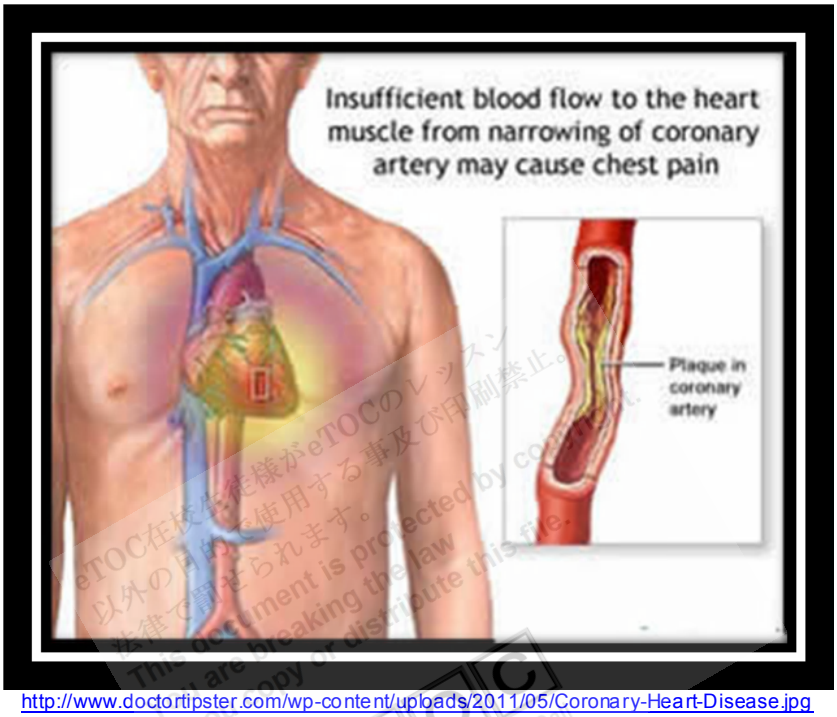
Coronary Artery Disease

Overview of Coronary Artery Disease



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Coronary artery disease *(CAD) involves impairment of blood flow through the coronary arteries, most commonly by* ***atheromas****. Clinical presentations include silent* ***ischemia****,* ***angina pectoris****,* ***acute coronary syndromes*** *(unstable angina, MI), and sudden cardiac death. Diagnosis is by symptoms, ECG, stress testing, and sometimes* ***coronary angiography****. Prevention consists of modifying reversible risk factors (eg,* ***hypercholesterolemia****,* ***hypertension****,* ***physical inactivity****,* ***obesity****, and* ***smoking****). Treatment includes drugs and procedures to reduce ischemia and restore or improve coronary blood flow.*

In developed countries, CAD is the leading cause of death in both sexes, accounting for about one third of all deaths. Mortality rate among white men is about 1/10,000 at ages 25 to 34 and nearly 1/100 at ages 55 to 64. Mortality rate among white men aged 35 to 44 is 6.1 times that among age-matched white women. For unknown reasons, the sex difference is less marked in nonwhites. Mortality rate among women increases after menopause and, by age 75, equals or even exceeds that of men.

Etiology

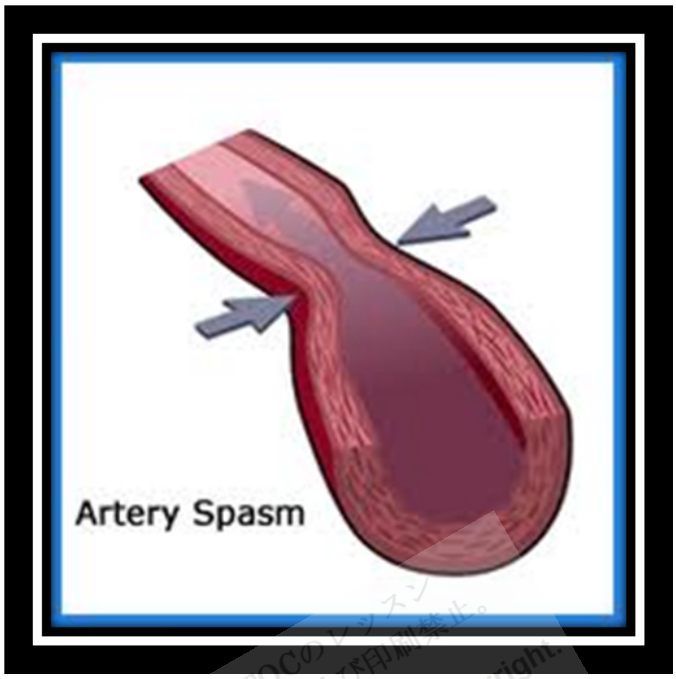
Usually, CAD is due to **subintimal** deposition of **atheromas** in large and medium-sized coronary arteries (**atherosclerosis**). Less often, CAD is due to coronary spasm. Rare causes include **coronary artery embolism, dissection, aneurysm** (eg, in Kawasaki disease), and **vasculitis** (eg, in **SLE**, **syphilis**).

Pathophysiology

Coronary atherosclerosis is often irregularly distributed in different vessels but typically occurs at points of turbulence (eg, **vessel bifurcations**). As the **atheromatous** plaque grows, the **arterial lumen** progressively narrows, resulting in **ischemia** (often causing **angina pectoris**). The degree of stenosis required to produce ischemia varies with O_2 demand.

Occasionally, an **atheromatous** plaque ruptures or splits. Reasons are unclear but probably relate to plaque morphology, **plaque Ca content**, and plaque softening due to an inflammatory process. Rupture exposes collagen and other **thrombogenic** material, which activates **platelets** and the coagulation cascade, resulting in an **acute thrombus**, which interrupts coronary blood flow and causes some degree of **myocardial ischemia**. The consequences of **acute ischemia**, collectively referred to as **acute coronary syndromes** (ACS), depend on the location and degree of obstruction and range from unstable angina to **transmural infarction**.

Coronary artery spasm is a transient, focal increase in vascular tone, markedly narrowing the **lumen** and reducing blood flow; **symptomatic ischemia** (**variant angina**) may result. Marked narrowing can trigger thrombus formation, causing infarction or life-threatening arrhythmia. Spasm can occur in arteries with or without **atheroma**. In arteries without atheroma, basal coronary artery tone is probably increased, and response to **vasoconstricting** stimuli is probably exaggerated. The exact mechanism is unclear but may involve abnormalities of nitric oxide production or an imbalance between endothelium-derived contracting and relaxing factors. In arteries with atheroma, the atheroma may cause local **hypercontractility**; proposed mechanisms include loss of sensitivity to **intrinsic vasodilators** (eg, **acetylcholine**) and increased production of **vasoconstrictors** (eg, **angiotensin II**, **endothelin**, **leukotrienes**, **serotonin**, **thromboxane**) in the area of the atheroma. Recurrent spasm may damage the intima, leading to atheroma formation. Use of vasoconstricting drugs (eg, cocaine, nicotine) and emotional stress also can trigger **coronary spasm**.



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Risk Factors

Risk factors for CAD are the same as those for **atherosclerosis**: high blood levels of **low-density lipoprotein** (LDL) cholesterol and lipoprotein a, low blood levels of high-density lipoprotein (HDL) cholesterol, **diabetes mellitus** (particularly type 2), smoking, obesity, and physical inactivity. Smoking may be a stronger predictor of MI in women (especially those <45). Genetic factors play a role, and several systemic disorders (eg, **hypertension**, **hypothyroidism**) and metabolic disorders (eg, **hyperhomocysteinemia**) contribute to risk. A high level of **apoprotein B** (**apo B**) is an important risk factor; it may identify increased risk when total cholesterol or LDL level is normal.

High blood levels of **C-reactive** protein indicate plaque instability and inflammation and may be a stronger predictor of risk of ischemic events than high levels of LDL. High blood levels of **triglycerides** and **insulin** (reflecting insulin resistance) may be risk factors, but data are less clear. CAD risk is increased by smoking; a diet high in fat and calories and low in phytochemicals (found in fruits and vegetables), fiber, and vitamins C and E; a diet relatively low in **ω-3** (**n-3**) **polyunsaturated fatty acids** (**PUFAs**), at least in some people; and poor stress management.

Anatomy

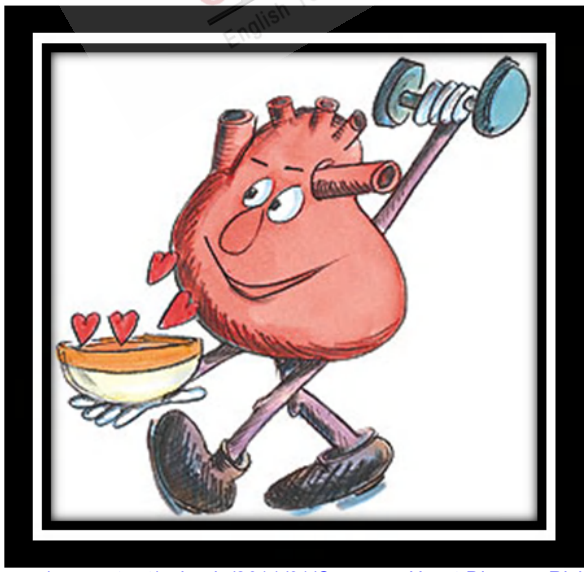
The right and left coronary arteries arise from the right and left **coronary sinuses** in the root of the **aorta** just above the **aortic valve orifice**. The coronary arteries divide into

large and medium-sized arteries that run along the heart's surface (**epicardial coronary arteries**) and subsequently send smaller **arterioles** into the **myocardium**. The left coronary artery begins as the left main artery and quickly divides into the **left anterior descending** (**LAD**) and **circumflex arteries**. The LAD artery usually follows the anterior interventricular groove and, in some people, continues over the apex. This artery supplies the anterior septum (including the **proximal conduction system**) and the anterior free wall of the left ventricle (LV). The circumflex artery, which is usually smaller than the LAD artery, supplies the lateral LV free wall. Most people have right dominance: The right coronary artery passes along the **atrioventricular** (AV) groove over the right side of the heart; it supplies the **sinus node** (in 55%), **right ventricle**, and usually the AV node and inferior **myocardial wall**. About 10 to 15% of people have left dominance: The **circumflex artery** is larger and continues along the **posterior AV groove** to supply the posterior wall and AV node.

Treatment

- **Percutaneous coronary intervention**
- For **acute thrombosis**, sometimes **fibrinolytic drugs**
- Coronary artery bypass grafting

Treatment generally aims to reduce cardiac workload, improve coronary artery blood flow, and, over the long term, halt and reverse the **atherosclerotic** process. Coronary blood flow can be improved by percutaneous coronary intervention (PCI) or **coronary artery bypass grafting** (**CABG**). An acute coronary thrombosis may sometimes be dissolved by **fibrinolytic drugs**.



http://kardiol.com/wp-content/uploads/2011/01/Coronary-Heart-Disease-Risk-Factors.jpg

PCI: At first, PCI was done with **balloon angioplasty** alone. However, roughly 50% of patients developed **restenosis** within 6 mo, and 1 in 3 ultimately required repeat **angioplasty** or **CABG**. Insertion of a bare-metal stent following angioplasty reduced the rate of restenosis, but many patients still required repeat treatment. Drug-eluting stents, which secrete an **antiproliferative** drug (eg, **sirolimus**, **paclitaxel**) over a period of several weeks, have reduced the rate of restenosis to about 10%. Now, most PCI is done with stents, and about three fourths of all stents used in the US are drug-eluting stents. With the recent controversy over drug-eluting stents and abrupt restenosis, use of the new drug-eluting stents appears to be decreasing in most centers. Patients with **acute stenoses** (ie, with **unstable angina** or **acute MI**) seem to do better with bare-metal stents. Patients without significant infarct or complications may quickly return to work and usual activities, but strenuous activities should be avoided for 6 wk.

In-stent thrombosis occurs because of the inherent **thrombogenicity** of metallic stents. Most cases occur within the first 24 to 48 h. However, late stent **thrombosis**, occurring after 30 days and as late as ≥ 1 yr, can occur with both bare-metal and drug-eluting stents, especially after cessation of **antiplatelet therapy**. Progressive **endothelialization** of the bare-metal stent occurs within the first few months and reduces the risk of thrombosis. However, the **antiproliferative drugs** secreted by drug-eluting stents inhibit this process and prolong the risk of thrombosis. Thus, patients who undergo stent placement are treated with various **antiplatelet drugs** and **anticoagulants**. The current standard regimen for patients with a bare-metal or drug-eluting stent consists of aspirin
given indefinitely, either **clopidogrel** or **prasugrel** for at least 12 mo, and **intraprocedural anticoagulation withheparin** or a similar agent (eg, **bivalirudin**, particularly those at high risk of bleeding). **Glycoprotein IIb/IIIa** inhibitors are no longer routinely used in stable patients (ie, no **comorbidities**, no **acute coronary syndrome**) having elective stent placement. Although controversial, they may be beneficial in some patients with an acute coronary syndrome but should not be considered routine. It is unclear whether it is beneficial to give glycoprotein IIb/IIIa inhibitors before arrival in the **cardiac catheterization laboratory**. After stent insertion, a **HMG-CoA reductase inhibitor** (**statin**) is added if one is not already being used.

Overall risk of **PCI** is comparable with that for **CABG**. Mortality rate is 1 to 3%; **MI** rate is 3 to 5%. In < 3%, intimal dissection causes obstruction requiring emergency CABG.

CABG: CABG uses sections of **autologous veins** (eg, **saphenous**) or, preferably, arteries (eg, internal mammary, radial) to bypass diseased segments. At 1 yr, about

85% of **venous bypass grafts** are patent, but after 10 yr, as many as 97% of internal **mammary artery grafts** are patent. Arteries also **hypertrophy** to accommodate increased flow.

CABG is typically done during **cardiopulmonary bypass** with the heart stopped; a bypass machine pumps and oxygenates blood. Risks of the procedure include stroke and MI. For patients with a normal-sized heart, no history of **MI**, good **ventricular function**, and no additional risk factors, risk is < 5% for perioperative MI, 2 to 3% for stroke, and ≤ 1% for mortality; risk increases with age and presence of underlying disease. Operative mortality rate is 3 to 5 times higher for a second bypass than for the first; thus, timing of the first bypass should be optimal.

After **cardiopulmonary bypass**, about 25 to 30% of patients develop cognitive dysfunction, possibly caused by **microemboli** originating in the bypass machine. Dysfunction ranges from mild to severe and may persist for weeks to years. To minimize this risk, some centers use a beating heart technique (ie, no cardiopulmonary bypass), in which a device mechanically stabilizes the part of the heart upon which the surgeon is working.

CAD may progress despite bypass surgery. Postoperatively, the rate of proximal obstruction of bypassed vessels increases. Vein grafts become obstructed early if **thrombi** form and later (several years) if **atherosclerosis** causes slow degeneration of the intima and media. Aspirin prolongs vein graft patency. Continued smoking has a profound adverse effect on patency.

Prevention

Prevention of CAD involves modifying **atherosclerosis** risk factors: smoking cessation, weight loss, a healthful diet, regular exercise, modification of serum lipid levels, and control of hypertension and diabetes. **Antihypertensives** should be used to achieve a goal blood pressure of < 130/80 mm Hg. Modification of **serum lipid levels** (particularly with statins) may slow or even partially reverse the progression of CAD. LDL targets are < 100 mg/dL (< 2.59 mmol/L) for patients with known CAD or 70 to 80 mg/dL (1.81 to 2.07 mmol/L) for those with a history of an **ischemic event**. Nicotinic acid or a fibrate should be added for patients with an HDL < 40 mg/dL (< 1.03 mmol/L).

Reference: http://www.merckmanuals.com