predisposing the atria to fibrillation might be somatic in nature.

Research efforts were focused on the *GJA5* gene, which encodes for a gap-junction protein called connexin 40. In humans, this gene is predominantly expressed in atrial tissue and has a role in mediating atrial conduction through electrical coupling between cells.

The investigators sequenced *GJA5* in genomic DNA isolated from resected cardiac tissue and peripheral lymphocytes from 15 patients with idiopathic AF. Novel heterozygous missense mutations were identified in four of these patients. In three of the patients the mutations were found in the cardiac tissue samples but not in the lymphocyte DNA, indicating that they were somatic in origin.

As their patient cohort was highly selected, the authors acknowledge that the prevalence of *GJA5* sequence variants might be different in a large, randomized cohort. Their findings do, however, suggest that mutations in *GJA5* could predispose patients to idiopathic AF, with mutations confined to the diseased tissue.

Original article Gollob MH *et al.* (2006) Somatic mutations in the connexin 40 gene (*GJA5*) in atrial fibrillation. *N Engl J Med* **354:** 2677–2688

Bosentan: a new therapy for Eisenmenger syndrome?

Eisenmenger syndrome is an advanced form of pulmonary arterial hypertension (PAH) related to congenital heart disease. Bosentan is a dual endothelin-1-receptor antagonist that effectively treats idiopathic PAH and PAH related to connective tissue disease. Following preliminary trials of bosentan for the treatment of Eisenmenger syndrome, the Bosentan Randomized Trial of Endothelin Antagonist Therapy-5 (BREATHE-5), was designed to confirm the drug's safety and efficacy.

Fifty-four patients with WHO functional class III Eisenmenger syndrome were randomized to receive therapy with either bosentan ($n=37$) or placebo ($n=17$). After 16 weeks of treatment, findings showed that bosentan did not compromise oxygen saturation. In addition, compared with placebo, bosentan therapy led to a decrease in pulmonary vascular resistance index (by 472.0 dynes/s/cm^{-5}; $P=0.0383$). Mean pulmonary arterial pressure was also diminished among patients treated with bosentan (by 5.5 mmHg; $P=0.0363$), while their exercise capacity (as measure by 6 min walking distance) increased by 53.1 m ($P=0.008$). A total of 18% of patients in the placebo group and 14% in the bosentan group had at least one serious adverse event.

These findings show that bosentan can improve the hemodynamics and exercise capacity of patients with Eisenmenger syndrome, without worsening peripheral levels of oxygen saturation. Furthermore, no unexpected adverse side effects were observed in patients who received bosentan therapy, and the profile of adverse events was comparable to that reported in other forms of PAH.

Original article Galie N *et al.* (2006) Bosentan therapy in patients with Eisenmenger syndrome: a multicenter, double-blind, randomized, placebo-controlled study. *Circulation* **114:** 48–54

Microvascular perfusion in the myocardium after infarction

After myocardial infarction, lack of microvascular perfusion is associated with poor outcome, even in patients with an open infarct-related artery. Researchers in Spain analyzed myocardial perfusion in 40 patients with open infarct-related arteries using first-pass perfusion cardiovascular MRI, 1 week and 6 months after infarction. A 16-segment model was used in analysis of the images.

At 1 week after infarction, 214 of the 290 segments served by the infarct-related artery exhibited normal perfusion; 76 segments had abnormal perfusion. After 6 months, the number of abnormal segments had decreased to 42, of which 13 segments were normal at 1 week and had worsened to abnormal perfusion by the 6-month measurement. Abnormal segments had thinner walls, reduced wall thickening, smaller contractile reserve and more-extensive necrosis than normally perfused segments. The extent of transmural necrosis did not change between measurements, but the number of segments with necrosis exhibiting normal perfusion increased from 38/103 to 69/102.

The authors conclude that in patients with an open infarct-related artery, more than half of myocardial segments with abnormal perfusion 1 week after infarction have normal perfusion after 6 months, with related improvements in