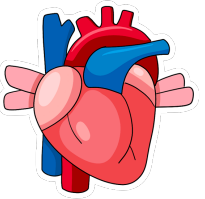
By H.T



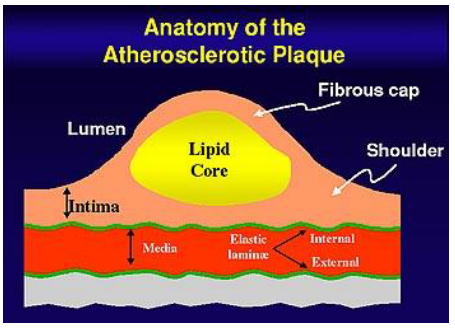
Atherosclerosis

A form of arteriosclerosis characterized by:
Atheromatous plaques containing cholesterol and lipids.
Found on the innermost layer of large and medium-sized arteries.
Etymology: From Greek "athero" (gruel/paste) and "sclerosis" (hardness).

Cell Types in Atherosclerosis

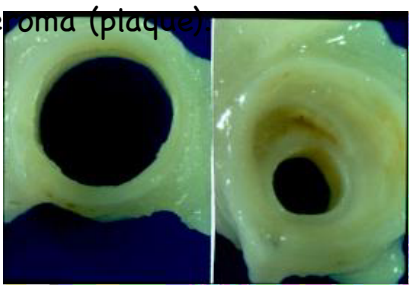
Key cell types involved:

Smooth muscle cells
Endothelial cells
Fibroblasts
Macrophages
Foam cells
T-lymphocytes
Mast cells



Normal vs. Atheromatous Coronary Artery

Normal coronary artery: Has a smooth lining without plaque.
Atherosclerotic coronary artery: Contains a fibrous cap over an atheroma (plaque).



Risk Factors for Atherosclerosis:

Non-Modifiable Risk Factors:

Age: Begins young, but organ injury occurs later.
Gender: Men are more prone; equal risk by age 60-70.
Family History: Genetic predisposition.

Modifiable Risk Factors:

Hyperlipidemia
Hypertension
Cigarette smoking
Diabetes Mellitus
Elevated homocysteine levels
Infections: e.g., Herpes virus, Chlamydia pneumoniae
Obesity, sedentary lifestyle, stress

Elevated serum cholesterol uniquely drives atherosclerosis.

Genetics of Atherosclerosis

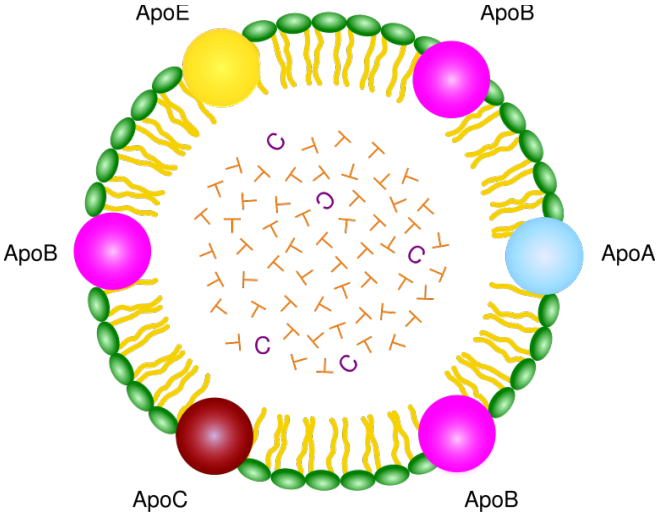
Familial Hypercholesterolemia (FH):
Caused by deficiency/mutation of LDL receptors leading to high cholesterol levels.

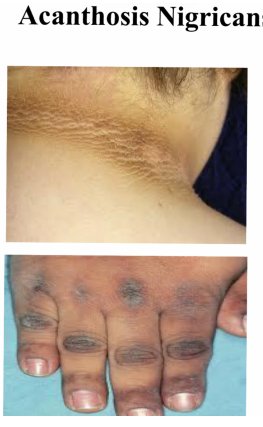
Cholesterol Mechanisms in Atherosclerosis

Sources of cholesterol:

Endogenous production (from the liver, ~1g/day)
Dietary intake (from animal sources)
LDL Cholesterol levels classification:

Optimal: Less than 100
Near Optimal: 100-129
Borderline High: 130-159
High: 160-189
Very High: 190 and above



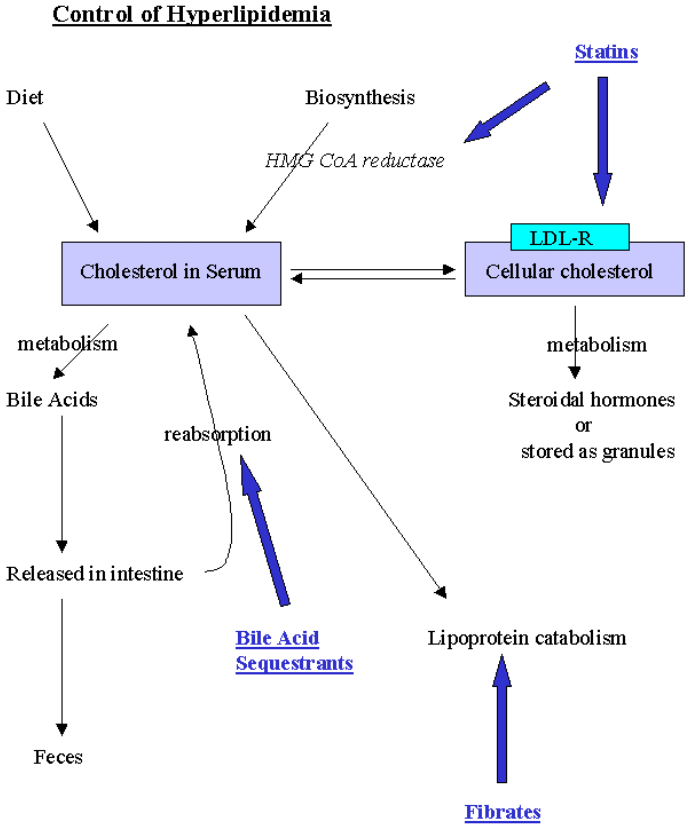


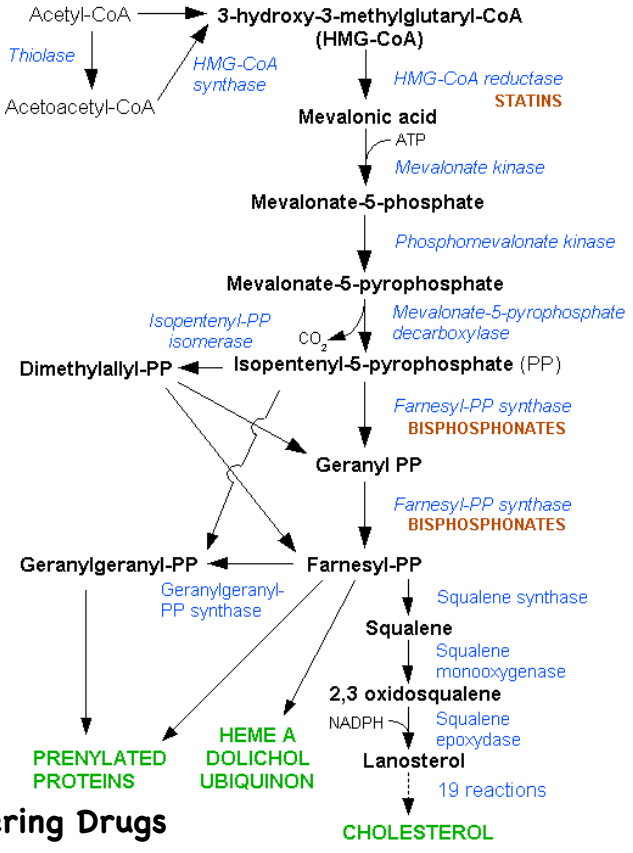
Lipid Transport Mechanisms

Cholesterol and fats are poorly soluble in blood; thus, they are transported via lipoproteins:
Chylomicrons
VLDL (Very Low-Density Lipoprotein)
IDL (Intermediate-Density Lipoprotein)
LDL (Low-Density Lipoprotein)
HDL (High-Density Lipoprotein)

Prevention and Lifestyle Changes for Atherosclerosis

Lifestyle Modifications:
Diet: Low in fat/cholesterol; increase fruits/ vegetables.
Physical activity: Increases HDL and helps control weight, diabetes, and blood pressure.
Reducing body weight increases HDL levels.
Avoid smoking and manage stress.





Treatment: Lipid-Lowering Drugs

Statins:
Examples: Simvastatin, Atorvastatin, Pravastatin.
Mechanism: Decrease LDL by 30-50% by blocking HMG-CoA reductase.
Increase LDL receptor expression in the liver, lowering circulating LDL.
Side effects: Myopathy, especially with combined therapy, and contraindicated in pregnancy.

Niacin for Lipid Lowering

Nicotinic Acid (Vitamin B3):
Functions by converting to NAD or NADP+.
Hypolipidemic effects:
Increases HDL-C by 35-40%.
Lowers triglycerides by 35-45%.
Decreases LDL-C production by 20-30%.
Mechanism: Inhibits triglyceride lipolysis in adipose tissue.

Fibrates for Lipid Lowering

Fibrates (e.g., Gemfibrozil, Fenofibrate):
Activate PPAR-α to stimulate fatty acid oxidation.
Decrease levels of VLDL and LDL while moderately increasing HDL.
Used in severe hypertriglyceridemia.
Side effects: Rashes, myopathy, and may interact with statins.

Bile Acid-Binding Resins

Examples: Colestipol, Cholestyramine, Colesevelam.
Mechanism: Bind bile acids in the intestine, preventing reabsorption, and increasing hepatic cholesterol synthesis.
Leads to increased LDL clearance but may elevate triglycerides due to HMG-CoA reductase upregulation.

Inhibitors of Sterol Absorption

Ezetimibe:
Reduces LDL by inhibiting cholesterol absorption in the intestine (NPC1L1).
Can reduce absorption by 54%, leading to increased cholesterol synthesis.
Works well with statins for enhanced LDL-C reduction (15-20%).
Possible side effects include allergic reactions and liver function impairment.