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Atherosclerosis and Coronary Heart Disease

Pronunciations: (Ath·er·o·scle·ro·sis)
Atherosclerosis is a form of arteriosclerosis that results in a buildup of fatty deposits (atheroma or plaque) within the intimal layers of medium and large sized arteries. It begins in childhood and slowly develops into old age, although rapid progression may be seen by the third decade of life.

Causes

Atherosclerosis is thought to occur when cholesterol or hypertension cause damage to the intima of the blood vessel wall. Platelets are sent to the site of injury, aggregate, and attach to the lesion. In addition, white blood cells (lymphocytes, macrophages, and monocytes) are also attracted to the inflamed area. Monocytes enter the intima of the arterial wall and are activated to macrophages by oxidized LDL. Oxidized LDL particles are also responsible for transforming macrophages into foam cells, which continue to collect cholesterol and other substances. Macrophages and foam cells express metalloproteinases and growth factors, resulting in smooth muscle and connective tissue growth. Over time, cholesterol, calcium, connective tissue, and cellular debris will continue to buildup (atheroma growth) causing hardening and narrowing of the arterial wall, which eventually will protrude into the artery channel and limit blood flow. Atherosclerosis develops progressively slow over time and is usually not a problem unless a rupture occurs. At that point, a clot will form in response to injury, which may break off and block blood flow to the heart (heart attack), brain (stroke), or arms and legs. Other factors that may be responsible for initiating the atherosclerotic process include: cigarette smoking, high triglyceride levels, low HDL levels, hyperhomocysteinemia, obesity, diabetes, *Chlamydia pneumoniae, Helicobacter pylori*, and lack of physical activity. Heart disease remains the number 1 killer in the United States and other Westernized countries.

Diagnosis

Symptoms:

Atherosclerosis is a disease with slow progression, therefore symptoms do not present themselves until its late stages. Narrowing of the interior portion of an artery by more than 70% may start to show signs of atherosclerosis. If the artery is in close proximity to the heart, angina (chest pain) usually occurs. Symptoms may not be present at all, which may result in a heart attack if an artery suddenly becomes blocked.

Other symptoms:

Chest pain during exercise
Leg pain

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Interpretation of Laboratory Tests

The following methods are frequently used to determine if atherosclerosis may be present. Selecting the type of test to order may depend on the severity of symptoms, confirming previously ordered tests, or availability of resources.
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BLOOD TESTS		
Test Name	Normal values	Indicators
White Blood Cell Count	4,500 to 10,000 cells/mcl	Normal-to-elevated levels may be associated with atherosclerosis and coronary heart disease[1]
Fibrinogen	200 to 400 mg/dl	High-normal levels may be associated with atherosclerosis[2]
RISK FACTOR TESTS		
Test Name	Normal values	Indicators
Cholesterol Test	Total Cholesterol: < 200 mg/dl (desirable) LDL: < 100 mg/dl (optimal) 100-129 (near optimal) HDL: ≥ 60 mg/dl (high)	Elevated total and LDL cholesterol, and low HDL levels may increase the risk of atheroma formation, as seen in familial hypercholesterolemia.
Serum Homocysteine	5.0 - 15.0 umol/mL (0.7 - 2.0 ug/mL)	Elevated levels may cause damage to arterial walls, thus increasing the risk for plaque formation
Triglyceride Levels	Less than 150 mg/dL	Elevated is a risk factor for heart disease
C-reactive Protein (CRP)	CRP < 1 mg/dl	CRP > 1 mg/dl (> 10 mg/dl often seen) suggests inflammation
Blood Pressure	Systolic (S):120 mmHg Diastolic (D):70 to 80 mmHg	Hypertension (S: 140 mmHg; D: 90 mmHg) often caused by atherosclerosis, is associated with cardiovascular disease risk
TESTS		
Test Name	Indicators	
Electrocardiogram (ECG or EKG)	Can help to determine if the heart is beating normally by measuring electrical activity. A normal heart rate is about 50 to 100 beats per minute (BPM), with consistent rhythmic beating. Abnormal results may show a myocardial defect or other diseases of the heart.	
Echocardiogram	Used to evaluate heart murmurs and pumping of the heart by assessing sound waves. Heart valves, chambers, arrythmias, and wall movements can be examined with this test.	

Thallium Stress Test	Often conducted with a treadmill exercise test. Radioactive thallium is injected once the patient achieves their maximal exercise level. A gamma camera is used to follow blood flow through the coronary arteries. The test can be used to determine if a blockage is present, if the blood is receiving enough blood during rest and/or exercise, and the presence of scar tissue.
Treadmill Test (or Stress Test)	Will determine how much workload the patient's heart can withstand. Heart and breathing rate, blood pressure, EKG and ECG, and fatigue are all examined.
Coronary Angiogram and Cardiac Catheterization	A catheter is inserted into a blood vessel and a dye (visible under X-ray) is injected into the blood stream. The test can determine a coronary blockage, location of the blockage, and severity.
Intravascular Ultrasound	More sensitive in detecting plaque and able to provide information regarding the plaque's composition.

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There are no blood tests that can be used as a definitive diagnosis for atherosclerosis, however, epidemiological studies have found fibrinogen, WBC counts, cholesterol, CRP and homocysteine levels associated with plaque formation and heart disease risk. The most widely used screening tool is coronary angiography with cardiac catheterization.

Common Current Treatments

The mainstay of treatment for atherosclerosis is prevention. There are several modifiable risk factors, if changed, may reduce the risk of suffering from heart-related complications in the future. For example, smoking, obesity, hypertension, lack of physical activity, and elevated total and LDL cholesterol levels are associated with heart disease risk. Once complications arise, treatment for a heart attack, angina, kidney failure, or heart failure, amongst others, will be required.

Medications

The following table lists some classes and examples of medications commonly prescribed to patients at risk or suffering from heart disease. The order of medications listed in the table is not intended to represent subsequent treatments; complementary medications may be needed to address multiple symptoms.
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LIPID LOWERING MEDICATIONS		
Indication	Class/Examples	Notes
Elevated Lipid Levels	HMG CoA Reductase Inhibitors (Statins): -Lovastatin -Pravastatin	May increase liver enzymes and myopathy occurrance
Elevated Lipid Levels	Bile Acid Sequestrants: -Cholestyramine	Can produce GI distress and impair the absorption of other drugs

	-Colestipol	
Elevated Lipid Levels	Fibrinates -Clofibrate -Gemfibrozil	Gallstone, dyspepsia, and myopathy may occur.
Elevated Lipid Levels	Nicotinic Acid	Flushing of the skin very common. May increase the risk for gout and hepatotoxicity.
Elevated Lipid Levels	Fish Oil: Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA)	2 to 4 grams each day effective in lowering TG levels. May lower total and LDL cholesterol.
BLOOD CLOT REDUCING AGENTS		
Indication	Class/Name	Notes
Delay Blood Clotting ("Blood Thinners")	Anticoagulants: -Warfarin -Coumadin -Heparin	
Prevention of Blood Clots	Antiplatelet Agents: -Aspirin	
BLOOD PRESSURE LOWERING AGENTS		
Indication	Class/Examples	Notes
High Blood Pressure	Diuretics -Amiloride -Spironolactone	
High Blood Pressure	**Angiotensin-Converting Enzyme (ACE) Inhibitors** **-Captopril** **-Fosinopril**	
High Blood Pressure	Beta-Blockers -Acebutolol -Sotolol	
High Blood Pressure	**Angiotensin-2-Receptor Antagonists** **-Losartan** **-Eprosartan**	

High Blood Pressure	Calcium Channel Blockers -Amlodipine -Felodipine	
High Blood Pressure	Alpha Blockers -Doxazosin mesylate -Prazosin hydrochloride	
High Blood Pressure	Combination Therapy -ACE inhibitor/calcium channel blocker - **Angiotensin II receptor antagonist/diuretic**	

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Dietary Interventions

The primary nutritional goal in the treatment of atherosclerosis is to reduce cholesterol and saturated fat intake. The optimal diet for heart disease prevention may be cholesterol intake around 100 mg/day, carbohydrates at about 65% of intake, including 11 to 15 grams of soluble fiber, protein intake around 15%, and 20% of calories from fat, with no more than 6% coming from saturated and rich in omega-3 and omega-6 fatty acids. The American Heart Association has recommended that individuals with heart disease ingest at least one gram each day of EPA and DHA to lower triglyceride levels. It is preferable to ingest these compounds through fatty fish (i.e. mackerel, herring) but capsule forms are also acceptable because cost may be a factor. Products such as Benecol® containing plant stanol esters have been shown to reduce cholesterol levels. Incorporation of such products into the diet requires minimal effort.
Weight control is very important, therefore, a weight loss regimen may be warranted to reduce blood pressure and blood lipid levels. Vegetarian diets have shown many benefits as well. Individuals on these diets tend to have lower bodyweights and less of a risk for developing heart disease. Risk factors (eg, smoking, hypertension) need to be aggressively handled because the effectiveness of following a low fat and cholesterol diet will be limited, until these factors are removed. Alcohol, especially red wine in moderation, may reduce the risk of heart disease but each situation must be considered separately before recommending this.

What to Tell the Patient and Family

When the patient's symptoms have subsided, it is important to emphasize the avoidance of foods high in saturated fat and cholesterol. Additional therapies may be warranted as well. For example: a smoking cessation program, weight reduction program, and overall dietary adherence may be needed. It is also important to instruct the whole family on all aspects of the diet and additional therapies. This applies to spouses or partners of patients.

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References

1.Kannel WB, Anderson K, Wilson PW. White blood cell count and cardiovascular disease. Insights from the Framingham Study. JAMA. 1992 Mar 4;267(9):1253-6.

2. Kannel WB, D'Agostino RB, Belanger AJ. Update on fibrinogen as a cardiovascular risk factor. Ann Epidemiol. 1992 Jul;2(4):457-66.