

Gene study links iron with cardiovascular disease risk

Haemochromatosis is an inherited disease in which too much iron is absorbed by the liver, heart, and pancreas. Overt symptoms occur only in people who are homozygous for a Cys282Tyr mutation in the protein coded for by *HFE* (*HLA-H*). This week, two independent groups report that people heterozygous for the mutation may be at increased risk of cardiovascular disease.

Mark Roest and colleagues (Utrecht University Medical Center, Netherlands) followed 12 239 women aged 51–69 years for a period of 16–18 years; 4% were heterozygous for the Cys282Tyr allele. Cardiovascular death rates were 1.6 times higher in heterozygotes than in women with two wild-type alleles (95% CI 1.1–2.4). The death rate from myocardial infarction was 1.5 times higher (0.9–2.5), and for stroke 2.4 times higher (1.3–4.4). Women who smoked, had hypertension, and were heterozygous for the Cys282Tyr mutation had a 19-fold increased risk of death from a heart attack or stroke compared with women without these three risk factors (*Circulation* 1999; 100: 1268–73).

In the second study, 1150 men aged 42–60 years were followed up as part of the population-based Kuopio Ischemic Heart Disease Risk Factor Study. Jukka Salonen's group (University of Kuopio, Finland) found that the incidence of acute myocardial infarction in men who were heterozygous for the Cys282Tyr allele was 2.3 times higher (1.1–4.8) than in men with two wild-type alleles (*Circulation* 1999; 100: 1274–79).

The prevalence of the Cys282Tyr allele in the European population is about 5%, but "in our study of Finnish men, we found a prevalence of 6.7%", says Salonen. He speculates that this finding might explain the higher rate of cardiovascular disease in Finland than in other European countries.

"The new data are highly supportive of the hypothesis that iron is an important risk factor for ischemic

heart disease in men and women", writes editorialist Jerome Sullivan (University of Florida, Gainesville, FL, USA). He adds that "a strong

case could now be made for recommending blood donation as a way to lower iron levels, thus lowering heart attack risk", and suggests that a consensus on specific public-health recommendations is now a priority.

Yvonne van der Schouw, co-author of the Dutch study, agrees with Sullivan and suggests that "the significant association between the Cys282Tyr allele and

heart-disease risk might in part explain why many women are protected from coronary heart disease until the menopause". The authors add that testing for this allele might help predict a postmenopausal woman's risk of cardiovascular death.



Hold back on the iron

Kathryn Senior

Amiodarone's benefit in cardiac arrest debated

Addition of the antiarrhythmic drug amiodarone to conventional cardiac life-support measures improves the rate of survival to hospital admission in patients with refractory ventricular fibrillation, report investigators from the University of Washington (Seattle, WA, USA). For every ten patients treated, "one additional person was successfully resuscitated and admitted", says lead author Peter Kudenchuk.

Kudenchuk and co-workers gave amiodarone to 246 patients who were not resuscitated after receiving three or more precordial shocks; 258 similar patients received placebo. 44% of patients in the amiodarone group survived to be admitted to the hospital compared with 34% of those given placebo

More patients in the amiodarone group had hypotension (59% vs 48%) or bradycardia (41% vs 25%; *N Engl J Med* 1999; 341: 871–78.)

The trial is the first to show a significant, independent benefit of an antiarrhythmic drug in improving survival to hospital admission in patients with refractory cardiac arrest, says Kudenchuk. The next step is to see whether giving the drug earlier will impact the real "bottom line"—survival to hospital discharge.

But hospital discharge, and the patient's functional state at discharge, might have been more appropriate endpoints for this study, comments Hasan Garan (Massachusetts General Hospital Boston, MA, USA). "For these parameters, there were no differ-

ences between the groups. And, of the 504 study patients, only 67 (13%) lived to be discharged."

The reported differences between amiodarone and placebo may have been because of "differences in underlying heart disease, time from onset of cardiac arrest to the arrival of paramedics, or to other more complex factors", he adds. And, even if there is a potential initial advantage of amiodarone, it "may be annulled by later deleterious effects such as hypotension and bradyarrhythmias, which may interfere with adequate perfusion of the CNS at a critical time. Thus, the possibility remains that the early benefit of amiodarone may not persist".

Khabir Ahmad