The sympathetic and parasympathetic innervation of the heart plays a major role in the regulation of myocardial function, heart rate, and myocardial blood flow (MBF), both in healthy subjects and in patients with heart disease. Important among these disorders are ischemic heart disease, heart failure, sudden death, and diabetes. It is known, for example, that $\alpha$-1 and $\alpha$-2 sympathetic receptor densities are different in large (conduit) vessels and in microvasculature. Vasoconstriction of the conduit vessels or of the small vessels has a profound effect on the regulation of MBF at rest and during stress.\(^1\) It is also known that denervation could occur on the basis of functional changes such as ischemia or as a result of structural changes such as myocardial infarction or heart transplantation.

Metaiodobenzylguanidine (MIBG) is an analog of the false neurotransmitter guanethidine. It is taken up by adrenergic neurons in a similar fashion to norepinephrine. It does not undergo intracellular metabolism (Figure 1). When tagged with iodine 123, it can be used to image adrenergic receptors in many organs, including the heart, with conventional planar or single photon emission computed tomography (SPECT) techniques.\(^2\)\(^-\)\(^5\) Such imaging allows the evaluation of receptor density and sympathetic tone. Other neuroimaging tracers allow the evaluation of both sympathetic and parasympathetic innervation through use of positron emission tomography (PET) (see below). This review will summarize current knowledge of neurocardiac imaging with SPECT and, briefly, with PET.

### Technique of I-123 MIBG Imaging

A dose of 4 mCi of I-123 MIBG is injected intravenously at rest (after thyroid uptake of I-123 is blocked). Planar followed by SPECT images are obtained 15 minutes after injection, and the planar images are repeated 4 hours later (Figure 2). The cardiac application of this tracer in the United States, at present, requires an investigative new drug application. On planar images, the heart-to-mediastinum uptake (H/M) ratio is determined from regions of interest on both the early and delayed images. The initial ratio reflects receptor density. A high ratio indicates predominant localization of the tracer in the myocardium, which is what is expected in normal hearts. As the ratio decreases, less uptake occurs in the myocardium and more in the extracardiac structures. This pattern reflects reduced adrenergic receptor density. Immediately after heart transplantation, no activity is detected in the myocardium, reflecting total denervation. In healthy subjects the activity is slightly lower in the inferior wall, probably because of attenuation, and the lower activity at the apex, compared with the base, may be due to the partial volume effect (Figure 3).\(^6\)\(^-\)\(^13\) The myocardial washout (normalized to mediastinal activity) is determined as the rate of decrease in myocardial counts over time between early and delayed imaging. This ratio reflects adrenergic activity and tone. A high washout rate means increased adrenergic activity. Normal myocardial MIBG results are shown in Table 1.\(^10\)\(^-\)\(^12\)\(^-\)\(^17\)

The SPECT (and planar) images depict a topography of the regional distribution of the tracer (Figure 2, B). As with perfusion imaging, the pressure of an abnormality could be assessed visually or semiquantitatively, and the extent of denervation may be expressed as percentage of left ventricular (LV) myocardium. The regional distribution could be compared with regional perfusion by acquisition of separate SPECT images with a perfusion tracer such as technetium 99m sestamibi or tetrofosmin. The 2 sets of images may yield a matched or mismatched pattern in terms of presence and extent of denervation versus perfusion abnormality. A mismatched pattern indicates that the denervation is larger than the corresponding perfusion abnormality. The difference corresponds to a region of denervated but perfused viable myocardium.

### MIBG Imaging in Ischemic Heart Disease

Sympathetic nerves extend from the base toward the apex of the left ventricle and penetrate the myocardium
from the epicardial to the endocardial surface alongside the coronary vessels. Parasympathetic fibers are much fewer in number and travel alongside the endocardial surface and penetrate the myocardium outward to the epicardial surface. Therefore acute myocardial infarction, whether transmural (Q wave) or nontransmural (non–Q wave), is expected to disrupt these nerve fibers. In a non–Q-wave infarction, the denervated area

Figure 1. Schema of sympathetic nerve terminals in the myocardium. NE, Norepinephrine; DOPA, dihydroxyphenylalanine.

Figure 2. A, Early (left) and 4-hour delayed (right) planar I-131 MIBG images. (Images courtesy of Nagara Tamaki, MD, Sapporo, Japan.) B, SPECT MIBG images in a healthy subject. (Images courtesy of Igansi Carrio, MD, Barcelona, Spain.)