

CONFERENCE REPORT

What role do genes play in abnormal HDL levels?

How do genetic abnormalities modulate the metabolism of high-density lipoprotein (HDL)? Medical geneticist Michael Hayden of the University of British Columbia asked and answered that question during a symposium at the Canadian Cardiovascular Society Congress, held in Vancouver Oct. 29. He began by highlighting the importance of HDL and noting that lowered HDL levels are responsible for at least 40% of premature heart disease. The higher the HDL, said Hayden, the lower the risk, even in the presence of elevated low-density lipoprotein (LDL) levels. He reviewed the hypothesis that HDL protects at the cellular level through its role in reverse cholesterol transport. In this process, cholesterol is

mobilized from peripheral sites and shuttled back to the liver for catabolism.

The consequences of defective reverse cholesterol transport are epitomized in patients with Tangier disease, a striking and severe expression of HDL deficiency. In addition to depressed HDL, patients with this disease have abnormal tissue deposition of cholesterol within the reticulo-endothelial system (giving rise to orange tonsils) and appear to be at high risk for atherosclerosis end points.

Hayden's group and others genetically mapped Tangier disease to chromosome 9q and then used fine-mapping techniques to isolate the causative gene. It turned out that the same gene defect that causes Tangier disease is also pre-

sent in a small but substantial proportion of patients with low HDL levels but without abnormal cholesterol deposits.

People who are heterozygous for this genetic defect have been found to develop vascular aging about 25 years faster than normal. An exciting implication of Hayden's work is the potential for novel drug development directed at raising HDL levels and thereby protecting against the development of atherosclerosis. — **This article was written by Dr. Paul Armstrong, an Edmonton cardiologist, and Dr. Robert Hegele, a symposium cochair. Physicians interested in submitting similar reports should contact John Hoey, 800 663-7336 x2118; hoeyj@cma.ca.**