EDITORIAL

Is Heart Disease All in the Family? Family History and Cardiovascular Disease

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Physicians often place special emphasis on a family history of coronary heart disease (CHD) in guiding their risk evaluation with their patients. But how important is a family history of premature CHD? Is a CHD family history independent of other risk factors? Should a negative family history mean not screening or treating CHD risk factors?

A family history of CHD increases CHD risk two to 11 times for first-degree family members (parents, siblings, children), and about 5 percent of families account for 50 to 60 percent of all CHD occurring in those younger than 55 years.[1,2] More than 70 percent of unaffected first-degree relatives will have one or more CHD risk factors, yet the majority of these family members will be unaware of their personal risk factors.[3] Research suggests that much of the risk for CHD is related to transferring either genetic, environmental, or behavioral risks through families, but that some of family history risk remains unexplained or independent of known risk factors.[2,4,5,6] How do these findings translate into practical strategies for health care providers to assist high-risk individuals and families?

In this issue of the *Journal*, Eaton and colleagues offer a new look at the role of family history in CHD.[4] This important study improves our understanding of the role of this history and provides insights into how best to care for our patients. This case-control study confirms that a family history of CHD is a powerful predictor of future heart disease, especially if a first-degree relative developed heart disease before the age of 60 years or there were more than one affected family members. It is also important to note, however, that 58 percent of those with CHD in this study did not have a family history of CHD.

Family history was also a strong marker for multiple risk factors in those with CHD in this study.[4] Family history remained an independent predictor of CHD even when controlling for traditional CHD risk factors and newly recognized risk factors such as lipoprotein (a), homocysteine, and fibrinogen. The newly discovered risk factors were predictive of CHD in this study but did not explain all of the family risk.[4]

The study by Eaton and colleagues is important because, although much of the development of CHD can be explained by known risk factors, we need to develop more comprehensive prevention strategies to assist high-risk families. Testing new risk factors for their effect on predicting CHD is a necessary step for screening and management guidelines. The Eaton et al study also emphasizes that family history is not just a yes-no or positive-negative issue; rather, the predictive value of family history depends on the many factors that create different degrees of risk in families. The important predictors from this and earlier studies are age of CHD onset, number of affected first-degree relatives, sex (same sex confers higher risk), how many risk factors the person being examined has, or how extreme the acquired risk factor is.[1-6]

The Eaton et al findings are not in complete agreement with those of all earlier studies. Lipoprotein (a) did account for most of the variance of family history not previously accounted for by traditional risk factors in another study.[7] Differing results might be due to study limitations, different study designs, or different study populations. A case-control study, such as the one by Eaton et al, can be affected by selection bias, recall bias, and self-reports, all of which can give rise to underestimation of risk factor prevalence in the study participants. In addition, it is difficult

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to account statistically for many of the metabolic interactions of risk factors,[6] especially if the sample size is small or if risk factors have been treated. That Eaton and colleagues included direct measures of many of the risk factors and standardized survey instruments, however, increases confidence in their findings.

As with most research, the Eaton et al findings point the way for future research. Many new risk factors are being discovered and will need to be studied in high-risk families. Some of the risk factors that are being considered include acquired differences in thrombotic factors (prostacyclin and thromboxane A_2 among others), metabolic factors (density and oxidative potential of various lipoproteins, apoproteins, converting enzymes, obesity, and glucose tolerance), and endothelial factors. Equally important is preventing the acquisition of negative behaviors, such as smoking, sedentary lifestyle, poor eating habits, and maladaptations to stress, which can be influenced by the family.

Although studies to determine why CHD is transmitted through the family are becoming increasingly based on epidemiology, biochemistry, and molecular biology, prevention strategies still depend on the physician and patient. Physicians' offices are ideal places to single out high-risk families through simple office screening and to develop strategies to reduce their risk.[2] Family history research suggests that the following practical approaches help primary care providers recognize high-risk families:

1. Routinely document and periodically update the family history of patients' first-degree relatives.[2]
2. Ask the age of onset of the disease in the affected family member(s) to determine whether the CHD was premature.
3. Ask about known risk factors in the affected family member. Such knowledge can point to potentially inherited risk factors in the patient and help determine whether the patient is similarly at risk.
4. Remember that family history is only one predictor of CHD; other risk factors and overall risk are still predictive. Consider treatment of risk factors regardless of a history of CHD in the family, because the absence of a family history of CHD does not mean the patient will not develop CHD.
5. Screen, including a full lipoprotein evaluation, first-degree relatives of those with premature CHD (less than age 60 years) for risk factors.

Knowing that CHD risk factors account for a considerable portion of family history risk is vital to our practices, our patients, and their families. Often patients and even their physicians view a family history of premature CHD as a death sentence and consider family history an unmodifiable risk factor. Dyslipidemia, diabetes, and hypertension are familial risk factors that might be primarily genetically determined, but they can be diagnosed and treated.[8] Lifestyles also cluster in families and can be improved with behavioral interventions by physicians.[2,3] From this point of view, family history is another risk factor that can be treated. The family with CHD offers family physicians an important opportunity to assist in the health care of all individuals in a family and to consider the family as the patient.[2,9]

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