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### **Cardiovascular Disease Risk Factors Part IX Family History**

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**Your Life Your Health**

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Among important risk factors for cardiovascular disease risk is family history, but it is not as simple as knowing that Aunt Susie had a heart attack. The following is information you need to know in order to determine whether or not you are at a higher risk of cardiovascular disease due to genetics, i.e., family history.

#### **Shared Genes in Blood Relatives**

- First Degree Relatives are your children, your parents or your brothers and sisters. You share 50% of your genes with these family members.
- Second-degree relatives are your aunts and uncles, grandparents, half siblings and nieces and nephews. You share 25% of your genes with these family members.
- Third-degree relatives are your cousins and great-grandparents. You share 12.5% of your genes with these family members.

Obviously, your risk of a genetically linked illness is four times higher if that illness is in a first-degree family member, as it is in a third-degree family member, as you share four times more genes with the first-degree relative as you do with the third-degree relative.

Consanguinity – the shared relationship of a common ancestor -- increases the percent of genes which you share with a relative. Consanguinity occurs when first cousins marry as is common in cultures such as Iraq where over 29% of marriages are between first cousins and 57% of marriages demonstrate some amount of consanguinity. A gene which has little potential for causing an abnormality has an increased probability in a person who has a shared common relative.

#### **Family History is Important**

The most useful family history includes medical, developmental and pregnancy outcome information for each of the above classes of relatives. Recently, the U.S. Preventive Services Task Force published a list of clinical preventive measures based on family history. Two of these recommendations were categorized as “Strongly recommended based on good evidence.” One of the two related to the use of daily aspirin for primary prevention of cardiovascular events for adults who are at increased risk of coronary heart disease due to age, sex, diabetes, elevated total cholesterol, low HDL cholesterol, elevated blood pressure, smoking and family history.

In searching for the significance of family history for cardiovascular disease, evaluation must also be made for the primary risk such as factors:

- Diabetes
- Cholesterol Abnormalities, including total cholesterol, Low HDL, High LDL and Lp(a), if known.
- Hypertension

However, a family history should take into account not only genetic factors which are based on the shared-gene pool with relatives, but also lifestyle including diet, activity, tobacco use, etc. A history of early cardiovascular disease in a parent may reflect a genetic predisposition, a mix of non-genetic risk factors or both. Effective early prevention may result in a parent with a history of medically treated hypercholesterolemia rather than a myocardial infarction. Likewise, a strong family history on the mother's side may be more evident in her male relatives than in her own medical history, due to the later onset of disease.

### **Here are some facts**

Family history as an isolated event for genetic implications of recurrence of disease is more suggestive when the illness occurs early. For instance, a first-degree male relative who has a cardiac event before age 55 and a female before 65 are far more predictive of risk than those who have events at older ages.

Multiple risk factors for cardiovascular disease increase that risk whether or not there is a family history of heart disease. For a non-smoking, normotensive 55-year-old man with a total cholesterol level less than 200 mg/dL, the probability of having a heart attack within 8 years is 31/1000. If he smokes, the risk is 46/1000. If he has high cholesterol (>260 mg/dL) and smokes, it is 64/1000. With the addition of hypertension (systolic greater than 150 mmHg) to smoking and hypercholesterolemia, his risk of myocardial infarction within 8 years is 95/1000.

In 2004, the *Journal of the American Medical Association* published a study entitled, "Parental Cardiovascular Disease as a Risk Factor for Cardiovascular Disease (CVD) in Middle-aged Adults." The study found that a parental history of cardiovascular disease is an independent predictor of cardiovascular events in middle-aged men and women. After adjustment for other risk factors, premature CVD in at least 1 parent was associated with a significant doubling (100% increase) in cardiovascular risk for men and a 70% increase in risk for women over 8 years. Premature parental CVD – cardiovascular before the age of 55 in men and 65 in women -- was found to indicate risk best among offspring who had intermediate levels of cardiovascular risk as predicted by Framingham Risk Score, i.e., a Framingham score between 10-20%.

The summary of the *JAMA* study stated: Among 2302 men and women (mean age, 44 years), 164 men and 79 women had cardiovascular events during follow-up. Compared with participants with no parental cardiovascular disease, those with at least 1 parent with

premature cardiovascular disease (onset age <55 years in father, <65 years in mother) had greater risk for events, with age-adjusted odds ratios of 2.6x for men and 2.3x for women. Nonpremature parental cardiovascular disease and parental coronary disease were weaker predictors. Addition of parental information aided in discriminating event rates, notably among offspring with intermediate levels of cholesterol and blood pressure, as well as intermediate predicted multivariable risk.

## **Clinical Implications**

These results help to inform clinicians and patients about use of parental history in risk stratification and treatment decisions. These results shed important light on the true magnitude of the association between offspring and parental CVD. It is likely that clinicians place greater importance on positive parental CVD in younger compared with older patients, which appears appropriate in terms of relative risk. However, at present it is difficult for clinicians and patients to know how to assess and incorporate into clinical practice the risk associated with parental CVD, independent of shared risk factors.

The *JAMA* study indicated that while family history was important in assigning risk that the modification of traditional risk factors – smoking, exercise, diet, cholesterol, diabetes, etc. – remain the most important focus of clinical efforts. Clinicians and patients must continue to focus on proven lifestyle and drug therapies to modify traditional risk factors and reduce risk.

The addition of parental data may aid in discriminating risk most among men and women at intermediate levels of predicted risk. Knowledge of parental CVD status may not change the magnitude of risk substantially for those at very high or very low predicted risk. For patients with intermediate predicted risk, however, the additional information provided by positive parental CVD may change the probability enough to consider altering the treatment of the patient. Treatment decisions in current guidelines are based on absolute risk levels. The *JAMA* study demonstrated a significantly higher 8-year rate of CVD among participants with borderline cholesterol or blood pressure levels and premature compared with no parental CVD. It is precisely these patients in whom decisions about lifestyle modification or drug treatment may be the most difficult. Thus, the *JAMA* study supports the emphasis placed by the ATP-III and JNC 7 guidelines on parental history to help guide treatment decisions for primary prevention.

Nothing can be done about your family history, but if you have a strong family history of cardiovascular heart disease, you can:

- Change your lifestyle:
- Lose weight
- Stop Smoking
- Exercise
- Eat less red meat
- Lower your cholesterol
- Control your diabetes
- Eat more fiber, more vegetables and fruit

- Decrease the inflammatory markers in your blood

Together, these measures can overcome your family history, if started early enough and practiced consistently enough. Remember, it is your life and it is your health.