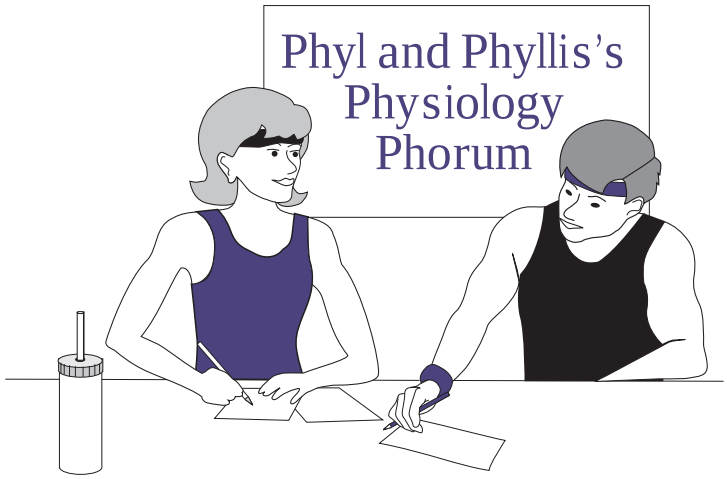
What is atherosclerosis?

What is cholesterol?

What are lipoproteins?

What determines whether cholesterol is "good" or "bad"?



Atherosclerosis is one of the two most common cardiovascular disorders; the other is high blood pressure or hypertension. Atherosclerosis is characterized by numerous lumps or plaques occurring within and throughout the walls of large and medium sized arteries. The most commonly affected arteries are the coronary arteries that serve heart muscle tissue and the carotid arteries that serve brain tissue.

Plaques begin to develop as a result of damage to the protective endothelial layer of cells that line the inner wall of arteries. The damage may be the result of chronic exposure to high blood pressure. It may also occur as a result of chronic exposure to high concentrations of "bad" cholesterol, also known as low-density lipoproteins.

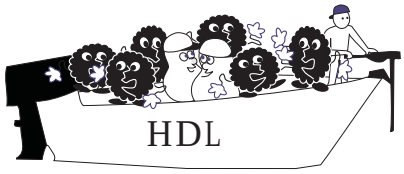
Atherosclerosis tends to run in families. However, there are such controllable risk factors as smoking, diets high in saturated fat and cholesterol, physical inactivity and the resulting obesity.

Cholesterol

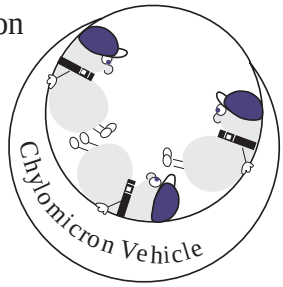
Low-Density Lipoprotein

Very-Low-Density Lipoprotein

High-Density Lipoprotein



Chylomicron



Although the disease process begins in childhood, it may not be detected until young adulthood. Because family history is an important predictor of cardiovascular disease, its manifestations should not be dismissed in childhood. Blood pressure measurement and examination of blood components should be a routine part of pediatric care.

Cholesterol is a fatty, waxy substance either brought into the body through the diet or made from fat inside the liver. Among other roles in the body, cholesterol serves as an important component of reproductive hormones and digestive materials. It is also an integral part of cell membranes.

As is the case with all lipids, or fatty substances, cholesterol is transported aboard protein structures to and from cells that use it. These carriers are called lipoproteins, the density of which depends upon what is being transported. There are several lipoproteins of varying density. Three of the most important are: very-low-density lipoproteins (VLDLs), low-density lipoproteins (LDLs) and high-density lipoproteins (HDLs).

Very-low-density lipoproteins (VLDLs) are constructed in the liver. They transport triglycerides and cholesterol to fat storage areas throughout the body. After the triglycerides are removed, the lipoprotein increases in density and becomes a low-density lipoprotein (LDL). LDLs are sometimes called “bad” cholesterol because of the risk they pose if they are trapped within blood vessel walls and go through a process called oxidation. Oxidized LDLs tend to form plaques associated with the development of atherosclerosis.

High-density lipoproteins (HDLs) are also constructed in the liver. They travel through the body collecting the excess cholesterol from arterial walls. Then they carry it back to the liver. HDLs are known as “good” cholesterol because their removal of cholesterol from arterial walls reduces the risk of the development of atherosclerosis. Chylomicrons are also carriers of fat, transporting the triglycerides contained in foods to fat storage areas.

Lipid Profile

Date Reported	Date Received	Patient Name - I.D.	Phone	Age	Sex
08–AUG-05	07-AUG-05	Phyllis Physiology	312-386-2782	45	F

Date Collected	Time Collected	Hospital I.D.	Requisition No.	Assession No.
07–AUG-05	8:30 am		361586829	2555006782-5

Client Name/Address	Test Requested
Lake Shore Cardiologist 27570-4 Chicago, IL [7]	Metabolic Panel, Comprehensive Lipid Panel Thyroid Panel with TSH.

Physician	Volume	Fasting	Patient SS#	Comments
Bergin, C		Yes		Copy sent to patient

TEST NAME	RESULT	UNITS	REFERENCE RANGE
Lipid Panel:			
Cholesterol	191	MG/DL	100-199
Triglycerides	110	MG/DL	20-199
HDL-Cholesterol	58	MG/DL	35-150
LDL (Calculated)	110	MG/DL	0-129
VLDL (Calculated)	18	MG/DL	(39

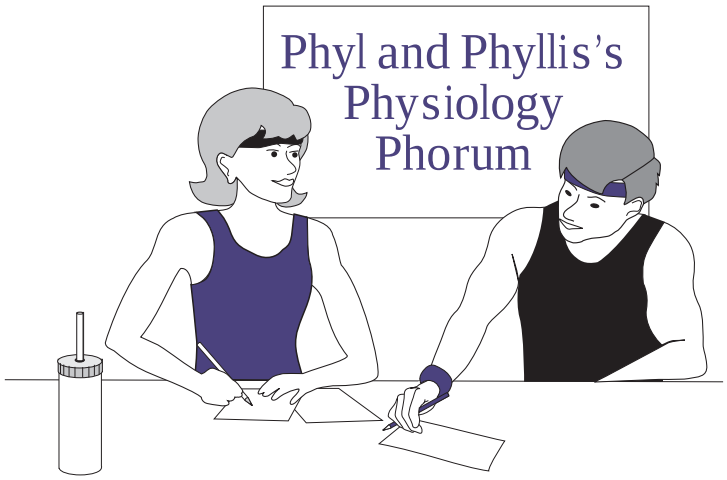
While lipids are essential for a variety of cellular functions and therefore must be transported in the blood to and from the liver, the transport must be rapid. The concentration of blood lipids fluctuates, but is lowest after fasting, which is when blood should be drawn for a lipid profile.

A lipid profile is a routine blood test that can be administered during an annual physical examination. It is a measurement of the concentration of blood lipids (in milligrams) dissolved in a deciliter of blood after a twelve-hour fast.

Desirable results are high concentrations of HDLs (≥60mg/dL), and low concentrations of LDLs (100 mg/dL). Triglyceride values should ideally be as low as possible (150 mg/dL).

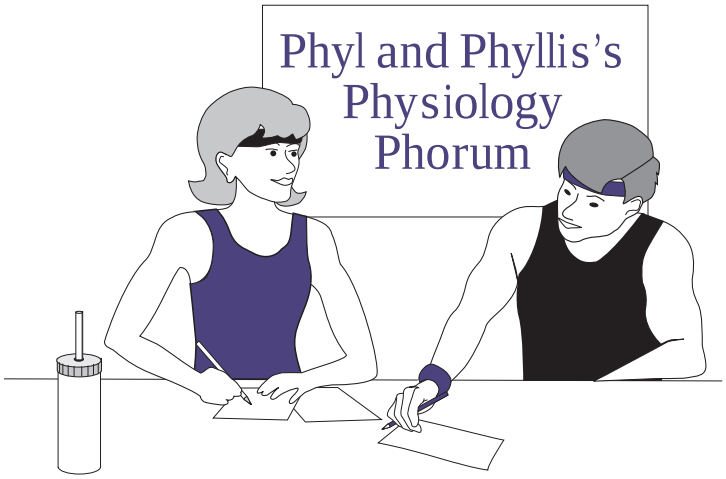
What is the relationship between LDL or "bad" cholesterol and the development of atherosclerosis?

How does this cause a heart attack or stroke?



The cells of healthy body tissues take up and use cholesterol for a variety of important functions. The remaining circulating LDLs must be removed from the blood. Both arterial endothelial cells and liver cells are equipped to remove them. The removal mechanism involves specially shaped proteins that are designed to bind with the LDL structure and remove its cholesterol.

While the primary mechanism provides effective cholesterol removal, chronically high concentrations of LDLs exhaust its ability to keep up. Thus, another mechanism is implemented—one that may be damaging to the protective endothelial lining of arterial walls. This alternative method of LDL removal involves a type of white blood cell called a monocyte, which changes into a macrophage. Macrophages gobble up excess LDL cholesterol.



Blood vessel walls that are continuously exposed to high concentrations of bad cholesterol must resort to calling in an army of macrophages to gobble up the excess LDLs. The removal process, however, disrupts the smooth cell-to-cell protective endothelial structure of the blood vessel walls. As with chronic high blood pressure, this disruption also allows the invasion of other blood constituents into vulnerable tissues beneath them. The damage to blood vessel walls caused by chronic high blood pressure and exposure to high concentrations of LDLs attracts blood cells called platelets to the areas of disrupted endothelium.

Platelets are important blood cells despite their small size. Platelets bunch together, or aggregate, when blood constituents or vessels are damaged. To control bleeding, they form a plug by releasing various sticky substances. The plug allows the body time to close up the wound. Platelet aggregation is an important process, but it sometimes occurs for no apparent reason. Fortunately, the body has safety mechanisms that dissolve unnecessary platelet aggregation or clotting.

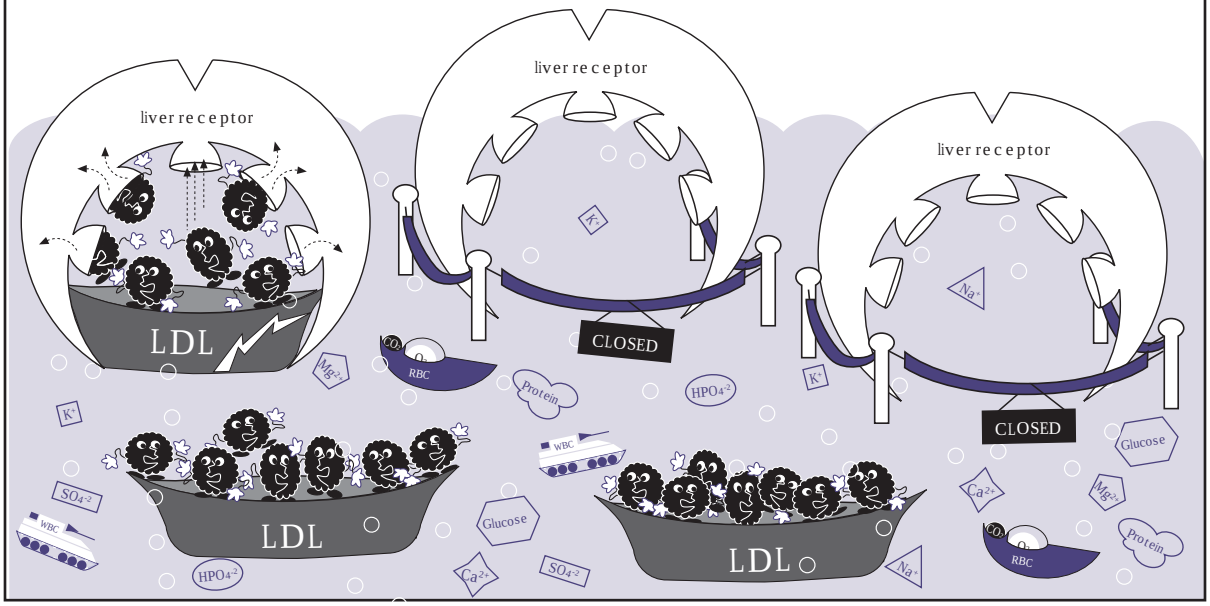
When the protective endothelial layer is disrupted, platelets are attracted to the area of inflammation and damage. Platelets release substances that seem to cause abnormal tissue growth in these areas. The abnormal tissue growth, combined with the fatty materials gobbled up by the macrophages begins to form mounds that grow and harden into plaques. Atherosclerosis is the result.

Arteries in this condition are no longer stretchy and pliable. They no longer can accommodate the loads of blood the heart pumps into them. The piping system becomes rigid and narrowed, creating more resistance against which the heart has to pump. This raises blood pressure. Eventually, the affected arteries can become virtually blocked, impeding adequate blood flow, and therefore much needed oxygen and nutrients, to the heart muscle or brain tissue.

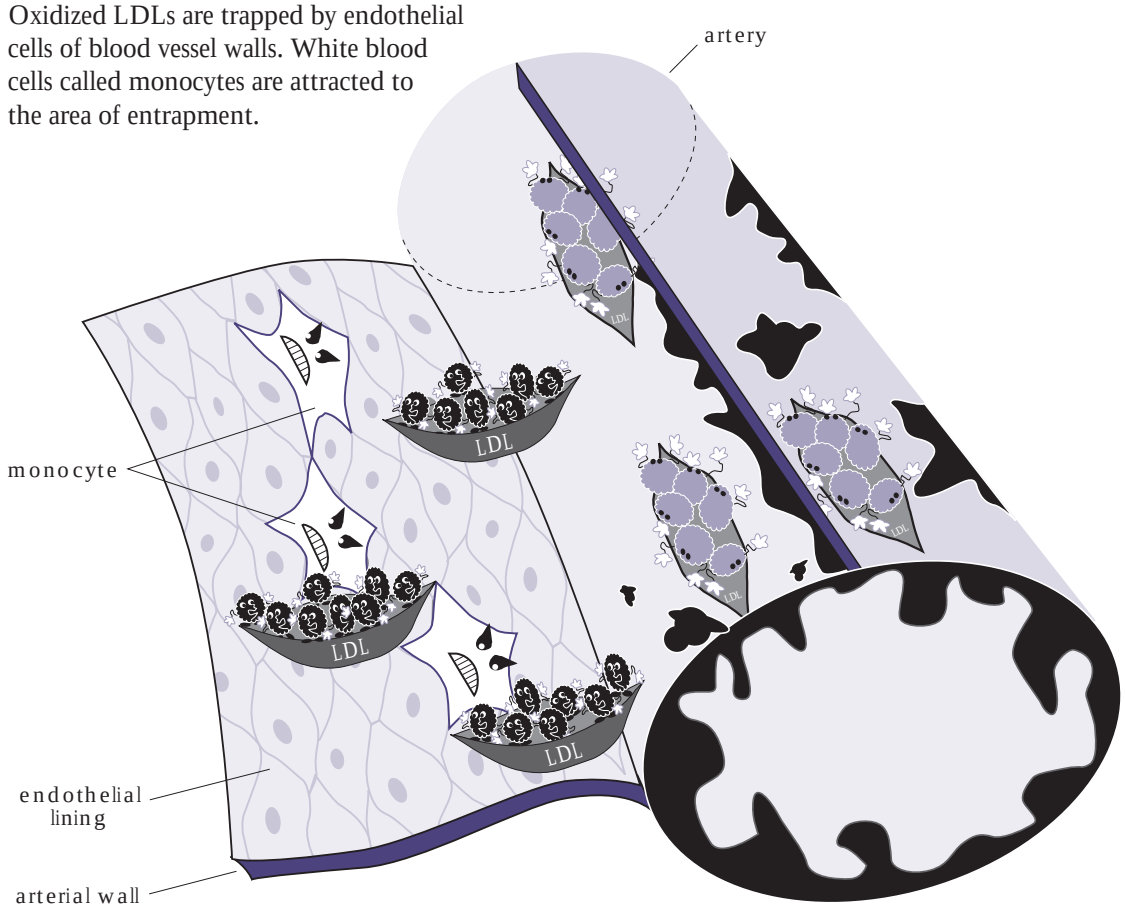
Plaque formation occurs throughout the cardiovascular system. Blood vessel walls that are hardened, bumpy and jagged like those affected by atherosclerosis are prone to cracking, promoting more platelet aggregation and clot formation. Should a clot attach to already existing plaques and get lodged in a small artery, it can block blood supply to heart muscle tissue, and cause a heart attack also known as a myocardial infarction. If a clot becomes lodged in an artery blocking blood supply to brain tissue, a stroke can result.

The Development of Atherosclerosis

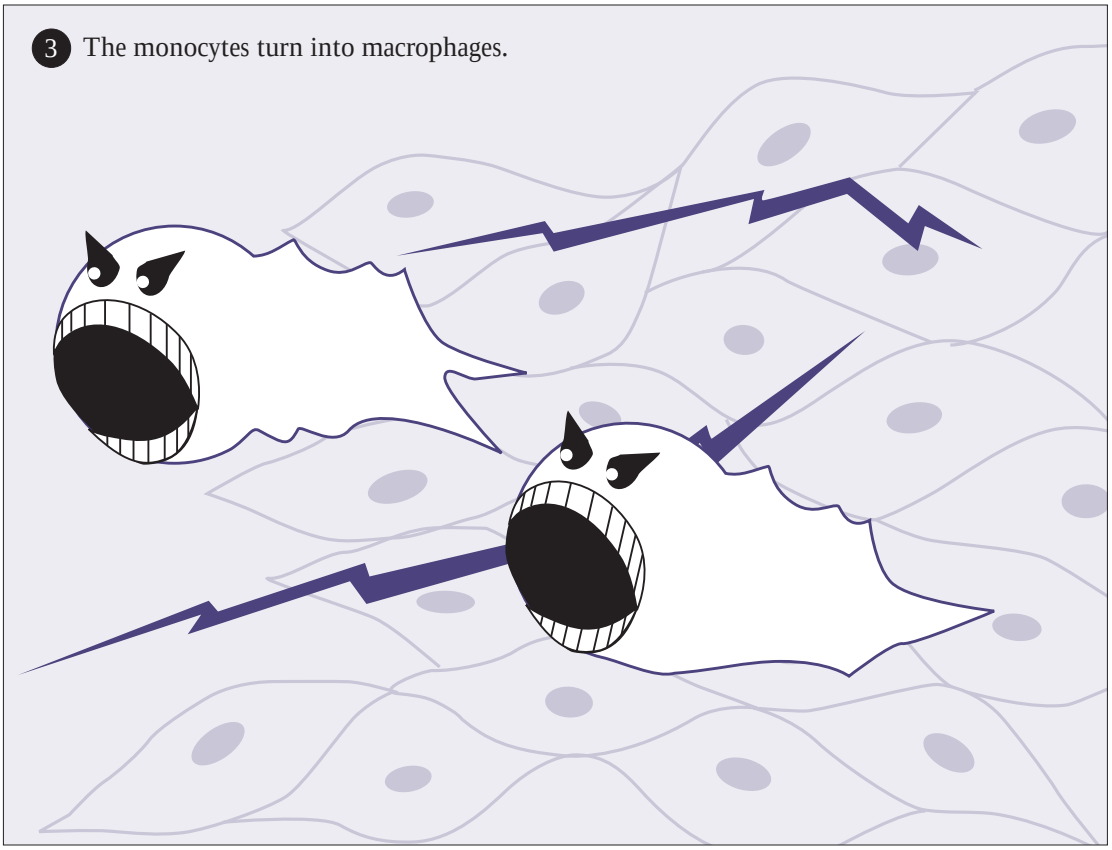
1 Body cells, especially liver cells, possess special receptors that bind with LDL cholesterol and remove it from circulating blood. Once cells have taken up all they need, the LDLs that remain in the circulation are susceptible to attack by unstable substances. Thus, they may be chemically altered through a process called oxidation.

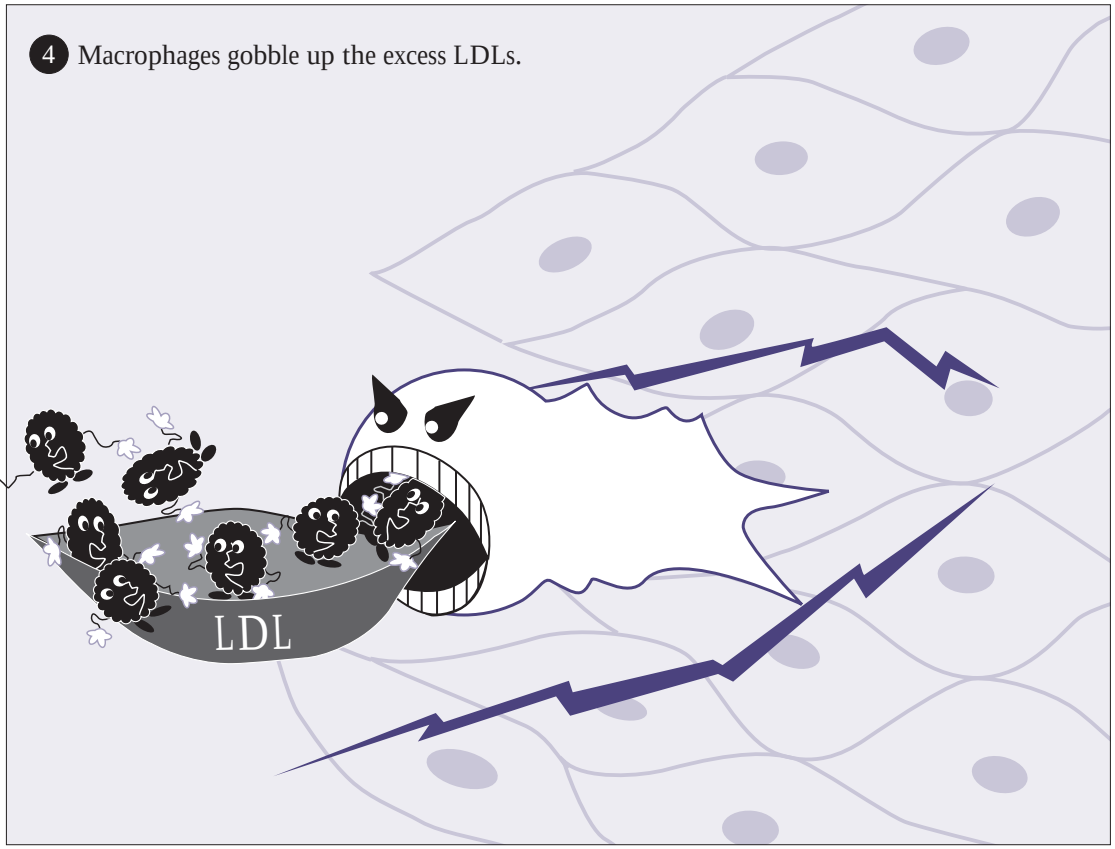


2 Oxidized LDLs are trapped by endothelial cells of blood vessel walls. White blood cells called monocytes are attracted to the area of entrapment.



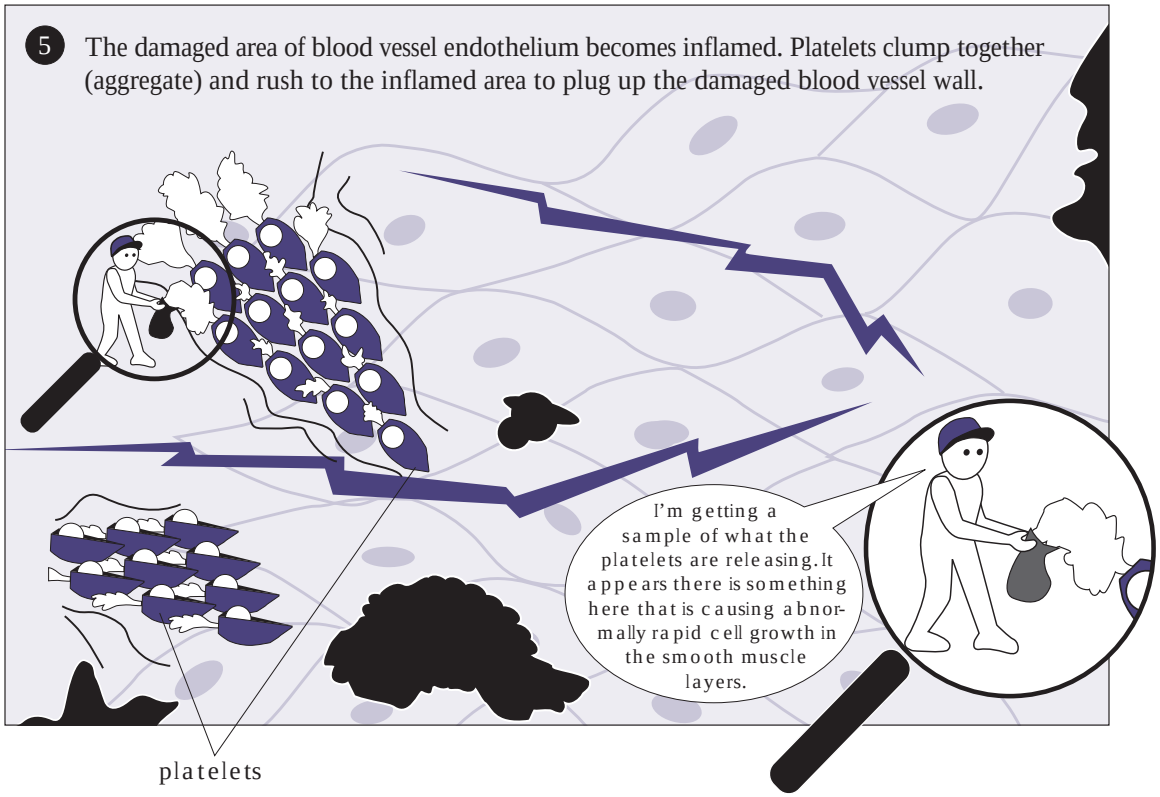
The Development of Atherosclerosis





The Development of Atherosclerosis

5 The damaged area of blood vessel endothelium becomes inflamed. Platelets clump together (aggregate) and rush to the inflamed area to plug up the damaged blood vessel wall.



6 The platelets produce sticky substances that not only draw more platelets and other fatty components but also cause abnormal cell growth in the area. Hardened walls form mounds called atherosclerotic plaques.