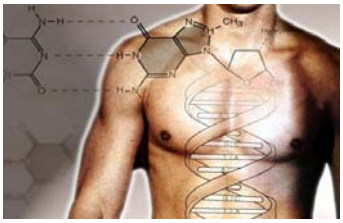
GENETICS AND CARDIOVASCULAR HEALTH

Many people wonder if their genetic makeup could potentially affect their cardiovascular health. Current literature states that it could. Two examples of this is autosomal dominant hypercholesterolemia and homocystenemia.



1. Autosomal dominant hypercholesterolemia

Autosomal dominant hypercholesterolemia (ADH) is a clinical disorder characterized by elevated plasma LDL-cholesterol which leads to premature atherosclerosis.

At least three genetic mutations with an autosomal dominant mode of inheritance have been reported in ADH.

-**(LDLR) gene mutation-** m/c form of familial hypercholesterolemia which causes defects in the LDL receptor.
- **apolipoprotein B mutation-** causes familial defective apolipoprotein B. It is less common and leads to impaired binding of LDL particles to the LDL receptor.
- **(PCSK9) gene mutation** (proprotein convertase subtilisin kexin 9)- these are rare; one or more mutations lead to reduced levels of the LDL receptor.

2.The MTHFR mutation and hyperhomocysteniemia

Hyper-homocysteine is a rare autosomal recessive disorder. An increase in homocystene has been reported to have primary atherogenic and prothrombotic properties.

The most common form of genetic hyperhomocysteinemia results from production of a thermolabile variant of methylene tetrahydrofolate reductase **(MTHFR)** with causes reduced enzymatic activity. The gene encoding for this variant results in an alanine-to-valine substitution at amino acid 677 (C677T).

Having these mutations results in predisposition to vascular injury which includes; intimal thickening, elastic lamina disruption, smooth muscle hypertrophy, marked platelet accumulation, and the formation of platelet-enriched occlusive thrombi.

Who should be tested?

-The general population should be tested for levels of total cholesterol/LDL/HDL/triglycerides.
-As a result of the frequency of familial disease and the associated risk, special screening of Lp(a) and apolipoproteins B and A-I; is recommended for first-degree relatives of patients with MI (particularly if premature). Approximately 25 percent of patients with premature CHD and a normal standard profile will have an abnormality in one of these factors
-All new patients could be screened for the MTHFR mutation

What will you gain from these laboratory tests?

-If you are found to have increased LDL cholesterol/LDL/triglycerides- life style modifying strategies (diet and exercise) will be advised, followed by initiation of lipid lowering drugs.
-Because increased blood levels of homocysteine may reflect deficiencies of folate, vitamin B6, and/or vitamin B12, increased doses of these vitamins could be initiated.
- Early detection of these abnormal blood tests will help your physician come up with a plan to prevent the progression of atherosclerosis, thus preventing ischemic coronary disease and stroke.

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