DEFINITIONS

- **IHD**: ↓ O₂ or blood supply to myocardium resulting from coronary artery narrowing or obstruction.

- **IHD may be asymptomatic or present as**:
  
  1. **Angina**:
     - Stable (exertional) angina
     - Vasospastic (variant or Prinzmetal) angina.
     - Unstable angina (US angina) [preinfarction angina]
  
  2. **Myocardial infarction (MI)**:
     - Non-ST-segment elevation MI (NSTEMI)
     - ST-segment elevation MI (STEMI)

**NB.: Acute coronary syndrome (ACS):** include US angina & MI
ETIOLOGY

(Imbalance between $O_2$ supply & $O_2$ demand)

1. **↓ quantity of coronary blood:** Atherosclerosis, thrombosis, spasm
2. **↓ quality of coronary flow:** Anemia
3. **↑ cardiac muscle demand that cannot be compensated**
   Severe exercise, tachycardia, thyrotoxicosis

- **Predisposing factors for atherosclerosis**
  1. Hereditary
  2. Smoking
  3. HTN
  4. DM
  5. Dyslipidemia
  6. Obesity

MANIFESTATION

- **Chest pain:**
  - **Site:** Retrosternal chest pain on exertion (?????) or rest (????). The pain may radiate to shoulder, left arm, or jaw.
  - **Type:** tightness, squeezing or burning
  - **Duration:** 0.5 – 30 minutes.
  - **Associated symptoms:** May be associated with SOB or vomiting

- **Signs:**
  - No specific signs.
  - However, ACS may present with signs of acute HF or arrhythmias.
DIAGNOSIS

1. **Laboratory tests**: Hb and fasting glucose & lipoprotein.
2. **ECG** is normal in about 50% of patients with angina.
3. **Stress ECG** or Exercise tolerance testing (ETT)
4. **Echocardiography**
5. **Pharmacologic stress echocardiography** (e.g., dobutamine, dipyridamole, or adenosine): In patients unable to exercise.
6. **Biochemical markers of MI**: Both troponins & CK-MB are detectable within 6 h of MI. Troponins remain elevated for up to 10 d, whereas CK-MB returns to normal within 48 h.
7. **Cardiac catheterization** & coronary angiography

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**1- Treatment of stable angina**

**Risk factor & life style modification**
- 1- Treat:
  - Obesity
  - Hyperlipidemia
  - DM
- 2- ↑ Physical activity
- 3- ↓ Smoking
- 4- Diet:
  - ↑ Vegetables & fruits
  - ↓ Saturated fats

**Pharmacological**
- 1- Organic nitrates
- 2- BB
- 3- CCB
- 4- Ranolazine
- 5- Antiplatelets

- **Short term goal**: relief of symptoms
- **Long term goal**: prevents sequences & complications (MI, arrhythmia, HF)
Organic nitrates

- **Mechanism of action:**
  - Nitrates (in the presence of SH group of tissues) $\rightarrow$ NO $\rightarrow$ GC $\rightarrow$ c.GMP $\rightarrow$ spasmytic & down platelet aggregation
  - It $\downarrow$ Cardiac work & $O_2$ consumption indirectly through:
    - Powerful venodilator $\rightarrow$ down preload
    - Mild arteriodilator $\rightarrow$ down afterload

- **Indications:**
  - 1st line in acute attack
  - May be used in prophylaxis, usually in combination with BB or CCB

Side effects

1. Allergy
2. **Headache** (the most common side effect & can be prevented by acetaminophen 15 – 30 min. prior to administration)
3. Hypotension $\rightarrow$ reflex tachycardia [add BB or CCB (Verapamil)]
4. Postural Hypotension $\rightarrow$ syncope
5. **Tolerance** $\rightarrow$ due to depletion of SH group & can be avoided by:
   - Allow 8-10 hours nitrate free / day or
   - Alternate with other antianginal every 2 weeks
6. Dependence $\rightarrow$ never stop suddenly
7. Formation of met hemoglobin
8. Formation of nitrosamine $\rightarrow$ carcinogenic
Preparations:

<table>
<thead>
<tr>
<th></th>
<th>Glyceryl trinitrate (nitroglycerine)</th>
<th>Isosorbid dinitrate (Isodril)</th>
<th>Isosorbid mononitrat (Imdur)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Sublingual</td>
<td>Dose: 0.5mg/15 min max. 3 dose</td>
<td>5 mg</td>
<td></td>
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<tr>
<td></td>
<td>Onset: 1-3 min</td>
<td>1-3 min</td>
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</tr>
<tr>
<td></td>
<td>Duration: 10-30 min</td>
<td>1 hour</td>
<td></td>
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<tr>
<td>2) Buccal</td>
<td>Dose: 0.4 / metered dose</td>
<td>1¼ / metered dose</td>
<td></td>
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<tr>
<td></td>
<td>Duration: 10-30 min</td>
<td>1½ hour</td>
<td></td>
</tr>
<tr>
<td>3) Oral</td>
<td>Dose: 6 ¼ - 12 ½ mg 2-4 times /d</td>
<td>10-40 mg t.d.s /4-6 h</td>
<td></td>
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<tr>
<td></td>
<td>Duration: 4-8 h</td>
<td>10-40 mg/ 12 h</td>
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<tr>
<td>4) T.D.S</td>
<td>- Ointment 2%</td>
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<tr>
<td></td>
<td>- Patch</td>
<td></td>
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<td></td>
<td>Dose: 1-1½ inch/4h</td>
<td></td>
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<tr>
<td></td>
<td>Duration: 3-6 h</td>
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<tr>
<td></td>
<td>Dose: One patch 25 mg /day</td>
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<tr>
<td></td>
<td>Duration: 8-12 h</td>
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**BETA BLOCKERS**

**Mechanism of action:**
1. −ve inotropic & chronotropic → ↓ cardiac work & O₂ consumption
2. −ve chronotropic (Bradycardia) → ↑ diastolic time → ↑ coronary perfusion time
3. antihypertensive effect → ↓ after load

- **NB.**
  - BB does not produce coronary V.D & non selective may cause even V.C [contra indicated in variant]
  - BB with ISA may be detrimental in patients with rest or severe angina (??)

**Classification & Side effects:** see before
- **Indications of BB:**
  1. 1st line in stable angina requiring daily maintenance therapy
  2. coexisting
     - 1. hypertension,
     - 2. supraventricular arrhythmias,
     - 3. postmyocardial infarction angina
     - 4. anxiety

- **Treatment objectives:**
  - ↓ resting HR to 50 - 60 beats/min
  - ↓ maximal exercise HR to 100 beats/min or less.

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**CALCIUM CHANNEL BLOCKERS**

- **Mechanism of action:**
  - VD of systemic arterioles & coronaries (nifedipine & amlodipine) ⇒ ↓ arterial pressure & coronary vascular resistance
  - –ve intotopic (Verapamil & diltiazem) ⇒ ↓contractility & \( O_2 \)

- **NB.:**
  - Reflex adrenergic stimulation overcomes much of the –ve inotropic effect,
  - –ve inotropic effect becomes clinically apparent only in:
    - the presence of LV dysfunction
    - when other –ve inotropics are used concurrently

- **Side effects & classification:** see before
Indications:

- Patients with contraindications to β-blockers: eg:
  1. Prinzmetal angina (CCB is the 1st choice)
  2. Concurrent:
     1. PVD,
     2. Severe ventricular dysfunction,
        (Amlodipine is the agent of choice in severe ventricular dysfunction & the other dihydropyridines should be used with caution if the EF is <40%)

- Concurrent hypertension

- NB.: coexisting conduction system disease excluding the use of verapamil & diltiazem

RANOLAZINE (Ranexa)

- Mechanism of action:
  - may be related to ↓ in Ca** overload in ischemic myocytes through inhibition of the late Na+ current.

- Indications:
  - should be reserved for patients who have not achieved adequate response to other antianginal drugs (because it prolongs QT interval)
  - Should be used in combination with amlodipine, βB, or nitrates.

- Dosing:
  - started at 500 mg twice daily & increased to 1 g twice daily if needed.

- Side effects:
  - Headache, constipation & nausea.
  - QT interval prolongation (baseline & follow up ECG should be obtained)
ANTIPLATELETS

Aspirin Small Dose (75-162 mg):
selective ↓ of platelet thromboxane $A_2$

Clopidogrel & Ticlopidine
Block ADP receptors
- Clopidogrel (Plavix): 75 mg
  - Used when aspirin is contraindicated
  - May be added to aspirin for 1 year
    (esp in patient undergoing PCI)
- Ticlopidine (Ticlid, Tilopin):
  used only if clopidogrel not available

Recommendations
- All patients with CAD should be given the following unless contraindications exist:
  1. Aspirin (Clopidogrel may be used if aspirin is contraindicated)
  2. ACEI to patients with diabetes or LV dysfunction
  3. β-Blockers with prior MI
  4. CCB or long-acting nitrates when βB are contraindicated OR failed
  5. Cholesterol (LDL) lowering therapy if LDL >130 mg/dL
  6. SL nitroglycerin for immediate relief of angina

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2- Treatment of variant angina

- **Acute attack:**
  - should be treated with nitrates

- **Prophylactic treatment for 6 -12 m:**
  - CCB (the drug of choice)
  - Long acting Nitrates
  - *NB: Avoid BB*

3- Treatment of acute coronary syndrome

- **General treatment**
- **Early therapy or CABG**
- **2ry prevention of MI**

1- Hospitalization & bed rest
2- O₂ (if saturation is < 90%)
3- Analgesics (morphine)
4- stools softeners to avoid Valsalva maneuver,
5- continuous ST-segment monitoring for arrhythmias & ischemia
**EARLY THERAPY**

**Early therapy for UA & NSTEMI**
1. SL NTG (or IV)
2. Antiplatelet (as aspirin)
3. Anticoagulant (UFH, LMWH [enoxaparin]).
4. β-blocker (orally, IV therapy optional);

**Early therapy for STEMI**
1. Reperfusion therapy: treatment of 1st choice:
   - Thrombolytics or PCI
2. SL NTG (or IV)
3. Antiplatelet (as aspirin)
4. anticoagulant (UFH, LMWH [enoxaparin]).
5. β-blocker (orally, IV therapy optional);
6. ACEI should be started within 24 h of presentation, esp. if EF ≤40%.

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**PCI (Percutaneous coronary artery intervention)**

A guide wire with a deflated balloon is passed through the catheter in the narrowed artery.

The balloon is then inflated to open the narrowed artery and the stent expands around the balloon.

The stent is removed and the stent is left in place to keep the artery open.

Dr. Ahmed Elberry, MD
2ry prevention after MI

1. SL NTG or lingual spray (PRN)
2. Antiplatelet therapy (Aspirin & Clopidogrel)
3. Anticoagulant therapy: warfarin for Selected patients (TED or history of TED, chronic AF)
4. β-blocker,

5. ACE inhibitor.
6. Annual influenza vaccination.

7. Control of risk factors as HTN, dyslipidemia & DM
   - Statins are the preferred agents for lowering LDL-C and should be prescribed at or near discharge in most patients.
   - Fibrates or Niacin should be considered in selected patients with low HDL-C (<40 mg/dL) and/ or TG (>200 mg/dL).

Thrombolytics

- Indications:
  - Should be considered in patients with persistent symptoms of ischemia who present within 12-24 hours of symptom onset.
  - It is preferred over PCI in patients presenting within 3 hours of symptom onset when there would be a delay in performing PCI.

- They include:
  1. Streptokinase (Obtained from streptococci)
  2. Anistreplase
  3. Urokinase
  4. Tissue plasminogen activator (t-PA): eg.: Alteplase
  5. t-PA analogue (long t½ allowing IV bolus). eg.: Reteplase - Tenecteplase
Side effects of thrompoliytics:
1- Bleeding (The most important & most common)
2- Allergy (especially with Streptokinase)
3- Fever

<table>
<thead>
<tr>
<th></th>
<th>Streptokinase (Streptase)</th>
<th>Alteplase (Activase)</th>
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<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>bind to plasminogen to form a complex &amp; this complex converts Plasminogen to Plasmin (fibrinolysin)</td>
<td>activate plasminogen that is bound to fibrin onto plasmin (it is fibrin selective)</td>
</tr>
<tr>
<td><strong>t₁/₂</strong></td>
<td>&lt; 30 min.</td>
<td>&lt; 5 min.</td>
</tr>
</tbody>
</table>

**DOSING:**

- **Streptokinase:** 1.5 million U in 50 mL of normal saline IV over 60 min.

- **Alteplase:** 15-mg IV bolus followed by 0.75-mg/kg infusion over 30 min, followed by 0.50 mg/kg infusion over 60 min.

- **Reteplase:** 10 U IV over 2 min, followed 30 min later with another 10 U IV over 2 min.

- **Tenecteplase:** A single IV bolus dose given over 5 seconds based on patient weight:
  - 30 mg if <60 kg;
  - 35 mg if 60 to 69.9 kg;
  - 40 mg if 70 to 79.9 kg;
  - 45 mg if 80 to 89.9 kg;
  - 50 mg if 90 kg or greater.
Contraindications

Absolute CI:
(1) active internal bleeding
(2) intracranial neoplasm
(3) structural vascular lesion
(4) suspected aortic dissection
(5) previous ICH at any time
(6) closed head trauma within 3 ms
(7) ischemic stroke within 3 ms

Relative CI:
(1) severe, uncontrolled HTN (>180/110 mm Hg)
(2) Current anticoagulant use;
(3) bleeding tendency
(4) pregnancy;
(5) active peptic ulcer;
(6) history of ischemic stroke longer than 3 ms
(7) major surgery within 3 ws;
(8) recent (within 2-4 ws) internal bleeding
(9) for streptokinase, prior administration (<5 days) or prior allergy

Primary PCI is preferred in these situations.

ANTIPLATELET THERAPY

1. **Drugs acting on Arachidonic acid metabolism:**
   1. ↓ Thromboxane A₂ synthesis
      Aspirin Small Dose (75-325 mg)
   2. Prostacyclin analogue:
      Epoprostenol but very short t ½

2. **Drugs acting on platelet receptors:**
   1. Block ADP receptors As:
      Clopidogrel & Ticlopidine
   2. Block GP IIb /IIIa receptors:
      Abciximab – Tirofiban – Eptifibatide
ASPIRIN

- **Indications:**
  - All patients without contraindications within the first 24 h of hospital admission.
  - For patients undergoing PCI

- **Dosing:**
  - 162 - 325 mg, chewed & swallowed as soon as possible.
  - Maintenance dose of 75 - 162 mg.

Thienopyridines

- **Clopidogrel (Plavix)**
  - **Indications:**
    - patients with aspirin allergy.
    - In combination with aspirin to reduce morbidity & mortality esp in patient undergoing PCI (for 1 year)
  - **Dose:** A 300- 600 mg loading dose on 1st hospital day, followed by a maintenance dose of 75 mg daily.
  - **Side effects:**
    - nausea, vomiting, & diarrhea (5% of patients).
    - Thrombotic thrombocytopenia purpura (rarely).
    - Hemorrhage (MOST SERIOUS).

- **Ticlopidine (Tilopin)**
  - is associated with neutropenia that requires frequent monitoring of the CBC during the 1st 3 months of use.
Glycoprotein IIb/IIIa Receptor Inhibitors

- **Abciximab** *(ReoPrp)* is preferred over **eptifibatide** & **tirofiban** because it is the most widely studied agent.

- **Benefit:**
  - Abciximab, in combination with aspirin, thienopyridine, & UFH reduces mortality and reinfarction.

- **Dose:**
  - 0.25 mg/kg IV bolus given 10-60 min before the start of PCI, followed by 0.125 mcg/kg/min (maximum 10 mcg/min) for 12 h.

- **Side effects:**
  - Bleeding
  - Thrombocytopenia

**GOOD LUCK**

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