state through the ^{201}Tl imaging protocol. Gastrointestinal uptake was negligible (Fig. 2, 3) and did not seem to change between rest and redistribution images. In addition, the absence of background subtraction in the quantitative analysis should overcome any artifact due to oversubtraction or undersubtraction in rest or redistribution images.

In conclusion, the study results suggest that myocardial segments with normal ^{201}Tl uptake on rest images and abnormal ^{201}Tl uptake on redistribution images (RR pattern A) have impaired function and are supplied by severely stenosed coronary arteries.

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EDITORIAL

Easy Come, Easy Go: Time to Pause and Put Thallium Reverse Redistribution in Perspective

For two decades, ^{201}Tl scintigraphy has withstood the test of time as the single-photon imaging gold standard of viability. Extensive clinical experience has taught the clinician that a reversible thallium defect represents jeopardized but viable myocardium, while a persistent defect represents scar or severe hypoperfusion, and may require delayed imaging or a second dose of thallium to distinguish the two. The phenomenon of the reverse redistributing thallium defect has continued to trouble the clinician, having evaded a clear understanding of its mechanisms and clinical significance.

Reverse redistribution has been most commonly observed following coronary thrombolysis, where it is frequently associated with patency of the infarct-related artery and relatively preserved infarct segment wall motion (*1,2*). It has also been described soon after angioplasty or bypass surgery (*3*), again in the presence of a patent graft or supplying artery. In a general referral population, reverse redistribution has been found to be associated with coronary artery disease of varying severity, using either exercise (*4*) or dipyridamole (*5*) stress. It is also observed in a variety of cardiomyopathies, including Chagas' disease and sarcoidosis (*6,7*).

In this issue of the *Journal*, Pace et al. further add to our knowledge on reverse redistribution in the setting of rest and delayed thallium images. They examine coronary angiography, ventricular function and rest uptake of ^{99m}Tc-sestamibi, in relation to rest-redistribution thallium scintigraphy in 25 patients with severe coronary disease. They report that segments with reverse redistribution are frequently subtended by occluded epicardial ves-

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sels (46%), often in association with "good collateral" circulation (58%). Such segments also had abnormal wall motion and decreased sestamibi uptake. This was especially true for defects that were present only in the redistribution study, but not on the initially injected scan. Pace et al. conclude that segments with reverse redistribution clinically resemble fixed defects.

Thus, reverse-redistributing defect appears to be associated with a variety of clinical conditions in diverse populations. Is there a potentially unifying concept that could put thallium reverse redistribution in perspective? We suggest that in times of uncertainty and confusion, we should pause and revisit the well established principles of thallium kinetics and generate a testable hypothesis.

The uptake of thallium in the initial scan is mainly dependent on myocardial blood flow in the setting of reverse redistribution, implying that if the initial scan is relatively normal in a reverse-redistributing defect, the bulk blood flow to the region is nonjeopardizing and comparable to adjacent regions at the time of initial thallium delivery. This would further imply a normal or, at most, a noncritical stenosis in the supplying coronary artery, or a coronary stenosis associated with the presence of adequate collaterals.

Thallium washout, on the other hand, depends on a combination of two main factors: (1) level of resting blood flow and its associated thallium content and (2) the ability of the myocardial cells to retain thallium. The latter is dependent on the number of functioning myocytes in the myocardium and the capacity of the membrane Na-K ATPase in each myocyte to maintain high intracellular levels of potassium or thallium. This was well demonstrated by a thallium kinetics study in a canine transient coronary occlusion model followed by reperfusion by Okada (*8*).

A reverse-redistributing defect suggests that there is more rapid thallium washout in a region than normal, resulting from either higher local blood flow at rest, or an inability of the local myocardium to hold onto the delivered thallium. Since the initial scan showed equal blood flow with other regions (i.e., not hyperemic), we propose that it is more often the latter situation of less-than-full complement of functioning myocytes that accounts for most of the reverse redistributions. This situation is best exemplified in the reperfused or infarcted myocardium, where there is a significant mixture of scar with stunned (transiently ischemic) or hibernating (persistently ischemic but viable) myocardium. This type of myocardium can receive the initially delivered thallium in the presence of nonlimiting flow, but cannot retain the thallium effectively with time.

Could this hypothesis explain existing clinical observations on reverse redistribution? In the reperfused myocardium, Weiss et al. found reverse redistribution to be associated with patent artery, improved thallium defect size and near normal wall motion (*1*). This is a classic condition of a mixture of stunned and nonviable myocardium in the face of restored coronary blood flow supply. Langer et al. also found reverse redistribution in 63 post-thrombolysis patients to have more widely patent coronary artery, and more significant transient regional functional improvement after sublingual nitroglycerin administration (*2*), further supporting our proposed hypothesis of a mixture of viable but possibly stunned with nonviable myocardium in the face of adequate perfusion. Similar arguments can be made for the study by Silberstein and DeVries, who found reverse redistributing defects in patients following bypass surgery to be associated with patent coronary grafts in regions of previous ischemia (*3*).

Is this hypothesis supported by the currently reported study by Pace et al.? They studied rest-redistribution thallium imaging, the main goal of which is the assessment of myocardial viability, and found reverse redistribution to be associated with occluded but well collateralized coronary circulation with compromised wall motion. In their population initial good myocardial perfusion is likely well maintained by excellent collaterals (58%). Why did they find more rapid washout in these segments? It is likely that a number of these segments had suffered previous coronary artery occlusion, leaving behind stunned or hibernating myocardium mixed with some scar and leading to early loss of the tracer. This is supported by the lower level sestamibi uptake in the same segments. It is appropriate to emphasize that there are still viable myocytes present, and that the perfusion is nonflow limiting at rest.

It is also important to consider the significance of reverse redistribution in normal subjects. Kaul et al. have demonstrated that regional scintigraphic myocardial thallium clearance can vary by as much as 98% within a single normal subject (*9*). They point out that this variability is likely a reflection of technical limitations of quantitative clinical scintigraphy. In particular, background subtraction of planar images can result in artifactual "reverse redistribution" (*10*).

How can we put the "reverse redistributing" thallium defect in clinical perspective? Perhaps three different approaches are required for three different clinical situations:

1. Early after reperfusion of acute myocardial infarction, reverse redistribution may be seen as evidence of infarct-related artery patency, with the extent of myocardial stunning/necrosis more accurately portrayed by the delayed images. It has a better prognosis than the classic reversible defect, and probably should be followed up with a repeat scan in several months' time to rule out a significant component of reversible ischemia.

2. In patients with known chronic coronary artery or myocardial disease, this finding can be interpreted, as concluded by Pace et al., as evidence of myocardial "scar" within a segment containing viable elements, whether normal, stunned or hibernating. A decision regarding revascularization will depend on the ultimate wall motion in the area, and the degree of ischemia in other myocardial segments. Clinically, it is still more

important to attend to the traditional reversible or persistent perfusion defects if they coexist in the same scan. A practical implication from this observation is that in a rest thallium study, the redistribution image is an integral part of the procedure, and should not be skipped just because the initial resting scan appears normal.

3. Finally, in subjects without significant pretest likelihood or overt evidence of heart disease, reverse redistribution may represent nothing more than normal variability of segmental thallium clearance, or an imaging artifact. This is consistent with the Bayesian theorem that false-positive results are frequent in patients with low pretest likelihood of the disease.

Reverse redistribution of thallium is a fascinating and perplexing observation which for too long has received too little attention. Improved understanding of this phenomenon is likely to enhance the diagnostic and prognostic value of thallium scintigraphy. Further experimental and clinical observations are required to shed light on reverse redistribution, and to test the approach we have proposed in this perspective.

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