Hypertension, Orthostatic Hypotension, Aneurysms, and Arterial Thrombi

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Hypertension

Overview and Definition

Hypertension is defined as a **sustained elevation in blood pressure**, with a systolic blood pressure of **130 mm Hg or higher** or a diastolic blood pressure of **80 mm Hg or higher**. Blood pressure becomes elevated when there is a long-term increase in **peripheral vascular resistance**, an increase in **blood volume or cardiac output**, or a combination of both. Hypertension is extremely common in adults, especially in older adults, and is a major cause of heart disease, kidney disease, and stroke.

Hypertension affects over half of adult males and nearly half of adult females in the United States. The prevalence increases significantly with age, and more than three-quarters of individuals over the age of 65 have hypertension. It is more common in Black individuals and in people with diabetes. Individuals with **elevated blood pressure** (systolic 120–129 mm Hg with normal diastolic pressure) are at high risk for developing hypertension if lifestyle changes are not made.

Classification of Blood Pressure

Normal blood pressure is defined as a systolic pressure below 120 mm Hg and a diastolic pressure below 80 mm Hg. Elevated blood pressure ranges from 120 to 129 mm Hg systolic with a diastolic pressure below 80 mm Hg. Stage 1 hypertension occurs when systolic pressure is between 130 and 139 mm Hg or diastolic pressure is between 80 and 89 mm Hg. Stage 2 hypertension is diagnosed when systolic pressure reaches 140 mm Hg or higher or diastolic pressure is 90 mm Hg or higher. A hypertensive crisis occurs when systolic pressure is 180 mm Hg or higher and/or diastolic pressure is 120 mm Hg or higher and requires urgent medical attention.

Types of Hypertension

Most people with hypertension (about 90–95%) have **primary or essential hypertension**, meaning no single cause can be identified. Primary hypertension develops slowly over time and

results from a complex interaction between genetics, lifestyle, metabolic changes, inflammation, and neurohormonal dysregulation.

Secondary hypertension accounts for about 5–10% of cases and is caused by an identifiable condition or medication. Common causes include kidney disease, endocrine disorders such as pheochromocytoma or thyroid disease, pregnancy, and structural abnormalities such as coarctation of the aorta. Certain medications, including NSAIDs, oral contraceptives, corticosteroids, acetaminophen, and antihistamines, can also raise blood pressure. If the underlying cause is treated early, blood pressure may return to normal.

Pathophysiology of Primary Hypertension

Primary hypertension develops from long-term changes in the body's systems that regulate blood pressure. These changes involve the kidneys, blood vessels, nervous system, hormones, metabolism, and immune system. Over time, these systems work abnormally together, leading to **vasoconstriction**, **salt and water retention**, and permanent elevation of blood pressure. Because of its close association with obesity, insulin resistance, and inflammation, primary hypertension is now considered a **metabolic disease**.

Role of the Kidneys and RAAS

The kidneys play a central role in regulating blood pressure. In hypertension, the **renin–angiotensin–aldosterone system (RAAS)** becomes overactive. When kidney blood flow is perceived as low, the kidneys release renin, which triggers a hormonal cascade that produces **angiotensin II**. Angiotensin II causes blood vessels to constrict and stimulates the release of aldosterone, which increases sodium and water retention. These effects raise blood pressure and blood volume.

Angiotensin II also promotes inflammation, insulin resistance, and structural changes in blood vessels and the heart, known as **vascular and myocardial remodeling**. These changes permanently increase peripheral resistance and contribute to coronary artery disease, left ventricular hypertrophy, and heart failure. Medications such as ACE inhibitors, angiotensin receptor blockers (ARBs), and aldosterone antagonists work by blocking these harmful RAAS effects.

A protective RAAS pathway also exists. Through the action of ACE-2, angiotensin II can be converted into substances that promote **vasodilation**, reduce inflammation, and protect the heart and blood vessels. In hypertension, the balance shifts toward the harmful RAAS pathway.

Sympathetic Nervous System (SNS)

The sympathetic nervous system is overactive in many individuals with hypertension. Increased SNS activity raises heart rate and causes widespread vasoconstriction, which increases both cardiac output and peripheral vascular resistance. The SNS also stimulates renin release, promotes sodium retention, contributes to insulin resistance, and increases blood clotting. These combined effects sustain elevated blood pressure and increase cardiovascular risk.

Natriuretic Hormones and Salt Retention

Natriuretic hormones such as **atrial natriuretic peptide (ANP)** and **B-type natriuretic peptide (BNP)** are released when the heart is stretched by increased blood volume. These hormones normally promote sodium and water excretion by the kidneys, reduce RAAS activity, and cause vasodilation. In primary hypertension, the kidneys become less responsive to these hormones. As a result, less salt and water are excreted, leading to increased blood volume and higher blood pressure.

This impaired response is called a **shift in the pressure–natriuresis relationship**, meaning higher blood pressures are required for the kidneys to eliminate sodium. High circulating levels of BNP and ANP therefore indicate dysfunction and are associated with heart failure, ventricular hypertrophy, and atherosclerosis. Reducing dietary sodium and using diuretics help counteract this problem.

Inflammation and Immunity

Chronic inflammation plays an important role in hypertension. Activation of the immune system damages the endothelium, reduces nitric oxide production, and increases vascular stiffness. Inflammatory cytokines also enhance the effects of angiotensin II and promote vascular remodeling. Obesity, poor diet, insulin resistance, and RAAS activation all contribute to this inflammatory state.

Obesity and Adipokines

Obesity is one of the strongest risk factors for primary hypertension. Fat cells release substances called **adipokines**, including leptin and adiponectin. In obesity, increased leptin and decreased adiponectin stimulate the sympathetic nervous system and RAAS, increase inflammation, promote insulin resistance, and contribute to cardiac hypertrophy. Fat accumulation around blood vessels also worsens vascular function. Weight loss significantly

lowers blood pressure, and in severe obesity, bariatric surgery may lead to long-term remission of hypertension.

Insulin Resistance and Metabolic Syndrome

Insulin resistance is common in individuals with hypertension, even without diabetes. It is associated with reduced endothelial vasodilation and increased renal sodium retention. More than half of individuals with diabetes have hypertension, and the combination greatly increases cardiovascular risk. Obesity, dyslipidemia, insulin resistance, and hypertension often occur together as **metabolic syndrome**, which significantly raises the risk of heart disease and stroke.

Vascular Changes

In hypertension, small arteries and arterioles become more sensitive to vasoconstrictors and less responsive to vasodilators. Abnormal calcium signaling in smooth muscle cells causes persistent contraction. Over time, smooth muscle hypertrophy, hyaline sclerosis, and atherosclerosis stiffen vessel walls and narrow the lumen. These changes increase peripheral resistance and cause damage to the eyes, kidneys, heart, and brain.

Clinical Manifestations of Hypertension

Hypertension is often called a **silent disease** because it usually causes no symptoms until organ damage occurs. Many individuals feel well for years while blood pressure remains elevated. When symptoms develop, they are usually related to damage in target organs such as the heart, kidneys, eyes, brain, or blood vessels. Complications typically appear in middle to late adulthood if hypertension is untreated.

Common complications include retinopathy with visual changes, kidney damage with proteinuria and renal failure, coronary artery disease, myocardial infarction, heart failure, stroke, and dementia.

Hypertensive Crisis

A hypertensive crisis occurs when blood pressure rises rapidly to **180/120 mm Hg or higher**. It may occur in people with chronic hypertension or as a result of pregnancy complications, stimulant drug use, medication reactions, or adrenal tumors. Severe elevations in blood

pressure cause capillary damage, tissue edema, retinal hemorrhages, cerebral edema, and encephalopathy. This condition is life-threatening and requires immediate treatment.

Evaluation and Treatment of Hypertension

Diagnosis

Hypertension is diagnosed using blood pressure measurements taken on at least two separate occasions. The patient should be seated, relaxed for at least five minutes, and should not have consumed caffeine or smoked in the previous 30 minutes. Blood pressure is initially measured in both arms. Additional evaluation may include ambulatory blood pressure monitoring, laboratory studies, ECG, and assessment for organ damage.

Treatment

Treatment begins with lifestyle modifications such as regular physical activity, dietary changes including sodium restriction, smoking cessation, and weight loss. Pharmacologic therapy is recommended for individuals with stage 1 hypertension who have high cardiovascular risk and for all individuals with stage 2 hypertension. First-line medications include diuretics, ACE inhibitors or ARBs, and calcium channel blockers. Medication selection depends on age, race, sex, and comorbid conditions. Blood pressure control significantly reduces the risk of stroke, heart failure, dementia, and kidney disease.

Orthostatic (Postural) Hypotension

Orthostatic hypotension is defined as a drop in systolic blood pressure of at least 20 mm Hg or a drop in diastolic pressure of at least 10 mm Hg within three minutes of standing. It is common in older adults and individuals with autonomic dysfunction and significantly increases the risk of falls.

Normally, standing triggers a reflex increase in sympathetic nervous system activity that constricts blood vessels and increases heart rate. In orthostatic hypotension, these compensatory mechanisms fail, causing blood to pool in the lower extremities and cerebral perfusion to decrease.

Orthostatic hypotension may be acute or chronic. Acute causes include dehydration, medications, prolonged immobility, and volume depletion. Chronic causes include neurologic

disorders such as Parkinson disease, diabetes-related autonomic neuropathy, adrenal insufficiency, and medication effects.

Symptoms include dizziness, blurred vision, syncope, and weakness, especially after standing, meals, or exercise. Treatment focuses on correcting underlying causes, increasing fluid and salt intake, using compression garments, and in some cases administering medications that increase blood volume or cause vasoconstriction.

Aneurysm

An aneurysm is a localized dilation of a blood vessel or cardiac chamber caused by weakening of the vessel wall. **True aneurysms** involve all three layers of the vessel wall, while **false aneurysms** involve blood collecting outside the vessel wall. **Dissecting aneurysms** occur when blood enters between layers of the vessel wall.

Aortic aneurysms most commonly occur in the thoracic or abdominal aorta. Risk factors include hypertension, smoking, atherosclerosis, older age, genetic disorders, infection, and trauma. Chronic hypertension contributes to vessel wall damage through increased mechanical stress and inflammation.

Aneurysms are often asymptomatic until rupture, which causes severe pain, hypotension, and shock. Diagnosis is confirmed with imaging such as CT angiography. Small aneurysms are managed medically, while larger or rapidly expanding aneurysms require surgical or endovascular repair.

Arterial Thrombus Formation

Arterial thrombi form when endothelial injury, inflammation, or blood flow abnormalities activate the coagulation system. Aneurysms and damaged vessels promote blood pooling and clot formation. Arterial thrombi can obstruct blood flow at the site of formation or dislodge and become emboli, causing ischemia in distant organs.

Diagnosis is confirmed with Doppler ultrasound or angiography. Treatment includes anticoagulants, thrombolytic therapy, and in some cases surgical removal of the clot.

Atherosclerosis

Learning Objective

Determine the **clinical course, complications, and management** of atherosclerosis.

Overview and Definition

Arteriosclerosis refers to thickening and hardening of the arterial walls. **Atherosclerosis** is a specific type of arteriosclerosis caused by the buildup of **lipid-laden macrophages** within the arterial wall. This buildup forms a lesion called a **plaque**. Atherosclerosis can affect arteries throughout the body and is the **leading cause of coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease (stroke)**.

Atherosclerosis is a **chronic inflammatory disease**, not simply a condition caused by cholesterol accumulation. Lipids, inflammation, immune responses, and endothelial dysfunction all contribute to plaque formation and progression.

Pathophysiology of Atherosclerosis

Atherosclerosis develops slowly over time through a predictable series of pathologic changes in the arterial wall. The disease begins with **endothelial injury and dysfunction**, progresses to **fatty streak formation**, advances to **fibrotic plaque**, and may ultimately become a **complicated lesion** that can rupture and cause thrombosis.

Endothelial Injury and Dysfunction

The initial event in atherosclerosis is damage to the **endothelium**, the inner lining of blood vessels. Common causes of endothelial injury include smoking, hypertension, diabetes, and dyslipidemia. Additional “nontraditional” risk factors include chronic kidney disease, systemic inflammation, infections, radiation exposure, certain medications, air pollution, and changes in the gut microbiome.

When endothelial cells are injured, they become inflamed and lose their normal protective functions. Healthy endothelium produces substances such as **nitric oxide**, which promote vasodilation and inhibit clot formation. Injured endothelial cells produce less nitric oxide and instead express **adhesion molecules** that attract inflammatory cells, including monocytes, macrophages, and platelets.

Inflammation and Lipid Oxidation

As inflammation develops, circulating **low-density lipoprotein (LDL)** particles move into the arterial intima. Inflammatory cells release toxic oxygen free radicals that **oxidize LDL**. Oxidized LDL is highly inflammatory and plays a central role in atherosclerosis progression.

Monocytes migrate into the arterial wall and differentiate into macrophages. These macrophages engulf oxidized LDL and become **foam cells**. Accumulation of foam cells forms an early lesion called a **fatty streak**. Fatty streaks can be seen even in young individuals and represent the earliest visible sign of atherosclerosis.

Foam cells and oxidized LDL continue to release inflammatory cytokines and free radicals, causing ongoing endothelial damage. Oxidized LDL and foam cells also act as **damage-associated molecular patterns (DAMPs)**, activating immune responses that recruit T lymphocytes and promote autoimmune injury to the vessel wall. Hypoxia within the plaque further stimulates chronic inflammation through inflammasome activation.

Plaque Formation and Vascular Remodeling

Macrophages in the lesion release growth factors that stimulate **smooth muscle cell proliferation**. Smooth muscle cells migrate from the media into the intima, where they produce collagen and extracellular matrix. This process forms a **fibrous cap** over a lipid-rich core, creating a mature **atherosclerotic plaque**.

As plaques enlarge, they may calcify and protrude into the vessel lumen, narrowing the artery and restricting blood flow. Reduced blood flow may be asymptomatic at rest but cause symptoms during increased demand, such as exercise. This explains exertional symptoms like **angina** or **intermittent claudication**.

Plaque Instability and Rupture

Not all plaques cause symptoms by obstructing blood flow. Many plaques are considered **unstable or vulnerable**, meaning they have thin fibrous caps and large lipid cores. These plaques may not significantly narrow the vessel lumen and are often clinically silent.

Inflammatory cytokines, enzymes, mechanical stress, and neurohumoral changes weaken the fibrous cap. When the plaque ruptures, the underlying lipid core and collagen are exposed to circulating blood. This triggers **platelet adhesion**, activation of the coagulation cascade, and rapid **thrombus formation**.

A ruptured plaque with associated thrombosis is called a **complicated plaque**. The thrombus may partially or completely occlude the vessel, leading to **acute ischemia or infarction**, such

as myocardial infarction or stroke. Antiplatelet agents such as aspirin are used to reduce this risk.

Clinical Manifestations

The clinical manifestations of atherosclerosis depend on the **location and severity** of arterial obstruction. Symptoms occur when blood flow is insufficient to meet tissue demands. Early in the disease, symptoms may occur only during physical exertion or stress, when oxygen demand increases.

Progressive plaque growth and superimposed thrombosis can result in **tissue infarction**. Obstruction of coronary arteries leads to myocardial ischemia and infarction. Atherosclerosis of peripheral arteries causes pain, weakness, and disability in the affected limbs. Cerebrovascular involvement leads to transient ischemic attacks or stroke.

Atherosclerosis often affects multiple vascular beds simultaneously. Therefore, the presence of disease in one area, such as the coronary arteries, indicates a high risk for ischemic events in other areas, such as the brain or peripheral circulation.

Evaluation of Atherosclerosis

Evaluation begins with a thorough **health history**, including assessment of cardiovascular risk factors and symptoms of ischemia. Physical examination may reveal **arterial bruits**, diminished pulses, cool extremities, or signs of impaired tissue perfusion.

Laboratory studies typically include lipid profiles, blood glucose levels, and markers of inflammation such as **high-sensitivity C-reactive protein (hs-CRP)**. Diagnostic imaging may include ECG, Doppler ultrasonography, CT or MR angiography, nuclear imaging, or invasive angiography to identify affected vessels and assess the severity of disease.

Treatment and Management

Management of atherosclerosis focuses on **early detection, risk factor modification, and prevention of plaque progression and rupture**. The goal is to stabilize plaques and reduce inflammation before acute complications occur.

Lifestyle modifications include smoking cessation, regular physical activity, weight management, and dietary changes to reduce cholesterol and improve metabolic health. Pharmacologic

therapy often includes lipid-lowering agents (such as statins), antihypertensives, antiplatelet agents, and glucose-lowering medications when indicated.

When atherosclerosis causes significant vessel obstruction or acute ischemia, treatment focuses on restoring blood flow through medications, interventional procedures, or surgery, depending on the affected vascular bed. Management strategies are tailored to the specific clinical condition, such as coronary artery disease or stroke.

Key Nursing Takeaway

Atherosclerosis is a **systemic, inflammatory, progressive disease** that develops silently over many years. Early intervention and aggressive management of risk factors are critical in preventing life-threatening complications such as myocardial infarction, stroke, and limb ischemia.

Peripheral Artery Disease (PAD)

Learning Objective

Describe the **clinical course and management** of peripheral artery disease.

Overview

Peripheral artery disease (PAD) is caused by **atherosclerosis of the arteries that supply the limbs**, most commonly the **lower extremities**. It affects millions of adults, especially those over age 40. The **risk factors for PAD are the same as for atherosclerosis**, including smoking, diabetes, hypertension, and dyslipidemia.

PAD develops when plaques narrow or block arteries, reducing blood flow to muscles and tissues of the legs and feet.

Pathophysiology

Lower-extremity ischemia in PAD can develop **gradually or suddenly**. In most individuals, PAD develops slowly as atherosclerotic plaques progressively narrow the arterial lumen. Endothelial

dysfunction occurs, along with reduced production of normal vasodilators and an increased tendency toward thrombosis.

As blood flow becomes restricted, tissues cannot meet oxygen demands during activity. This causes **exercise-induced ischemia**, which is the hallmark of early PAD. When PAD affects the iliofemoral arteries, it produces **intermittent claudication**, which is cramping or pain in the legs during walking that is relieved by rest.

In some cases, a **thrombus forms on top of an existing plaque**, causing sudden and complete obstruction of blood flow. Acute arterial occlusion results in **severe pain, pallor, loss of pulses, and changes in skin temperature and color**, and is a medical emergency.

Clinical Manifestations

PAD symptoms result from **reduced blood flow to the extremities**. Early disease may be asymptomatic. As disease progresses, patients develop exertional leg pain, weakness, numbness, or fatigue. Advanced PAD can cause rest pain, nonhealing wounds, skin breakdown, and tissue necrosis.

Evaluation

Diagnosis of PAD begins with a careful **history and physical examination**, focusing on symptoms of ischemia and signs of atherosclerosis such as bruits or diminished pulses. One of the most important screening tools is the **ankle-brachial index (ABI)**, which compares blood pressure in the ankle to blood pressure in the arm. A lower ankle pressure indicates arterial obstruction.

Additional testing may include **duplex ultrasonography**, CT angiography (CTA), or MR angiography (MRA) to assess blood flow and identify areas of narrowing or occlusion.

Management and Treatment

Treatment of PAD focuses first on **risk factor modification**, including smoking cessation, regular exercise, management of diabetes and hypertension, and treatment of dyslipidemia. Proper **foot and skin care**, including toenail care and well-fitting footwear, is essential to prevent ulcers and infections.

Symptomatic PAD is treated with **vasodilators and antiplatelet therapy** to improve blood flow and reduce thrombosis risk. Newer medications such as **cilostazol** and anticoagulants like **rivaroxaban** may be used in selected patients.

If symptoms are severe, acute, or do not respond to medical therapy, **revascularization** using catheter-based or surgical techniques may be necessary to restore blood flow.

Coronary Artery Disease (CAD), Myocardial Ischemia, and Acute Coronary Syndromes

Learning Objective

Describe the **pathophysiology, clinical manifestations, evaluation, and treatment** of coronary artery disease, myocardial ischemia, and acute coronary syndromes.

Overview

Coronary artery disease (CAD) is caused by atherosclerosis of the coronary arteries and is a leading cause of morbidity and mortality. CAD reduces blood flow to the myocardium, resulting in **myocardial ischemia**. Persistent ischemia or sudden coronary artery occlusion leads to **acute coronary syndromes**, including unstable angina and myocardial infarction (MI).

CAD is extremely common and remains the **leading cause of death** in both men and women.

Pathophysiology

As atherosclerotic plaques form in the coronary arteries, the myocardial blood supply becomes inadequate to meet oxygen demands. Initially, ischemia occurs during exertion or stress and may be reversible. As disease progresses, ischemia becomes more severe and prolonged.

If a plaque ruptures and a thrombus forms, blood flow may be partially or completely blocked. This results in **acute myocardial ischemia and infarction**, causing irreversible myocardial injury if not promptly treated.

Risk Factors for CAD

Risk factors for CAD are divided into **nonmodifiable** and **modifiable** categories.

Nonmodifiable risk factors include **advanced age, male sex or postmenopausal status, and family history**. Aging and menopause reduce endothelial repair and increase exposure to cardiovascular risk factors.

Modifiable risk factors include **dyslipidemia, hypertension, smoking, diabetes, obesity, sedentary lifestyle, and poor diet**. Addressing these factors can significantly reduce CAD risk.

Nontraditional risk factors include chronic inflammation, chronic kidney disease, air pollution, radiation exposure, medications, infection, and alterations in the microbiome.

Role of Genetics

Genetic variations influence lipid metabolism, vascular function, and inflammation. Many inherited traits increase susceptibility to CAD by affecting cholesterol levels, blood pressure, and glucose metabolism. Environmental factors such as diet can alter gene expression through **epigenetic mechanisms**, further influencing disease risk.

Dyslipidemia and CAD

Dyslipidemia refers to abnormal levels of lipoproteins in the blood and is a major contributor to CAD. LDL cholesterol delivers cholesterol to tissues and arterial walls. Elevated LDL and ApoB levels strongly increase coronary risk.

Excess LDL becomes oxidized in the arterial wall, triggering inflammation and foam cell formation, which drives atherosclerosis. Genetic defects in LDL receptors and diets high in saturated fats worsen LDL accumulation.

HDL cholesterol removes excess cholesterol from tissues and returns it to the liver. Low HDL levels increase coronary risk, while higher levels are protective. Lifestyle interventions such as

exercise and weight loss modestly increase HDL, but medications to raise HDL have not reduced CAD risk.

Triglycerides and lipoprotein(a) also contribute to CAD, especially in individuals with diabetes. Elevated Lp(a) is genetically determined and promotes inflammation and thrombosis.

Management of Dyslipidemia

Screening for dyslipidemia is a key part of preventive care. Treatment focuses on lowering LDL cholesterol using **dietary changes and medications**, primarily **statins**, which reduce cholesterol synthesis and stabilize plaques.

For individuals who cannot tolerate statins or require additional LDL reduction, medications such as **ezetimibe** and **PCSK9 inhibitors** may be used.

Hypertension

Hypertension increases CAD risk by causing endothelial injury and increasing myocardial oxygen demand. Overactivation of the RAAS and sympathetic nervous system promotes inflammation and plaque formation. Treating hypertension significantly reduces cardiovascular risk.

Cigarette Smoking

Smoking directly damages the endothelium, promotes inflammation, increases LDL levels, lowers HDL levels, and increases myocardial oxygen demand. Both active and passive smoking significantly increase CAD risk. Smoking cessation is one of the most effective preventive interventions.

Diabetes Mellitus

Diabetes and insulin resistance cause chronic vascular inflammation, endothelial dysfunction, increased thrombosis, and dyslipidemia. Tight glycemic control reduces CAD risk. Certain diabetes medications also lower cardiovascular risk, even in patients without diabetes.

Obesity and Sedentary Lifestyle

Obesity promotes inflammation, insulin resistance, dyslipidemia, and hypertension. Excess adipose tissue releases inflammatory cytokines that accelerate atherosclerosis. Physical inactivity independently increases CAD risk, while regular exercise improves endothelial function and reduces mortality.

Diet and Inflammation

Diet plays a major role in CAD risk. Diets high in saturated fats, trans fats, salt, and refined carbohydrates increase risk. The **Mediterranean diet** is especially effective in reducing cardiovascular risk due to its antiinflammatory and metabolic benefits.

Markers of inflammation such as **high-sensitivity C-reactive protein (hs-CRP)** help identify individuals at higher risk and guide treatment decisions.

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

CKM syndrome describes the interconnected relationship between obesity, diabetes, chronic kidney disease, and cardiovascular disease. These conditions amplify inflammation, vascular dysfunction, and neurohumoral activation. Managing CKM syndrome is critical for preventing CAD, PAD, and stroke.

Environmental and Other Factors

Air pollution, ionizing radiation, certain medications, infections, and alterations in the gut microbiome all contribute to vascular inflammation and plaque progression. Chronic inflammatory states increase the likelihood of plaque instability and acute coronary events.

Key Takeaway

Peripheral artery disease and coronary artery disease are **manifestations of systemic atherosclerosis**. Both develop silently over time, are driven by inflammation and lipid abnormalities, and can lead to severe ischemic complications. Early detection, aggressive risk factor modification, and appropriate medical or interventional therapy are essential to improving outcomes.

Transient Myocardial Ischemia

Coronary artery disease (CAD) reduces blood flow to the heart muscle. When this reduction happens gradually, the heart may temporarily not get enough oxygen, especially during times of increased demand such as exercise or stress. If blood flow returns before permanent damage occurs, the result is **transient myocardial ischemia**. This is commonly called **chronic coronary disease**. It may cause chest pain (angina), or it may occur without any noticeable symptoms. Ischemia can also happen when coronary arteries suddenly constrict (vasospasm), even if there is no atherosclerosis.

Pathophysiology of Myocardial Ischemia

Myocardial ischemia occurs when the heart's oxygen supply does not meet its metabolic needs. This imbalance can happen either because blood flow is reduced or because the heart is working harder than usual.

The most common cause of reduced blood flow is **atherosclerosis**, where plaques build up in coronary arteries and narrow the vessel. As plaques grow, they limit blood flow, especially during exercise when the heart needs more oxygen. Even plaques that grow slowly and appear "stable" can still suddenly cause serious events.

Other causes of reduced oxygen supply include coronary artery spasm, low blood pressure, abnormal heart rhythms, or reduced oxygen in the blood, such as with anemia or lung disease. Increased oxygen demand occurs with conditions like fast heart rates, exercise, high blood pressure (which causes heart muscle thickening), and valvular heart disease.

When ischemia begins, heart cells are affected within seconds. Aerobic metabolism stops, anaerobic metabolism takes over, and lactic acid builds up. Within minutes, the heart muscle loses its ability to contract effectively, lowering cardiac output. Heart cells can survive for about 20 minutes under these conditions. If blood flow is restored in time, the cells recover. If not, myocardial infarction (MI) occurs.

Both short-term and prolonged ischemia can disrupt electrical signaling in the heart, leading to dangerous heart rhythms. These rhythm problems can impair pumping, cause heart failure, or lead to sudden death.

Clinical Forms of Transient Myocardial Ischemia

People with transient ischemia can present in several ways:

Stable angina occurs when coronary arteries are partially blocked by plaques that prevent adequate dilation during exertion.
Vasospastic angina results from sudden constriction of coronary arteries and is unpredictable.
Silent ischemia occurs without noticeable chest pain.

Stable Angina Pectoris

Stable angina is chest pain caused by temporary myocardial ischemia. It usually happens during physical exertion or emotional stress and is relieved by rest or nitrate medications. Blood flow returns before permanent damage occurs.

The pain is caused by lactic acid buildup or stretching of ischemic heart muscle, which stimulates nerve fibers. Because these nerves enter the spinal cord at levels C3–T4, pain may radiate to the neck, jaw, left arm, shoulder, back, or occasionally the right arm.

People often describe the discomfort as pressure, heaviness, or tightness in the chest. It can resemble indigestion or other noncardiac conditions, which is why chest pain is initially classified as cardiac, possibly cardiac, or noncardiac until proven otherwise.

During angina episodes, individuals may appear pale, sweaty, or short of breath. Between episodes, the physical exam is often normal. Findings such as xanthelasmas, arcus senilis, or arterial bruits suggest underlying atherosclerosis.

Diagnosis includes ECG, chest X-ray, and cardiac biomarkers. During ischemia, ECG typically shows ST-segment depression and T-wave inversion. Troponin levels remain normal because no myocardial cell death has occurred. Stress testing and imaging studies help assess disease severity.

Treatment focuses on increasing blood flow, reducing oxygen demand, and preventing heart attacks. Medications such as nitrates, beta blockers, calcium channel blockers, and antiplatelet agents are commonly used. PCI can improve symptoms but does not reduce long-term risk of MI or death. Severe disease may require coronary artery bypass surgery.

Preventing CAD is essential. This includes lifestyle changes, blood pressure and cholesterol control, and diabetes management. Risk reduction before an MI is primary prevention; after an MI it is secondary prevention.

Coronary Vasospasm

Many people with angina do not have significant coronary artery blockage. Instead, they experience **vasospastic angina**, where coronary arteries suddenly constrict. This type of angina often occurs at rest and unpredictably.

Vasospasm can be triggered by stress, smoking, alcohol, stimulants, hyperventilation, or sleep. It is related to abnormal smooth muscle contraction and endothelial dysfunction. Diagnosis is based on symptoms and ECG changes during pain. Treatment focuses on avoiding triggers and using calcium channel blockers.

Although usually benign, vasospastic angina can sometimes lead to arrhythmias or infarction.

Coronary Microvascular Dysfunction (CMD)

CMD affects the small coronary vessels deep within the heart muscle. It is especially common in women and often causes atypical symptoms such as fatigue, palpitations, or vague chest discomfort rather than classic angina.

CMD is caused by endothelial dysfunction, inflammation, and impaired vasodilation. It is often misdiagnosed. Specialized imaging tests help identify it. Treatment improves symptoms but patients remain at higher cardiovascular risk.

Takotsubo Syndrome

Takotsubo syndrome is a stress-related, reversible form of heart failure caused by intense catecholamine release. It mainly affects postmenopausal women and increased during the COVID-19 pandemic.

ECG changes, modest troponin elevation, and characteristic ventricular ballooning are seen. Treatment includes beta blockers and supportive care. Although reversible, it can cause serious complications and death.

Silent Ischemia

Silent ischemia is myocardial ischemia without chest pain. People may only notice fatigue or shortness of breath. It is common in individuals with diabetes due to autonomic nerve dysfunction.

Despite the lack of symptoms, silent ischemia is dangerous and increases the risk of future cardiac events. It is detected through stress testing and imaging and treated based on severity.

Acute Coronary Syndromes

Acute coronary syndromes occur when an atherosclerotic plaque suddenly ruptures and a clot forms. This can cause unstable angina, myocardial infarction, or sudden cardiac death.

Unstable angina occurs when a clot briefly blocks a coronary artery but dissolves before extensive damage occurs. It signals a high risk of impending MI.

If obstruction lasts longer, myocardial infarction occurs. Non-STEMI involves partial-thickness damage, while STEMI involves full-thickness heart muscle death and is more severe.

Myocardial Infarction

MI occurs when prolonged ischemia causes irreversible heart muscle death. Oxygen deprivation leads to anaerobic metabolism, lactic acid accumulation, loss of contractility, and electrical instability.

Cell death triggers inflammation, followed by scar formation. Scar tissue restores structural integrity but cannot contract, leading to long-term heart dysfunction and possible heart failure.

Restoring blood flow is essential, but reperfusion itself can cause further injury through oxidative stress and calcium overload.

Surrounding heart muscle may be stunned or hibernating. These areas can recover function if blood flow is restored. Over time, structural changes called remodeling can worsen heart function unless treated with medications such as beta blockers and ACE inhibitors.

Clinical Manifestations of MI

MI pain is more severe and longer lasting than angina and often described as crushing or heavy. Pain may radiate widely. Some people, especially older adults or those with diabetes, have no pain at all.

Other findings include rapid heart rate, abnormal heart sounds, pulmonary congestion, cool clammy skin, nausea, and vomiting.

Evaluation and Treatment of MI

MI diagnosis is based on symptoms, ECG changes, and elevated cardiac troponins. ECG helps localize the infarction. Troponins rise within hours and indicate the extent of damage.

Treatment requires immediate hospitalization. Aspirin, nitrates, pain control, antithrombotic therapy, and continuous monitoring are essential. STEMI requires urgent PCI. Long-term care focuses on preventing recurrence through medications and lifestyle changes.

Heart Failure

Heart failure is a clinical syndrome in which the heart cannot pump enough blood to meet the body's needs or cannot fill properly without increasing pressure in the heart. This leads to poor tissue perfusion, fluid buildup, or both. In many cases, the left ventricle develops high filling pressures, which raises pressure in the lungs and causes congestion.

Heart failure affects millions of people in the United States, and its prevalence continues to rise. The most important risk factors are ischemic heart disease and hypertension. Diabetes also greatly increases risk by directly damaging the heart muscle. Other contributing factors include aging, obesity, kidney disease, valvular and congenital heart disease, cardiomyopathies, myocarditis, abnormal heart rhythms, endocrine disorders, cancer treatments, and substance use such as alcohol or stimulants. Genetic factors affecting heart muscle and neurohormonal systems also play a role.

Most cases of heart failure involve dysfunction of the **left ventricle**, although the right ventricle can fail as well, especially in lung disease. In some conditions, the heart pumps large amounts of blood but still cannot meet metabolic demands; this is called **high-output heart failure**.

Left-Sided Heart Failure (Congestive Heart Failure)

Left-sided heart failure occurs when the left ventricle cannot pump or fill effectively. It is divided into two major types:
heart failure with reduced ejection fraction (HFrEF) and **heart failure with preserved ejection fraction (HFpEF)**. Some people have features of both.

Heart Failure With Reduced Ejection Fraction (HFrEF)

HFrEF, also called systolic heart failure, occurs when the left ventricle cannot contract forcefully enough to eject blood. The ejection fraction is 40% or less, meaning a reduced amount of blood leaves the heart with each beat.

The most common cause is myocardial infarction, which damages heart muscle and reduces contractility. Other causes include myocarditis and cardiomyopathies. As contractility decreases, less blood is pumped out, and more blood remains in the ventricle after each beat. This increases preload and causes the ventricle to dilate.

Increased preload stretches the heart muscle. At first this helps improve contraction, but over time excessive stretching damages the muscle and worsens heart failure. Preload can also rise from excess fluid, kidney failure, or valve disease.

Afterload also plays a major role. High blood pressure increases resistance to ventricular ejection, forcing the heart to work harder. Over time, this leads to ventricular remodeling, thickening of the heart muscle, increased oxygen demand, and relative ischemia, which further reduces contractility.

As cardiac output falls, kidney perfusion decreases. This activates the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system. These systems increase fluid retention and vasoconstriction, raising preload and afterload even more. This creates a **vicious cycle** that progressively worsens heart failure.

Many neurohormonal and inflammatory processes contribute to disease progression. Angiotensin II, aldosterone, catecholamines, and antidiuretic hormone cause direct myocardial damage, fibrosis, and fluid retention. Inflammatory cytokines contribute to muscle wasting and weakness. Metabolic changes reduce the heart's ability to generate energy. These mechanisms explain why modern treatment targets neurohormonal pathways, not just symptoms.

Clinical Manifestations of HFrEF

Symptoms result from lung congestion and poor blood flow to tissues. Common findings include shortness of breath, difficulty breathing when lying flat, fatigue, cough with frothy sputum, reduced urine output, and swelling. On exam, pulmonary crackles, pleural effusions, abnormal heart sounds (especially an S3 gallop), and signs of underlying coronary disease may be present.

Diagnosis is confirmed with echocardiography showing reduced ejection fraction and an enlarged heart. BNP levels are often elevated and reflect disease severity.

Treatment of HFrEF

Acute treatment focuses on breaking the cycle of worsening contractility, preload, and afterload. Oxygen, nitrates, and morphine improve oxygen delivery and reduce preload. Diuretics remove excess fluid. Inotropic medications may be needed to support blood pressure and cardiac output. ACE inhibitors, ARBs, and aldosterone antagonists reduce neurohormonal activation.

Severe cases may require mechanical support such as intraaortic balloon pumps or left ventricular assist devices.

Chronic management depends on disease stage. Lifestyle changes are critical in early stages. In symptomatic heart failure, guideline-directed therapy includes angiotensin receptor–neprilysin inhibitors, beta blockers, mineralocorticoid antagonists, and SGLT inhibitors. These medications reduce hospitalizations, improve quality of life, and prolong survival. Advanced disease may require device therapy, revascularization, transplant evaluation, or palliative care.

Heart Failure With Preserved Ejection Fraction (HFpEF)

HFpEF occurs when individuals have heart failure symptoms but a normal or near-normal ejection fraction (≥50%). It accounts for more than half of left-sided heart failure cases and is especially common in older adults and women.

Major risk factors include hypertension, obesity, diabetes, aging, ischemic heart disease, atrial fibrillation, and valvular disease. Outcomes are often poor, with frequent hospitalizations and reduced quality of life.

In HFpEF, the problem is **impaired relaxation**, not contraction. Chronic inflammation and endothelial dysfunction lead to ventricular hypertrophy, fibrosis, and stiffening of the myocardium. The ventricle becomes less compliant and cannot fill properly during diastole.

Because the ventricle is stiff, even normal filling volumes cause abnormally high pressures. These pressures are transmitted backward to the left atrium and pulmonary circulation, leading to congestion and symptoms. Symptoms worsen with tachycardia because rapid filling increases pressure even more.

Clinical Manifestations of HFpEF

Early symptoms include shortness of breath with exertion and fatigue. Pulmonary edema may be absent initially. An S4 gallop is common due to atrial contraction against a stiff ventricle. Advanced disease may cause nocturnal dyspnea, jugular venous distension, and liver enlargement.

ECG often shows left ventricular hypertrophy. Chest x-ray may reveal pulmonary congestion without heart enlargement.

Evaluation and Treatment of HFpEF

Diagnosis requires heart failure symptoms, preserved ejection fraction, and evidence of diastolic dysfunction on echocardiography. BNP levels are usually elevated.

Treatment focuses on controlling blood pressure, managing comorbidities, improving diastolic filling, and reducing congestion. Current guidelines recommend mineralocorticoid antagonists, angiotensin receptor–neprilysin inhibitors, angiotensin receptor blockers, SGLT inhibitors, and exercise training.

Right-Sided Heart Failure

Right heart failure occurs when the right ventricle cannot pump blood effectively into the pulmonary circulation. Most often, it results from left heart failure, where increased pulmonary pressures overload the right ventricle.

As the right ventricle fails, pressure builds up in the systemic venous circulation, leading to peripheral edema, ascites, and liver enlargement. Treatment focuses on managing the underlying left-sided heart failure.

Right heart failure can also occur independently, usually due to chronic lung disease such as COPD or pulmonary hypertension. Myocardial infarction, cardiomyopathies, and pulmonic valve disease can also impair right ventricular contractility.

High-Output Heart Failure

In high-output heart failure, cardiac output is increased, but tissue oxygen demands are still not met.

Anemia reduces oxygen-carrying capacity, forcing the heart to pump faster and harder. Severe infection causes systemic vasodilation and metabolic dysfunction. Hyperthyroidism increases metabolic demand beyond what the heart can supply. Thiamine deficiency impairs myocardial metabolism and causes vasodilation, triggering excessive cardiac output that eventually leads to failure.

Dysrhythmias

Dysrhythmias are abnormalities in heart rhythm caused by problems with impulse formation or conduction. They may originate from the sinoatrial node or from abnormal electrical activity elsewhere in the heart.

Causes include ischemia, infection, inherited disorders, medications, electrolyte disturbances, and cardiac procedures. Symptoms depend on how much cardiac output is affected and range from none at all to syncope, shock, or sudden death.

Diagnosis relies on ECG findings and evaluation of underlying causes. Treatment aims to maintain adequate cardiac output using medications or electrical therapies such as cardioversion, pacemakers, or resynchronization while addressing the cause of the rhythm disturbance.

Dysrhythmias are broadly classified into atrial dysrhythmias, ventricular dysrhythmias, and conduction or sinus node disorders, with management guided by current clinical guidelines.