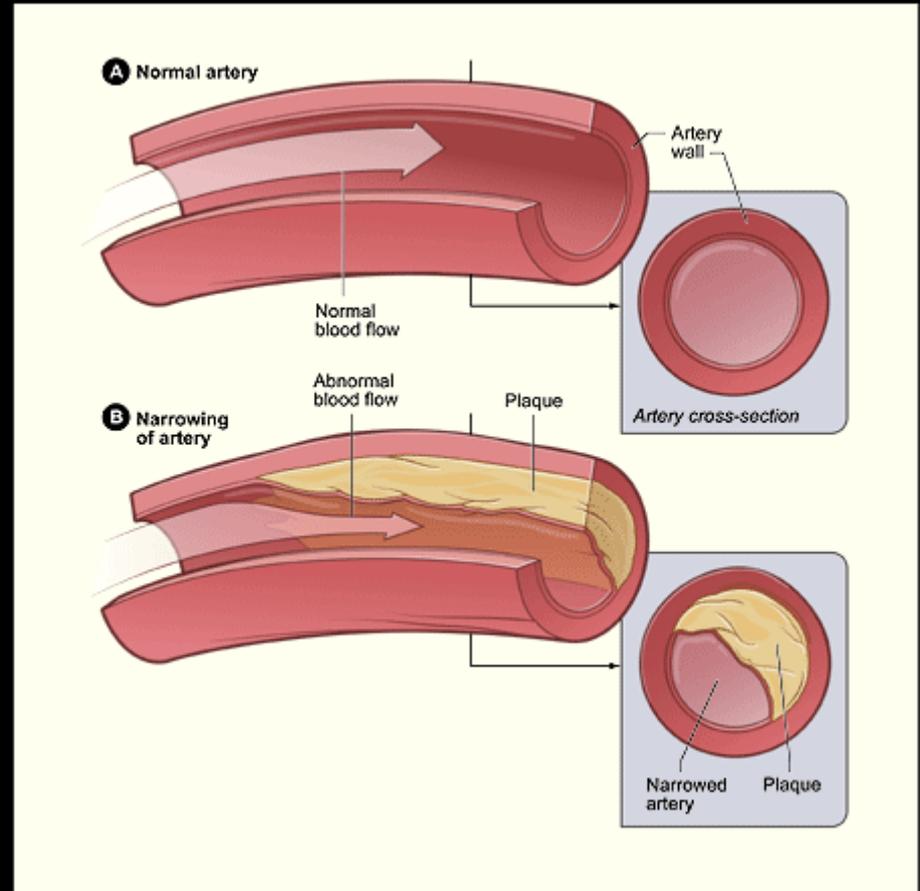


**Mitochondrial Implications
in
Coronary Heart Disease
(Pre-Ischemia)**

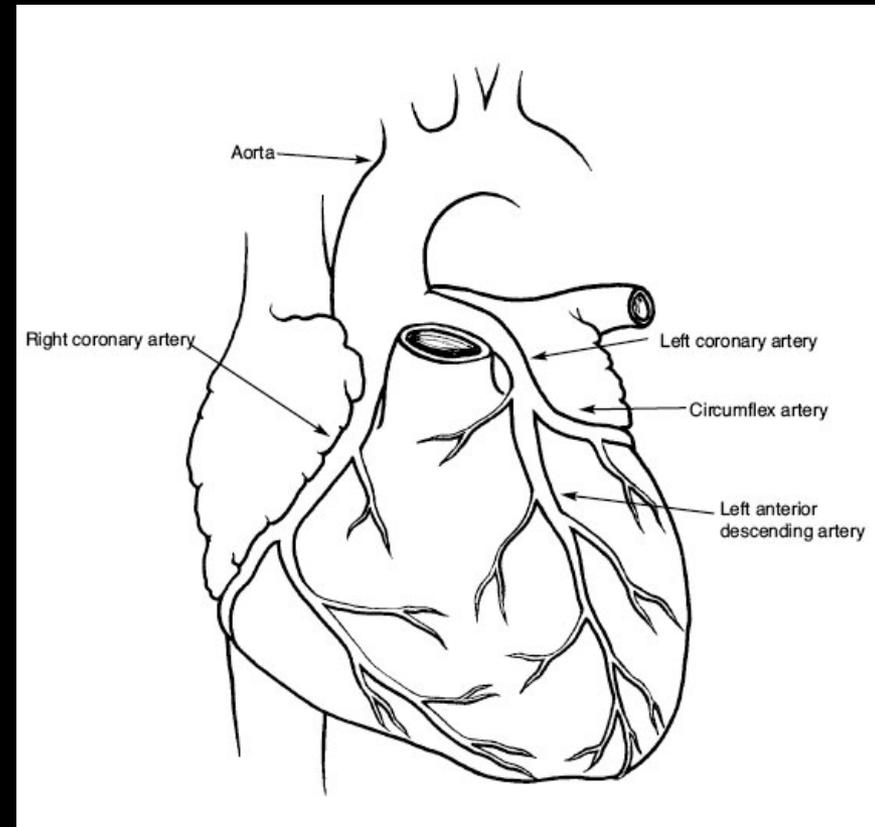
Arteriosclerotic Vascular Disease (ASVD)

- ASVD is the build up of plaque along arterial walls.
- Plaque is composed of cholesterol, fat, calcium, and other substances from the blood.
- Plaque build up leads to narrowing of the arteries, and consequently blood clots.
- When ASVD occurs in the coronary arteries, it is classified as Coronary Heart Disease.

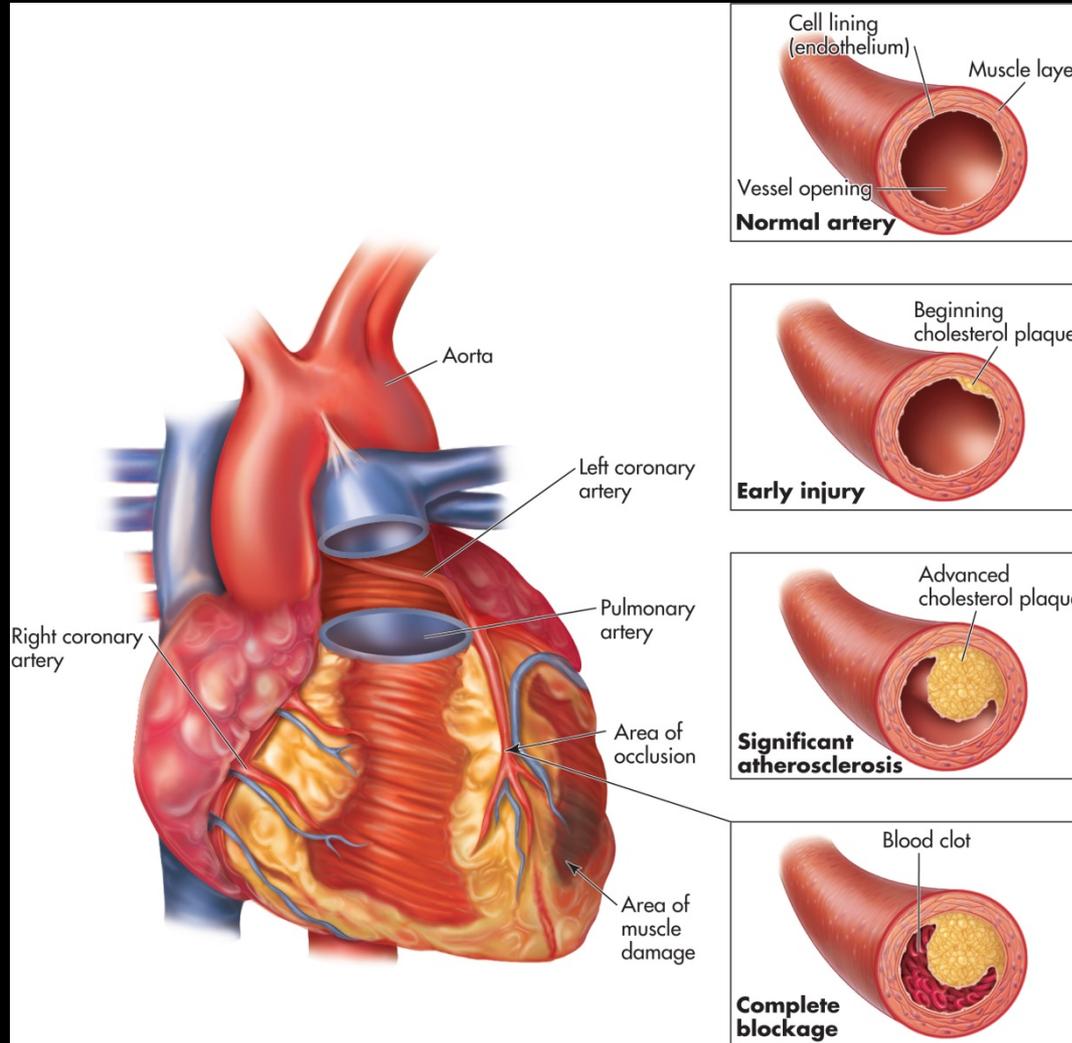


Coronary Heart Disease (CHD)

- Coronary arteries are responsible for the supply of oxygenated blood to the heart itself.
- The coronary arteries diverge from the aorta almost immediately after it branches off from the left ventricle of the heart.
- The left coronary artery further diverges into the left circumflex (LCX) and the left anterior descending (LAD), while the right coronary artery has only one major branch.
- When atherosclerosis occurs in any of the coronary arteries, blood supply to the heart is slowed or blocked.



Stages of CHD



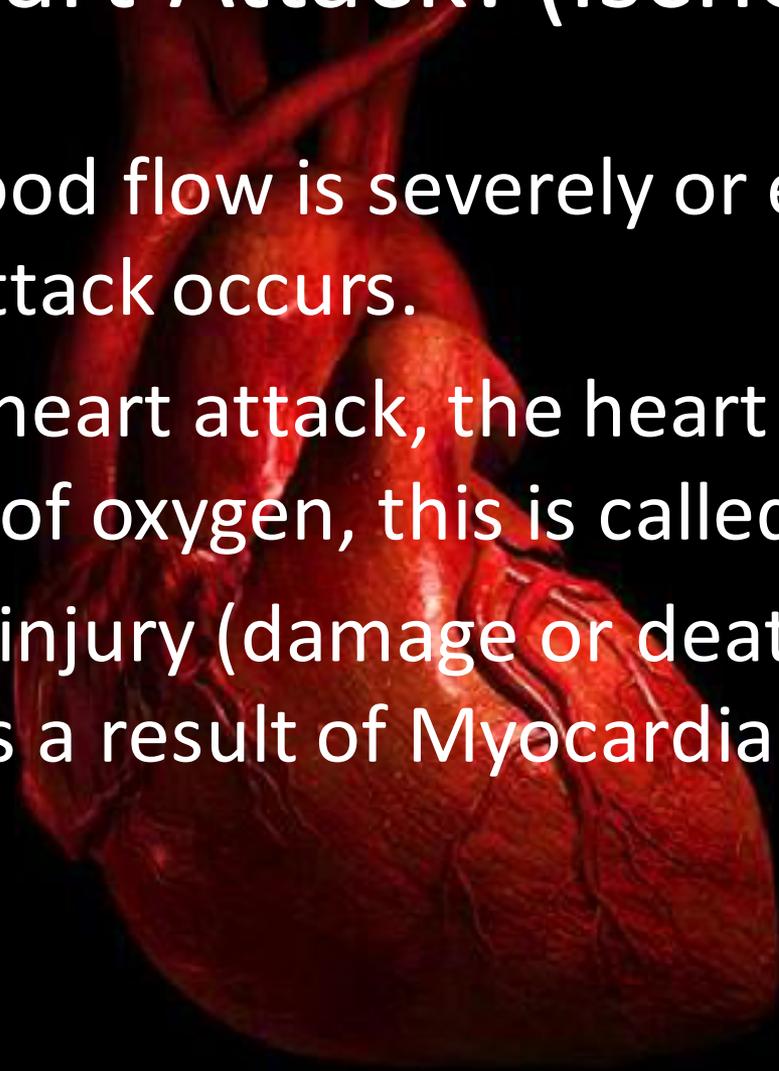
Symptoms of CHD

- Angina (chest pain)
- Shortness of breath
- Fatigue

The decreased efficiency of the blood flow causes the muscle to be easily exhausted, often resulting in a tight, squeezing sensation in the chest, neck, arms, stomach, or upper back. Pain typically worsens with (but is not limited to) physical activity and emotions, and subsides with rest and treatment with nitroglycerin.

Heart Attack! (Ischemia)

- When blood flow is severely or entirely cut off, a heart attack occurs.
- During a heart attack, the heart muscle is deprived of oxygen, this is called ischemia.
- Ischemic injury (damage or death to the heart muscle) is a result of Myocardial Infarction (MI).



Arteriosclerotic Vascular Disease Inheritance

Pathogenesis:

- The disease can occur by behavioral induction.
- There is also a strong hereditary correlation, though the exact genetic contributing factors are not understood in their entirety.
- The mitochondrial genome (mtDNA) has been implicated as a maternally inherited predisposatory factor.

Mitochondrial Implications

- Reactive oxygen species (ROS) formed during oxidative phosphorylation cause oxidative stress. Oxidative stress elevates mitochondrial DNA (mtDNA) damage and mutation levels.
- Excessive mitochondrial damage in both proteins and DNA decreases efficiency and can also result in apoptosis, a mitochondrial mediated programmed cell death.
- The decreased efficiency and apoptosis in smooth muscle cells are contributors to plaque progression.
- Mutations/damage in DNA also show a direct correlation with the presence of CHD.

Evidence of Implications

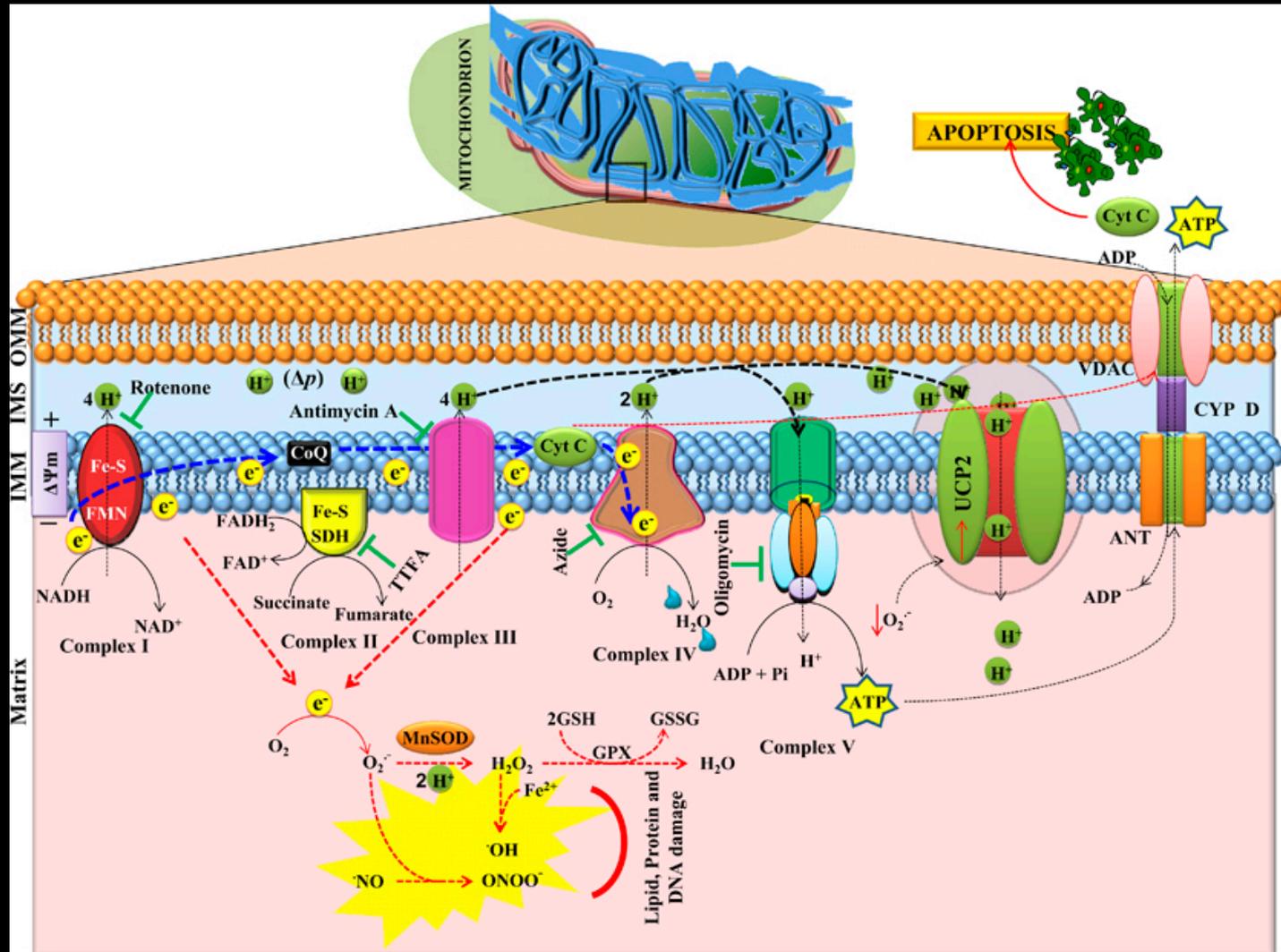
In the experimental examination of tissue from atherosclerotic coronary plaque, the following observations were made:

- 1) The mean level of heteroplasmy in a specific set of five mitochondrial genes was significantly higher in the diseased tissue¹.
- 2) Presence of molecular markers specific to apoptosis was significantly higher in the atherosclerotic tissue⁶.
- 3) Vasoactive markers that control apoptosis in the smooth muscle cells and endothelial cells were altered during the progression of atherosclerosis⁶.
- 4) The abundant presence of matrix metalloproteinases in the atherosclerotic tissue caused lots of cellular stress sometimes followed by apoptosis¹¹.

Mitochondria: Main Functions

- Oxidative Phosphorylation
- Regulation of Cellular Metabolism
- Apoptosis
- Calcium Signaling
- Lipid Transfer

Normal Oxidative Phosphorylation in a Mitochondrion



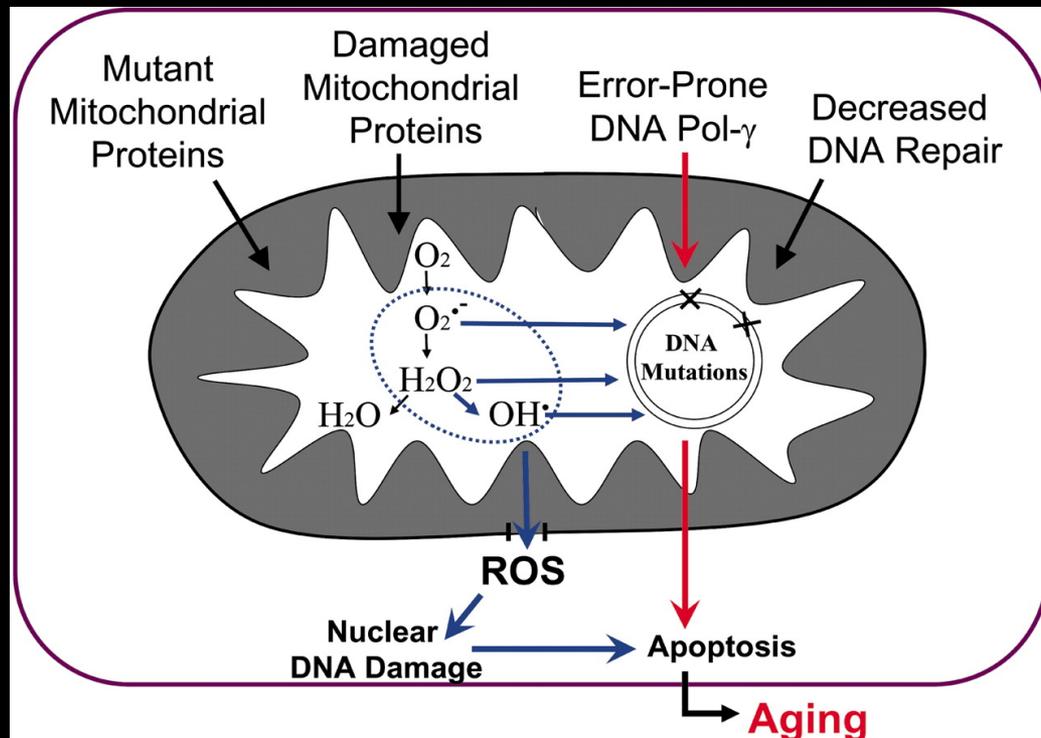
Reactive Oxygen Species



- **Formation:** 0.4-4.0% of all oxygen consumed in oxphos is converted into a superoxide radical. This occurs when oxphos malfunctions and reduces oxygen, forming a superoxide radical. The superoxide radical is then converted into hydrogen peroxide by a superoxide dismutase enzyme, and then the hydrogen peroxide is converted into water by a glutathione peroxidase enzyme. If the enzymes do not catalyze the changes adequately or efficiently enough, a ROS is formed causing oxidative stress.
- Reactive oxygen species are capable of damaging both protein and DNA. mtDNA is especially susceptible due to its lack of histones, like nuclear DNA.
- mtDNA, when functional, repairs the damage by molecular remodeling. However, mutations and damage still accumulate over time. Damage may ultimately result in apoptosis.

Oxidative Stress Effects

- ROSs have also been implicated in: aging, schizophrenia, bipolar disorder, dementia, Alzheimer's, epilepsy, chronic migraines, strokes, neuropathic pain, Parkinson's, ataxia, transient ischemic attack, cardiomyopathy, chronic fatigue syndrome, fibromyalgia, diabetes, Hepatitis C, etc... as well as CHD.



Prevention

- **Healthy Balanced Diet:**

- low intake of saturated and trans-fat

- high fiber

- fruits & vegetables

- whole grain

- some unsaturated fat: avocado, oily fish, nuts and seeds...



- **Physical Activity:** Lower BMI and Blood Pressure

- **Reduce drinking... Give up smoking...**

- **Manage Stress!**



Screening

Detection methods include:

- Exercise stress test
- Heart CT scan
- Nuclear stress test
- Echocardiogram stress test
- Electrocardiogram (ECG)
- Coronary angiography- an invasive test that evaluates the heart arteries under x-ray
- Electron-beam computed tomography (EBCT) to look for calcium in the lining of the arteries -- the more calcium, the higher your chance for CHD



Prognosis

- Outcomes differ by severity and individual. With early detection, lifestyle changes can be adequate treatment.

In more severe and advanced cases, surgery (bypass, stent placement, angioplasty) or death are possible outcomes.



Conclusion

- Behavioral habits contribute to the risk of Arteriosclerotic Coronary Heart Disease.
- Still, many individuals are hereditarily predisposed through both the mitochondrial genome as well as the nuclear genome.
- There are multiple factors that contribute to the production of ROSs and the induction of apoptosis, both symptoms and causes of CHD.
- Lifestyle changes in diet, exercise, smoking, etc. can aid in both the prevention and combat of coronary heart disease.

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