necessary to achieve the higher figure. The prediction of the extent of coronary disease from ^{201}Tl images is less reliable. An abnormal ^{201}Tl image is not entirely specific for coronary artery disease and the likelihood of an abnormal image being due to this diagnosis varies according to the clinical circumstances.

The main clinical value of ^{201}Tl myocardial imaging is likely to be in the noninvasive screening of patients with atypical chest pain or with ambiguous findings on stress electrocardiographic tests. It has also proved useful in studying patients with variant angina or following a coronary bypass operation. It is doubtful whether the technique is clinically helpful in most patients with suspected or established acute myocardial infarction.

Imaging of organs other than the heart with ^{201}Tl has received much less attention but has been reported in patients with peripheral vascular disease and various primary and secondary neoplasms.

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IN 1941 Noonan and co-workers[1] showed that following intraperitoneal injection of potassium 42 into rats, there was rapid accumulation of radioactivity in the myocardium. In the early 1950's, work by Burch and associates[2-6] showed that radioactive rubidium could be regarded as an analog of potassium in tracer studies, though the behavior of the two elements was not identical. Similar properties were also described for radioactive cesium.[2]

The demonstration by Burch and colleagues of rapid myocardial uptake of rubidium 86 suggested to Carr and colleagues[7] the possibility of showing the myocardium by photoscanning after the administration of the radioactive isotope. They confirmed the feasibility of imaging the beating myocardium of dogs using ^{86}Rb and a rectilinear scanner, but found that areas of decreased isotope uptake due to experimental myocardial infarction could be identified reliably only after excision of the heart.[7] They considered ^{86}Rb unsuitable for in vivo imaging of the myocardium and turned their attention to cesium 131. Using this tracer, they reported the first successful imaging of normal myocardium in humans, and also showed that the images were abnormal in patients with acute myocardial infarction.[8]

Between 1964 and 1975 a variety of radioactive isotopes of potassium, rubidium and cesium were examined as possible myocardial imaging agents; however, for physical or biological reasons none was suitable for widespread use.[9] In 1976, however, the introduction of thallium 201 made myocardial imaging generally feasible,[10] and this has now become established as a clinically useful tool for investigation.

The heavy metal thallium was discovered and named in 1861 by the English chemist Sir William Crookes, the name being derived from the Greek word *thallos* (a budding twig), "a word which is frequently employed to express the beautiful green tint of vegetation and which I chose on account of the green line which it communicated to the spectrum, recalling with particular vividness the fresh colour of early spring."[11]

Physical and Biologcal Properties of Thallium

Thallium (atomic number 81) belongs to group III of the periodic table whereas potassium, rubidium and cesium are group I elements. However, in 1960 Mullins and Moore, noting that the univalent thallium cation had a crystal radius between that of potassium and cesium, felt that their physiological properties might be similar and showed that this was so in the isolated frog sartorius muscle preparation.[12] The biological similarities between potassium and thallium were confirmed by Gehring and Hammond in rabbit erythrocytes[13] and in studies in rats and dogs.[14] The first suggestion of thallium as a potassium analog for use in nuclear medicine was by Kawana and co-workers[15] in 1970. Using thallium 199, they showed the possibility of imaging the human myocardium; however, the images were of poor quality because of high energy gamma rays present, which caused excitation of the lead in the collimator. They suggested that thallium 201 might be more suitable. This was eventually produced from Brookhaven National Laboratory[10] and, in the form of a sterile solution of carrier-free thallous chloride in saline, is now the standard agent for noninvasive imaging of normal myocardium.

Thallium 201 has a physical half-life of 73.5 hours and decays by electron capture to mercury 201, emitting gamma rays of 137 and 167 keV. The ^{201}Hg then decays with emission of 65 to 82 keV x-rays. The gamma rays have suitable energies for scintillation camera imaging but are present in low incidence so that the use of the mercury x-rays is usually recommended. Atkins and colleagues[16] found that the count rate obtained using the x-rays was seven times greater than that with the gamma rays.

The mercury x-rays are not ideal for imaging. The relatively low energy leads to substantial tissue attenuation. In addition, the intrinsic resolution obtained with the scintillation camera using ^{201}Tl may be as much as 50 percent less than that with technetium 99m (6.7 mm versus 4.7 mm in one study[17(pp73-74)]).

Following intravenous injection, the uptake of ^{201}Tl occurs rapidly, with maximal myocardial uptake at rest occurring some 5 to 15 minutes after injection in different species.[16,18,19] The first pass extraction of the isotope from coronary arterial blood is of the order of 85 percent.[20,21] The myocardial-to-liver activity ratio obtained with thallium 201 is superior to that obtained with rubidium and cesium radionuclides,[22,23] and also to that with potassium 43.[19] Thallium is also superior to potassium radioactive isotopes in showing longer myocardial retention[19] so that multiple images are easier to obtain. Approximately 4

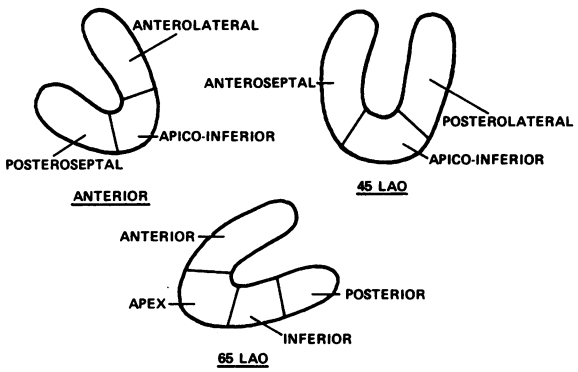

Figure 1.—Diagram of left ventricular regions seen in some standard projections for thallium 201 imaging. Note superimposition of apical and inferior myocardium on anterior and 45° left anterior oblique (LAO) projections.

percent of the injected dose of ^{201}Tl is taken up by myocardium.[10,24]

The myocardial uptake of ^{201}Tl, like that of the other potassium analogs, reflects two main factors —the regional myocardial blood flow and the metabolic integrity of the myocardial cells. In studies in animals there is good correspondence between decrease in coronary flow during experimental coronary occlusion and decrease of myocardial ^{201}Tl.[22] During coronary hyperemia, myocardial uptake of the isotope increases but to a lesser extent than myocardial blood flow.[22,24] The actual uptake of thallium by the myocardial cell is an active process which appears to use the adenosine triphosphatase-dependent sodium-potassium pump,[12-14] though there is some evidence to suggest that the mechanism of thallium uptake is not identical to that of potassium.[25] There is conflicting evidence at present as to whether reduced myocardial perfusion results in decreased myocardial ^{201}Tl uptake in the absence of myocardial ischemia, that is, disordered metabolism.[26-28]

Because myocardial uptake of potassium tracers is dependent on the integrity of each myocardial cell, metabolic effects may influence the trapping. Studies in animals have shown that hypoxia in the absence of any flow change will decrease the myocardial extraction rate of ^{201}Tl, and that metabolic acidosis has a similar effect.[20] Metabolic alkalosis, by comparison, augments myocardial ^{201}Tl uptake.[20,29]

The influence of some cardioactive drugs on ^{201}Tl uptake by the myocardium has also been studied. Two studies have reported depression of ^{201}Tl uptake after intravenous injection of propranolol or a cardiac glycoside,[24,30] though a third study failed to confirm this.[20] The administration of these drugs does not significantly degrade the quality of the in vivo myocardial image.[24] Insulin and glucose have been reported to cause substantial increase in myocardial uptake of potassium, rubidium and cesium,[3] but this effect has not been confirmed with thallium.[20] The myocardial uptake of ^{201}Tl is also increased following intravenous administration of dipyridamole, perhaps as a result of the coronary hyperemia that this drug induces.[24]

Methods

Myocardial imaging is carried out shortly after intravenous injection of thallous chloride Tl 201. The usual dosage used is limited to 1.5 to 2 mCi because of radiation dosimetry considerations (see below).

Images are obtained with a modern, standard field of view scintillation camera, though large field of view cameras can also be used. The spectrometer of the camera is centered over the 65 to 82 keV x-rays, usually with a 20 percent window. The collimation most frequently used is the general purpose, low-energy, high-resolution collimator, and this gives satisfactory images in most circumstances.[32] Acceptable images can also be obtained using a high-sensitivity collimator. Increased resolution can be obtained using a pinhole collimator but the low sensitivity precludes its general use.[32] Converging collimators have also been used, though there is some evidence that their ability to detect lesions is poor.[32] Recently, a multipinhole collimator system has been described which allows reconstruction tomography of the myocardium using ^{201}Tl.[33] This technique is still under investigation, but early results suggest a clinically significant improvement in the images.[34]

In most centers, images containing 250,000 to 500,000 counts are obtained, requiring some five to ten minutes for each image. Usually the images are "ungated," that is, they are recorded during all phases of the cardiac cycle and, thus, are blurred by cardiac motion. Gating the gamma camera by the patient's electrocardiogram (ECG) allows this blurring to be eliminated but prolongs the imaging time. There may, however, be important improvement in lesion detection with ECG gating.[35,36]

In a standard ^{201}Tl study, the principal contri-

bution to the left ventricular image is made by areas of myocardium that are perpendicular to or almost perpendicular to the front of the gamma camera.[37] Thus, by obtaining multiple projections, it is possible to view the different areas of the myocardium separately. These include an anterior view and one or more left anterior oblique views, as well as possibly a left lateral image. The images are usually obtained with the patient in a supine position, but two recent studies suggested that it is important to obtain the left lateral view with the patient lying on his right side. This is to avoid false posteroinferior defects being produced by attenuation of the low energy x-rays by the diaphragm.[38,39]

The precise anatomical areas of the left ventricle seen in any projection will vary somewhat depending on the orientation of the ventricle in the chest. Figure 1 shows one accepted system of nomenclature.

The two principal types of thallium 201 myocardial imaging studies are those carried out after injection of the tracer with the patient at rest and those after the tracer has been injected at the peak of a stress test.

Rest imaging should be done after the patient has been sitting quietly for a time. Rest images are characterized by a relatively poor ratio of myocardial-to-background activity with noticeable splanchnic, particularly hepatic, uptake. It is possible to reduce hepatic activity by injecting the patient in an upright position[40] and after some hours of fasting.[16,41]

Early studies with potassium analogs other than ^{201}Tl showed that acute myocardial infarction or myocardial scarring due to previous infarction could be shown by myocardial imaging after injection of the tracer at rest.[8,42-44] Such rest studies, however, usually showed no abnormalities in patients with coronary disease but no infarction. This is not surprising. As discussed above, regional myocardial perfusion is one of the two principal determinants of myocardial uptake of potassium analogs, and various studies using inert gas washout techniques have shown that regional myocardial perfusion may not be significantly changed at rest in patients with coronary disease and no infarction.[45,46] A very different circumstance exists during stress, however, as indicated by the elegant experiments carried out by the Seattle group. Both in animal and clinical studies they have shown that whereas myocardial perfusion distal to a coronary stenosis remains normal at rest until the lesion occupies 85 percent to 90 percent of the luminal diameter, during stress the normal augmentation in myocardial blood flow is decreased distal to stenoses of 50 percent or more.[47-49] The development of myocardial perfusion abnormalities during stress in patients with coronary artery disease, for whom results at rest were normal, has been confirmed using inert gas washout techniques.[50]

The radionuclide detection of relatively decreased perfusion distal to significant coronary artery occlusions during exercise predated the above investigations. In 1973 Strauss and coworkers[51] introduced the concept of stress myocardial imaging. They found that if ^{43}K was injected intravenously at the end point of a symptom-limited exercise test, abnormal myocardial images could be obtained in patients with coronary artery disease in whom rest myocardial images were normal.

The technique of stress imaging is now widely used. The patient exercises either on a bicycle ergometer or treadmill, under ECG control and with full resuscitation facilities available. When a standard exercise end point, such as chest pain, fatigue, maximal predicted heart rate or ST segment changes, is reached, the isotope is injected intravenously as a bolus and the patient is asked to continue exercising for at least 30 to 60 seconds more to allow fixing of the ^{201}Tl by the myocardium in its stressed state. Imaging then proceeds in the standard fashion. If imaging of the patient is done on two occasions after injection at the same exercise end point, the results are highly reproducible.[52]

Two pharmacological interventions have recently been described as alternatives to exercise stress testing. The intravenous injection of dipyridamole produces coronary vasodilatation and increased coronary artery blood flow[53] with increased myocardial uptake of ^{201}Tl in experimental animals.[24] Pharmacological dilatation of the coronary arterial tree using dipyridamole may be a satisfactory alternative to exercise stress testing for ^{201}Tl myocardial imaging in humans.[54,55] Imaging during an intravenous infusion of isoproterenol hydrochloride (Isuprel) has also been suggested as an alternative to exercise imaging.[56]

In 1977 Pohost and colleagues described the technique of redistribution imaging.[57] If the isotope is injected during stress, the images obtained

in the next 30 to 45 minutes reflect the distribution of uptake during stress. Over the next four to six hours, however, the thallium redistributes within the myocardium so that a delayed image obtained at that time, without further injection of tracer, is more a reflection of functional myocardial cell mass than myocardial perfusion.[58] Thus, it has been suggested that an ischemic area of myocardium will be abnormal on the images immediately following exercise but normal on the delayed images, whereas areas of infarction will be abnormal on both sets of images.[57,59] The value of delayed images following exercise in replacing separate rest studies will be discussed further in the section on coronary artery disease.

Interpreting Thallium 201 Myocardial Images

A variety of methods exist for interpreting ^{201}Tl myocardial images. Initial studies used unprocessed images recorded from the camera oscilloscope onto Polaroid or x-ray film, and in many centers this method is still used. Another approach has been to use computer-generated images, either in black and white or in color, and apply uniform background subtraction or contrast enhancement to them. Some observers have claimed that use of such processing improves the accuracy of interpretation of ^{201}Tl images,[60] but others believe it merely increases sensitivity at the expense of specificity.[61,62] A refinement of background subtraction is "interpolative background subtraction," which makes allowance for the differing background contribution in different tissues surrounding the myocardial image.[63]

Various methods of quantitative analysis of myocardial images have also been described recently. Attempts have been made to compare myocardial uptake of the radionuclide with activity in other organs.[64,65] However, such methods have been frustrated by the many factors which may alter such ratios. For example, hepatic activity is increased by a recent meal[16,41] or by injecting the patient when supine,[40] while lung uptake is increased and prolonged in smokers[66] and is frequently increased in multiple-vessel coronary artery disease after exercise—perhaps due to impaired left ventricular function.[67]

The alternative approach to "quantitation" has been to measure relative activity in different areas of the myocardium, and a variety of techniques have been described.[61,68-71] Use of such computer processing has not yet been clearly shown to produce significant improvement in interpretation of myocardial images when compared with visual analysis, but there have been some promising preliminary reports.[61,69,72]

The Normal Thallium 201 Myocardial Image

The normal left ventricular myocardium is seen on the ^{201}Tl image as a horseshoe shape, or sometimes a doughnut, of relatively uniform activity, with a central colder area corresponding to the left ventricular cavity (Figure 2). Even in the normal myocardium, uptake is not entirely uniform,[18,40,70,73] with the nonhomogeneity being more pronounced in rest than in stress studies.[40,70] The apex frequently appears as an area of thinning on normal images,[40] and decreased uptake is usually seen at the base of the heart at the sites of valve insertion.[40] In addition to more homogeneous cardiac uptake, the stress study is characterized by a higher myocardial-to-background activity ratio when compared with rest images.[40]

Visualization of the right ventricle is unusual on the rest image,[40] and if seen, suggests right ventricular overload or hypertrophy.[74,75] However, the right ventricle is frequently visualized on normal stress images (Figure 2).[40]

Safety of Myocardial Imaging

Like most heavy metals, thallium is a toxic substance, and serious (sometimes fatal) side effects to the central nervous system and gastrointestinal tract resulted from its use as a depilatory agent in the treatment of ringworm of the scalp.[76] Thallium salts have been used for homicidal poisoning both in fiction[77] and in fact.[78] Therapy for thallium poisoning is essentially supportive, though excretion may be promoted by potassium salts.[79]

The minimum lethal dose of thallium in humans is thought to be 8 to 12 mg per kg of body weight,[80] though nonfatal side effects have been reported with doses as low as 0.1 mg per kg.[18] Thallium 201 supplied for myocardial imaging is virtually carrier-free and the dose administered during diagnostic studies using 2 mCi of the radionuclide has been calculated to be of the order of 0.07 to 0.15 ng per kg of body weight,[73] so that there is a very large margin of safety, even when repeat studies are done. As yet there have

been no reports of ill effects following administration of this radioactive pharmaceutical agent.

The whole body radiation dose from ^{201}Tl is in the range of 0.07 to 0.24 rads per mCi.[16,18,58,81,82] The kidney is the critical organ, receiving a radiation dose of 0.39 to 1.17 rads per mCi. The renal medulla accumulates considerably more ^{201}Tl than the cortex.[18,24] The radiation dose sustained by the kidney during myocardial imaging is unlikely to produce any renal damage as no significant long-term functional or anatomical changes were seen in dog kidneys irradiated with 400 rads.[83]

The final potential hazard involved in myocardial imaging is that of exercising patients with suspected cardiac disease. Exercise testing for ECG studies in this group of patients is surprisingly safe, with a mortality of 0.5 to 1 per 10,000 and a nonfatal serious complication rate of 3 to 9 per 10,000 tests reported from two questionnaire surveys of many centers.[84,85] The hazard of exercising for stress myocardial imaging should be similar, but it is essential that (1) patients be assessed before the study for any known contraindications to exercise testing,[85] (2) the test be conducted by personnel fully trained in exercise testing, with full monitoring of the patient (including ECG) during and after exercise, and (3) that full resus-

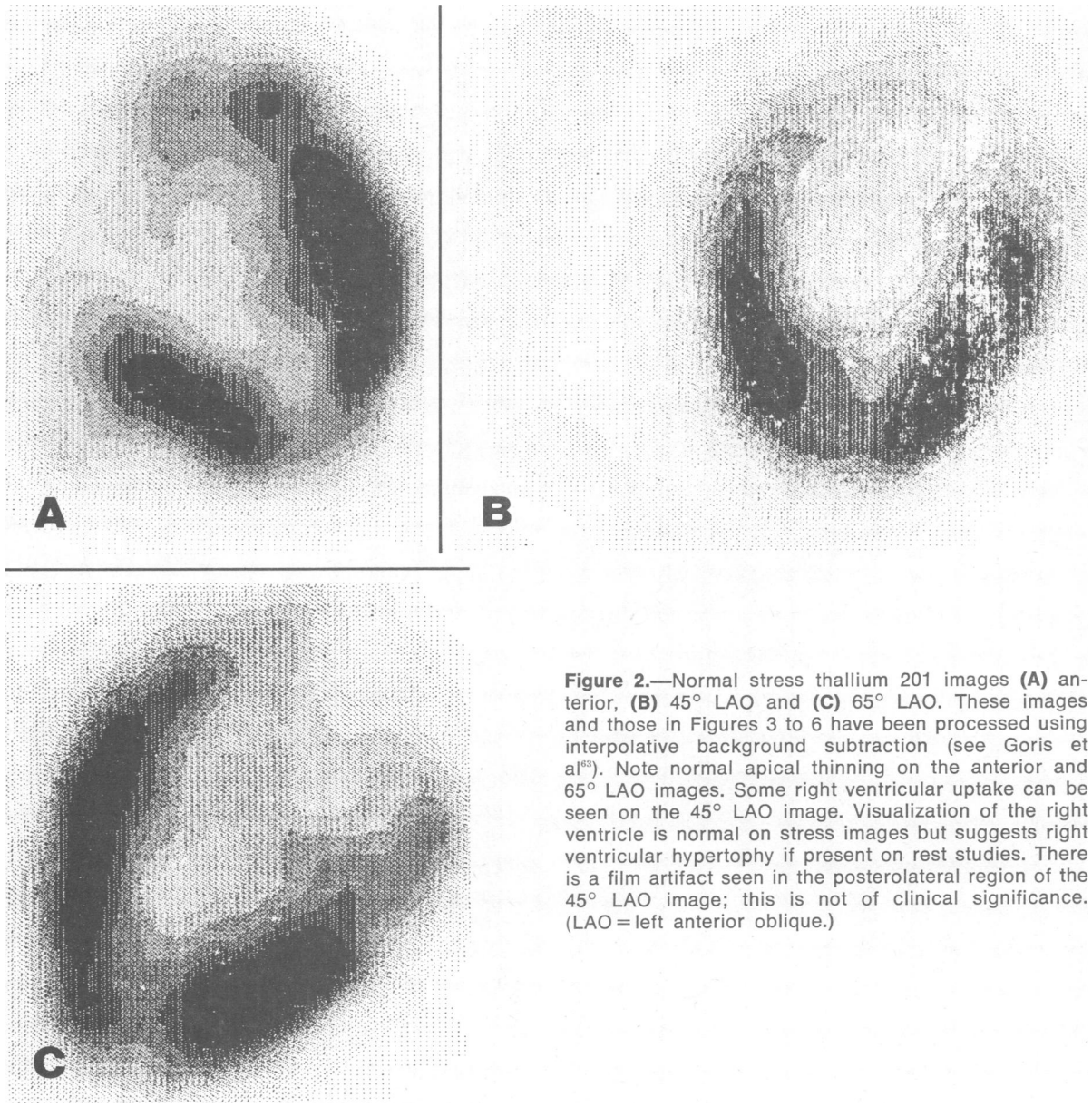

Figure 2.—Normal stress thallium 201 images **(A)** anterior, **(B)** 45° LAO and **(C)** 65° LAO. These images and those in Figures 3 to 6 have been processed using interpolative background subtraction (see Goris et al[63]). Note normal apical thinning on the anterior and 65° LAO images. Some right ventricular uptake can be seen on the 45° LAO image. Visualization of the right ventricle is normal on stress images but suggests right ventricular hypertophy if present on rest studies. There is a film artifact seen in the posterolateral region of the 45° LAO image; this is not of clinical significance. (LAO = left anterior oblique.)

citation facilities be available immediately if needed.

Clinical Applications of Thallium 201 Imaging

Ischemic Heart Disease

Acute myocardial infarction. The diagnosis of acute myocardial infarction often can be strongly suspected on clinical grounds. However, because of the large number of other conditions which may cause anterior chest pain and because of the serious implications that this diagnosis has for a patient's physical and psychosocial well-being both in the short and long term, the diagnosis should always be confirmed by appropriate laboratory investigations. The standard tests of serial electrocardiograms and serum enzyme determinations are adequate in most patients, but in some the diagnosis remains in doubt.

Thallium 201 myocardial imaging at rest has been proposed as a useful procedure in patients with suspected acute infarction.[86] Infarcted myocardium characteristically appears on the rest ^{201}Tl image as an area of moderately to substantially reduced tracer uptake in the left ventricular wall (Figure 3). The demonstration of such an abnormality, however, does not differentiate between acute and old infarction. Rest ^{201}Tl image abnormalities are also seen in some patients with (1) unstable angina,[87] (2) stable angina,[88] (3) acute myocardial ischemia,[89] and (4) coronary artery spasm.[90,91] It may be possible to differentiate infarction and ischemia by the reversibility of the ischemic defect when the patient is reimaged some hours later[88,89]; however, there is no means of differentiating acute and old myocardial infarction on ^{201}Tl imaging.

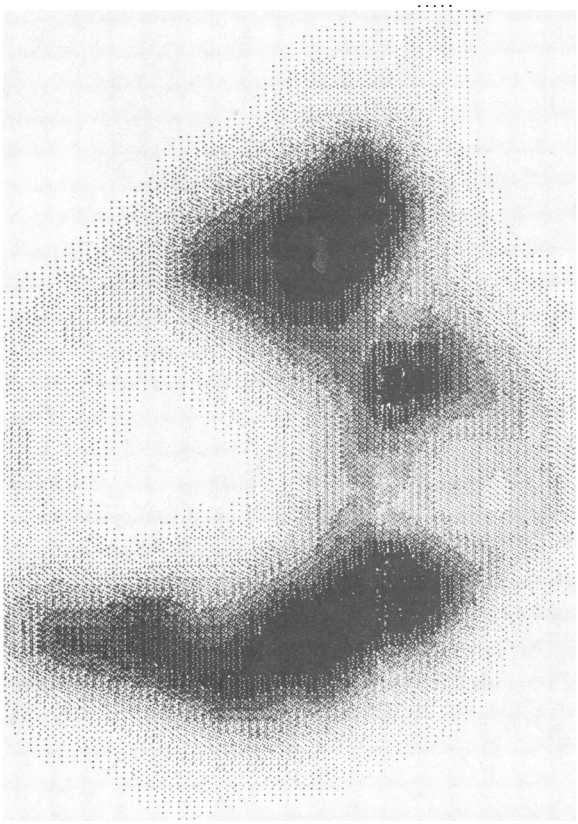

Figure 3.—65° left anterior oblique rest image from a patient with previous anterior myocardial infarction. There is substantially decreased tracer uptake in the anterior and apical regions.

The sensitivity of rest ^{201}Tl myocardial imaging for the detection of acute myocardial infarction is dependent both on the time elapsed from the onset of symptoms and on the size of the infarct.[92,93] In one study of 200 patients with documented acute myocardial infarction,[92] all patients studied within six hours of onset of symptoms had abnormal images, whereas only 72 percent of those studied more than 24 hours later showed image defects.

Because of the high sensitivity of studies shortly after onset of symptoms, rest ^{201}Tl myocardial imaging at the time of admission has been suggested as a means of selecting patients with chest pain for the coronary care unit (CCU).[94] To implement such a policy would require constant availability of the radioactive pharmaceutical agent and either a mobile gamma camera or one permanently situated in the CCU or emergency room. In addition, the patient would have to be seen within six hours of the onset of symptoms—and many patients have a longer delay than this before admission to hospital.[95] Thallium 201 imaging, therefore, is not an appropriate screening test for admission to CCU in many hospitals.

The reduced sensitivity of imaging more than 24 hours after the onset of symptoms is due principally to failure to visualize smaller, usually subendocardial, infarcts.[92,93] If sequential imaging of myocardial infarcts is done (using repeated doses of ^{201}Tl), the image defect is often larger on the study at less than six hours compared with that seen on the image made 24 hours to a week later.[92] The decrease in size of the defect with time presumably reflects resolution of peri-infarctional ischemia and edema. Detection by myocardial imaging of small infarcts in the early stages of evolution may, therefore, depend on reversible

peri-infarctional changes; late imaging fails to show the infarct because it is too small to be detected with the somewhat limited resolution available with ^{201}Tl.[96] The decreased sensitivity of late imaging and the nonspecificity of a defect for acute infarction are important shortcomings when ^{201}Tl imaging is used to attempt to clarify equivocal or conflicting ECG and enzyme studies: an abnormal image does not necessarily indicate acute infarction while a normal image does not absolutely exclude acute infarction.[93]

Thallium 201 myocardial imaging has been proposed as a means of localizing and measuring the extent of acute myocardial infarctions, factors which are related closely to a patient's prognosis. A clinicopathologic study of 23 patients who died of complications resulting from acute myocardial infarction within a few days after the ^{201}Tl imaging disclosed a slightly better correlation between postmortem location of the infarcts and findings on myocardial images than between postmortem evidence and ECG's.[97] This investigation also showed a reasonable correlation between infarct size at postmortem and the size estimated from the thallium 201 studies. In another series,[98] there was good correlation between estimation of infarct size from ^{201}Tl images obtained in the first 12 hours after symptoms and that estimated from serial serum creatinine phosphokinase measurements. However, as noted above, the size of the ^{201}Tl image defect tends to decrease in the days after the myocardial infarction.[92] Similar findings have been described in patients with acute infarctions imaged with nitrogen 13 ammonia[99] and in dogs with experimental myocardial infarction imaged with ^{201}Tl.[100] Therefore, the clinical reliability of measuring the size of acute infarcts from ^{201}Tl images is dubious, and it is unlikely that the technique will be accurate enough to judge the effect of therapies aimed at limiting infarct size. In the longer term, the ^{201}Tl image may have some prognostic value by indicating the amount of viable myocardium remaining, and in groups of patients with prior myocardial infarction, abnormalities seen on the rest myocardial scintigrams correlated well with the extent of wall-motion abnormalities at ventriculography.[69,101,102] Once again, some caution is necessary as rest image abnormalities do not always indicate earlier infarction.[88,89,102] Also, data from serial studies with rubidium 81 from 1 to 510 days after acute infarction[103] show a decrease in the size of the image defect in the late postinfarction period, possibly as the result of fibrotic shrinkage of the scar tissue.

Angina and atypical chest pain. The widest clinical application of ^{201}Tl myocardial imaging has been in the study of patients with angina

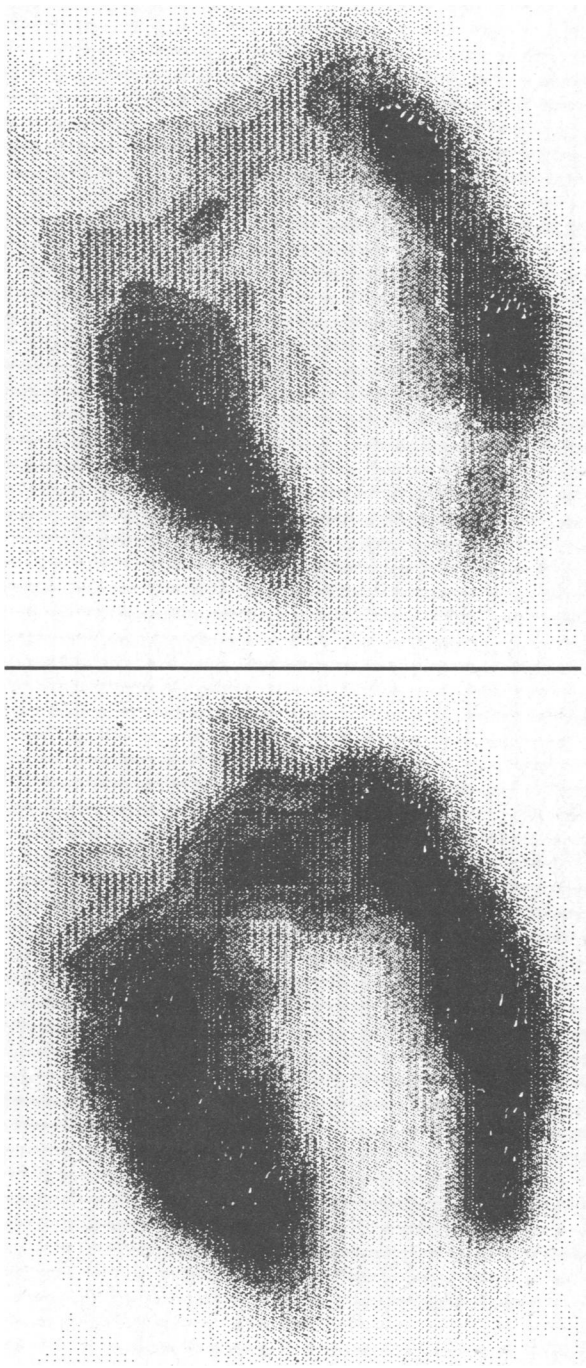

Figure 4.—Anterior images from a patient with previous myocardial infarction. The apico-inferior defect on the stress image **(above)** does not change signficantly on the rest image **(below).** A fixed defect of this type is characteristic of myocardial scarring.

pectoris or atypical chest pain. In such patients the usual procedure is to carry out a stress study first. If this is normal, then, ordinarily, no further studies are carried out. If the stress images are abnormal, they are compared with either rest images or images obtained some hours (usually about four) after the stress injection (redistribution study). Improvement of the image abnormality either at rest or on the redistribution study suggests myocardial ischemia while absence of change is usually interpreted as myocardial scarring. Figure 4 shows a "fixed" defect due to previous infarction and Figure 5, a reversible abnormality produced by myocardial ischemia.

Figure 5.—45° left anterior oblique images from a patient with exertional angina. There is a pronounced posterolateral abnormality on the stress image (above), which has completely reversed on the rest image (below). These appearances suggest ischemia in the territory of the left circumflex coronary artery which was significantly stenosed at arteriography.

As discussed above, some caution is needed in interpreting rest image abnormalities as showing myocardial scarring, particularly when they are associated with ventriculographic evidence of normal or only slightly abnormal left ventricular wall motion.[88,102] In such patients, re-imaging two to four hours after the rest injection may be valuable as a means of differentiating more accurately between infarction and ischemia.[88]

There is some debate at present as to whether the redistribution technique[57] yields the same information as rest imaging. If it did so, only one injection of ^{201}Tl would be necessary, with both financial savings (of approximately $200) and decrease in radiation dosage for the patient. However, several recent publications have suggested that in at least a proportion of patients the two studies are not identical.[104-106] Figure 6 illustrates a study showing differences between rest and redistribution images.

Blood and co-workers[104] have reported that in 62 patients with coronary artery disease, 16 showed defects on redistribution images which were not present on the rest images. Of these patients, 11 had evidence of previous transmural myocardial infarction. They concluded that redistribution studies were more sensitive than rest images for detecting previous myocardial infarctions, especially of the inferior wall. Ritchie and colleagues[105] found discrepancies between the rest and redistribution images in 12 of 27 patients with coronary artery disease. However, they were unable to correlate the differences with presence of earlier infarction, disturbances of regional wall motion or severity of coronary stenosis. They concluded that while some redistribution occurred in most patients with exercise-induced defects, the use of the redistribution image may lead to overestimation of the extent of previous infarction. Verani and co-workers[106] found that there was a considerable overlap in redistribution scintigrams in patients with coronary disease with and without previous infarction, with a high incidence of stress-induced hypoperfusion both in infarcted and non-infarcted myocardium. They also found that good

quality collateral vessels allowed redistribution even to some areas of previous infarction.

Until the controversy over the significance of the redistribution image is resolved, it seems reasonable to carry out separate rest studies in patients who have persistent abnormalities on their redistribution scintigrams, especially if there is no history of previous infarction.

Numerous series have now been published on the sensitivity and specificity of ^{201}Tl myocardial imaging for the detection of angiographically proved coronary artery disease in patients with chest pain.[36,71,107-121] Some results are summarized in Table 1. The sensitivity of ^{201}Tl imaging for detecting significant coronary artery disease ranges from 68 percent to 100 percent, with most recent series giving figures of 75 percent to 90 percent. Comparison between different series is difficult, but factors producing the differences in sensitivity may include (1) differing criteria for the severity of stenoses considered significant, (2) whether the sensitivity reported represents only "new" lesions

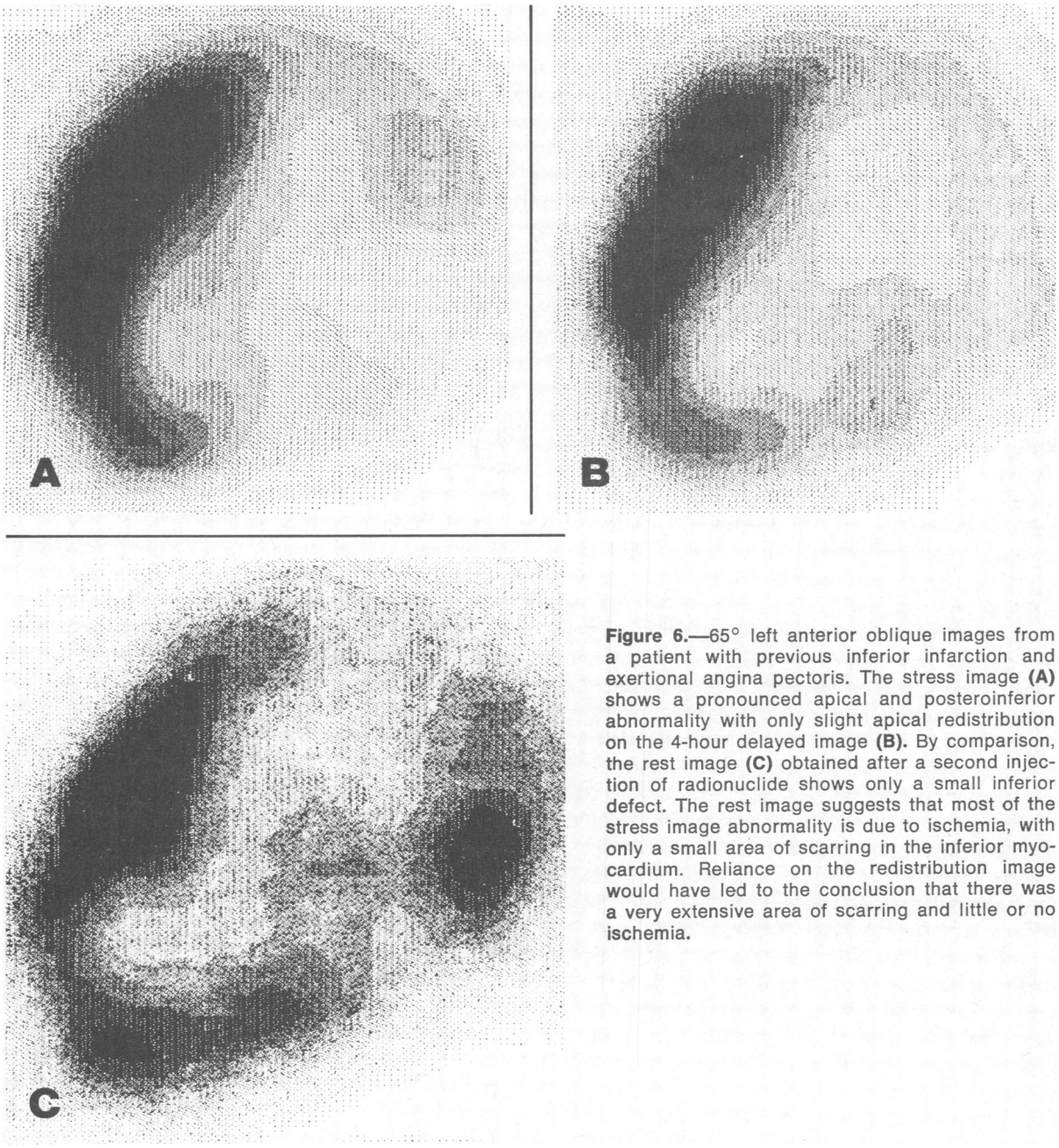

Figure 6.—65° left anterior oblique images from a patient with previous inferior infarction and exertional angina pectoris. The stress image **(A)** shows a pronounced apical and posteroinferior abnormality with only slight apical redistribution on the 4-hour delayed image **(B).** By comparison, the rest image **(C)** obtained after a second injection of radionuclide shows only a small inferior defect. The rest image suggests that most of the stress image abnormality is due to ischemia, with only a small area of scarring in the inferior myocardium. Reliance on the redistribution image would have led to the conclusion that there was a very extensive area of scarring and little or no ischemia.

seen at stress or also includes those which do not change between rest and exercise, (3) differences in patient populations; for example, the proportion of patients with multiple-vessel disease or with good collateral circulation may be important, and (4) the method of analysis of the scintigrams. As discussed above, there is some preliminary evidence that various forms of image processing may influence the sensitivity. When particular vessels are considered, the sensitivity of detection is greatest for left anterior descending artery disease and lowest for left circumflex vessel disease.[36,117]

The specificity of thallium 201 imaging for the detection of coronary artery disease has been of the order of 80 percent to 100 percent, though a few series have produced much lower figures. The false-positive results are probably due to several factors. For instance, the criteria adopted for judging abnormalities of the images vary in different centers as does the method of processing. Use of flat background subtraction may cause a reduction in specificity.[61,62] Also, because myocardial thallium uptake is dependent on regional sodium-potassium pump function as well as myocardial blood flow, any myocardial pathology may produce an abnormal image. Such abnormalities are usually present on the rest image, but reversible "ischemic"-type defects can also be seen occasionally in noncoronary disease.[122,123]

In several studies ^{201}Tl imaging has been compared with electrocardiography. Most series (for example, see references 108, 112, 116, 124) have found myocardial imaging to have a higher sensitivity than ECG's for detecting coronary artery disease, though not all authors agree on this point.[114] Specificity for the two techniques was not significantly different in some series,[112,114] but others have indicated increased specificity for radionuclide imaging.[106,117] It has been reported in three studies[119-121] that the results of myocardial imaging are normal more frequently than those of electrocardiography in patients with chest pain and normal coronary arteriograms. Berman and colleagues[125] carried out myocardial imaging in 21 asymptomatic subjects with positive stress ECG's. The ^{201}Tl images were abnormal in six of seven patients with coronary artery disease and normal in all 14 with normal arteriograms.

The relationship between the extent of coronary artery disease and the findings on thallium 201 imaging has also received some attention. Wainwright and co-workers[115] reported a high degree of accuracy in predicting the extent of disease from myocardial images while Weisberger[126] reported a specific scintigraphic pattern for left main stem disease. Massie and colleagues[110] concluded that stress perfusion scintigraphy was a useful adjunct in identification of patients with high-risk coronary artery disease. By contrast, some of the earlier studies, without giving exact details, commented on a generally poorer correlation between the ^{201}Tl image and the coronary arteriogram in patients

TABLE 1.—*Sensitivity and Specificity of Thallium 201 Myocardial Imaging and Electrocardiography for Detection of Coronary Artery Disease in Patients With Chest Pain Who Had Undergone Coronary Arteriography**

Reference No.	No. of Patients	Thallium 201 Imaging		Electrocardiography		Comments
		Sensitivity Percent	Specificity Percent	Sensitivity Percent	Specificity Percent	
35	85	97	71	59	64	.....
70	46	96	90	81	65	.....
107	83	75	100	65	100	.....
108	65	85	89	67	63	.....
109	70	95	93	..	..	.....
110	32	97	..	66	..	All 2- or 3-vessel disease
111	161	88	..	..	..	.....
112	101	91	96	65	84	.....
113	22	93	86	..	..	.....
114	75	68	97	71	79	No patients with previous myocardial infarction
115	111	99	56	55	..	.....
116	95	75	91	71	86	.....
117	50	91	83	76	..	.....
118	190	78	88	..	..	Multicenter study
119	55	84	85	76	52	.....
120	53	..	91	..	77	Patients with chest pain and normal coronary angiography
121	9	..	100	..	44	Patients with chest pain and normal coronary angiography

*Sensitivities and specificities quoted are calculated from rest or exercise abnormalities, or both, where this information is available.

with multiple-vessel disease compared with patients with single-vessel disease,[109,113] while Rehn and co-workers[111] felt that myocardial imaging was sensitive but not specific in detecting left main artery disease. Three recent studies[127-129] have commented on the frequent underestimation of the extent of disease when predictions are made from myocardial images in patients with multiple-vessel disease.

The discrepancy found in many patients between estimates based on ^{201}Tl imaging and the arteriographic extent of disease may have several causes. First, coronary arteriography is open to some error of interpretation,[130] although when arteriography is compared with postmortem findings, the arteriography will underestimate more often than overestimate the extent of coronary artery disease.[131,132] Second, the presence of an anatomic stenosis at arteriography does not necessarily imply distal abnormal flow and ischemia. Two studies[17(pp84-142),133] have suggested that the presence of collateral circulation to the territory of an abnormal vessel reduces the likelihood of a radionuclide image abnormality in that region, if the area has not been the site of previous infarction. The same two studies have also shown that the differing severity of individual stenoses in multiple-vessel disease may also be important, with image defects developing only in the territory of the most abnormal vessel.[17(pp84-142),133] This may be due to pain from ischemia in this area limiting exercise before flow becomes abnormal in the territory of a less severely occluded vessel. An alternative explanation is that although the flow in the less stenosed vessels is abnormal in absolute terms, this is not detected on a myocardial image that reflects only *relative* regional perfusion. A third factor making prediction of extent of disease from myocardial images difficult is the variability of territories of the coronary arteries, especially the reciprocal relationship between the right and left circumflex vessels.[134,135] As a result, an image defect in certain areas may represent abnormalities in the territories of one or both vessels.[128]

What then is the role of ^{201}Tl myocardial imaging in a patient with possible ischemic heart disease? The patient with classic angina pectoris and an abnormal ECG has a high probability of having coronary artery disease, and the results of myocardial imaging will not produce any significant change in this probability.[138] Myocardial imaging, therefore, has very limited value as a diagnostic procedure for coronary artery disease in this group of patients. Patients with abnormalities on the myocardial scintigrams that suggest multiple-vessel disease, usually have more than one abnormal vessel at arteriography, but as noted above, the extent of disease is often underestimated from the myocardial images. Therefore, high-risk coronary disease may be suggested from ^{201}Tl images, but cannot be excluded by them. Thallium 201 imaging is thus not reliable in identifying patients who require more invasive studies as a prelude to possible coronary artery operations. The findings on rest myocardial imaging may have some prognostic value by showing the extent of irreversibly damaged (or very severely ischemic) myocardium. Similarly, the findings of only small areas of ischemic defects during stress may be a good prognostic sign by indicating single-vessel disease or multiple-vessel disease with good collateralization. These prognostic points, however, remain speculative at present. Finally, preoperative myocardial imaging in this group of patients would be valuable when a decision has been made to carry out a bypass surgical operation. Comparison of preoperative and postoperative images may be of value in assessing the adequacy of myocardial revascularization (see below).

Thallium 201 myocardial imaging is of great clinical use in patients with various atypical chest pain syndromes which may be associated with coronary artery disease. For such patients stress myocardial imaging is usually combined with stress electrocardiography. If results of both investigations are normal, the probability of significant cardiac disease is low, and further investigation is not indicated. By comparison, if abnormal studies are obtained, further cardiac investigation should be instituted. It should be noted that while an abnormal myocardial image in a patient with atypical chest pain is most often due to coronary artery disease, it is not specific for this diagnosis and may be produced by a variety of other myocardial pathologies.

A further indication for ^{201}Tl myocardial imaging is in assessing the functional significance of coronary artery lesions which are borderline at coronary arteriography. The uptake of the radionuclide by the myocardium reflects regional small-vessel blood flow and myocardial cell function. A normal stress myocardial image in the territory of a borderline abnormal vessel suggests that the stenosis is not of hemodynamic significance. By

comparison, a reversible stress image abnormality in that territory is an indication that the occlusive lesion is producing regional myocardial ischemia.

A major indication for myocardial imaging is in the clarification of equivocal ECG changes in patients with atypical chest pain or the presence of abnormal ECG findings in asymptomatic subjects.[139] Normal stress images considerably reduce the probability of coronary artery disease in such patients and, depending on the clinical setting, may obviate the need for further investigation. Myocardial imaging is also very valuable in a patient whose stress ECG cannot be interpreted; for example, because of digoxin effect or left bundle branch block (LBBB). The finding of a reversible stress image abnormality is highly suggestive of ischemic heart disease. The significance of rest image abnormalities in patients with LBBB is less clear. Studies using ^{43}K and ^{81}Rb showed septal abnormalities at rest in patients with LBBB and no coronary disease.[136] By contrast, in patients with suspected acute myocardial infarction and LBBB, rest ^{201}Tl image abnormalities occurred only in those patients subsequently shown to have acute infarction.[137]

Because of the high cost of the test, the sensitivity and specificity obtained and the low yield to be expected, it is unlikely that myocardial imaging will be a suitable screening test for coronary artery disease in large asymptomatic populations.[138] Myocardial imaging may be useful, however, as a noninvasive screening test both at the time of presentation and during follow-up of patients with known high-risk factors for coronary atherosclerosis, such as hyperlipidemia.

After coronary artery bypass operations. Myocardial imaging has been used as a method of assessing the adequacy of myocardial revascularization after a coronary artery bypass operation. When comparing myocardial imaging and postoperative arteriography, it is important to remember that myocardial revascularization and anatomic graft patency are not necessarily synonymous.[140] Thus, a patent graft may supply an area of myocardial infarction[141] which would appear abnormal on the myocardial image. Similarly, collaterals to the grafted vessel from nondiseased vessels may develop after the operation,[142] and it is possible, at least theoretically, that this might maintain myocardial perfusion in spite of proximal graft occlusion.

The success of showing improved myocardial perfusion after an operation using potassium 43,[143] and rubidium 81[144] has been followed by similar applications of thallium 201 imaging.[113,145-152]

Overall, postoperative improvement in stress myocardial images has been associated with a high frequency of graft patency.[145-148] Rest myocardial images may also improve following a bypass procedure, especially in segments not associated with Q waves on ECG.[151] Similarly, abnormalities present on postoperative stress images correspond well to incomplete revascularization, either due to graft occlusion or to disease of ungrafted vessels.[144,146,147,150] One must be cautious in interpreting apical abnormalities because in some patients after operation there may be apical defects more pronounced than normal thinning without coronary occlusion, perhaps due to insertion of a vent into the apex of the left ventricle during the operation.[17(pp149-163)] It should be noted that absence of improved results on myocardial imaging after the operation does not preclude alleviation of angina and increased exercise tolerance.[149] Although overall correlation between improvement or continued abnormal findings on the postoperative scintigram and arteriogram is fair, prediction of occlusion or patency of individual grafts or ungrafted vessels has been less successful in several series.[145,146,148,150,152] The ability to predict the patency of individual grafts is improved if there is an abnormality in that vessel's territory on the preoperative study.[152]

Because of the limitations of ^{201}Tl imaging in predicting the status of individual grafts, its main value in the postoperative assessment of a patient who has had good symptomatic relief is to serve as a baseline for future comparison. If, however, the patient continues to have chest pain after the operation, the presence of abnormal findings on the scintigram is highly suggestive of incomplete revascularization. By comparison, the conversion of an abnormal preoperative to a normal postoperative study indicates that the pain is more likely to be noncardiac in origin.

Variant angina. Myocardial ischemia due to coronary artery spasm is associated with reduction in myocardial perfusion, which can be shown by ^{201}Tl imaging.[90] Images obtained during a spontaneous attack show transmural reduction in ^{201}Tl uptake in the affected myocardial territory, with reversal of the abnormality on redistribution images or on separate rest images obtained when the patient is free of pain.[90] Similar reduction in ^{201}Tl uptake can be shown when attacks are induced pharmacologically in affected subjects through adminis-

tration of ergonovine maleate.[36,90,91,153] Thallium 201 myocardial imaging after the patient has been given this drug is a useful means of showing the effect of coronary spasm on myocardial perfusion and metabolism, and may be a method of assessing the value of proposed therapies. However, because of the danger of inducing spasm in patients with arteriosclerotic coronary disease, such provocative tests should be carried out only after fixed coronary occlusion has been excluded by standard rest and exercise myocardial imaging or by coronary arteriography.

Noncoronary Disease

Valvular heart disease. Thallium 201 myocardial imaging has been applied in patients with aortic valve disease to determine whether they also have coronary artery disease, because this has important prognostic and therapeutic implications. Two studies, the first including patients with pure aortic stenosis[154] and the second including some patients with aortic stenosis and others with combined aortic stenosis and regurgitation,[155] have shown that in patients with these conditions, abnormal stress myocardial images can be obtained in some patients with no significant coronary artery disease while a normal image does not exclude obstructive coronary disease. The false-negative studies may be related to the patient's exercise capacity being limited by low cardiac output before myocardial ischemia develops.

The explanation for positive studies in patients without coronary disease is unclear. Similar false-positive studies in cases of aortic stenosis have been recorded with ^{43}K.[122] It does appear, however, that potassium analog myocardial imaging cannot be used to exclude or to confirm the presence of occlusive coronary disease in patients with aortic valve disease.

Mitral valve prolapse may be accompanied by atypical chest pain, false-positive electrocardiograms and arrhythmias, and may thus mimic coronary disease. Thallium 201 imaging has been investigated in this group of patients.[156-159] The weight of evidence in the literature suggests that the technique is valuable in differentiating patients with prolapse who have coronary disease from those who do not, abnormal results on scintigrams being found only in the former group.

Nonischemic cardiomyopathy. Although myocardial imaging has proved most useful for studying coronary artery disorders, it has also been applied to certain noncoronary cardiomyopathies.[65,122,123,160-163] The myocardial images usually have a nonspecific appearance in noncoronary cardiomyopathy and do not usually help in distinguishing the cause.[163] Rather, they show the effect of the disease process on myocardial anatomy and function, and can be used in assessing whether hypertrophy or dilatation of either ventricle is present.[65,122,163] Focal abnormalities appearing during stress are not entirely specific for occlusive coronary artery disease and may also be seen occasionally in patients with noncoronary cardiomyopathy.[122,123,164]

A more specific pattern of abnormality has been reported in idiopathic hypertrophic subaortic stenosis (IHSS), where the ratio of thickness of the septum to that of the free left ventricular wall exceeds 1.7.[160] In addition, the posterior left ventricular free wall is thicker in the obstructive compared with the nonobstructive form of the disease.[160] Patients with IHSS may show stress-induced focal defects of ^{201}Tl uptake in the absence of significant coronary disease.[164] It should be noted, however, that the noninvasive diagnosis of IHSS, and left ventricular hypertrophy in general, is best made from the ECG and echocardiography rather than from ^{201}Tl imaging.

Focal myocardial image abnormalities at rest are found in patients with myocardial sarcoid granulomata, and this study may be a useful means of differentiating cardiac dysfunction due to cor pulmonale from that resulting from direct myocardial involvement.[161] In a recent study myocardial image abnormalities were reported in almost a third of 50 patients with sarcoidosis who did not have cardiovascular symptoms.[162]

Miscellaneous conditions. Visualization of the right ventricle on rest ^{201}Tl images may occur in acute pulmonary embolism.[163] As noted earlier,[74,75] chronic pulmonary hypertension and right ventricular hypertrophy result in visualization of the right ventricle on rest images.

Thallium 201 imaging is possible in neonates and young children and can be used to differentiate global "transient myocardial ischemia" from focal ischemia resulting from an anomalous left coronary artery.[165] Myocardial imaging can also be used to assess myocardial perfusion following surgical intervention for an anomalous left coronary artery.[166] Thallium 201 imaging has also allowed successful differentiation between tetralogy of Fallot and single ventricle disease.[66]

Finally, it may be possible to recognize the presence of pericardial effusion from a halo of sub-

stantially decreased background activity around the heart on rest myocardial images.[163]

Noncardiac Applications of Thallium 201 Imaging

The whole body distribution of ^{201}Tl following intravenous injection parallels regional blood and regional metabolic activity, and the fractional distribution of the isotope has been suggested as a method of studying the regional distribution of cardiac output.[167] This approach has been questioned because of the many factors other than regional blood flow that might alter the distribution of ^{201}Tl.[168] Imaging of the lower limbs after injection of ^{201}Tl at rest and during exercise has been done in patients with peripheral vascular disease, and has been proposed as a method of studying the functional result of major vessel occlusion.[169]

In addition to metabolically active normal tissues, ^{201}Tl has been found to accumulate in certain pathological tissues. Cox and colleagues[170] reported an abnormal concentration of ^{201}Tl in the primary tumor of a man with bronchial carcinoma. They also showed that the nuclide was taken up by rhabdomyosarcoma implants in rats. Tonami and associates[171] investigated ^{201}Tl as a tumor-imaging agent in humans. They found abnormal uptake of the isotope in 14 of 15 patients with hepatomas but in none of 8 with hepatic metastasis. In patients with thyroid nodules, 14 of 15 with thyroid cancer had a hot spot on ^{201}Tl imaging, whereas in only 6 of 19 patients, benign adenomas which were "cold" on technetium 99m imaging concentrated ^{201}Tl. The same group have also reported ^{201}Tl uptake in primary lung and esophageal carcinomas.[172] Thallium 201 uptake has also been recorded in single cases of lymph node metastasis from thyroid carcinoma,[173] in a benign parathyroid adenoma[174] and in two cases of subacute thyroiditis.[175]

Conclusion

Thallium 201 myocardial imaging, though a relatively new technique, has been the subject of extensive evaluation. Its clinical use in several situations is still unresolved, but the following indications for carrying out the procedure are now generally accepted:

- The study of patients with symptoms suggestive of coronary artery disease, especially those with atypical chest pain or ECG findings that are equivocal or cannot be clearly interpreted. (Its value in identifying patients with high-risk coronary disease remains controversial.)
- The clarification of the significance of an abnormal ECG discovered during routine screening of an asymptomatic subject.
- The assessment of the hemodynamic significance of a borderline lesion seen at coronary arteriography.
- The follow-up of patients after coronary artery bypass operations.
- The exclusion of coexistent coronary disease in patients with mitral valve prolapse—thallium 201 imaging cannot be used to confirm or exclude coronary disease in aortic valve disease.
- A normal myocardial image obtained in the few hours after the onset of acute chest pain virtually excludes acute myocardial infarction. Studies delayed beyond this time are less valuable, and there are difficulties in using the technique to quantitate infarct size accurately.
- Thallium 201 imaging in patients with possible variant angina due to coronary artery spasm.
- The noninvasive detection of right ventricular hypertrophy.

REFERENCES

1. Noonan TR, Fenn WO, Haege L: The distribution of injected radioactive potassium in rats. Am J Physiol 132:474-488, Mar 1941
2. Love WD, Burch GE: A comparison of potassium^{42}, rubidium^{86} and caesium^{134} as tracers of potassium in the study of cation metabolism of human erythrocytes in vivo. J Lab Clin Med 41: 351-362, Mar 1953
3. Love WD, Romney RB, Burch GE: A comparison of the distribution of potassium and exchangeable rubidium in the organs of the dog, using rubidium-86. Circ Res 2:112-122, Mar 1954
4. Burch GE, Threefoot SA, Ray CT: The rate of disappearance of Rb^{86} from the plasma, the biologic decay rates of Rb^{86} and the applicability of Rb^{86} as a tracer of potassium in man with and without chronic congestive failure. J Lab Clin Med 45:371-394, Mar 1955
5. Threefoot SA, Ray CT, Burch GE: Study of the use of Rb^{86} as a tracer for the measurement of Rb^{86} and K^{39} space and mass in intact man with and without congestive heart failure. J Lab Clin Med 45:395-407, Mar 1955
6. Ray CT, Threefoot SA, Burch GE: The excretion of radiorubidium Rb^{86}, radiopotassium, K^{42}, and potassium, sodium and chloride by man with and without congestive heart failure. J Lab Clin Med 45:408-430, Mar 1955
7. Carr EA, Beierwaltes WH, Patno ME, et al: The detection of experimental myocardial infarcts by photoscanning. Am Heart J 64:650-660, Nov 1962
8. Carr EA, Gleason G, Shaw J, et al: The direct diagnosis of myocardial infarction by photoscanning after administration of caesium-131. Am Heart J 68:627-636, Nov 1964
9. Poe ND: Rationale and radiopharmaceuticals for myocardial imaging. Sem Nucl Med 7:7-14, Jan 1977
10. Lebowitz E, Greene MW, Fairchild R, et al: Thallium-201 for medical use. I. J Nucl Med 16:151-155, Feb 1975
11. Crookes W: Preliminary researches on thallium. Proc Roy Soc 12:150-159, 1862
12. Mullins LJ, Moore RD: The movement of thallium ions in muscle. J Gen Physiol 43:759-773, Mar 1960
13. Gehring PJ, Hammond PB: The uptake of thallium by rabbit erythrocytes. J Pharmacol Exp Therap 145:215-221, Aug 1964
14. Gehring PJ, Hammond PB: The interrelationship between thallium and potassium in animals. J Pharmacol Exp Therap 155: 187-201, Jan 1967
15. Kawana M, Krizek H, Porter J, et al: Use of ^{199}Tl as a potassium analog in scanning. J Nucl Med 11:333, 1970 (abst)
16. Atkins HL, Budinger TF, Lebowitz E, et al: Thallium-201 for medical use—Part 3: Human distribution and physicial imaging properties. J Nucl Med 18:133-140, Feb 1977

17. McKillop JH: An Evaluation of the Role of Thallium-201 Myocardial Imaging in the Investigation of Ischaemic Heart Disease, PhD thesis. University of Glasgow, 1979

18. Bradley-Moore PR, Lebowitz E, Greene MW, et al: Thallium-201 for medical use—II: Biologic behaviour. J Nucl Med 16:156-160, Feb 1975

19. Nishiyama H, Sodd VJ, Adolph RJ, et al: Intercomparison of myocardial imaging agents ^{201}Tl, ^{129}Cs, ^{42}K, ^{81}Rb. J Nucl Med 17:880-889, Oct 1976

20. Weich HF, Strauss HW, Pitt B: The extraction of thallium-201 by the myocardium. Circulation 56:188-191, Aug 1977

21. Abbate A, Maseri A, Biagini A, et al: Study of early and late myocardial kinetics of ^{201}Tl in man at rest, *In* Symposium on Radionuclides in the Diagnosis of Myocardial Infarction. Lund, Sweden, Jun 1977

22. Strauss HW, Harrison K, Langan JK, et al: Thallium-201 for myocardial imaging: Relation of thallium-201 to regional myocardial perfusion. Circulation 51:641-645, Apr 1975

23. Schelbert HR, Henning H, Rigo P, et al: Considerations of ^{201}Tl as a myocardial radionuclide imaging agent in man. Invest Radiol 11:163-171, May 1976

24. Hamilton GW, Narahara KA, Yee H, et al: Myocardial imaging with thallium-201: Effect of cardiac drugs on myocardial images and absolute tissue distribution. J Nucl Med 19:10-16, Jan 1978

25. Britten JS, Blank M: Thallium activation of the (Na+-K+) activated ATP-ase of rabbit kidney. Biochim Acta 159:160-166, Apr 1968

26. Selwyn AP, Welman E, Pratt TA, et al: The interpretation of the thallium-201 cardiac scintigram—Studies in experimental ischemic heart disease in dogs. Circ Res 43:287-293, Aug 1978

27. Adolph RJ, Nishiyama H, Franklin DW, et al: Correlative studies of effects of perfusion and ischemia on thallium-201 uptake. Am J Cardiol 43:357, Feb 1979 (abst)

28. Strauer BE, Büll U, Burger S: Clinical studies concerning the determinants of myocardial ^{201}thallium uptake. Basic Res Cardiol 73:365-379, 1978

29. Hetzel KR, Westerman BR, Quinn JL III, et al: Myocardial uptake of thallium-201 augmented with bicarbonate. J Nucl Med 18:24-25, Jan 1977

30. Costin JC, Zaret BL: Effect of propranolol and digitalis upon radioactive thallium and potassium uptake in myocardial and skeletal muscle. J Nucl Med 17:535, Jun 1975 (abst)

31. Schelbert HR, Ashburn WL, Chauncey DM, et al: Comparative myocardial uptake of intravenously administered radionuclides. J Nucl Med 15:1092-1100, Dec 1974

32. Nishiyama H, Romhilt DW, Williams CC, et al: Collimator evaluation for Tl-201 myocardial imaging. J Nucl Med 19:1067-1073, Sep 1978

33. Vogel RA, Kirch D, LeFree M, et al: A new method of multiplanar emission tomography using a seven pinhole collimator and an Anger scintillation camera. J Nucl Med 19:648-654, Jun 1978

34. Vogel RA, Kirch DL, LeFree MT, et al: Thallium-201 myocardial perfusion scintigraphy: Results of standard and multipinhole tomographic techniques. Am J Cardiol 43:787-793, Apr 1979

35. Hamilton GW, Narahara KA, Trobaugh GB, et al: Thallium-201 myocardial imaging: Characterization of the ECG synchronized images. J Nucl Med 19:1103-1110, Oct 1978

36. Buda AJ, Goris ML, Doherty PW, et al: Results of computer processing in thallium-201 myocardial perfusion imaging. Comput Cardiol, Sep 1978, pp 11-18

37. Wackers FJTh, Sokole EB, Samson G, et al: Atlas of ^{201}Tl myocardial scintigraphy. Clin Nucl Med 2:64-74, Feb 1977

38. Johnstone DE, Wackers FJTh, Berger HJ, et al: Effect of patient positioning on left lateral thallium-201 myocardial images. J Nucl Med 20:183-188, Mar 1979

39. Gordon DG, Pfisterer M, Williams R, et al: The effect of diaphragmatic attenuation on ^{201}Tl images. Clin Nucl Med 4:150-151, Apr 1979

40. Cook DJ, Bailey I, Strauss HW, et al: Thallium-201 for myocardial imaging: Appearance of the normal heart. J Nucl Med 17:583-589, Jul 1976

41. Wackers FJTh, deJong RBJ: Myocardial imaging with thallium-201. Medicamundi 21(2):103-113, 1976

42. McGeehan JT, Rodriguez-Antunez A, Lewis RC: Cesium-131 photoscan—Aid in diagnosis of myocardial infarction. JAMA 204:585-589, May 1968

43. Hurley PJ, Cooper M, Reba RC, et al: ^{43}KCl: A new radiopharmaceutical for imaging the heart. J Nucl Med 12:516-519, Jul 1971

44. Bennett KR, Smith RO, Lehan PH, et al: Correlation of myocardial ^{42}K uptake with coronary arteriography. Radiology 102:117-124, Jan 1972

45. Schwartz L, Froggart G, Covvey HD, et al: Measurement of left anterior descending coronary arterial blood flow—Technique, methods of blood flow analysis and correlation with angiography. Am J Cardiol 32:679-685, Oct 1973

46. Cannon PJ, Dell RB, Dwyer EM Jr: Regional myocardial perfusion rates in patients with coronary artery disease. J Clin Invest 51:978-994, Apr 1972

47. Gould KL, Lipscomb K, Hamilton GW: Physiologic basis for assessing critical stenosis: Instantaneous flow response and regional distribution during coronary hyperaemia as measures of coronary flow reserve. Am J Cardiol 33:87-94, Jan 1974

48. Gould KL, Hamilton GW, Lipscomb K, et al: Method for assessing stress induced regional malperfusion during coronary arteriography—Experimental validation and clinical application. Am J Cardiol 34:557-564, Oct 1974

49. Ritchie JL, Hamilton GW, Gould KL, et al: Myocardial imaging with indium-113m and technetium-99m macroaggregated albumin—New procedure for identification of stress induced regional ischemia. Am J Cardiol 35:380-389, Mar 1975

50. Schmidt DH, Weiss MB, Casarella WJ, et al: Regional myocardial perfusion during atrial pacing in patients with coronary artery disease. Circulation 53:807-819, May 1976

51. Strauss HW, Zaret BL, Martin ND, et al: Noninvasive evaluation of regional myocardial perfusion with potassium-43—Technique in patients with exercise-induced transient myocardial ischemia. Radiology 108:85-90, Jul 1973

52. McLaughlin PR, Martin RP, Doherty P, et al: Reproducibility of thallium-201 myocardial imaging. Circulation 55:497-503, Mar 1977

53. Gregg DE: Physiology of the coronary circulation—The George E. Brown Memorial Lecture. Circulation 27:1128-1137, Jun 1963

54. Büll U, Strauer BE, Burger S, et al: Effect of physical stress and pharmacologically induced coronary dilation on myocardial and non myocardial ^{201}thallium uptake. Europ J Nucl Med 3:19-27, 1978

55. Albro PC, Gould KL, Westcott RJ, et al: Myocardial perfusion imaging during pharmacologic coronary vasodilatation in assessing coronary disease. Am J Cardiol 41:378, Feb 1978 (abst)

56. Duperrier C, Devaux J-Y, Roucayrol JC, et al: 201 Thallium myocardial scintigraphy during IV perfusion of Isuprel—Preliminary report. Trans Europ Soc Cardiol 1:134, Jun 1978 (abst)

57. Pohost GM, Zir LM, Moore RH, et al: Differentiation of transiently ischemic from infarcted myocardium by serial imaging after a single dose of thallium-201. Circulation 55:294-302, Feb 1977

58. Adelstein SJ, Maseri A: Radio-indicators for the study of the heart: Principles and applications. Prog Card Dis 20:3-17, Jul 1977

59. Hor G, Sebening H, Sauer F, et al: Thallium-201 redistribution in coronary heart disease (CHD)—Early and delayed myocardial scans. J Nucl Med 18:599, Jun 1977 (abst)

60. Berger HJ, Gottschalk A, Zaret BL: Dual radionuclide study of acute myocardial infarction—Comparison of thallium-201 and technetium-99m stannous pyrophosphate imaging in man. Ann Intern Med 88:145-154, Feb 1978

61. Fletcher JW, Walter KE, Witztum KF, et al: Diagnosis of coronary artery disease with ^{201}Tl—Computer analysis of myocardial perfusion images. Radiology 128:423-427, Aug 1978

62. Massie B, Botvinick E, Arnold S, et al: Effect of contrast enhancement on the sensitivity and specificity of Tl-201 scintigraphy. Am J Cardiol 43:357, Feb 1979 (abst)

63. Goris ML, Daspit SG, McLaughlin P, et al: Interpolative background subtraction. J Nucl Med 17:744-747, Aug 1976

64. Pitt B, Strauss HW: Myocardial imaging in the noninvasive evaluation of patients with suspected ischemic heart disease. Am J Cardiol 37:797-806, Apr 1976

65: Büll U, Niendorf HP, Strauer BE: Evaluation of myocardial function with the ^{201}thallium scintimetry in various diseases of the heart. Eur J Nucl Med 1(3):125-136, Aug 12, 1976

66. Strauss HW, Pitt B: Thallium-201 as a myocardial imaging agent. Sem Nucl Med 7:49-58, Jan 1977

67. Kushner FG, Okada RD, Kirshenbaum HD, et al: Stress induced pulmonary thallium-201 uptake in patients with coronary artery disease. J Nucl Med 20:649, Jun 1979 (abst)

68. Wainwright RJ: Radioisotopes in cardiology. *In* Besser GM (Ed): Advanced Medicine, 13th Ed. Tunbridge Wells, England, Pitman Medical, 1977, pp 462-487

69. Meade RC, Bamrah VS, Horgan JD, et al: Quantitative methods in the evaluation of thallium-201 myocardial perfusion images. J Nucl Med 19:1175-1178, Oct 1978

70. McKillop JH, Bessent RG, Murray RG, et al: A quantitative approach to the analysis of the normal thallium-201 myocardial image. Europ J Nucl Med 3(4):223-225, 1978

71. Corne RA, Gotsman MS, Weiss A, et al: Thallium-201 scintigraphy in the diagnosis of coronary stenosis. Br Heart J 41:575-583, May 1979

72. McKillop JH, Murray RG, Turner JG, et al: A comparison of visual and semiquantitative analysis of stress thallium-201 myocardial images in patients with suspected ischemic heart disease. Radiology (in press) 1980

73. Schelbert HR, Henning H, Rigo P, et al: Considerations of ^{201}Tl as a myocardial radionuclide imaging agent in man. Invest Radiol 11:163-171, May 1976

74. Cohen HA, Baird MG, Rouleau JR, et al: Thallium-201 myocardial imaging in patients with pulmonary hypertension. Circulation 54:790-795, Nov 1976

75. Khaja F, Alam M. Goldstein S, et al: Diagnostic value of visualization of the right ventricle using thallium-201 myocardial imaging. Circulation 59:182-188, Jan 1979

76. Munch JC: Human thallotoxicosis. JAMA 102:1929-1934, Jun 1934

77. Christie A: The Pale Horse. New York, Pocket Books, Simon and Schuster, 1975

78. Cavanagh JB, Fuller NH, Johnson HRM, et al: The effects of thallium salts with particular reference to the nervous system changes. Quart J Med (new series) 43:293-319, Apr 1974

79. Reed D, Crawley J, Faro SN, et al: Thallotoxicosis—Acute manifestations and sequelae. JAMA 183:516-522, Feb 1963

80. Browning E: Thallium, chap 39, *In* Toxicity of Industrial Metals. London, Butterworths, 1961, pp 282-287

81. Feller PA, Sodd VJ: Dosimetry of four heart imaging radionuclides ^{43}K, ^{81}Rb, ^{129}Cs and ^{201}Tl. J Nucl Med 16:1070-1075, Nov 1975

82. Budinger TF, Rollo FD: Physics and instrumentation. Prog Card Dis 20:19-53, Jul 1977

83. Maier JG, Casarett G: Pathophysiologic aspects of radiation nephritis in dogs. University of Rochester AEC Report UR 626, 1963

84. Rochmis P, Blackburn H: Exercise tests—A survey of procedures, safety and litigation experience in approximately 170,000 tests. JAMA 217:1061-1066, Aug 1971

85. Ellestad MH, Cooke BM, Greenberg PS: Stress testing: Clinical application and predictive capacity. Prog Card Dis 21: 431-460, Jun 1979

86. Wackers FJTh, Schoot JBvd, Sokole EB, et al: Noninvasive visualisation of acute myocardial infarction in man with thallium-201. Br Heart J 37:741-744, Jul 1975

87. Wackers FJTh, Lie KI, Liem KL, et al: Thallium-201 scintigraphy in unstable angina pectoris. Circulation 57:738-750, Apr 1978

88. Gewirtz H, Beller GA, Strauss HW, et al: Transient defects of resting thallium scans in patients with coronary artery disease. Circulation 59:707-713, Apr 1979

89. Pond M, Rehn T, Burow R, et al: Early detection of myocardial infarction by serial thallium-201 imaging. Circulation 56: III 230, Oct 1977 (abst)

90. Maseri A, Parodi O, Severi S, et al: Transient transmural reduction of myocardial blood flow, demonstrated by thallium-201 scintigraphy, as a cause of variant angina. Circulation 54:280-288, Aug 1976

91. McLaughlin PR, Doherty PW, Martin RP, et al: Myocardial imaging in a patient with reproducible variant angina. Am J Cardiol 39:126, Jan 1977

92. Wackers FJTh, Sokole EB, Samson G, et al: Value and limitations of thallium-201 scintigraphy in the acute phase of myocardial infarction. N Engl J Med 295:1-5, Jul 1976

93. McKillop JH, Gray HW, Turner JG, et al: The clinical value of delayed thallium-201 myocardial imaging in suspected acute myocardial infarction. Br Heart J 40:870-873, Aug 1978

94. Wackers FJTh, Lie KI, Sokole EB, et al: Prospective study of value of thallium-201 scintigraphy for selection of CCU patients. Circulation 54:II 216, Oct 1976 (abst)

95. McNeilly RH, Pemberton J: Duration of last attack in 998 fatal cases of coronary artery disease and its relation to possible cardiac resuscitation. Br Med J 3:139-142, Jul 1968

96. Mueller TM, Marcus ML, Ehrhardt JC, et al: Limitations of thallium-201 myocardial perfusion scintigrams. Circulation 54: 640-646, Oct 1976

97. Wackers FJTh, Becker AE, Samson G, et al: Location and size of acute transmural myocardial infarction estimated from thallium-201 scintiscans—A clinicopathological study. Circulation 56:72-78, Jul 1977

98. Fletcher JW, Rao PS, Herbig FK, et al: Tl-201 assessment of infarct size in early infarction. J Nucl Med 19:680, Jun 1978 (abst)

99. Karunaratne H, Cantez S, Harper P, et al: The natural history of myocardial perfusion defects in patients with uncomplicated myocardial infarction. Am J Cardiol 41:360, Feb 1978 (abst)

100. Misbach GA, Botvinick EH, Shames DM, et al: Serial changes in scintigraphic measures of ischemia and infarction and in left ventricular function following coronary occlusion in dogs. Am J Cardiol 41:380, Feb 1978 (abst)

101. Niess GS, Logic JR, Russell RD, et al: Usefulness and limitations of thallium-201 myocardial scintigraphy in delineating location and size of prior myocardial infarction. Circulation 59: 1010-1019, May 1979

102. McKillop JH, Murray RG, Bessent RG, et al: The significance of the abnormal rest thallium-201 myocardial image in coronary artery disease. Eur J Nucl Med 4(1):83-86, 1979

103. Schelbert HR, Henning H, Rigo P, et al: Intravenous myocardial imaging performed serially early and late after acute myocardial infarction. Eur J Nucl Med 2(2):75-83, Jun 30, 1977

104. Blood DK, McCarthy DM, Sciacca RR, et al: Comparison of single-dose and double dose thallium-201 myocardial scintigraphy for the detection of coronary artery disease and prior myocardial infarction. Circulation 58:777-788, Nov 1978

105. Ritchie JL, Albro PC, Caldwell JH, et al: Thallium-201 myocardial imaging: A comparison of redistribution and rest images. J Nucl Med 20:477-483, Jun 1979

106. Verani MS, Jhingran S, Attar M, et al: Post stress redistribution of thallium-201 in patients with coronary artery disease, with and without prior myocardial infarction. Am J Cardiol 43: 1114-1122, Jun 1979

107. Bailey LK, Griffith LSC, Rouleau J, et al: Thallium-201 myocardial perfusion imaging at rest and during exercise—Comparative sensitivity to electrocardiography in coronary artery disease. Circulation 55:79-87, Jan 1977

108. Botvinick EH, Taradash MR, Shames DM, et al: Thallium-201 myocardial perfusion scintigraphy for the clinical clarification of normal, abnormal and equivocal electrocardiographic stress tests. Am J Cardiol 41:43-51, Jan 1978

109. Lenaers A, Block P, Van Thiel E, et al: Segmental analysis of Tl-201 stress myocardial scintigraphy. J Nucl Med 18:509-516, Jun 1977

110. Massie B, Dash H, Botvinick E, et al: Identification of high risk coronary disease by myocardial perfusion scintigraphy during exercise testing. Am J Cardiol 41:413, Feb 1978 (abst)

111. Rehn T, Griffith L, Achuff S, et al: Rest and stress thallium 201 imaging in left main coronary disease: Sensitive but not specific. Am J Cardiol 41:413, Feb 1978 (abst)

112. Ritchie JL, Trobaugh GB, Hamilton GW, et al: Myocardial imaging with thallium-201 at rest and during exercise—Comparison with coronary arteriography and resting and stress electrocardiography. Circulation 56:66-71, Jul 1977

113. Rosenblatt A, Lowenstein JM, Kerth W, et al: Post exercise thallium-201 myocardial scanning: A clinical appraisal. Am Heart J 94:463-470, Oct 1977

114. Turner DA, Battle WE, Deshmukh H, et al: The predictive value of myocardial perfusion scintigraphy after stress in patients without previous myocardial infarction. J Nucl Med 19:249-255, Mar 1978

115. Wainwright RJ, Maisey MN, Sowton E: Segmental quantitative thallium scintigraphy in diagnosis of coronary artery disease—Correlation with coronary arteriography and exercise stress testing. Br Heart J 40:447, Apr 1978 (abst)

116. Bodenheimer MB, Banka VS, Fooshee CM, et al: Extent and severity of coronary heart disease—Determination by thallous chloride Tl 201 myocardial perfusion scanning and comparison with stress electrocardiography. Arch Intern Med 139:630-634, Jun 1979

117. Murray RG, McKillop JH, Bessent RG, et al: Evaluation of thallium-201 exercise scintigraphy in coronary heart disease. Br Heart J 41:568-574, May 1979

118. Ritchie JL, Zaret BL, Strauss HW, et al: Myocardial imaging with thallium-201 at rest and exercise: A multicentre study—Coronary angiographic and electrocardiographic correlations. J Nucl Med 18:642, Jun 1977 (abst)

119. Meller J, Goldsmith SJ, Rudin A, et al: Spectrum of exercise thallium-201 myocardial perfusion imaging in patients with chest pain and normal coronary angiograms. Am J Cardiol 43:717-723, Apr 1979

120. Pond M, Rehn T, Bailey I, et al: Specificity of thallium-201 myocardial imaging in patients with chest pain and suspected coronary artery disease. Am J Cardiol 41:442, Feb 1978 (abst)

121. Raphael LD, Cowley MJ, Logic JR, et al: ^{201}Thallium exercise myocardial scintigraphy in patients with "angina and normal coronary arteriograms." Circulation 54 II 217, Oct 1976 (abst)

122. Poe ND, Eber LM, Norman AS, et al: Myocardial images in nonacute coronary and noncoronary heart diseases. J Nucl Med 18:18-23, Jan 1977

123. Feiglin D, Huckell V, Staniloff H, et al: Demonstration of segmental thallium perfusion defects in cardiomyopathies having normal coronary arteries. J Nucl Med 19:704, Jun 1978 (abst)

124. Bailey I, Strauss HW, Pitt B: Thallium-201 myocardial perfusion imaging at rest and stress: Sensitivity for detection of coronary artery disease. J Nucl Med 17:522, Jun 1976 (abst)

125. Berman DS, Amsterdam EA, Jove JA, et al: Thallium-201 stress myocardial scintigraphy—Application in asymptomatic patients with positive exercise electrocardiograms. Am J Cardiol 41: 380, Feb 1978 (abst)

126. Weisberger CL: Debate on coronary bypass (Letter). N Engl J Med 297:1466, Dec 1977

127. Rigo P, Bailey IK, Griffith LSC, et al: Value and limitations of segmental analysis of stress thallium myocardial imaging for localization of coronary artery disease. Circulation 61:973-981, May 1980

128. McKillop JH, Murray RG, Turner JG, et al: Can the extent of coronary artery disease be predicted from thallium-201 myocardial images? J Nucl Med 20:715-719, Jun 1979

129. Massie BM, Botvinick EH, Brundage BH: Correlation of thallium-201 scintigrams with coronary anatomy—Factors affecting region by region sensitivity. Am J Cardiol 44:616-622, Oct 1979

130. DeRouen TA, Murray JA, Owen W: Variability in the analysis of coronary arteriograms. Circulation 55:324-328, Feb 1978

131. Vlodaver Z, Frech R, Van Tassel RA, et al: Correlation of the antemortem coronary arteriogram and the postmortem specimen. Circulation 47:162-169, Jan 1973

132. Schwartz JN, Kong Y, Hackel DB, et al: Comparison of angiographic and postmortem findings in patients with coronary artery disease. Am J Cardiol 36:174-178, Aug 1975

133. Rigo P, Becker LC, Griffith LSC, et al: Influence of coronary collateral vessels on the results of thallium-201 myocardial stress imaging. Am J Cardiol 44:452-458, Sep 1979

134. Fulton WFM: The Coronary Arteries. Springfield, IL, Charles C Thomas, 1965, pp 49-71

135. Kalbfleisch H, Hort W: Quantitative study on the size of coronary artery supplying areas postmortem. Am Heart J 94: 183-188, Aug 1977

136. McGowan RL, Welch TG, Zaret BL, et al: Noninvasive myocardial imaging with potassium-43 and rubidium-81 in patients with left bundle branch block. Am J Cardiol 38:422-428, Oct 1976

137. Wackers FJ, Lie KI, Sokole E, et al: Thallium-201 for localization of acute myocardial infarction in the presence of left bundle branch block—Correlation between site of infarction and ECG changes. Circulation 52:II 54, Oct 1975 (abst)

138. Hamilton GW, Trobaugh GB, Ritchie JL, et al: Myocardial imaging with ^{201}thallium: An analysis of clinical usefulness based on Bayes' theorem. Sem Nucl Med 8:358-364, Oct 1978

139. Caralis DG, Bailey I, Kennedy HL, et al: Thallium-201 myocardial imaging in evaluation of asymptomatic individual with ischemic ST segment depression on exercise electrocardiogram. Br Heart J 42:562-567, Nov 1979

140. Frick MH: An appraisal of symptom relief after coronary bypass grafting. Postgrad Med J 52:765-769, Dec 1976

141. Bulkley BH, Hutchins GM: Myocardial consequences of coronary artery by-pass graft surgery—The paradox of necrosis in areas of revascularization. Circulation 56:906-913, Dec 1977

142. Di Luzio V, Roy PR, Sowton E, et al: Fate of coronary collateral circulation after aortocoronary saphenous vein bypass grafts. Br Heart J 37:397-400, Apr 1975

143. Zaret BL, Martin ND, McGowan RL, et al: Rest and exercise potassium-43 myocardial perfusion imaging for the noninvasive evaluation of aortocoronary bypass surgery. Circulation 49:688-695, Apr 1974

144. Lurie AJ, Salel AF, Berman DS, et al: Determination of improved myocardial perfusion after aortocoronary bypass surgery by exercise rubidium-81 scintigraphy. Circulation 54:III20-III23, Dec 1976

145. Ritchie JL, Narahara KA, Trobaugh GB, et al: Thallium-201 myocardial imaging before and after coronary revascularization. Circulation 56:830-836, Nov 1977

146. Ormand J, Platt M, Mills L, et al: Thallium-201 scintigraphy and exercise testing in evaluating patients prior to and after coronary bypass surgery. Circulation 56:III 131, Oct 1977 (abst)

147. Sharboro JA, Karunaratne H, Cantez S, et al: Thallium-201 imaging in assessment of aortocoronary bypass grafting. Br Heart J 42:553-561, Nov 1979

148. Greenberg BH, Hart R, Botvinick EH, et al: Thallium-201 myocardial perfusion scintigraphy to evaluate patients after coronary bypass surgery. Am J Cardiol 42:167-176, Aug 1978

149. Verani MS, Marcus ML, Spoto G, et al: Thallium-201 myocardial perfusion scintigrams in the evaluation of aortocoronary saphenous bypass surgery. J Nucl Med 19:765-772, Jul 1978

150. Murray RG, McKillop JH, Tweddel A, et al: The value of thallium-201 exercise scintigraphy in predicting coronary artery graft status. Br Heart J 41:369, Mar 1979 (abst)

151. Berger BC, Watson DD, Burwell LR, et al: Improvement in resting thallium-201 uptake following coronary artery bypass surgery. Am J Cardiol 43:383, Feb 1979 (abst)

152. Rehn T, Griffith L, Achuff S, et al: Value and limitations of thallium-201 imaging to detect bypass graft patency. Am J Cardiol 43:434, Feb 1979 (abst)

153. Rothman M, Bergman G, Atkinson L, et al: Value and limitation of ergometrine in predicting vasospastic angina. Br Heart J 41:370-371, Mar 1979 (abst)

154. Bailey IK, Come PC, Kelly DT, et al: Thallium-201 myocardial perfusion imaging in aortic valve stenosis. Am J Cardiol 40:889-899, Dec 1977

155. McKillop JH, Murray RG, Turner RG: Thallium-201 myocardial imaging in aortic valve disease. Proceedings of the 16th International Annual Meeting of the Society of Nuclear Medicine (in press)

156. Massie B, Botvinick EH, Shames D, et al: Myocardial perfusion scintigraphy in patients with mitral valve prolapse—Its advantage over stress electrocardiography in diagnosing associated coronary artery disease and its implications for the aetiology of chest pain. Circulation 57:19-26, Jan 1978

157. Gaffney FA, Wohl AJ, Blomquist CC, et al: Thallium-201 myocardial perfusion studies in patients with the mitral valve prolapse syndrome. Am J Med 64:21-26, Jan 1978

158. Klein GJ, Kostuk WJ, Boughner DR, et al: Stress myocardial imaging in mitral valve leaflet prolapse syndrome. Am J Cardiol 42:742-750, Nov 1978

159. Tresch DD, Soin S, Siegel R, et al: Mitral valve prolapse —Evidence for a myocardial perfusion abnormality. Am J Cardiol 41:441, Feb 1978 (abst)

160. Bulkley BH, Rouleau J, Strauss HW, et al: Idiopathic hypertrophic subaortic stenosis: Detection by thallium-201 myocardial perfusion imaging. N Engl J Med 293:1113-1116, Nov 1975

161. Bulkley BH, Rouleau JR, Whitaker JQ, et al: The use of 201-thallium for myocardial perfusion imaging in sacroid heart disease. Chest 72:27-32, Jul 1977

162. Kinney EL, Jackson GL, Reeves WC, et al: The prevalence of sarcoid heart disease detected by thallium scanning. Am J Cardiol 43:437, Feb 1979 (abst)

163. Wackers FJTh, Sokole EB, Samson G, et al: Imaging in non-coronary heart disease, *In* Ritchie JL, Hamiton GW, Wackers FJTh (Eds): Thallium-201 Myocardial Imaging. New York, Raven Press, 1978, pp 111-120

164. Pitcher DW, Wainwright RJ, Maisey MN, et al: Assessment of chest pain in hypertrophic cardiomyopathy by thallium-201 myocardial scintigraphy. Br Heart J 41:379-380, Mar 1979 (abst)

165. Gilday DL, Howman-Giles R, Rowe R: The benefit of thallium-201 myocardial perfusion studies in neonates. Am J Cardiol 41:380, Feb 1978 (abst)

166. Finley JP, Howman-Giles R, Gilday DL, et al: Thallium-201 myocardial imaging in anomalous left coronary artery arising from the pulmonary artery. Am J Cardiol 42:675-680, Oct 1978

167. Strauss HW, Harrison K, Pitt B: Thallium-201: Noninvasive determination of the regional distribution of cardiac output. J Nucl Med 18:1167-1170, Dec 1977

168. Bossuyt A, Jonckheer MH: Noninvasive determination of the regional distribution of cardiac output: Effect of pharmacological agents on the distribution of Tl-201 (Letter). J Nucl Med 19:973, Aug 1978

169. Christenson J, Larsson I, Svensson S-E, et al: Distribution of intravenously injected 201 thallium in the legs during walking —A new test for assessing arterial insufficiency in the legs. Eur J Nucl Med (2):85-88, Jun 30, 1977

170. Cox PH, Belfer AJ, van der Pompe WB: Thallium-201 chloride uptake in tumours, a possible complication in heart scintigraphy. Br J Radiol 49:767-768, Sep 1976

171. Tonami N, Michigishi T, Bunko H, et al: Clinical tumour scanning with ^{201}Tl-chloride. J Nucl Med 18:617, Jun 1977 (abst)

172. Tonami N, Hisada K: Clinical experience of tumor imaging with ^{201}Tl-chloride. Clin Nucl Med 2:75-81, Mar 1977

173. Fukuchi M, Tachibana K, Kuwata K, et al: Thallium-201 imaging in thyroid carcinoma—Appearance of a lymph node metastasis. J Nucl Med 19:195-196, Feb 1978

174. Fukunaja M, Morita R, Yonekura Y, et al: Accumulation of ^{201}Tl chloride in a parathyroid adenoma. Clin Nucl Med 4: 229-230, Jun 1979

175. Tonami N, Bunko H, Kuwajima A, et al: Increased localization of ^{201}Tl-chloride in subacute thyroiditis. Clin Nucl Med 4:3-5, Jan 1979