What is the importance of a family history of Cardiovascular Disease?

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Family history is an important contributor to cardiovascular risk, and is not always fully assessed and incorporated into an individual's risk calculation. CVD risk relates to the interaction between an individual's genetic background and the environmental factors operating

Assessing the genetic contribution

Some individuals will inherit single gene disorders giving rise to cardiovascular disease, but in many in the population there will be contributions from multiple genes that are currently poorly understood. Clinically, the genetic contribution should be assessed by enquiry of family history, of the presence of macrovascular disease in parents together with its nature, age of initial onset and presence of known risk factors. Age of onset in first degree male relatives before the age of 55, and in females before 65 years, is clearly likely to be of importance. Enquiry should also be made of uncles, aunts, siblings and children. Taking into account the number of such relatives, the greater the number and the earlier the age of onset of disease provides some guide to the genetic component and to the risk. The guidelines of the Joint British Societies published in December 2005 suggest that the calculated risk should be augmented by about 1.3

Specific single gene disorders

Where specific single gene disorders are encountered in a family, then this is of major significance, and it may well be possible to identify at-risk members of the family. The classic example is familial hypercholesterolaemia affecting 1 in 500 of the population in the heterozygous form, and 1 in 1,000,000 in the homozygous form. The gene defect can be identified in around 50-75% of those affected, but as there are more than 700 known defects in the gene it may not be that straight forward, unless a defect has already been found in another family member. Finding the gene defect does not currently influence treatment. Where one person has been found to have familial hypercholesterolaemia, then one parent is an obligate heterozygote, and each sibling and child has a 50% risk.

A further rare condition is familial dysbetalipoproteinaemia (remnant lipaemia, type III hyperlipidaemia) where there is homozygosity for the E2 pattern of apolipoprotein E. About 1% of the population has this, but only about 2% of these then develop severe mixed hyperlipidaemia, nearly always when there is at least one other disease, environmental or inherited factor. Here premature CHD and peripheral vascular disease can present at a very early age but the hyperlipidaemia and the risk respond well to diet and weight loss treatment, and if necessary to fibrate treatment. Fibrates are the drug of first choice, but statins can be very helpful, and in a few patients a statin-fibrate (usually with fenofibrate not gemfibrozil) is needed. Other siblings and members of the family may also be affected. A fibrate drug may be the drug of choice (a statin being second in line) in individuals with remnant lipaemia inadequately responding to diet and lifestyle change.

Screening family members

Whether there is a clear single gene disorder or a possible polygenic contribution to a family history of vascular disease, it is of considerable importance to ensure that other first degree relatives of the family are screened (and any second degree relatives where a further family member is found with hyperlipidaemia) These relatives are often not patients of the proband's doctor, and the proband needs to be strongly encouraged to contact all the family to obtain lipid profiles.

In 2004, the UK Department of Health agreed to initiate a cascade screening programme, where specially trained nurses in the community would contact the first degree relatives of patients with familial hypercholesterolaemia to check their profiles, since 50% of these individuals will also be affected. Where such an individual is so affected, their relatives in turn will be approached. It is hoped that the pilot studies will be the prelude to a national roll out, for only 10-15% of affected individuals are currently identified.

Extracted from "Lipid Disorders – Your Questions Answered" by John Reckless and Jonathan Morre