ISCHEMIC HEART DISEASE

cardiac function is strictly dependent upon the continuous flow of oxygenated blood through the coronary arteries.

Ischemic heart disease (IHD) is an imbalance between cardiac blood supply (perfusion) and myocardial oxygen and nutritional requirements.

Despite dramatic improvements in therapy in the past quarter-century, IHD in its various forms remains the leading cause of mortality in the United States and other developed nations, accounting for 7 million deaths worldwide each year.

The manifestations of IHD are a direct consequence of the insufficient blood supply to the heart.

The clinical presentation may include one or more of the following *cardiac syndromes*:

• ***Angina pectoris*** (literally, "chest pain"): Ischemia induces pain but is insufficient to cause myocyte death. Angina can be *stable* (occurring predictably at certain levels of exertion), can be caused by vessel spasm , or can be *unstable* (occurring with progressively less exertion or even at rest).

• ***Acute myocardial infarction* (*MI*):** The severity or duration of ischemia is sufficient to cause cardiomyocyte death.

• ***Chronic IHD with CHF***:

• ***Sudden cardiac death (SCD)***

PATHOGENESIS

IHD is primarily a consequence of inadequate coronary perfusion relative to myocardial demand. This imbalance occurs as a consequence of the combination of preexisting ("fixed") atherosclerotic occlusion of coronary arteries and new, superimposed thrombosis and/or vasospasm.

The following elements contribute to the development and consequences of coronary atherosclerosis:

• **Inflammation**

• **Thrombosis associated with a disrupted plaque often triggers the acute coronary syndromes.**

• **Vasoconstriction**

Angina Pectoris

Angina pectoris is an intermittent chest pain caused by transient, *reversible myocardial ischemia.*

The pain probably is a consequence of the ischemia-induced release of adenosine, bradykinin, and other molecules that stimulate the autonomic afferents.

Three variants are recognized:

• ***Typical* or *stable angina*** is predictable episodic chest pain associated with particular levels of exertion or some other increased demand (e.g., tachycardia). The pain is classically described as a crushing or squeezing sub sternal sensation, that can radiate down the left arm or to the left jaw (*referred pain*).

The pain usually is relieved by rest (reducing demand) or by drugs such as nitroglycerin, a vasodilator that increases coronary perfusion.

• ***Prinzmetal* or *variant angina*** occurs at rest and is caused by coronary artery spasm.

• ***Unstable angina* (also called *crescendo angina*)** is characterized by increasingly frequent pain, caused by complete vascular occlusion.

Myocardial Infarction

Myocardial infarction (MI), also commonly referred to as “heart attack,” is *necrosis of heart muscle resulting from ischemia.* Roughly 1.5 million people per year in the United States suffer an MI; of these, one third

die—half before they can get to the hospital. The major underlying cause of IHD is atherosclerosis; while MIs can occur at virtually any age, *the frequency rises progressively with increasing age and with increasing atherosclerotic risk factors*.

PATHOGENESIS

The vast majority of MIs are caused by acute coronary artery thrombosis.

Coronary Artery Occlusion. In a **typical MI,** the following sequence of events takes place:

• An atheromatous plaque is suddenly disrupted by intraplaque hemorrhage or mechanical forces, exposing subendothelial collagen and necrotic plaque contents to the blood.

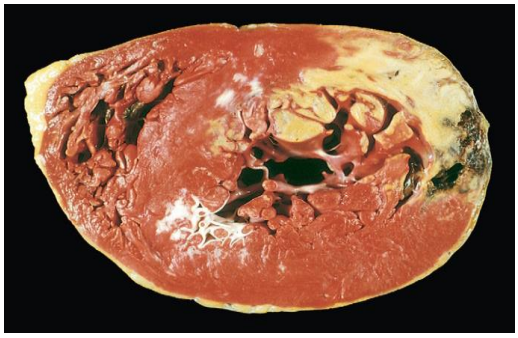
• Platelets adhere, aggregate, and are activated, releasing thromboxane A2, adenosine diphosphate (ADP), and serotonin—causing further platelet aggregation and vasospasm

• Activation of coagulation by exposure of tissue factor and other mechanisms adds to the growing thrombus.

• Within minutes, the thrombus can evolve to completely occlude the coronary artery lumen.

MORPHOLOGY

The gross and microscopic appearance of an MI depends on the age of the injury. Areas of damage progress through a highly characteristic sequence of morphologic changes from coagulative necrosis, to acute and then chronic inflammation, to fibrosis.



Clinical Features

The classic MI is heralded by severe, crushing substernal chest pain (or pressure) that can radiate to the neck, jaw, epigastrium, or left arm.

In contrast to angina pectoris, the associated pain typically lasts several minutes to hours, and is not relieved by nitroglycerin or rest.

The pulse generally is rapid and weak, and patients are often diaphoretic and nauseous.

The *laboratory evaluation* of MI is based on measuring blood levels of macromolecules that leak out of injured myocardial cells through damaged cell membranes.

Troponins have high specificity and sensitivity for myocardial damage.