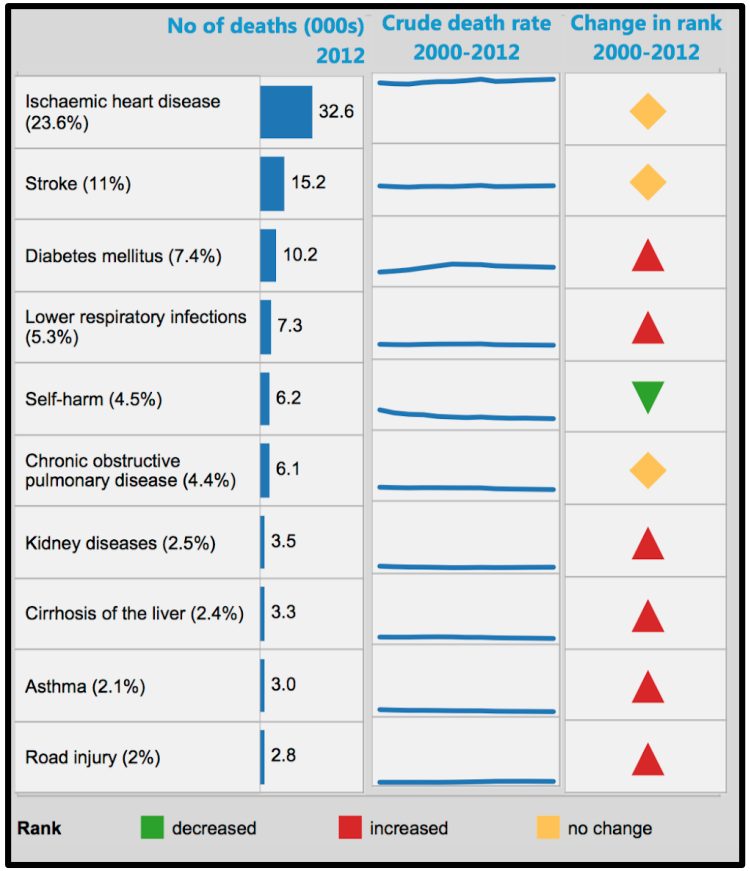
Ischaemic Heart Disease (IHD) and Acute Coronary Syndromes (ACS)

Bridget O’Brien

Lecture Objectives:

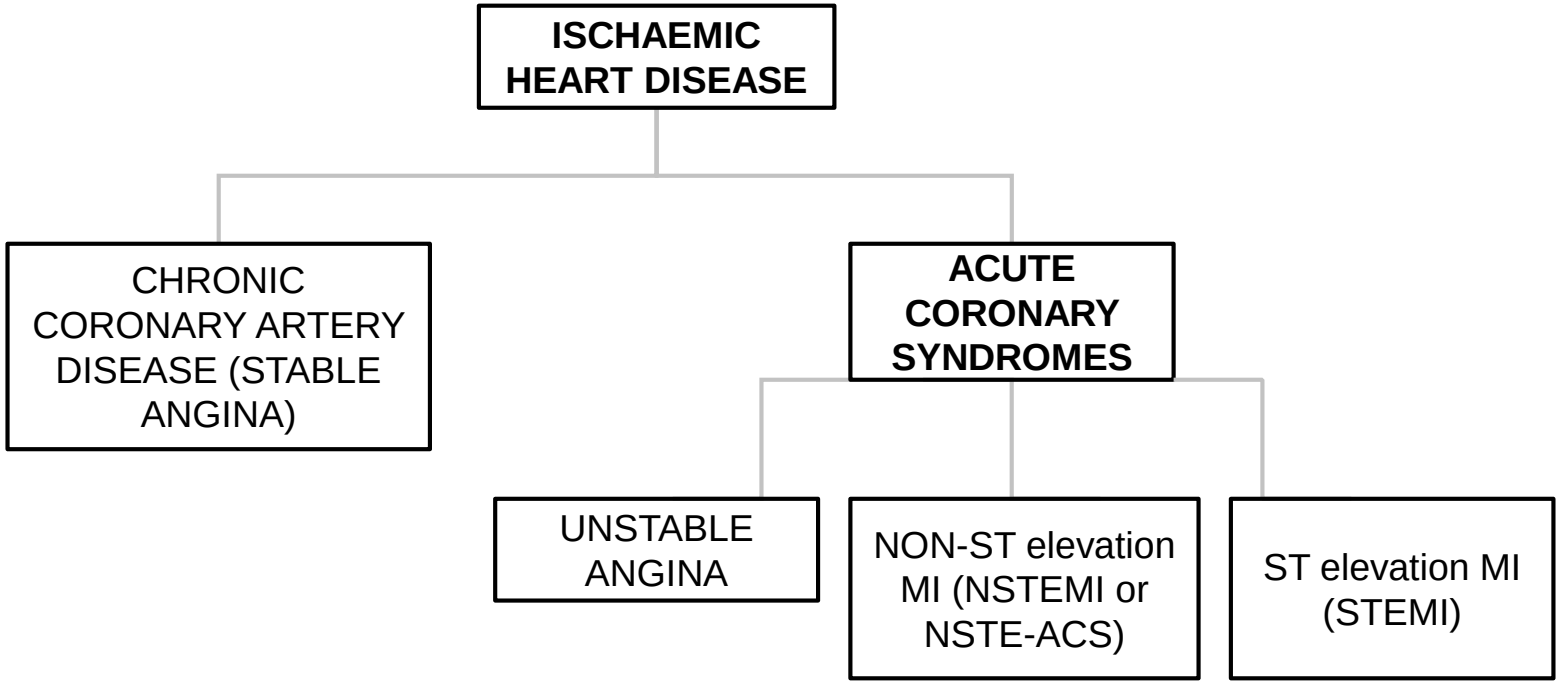
- Classify ischaemic heart disease (IHD) and risk factors.
- Discuss acute coronary syndrome (ACS) types & diagnostics.
- Review medication therapies involved in management of ACS.
- Discuss lifestyle modifications recommended in IHD.
- Review key counselling points and the role of a pharmacist in patient care.

Top 10 Causes of Death in Sri Lanka:



WHO Statistical Profile 2015

Ischaemic Heart Disease:



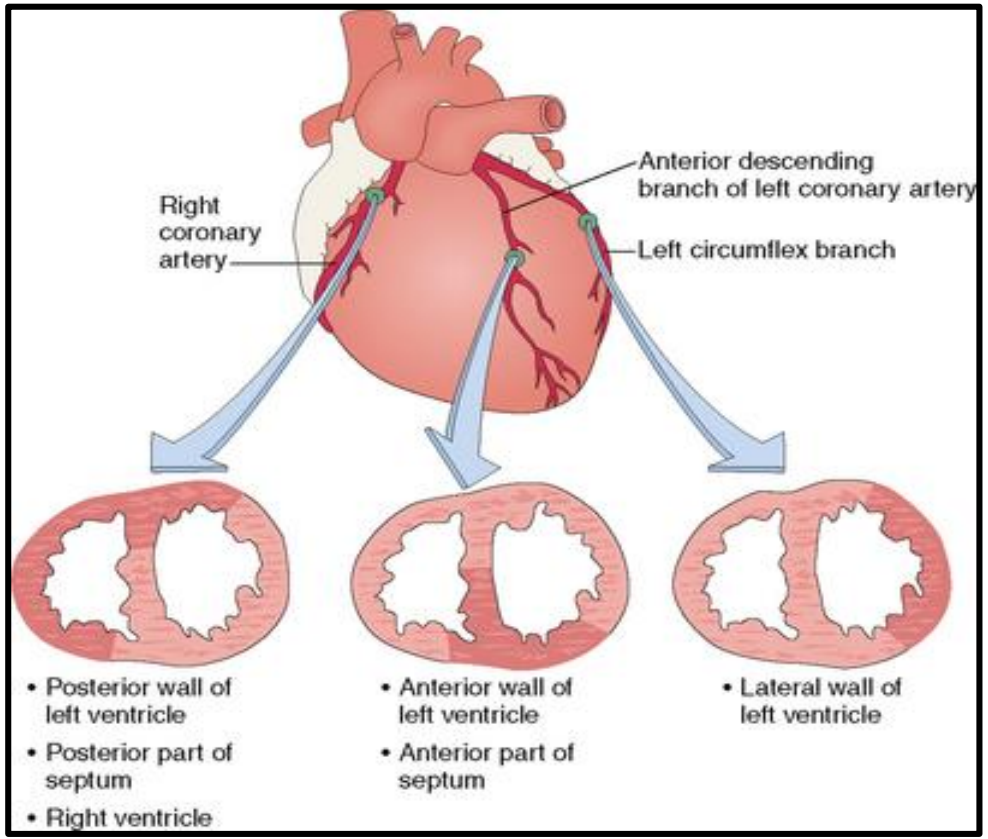
Simple (!) Coronary Vasculature Anatomy:

Right coronary artery (RCA)

Left coronary artery

-Left anterior descending (LAD)

-Left circumflex artery (LCX)



Pathophysiology of IHD:

Cardiac ischaemia = imbalance between myocardial oxygen **supply** and **demand**.

No oxygen → muscle cell death.

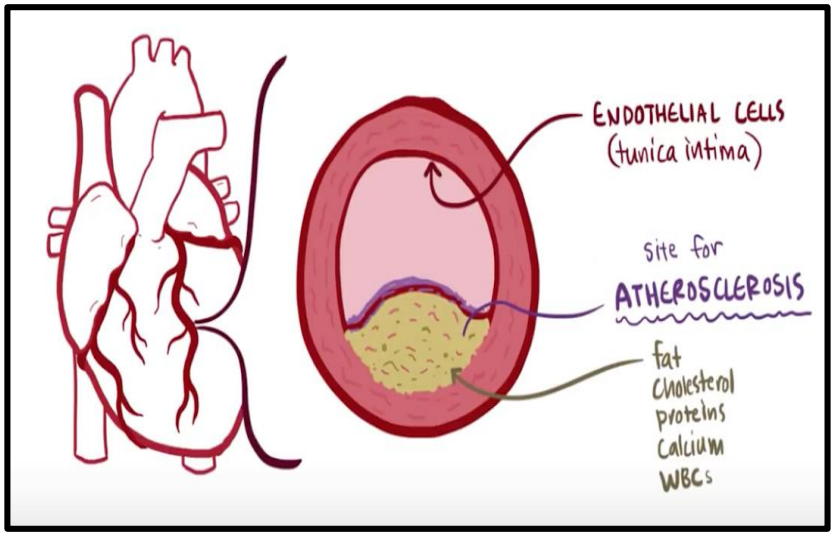
Typically caused by rupture or erosion of an atherosclerotic plaque, followed by the formation of a platelet-rich thrombus.

Ischaemia less typically occur secondary to other causes not associated with atherosclerotic plaques.

Reduced Coronary Flow: Coronary Atherosclerosis

Atherosclerosis (hardening of an artery due to an atherosclerotic plaque) → thought to be triggered by physical or chemical insults to artery endothelium.

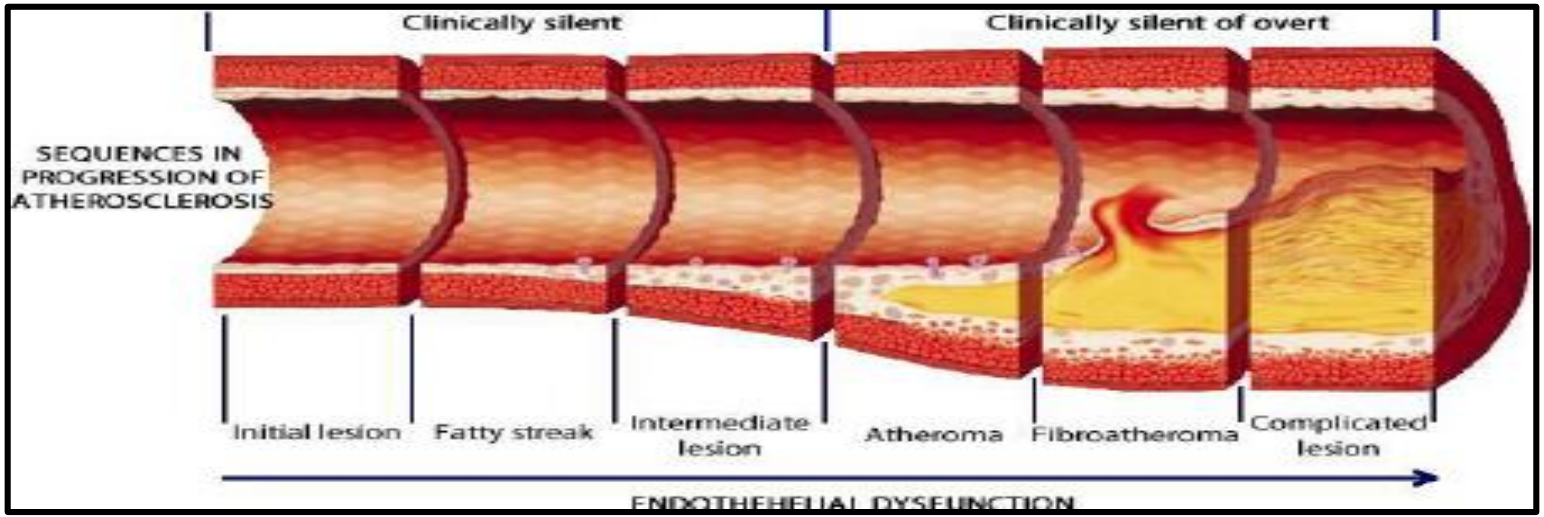
- Trauma/hypertension
- Smoking/air pollutants
- Hyperlipidaemia
- Chronically elevated blood glucose levels
- Turbulent blood flow
- Genetic factors



Risk factors for IHD:

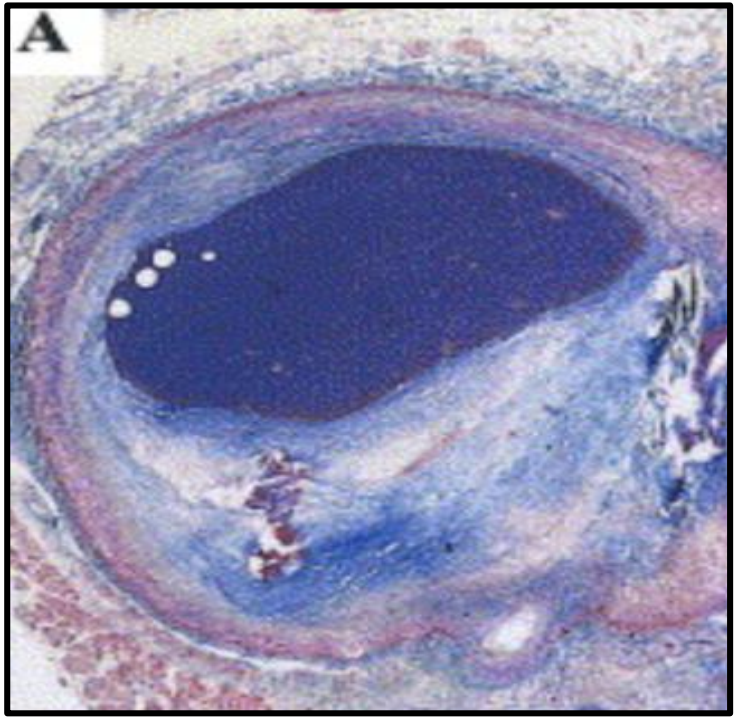
MODIFIABLE RISK FACTORS (the things we can help with!) 👍	NON-MODIFIABLE RISK FACTORS (the things we can't change) 👎
Smoking	Increased age
Dyslipidaemia	Being male
Hypertension	Family/personal history of cardiovascular disease
Diabetes (insulin dependent + non-insulin dependent)	Post-menopausal women
Obesity	
Physical inactivity	

Progression of Atherosclerosis:

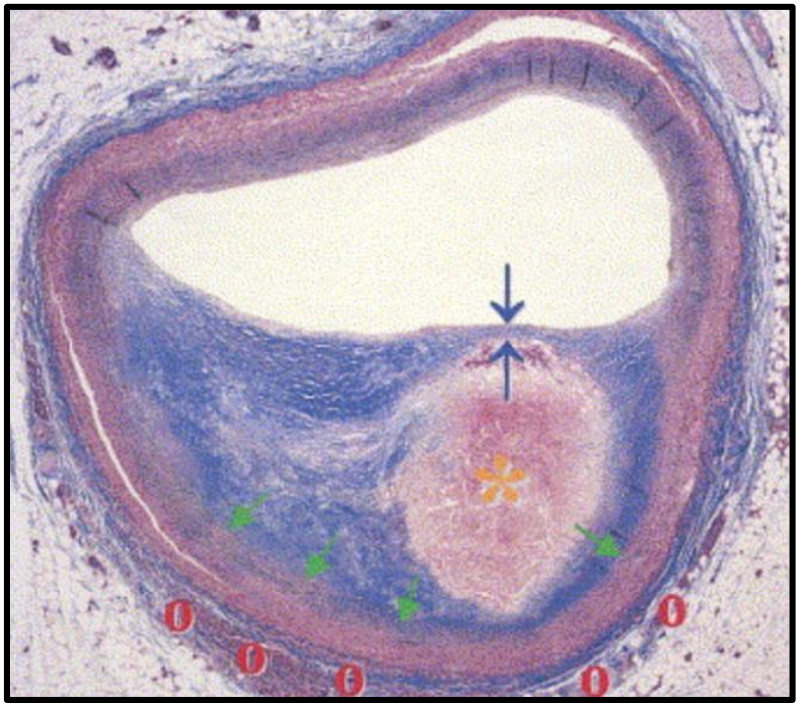


Atherosclerosis is an ongoing process, mainly affecting large and medium sized arteries.

Atherosclerotic Plaques:



Stable plaque - fibrotic and partly calcified atherosclerotic plaque (angina)



Rupture-prone plaque showing a large lipid rich necrotic core and thin fibrous cap (unstable angina)

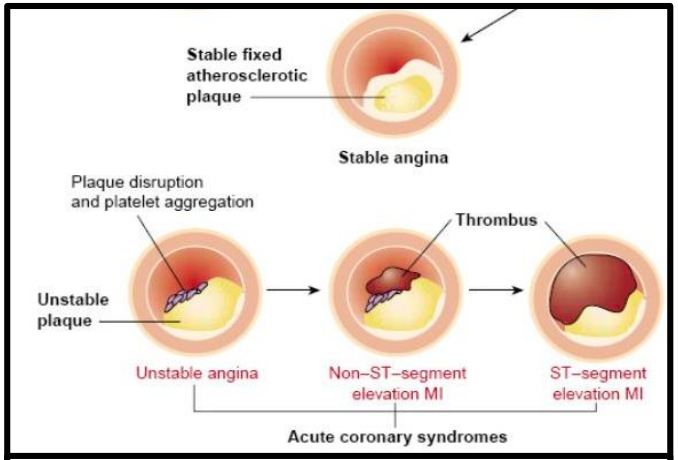
Clinical Manifestations of IHD:

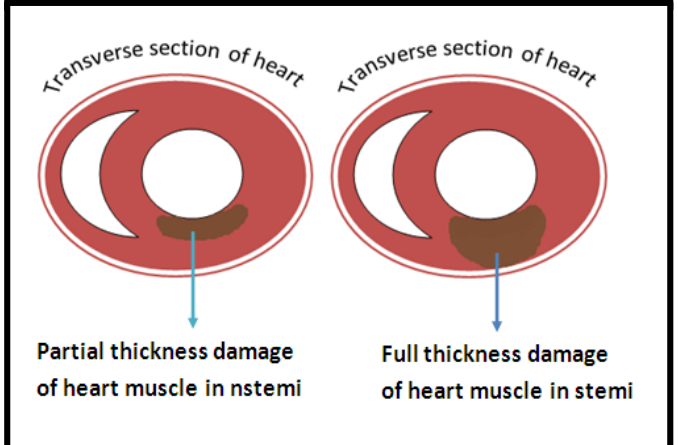
Chronic stable angina:
Chest pain at **reproducible** workloads (ie. walking up a flight of stairs) that is **relieved with rest.**

Unstable angina:
Increased *frequency* or *severity* of chest pain that occurs abruptly **AT REST.**

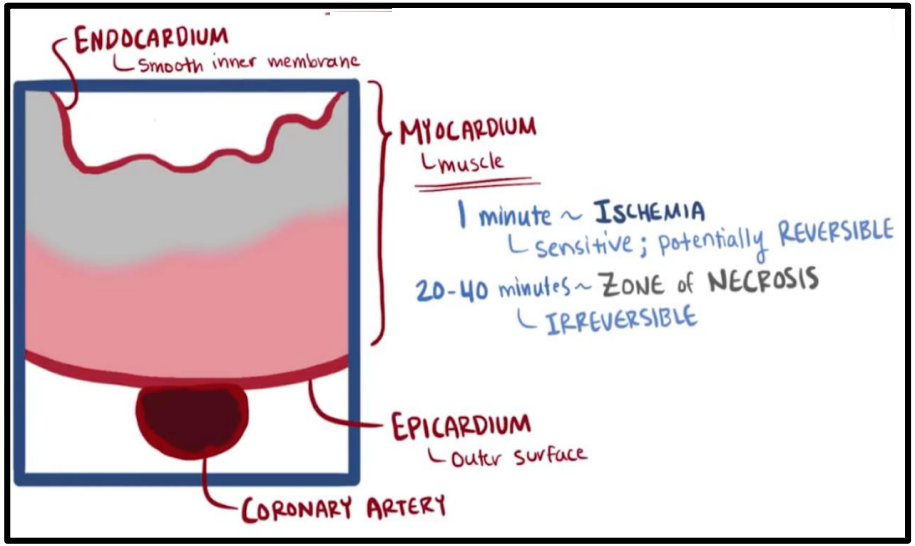
Non-ST elevation ACS (NSTEMI):
Thrombus significantly compromises but does not completely occlude the coronary artery = PARTIAL thickness damage to heart muscle.

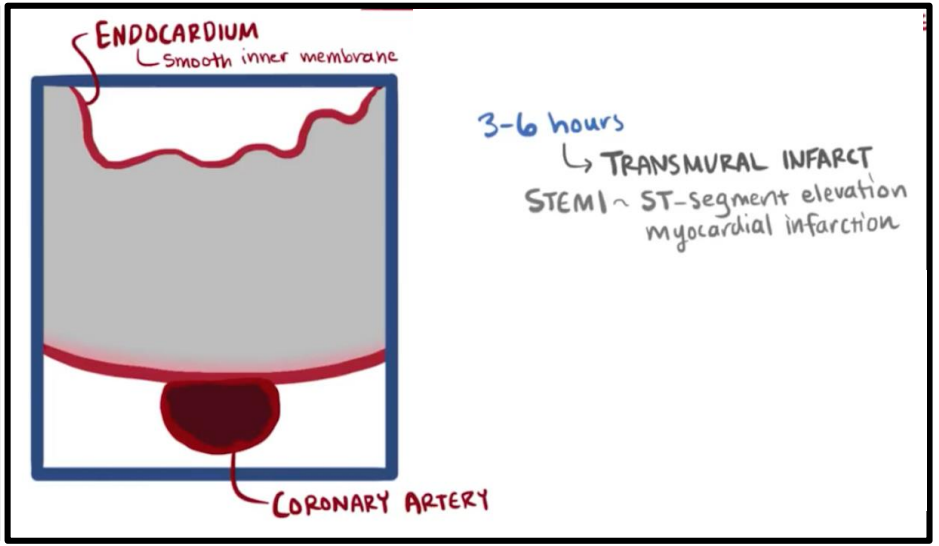
ST elevation ACS (STEMI):
Thrombus **completely** occludes the coronary artery at the site of plaque rupture. No blood flow beyond the point of obstruction = FULL thickness damage to heart muscle.





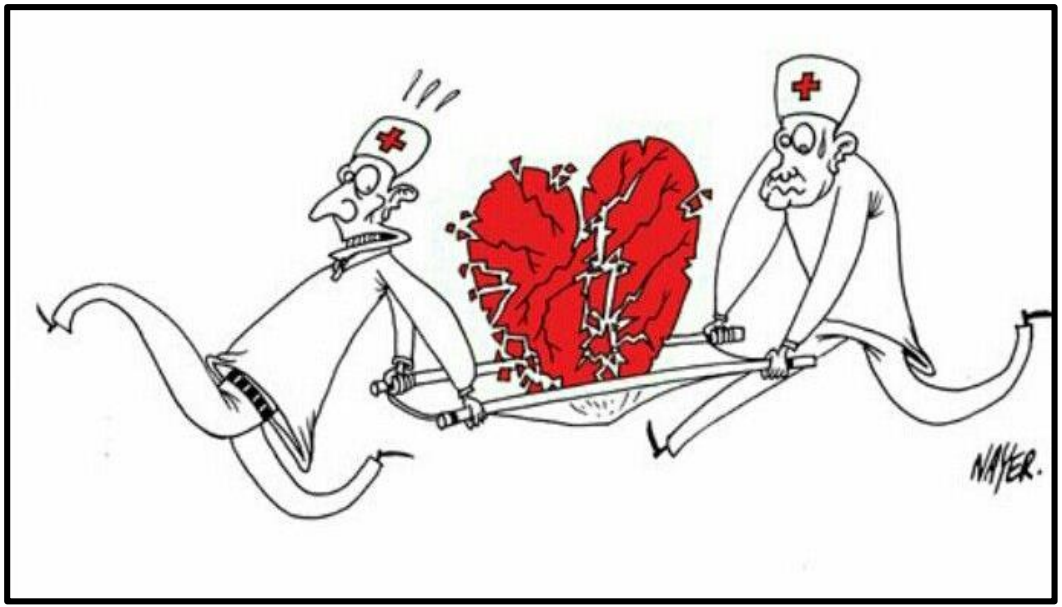
Remember (!!) Time = Muscle:





Acute Coronary Syndromes:

- Unstable angina
- NSTEMI
- STEMI



Case 1: Mr IR

55 year old male presented to hospital with sudden onset chest pain (radiating to arm) and tightness while on evening walk; pain persisted despite rest.

Smoker ~10/day; ETOH ~6 standard drinks/night Saturday + Sunday; Weight 109kg

Nil known drug allergies

<u>PMHx:</u>
HTN (perindopril 5mg / amlodipine 5mg mane)
Hypercholesterolaemia (no treatment)
Gout (allopurinol 400mg mane)

<u>Family Medical History:</u>
Mother had triple CABG ~ 65 years.

QUESTIONS

1. What risk factors does Mr IR possess?

   Smoker; HTN; dyslipidaemia; obesity; male; family history

2. What could be an initial differential diagnosis based on his presenting complain, risk factors and family history?

   Abrupt and ongoing chest pain not relieved by rest + risk factors + family history. Further investigation required. Consider ACS.

3. What initial diagnostics do you think would be required to confirm ACS?

   - Symptoms (+risk factors)
   - 12-lead ECG
   - Biochemical cardiac markers

Diagnostics:

1. Symptoms

2. 12-lead ECG

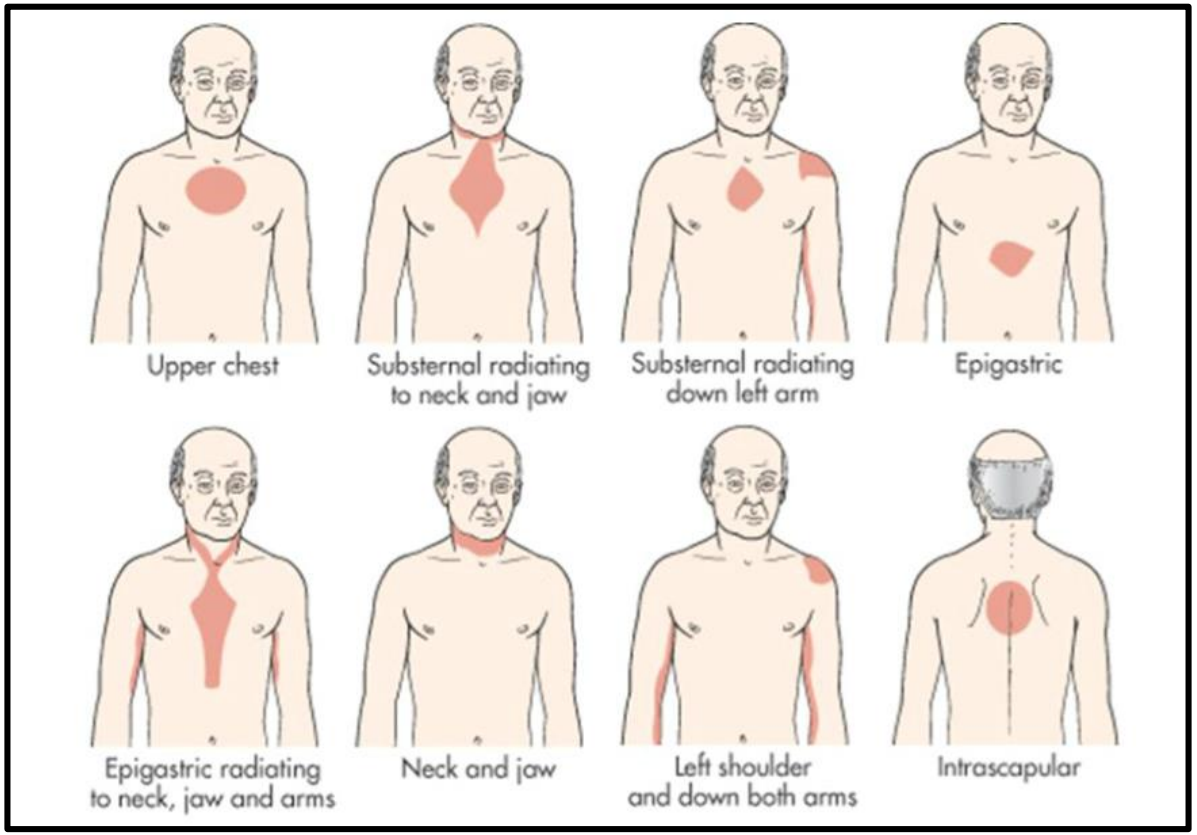
3. Biochemical cardiac markers (= bio-markers)

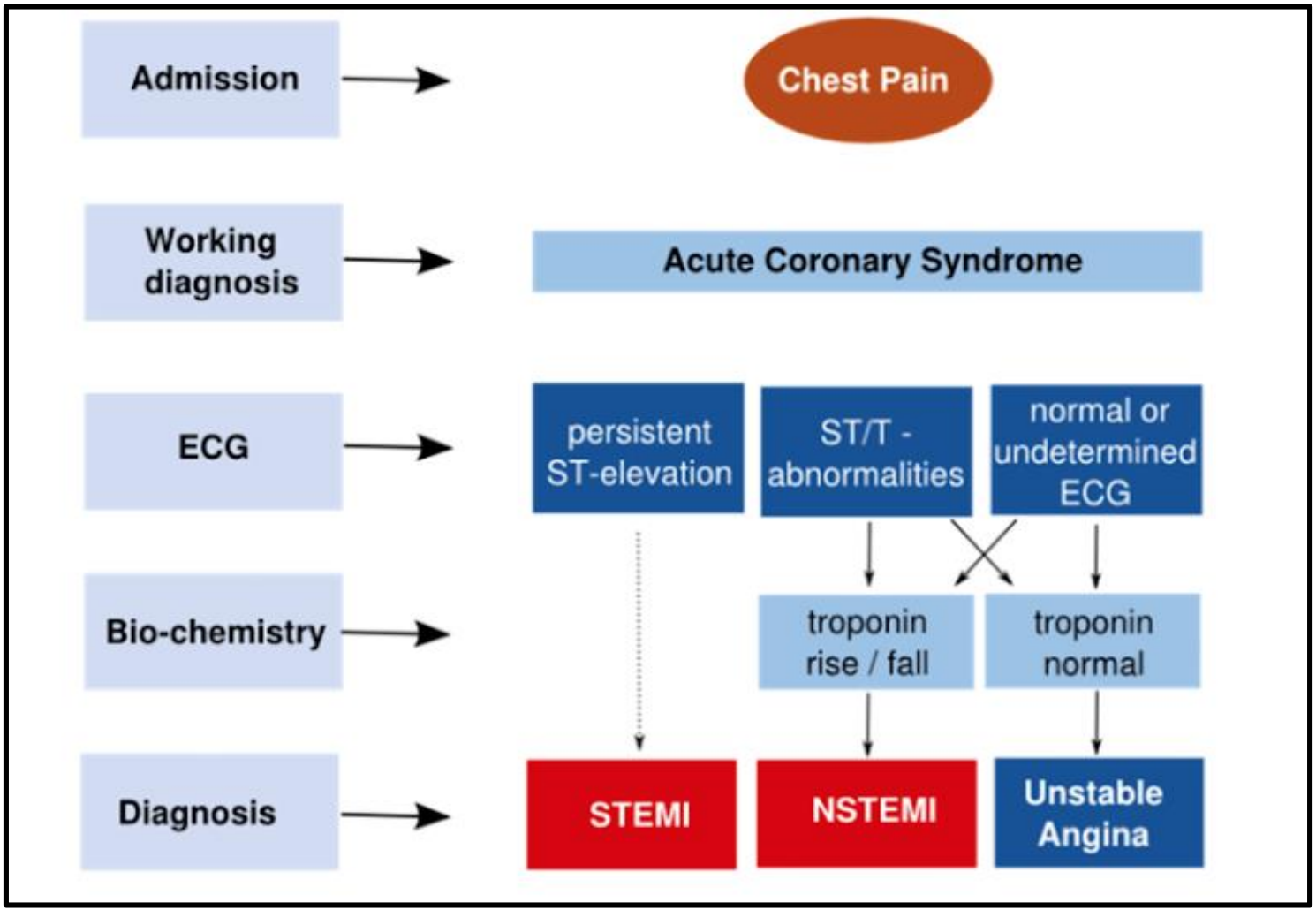
Diagnostics - Symptoms:

- Chest pain (hallmark symptom)
  - Tightness = sensation of pressure
  - Radiation to other areas (e.g. jaw, arm)
- Nausea (vomiting more common with inferior infarcts)
- Sweating / Perspiration
- Shortness of breath

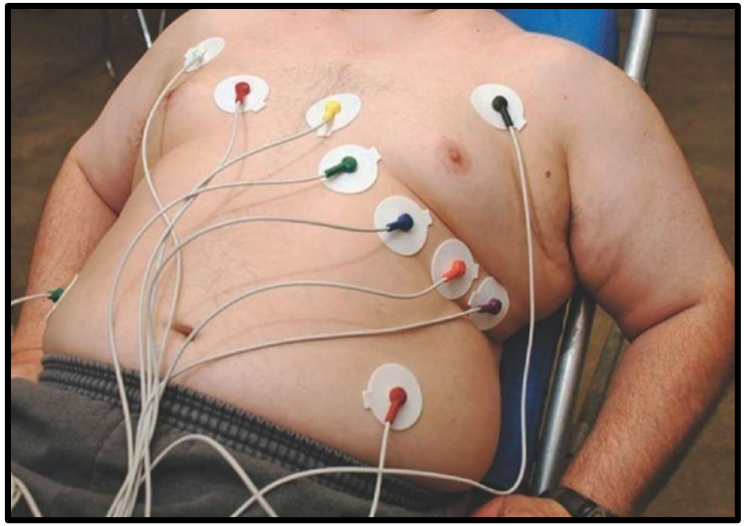
- Atypical chest pain is more common in women (important when counselling)

Diagnostics - Symptoms: Chest Pain



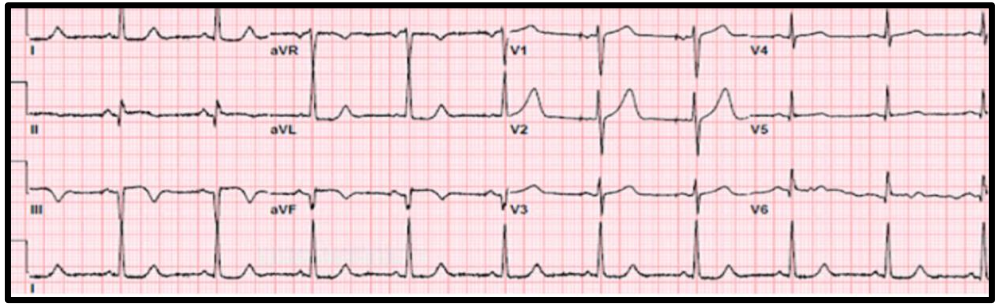

Admission
Chest Pain
Working diagnosis
Acute Coronary Syndrome
ECG
persistent ST-elevation
ST/T - abnormalities
normal or undetermined ECG
Bio-chemistry
troponin rise / fall
troponin normal
Diagnosis
STEMI
NSTEMI
Unstable Angina

Diagnostics - 12-lead ECG

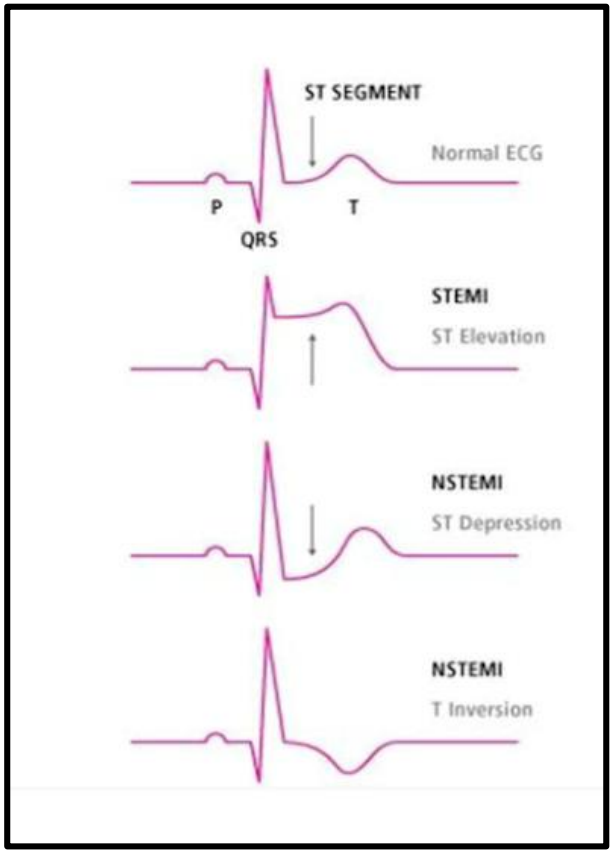


ECG = electrocardiogram

Electrodes record small voltage (electrical) changes arising from the heart muscles → useful in detecting cardiac abnormalities.



Diagnostics - 12-lead ECG



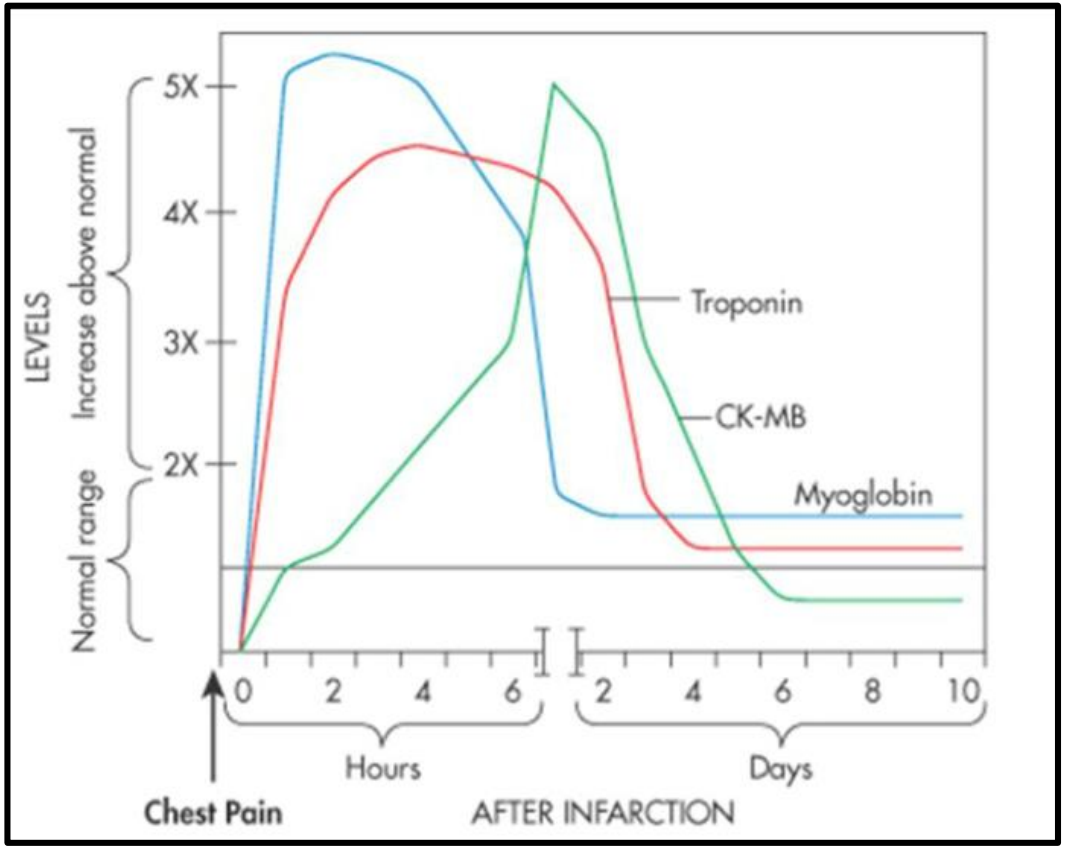
Provides clues as to where the myocardial ischaemia may be occurring.

Rapidly identifies patients with an acute STEMI who require emergency reperfusion.

<u>STEMI:</u> ST-segment elevated (tombstone) → sole test required to select patients for emergency reperfusion.

<u>NSTEMI:</u> ST-depression *OR* T-inversion

Diagnostics - Biochemical Cardiac Markers



Rise in the setting of ACS

ECG = high specificity but poor sensitivity → therefore, need cardiac biomarkers also.

Diagnostics - Bio-markers: Troponin

Cardiac troponins = most *sensitive* and *specific* biomarker for myocardial injury and infarction.

Increases transiently secondary to ischaemic myocardial injury, however troponin increases are not specific for MI only (cardiac + non-cardiac causes including PE, sepsis, burns).

Troponin levels become elevated in the bloodstream within 1 to 3 hours after an acute MI.

A rise*/fall in troponin is suggestive of an acute MI:

- Serial / repeat sampling is necessary to assess trend. **Trend is more important than a single value.**
- To rule out MI → need unchanged troponin on repeat samples.

Continued - Mr IR: Investigations / Diagnostics

Symptoms:

Chest pain and tightness (radiating to arm) not relieved by rest PLUS risk factors (male, smoking, overweight, HTN, dyslipidaemia) PLUS strong family history.

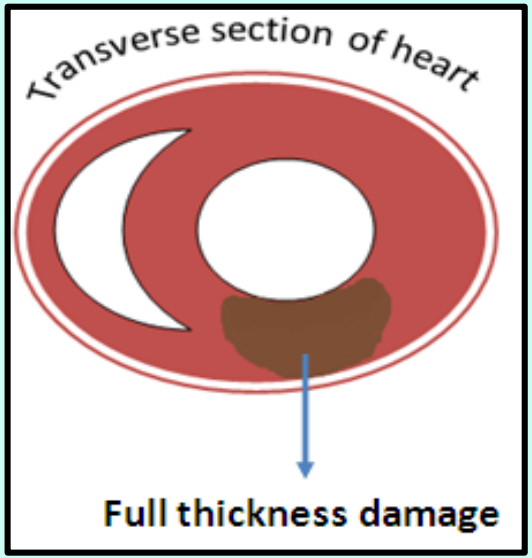
12-lead ECG:

ST-elevation noted.

Bio-markers:

Initial troponin = 6.8 (Ref range: <0.040)

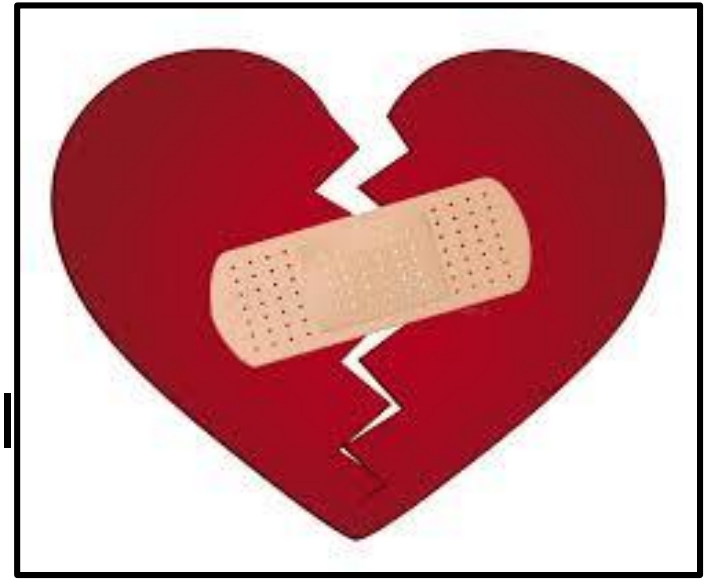
2-hour troponin = 19 (Ref range: <0.040)



Diagnosis: STEMI

Treatment Objectives:

1. Relieve symptoms
2. Prevent further myocardial injury
3. Optimise remaining myocardial function



Emergency Treatment of ACS:

1. Glyceryl Trinitrate (GTN) sublingual tablet/spray administered every FIVE minutes SOS for up to three doses. Consider IV GTN if symptoms unrelieved.

2. Aspirin 300mg should be given as soon as possible after presentation in ALL patients with possible ACS (without contraindications).

3. Consider IV morphine or fentanyl for ongoing chest discomfort at any point.

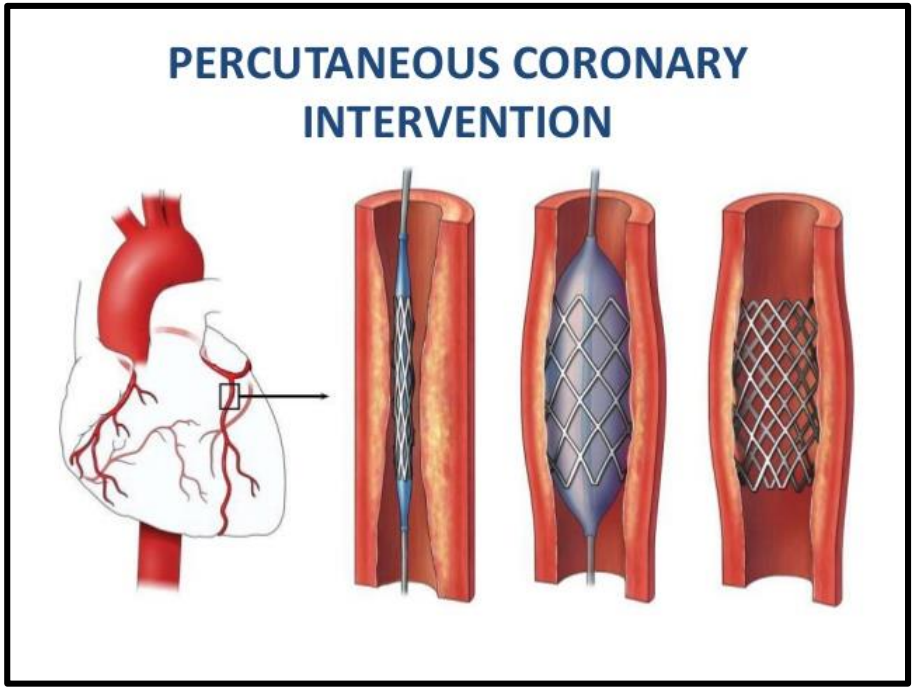
Acute Management: STEMI & NSTEMI

STEMI: aim to **re-establish blood flow** (reperfusion) → achieved by ***percutaneous coronary intervention*** *(PCI aka stent) or* ***fibrinolytic therapy*** *(Alteplase, Tenecteplase, Reteplase).*

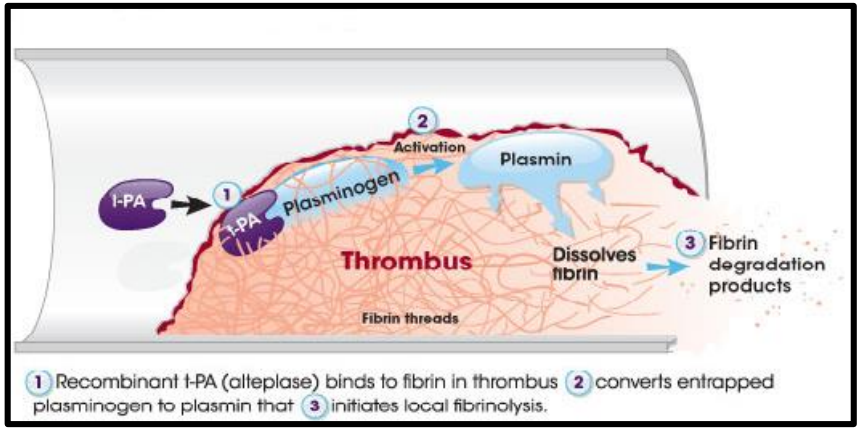
NSTEMI: aim to **stabilise plaque** and the **prevent coronary occlusion** → achieved with ***medical therapy***, and, if appropriate, ***revascularisation*** (ie stenting or bypass surgery).

Fibrinolytic therapy is NOT used to treat NSTEMI

STEMI - Re-establishing Flow (=reperfusion)



Option 1: PCI = stent (also used in NSTEMI dependent on patient risk).



Option 2: Fibrinolytic therapy → Break down clots through the lysis of fibrinogen bonds. (Not used in patient presenting with NSTEMI).

STEMI - Re-establishing Flow (=reperfusion)

Reperfusion therapy → minimises infarct size, relieves symptoms, prevents complications and improves outcomes.

PCI is more beneficial than fibrinolytic therapy in reducing mortality, recurrent MI and stroke.

PCI is preferred if it can be performed within 90 minutes of first medical contact.

If this is not possible, fibrinolysis should be given within 30 minutes of arrival to hospital (where no contraindications exist).

Acute Medication Management: STEMI & NSTEMI

1. Dual Antiplatelet Therapy (=DAPT) (Aspirin + Clopidogrel/Ticagrelor/Prasugrel)

2. Parenteral Anticoagulants (UFH/enoxaparin/dalteparin)

DAPT = Dual Antiplatelet Therapy

- Patients at high or very high acute risk of mortality and recurrent cardiovascular events should be *immediately* started on DAPT.
- Aspirin 300mg for the first dose, then 100mg daily.

Patients undergoing PCI / ACS	Clopidogrel 300 - 600mg stat then 75mg daily
	Ticagrelor 180mg stat then 90mg TWICE daily
	Prasugrel 60mg stat then 10mg daily*
Patients receiving fibrinolytic therapy	Clopidogrel 300mg stat then 75mg daily

*Do not use Prasugrel if <60kg, >75 years, PMHx stroke of TIA (increased bleeds risk)

Parenteral Anticoagulation

STEMI: UFH IV infusion OR enoxaparin should be given with fibrinolytic therapy as per local guidelines.

High or Very High Risk NSTEMI:
-Enoxaparin 1mg/kg subcut BD (CrCl >30mL/min) OR 1mg/kg subcut DAILY (CrCl <30mL/min) **OR**
-Dalteparin 120 units/kg subcut (CrCl >30mL/min) **OR**
-UFH as per local protocol (for patients with severe kidney impairment or high risk of active bleeding **OR**
-Bivalirudin as per local protocol (CrCl >30mL/min) (if invasive management is planned for patient with high risk of bleeding)

Therapy is continued until angiography (or longer depending on clinical response)

Case Continued – Mr IR: Initial Treatment

Q1/ Mr IR has been diagnosed with a STEMI and can not be transferred to a PCI capable hospital within 90 to 120 minutes. What are Mr IR's short-term treatment goals? (Pick all that apply)

- Prevent platelet aggregation
- Prevent further myocardial ischaemia/infarction
- Provide pain relief of symptoms
- Encourage weight loss
- Initiate fibrinolytic therapy

Q2/ Would your answer be different if Mr IR had experience a NSTEMI?

Nil ST-elevation, nil fibrinolytic needed.

Q3/ Would your choice of P2Y12-inhibitor be different if he received fibrinolytic therapy vs PCI?

Only clopidogrel is indicated in patients who have been fibrinolysed.

Case Continued - Mr IR: Initial Treatment

Transferred to PCI-capable hospital. Underwent angiogram + PCI within 24 hours.

Medications at time of review:

-Tenectaplase 50mg IV bolus → prior to arrival at PCI-capable centre.
-Enoxaparin 100mg subcut 12-hourly → ceased post angiogram.
-Aspirin 100mg mane
-Clopidogrel 75mg mane
-Metoprolol 25mg TWICE daily
-Perindopril 5mg mane
-Atorvastatin 80mg mane
-GTN spray 0.4mg PRN
-Morphine 2.5mg IV 2hrly PRN

Long-Term Medication Management: STEMI & NSTEMI

1. Dual Antiplatelet Therapy
2. Beta-blockers
3. ACEI / ARB
4. Statin
5. SOS sublingual nitrates

DAPT:

Treatment duration = 12 months after ACS, then single antiplatelet lifelong (usually aspirin) (can vary based on patient factors)

Aspirin 100mg to 150mg daily (unless true contraindication)

Three choices for second agent:

Clopidogrel: preferred in elderly patients, those with previous stroke/TIA, bleeding risk++ (inc. those on anticoagulant).

Ticagrelor and Prasugrel: proven benefit over clopidogrel, however increased risk of bleeding compared to clopidogrel.

DAPT Counselling Points:

Reduces chance of unwanted blood clots forming and further MI (high risk of further events).

You may notice cuts, wounds and nose bleeds take slightly longer than usual to stop bleeding. There's generally no need to worry, but tell your doctor if you are concerned.

Seek immediate medical attention if you notice dark, tarry stools, blood in urine or unexplained bruising.

Treatment should not be ceased early unless advised by your cardiologist. Inform other health professionals that you are being treated with antiplatelet therapy → consider a patient alert card.

Beta-Blockers:

Reduce total mortality, re-infarction and sudden cardiac death post-ACS, particularly in patients with LV systolic dysfunction.

Work by:
-Preventing arrhythmias
-Reducing oxygen demand on ventricular muscle.
-Potentially limiting infarct size (effect lost after ~30 days).

Historical evidence for use pre-dates current practice → current benefit is not well established and likely to be small in patients with successful re-vascularisation, preserved LV function, and *no ongoing angina or residual ischaemia.*

In asymptomatic patients or those with preserved LV ejection fraction → consider cessation after 12 months if commenced.
Continue indefinitely if LV dysfunction or ongoing ischaemia/angina.

ACE-I/ARB:

Cardio-protective → long-term use reduces cardiovascular mortality, non-fatal MI, and stroke.

Work by:
-Limiting infarct size.
-Reducing ventricular remodelling (especially in STEMI population).

Usually commenced within 24 - 48 hours and continued indefinitely in patients with evidence of heart failure, LV systolic dysfunction, diabetes, anterior MI or co-existing hypertension.

Statins:

Reducing premature death, myocardial infarction and other cardiovascular events irrespective of lipid levels.

Work by:
-Reducing low-density lipoprotein-cholesterol (LDL-C = the bad stuff!)
-Reducing arterial inflammation
-Stabilising the lipid core in atherosclerotic plaques
-Helps regress atherosclerotic plaque

Commenced as **early** as possible at the **highest tolerated dose** and continued indefinitely.

SOS Sublingual Nitrates:

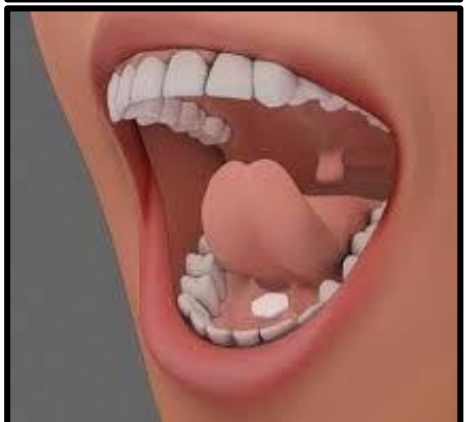
Vasodilator → reduces venous return and preload to the heart, reducing myocardial oxygen requirements. Relieves acute angina.

Counselling:
-Use during episodes of angina or before an activity expected to bring on angina.
-Sit or lie down before use as it may cause dizziness.
-Call an ambulance if symptoms are severe, get worse quickly or last for 10 minutes.

Tablets: Place half to one tablet under your tongue, do not swallow. After the pain has been relieved, spit out or swallow what is left of the tablet to avoid adverse effects.

Spray: Prime the spray before using it for the first time by pressing the nozzle 5 times, spraying it into the air. Prime it with 1 spray if it hasn't been used for 7 days. Prime with 5 sprays if it hasn't been used for more than 4 months. Do NOT inhale spray.

SOS Sublingual Nitrates:



- Ask the patient to **describe** the symptoms of chest pain that brought them into hospital. Advise them to use this medication if they experience similar symptoms.
- Explain **why** this medication is to be administered under the tongue.
- Ensure they understand that they need to **call for assistance** if no relief after 10 minutes.
- This medication is for acute pain which can occur at any time → needs to be accessible at all times.
- Ensure it is stored correctly and is in date / expiry (!)

Case Continued - Mr IR: Long-Term Treatment

Q1/ What medications would you expect Mr IR to be discharged home on?

1. Dual Antiplatelet Therapy, 2. ACE-I, 3. B-blocker, 4. Statin, 5. GTN SOS (AAABC + G)

Q2/ What is the expected duration of dual antiplatelet therapy?

12 months

Q3/ What is the expected duration of beta-blocker therapy? What factors do we need to consider when assessing this?

Review after 12 months. If reduced LVEF or ongoing angina, continue treatment indefinitely.

Case Continued - Mr IR: Long-Term Treatment

Medications on discharge:

-Aspirin 100mg mane (indefinitely) (antiplatelet – STEMI) (NEW)
-Clopidogrel 75mg mane (12 months) (antiplatelet – STEMI) (NEW)
-Perindopril 5mg mane (HTN/STEMI) (UNCHANGED)
-Metoprolol 25mg BD (STEMI) (NEW)
-Atorvastatin 80mg nocte (STEMI) (NEW)
-GTN spray PRN (IHD) (NEW)
-Allopurinol 400mg mane (Gout) (UNCHANGED)

Q: Mr IR was previously on amlodipine, which has been ceased during admission. Why do you think amlodipine was ceased? Was this appropriate? Should he be restarted on this medication on discharge?

Lifestyle Advice: Target Modifiable Risk Factors!

Diet: address healthy eating habits in overweight patients. Promote fresh food, reduce portion sizes, and water (!) as the drink of choice.

Exercise: regular light-to-moderate exercise (increased breathing while able to sustain a conversation) is preferred to vigorous exercise. Reassure patients that exercise-induced cardiac events are negligible in comparison to risk associated with a sedentary lifestyle.

Smoking cessation: smoking and second-hand smoke can contribute to heart disease. Discuss strategies to stop smoking with your patients.

Hypertension: patients may not know if they are hypertensive -> recommend monitoring and treatment if history of HTN.

Glycaemic control: poor glycaemic control can increase risk of heart attack -> ensure patients are compliant with medications and monitor appropriately.

How can Pharmacists Make a Difference?

1. Clear, concise medication counselling (what, why, when + side-effects). Incorporate written material where available.

2. Ensure patient has a heart attack action plan (recognises symptoms, knows when to use GTN/call ambulance).

3. Monitor and advise on compliance -> why it's important to continue these medications, strategies to remember to take medications.

4. Lifestyle modification advice.

Conclusion:

Understanding pathophysiology of ACS helps to understand treatment goals.

Goals of ACS treatment are similar → relieve symptoms, prevent further myocardial injury, optimise remaining myocardial function.

Initial and long-term medication management extremely important → lots of space for pharmacy intervention.

Role of pharmacist in prevent further complications important:

- Provide clear, concise counselling (with written aids where possible)
- Suggest strategies to aid compliance (alarms, dosette box, ?phone APPs)
- Educate on lifestyle choices and modifications -> smoking cessation, diet (sugary drinks), exercise.

Helpful Resources If You'd Like to Learn More:

International Guidelines:

Australian Heart Foundation - https://www.heartfoundation.org.au

-Access to guidelines (abridged versions) and online learning modules

-Patient information

American Heart Association - https://professional.heart.org

-Free Pocket Guidelines and APP available for guidelines on-the-go

-Access to webinar lectures, online courses (free)

European Society of Cardiology - https://www.escardio.org

-Exams and clinical scenarios to test your knowledge

-Access to webinar lectures and guidelines

NPS MedicinesWise - https://www.nps.org.au

-Management of Acute Coronary Syndrome (+many more modules)

QUESTIONS?

QUICK FIRE CASE (+Australian Treat time!):

Case 2: Mr JJ

63 year old male BIBA with sudden onset chest pain (nil radiation). Patient took own GTN spray prior to calling ambulance (nil effect).

Smoker ~4/day; ETOH++.

Weight 81kg, CrCl = >90
Allergy: morphine (disorientated)

PMHx:
-HTN (perindopril 5mg mane)
-Hypercholesterolaemia (nil treatment)
-NSTEMI 2017 (<12months) → stent in situ (aspirin 100mg mane, GTN 0.4mg spray SOS)
-LVEF = 58% (2017)

Case 2: Mr JJ continued

Initial Diagnostics:

-Risk factors → male, smoker, HTN, hypercholesterolaemia, previous NSTEMI (+non-compliance to medications)

-ST depression noted on 12-lead ECG (when in pain).

-Troponin: 0.89 (on presentation), 2.1 (hour 6)

Initial Medication:

Enoxaparin 80mg subcut BD

Aspirin 100mg mane (initial load of 300mg in ambulance)

Clopidogrel 75mg mane (initial load of 300mg in ED)

Atorvastatin 80mg nocte

Metoprolol 25mg BD

Perindopril 5mg mane

GTN spray 0.4mg SOS

Case 2: Mr JJ continued

Angiogram:

Severe circumflex coronary artery disease

Successful PCI of the proximal circumflex coronary artery with drug eluting stent

Discharge Medication Plan:

Aspirin 100mg mane

Clopidogrel 75mg mane

Atorvastatin 80mg nocte

Metoprolol 25mg BD

Perindopril 5mg mane

GTN spray 0.4mg PRN