Genetic Sub-Study

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ANBP2 offers a unique opportunity to study important genetic issues in relation to hypertension, response to treatment and cardiovascular outcome. Advances in molecular biology are likely to allow improved detection of predisposition for hypertension and cardiovascular disease and the implementation of early preventive strategies. Defining genetic causes will also provide some insight into basic pathophysiological mechanisms and, therefore, more logical approaches to treatment.

Existing cross-sectional studies of genetic markers are incomplete in that they do not provide a true estimate of predictive value for cardiovascular disease because of bias related to premature death, increased survival associated with certain genotypes or the effects of distortion of population distributions of alleles. With a prospective cohort study such as ANBP2, these problems are minimised. Thus, it should be possible not only to identify genetic markers of hypertension but also those related to complications such as cardiac hypertrophy and coronary heart disease. In addition, those markers that might predict response to treatment may be elucidated.

The renin-angiotensin system features in the complications, treatment and genetics of hypertension. Recent studies of hypertension and ischaemic heart disease have drawn attention to two particular genes relevant to the renin-angiotensin system: the angiotensin converting enzyme (ACE) gene and the angiotensinogen gene. With the genetics sub study, participants agree to have 20-30 ml of blood collected for DNA analysis. The blood is genotyped for informative alleles at the ACE and angiotensinogen genes.

The genetic information will be used to address 4 broad issues:

1. Case-control study of the genetics of hypertension. Genotype frequencies for the ACE and angiotensinogen genes will be compared between cases who are enrolled as part of ANBP2 and age- and sex-matched controls selected from the Victorian Family Heart Study.

2. Genetics of cardiac hypertrophy. In those subjects undergoing echocardiography for measurement of left ventricular dimensions, genotype frequencies will be compared in those with higher or lower left ventricular mass indices.

3. Genetic markers of response to treatment. The genetic information will be utilised to determine whether the blood pressure response and any side-effects exhibited by hypertensive subjects to classes of antihypertensive treatment can be predicted using genetic markers.

4. Genetic markers of cardiovascular outcome. The ACE and angiotensinogen genotype frequencies will be compared in the cohort to determine in a prospective manner whether it is possible to predict outcome for the main cardiovascular end-points.

This study is operating in all mainland states with 2 analysis sites established, the Department of Medicine, University of Queensland, Prince Charles Hospital and the Department of Physiology, University of Melbourne. At present, blood has been collected from over 1000 subjects with duplicate samples present at each analysis site. With about 4000 subjects due to be recruited to ANBP2 for 1997, the number of duplicate genetic samples should reach the 5000 mark. The collection of DNA from such a large group of hypertensives will establish a resource unmatched internationally, and provide the opportunity to answer many questions relating to the prevention and treatment of hypertension and its complications.

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