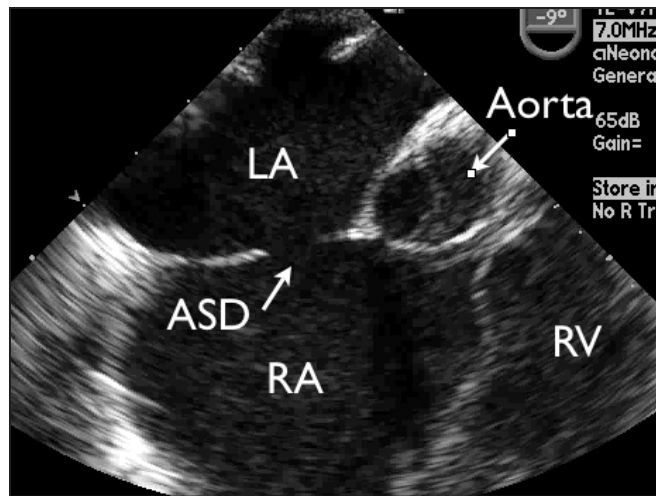




A CT scan with three-dimensional reconstruction shows a stent placed in this patient to aortic coarctation. With three-dimensional echocardiography, physicians can obtain real-time images of the atrial septum, mitral valve, and aortic valve structure.



A transesophageal echocardiogram shows a secundum atrial septal defect (ASD) in a toddler. This technology provides excellent anatomic definition because lungs, bone, and muscle do not interfere with the imaging (LA, left atrium; RA, right atrium; RV, right ventricle).

PHOTOS COURTESY DR. ALAN FRIEDMAN

Continued from previous page

measurement of right and left ventricular function. Unlike echocardiography, its results are not subject to variable interobserver interpretation. He recommended PET scanning for assessing myocardial metabolism, perfusion, and viability.

Dr. Friedman said ultrafast CT scanning produces very-high-resolution images that can provide excellent information on blood flow and cardiac function. It also can assess areas of stenosis, particularly in the distal pulmonary artery, that are missed by echocardiography.

Although not yet portable, MRI and MR angiography also offer excellent resolution, according to Dr. Friedman, but without the high doses of radiation with CT scanning. Three-dimensional images are already available for surgical planning, he said, and MR cardiac catheterization laboratories are being developed. ■

## Doppler Able to Determine the Nature of HCM

Doppler myocardial imaging to assess systolic activation delay can help determine whether a condition is hypertrophic cardiomyopathy or merely the result of athletic training—and help predict serious adverse cardiac events, Italian researchers reported.

Dr. Antonello D'Andrea of the Second University of Naples (Italy) and colleagues followed 70 patients with hypertrophic cardiomyopathy (HCM) and 85 age- and sex-matched competitive athletes with enlarged left ventricles and interventricular septa thicker than 12 mm (*Br. J. Sports Med.* 2006;40:244-50).

During the 4-year follow-up, the study's primary end point was cardiovascular mortality. Eight HCM patients died during follow-up; none of the athletes had a cardiovascular event. The participants were aged 29 years on average and were matched for blood pressure. Eighty percent of them were male. All had standard pulsed Doppler echocardiography and pulsed Doppler myocardial imaging in six myocardial segments. HCM patients showed a "significant global Doppler interventricular delay," the authors said. One-fifth of the HCM patients had a relative who had died from an HCM-related cardiac event.

—John R. Bell

levels are at least partly associated with impaired ET<sub>B</sub> receptor-mediated clearance.<sup>13</sup> Furthermore, the long-term administration of a selective ET<sub>B</sub> receptor antagonist was found to have unfavorable effects on vascular remodeling.<sup>4</sup> This is in sharp contrast to the benefits of selective ET<sub>A</sub> antagonism.<sup>14</sup>

### THE DIFFERENCE LIES IN ET<sub>A</sub> SELECTIVITY

Vasoconstriction, cellular proliferation, and vascular remodeling are the hallmarks of PAH.<sup>12</sup> Studies have demonstrated that selective ET<sub>A</sub> antagonists play a pivotal role in the regulation of ET-1 levels in PAH and have been beneficial for vascular remodeling.<sup>4,7,13</sup>

### ET-1 AND RECEPTOR-MEDIATED ACTIVITIES

Highly selective ET<sub>A</sub> blockade maintains ET-1 clearance, NO and PGI<sub>2</sub> levels, and reduces or maintains circulating ET-1 levels, resulting in vasodilation, increased blood flow, and repair of remodeled vasculature compared to less selective agents.<sup>5-7,14</sup> (See Figures 1,2)

### HOW SELECTIVE TO ET<sub>A</sub> SHOULD TREATMENT BE?

The more selective, the better. One should always be aware of the varying degrees of selectivity, as they equate to differences in blockade of the ET<sub>A</sub> and ET<sub>B</sub> receptors and resulting levels of ET-1.<sup>8,15,16</sup> Figure 3 illustrates the difference between a less selective agent and highly selective agents. These in vitro selectivity ratios demonstrate the stark differences in ET<sub>A</sub> selectivity. Figure 4 depicts how agents with low selectivity of the ET<sub>A</sub> receptor (<2400) increase ET-1 levels whereas highly selective ET<sub>A</sub> receptor (>2400) antagonists have been shown to

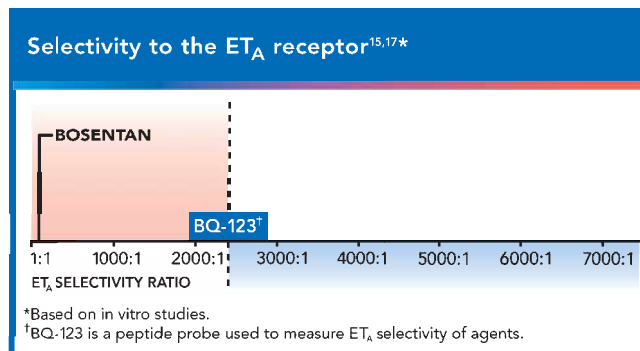


Figure 3

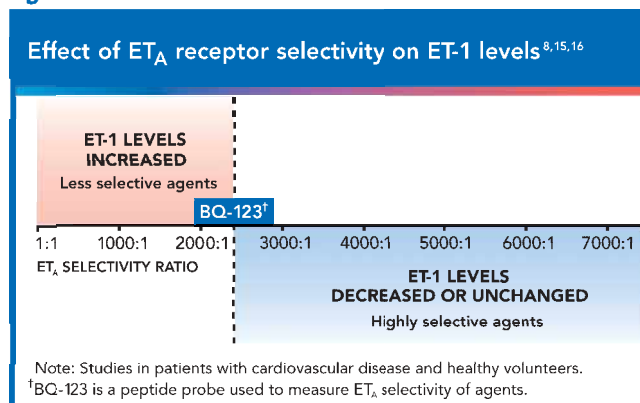


Figure 4

decrease ET-1 levels or leave them unchanged.<sup>6,8,15</sup> The benefits of ET<sub>A</sub> selectivity are being recognized.

### TOWARD BETTER OUTCOMES IN PAH

Currently, there are no highly selective ET<sub>A</sub> antagonists available for the treatment of PAH. In vivo studies have shown that highly selective ET<sub>A</sub> antagonism may lead to better overall outcomes.<sup>7,8,12</sup>

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