"Ischemic Heart Disease (IHD)"

📘 Definition

Ischemic heart disease (IHD) refers to a group of closely related clinical syndromes caused by an imbalance between myocardial blood supply (perfusion) and myocardial oxygen & nutritional demand.

👉 In simple terms:
Heart needs more oxygen than the coronary arteries can deliver → ischemia → clinical disease.

✨ *High-yield exam line:*

> IHD results from insufficient coronary perfusion relative to myocardial metabolic demands.

🔗 IHD ≈ Coronary Artery Disease (CAD)

- >90% of IHD cases are due to obstructive atherosclerosis of coronary arteries

- Hence, IHD is usually synonymous with CAD, unless stated otherwise

🧠 Key Concept:

Coronary atherosclerosis is a slow, progressive process developing over decades, but its manifestations are often sudden and catastrophic.

⚖️ Pathophysiology: Supply–Demand Imbalance

🔻 Decreased Oxygen Supply (Most common)

- Coronary atherosclerosis (plaque + thrombosis)
- Coronary artery spasm
- Hypotension / shock
- Reduced blood volume
- Reduced blood oxygenation
    - Pneumonia
    - Congestive heart failure (CHF)
- Reduced oxygen-carrying capacity
    - Anemia

- Carbon monoxide poisoning

🔺 Increased Oxygen Demand

- Increased heart rate (tachycardia)
- Hypertension
- Increased myocardial wall stress

🧬 Why the Heart Is So Vulnerable to Ischemia

- Cardiac myocytes:
  - Rely almost exclusively on mitochondrial oxidative phosphorylation
  - Have minimal anaerobic reserve
- Therefore:
  - Continuous oxygenated blood flow is essential
  - Even brief ischemia → functional impairment

✨ *Exam pearl:*

Myocardial cells are highly sensitive to hypoxia due to dependence on aerobic metabolism.

🔁 Pathogenesis of Ischemic Heart Disease (Flowchart)

Coronary atherosclerosis → Progressive luminal narrowing → Reduced coronary blood flow → Myocardial ischemia → ↓ ATP production → Impaired contractility ± electrical instability → Clinical manifestations of IHD

🩺 Clinical Syndromes of IHD

❗ Angina Pectoris ("Chest pain")

- Reversible myocardial ischemia
- No myocyte death

Types:

- Stable angina
  - Occurs predictably with exertion
  - Due to fixed atherosclerotic narrowing
- Unstable angina

    - Occurs with minimal exertion or at rest
    - Due to plaque rupture + thrombosis
- Vasospastic (Prinzmetal) angina
    - Due to coronary artery spasm
    - Often occurs at rest

📝 *Exam tip:*

Angina = ischemia without necrosis

2️⃣ Myocardial Infarction (MI)

- Prolonged or severe ischemia
- Irreversible injury → cardiomyocyte death
- Usually due to acute plaque rupture + thrombosis

📝 *One-liner:*

MI is ischemia severe enough to cause myocardial necrosis.

3️⃣ Chronic IHD with Congestive Heart Failure (CHF)

- Develops due to:
  - Previous large MI
  - Repeated small ischemic insults
- Leads to:
  - Progressive myocardial dysfunction
  - Mechanical pump failure

Flow idea:

Repeated ischemia / MI → Loss of functional myocardium → Ventricular remodeling → ↓ Cardiac output → CHF

4️⃣ Sudden Cardiac Death (SCD)

- Unexpected death due to:
  - Lethal ventricular arrhythmias (usually ventricular fibrillation)
- Often:
  - Occurs without warning

- Underlying CAD is usually present

⚡ *Important point:*

Death occurs due to electrical instability, not pump failure.

🚨 Acute Coronary Syndrome (ACS)

Acute coronary syndrome includes the three catastrophic manifestations of IHD:

- Unstable angina
- Myocardial infarction
- Sudden cardiac death

🧠 *Exam favorite:*

ACS reflects acute myocardial ischemia due to sudden reduction in coronary blood flow.

🌍 Epidemiology

📊 Burden of Disease

- ~800,000 MIs/year in the United States
- ~50% mortality among affected individuals
- Globally:
  - ~7.5 million deaths/year
  - Leading cause of mortality in high-income nations

📉 Decline in Mortality (Since 1963)

- ~50% reduction in IHD-related mortality
- Major contributors:

🛡️ Risk Factor Modification (Most important)

- Smoking cessation 🚭
- Hypertension control
- Diabetes management
- Cholesterol-lowering therapy (statins)

🏥 Medical & Surgical Advances

- Aspirin prophylaxis
- Better arrhythmia control
- Coronary care units
- Thrombolysis for MI
- Percutaneous coronary intervention (angioplasty & stenting)
- Coronary artery bypass grafting (CABG)
- Ventricular assist devices

⚠️ Future Challenges

- Increased life expectancy (aging population)
- Global obesity epidemic 🍔
- Rising diabetes prevalence

✨ *Concluding exam line:*

> Despite therapeutic advances, IHD remains a major public health challenge worldwide.

🧬 Mechanisms of Pathogenesis of Ischemic Heart Disease (IHD)

🔑 Core Principle

Ischemic heart disease results from inadequate coronary perfusion relative to myocardial oxygen demand.

In the vast majority of patients, this imbalance is caused by one or both of the following mechanisms:

1. Pre-existing ("fixed") atherosclerotic narrowing of coronary arteries
2. Acute plaque change with superimposed thrombosis and/or vasospasm

---

🔁 Overview Flowchart (High-Yield)

Coronary atherosclerosis → Fixed luminal narrowing ± plaque disruption → Reduced coronary blood flow → Myocardial ischemia → Angina / MI / Sudden cardiac death

🟦 I. Chronic Vascular (Fixed) Occlusion

📌 Degree of Luminal Narrowing & Clinical Correlation

% Luminal Occlusion	Clinical Effect
< 70%	Usually asymptomatic, even with exertion
≥ 70%	Critical stenosis → ischemia during increased demand → stable angina
≥ 90%	Inadequate flow even at rest → unstable angina

✨ *Exam favorite:*

Stable angina is typically due to fixed coronary stenosis >70%.

🔍 Coronary Arteries Commonly Involved

- Left anterior descending (LAD) – most commonly affected
- Left circumflex (LCX)

- Right coronary artery (RCA)

📍 Typical locations:

- Proximal LAD & LCX (first few cm from aorta)
- Entire length of RCA
- May also involve secondary branches:
  - Diagonal branches (LAD)
  - Obtuse marginal branches (LCX)
  - Posterior descending artery (RCA)

🔄 Collateral Circulation – A Protective Mechanism

- Slowly progressive occlusion (over years) → Remodeling of adjacent vessels → Development of collateral circulation → Can protect myocardium even if original artery becomes fully occluded

⚠️ Acute occlusion

- No time for collateral development
- Sudden ischemia → myocardial infarction

🔺 Role of Vasoconstriction

🧠 How Vasospasm Worsens Ischemia

- Directly reduces lumen diameter
- Increases mechanical shear stress
- Can trigger plaque disruption

🔥 Triggers of Vasoconstriction

- Circulating adrenergic agonists
- Platelet-derived substances
- Endothelial dysfunction:
  - ↓ Nitric oxide (vasodilator)
  - ↑ Endothelin (vasoconstrictor)
- Mediators from perivascular inflammatory cells

✨ *Key link:*

Endothelial dysfunction converts a protective vessel into a pro-ischemic one.

🟥 II. Acute Plaque Change (Most Dangerous Mechanism)

🚨 Clinical Significance

- Responsible for:
  - Unstable angina
  - Myocardial infarction
  - Sudden cardiac death
- Collectively termed Acute Coronary Syndrome (ACS)

🔁 Sequence of Events (Flowchart)

Atherosclerotic plaque → Sudden plaque rupture / erosion → Exposure of thrombogenic material → Platelet activation + coagulation → Rapid thrombus formation → Partial or complete luminal occlusion → Myocardial ischemia / infarction

---

🧨 Mechanisms of Acute Plaque Change

❗ Plaque Rupture

- Fissuring, ulceration, or rupture of fibrous cap
- Exposes:
    - Thrombogenic plaque contents
    - Subendothelial basement membrane

2️⃣ Plaque Erosion

- Loss of endothelial cells without rupture
- Due to:
    - Endothelial injury
    - Apoptosis
    - Inflammatory & toxic insults

🩸 Additional Contributors

- Intraplaque hemorrhage
    - Expands plaque volume
    - Acutely worsens luminal narrowing
- Mural (non-occlusive) thrombus
    - May embolize distally
    - Causes microinfarcts in intramyocardial vessels

💔 Outcome Based on Thrombus Size

Thrombus Type	Result
Partial occlusion	Subendocardial infarction
Complete occlusion	Transmural MI
Distal emboli	Microinfarcts

🧱 Vulnerable Plaques – The Real Culprits

🧠 Characteristics of Vulnerable Plaques

- Large lipid (atheromatous) core
- Thin fibrous cap
- High macrophage content
- Low smooth muscle cell content

📍 Common site of rupture:

- Junction of fibrous cap and adjacent normal artery
- Area of maximum mechanical stress

🔬 Fibrous Cap Stability – A Balance

Smooth muscle cells → Collagen synthesis → Cap strength

Macrophages → Metalloproteases → Collagen degradation → Cap weakening

⚖️ Net balance determines plaque stability

💊 Role of Statins (Beyond Cholesterol)

- Reduce circulating cholesterol
- Improve endothelial function
- Decrease plaque inflammation
- Stabilize vulnerable plaques

✨ *Exam insight:*

Statins reduce MI risk even when plaque size changes are modest.

⚠️ A Crucial Exam Concept: Degree of Stenosis Before Rupture

- Majority of culprit plaques are:
  - Not critically stenotic
  - Often asymptomatic before rupture

📊 Key Data:

- ~⅔ of ruptured plaques: ≤50% stenosis
- 85%: ≤70% stenosis before rupture

🧠 *Take-home message:*

Severity of stenosis ≠ risk of rupture

🔁 Silent Plaque Disruption & Disease Progression

- Plaque rupture + non-occlusive thrombosis can be:
  - Repetitive
  - Clinically silent

- Healing of these micro-events: → Progressive plaque enlargement → Worsening atherosclerosis over time

---

✅ Final Exam Summary Line

Ischemic heart disease arises from chronic fixed coronary narrowing and acute plaque disruption with thrombosis, the latter being the major cause of myocardial infarction and sudden cardiac death.

🫀 Angina Pectoris

📘 Definition

Angina pectoris is intermittent chest pain or discomfort caused by transient, reversible myocardial ischemia that is insufficient to produce myocyte necrosis.

🧠 *Key distinction:*

Angina = ischemia without cell death

🧬 Mechanism of Pain (Why angina hurts)

Myocardial ischemia → ↓ ATP production → Accumulation of metabolites → Release of adenosine, bradykinin & other mediators → Stimulation of cardiac autonomic nerves → Chest pain (angina)

✨ *Exam pearl:*

Pain in angina is chemically mediated, not due to tissue necrosis.

🔹 Types of Angina Pectoris

❗ Stable (Typical) Angina

🔍 Key Features

- Predictable, episodic chest discomfort
- Occurs with exertion or increased demand

    - Exercise
    - Tachycardia
    - Emotional stress
- Caused by fixed atherosclerotic coronary narrowing

🩺 Pain Description

- Crushing / squeezing substernal pain
- Radiates to:
    - Left arm
    - Left shoulder
    - Left jaw (referred pain)

💊 Relief

- Rest → reduces myocardial oxygen demand
- Nitroglycerin → vasodilation → ↑ coronary perfusion

✨ *High-yield line:*

Stable angina occurs when myocardial demand exceeds supply in the presence of fixed coronary stenosis.

2️⃣ Prinzmetal (Variant) Angina

🔍 Key Features

- Occurs at rest
- Due to coronary artery vasospasm
- Can involve:
  - Atherosclerotic arteries
  - Or completely normal coronary vessels

💊 Treatment Response

- Rapid response to:
  - Nitroglycerin
  - Calcium channel blockers

✨ *Exam favorite:*

Prinzmetal angina is caused by transient coronary vasospasm rather than fixed obstruction.

3️⃣ Unstable Angina

🔍 Key Features

- Increasing frequency and severity of chest pain
- Occurs with:
  - Progressively less exertion
  - Or at rest
- Considered part of acute coronary syndrome (ACS)

🧬 Underlying Mechanisms

- Plaque disruption
- Superimposed thrombosis
- Distal thromboembolization
- Vasospasm

⚠️ Clinical Importance

- Many patients show evidence of myocyte injury
- High risk of progression to MI
- Requires aggressive management

✨ *Exam line:*

Unstable angina represents a pre-infarction state.

🆚 Comparison of Angina Types (High-Yield Table)

Feature	Stable Angina	Prinzmetal Angina	Unstable Angina
Occurs with	Exertion	Rest	Minimal exertion or rest
Cause	Fixed stenosis	Vasospasm	Plaque disruption ± thrombosis
Necrosis	❌ No	❌ No	❌ / ⚠️ Minimal
ACS	❌	❌	✅ Yes
Response to nitrates	✅	✅	Variable

❤️ Myocardial Infarction (MI)

📘 Definition

Myocardial infarction (MI) is necrosis of cardiac muscle resulting from prolonged ischemia.

📜 2018 Universal Definition of MI:

Acute myocardial injury (↑ cardiac biomarkers) with evidence of acute myocardial ischemia

---

🧠 Epidemiological Highlights

- Risk increases with:
  - Age
  - Atherosclerotic risk factors
- ~10% occur before 40 years
- ~45% occur before 65 years
- Men > women, but difference narrows with age
- Premenopausal women are relatively protected
  → Loss of estrogen after menopause increases CAD risk

✨ *Exam point:*

IHD is the leading cause of death in older women.

🧬 Pathogenesis of Myocardial Infarction

🔁 Common Mechanism (≈90%)

Atherosclerotic plaque → Plaque rupture / erosion → Acute coronary thrombosis → Sudden vascular occlusion → Severe ischemia → Myocardial necrosis (MI)

🔀 Less Common Mechanisms (~10%)

1️⃣ Vasospasm-induced MI

- Severe coronary artery spasm
- Can occur without significant atherosclerosis

2️⃣ Embolic MI

- Emboli from:
  - Mural thrombi (e.g., atrial fibrillation)
  - Valve vegetations (infective endocarditis)

🧱 Subendocardial Infarction (Special Mechanism)

Severe fixed coronary stenosis → Marginal baseline perfusion → Prolonged increased demand (tachycardia / hypertension) → Ischemia of subendocardium → Subendocardial infarction

🧠 *Why subendocardium?*

- Farthest from epicardial coronary vessels
- Most vulnerable to hypoperfusion

🧬 MI Without Major Epicardial Disease

Ischemia may occur due to disease of small intramyocardial vessels, such as:

- Vasculitis
- Amyloid deposition
- Sickle cell disease (vascular stasis)

✨ *Exam insight:*

Not all MIs are due to epicardial coronary thrombosis.

📝 Final Exam Takeaway

- Angina → reversible ischemia, no necrosis
- MI → prolonged ischemia with irreversible myocyte death
- Unstable angina & MI form a spectrum of acute coronary syndromes

---

🫀 Coronary Artery Occlusion in Myocardial Infarction

📌 Overview

In a typical myocardial infarction (MI), acute coronary artery occlusion occurs due to superimposed thrombosis on a disrupted atherosclerotic plaque, leading to sudden and severe myocardial ischemia.

🔁 Sequence of Events in Coronary Artery Occlusion (Flowchart)

Atherosclerotic plaque → Plaque erosion / rupture (due to endothelial injury, intraplaque hemorrhage, or mechanical stress) → Exposure of subendothelial collagen & necrotic plaque core → Platelet adhesion, aggregation & activation → Release of platelet mediators (Thromboxane A_2 , ADP, Serotonin) → Further platelet aggregation + vasospasm → Activation of coagulation cascade (via tissue factor) → Progressive thrombus enlargement → Complete coronary artery occlusion (within minutes) → Acute myocardial ischemia → MI

✨ *Exam favorite:*

> Most MIs are caused by acute thrombosis superimposed on a disrupted atherosclerotic plaque.

🧠 Evidence Supporting This Mechanism

- Autopsy studies of patients dying from acute MI
- Coronary angiography findings:
    - Within 4 hours of MI onset → ~90% show coronary thrombosis
    - At 12–24 hours → thrombosis seen in only ~60% (even without treatment)

🔍 Why the decrease later?

- Spontaneous thrombolysis
- Relaxation of vasospasm

💊 Therapeutic Implications (Very High-Yield)

Early intervention → Thrombolysis and/or angioplasty → Restoration of coronary blood flow → Limitation of myocardial necrosis

🕑 *Golden window:*

Myocardial salvage is greatest when reperfusion occurs within the first few hours.

❤️ Myocardial Response to Ischemia

⚡ Immediate Biochemical & Functional Changes

Coronary occlusion → Cessation of aerobic metabolism → ↓ ATP production → Accumulation of lactic acid & other toxic metabolites → Rapid loss of myocardial contractility (within minutes)

🧠 *Key concept:*

Early ischemic changes are reversible.

⏳ Time-Dependent Progression of Injury

Duration of Ischemia	Myocardial Effect
Seconds–minutes	Loss of contractility
< 20 minutes	Reversible injury
20–40 minutes	Irreversible injury begins

> 40 minutes	Coagulative necrosis

🔬 Earliest Marker of Myocyte Necrosis

- Sarcolemmal membrane disruption
- Leakage of intracellular contents into:
  - Cardiac interstitium
  - Bloodstream

📌 *Clinical relevance:*

Basis for detection of cardiac biomarkers (e.g., troponins).

🔁 Reperfusion: Benefit & Risk

✅ Benefits

- Restores oxygen & nutrients
- Preserves viable myocardium
- Limits infarct size

⚠️ Potential Harm

- Reperfusion injury due to:
  - Reactive oxygen species
  - Calcium influx
  - Inflammation

😵 Stunned Myocardium

Timely reperfusion → Myocytes survive → Persistent biochemical abnormalities → Transient noncontractile state → Stunned myocardium

📌 Characteristics:

- Reversible
- Lasts days
- May cause temporary heart failure

⚡ Ischemia & Arrhythmias

Myocardial ischemia → Electrical instability (irritability) → Ventricular arrhythmias → Ventricular fibrillation

📊 *Crucial exam stat:*

80–90% of ischemic cardiac deaths are due to ventricular fibrillation, not pump failure.

🧱 Pattern of Myocardial Necrosis

📍 Initial Site of Irreversible Injury

- Subendocardial zone

🧠 *Why subendocardium is most vulnerable:*

- Farthest from epicardial coronary arteries
- Exposed to highest intramural pressure
- Blood inflow is easily compromised

🌊 Wavefront Phenomenon (Flowchart)

Prolonged ischemia → Subendocardial necrosis → Progressive tissue edema → Release of ROS & inflammatory mediators → Spread of necrosis toward epicardium → Transmural infarction (if untreated)

🧠 Final Extent of Infarction

- Infarct size becomes complete in 3–6 hours
- Without intervention:
  - Occlusion of epicardial artery → Full-thickness (transmural) MI

✨ *Clinical takeaway:*

Early reperfusion within the 3–6 hour window can significantly reduce infarct size.

📝 One-Line Exam Summary

Myocardial infarction results from acute coronary thrombosis leading to time-dependent, wavefront progression of ischemic myocyte necrosis, beginning in the subendocardium and potentially becoming transmural.

📌 Determinants of Infarct Pattern

The location, size, and morphology of an acute myocardial infarction (MI) depend on several interrelated factors:

- Size & distribution of the involved coronary vessel
- Rate of development and duration of occlusion
- Metabolic demands of myocardium
  (↑ heart rate, ↑ blood pressure → ↑ demand)
- Extent of collateral circulation

✨ *Exam insight:*

Infarct severity is not determined by occlusion alone, but by the balance between ischemic duration, demand, and collateral flow.

🔴 Coronary Artery Involvement & Infarct Location (Very High-Yield)

🩸 Left Anterior Descending (LAD) Artery

- Most common vessel involved
- 40–50% of all MIs
- Proximal LAD occlusion → infarction of:
  - Anterior wall of left ventricle
  - Anterior two-thirds of interventricular septum
  - Apex of the heart
- Often fatal if proximal
- Distal LAD occlusion → may affect apex only

🩸 Left Circumflex (LCX) Artery

- 15–20% of MIs
- Proximal occlusion → infarction of:
  - Lateral wall of left ventricle

🩸 Right Coronary Artery (RCA)

- 30–40% of MIs
- Proximal occlusion → infarction of:
  - Much of the right ventricle
  - Inferior/posterior LV (depending on dominance)

🧭 Coronary Dominance (Exam Favorite Concept)

📍 Posterior Descending Artery (PDA)

- Supplies:
  - Posterior one-third of interventricular septum
  - Inferior & posterior LV walls

🔹 Right-Dominant Circulation (≈90%)

- PDA arises from RCA
- RCA occlusion →

  Posterior septal + posterior wall ischemia

🔹 Left-Dominant Circulation (≈10%)

- PDA arises from LCX
- LCX occlusion →
  Lateral wall + posterior septum + inferior/posterior LV infarction

✨ *One-liner:*

The artery giving rise to the PDA is termed the dominant vessel.

🌱 Collateral Circulation – A Natural Defense

- Major coronary arteries are functional end arteries
- However, they are connected via anastomotic channels

⚠️ Gradual arterial narrowing → Pressure gradient develops
→ Blood diverted through collaterals → Progressive

collateral dilation → Adequate perfusion despite epicardial occlusion

⚠️ Acute occlusion → No time for collateral adaptation → Large infarct

---

🔷 Patterns of Myocardial Infarction

❑ Transmural Infarction

📘 Definition

- Infarction involving the full thickness of ventricular wall

🧬 Cause

- Epicardial coronary artery occlusion
- Plaque rupture + occlusive thrombosis

📌 Key Points

- Most common pattern
- Usually involves:

- Left ventricle
- Interventricular septum

✨ *Exam line:*

Transmural infarcts are caused by complete occlusion of an epicardial artery.

2️⃣ Subendocardial Infarction

📘 Definition

- Infarction limited to the inner one-third of myocardium

🧬 Mechanisms

- Plaque disruption with:
  - Transient thrombus (spontaneously or therapeutically lysed)
- Severe coronary atherosclerosis with:
  - ↓ oxygen delivery (hypotension, anemia, pneumonia)

- ↑ oxygen demand (tachycardia, hypertension)

🧠 Why subendocardium?

- Farthest from epicardial vessels
- Highest intramural pressure
- Most vulnerable to hypoperfusion

3️⃣ Microscopic (Microinfarcts)

📘 Definition

- Tiny infarcts due to small-vessel occlusion
- Often ECG-negative

🧬 Causes

- Vasculitis
- Embolization:
  - Valve vegetations
  - Mural thrombi
- Vasospasm:
  - Extreme emotional stress

- Pheochromocytoma
- Cocaine use

✨ *Exam pearl:*

Microscopic infarcts may be clinically silent yet pathologically significant.

🧠 Morphology of Myocardial Infarction

📌 General Principles

- Nearly all transmural infarcts involve:
  - Left ventricle ± septum
- 15–30% of posterior or posteroseptal MIs → extend into right ventricle
- Isolated RV infarcts → rare (1–3%)

🧬 Evolution of Morphologic Changes

🔁 Healing Sequence (Flowchart)

Ischemic injury → Coagulative necrosis → Acute inflammation → Macrophage-mediated clearance → Granulation tissue formation → Collagen deposition → Fibrous scar (no regeneration)

✨ *Important:*

Myocardium heals by scarring, not regeneration.

👁️ Gross Morphology (Time-Dependent)

⏱️ Early Phase

- < 12 hours → usually not grossly visible
- > 3 hours:
  - Vital stains (Triphenyl tetrazolium chloride)
  - Infarct appears pale (enzyme leakage)

⏱️ 12–24 hours

- Red-blue discoloration
- Due to trapped stagnant blood

⏱️ 3–7 days

- Soft, yellow-tan infarct center

⏱️ 10–14 days

- Hyperemic border
- Granulation tissue rim

⏱️ Weeks later

- Gray-white fibrous scar

🔬 Microscopic Morphology (High-Yield Timeline)

🧠 Reversible Injury (0–30 min)

- Myofibril relaxation
- Glycogen depletion
- Mitochondrial swelling

☠️ Irreversible Injury

½–4 hours

- Sarcolemmal disruption
- Wavy fibers at borders
- Mitochondrial amorphous densities

4–12 hours

- Early coagulative necrosis
- Edema & hemorrhage

12–24 hours

- Hypereosinophilic myocytes
- Nuclear pyknosis
- Early neutrophilic infiltrate
- Contraction band necrosis

🔥 Inflammatory Phase

1–3 days

- Extensive coagulative necrosis

- Loss of nuclei & striations
- Dense neutrophilic infiltrate

3–7 days

- Macrophages replace neutrophils
- Phagocytosis of dead myocytes
- Tissue softening (⚠️ rupture risk)

🌱 Repair Phase

7–10 days

- Well-developed macrophages
- Early granulation tissue

10–14 days

- Prominent granulation tissue
- Neovascularization
- Collagen deposition begins

🧱 Scar Formation

2–8 weeks

- Increasing collagen
- Decreasing cellularity

> 2 months

- Dense collagenous scar
- Age of scar cannot be determined

✨ *Exam favorite:*

Once healed, MI scars look identical whether 8 weeks or 10 years old.

⚠️ Factors Delaying Healing

- Large infarct size
- Poor vascular supply
- Malnutrition
- Corticosteroid therapy

Healing proceeds:

→ From margins toward center

→ Large infarcts heal slowly & incompletely

📝 Final Exam Summary

- MI patterns depend on vessel involved, dominance, duration of ischemia, and collateral flow
- Transmural infarcts result from complete epicardial occlusion
- Subendocardium is most vulnerable to ischemia
- Myocardial healing occurs via fibrous scarring only

Infarct Modification by Reperfusion

🎯 Therapeutic Goal in Acute Myocardial Infarction

The primary objective in acute MI management is rapid restoration of myocardial blood flow.

📌 *Core principle:*

"Time is myocardium" ⏱️ → The longer the ischemia, the greater the irreversible myocardial damage.

🩺 Methods of Reperfusion

- Thrombolysis
  → Dissolution of thrombus using tissue plasminogen activator (tPA)
- Percutaneous coronary intervention (PCI)
  → Balloon angioplasty ± stent placement
- Coronary artery bypass graft (CABG)

✔️ Early reperfusion:

- Salvages reversibly injured but viable myocardium
- Improves short- and long-term survival

⚠️ However, reperfusion is not entirely beneficial due to a phenomenon called reperfusion injury.

⚠️ Reperfusion Injury

Reperfusion injury refers to additional myocardial damage occurring after blood flow is restored to ischemic tissue.

📌 *Key concept:*

> Reperfusion can save viable cells but may also exacerbate injury in irreversibly damaged cells.

🔬 Mechanisms of Reperfusion Injury (Very High-Yield)

❶ Mitochondrial Dysfunction ⚡

- Ischemia alters mitochondrial membrane permeability
- Leads to:
  - Mitochondrial swelling
  - Rupture of outer mitochondrial membrane
- Release of pro-apoptotic proteins
  → Apoptosis of myocytes

✨ *Exam line:*

Mitochondrial damage is a major trigger for apoptosis in reperfused myocardium.

2️⃣ Myocyte Hypercontracture 💥

- Ischemia causes:
  - ↑ Calcium influx through damaged sarcolemma
  - ↑ Calcium release from intracellular stores

↑ Intracellular Ca^{2+} → Excessive cytoskeletal contraction → Uncontrolled myofibril shortening → Cell death

📌 *Why fatal?*

In the absence of ATP, myofibrils cannot relax, resulting in irreversible injury.

3️⃣ Free Radical (ROS)-Mediated Injury 🧪

Within minutes of reperfusion, there is a burst of reactive oxygen species (ROS):

- Superoxide anion ($O_2^{\bullet -}$)
- Hydrogen peroxide (H_2O_2)
- Hydroxyl radical ($^{\bullet}OH$)
- Hypochlorous acid ($HOCl$)
- Peroxynitrite (from nitric oxide)

🧬 Effects of ROS:

- Lipid peroxidation of cell membranes
- Protein denaturation
- DNA damage

Additional source:

- ROS released by infiltrating neutrophils

✨ *One-liner:*

Free radicals are central mediators of reperfusion injury.

4️⃣ Leukocyte-Mediated Microvascular Obstruction 🚫

- Reperfusion → leukocyte adhesion & aggregation
- Leads to:
    - Capillary plugging
    - Microvascular occlusion

This causes the "No-Reflow Phenomenon":

Restored epicardial blood flow → Microvascular obstruction persists → Tissue remains ischemic

🔬 Mediated partly by:

- Activation of phospholipase A_2
- Production of arachidonic acid metabolites
- Prostaglandin-mediated acute inflammation

🇸 Platelet & Complement Activation 🩸

- Platelet activation → microthrombi formation
- Complement activation → endothelial injury

📌 Complement-mediated effects:

- Endothelial swelling
- Increased vascular permeability
- Worsening of no-reflow phenomenon

🧠 Summary Flowchart: Reperfusion Injury

Reperfusion of ischemic myocardium → Sudden oxygen & calcium influx → ROS generation + mitochondrial damage → Leukocyte & platelet activation → Microvascular obstruction → Additional myocyte death

---

🔴 Morphology of Reperfused Myocardium

👁️ Gross Appearance

- Infarct appears hemorrhagic
- Due to:
    - Vascular injury
    - Increased vascular permeability
    - Leakage of blood into necrotic tissue

🔬 Microscopic Appearance: Contraction Band Necrosis (Very Important)

📘 Definition

A characteristic form of myocyte necrosis seen after reperfusion.

🔬 Features

- Intense eosinophilic transverse bands
- Hypercontracted sarcomeres
- Caused by sudden calcium influx

🧠 Pathogenesis

Calcium influx → Excessive sarcomere contraction → ATP depletion → Sarcomeres fixed in agonal tetanic state

✨ *Exam favorite line:*

> Contraction band necrosis is a hallmark of reperfusion injury.

⚖️ Key Concept to Remember

- Reversibly injured cells → may recover after reperfusion
- Irreversibly injured cells → die, but show altered morphology due to reperfusion

---

🩺 Clinical Features of Myocardial Infarction

🔔 Chest Pain

- Severe, crushing substernal pain
- Radiates to:
  - Left arm
  - Neck
  - Jaw
  - Epigastrium
- Lasts minutes to hours
- Not relieved by rest or nitroglycerin

📌 *Difference from angina:*

Angina → relieved by rest

MI → persistent pain

🤫 Silent Myocardial Infarction

- Occurs in up to 25% of patients
- Common in:
  - Diabetics (autonomic neuropathy)
  - Elderly patients

✨ *Exam pearl:*

Absence of pain does not exclude MI.

🫀 Systemic Signs

- Rapid, weak pulse
- Diaphoresis 😓
- Nausea & vomiting (especially posterior wall MI)

- Dyspnea:
  - Due to ↓ LV contractility
  - Mitral valve dysfunction
  - Acute pulmonary edema

⚠️ Cardiogenic Shock

- Occurs when >40% of LV myocardium is infarcted
- Results in:
  - Hypotension
  - Reduced tissue perfusion
  - High mortality

⚡ Arrhythmias (Most Common Cause of Early Death)

- Due to ischemic damage to:
  - Conduction system
  - Myocardial electrical stability

📌 *Important:*

Sudden cardiac death due to arrhythmia is the leading cause of MI-related deaths before hospitalization.

📈 ECG Changes in MI

Common ECG Abnormalities

- Pathological Q waves
- ST-segment elevation or depression
- T-wave inversion

🩺 ECG-Based Classification of MI

🔴 STEMI

- Caused by complete coronary artery occlusion
- Represents transmural infarction
- Requires urgent reperfusion (thrombolysis or PCI)

🟡 NSTEMI

- Due to partial or transient occlusion
- No full-thickness infarction
- Often managed conservatively

🧪 Laboratory Diagnosis of MI (Very High-Yield)

🔬 Principle

Necrotic myocytes → Loss of membrane integrity → Leakage of intracellular proteins into blood

---

📊 Cardiac Biomarkers Comparison Table

Biomarker	Rise	Peak	Return to Normal	Key Use
CK-MB	2–4 h	24–48 h	~72 h	Detect reinfarction
Troponin I / T	2–4 h	~48 h	7–10 days	Most sensitive & specific

Myoglobin	1–2 h	Early	Rapid	Low specificity

🧠 Troponins (TnI & TnT) ⭐

- Normally absent in blood
- Highly specific for myocardial injury
- Remain elevated for 7–10 days

✨ *Clinical advantage:*

Allows diagnosis of MI long after CK-MB normalizes.

🔄 Effect of Reperfusion on Biomarkers

Reperfusion

→ Rapid washout of enzymes

→ Earlier peak levels of CK-MB and troponins

📝 Final Exam Takeaways

- Reperfusion saves myocardium but can cause reperfusion injury
- Key mechanisms: ROS, Ca^{2+} overload, mitochondrial damage
- Contraction band necrosis is characteristic of reperfused MI
- Troponins are the gold-standard biomarkers
- STEMI = transmural infarct + complete occlusion

Consequences and Complications of Myocardial Infarction

📊 Mortality After Acute MI (High-Yield Stats)

- Overall in-hospital mortality: ~ 7–8%
- STEMI mortality: ~ 10%
- NSTEMI mortality: ~ 6%

📉 With advances in early reperfusion and intensive care, this gap is narrowing.

⚠️ Out-of-Hospital Mortality

- ~33% of STEMI patients die outside the hospital
- Most deaths occur:
    - Within 1 hour
    - Due to fatal arrhythmias (especially ventricular fibrillation)

🌍 This highlights the major public health burden of CAD in low-income countries with limited emergency care.

☠️ Major Complications of Acute MI

📌 Nearly 75% of patients develop one or more complications.
Among these, three are classically life-threatening.

🔴 Lethal Mechanical Complications (Must-Remember)

i. Myocardial Rupture 💥

Occurs in 1–5% of MIs and is often fatal.

Types of Rupture (in decreasing severity):

1. Ventricular septal rupture → Ventricular septal defect (VSD)
2. Papillary muscle rupture → Acute severe mitral regurgitation
3. Left ventricular free wall rupture → Hemopericardium → Cardiac tamponade (most serious)

⏱️ Timing

- 3–7 days post-MI

📌 *Why this timing?*

This is when:

- Necrotic myocardium undergoes maximal enzymatic degradation
- Infarcted tissue is replaced by soft, friable granulation tissue

---

🧠 Flowchart: Myocardial Rupture

Acute MI → Coagulative necrosis → Enzymatic digestion of dead myocytes → Weak, friable myocardial wall → Rupture (3–7 days)

---

ii. Contractile Dysfunction (Pump Failure) 🫀

- LV systolic function is impaired proportionally to infarct size
- Common manifestations:
  - Hypotension
  - Pulmonary congestion
  - Pulmonary edema

⚠️ Cardiogenic Shock

- Occurs in ~ 10% of transmural MIs
- Usually when ≥40% of LV myocardium is damaged
- Major cause of early mortality

✨ *Exam line:*

Cardiogenic shock reflects severe loss of functional myocardium.

---

iii. Papillary Muscle Dysfunction 🩹

- Due to ischemia or necrosis of papillary muscles
- Results in mitral regurgitation

Mechanisms

- Early: ischemia → reduced contractility
- Late:
  - Fibrosis and shortening of papillary muscles
  - Global LV dilation → altered valve geometry

📌 Leads to:

- Pulmonary edema
- Worsening heart failure

---

iv. Right Ventricular Infarction 🫀

- Isolated RV infarction: 1–3%
- More commonly seen with RCA occlusion
- Often associated with concurrent LV infarction

Clinical Consequences

- Right-sided heart failure:
  - Venous pooling
  - Systemic hypotension
  - Reduced LV preload

---

v. Arrhythmias (Most Common Complication) ⚡

- Occur in ~90% of MI patients
- More frequent in STEMI

Types

- Heart block (partial → complete)
- Asystole
- Bradycardia
- Supraventricular tachyarrhythmias

- Ventricular premature beats
- Ventricular tachycardia
- Ventricular fibrillation (most lethal)

⏱️ Highest risk: first 1 hour after MI
Risk declines thereafter.

✨ *Very important exam point:*

> Most early MI deaths are due to arrhythmias, not pump failure.

---

vi. Pericarditis After MI 🩸

🟡 Early Pericarditis

- Occurs 2–3 days post-MI
- Seen in transmural infarctions
- Type: Fibrinohemorrhagic pericarditis

Clinical Features

- Anterior chest pain

- Pericardial friction rub

Usually self-limited, resolving over days.

🔵 Late Pericarditis (Dressler Syndrome)

- Occurs weeks after MI
- Due to autoimmune response against myocardial antigens
- Less common

🧠 Flowchart: Pericarditis After MI

Transmural MI → Epicardial inflammation → Fibrin deposition on pericardium → Chest pain + friction rub

Weeks later → Autoantibody formation → Dressler syndrome

---

vii. Chamber Dilation 📐

- Necrotic myocardium loses tensile strength
- Leads to:
  - Stretching
  - Thinning
  - Dilation of infarcted region

📌 Especially common in:

- Anteroseptal infarcts

---

viii. Mural Thrombus 🩸

Pathogenesis

Three factors act together:

1. Reduced myocardial contraction → Blood stasis
2. Chamber dilation
3. Endocardial injury (thrombogenic surface) → Mural thrombus formation

Consequences

- Systemic thromboembolism
  - Stroke
  - Renal infarcts
  - Limb ischemia

---

ix. Ventricular Aneurysm (Late Complication) 🎈

- Develops from:
  - Large transmural anteroseptal MI
- Heals by:
  - Formation of thin fibrous scar

Features

- Thinned, bulging ventricular wall
- Does not rupture (important!)

Complications

- Mural thrombus
- Arrhythmias
- Chronic heart failure

✨ *Exam favorite:*

Ventricular aneurysms do not rupture but predispose to thrombosis and arrhythmias.

---

x. Progressive Heart Failure 💔

- Result of:
  - Loss of contractile myocardium
  - Ventricular remodeling
- Discussed under Chronic Ischemic Heart Disease

📈 Long-Term Prognosis After MI

Depends mainly on:

1. Residual left ventricular function
2. Severity of atherosclerosis in remaining coronary vessels

Chronic Ischemic Heart Disease (Ischemic Cardiomyopathy)

📘 Definition

Chronic IHD is progressive heart failure due to long-standing ischemic myocardial damage.

🧬 Pathogenesis

Common Scenario

Previous MI(s) → Loss of myocardium → Compensatory hypertrophy of remaining myocytes → Eventual failure of compensation → Chronic heart failure

---

Alternate Scenario

Severe CAD without overt MI → Repeated ischemia → Micro-infarctions → Replacement fibrosis → Diffuse myocardial dysfunction

---

🩺 Clinical Features

- Severe chronic heart failure
- Intermittent angina
- Recurrent infarctions
- Arrhythmias

📌 Major causes of morbidity & mortality:

- Arrhythmias
- Congestive heart failure
- Recurrent MI

🧠 One-Look Summary Flowchart

Acute MI → Myocyte necrosis → Mechanical + electrical complications → Healing with fibrosis → Ventricular remodeling → Chronic ischemic heart disease

---

📝 Final Exam Pearls

- 3–7 days post-MI = highest risk of rupture
- Arrhythmias are the leading cause of early death
- Ventricular aneurysms do not rupture
- Dressler syndrome = autoimmune pericarditis
- Chronic IHD = ischemic cardiomyopathy

<-- The End -->