Lesson 3: CHD & Atherosclerosis

- **Coronary heart disease (CHD)** is the leading cause of death killing millions of people worldwide every year. It has been known for a long time that there is a direct and **profound correlation between dyslipidemia and atherosclerosis**. So high plasma cholesterol levels, high triglyceride levels, and low HDL levels all are known to contribute to the progression of atherosclerotic lesions. In addition, there are other risk factors that either play a role independently or compound the effects of dyslipidemia. These risk factors include Hypertension, Diabetes, Obesity, Smoking, and family history of CHD.

- **The coronary arteries** are the major blood vessels that supply oxygenated blood to the heart muscle or the myocardium. Since the heart muscle needs a constant supply of oxygen and glucose, any blockage within these arteries will lead to damage or death to the myocardium, and if the damaged area is large enough, it would lead to an irreversible heart failure and death. The major cause of blockage of course is atherosclerosis, sometimes simply referred to as **plaque** within the coronary arteries.

- **Atherosclerosis**: The innermost layer of the artery is made up of endothelial cells, and this endothelial barrier tends to be **semi porous** in that it is **permeable to certain lipoproteins and phagocytic cells** such as macrophages. Under normal circumstances, the lumen of the artery is large enough to allow all cells to go through. Some LDL particles, particularly those that happen to be very small tend to easy penetrate the endothelial barrier and make it into the intima proper of the artery. Once inside, the LDL particle will **undergo oxidation**. Macrophages in circulation are attracted to this oxidized LDL and they enter the intima and phagocytose these oxidized LDL particles. As they engulf more and more
oxidized LDL, these macrophages become bloated with lipids and are known as **Foam Cells**. If the foam cells continue to get bigger, at some point the lipid content will prove **toxic** and the cell will die by **apoptosis or necrosis**.

- Cell death causes recruitment of other white blood cells that accumulate in the area and release **inflammatory cytokines**, resulting in damage to the endothelial layer. The body’s attempt to contain and repair this damage results in a **scar or plaque** that is particularly enriched in lipids. After some time, the atherosclerotic plaque may also be fortified by calcium deposits.

- The presence of atherosclerotic plaque causes **narrowing of the artery** in the region. Red blood cells may be small enough to pass through this narrowing, but if there is a **clot present in the arterial circulation** and if it is too big to pass through the narrowing, it will lodge into place and cut off the circulation downstream, resulting in a heart attack.

- When there is a **stenosis** or narrowing of an artery due to a plaque, the endothelial layer of the artery will respond by producing and **releasing nitric oxide**, which acts on the muscles of the artery, causing **dilation as a compensatory mechanism** to allow the blood flow. When this compensatory dilation is not sufficient, the patient gets **ischemic chest pains** that can be relieved by taking nitroglycerine. Severe blockages, if detected early enough, can be treated by **balloon angioplasty**. A **stent** with balloon is inserted into the artery and when it reaches the site of stenosis or narrowing, the balloon is inflated, which expands the stent in place. The balloon is then removed and the stent stays in place to keep the artery open.
• **A stable plaque** is the one that causes the narrowing of the artery but doesn’t undergo any dramatic change. However, for reasons that are still not understood very well, some plaques become **unstable and are ruptured**. Meaning that the anchors that hold plaque in place are severed so that the plaque is **dislodged** and it breaks through the endothelial layer and enters the lumen of the artery. The endothelial damage that occurs during this rupturing process recruits platelets that forms a clot. The clot further increases the risk of a severe infarct. Ruptured plaques that originate in carotid artery as well as clots can also cause **cerebral infarcts** when they reach cerebral circulation.

• **Atherosclerosis and Beneficial effects of HDL:**
  1. HDL is known to have antioxidant activity that attenuates the oxidation of LDL particles.
  2. Reverse Cholesterol Transport: HDL removes cholesterol from foam cells and prevents them from becoming necrotic.
  3. HDL stimulates production of nitric oxide by the endothelium, thus causing increased vasodilation.
  4. HDL has anti-inflammatory properties that inhibit the process of atherosclerosis.
  5. HDL has anti-thrombotic effects. It has fibrinolytic properties that help reduce clot size.