📘 Lecture 1: Ischemic Heart Disease (IHD)

🔷 Page 1: General Overview & Coronary Physiology

🟥 General Characteristics

1. **Heart Anatomy**
- Size: Approximately the size of a closed fist.
- Average heart rate: ~70 beats per minute.
- Average blood pumped: 6–7.5 liters per day.

2. **Coronary Artery ECG Leads**
- **Anterior leads**: V1–V4 → LAD
- **Inferior leads**: II, III, aVF → RCA
- **Lateral leads**: V5, V6, aVL, lead I

3. **Coronary Circulation Physiology**
- **Flow at rest**: ~60–90 mL/min/100 g tissue
- **Flow during exercise**: ↑ up to 300–400 mL/min/100 g
- **Oxygen extraction**: ~65–75% (already near max → compensation must occur by ↑ blood flow)
- **80% of coronary perfusion occurs during diastole** (In contrast to most other organs where it occurs during systole)
- **Collateral vessels**:
- Anatomically present but usually **non-functional** unless activated by ischemia.
- **Clinical Pearl**: A patient with prior angina is more likely to have developed collateral circulation → better outcomes in MI than someone with a first-time event.

→ Not by more O_2 extraction

→ Since in systole, contraction would puts more pressure on the vessels

🟨 Physiology of Coronary Circulation

💙 Normal Myocardial Oxygen Dynamics

Myocardial O_2 Demand	Myocardial O_2 Supply
1. Heart rate	1. Coronary flow (vessel patency)
2. Contractility	2. Hemoglobin level
3. Wall tension	3. Oxygen extraction
4. Muscle mass (wall thickness)	4. Arterial oxygen saturation

🟧 Causes of Myocardial Ischemia

🔻 Reduced Oxygen Supply

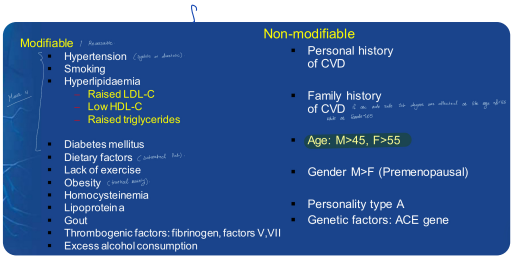
1. Coronary artery disease (atherosclerosis or non-atherosclerotic)
2. Decreased oxygen content in blood:
- Severe anemia
- Carboxyhemoglobinemia (e.g., CO poisoning)
- Hypotension

🔺 Increased Oxygen Demand

1. **Left Ventricular Hypertrophy**
- Due to hypertension, aortic stenosis, hypertrophic cardiomyopathy
2. **Increased Cardiac Output**
- Conditions such as thyrotoxicosis, rapid tachyarrhythmias

🟫 Causes of Coronary Artery Disease (CAD)

🩸 Atherosclerotic (95%)



⚠️ Non-Atherosclerotic Causes

1. Arteritis: e.g., SLE, RA, Takayasu arteritis
2. Embolism
3. Mural thickening: e.g., amyloidosis, post-radiation fibrosis
4. Luminal narrowing: spasm or aortic dissection
5. Congenital anomalies

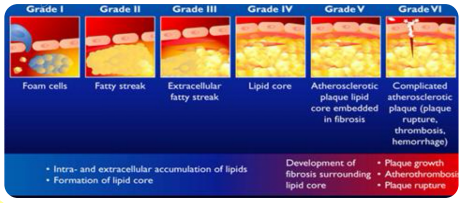
📊 **Local Context: CAD in Jordan**

- **98%** of the population have **at least 1 modifiable risk factor**.
- Most people have **≥3 risk factors**.
- **Risk is exponential**, not additive: Multiplitive
- Hypertension = 3× risk of CAD
- High LDL = 4× risk
- Together = 12× risk

🧬 **Pathogenesis of Atherosclerotic Plaques**

🟥 **Step-by-Step Pathogenesis**

1. **Endothelial Injury (Dysfunction)**
- Caused by hypertension, smoking, diabetes, hyperlipidemia, etc.
- Leads to loss of nitric oxide (vasodilator), increased permeability, and pro-inflammatory state.
2. **Protective Response**
- Activated endothelium expresses **cell adhesion molecules**:
- **Cytokines**: IL-1, TNF-α
- **Chemokines**: MCP-1, IL-8
- **Growth Factors**: PDGF, FGF
- These attract **T-cells and monocytes** and promote **smooth muscle proliferation**.
3. **Monocyte and T-cell Recruitment**
- These immune cells adhere to the sticky surface of activated endothelium.
4. **Migration to Subendothelial Space**
- Monocytes penetrate the intima and mature into **macrophages**.
5. **Lipid Uptake**
- Macrophages engulf oxidized LDL → become **foam cells**.
6. **Formation of Fatty Streaks**
- Clusters of foam cells accumulate → earliest visible lesion in atherosclerosis.
7. **Progression to Plaque**
- Foam cells + lipid pools + migrating smooth muscle cells form a fibrous plaque.



🟦 **Plaque Types: Stable vs. Unstable**

Stable Plaque	Unstable Plaque
1. More smooth muscle cells	1. More inflammatory cells
2. Fewer inflammatory cells	2. Fewer smooth muscle cells
3. Thick fibrous cap	3. Thin fibrous cap
4. Small lipid pool	4. Large lipid pool

🔍 **Unstable plaques** are prone to **rupture**, causing **thrombosis → MI or ACS**.

📌 **Clinical Note:**

"Atherosclerosis begins early in life, but by the time the patient becomes symptomatic, it is often **already advanced**."
🧠 This is why **screening and primary prevention** (controlling BP, lipids, etc.) is so critical even in asymptomatic patients.

🧭 **Clinical Manifestations of Atherosclerosis**

Varies by **artery affected**:

1. **Coronary Arteries**
- Asymptomatic → Stable angina → Unstable angina → MI → CHF → Arrhythmia → Sudden cardiac death
2. **Cerebrovascular Arteries**
- TIA, ischemic stroke
3. **Peripheral Arteries**
- Claudication, gangrene, cold/painful feet, impotence (e.g., Leriche syndrome)

❤️‍🔥 **Stable Angina**

"**Fixed plaque** narrowing a major coronary artery → mismatch between **oxygen demand and supply**" → Mainly ↑ O_2 demand

🩺 Clinical Features:

- **Chest pain**:
- Retrosternal, pressure-like, heaviness
- Gradual onset
- Triggered by **exertion**, **stress**, or drugs (e.g., cocaine, methamphetamines)
- Duration: <30 min (usually 5–10 minutes)
- Relieved by **rest** or **sublingual nitroglycerin**
- May radiate to **left arm, jaw, or neck**
- Rare in HIV or unrelated systemic disease

🔥 Pain pattern is predictable. If it occurs at rest or gets worse → it's no longer "stable" → likely unstable angina or variant.

🟦 Classification & Diagnosis of Angina

🟨 Angina Classification (Canadian Cardiovascular Society – same as NYHA for dyspnea)

Class	Description
I	No symptoms with ordinary activity
II	Symptoms with **more than** ordinary exertion
III	Symptoms with **less than** ordinary exertion
IV	Symptoms **at rest**

🧠 Used to **grade severity and functional limitation** of angina. Class III and IV are considered high risk.

🟨 Causes of Angina (Not all ischemia is coronary!)

1. **Coronary artery disease (CAD)** – most common
2. **Severe anemia** – ↓ O_2 delivery
3. **Hypertrophic cardiomyopathy (HCM)** – impaired diastolic filling, increased O_2 demand
4. **Hypertension (HTN)** – ↑ afterload
5. **Aortic stenosis (AS)** – ↓ perfusion, ↑ LV work
6. **Rapid tachyarrhythmia** – ↑ demand, ↓ filling time

🩺 Diagnosis of Stable Angina

Step 1: History

Clinical diagnosis based on characteristic chest pain pattern.

Step 2: Physical Examination

Often **normal** unless angina is complicated by HF or valvular disease.

Step 3: Resting ECG

- Often **normal** because stable angina is **exertional**
- But: **Pathologic Q wave** may be present → suggests **previous MI**

🧠 *Q wave = old infarction marker, especially if seen in ≥2 contiguous leads*

Step 4: Stress Testing

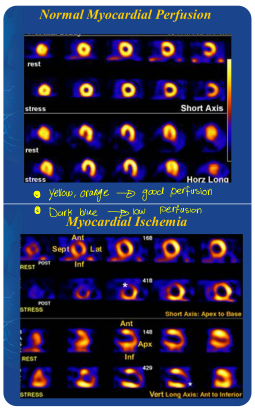
Type	What to look for
A. Stress ECG	Done before, during, after exercise
	Positive if you see **ST depression**
	→ Perform **cardiac catheterization**
Clinical Note	Patients with:

- LBBB
- LV hypertrophy
- Baseline ST abnormalities Should **not undergo stress ECG**, because interpretation is unreliable

B. Stress Echo (with exercise or dobutamine)

- Looks for **wall motion abnormalities**:
- **Akinesis** or **hypokinesis** during stress
- **More sensitive** than ECG
- Also shows **LV function and size**

C. Nuclear Imaging (e.g., thallium, dipyridamole scan)

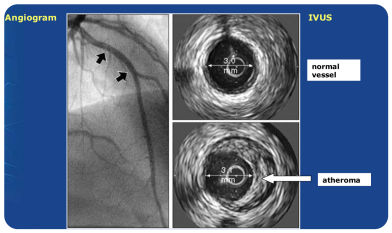


- Looks for **decreased isotope uptake during stress**
- **High sensitivity**
- Useful when other tests are equivocal

Step 5: Laboratory Workup

- **Serum lipids**: LDL, HDL, triglycerides
- **Fasting glucose**
- **CBC** (anemia can mimic angina)

Step 6: Coronary Angiography



Definitive test for CAD Direct visualization of coronary vessels Indicated if:

- Symptoms are moderate/severe (1)
- Stress test is positive (2)
- Revascularization is being considered (?)

Imaging for Atherosclerosis

Invasive	Non-Invasive
Coronary angiography	MRI, CT angiography
Intravascular ultrasound (IVUS)	B-mode ultrasound

*Atheroma is considered significant if vessel narrowing is **>3.0 mm**.*

Clinical Tips:

- **Normal tests do NOT rule out stable angina.** You need **provocative testing** to unmask exertional ischemia.
- Always assess the **functional impact** and decide on risk stratification and possible revascularization.

Diagnostics & Prognosis + Beginning of Management

Nuclear Perfusion Imaging

(Top left panel: "Normal Myocardial Perfusion")

What you're seeing:

- **Short axis + long axis views**
- Images during **rest and stress**
- **Yellow/orange** areas = good perfusion
- **Dark blue/purple** = poor perfusion = **ischemia**

Clinical Pearl:

This is one of the most sensitive non-invasive tools for detecting **reversible ischemia** — i.e., perfusion is fine at rest but drops during exertion.

Prognosis of CAD

Factors that determine risk:

Ejection Fraction (EF)	Vessel Involvement	Prognosis
Normal EF = **60–75%**	Single-vessel disease	Good prognosis
↓ EF (<50%)	LAD or multi-vessel	Poorer outcome
Involves **LAD**	2–3 vessels	High-risk → often consider CABG

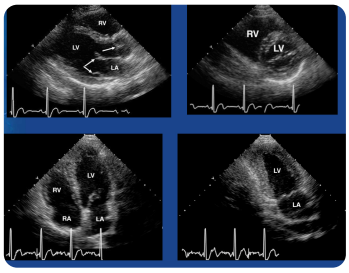
LAD = the "**widowmaker**" if proximal.

*Questions: if we have LAD involvement and 80% EF we would still have Good pr.

Echocardiography Findings

(Top middle panel: 4 ultrasound views)

- Shows **RV, LV, LA, RA** chambers
- Assesses:
- Wall motion
- LV size
- EF
- Diastolic function
- Valvular abnormalities



🧭 Management of Stable Angina

🔷 1. Risk Factor Modification

(Always first step unless unstable)

- **Smoking cessation** (benefits within 1 year)
- Control **comorbidities**: DM, HTN, lipids
- **Weight loss**
- **Aerobic exercise** — improves functional capacity and symptoms

🔷 2. Medical Therapy

A. 🎯 Medications that Improve Mortality:

1. **Aspirin**
- Antiplatelet; reduces thrombotic events (irreversible inhibition of COX 1 – which inhibits TAX2)
2. **Statins**
- Stabilize plaques, reduce LDL, improve endothelial function
3. **ACE inhibitors**
- Especially beneficial in patients with DM, HTN, or low EF

B. 💊 Medications for Symptom Relief:

1. **β-blockers**
- ↓ HR, ↓ BP, ↓ myocardial O_2 demand
- **Can be taken before exertion** to prevent angina
2. **Nitrates** (Nitrates not B-blocker)
- Vasodilate → reduce preload → lower O_2 demand
- Fast acting (sublingual) or long-acting (patch, oral)
3. **CCBs (Calcium Channel Blockers)**
- ↓ contractility and afterload
- Often used if beta-blockers contraindicated or ineffective

💊 Advanced Medical Therapy & Revascularization

🟦 Management of Stable Angina (continued)

🔷 Risk Factor Modification

- Smoking cessation
- Weight reduction
- Control of comorbidities (diabetes, hypertension)
- **Aerobic exercise**: improves both **functional capacity** and **angina symptoms**

🔷 Increase Oxygen Supply vs Decrease Oxygen Demand

This is one of the **core frameworks** of angina therapy:

To Increase O_2 Supply	To Decrease O_2 Demand
1. ↑ Diastolic time → **β-blocker**	1. ↓ Heart rate → **β-blocker, CCB**
2. ↓ Coronary tone → **Nitrate, CCB**	2. ↓ Contractility → **β-blocker, CCB**
3. ↓ LV diastolic pressure → **Nitrates**	3. ↓ Wall tension (↓ preload/afterload) → **nitrates**
4. Correct stenosis → **PCI or CABG**	4. Shift metabolism → **trimetazidine**
5. ↑ O_2-carrying capacity → **transfusion if anemic**	

🧠 Angina occurs when supply < demand. So treatment either **enhances supply** (flow, O_2 content) or **lowers demand** (workload).

🔧 **When to Revascularize**

"Revascularization is indicated when **medical therapy fails**"

- **PCI**: Percutaneous Coronary Intervention
- **CABG**: Coronary Artery Bypass Graft Used when:
- Angina persists despite optimal medication
- High-risk coronary anatomy
- Left main or triple-vessel disease
- Reduced EF

🚀 **New Medical & Invasive Therapies for Refractory Angina**

Patients with angina that persists **despite optimized conventional therapy** are considered to have **refractory angina**.

💊 **Metabolic Modulators**

Drug	Mechanism
Trimetazidine	Shifts metabolism from fatty acid to glucose oxidation
Ranolazine	Inhibits late Na^+ current → ↓ intracellular Ca^{2+}
Ivabradine	Inhibits SA node → ↓ HR without ↓ contractility
Nicorandil	Potassium channel opener + nitrate-like effect
Bosentan	Endothelin receptor blocker → improves endothelial function
Testosterone	May improve endothelial vasodilation (experimental)

⚙️ **Invasive Non-Pharmacologic Options**

1. **Enhanced External Counterpulsation (EECP)**
- Cuffs on legs inflate during diastole → improve coronary perfusion
2. **Spinal Cord Stimulation**
- Modulates pain transmission, may improve myocardial perfusion reflexively
3. **Laser Revascularization & Angiogenesis**
- Still experimental — aims to induce new vessel growth in ischemic myocardium

📌 **Differential Diagnosis of Angina-like Chest Pain**

Some non-cardiac causes to always rule out in atypical angina cases:

1. **Neuromuscular disorders** (e.g., cervical radiculopathy)
2. **Respiratory conditions** (e.g., pleuritis, PE, pneumothorax)
3. **Upper GI disorders** (GERD, spasm, ulcer)
4. **Psychological causes** (e.g., anxiety, panic attacks)
5. **Syndrome X** (covered on next page)

🧠 Don't call it "angina" until you've ruled out these mimics — especially in women, young patients, and those with normal coronaries.

🔍 **Special Forms of Angina & Therapy Stratification**

🟦 **Syndrome X (Microvascular Angina)**

📖 **Definition:**

"Exertional angina with normal coronaries on angiography"

- Presents like typical stable angina: **exertional chest pain**
- BUT: **Cardiac catheterization shows no significant stenosis**
- Stress testing and nuclear imaging still show **objective evidence of ischemia**

🧠 **Pathophysiology:**

- **Microvascular dysfunction**:
- Coronary microvessels (not visible on angiography) fail to **dilate appropriately**
- Endothelial dysfunction is the key

👩 **Classic Patient:**

- **Middle-aged woman**
- Normal ECG at rest
- Positive stress ECG (ST depression)
- Normal angiogram

📌 **Prognosis:**

- Generally **excellent**
- Risk of infarction/death is **low**, but symptoms can be **persistent and frustrating**

🟦 **Variant Angina (Prinzmetal)**

"Rest angina associated with ST elevation and ventricular arrhythmias"

📖 **Key Features:**

- Occurs **at rest**, often **at night or early morning**
- Caused by **transient spasm** of coronary arteries
- **Not** related to exertion or plaque burden

🧪 **ECG Findings:**

- **Transient ST elevation**
- May return to normal between attacks

🩺 **Diagnosis:**

- Often confirmed by **provocative testing during angiography**
- **IV acetylcholine** or **ergonovine** used to induce spasm
- ST elevation + no obstructive disease on cath = diagnostic

❌ **β-blockers are contraindicated**

- They may **worsen coronary spasm** by unopposed alpha stimulation

✅ **Treatment:**

- **Nitrates**: relieve acute spasm
- **Calcium channel blockers (CCBs)**: prevent recurrence

📌 **Associated Conditions:**

- Migraine
- Raynaud's phenomenon
- Other vasospastic syndromes

🟨 **Stratified Management of Angina by Severity**

🟩 **Mild Angina**

- EF: Normal
- Symptoms: Mild
- Anatomy: Single-vessel disease

🔷 **Treatment**:

- **β-blockers + nitrates**
- Add **CCB** if symptoms persist
- Focus on medical therapy

🟨 **Moderate Angina**

- EF: Normal
- Symptoms: Moderate
- Anatomy: 2-vessel disease

🔷 If medical therapy fails → **Consider coronary angiography** To assess whether PCI or CABG is suitable

🟥 **Severe Angina**

- EF: **Reduced**
- Symptoms: **Severe**
- Anatomy: 3-vessel or **left main disease**

🔷 Proceed directly to:

- **Coronary angiography**
- Likely **CABG** preferred over PCI
- **Avoid CCBs** in reduced EF patients

🧠 CCBs can **worsen systolic dysfunction** — especially nondihydropyridines like verapamil/diltiazem

RECAP

❤️ **1. Basic Cardiac & Coronary Physiology**

Concept	Value/Detail
Heart rate	~70 bpm
Output	~6–7.5 L/day
Perfusion	80% in **diastole**
O_2 extraction	Already ~75% → supply is flow-dependent
Collaterals	Exist but require ischemia to activate

🧠 **2. O_2 Demand vs Supply (Core Angina Mechanism)**

↑ Demand	↓ Supply
↑ HR, ↑ contractility, wall tension	CAD (atherosclerosis)
LVH (HTN, AS, HCM)	Severe anemia
Tachyarrhythmia	Carboxyhemoglobinemia (CO)
Thyrotoxicosis	Hypotension

🧬 **3. Atherosclerosis Pathogenesis**

1. Endothelial injury (HTN, smoking, etc.)
2. Cytokine, chemokine, GF release
3. Monocyte migration → macrophages
4. LDL oxidation → foam cells
5. Fatty streak → fibrous cap → plaque

🧠 **Stable vs. Unstable Plaque**:

Stable	Unstable
Thick cap	Thin cap
Small lipid core	Large lipid core
Few inflammatory cells	Many inflammatory cells

🩺 **4. Clinical Manifestations by Territory**

Artery	Disease
Coronary	Angina, MI, CHF, arrhythmia, sudden death
Carotid/cerebral	TIA, stroke
Peripheral	Claudication, gangrene, impotence

🫀 **5. Types of Angina**

Type	Key Feature	Cause	ECG	Treatment
Stable	Predictable, exertional	Fixed plaque	Often normal	BB, nitrates, CCB
Syndrome X	Normal coronaries + ischemia	Microvascular dysfunction	ST ↓ on stress	BB, CCB (limited effect)
Variant (Prinzmetal)	Rest pain, ST elevation	Coronary spasm	ST ↑ at rest	Nitrates + CCB (no BB)

Unstable	Rest pain, worsening, new pattern	Plaque rupture + thrombus	ST ↓ ± T inv	ACS protocol (next lecture)

🧪 6. Diagnostic Approach for Stable Angina

Test	Purpose
History + ECG	Clinical diagnosis
Stress ECG	ST depression = ischemia
Stress Echo	Wall motion abnormality (e.g. hypokinesis)
Nuclear Scan	↓ Isotope uptake during stress
Coronary Angiography	Gold standard, anatomical

🧠 7. Stress Test Interpretation

- **Positive test**: ST depression ≥1 mm → move to angiography
- Avoid stress ECG if:
- LBBB
- LVH
- Baseline ST abnormality → Use **stress echo** or **nuclear scan**

💊 8. Medical Therapy Framework

Goal	Medications
↓ Mortality	**Aspirin, statins, ACE inhibitors**
↓ Symptoms	**BB, nitrates, CCB**
Advanced	**Ranolazine, trimetazidine, ivabradine**
Refractory	EECP, spinal stim, laser, PCI, CABG

⚠️ 9. Who Gets Revascularized?

Severity	Clues	Management
Mild	Single-vessel, normal EF	Medical
Moderate	2-vessel, normal EF	Maybe PCI/CABG
Severe	↓ EF, 3-vessel or left main	Likely CABG

🚫 10. Contraindications You Must Remember

- **β-blockers contraindicated** in **variant angina**
- **CCBs avoided** in **reduced EF**
- Don't rely on normal ECG to rule out ischemia