incidence of CHD is especially great in women with diabetes. One reason for the increased risk is that elevated triglycerides, low HDL cholesterol, high blood pressure, and obesity, all of which are risk factors for CHD, are more common in people with diabetes. In addition, diabetes itself imparts other, as-yet-unidentified mechanisms for increasing the risk of CHD. For example, young women with diabetes lose the protection that other premenopausal women have against CHD; in fact, these women have the same frequency of CHD as do men of the same age without diabetes.

Moreover, people with pre-diabetes (blood glucose levels higher than normal but not quite in the diabetes range) are at increased risk for CHD. Pre-diabetes is diagnosed when blood glucose levels are between 100 and 125 mg/dL on a fasting blood glucose test or between 140 and 199 mg/dL on an oral glucose tolerance test.

Careful control of blood glucose levels with diet and drug therapy may reduce the increased risk of CHD associated with diabetes, but it does not completely eliminate the risk. Therefore, it is particularly important for people with diabetes or pre-diabetes to control other risk factors for CHD.

Cerebrovascular disease. CHD is the most likely cause of death in people with cerebrovascular disease (blockage of an artery that supplies blood to the brain). People with evidence of blockage in these arteries invariably have CHD as well.

Peripheral arterial disease. CHD is also the most likely cause of death in people with peripheral arterial disease (narrowing of the arteries that supply blood to the extremities, especially the legs). Just as with cerebrovascular disease, people with narrowed peripheral arteries also have CHD. Reduced blood pressure measured at the ankles or painful cramping in the legs upon exertion are signs of peripheral arterial disease.

Blood-clotting factors (fibrinogen, factor VII, platelets, PAI-1, and PLA-2). Efforts to find a consistent clotting abnormality in people prone to heart attacks have not been successful. However, a number of studies have found an association between increased heart attack risk and an elevation in blood levels of fibrinogen or factor VII (two clotting proteins), or an over-responsiveness of platelets to certain stimuli. Elevated levels of plasminogen activator inhibitor type 1 (PAI-1), a substance that inhibits the breakdown of blood clots, are also associated with increased cardiovascular risk, including heart attack risk.

A variation in platelet antigen-2 (PLA-2), one of the proteins involved in platelet binding of fibrinogen, was the first inherited

NEW RESEARCH

Premature CHD in Sibling Raises Risk of Atherosclerosis

A new study from Johns Hopkins finds that the risk of coronary artery calcification—a sign of atherosclerosis—is particularly high if the person has a sibling history of premature CHD.

The study involved 8,549 people, average age 52, with no symptoms of CHD. Of those, 27% had a family history of premature CHD—a heart attack, bypass surgery, or angioplasty before age 55. The researchers used electron-beam computed tomography to detect calcium deposits in the coronary arteries.

Calcium deposits were more frequent in people with a family history of premature CHD than in those without such a history. The prevalence of calcium deposits was 30% higher if the family history was in a parent, but was more than twice as high if the family history occurred in a sibling. Compared with people without a family history of premature CHD, the risk of advanced calcified plaques was four times greater in people with a sibling history and two times greater in people with a parental history.

It is unclear why sibling history may play a greater role in atherosclerosis than parental history. One possible explanation is that siblings are more likely than parents and children to share environmental CHD risk factors, such as smoking, obesity, and a high-fat diet, since they grow up in the same household.

CIRCULATION
Volume 110, page 2150
October 12, 2004