atherosclerosis & blood clotting

atherosclerosis

1. The endothelium becomes damaged. This could be because of a variety of reasons, including smoking and high blood pressure. This damage causes an inflammatory response, and white blood cells leave the blood flow into the endothelium. They attract collagen-producing enzymes.

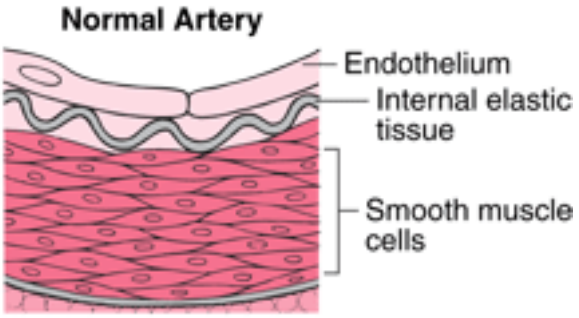
2. These white blood cells are called monocytes. Monocytes are only attracted to the cell wall where there is no creation of NO (Nitrous Oxide). The production of NO can be limited by factors such as high blood pressure, diabetes or smoking. Instead these cells produce CAM (cell adhesion molecules). Once inside the cell wall the monocytes are converted to macrophage foam cells. These accumulate 'Low Density Lipoproteins' which is 'bad' cholestrol. This build up of chemicals and cholesterol is known as an atheroma.

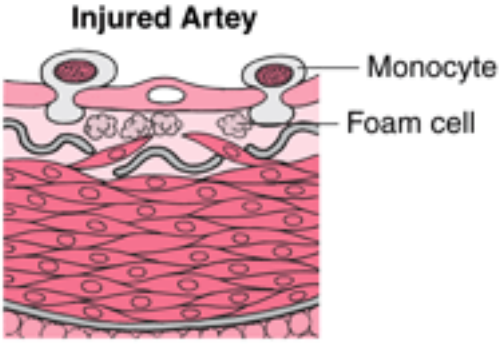
3. There is also a build up of calcium salts and vitamin K from the blood plasma. This causes a hard swelling known as a plaque, which also consists of collagen. The plaques are usually filled with cholesterol and can have calcium deposits.

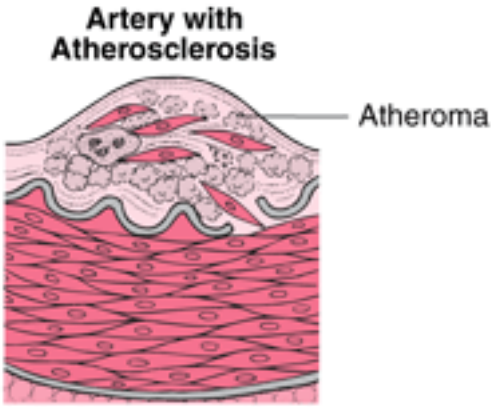
4. The plaques cause the arteries to become smaller. This increases blood pressure, causing positive feedback; plaques cause high blood pressure, which in turn makes the likelihood of more plaques developing higher.

5. Often atherosclerosis can go hand in hand with blood clotting. This is most likely to occur if an atheroma bursts. In the coronary arteries, this can cause a heart attack if the heart tissue doesn't recieve enough oxygen to function properly.

Atherosclerosis only affects arteries. This is because the blood pressure in veins is always of a safe level, and atheromas will tend not to develop, as the lumen walls are unlikely to sustain damage.







http://www.merck.com/mmhe/sec03/ch032/ch032a.html

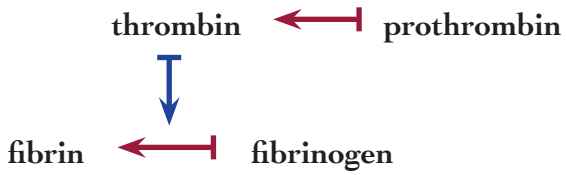
blood clotting

1. If a cell wall is damaged, platelets, carried in the plasma, change from flat disc shaped cells to long, projections. These stick to the damaged areas of the wall, which consist of exposed collagen, and form a 'platelet plug'. They release ADP, a substance which attracts more platelets to the scene.

2. Damage to the cell wall brings blood into direct contact with the collagen inside the wall. This brings about a rapid cascade of chemical changes:

- Soluble prothrombin is converted into insoluble thrombin. This catalyses the conversion of:
- Fibrinogen, another soluble protein, into fibrin, which is made up of long thin strands that form a mesh which catch blood cells, causing a clot.

3. A blood clot of this nature is known as a thrombosis. It can cause myocardial infarction if it occurs in the coronary arteries, or a stroke.



macrophage foam cells

Within a foam cell there are a variety of proteins that can have a radical affect upon the formation of a plaque.

i. The first of these is MMP-12. This is an enzyme which causes the degradation of cellulose, thus further damaging the cell wall. This increase the size of a plaque. The concentration of MMP-12 has been found to increase as a plaque grows older.

ii. However, there is another variety of proteins, TIMP 3s (Tissue inhibitors of MMP 3), which nullify the collagen degradation affects of the MMPs. Those cells lacking TIMP 3 are 3 x more likely to rupture, releasing their fatty contents and causing either thrombosis, a blood clot, or detaching entirely and causing an embolism, which will block elsewhere in the artery.

Worryingly, the amount of TIMP3 decreases over time, rendering the increased presence of MMP-12 all the more dangerous.