Ischemic Heart Disease (IHD)
Definition

anskhon = strangling
pectis = chest

**basic cause:**
coronary blood flow failure to meet myocardial oxygen requirements (myocardial ischemia):

- $\uparrow O_2$ demand (physical activity)
- $\downarrow O_2$ supply (blood flow obstructed)
Pathophysiology

O₂ supply
- coronary blood flow
- O₂ availability

O₂ demand
- heart rate
- contractility
- cardiac wall tension
Pathophysiology

O₂ supply
- coronary blood flow
- O₂ availability

O₂ demand
- heart rate
- contractility
- cardiac wall tension

IHD
Clinical presentation

- **chest discomfort:**
  - pressure/tightness
  - burning
  - choking/breathlessness
  - pain

- **discomfort at other sites:**
  - epigastrum
  - shoulders/arms
  - neck/jaw

- **nausea**

- **diaphoresis**

**duration:**
- typically 1-5 minutes
- range 15sec-15min
Angina classification

1. stable (typical) angina

- the most common form of angina
- consequence of coronary atherosclerosis
- presents in physical activity, emotional stress etc.
- predictable, reproducible (exertion)
- worse in cold conditions and after meals
2. unstable angina (crescendo/pre-infarction angina)

- intermediate state between stable angina and MI
- a presentation of “acute coronary syndromes” (ACS)
- may appear unexpectedly, at rest
- often not associated with physical activity
- usually a consequence of severe coronary atherosclerosis possibly complicated by a rupture and thrombus formation
- management similar to that of MI
Angina classification

3. Prinzmetal angina (variant/vasospastic angina)

- an uncommon form of angina
- consequence of coronary artery spasm
- occurs at rest
- patients may be younger, with lower risk
- typical ECG profile
## Angina classification

Insufficient blood flow to the heart muscle from narrowing of coronary artery may cause chest pain.

<table>
<thead>
<tr>
<th>coronary artery obstruction</th>
<th>angina</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>potential</td>
</tr>
<tr>
<td>70%</td>
<td>stable (exercise-induced)</td>
</tr>
<tr>
<td>90%</td>
<td>unstable (at rest)</td>
</tr>
</tbody>
</table>
Angina classification

Risk factors

- smoking
- HTN
- hyperlipidemia
- diabetes
- overweight
- sedentary lifestyle
- family history
- male gender
Non-pharmacological Tx

**lifestyle modifications**

- increased, controlled physical activity (exercise training)
- smoking cessation
- weight management, balanced diet

**invasive interventions**

- PCI - percutaneous coronary intervention:
  - balloon angioplasty
  - stent placement
- CABG - coronary artery bypass grafting
- EECP - enhanced external counter-pulsation
Pharmacotherapy

Three major drug classes:

- β-blockers
- organic nitrates
- CCBs
Pharmacotherapy

Three major drug classes:

- β-blockers
- organic nitrates
- CCBs
Pharmacotherapy

β-blockers

cardiac $\beta_1$ receptor antagonism

- blood pressure
- myocardial contractility

- myocardial O2 demand

- relief of angina symptoms
Pharmacotherapy

β-blockers - clinical considerations

• 1\textsuperscript{st} line in stable angina
• long-acting $\beta_1$-selective preferred (atenolol, metoprolol)
• anti-anginal effect is dose-dependent
• titrate dose to alleviate symptoms and HR=50-60, considering ADEs
• very effective in prevention of exertional angina
• reduce morbidity and mortality (post-MI)
• ineffective, \textit{potentially harmful} in Prinzmetal angina (induction of vasospasms)
Pharmacotherapy

Three major drug classes:

• β-blockers
• organic nitrates
• CCBs
Pharmacotherapy

Organic nitrates:

- nitroglycerin (NTG)
Pharmacotherapy

Organic nitrates:

- nitroglycerin (NTG)
- isosorbide dinitrate (ISDN)
- isosorbide mononitrate (ISMN)

IHD
Pharmacotherapy

Organic nitrates - mechanism of action

Endogenous sources
- arginine + $O_2$

Nitric oxide (NO)
- nitrite
- vascular smooth muscle relaxation
- venous and coronary vasodilation
- small hypotensive effect
- minor effect on arteries

Nitrate
- ISDN
- ISMN
- NTG

IHD
Pharmacotherapy

Organic nitrates:

- nitroglycerin (NTG):
  

- isosorbide dinitrate (ISDN):
  
  \textit{Isoket}® \textit{(spray)}, \textit{Cordil}®, \textit{Isolong}®

- isosorbide mononitrate (ISMN):
  
  \textit{Monolong}®, \textit{Mononit}®, \textit{Monocord}®
Pharmacotherapy

Organic nitrates - ADEs:

- headache
- facial flushing
- hypotension
- bradycardia

Organic nitrates - DDIs:

- PDE-5 inhibitors (sildenafil = Viagra®, severe hypotension)
- alcohol (hypotension)
Pharmacotherapy

Organic nitrates - use:

<table>
<thead>
<tr>
<th>nitrate</th>
<th>clinical use</th>
<th>mode of administration</th>
<th>onset of effect</th>
<th>duration of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTG</td>
<td>acute angina</td>
<td>sublingual/IV</td>
<td>rapid</td>
<td>short</td>
</tr>
<tr>
<td></td>
<td>chronic angina</td>
<td>transdermal</td>
<td>rapid</td>
<td>long</td>
</tr>
</tbody>
</table>
Pharmacotherapy

**Organic nitrates - tolerance:**

**presentation:**

- reduced effect following long-term use
- effect restored after “nitrate-free interval”

**proposed mechanisms:**

- decrease in NO formation
- decrease in NO effect
- activation of vasoconstricting RAAS
Pharmacotherapy

Organic nitrates - tolerance:

prevention:

• asymmetrical dosing allowing for 8-12hr “nitrate-free intervals”:

<table>
<thead>
<tr>
<th>nitrate</th>
<th>dosage form</th>
<th>recommended dosing regimen</th>
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<tbody>
<tr>
<td>ISDN</td>
<td>IR</td>
<td>BID: 7/12; TID: 7/12/17</td>
</tr>
<tr>
<td></td>
<td>SR</td>
<td>BID: 8/14; OD: morning</td>
</tr>
<tr>
<td>ISMN</td>
<td>IR</td>
<td>BID: 8/15</td>
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<td></td>
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<td>OD: morning</td>
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IR/SR: immediate/sustained release; OD - ×1/d; BID - ×2/d; TID - ×3/d
Pharmacotherapy

Organic nitrates - clinical considerations:

- sublingual NTG/ISDN for acute angina and for prophylaxis
- ISDN/ISMN for chronic angina: daytime for exertional angina, nighttime for nocturnal angina
- prevention of nitrate tolerance
- improve exercise duration; not shown to ↓ mortality
Pharmacotherapy

**Three major drug classes:**

- β-blockers
- organic nitrates
- CCBs
Pharmacotherapy

CCBs

- peripheral vasodilation
- coronary vasodilation
- negative chronotropic effect
- negative inotropic effect
Pharmacotherapy

**CCBs - subclasses**

Dihydropyridines (nifedipine, amlodipine)

- arterial vasodilation
- minimal effect on cardiac rate/conduction
- avoid short acting (BP drop, reflex tachycardia, ↑ mortality)

<table>
<thead>
<tr>
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<th>diltiazem</th>
<th>verapamil</th>
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<tr>
<td><strong>cardiac</strong> Ca$^{++}$ channels</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>vascular</strong> Ca$^{++}$ channels</td>
<td>+++</td>
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<td>+</td>
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IHD
Pharmacotherapy

CCBs - subclasses

Non-dihydropyridines: verapamil (phenylalkylamine)

- cardiac conduction effect  >  vasodilating effect
- negative chronotrope/inotrope

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Avoid in cardiac depression

IHD

Less headache, edema...
Pharmacotherapy

CCBs - subclasses

Non-dihydropyridines: diltiazem (benzothiazepine)

• intermediate properties

• coronary vasodilator (mild arterial vasodilator);
  negative chronotrope (not negative inotrope)

• useful in variant angina (relieves coronary artery spasm)

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Pharmacotherapy

![Graph showing cumulative procedure rate percent over months for Placebo and Amiodipine.](image)
Pharmacotherapy

ACEIs in stable angina?

- some ACEIs have been shown to ↓ M&M
- mechanism of benefit unclear
  - anti-inflammatory effect in plaque?
  - reduction of LV hypertrophy
- consider adding in non-responders
- no clinical evidence regarding ARBs
Pharmacotherapy

**Anti-platelet Tx in stable angina?**

- for prevention of thrombus formation
- aspirin generally accepted for 1°/2° prevention
- also indicated in unstable angina
- addition of clopidogrel
Pharmacotherapy

Stable angina

- 1st-line: β-blocker (prevent progression to MI)
- combine as needed with nitrate/CCB
  - nitrates advantageous in LV dysfunction
  - CCBs advantageous in HTN
- triple therapy as needed
- consider ACEI
Pharmacotherapy

Unstable angina (non-acute Tx)

- 1st-line: β-blocker (prevent progression to MI)
- nitrate
- CCB - for refractory cases
- aspirin +/- clopidogrel
- statin
- ACEI (ARB)
- aldosterone antagonist in some
Pharmacotherapy

Prinzmetal angina

• 1\textsuperscript{st}-line: CCBs (antispastic effect)
• if uncontrolled - combine a nitrate
• β-blockers not indicated (may induce vasospasms)
Myocardial infarction

Pathophysiology

- deterioration of unstable angina
- atherosclerotic thrombus formation
- complete occlusion of coronary artery
- massive cellular necrosis/death
- rarely caused by vasospasms w/o atherosclerosis
Myocardial infarction

Presentation

• chest pain, may radiate to arms/neck/jaw etc.
• shortness of breath
• diaphoresis
• nausea
• ~20% “silent MI”
Myocardial infarction

Diagnosis

- symptoms
- ECG
- cardiac enzymes
Myocardial infarction

Pharmacotherapy

- thrombolytics
- antiplatelet/anticoagulant Tx
- β-blockers
- CCBs
- nitrates
- anti-arrhythmics
- analgesics
- stool softeners
DRUGS FOR EXAM

• isosorbide mononitrate