Coronary Heart Disease, Angina, MI, Embolism

Year 1 Cardiovascular System

Ranil de Silva FRCP PhD

Senior Lecturer in Clinical Cardiology

Consultant Interventional Cardiologist

r.desilva@imperial.ac.uk

Imperial College London

Royal Brompton & Harefield NHS Foundation Trust

NHS National Institute for Health Research

How does coronary artery disease present?

- Sudden cardiac death
- Acute coronary syndrome
  - Acute myocardial infarction
  - Unstable angina
- Stable angina pectoris
- Heart failure
- Arrhythmia

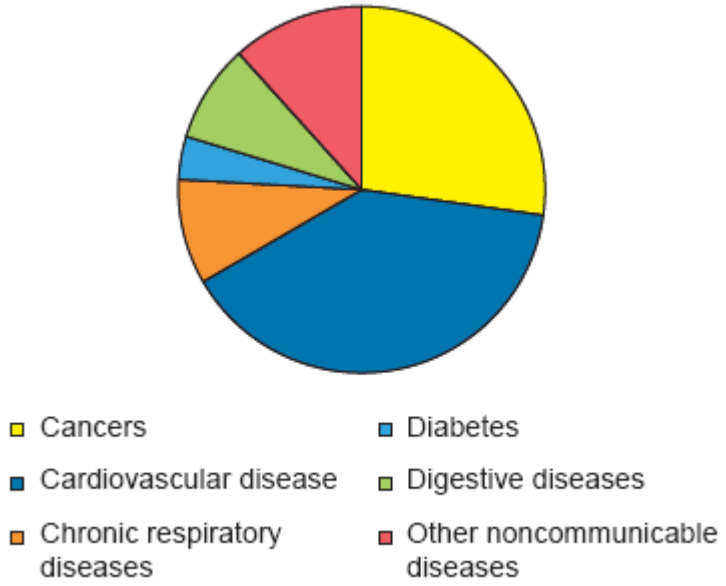
Epidemiology – Determinants of Risk

- Tobacco use, physical inactivity, harmful use of alcohol, unhealthy diet accounts results in:
  - Hypertension
  - Obesity
  - Diabetes mellitus
  - Hyperlipdaemia

- Responsible for ~80% of CHD

Global Burden of CVD

- Cardiovascular disease accounts for ~17M deaths per year.
- Leading cause of death in both developed and low/medium income countries
- Leading cause of death in age <70y
- Leading cause of death in women



WHO Global Status Report on Non-communicable disease 2010

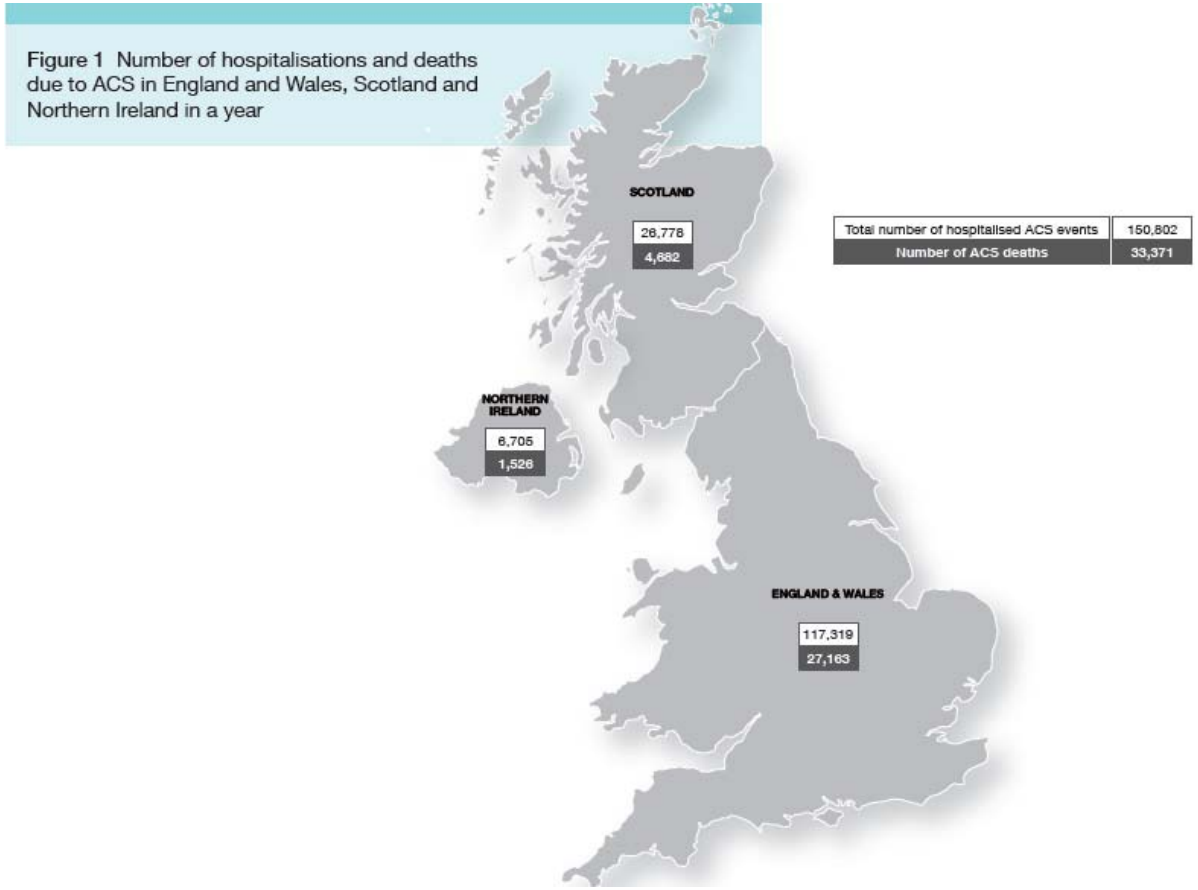
UK Burden of CHD

- 88,000 CHD deaths per year, commonest cause of death
- CHD accounts for 18% deaths in men and 10% deaths in women <75y, commonest cause of premature death
- While rates are falling, UK mortality still greater than most of Western Europe

Coronary Heart Disease Statistics 2010

UK MI Statistics (2009-10)

- 124,000 MI's per yr
- ~99,000 hospital admissions per year
- ~33,000 deaths per year (~6% of all deaths in UK)
- £3.6 billion per year



Epidemiology of Stable Angina

- Incidence increasing
- ~2M cases in UK
- Age 55-64y
  - Affects 8% ♂ and 3% ♀
- Age 65-74y
  - Affects 14% ♂ and 8% ♀

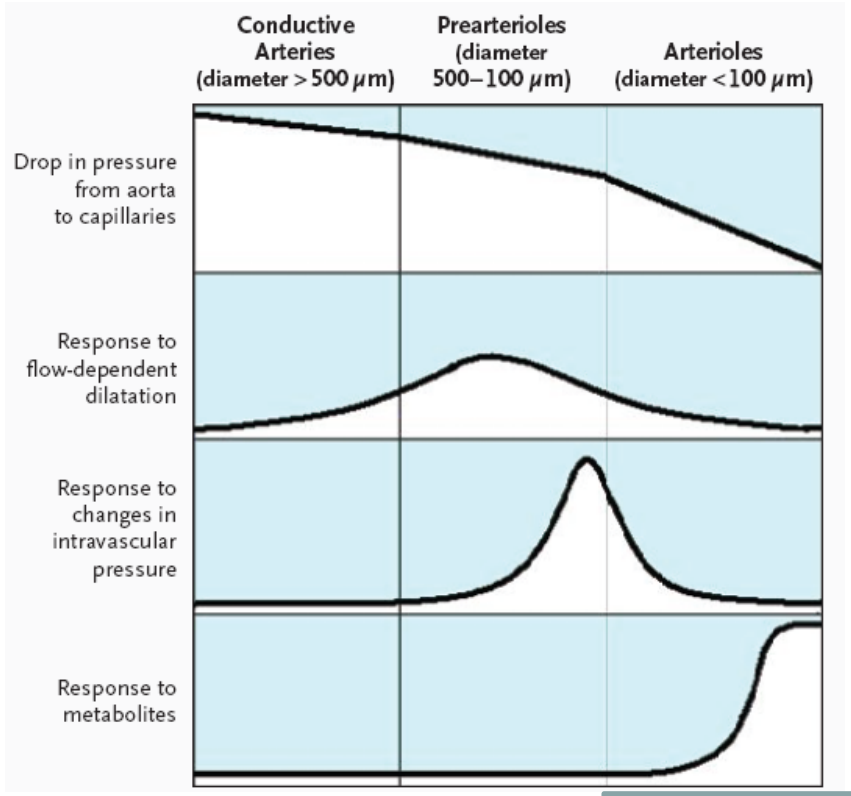
Epidemiology of Stable Angina

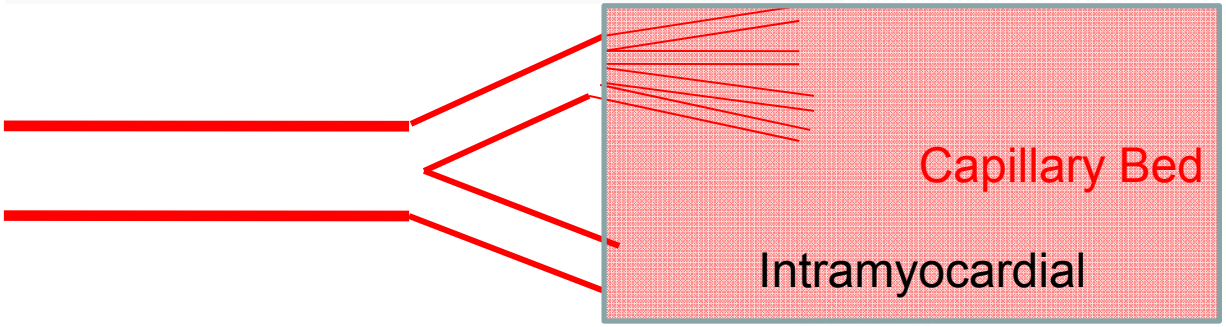
- In 2009/10 ~45K admission → ~65K bed days
- ~67,000 elective PCI's per year
- ~50% of patients undergoing PCI are on no or suboptimal medical Rx
- In 2009/10, ~300K angina patients attended Cardiology Outpatient appointments

Myocardial Ischaemia

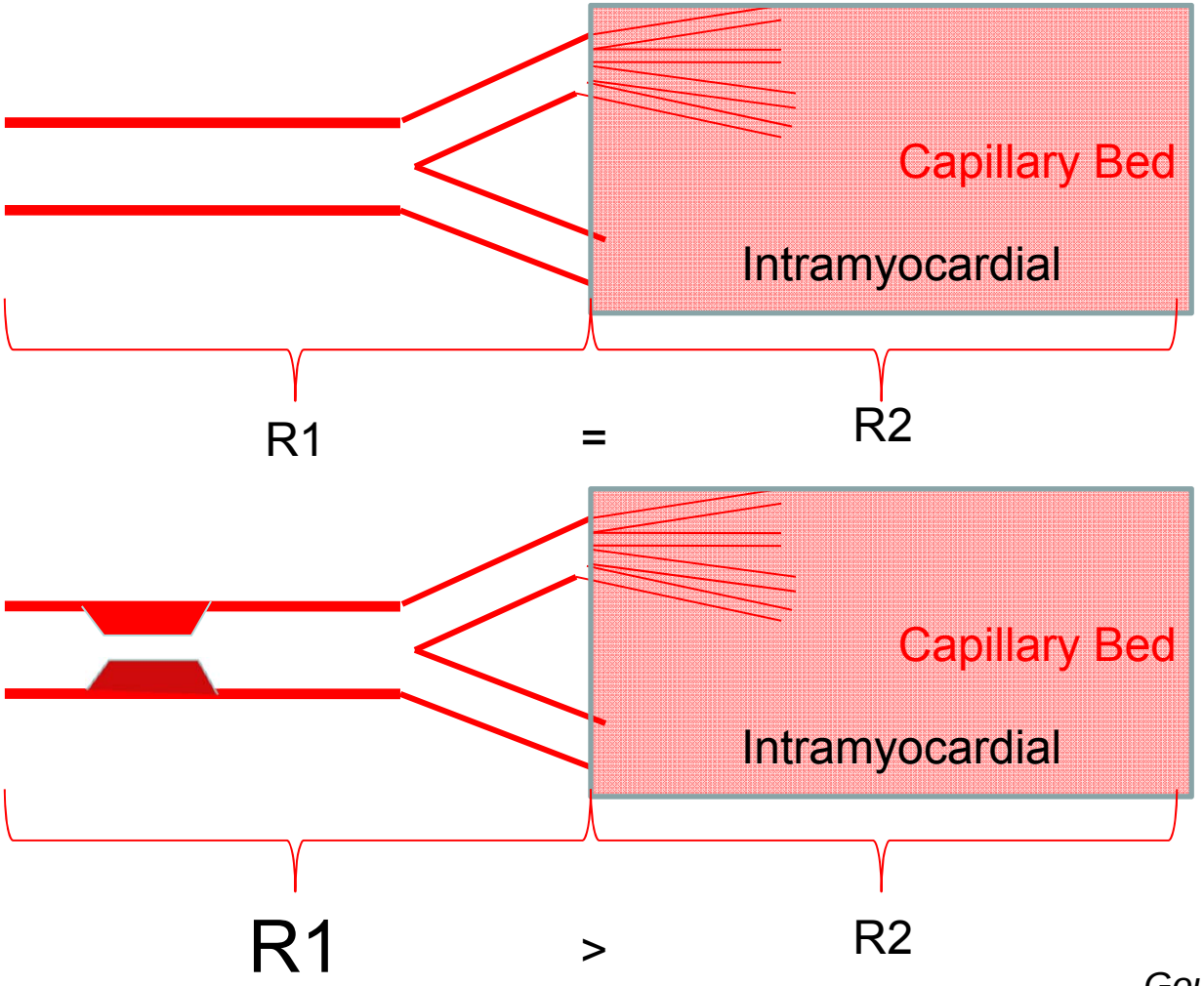
- Mismatch between myocardial oxygen supply and demand
- Primary reduction in blood flow
- Inability to increase blood flow to match increased metabolic demand

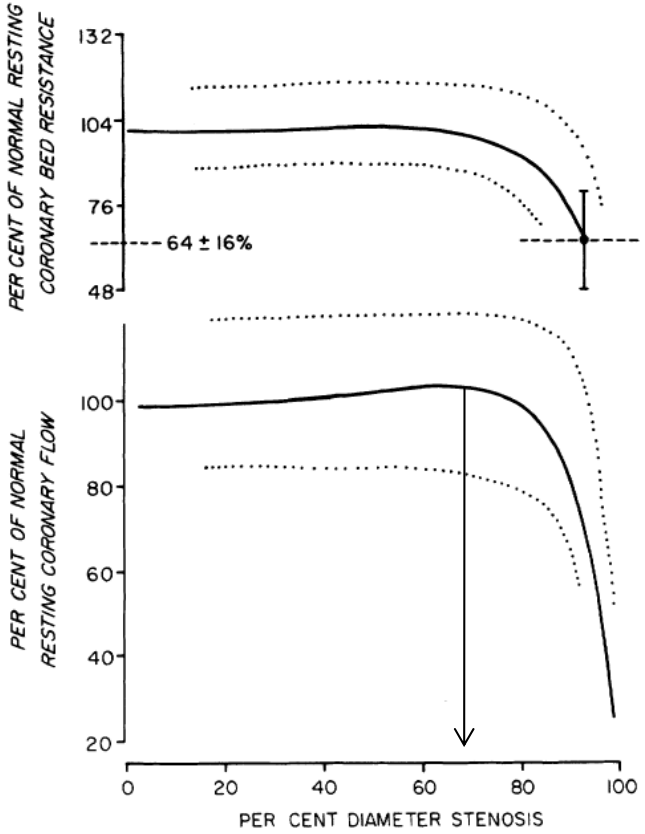
Functional Anatomy of Coronary Circulation





Effect of Epicardial Stenosis on Resting Coronary Resistance and Flow





Gould, Lipscomb, Calvert Circulation 1975

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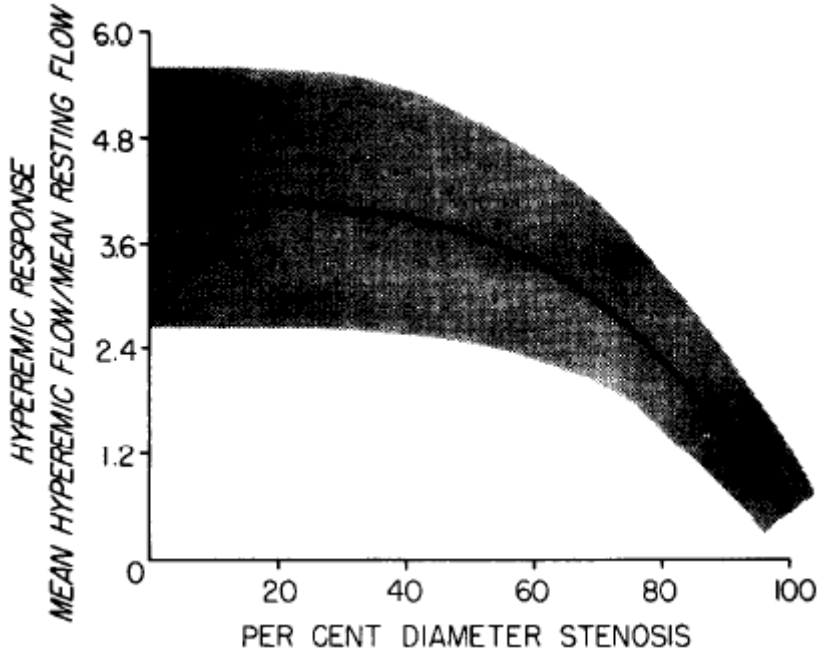
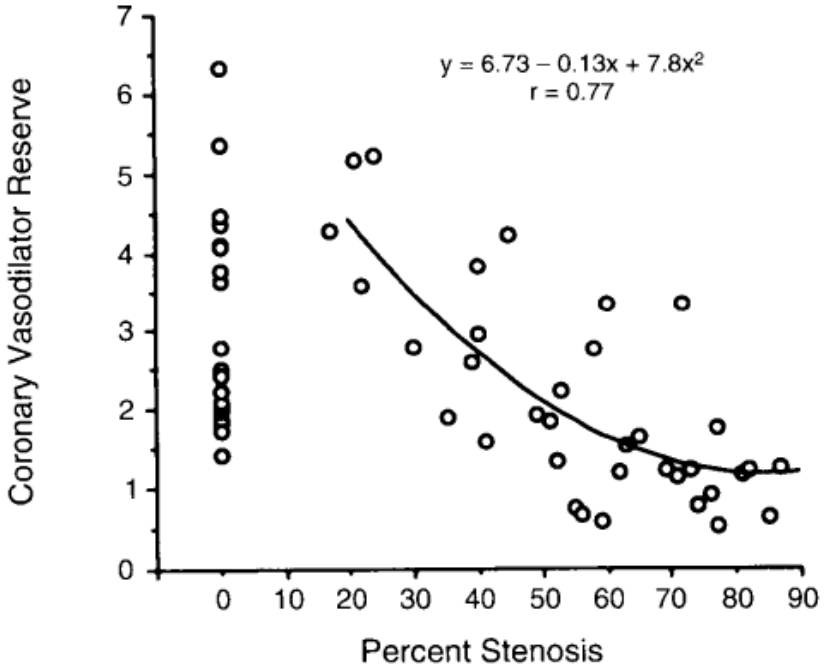
Effect of Coronary Stenosis on Flow Response to Vasodilators



Gould and Lipscomb Am Heart J 1974



Uren et al. N Engl J Med 1994

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MEDICAL TRANSACTIONS,

PUBLISHED BY THE

COLLEGE OF PHYSICIANS

IN

LONDON.

VOLUME THE SECOND.

LONDON:
Printed for S. BAKER, and J. DODSLEY.
M.DCC.LXXII.

VI. *Some Account of a Diſorder of the Breaſt.* By WILLIAM HEBERDEN, *M. D. F. R. S.*

Read at the COLLEGE, JULY 21, 1768.

THERE is a diſorder of the breaſt, marked with ſtrong and peculiar ſymptoms, conſiderable for the kind of danger belonging to it, and not extremely rare, of which I do not recollect any mention among medical authors. The ſeat of it, and ſenſe of ſtrangling and anxiety with which it is attended, may make it not improperly be called Angina pectoris.

THOSE, who are afflicted with it, are ſeized, while they are walking, and more particularly when they walk ſoon after eating, with a painful and moſt diſagreeable ſenſation in the breaſt, which ſeems as if it would

Angina Pectoris

- Angina pectoris is a clinical diagnosis
- Discomfort in the chest, jaw, shoulders, arms, or back.
- Provoked by exertion or emotional stress
- Relieved by rest or s.l. GTN in < 5min

Investigation for Stable CHD

- To confirm the clinical diagnosis
  - Demonstrate myocardial ischaemia
- To assess risk of future adverse cardiovascular events
  - Burden of myocardial ischaemia
  - Anatomic severity coronary artery disease
  - LV function
- Choice of test dependent on clinical probability of CHD

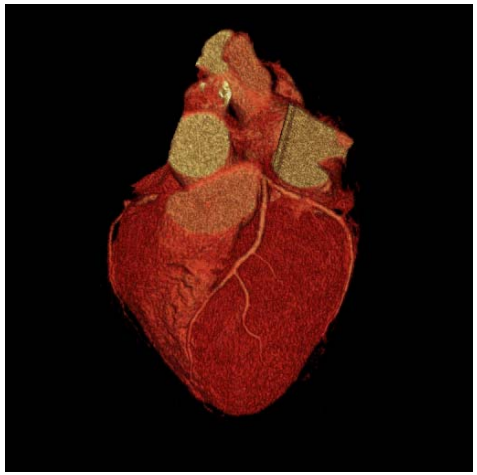
Investigation of CHD

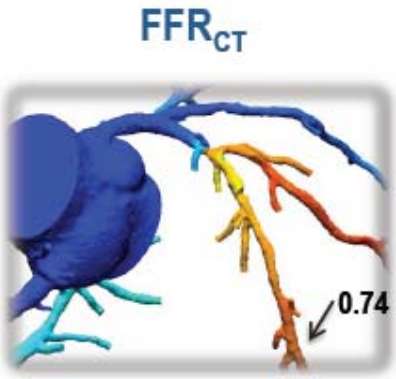
	Functional	Anatomical
Non-invasive	Exercise ECG Stress echo Stress cardiac MRI *PET/CT* *Stress nuclear MPS* *FFR_{CT}*	*CT coronary calcium score* *CT coronary angiogram*
Invasive	*CFR* *Pressure wire (FFR)* *iFR* *IVUS* *OCT*	*Coronary angiogram*

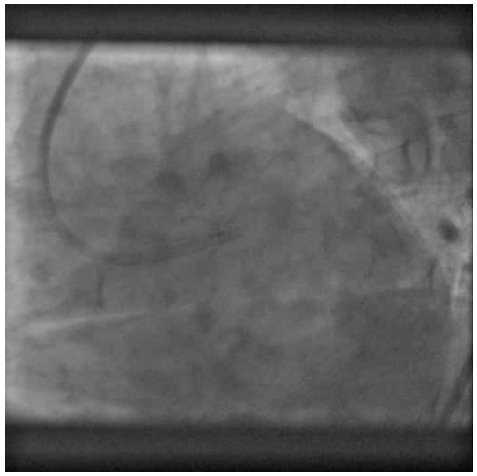
Involves exposure to ionising radiation

How do we diagnose CHD?

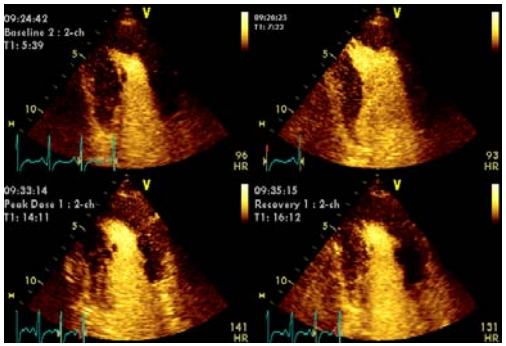
Anatomical

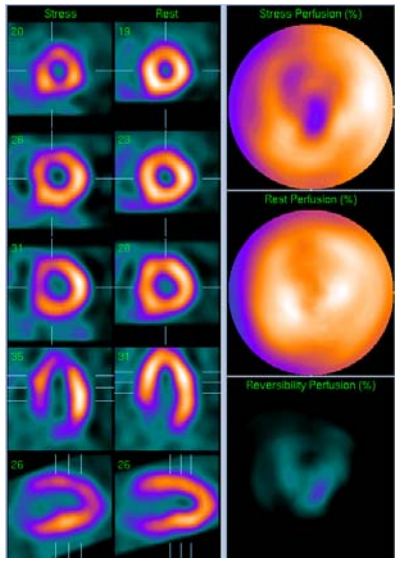


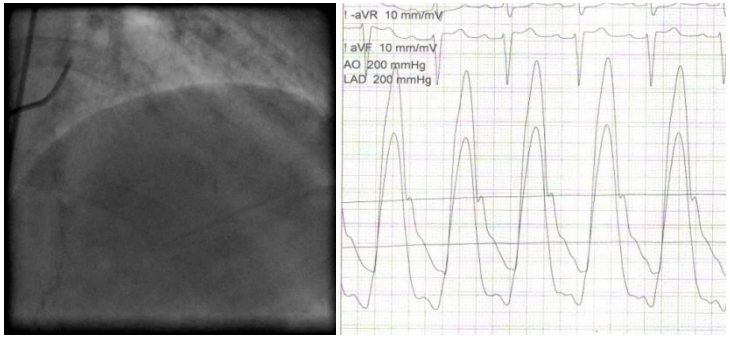


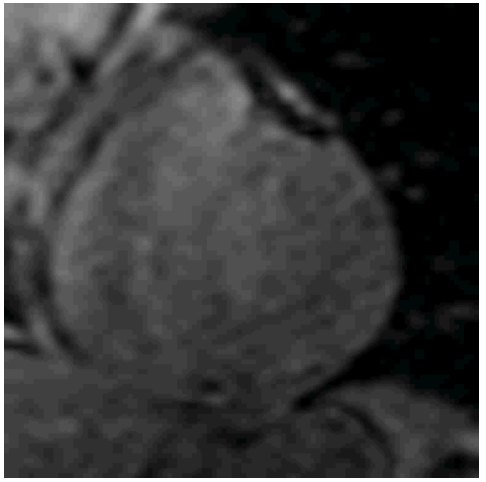


Functional









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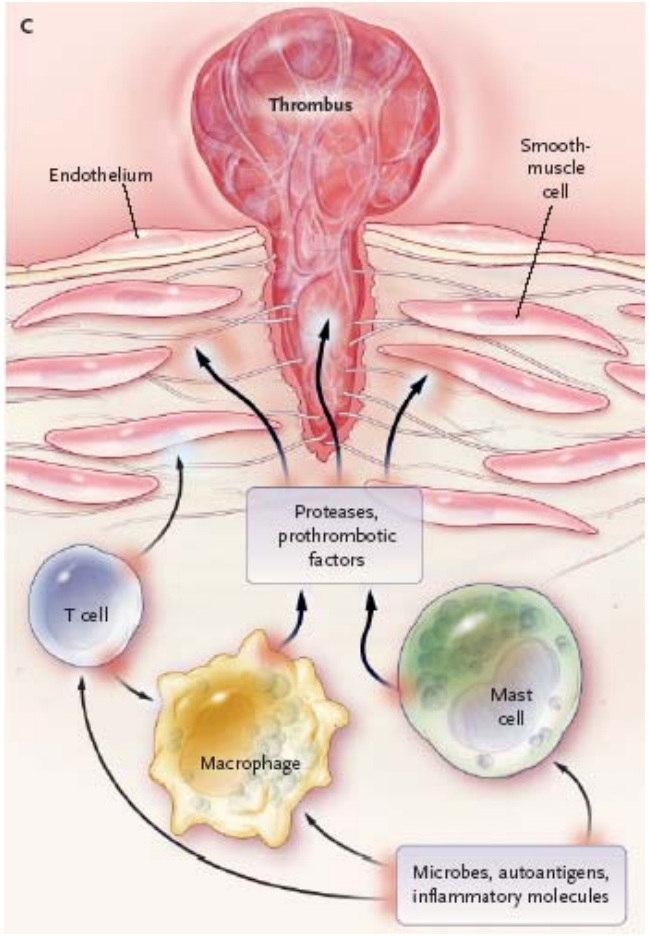
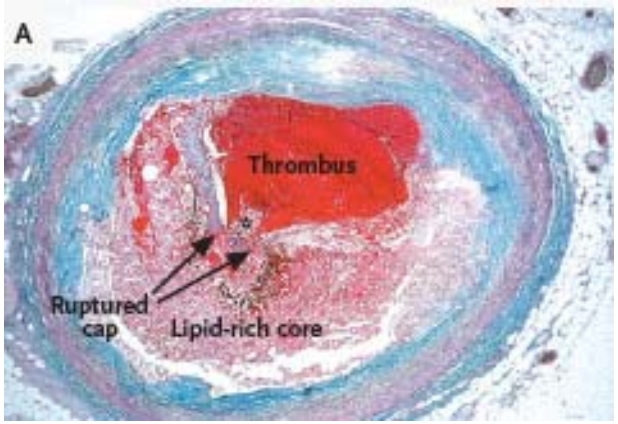
Treatment Strategies

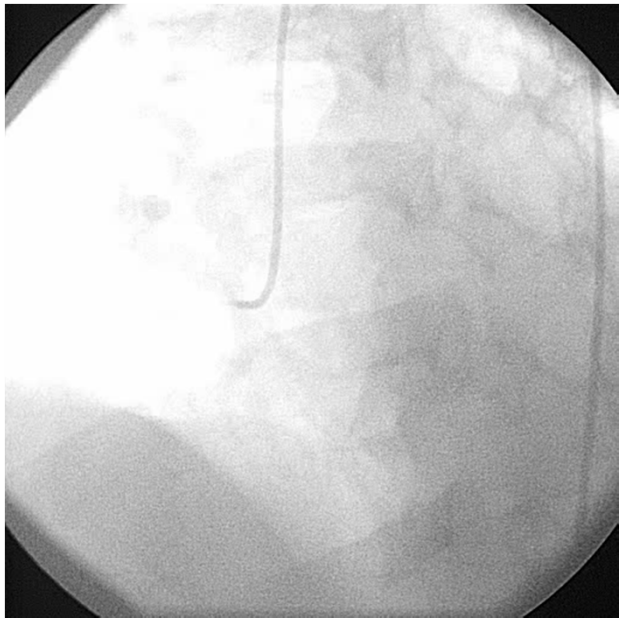
- Prevent atherosclerosis progression and risk of death/MI
  - Education
  - Lifestyle modification
  - Aspirin, statins, ACE inhibitors
- Reduce myocardial oxygen demand
  - HR (β blockers, Ca antagonists, I_f blockers)
  - wall stress (ACE inhibitors, Ca antagonists)
  - Metabolic modifiers
- Improve blood supply
  - Vasodilators (nitrates, nicorandil, Ca antagonists)
  - Revascularisation (PCI, CABG)

Acute MI

Acute Coronary Syndromes







- **Inflammation**
  - Systemic
  - Local
- **Plaque**
  - Rupture
  - Erosion
- **Thrombosis**

Hansson N Engl J Med 2005

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Mechanisms Underlying MI

- Myocardial cell death arising from interrupted blood flow to the heart
  - Coronary plaque rupture
  - Coronary plaque erosion
  - Coronary dissection

- Mechanisms of myocardial cell death
  - Oncosis
  - Apoptosis

“Man lives with atherosclerosis but dies from thrombosis”

Didischem 1957

ACS

THROMBOSIS

20-30 %
PLAQUE EROSION

70-80 %
PLAQUE RUPTURE

Thrombosis - Virchow's Triad

- Abnormal vessel wall (**endothelial dysfunction**, inflammation, atherosclerosis)
- Abnormal blood flow (**endothelial dysfunction**, turbulent flow at bifurcations and stenoses, stasis)
- Abnormal blood constitutents (**endothelial dysfunction**, hypercoagulability, abnormal platelet function, altered fibrinolysis, metabolic, hormonal factors)

Thrombosis

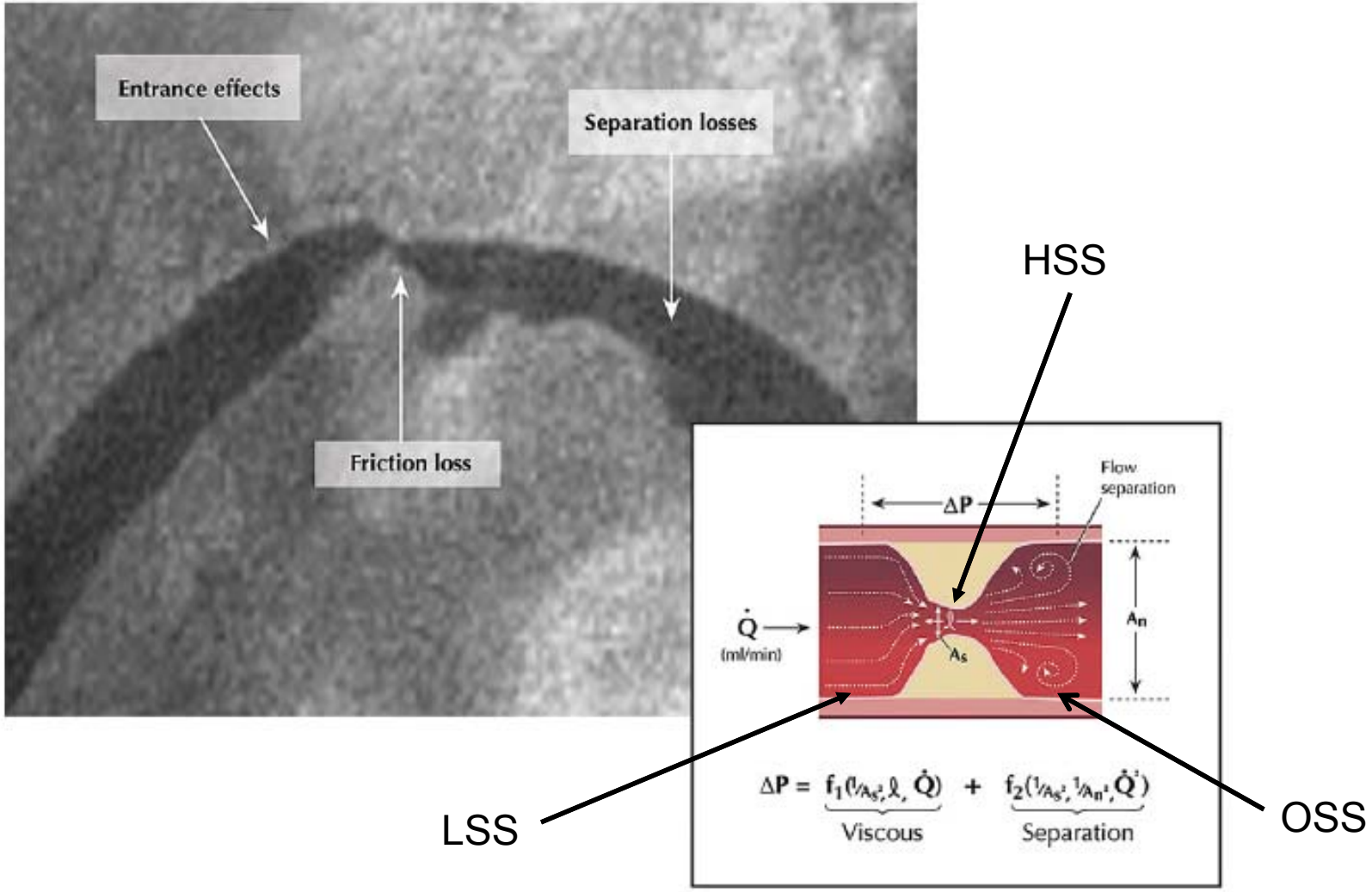
White Thrombus

- Platelet rich
- Common in arterial thrombosis (high pressure/turbulent circulation)
- Benefit from antiplatelet therapy

Red Thrombus

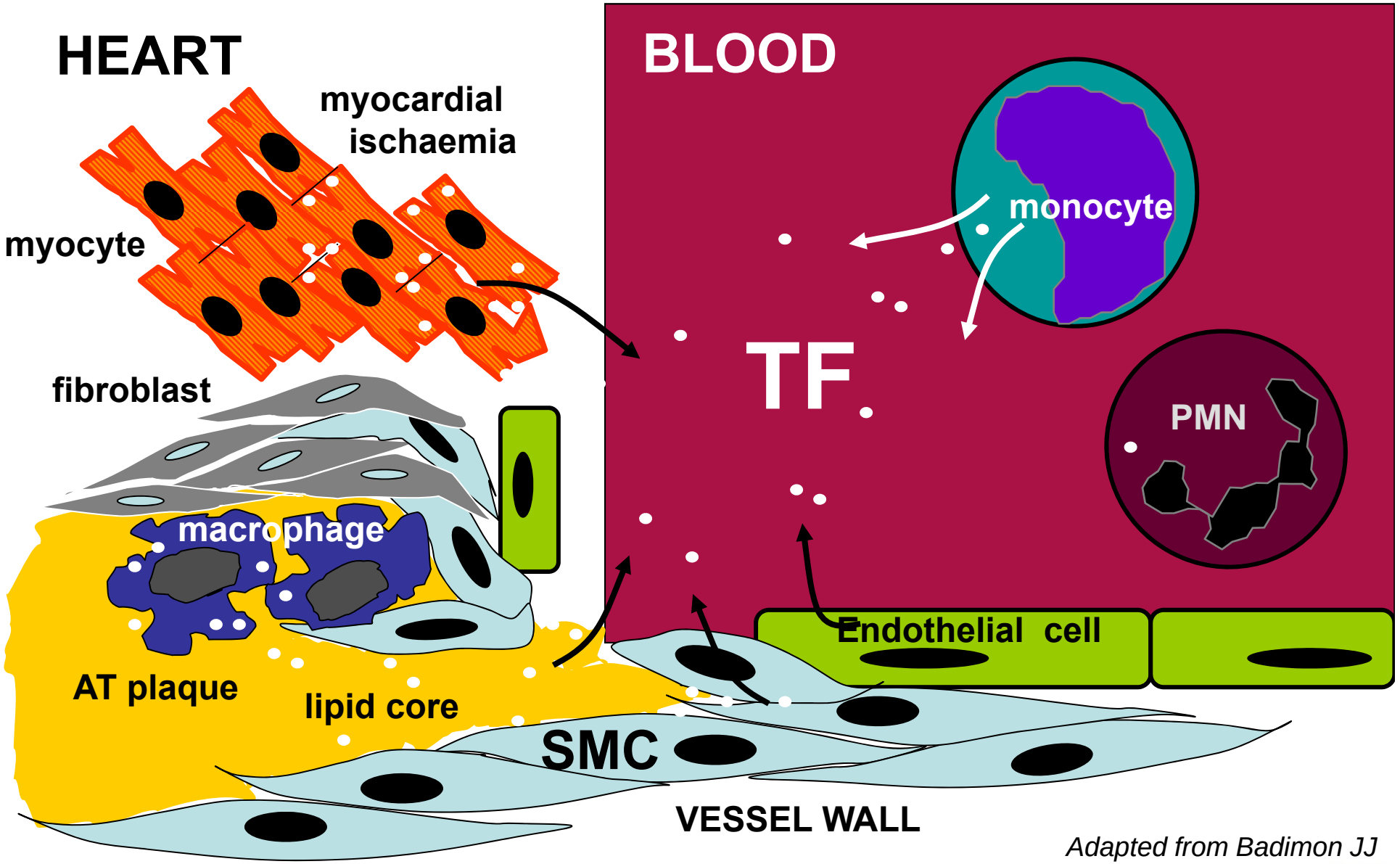
- Fibrin rich, with trapped erythrocytes
- Common in venous or low pressure situations (stasis)
- Benefit from anticoagulant or anti-fibrinolytic therapy

Effect of Coronary Stenosis on Haemodynamics



Kern et al. JACC 2010

TF Circulates in Blood: Possible Cellular Sources



Adapted from Badimon JJ

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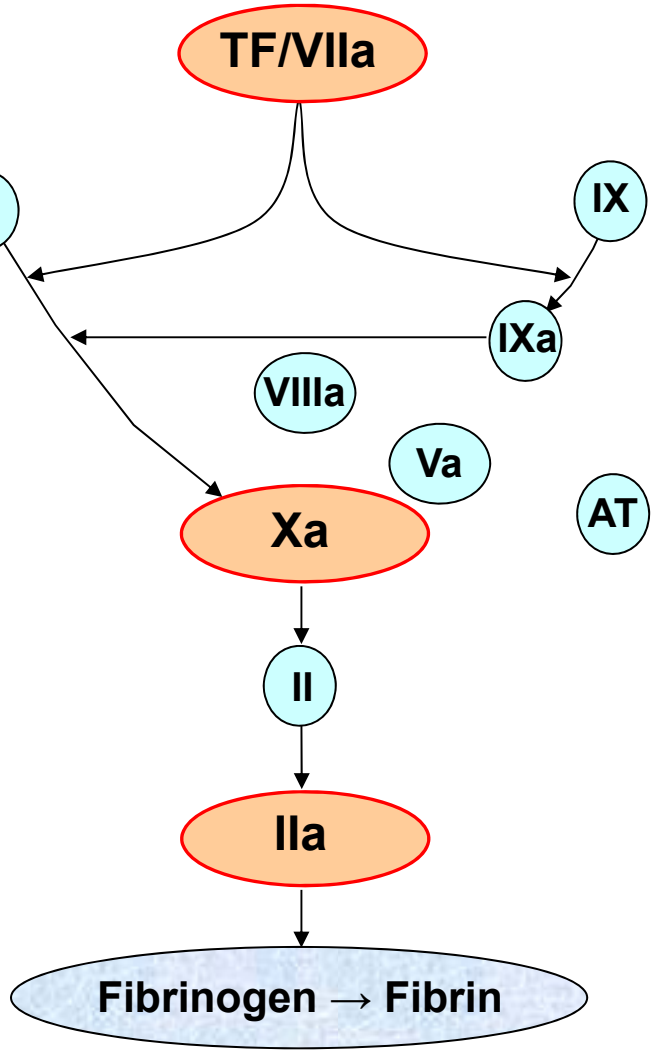
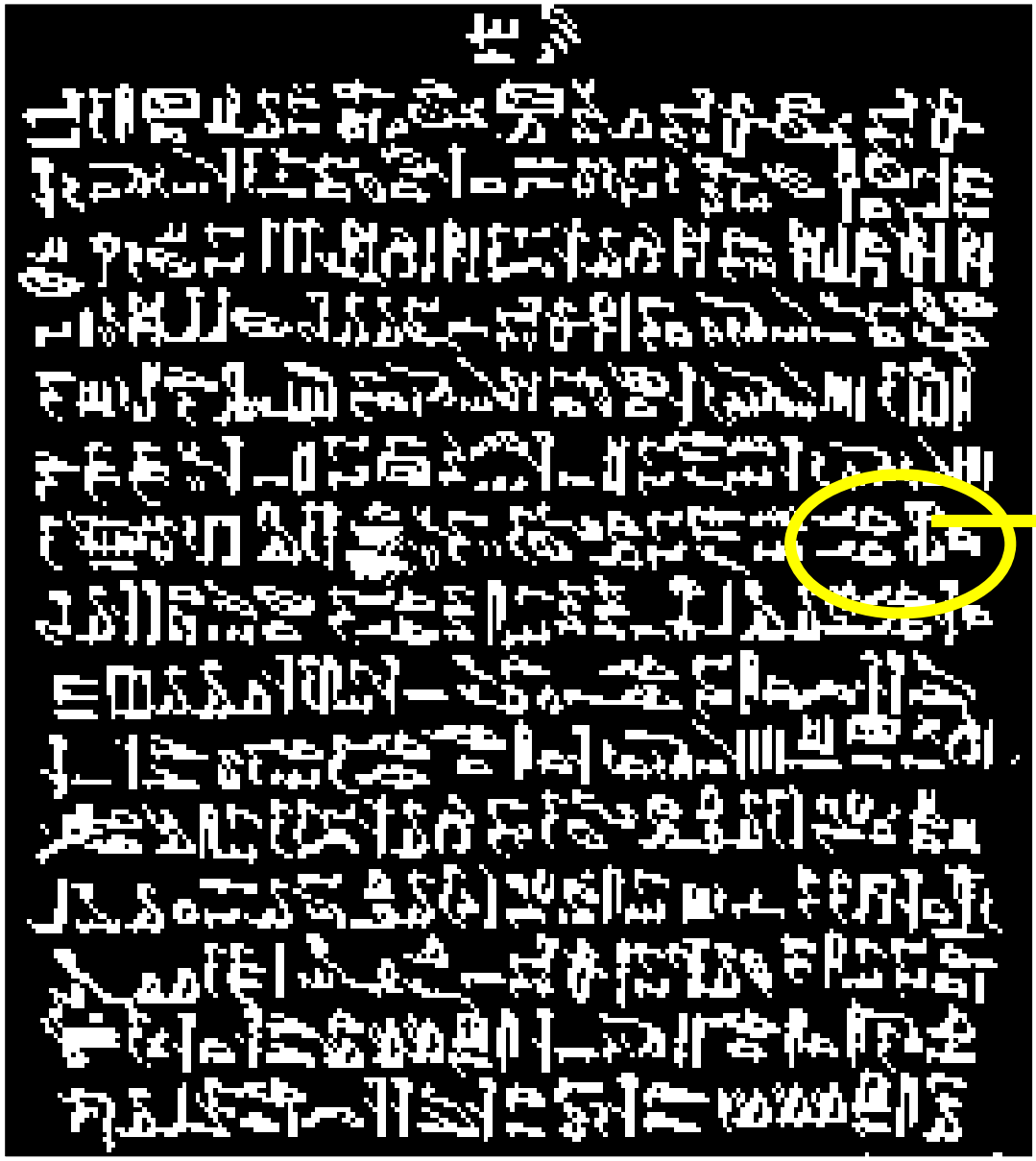
Tissue Factor as a Determinant of Thrombosis



Adapted from Weitz JI: *J Throm Haemost. 2007 Jul 5 Suppl 1:65-7*



…a man with severe chest pain going down the arms: Death is near …

The Ebers Papyrus 2600 B.C.

with kind permission from J.C. Kaski

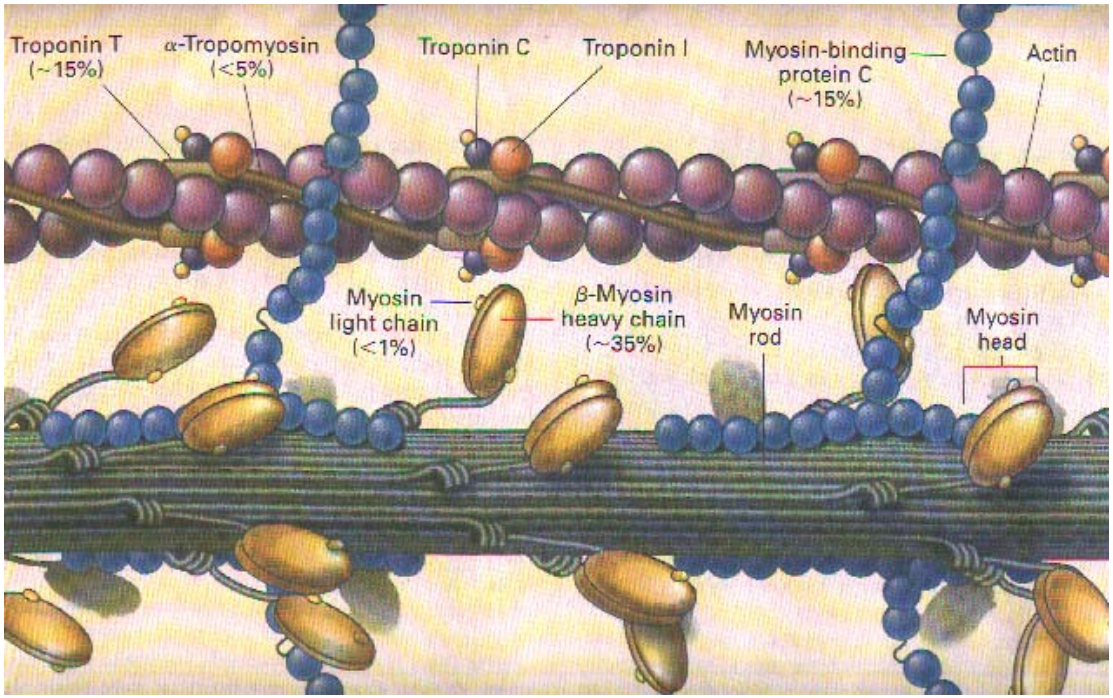
Clinical Assessment in Suspected Acute MI

Feature	High Likelihood *Any of the following:*	Intermediate Likelihood *Absence of high-likelihood features and presence of any of the following:*	Low Likelihood *Absence of high- or intermediate-likelihood features but may have:*
History	Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina Known history of CAD, including MI	Chest or left arm pain or discomfort as chief symptom Age greater than 70 years Male sex Diabetes mellitus	Probable ischemic symptoms in absence of any of the intermediate likelihood characteristics Recent cocaine use
Examination	Transient MR murmur, hypotension, diaphoresis, pulmonary edema, or rales	Extracardiac vascular disease	Chest discomfort reproduced by palpation
ECG	New, or presumably new, transient ST-segment deviation (1 mm or greater) or T-wave inversion in multiple precordial leads	Fixed Q waves ST depression 0.5 to 1 mm or T-wave inversion greater than 1 mm	T-wave flattening or inversion less than 1 mm in leads with dominant R waves Normal ECG
Cardiac markers	Elevated cardiac TnI, TnT, or CK-MB	Normal	Normal

Universal Definition Acute MI (2012)

- Detection of a rise or fall in a biomarker (**troponin**) with at least one value >99th centile upper reference limit **AND** at least one of:
  - Symptoms suggestive of ischaemia
  - New or presumed new ST-T changes or LBBB on ECG
  - Development of pathological Q waves on ECG
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
  - Identification of intracoronary thrombus on angiography or at autopsy

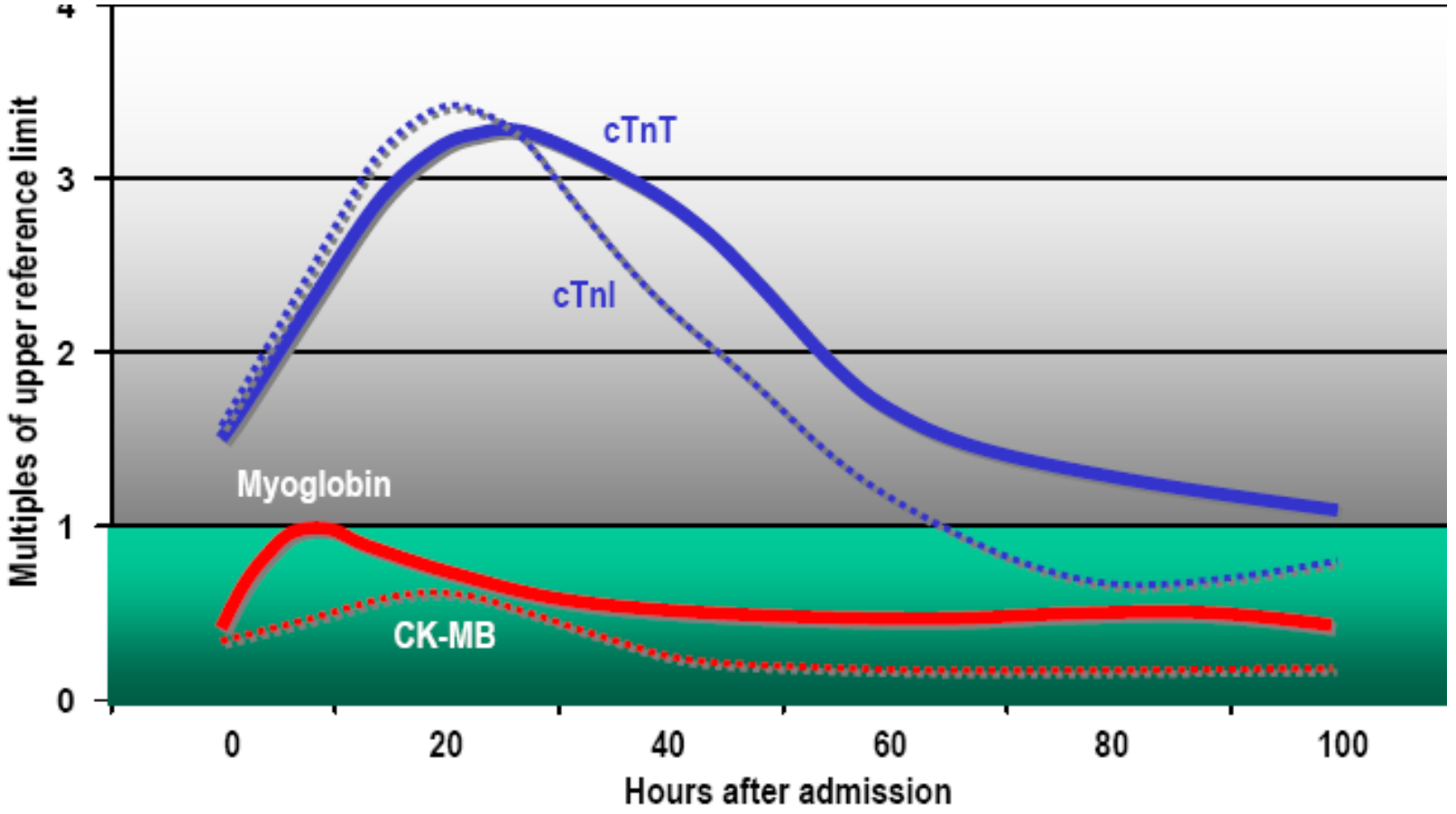
Cardiac Troponin



cTn can be released transiently without cardiomyocyte death

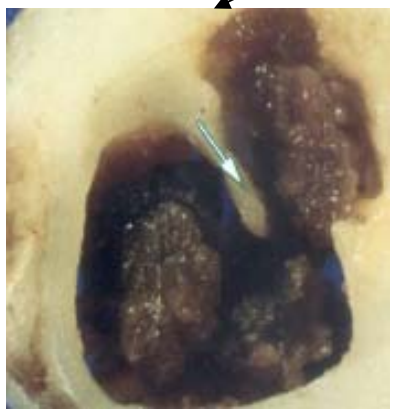
- cTn complex – thin filament of striated muscle
- 3 components, coded by separate genes
- Critical role in E-C coupling
- cTnI (23kDa)
- cTnT (35 kDa)
- cTnC (18 kDa)
- cTnI and T are highly specific for cardiac muscle
- ~5% in cytosolic/early appearing pool, ~95% in structural pool
- Proteolytic cleavage during myocardial ischaemia
- Circulating cTn: post-translational modified, degraded and truncated forms

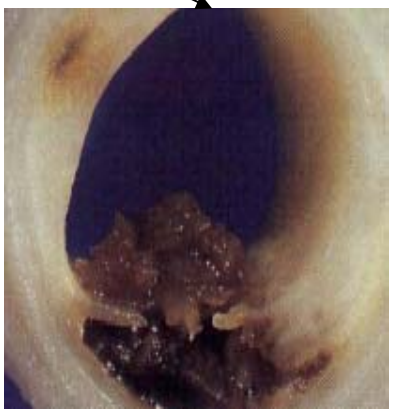
Timing of Cardiac Enzyme Release in ACS

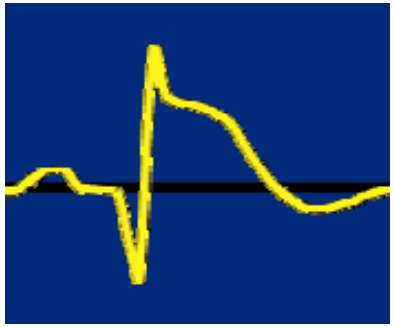


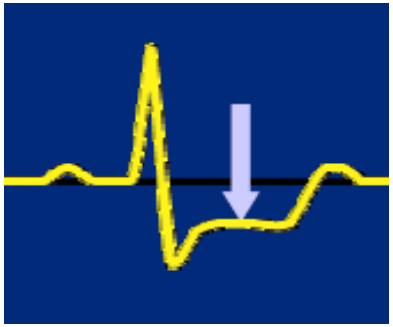
ESC NSTE-ACS Guidelines 2007

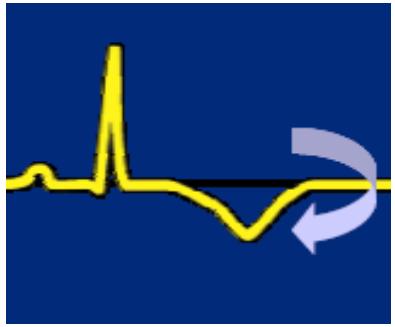
Acute Coronary Syndromes











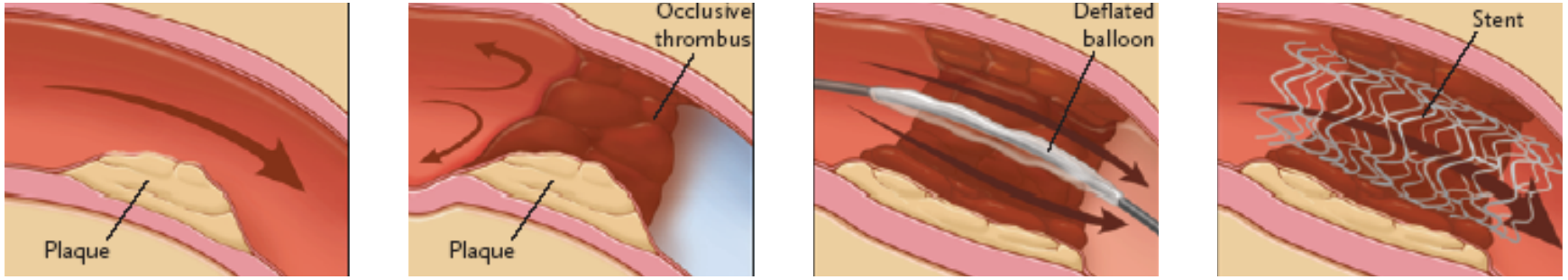
ST elevation

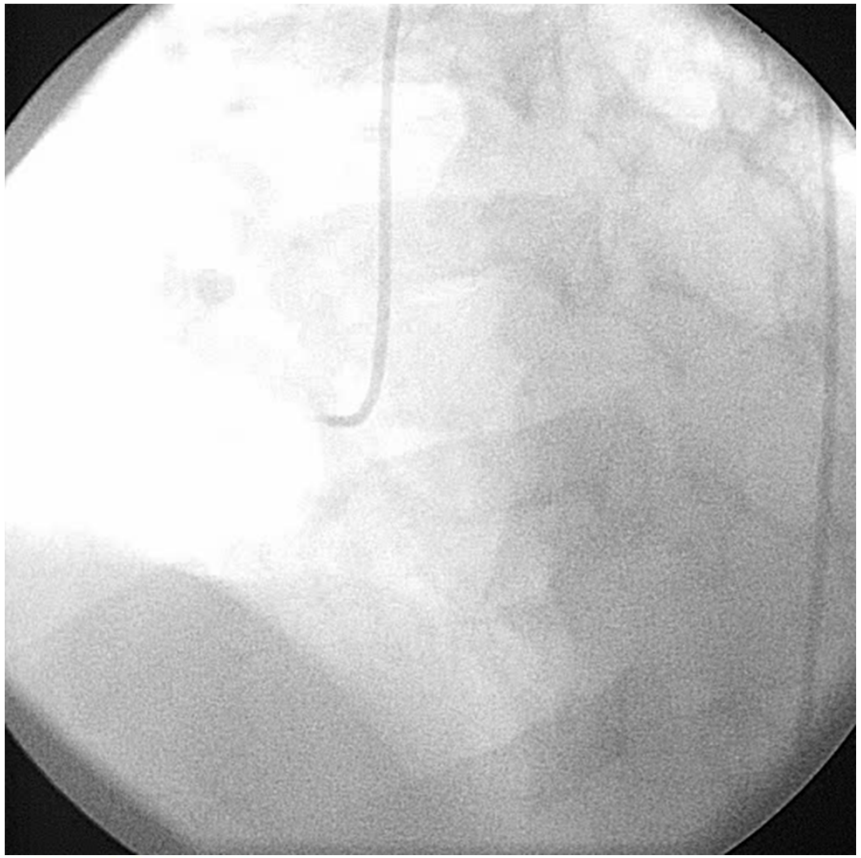
ST depression

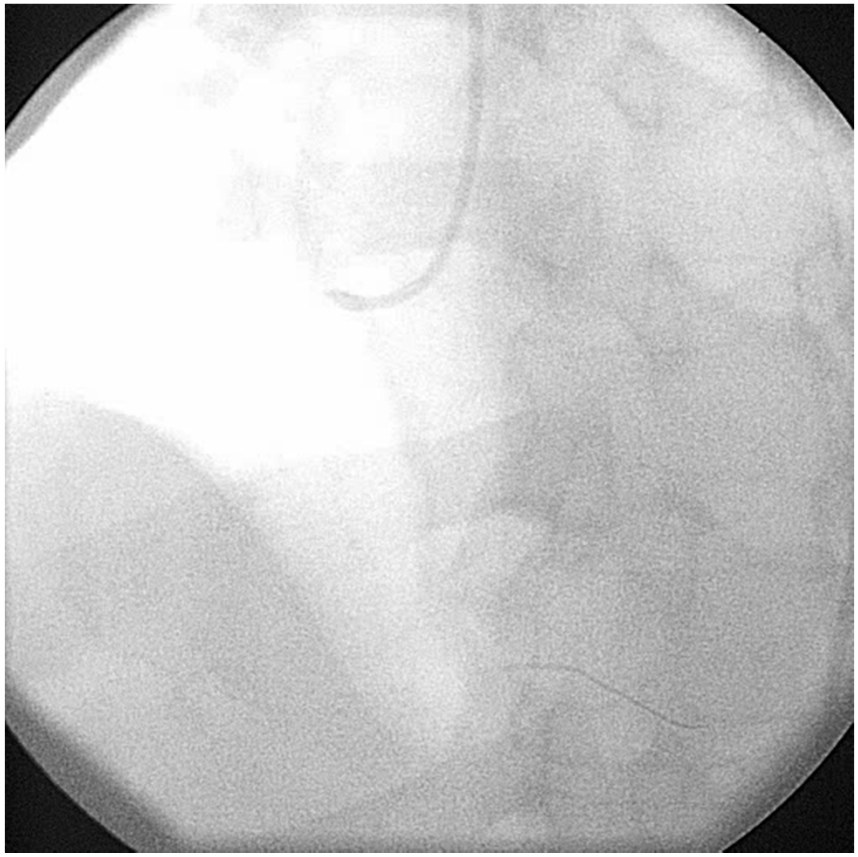
T wave inversion or normal ECG

ESC NSTE-ACS Guidelines 2007

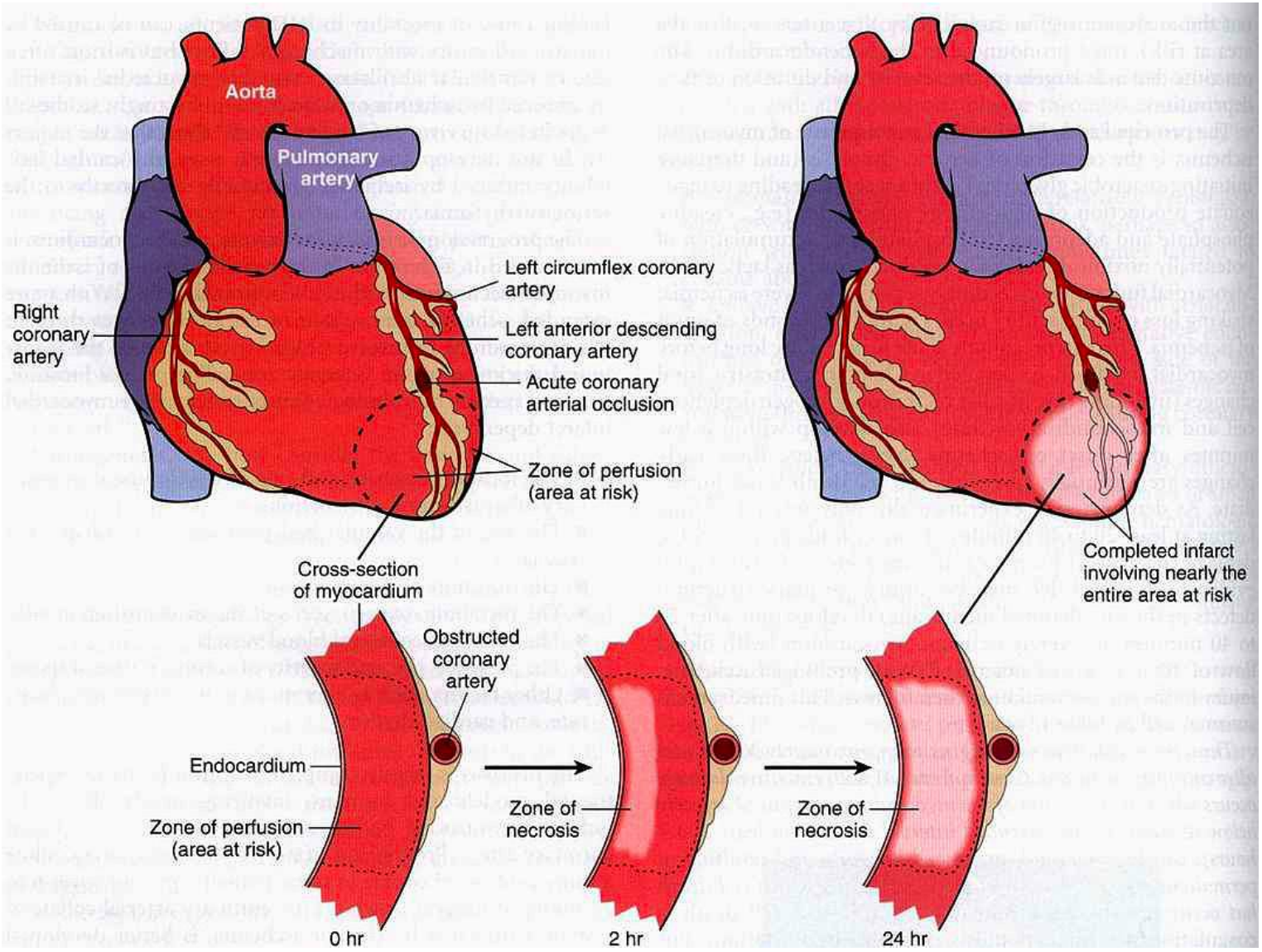
PPCI for STEACS



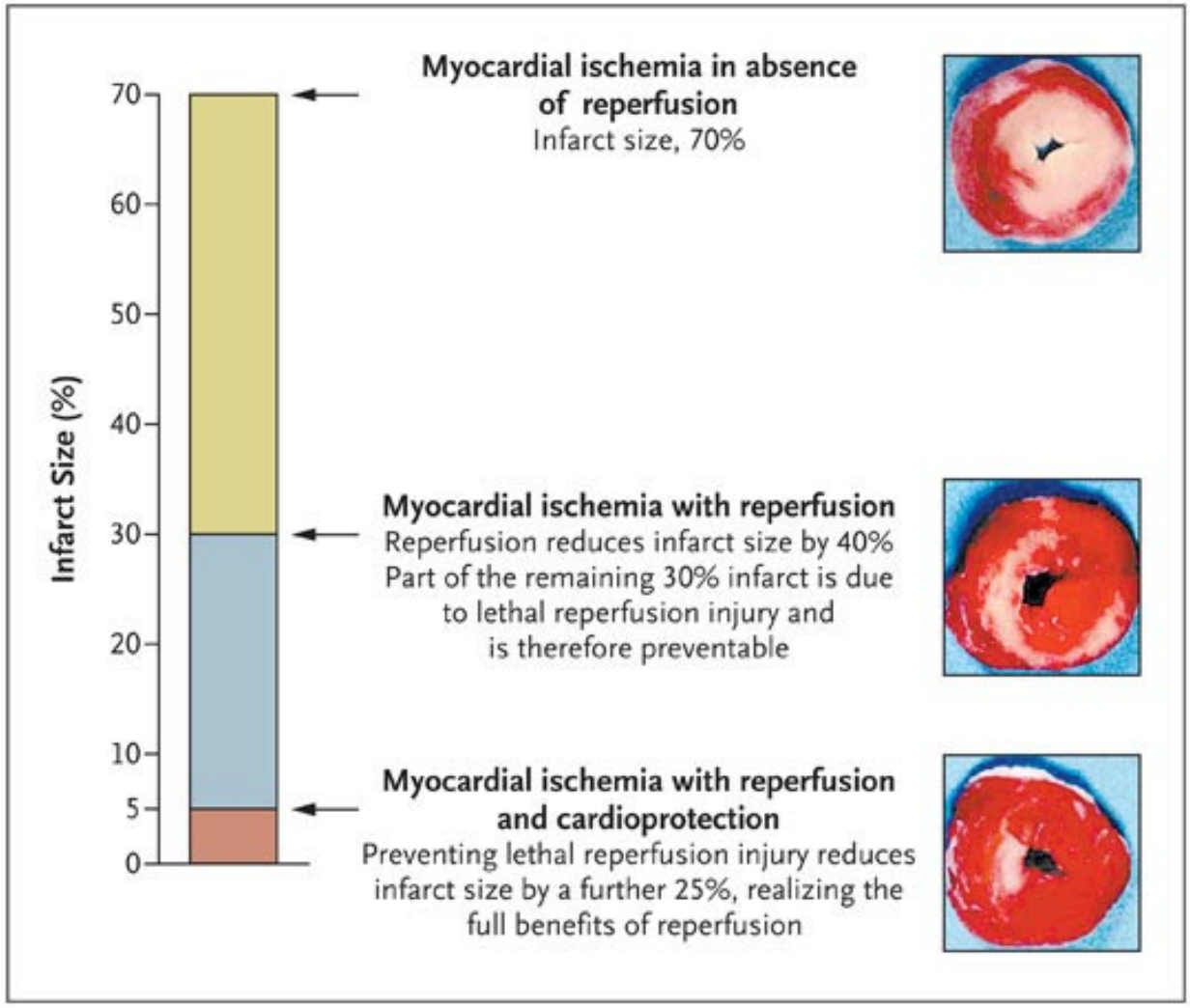




Development of Infarction

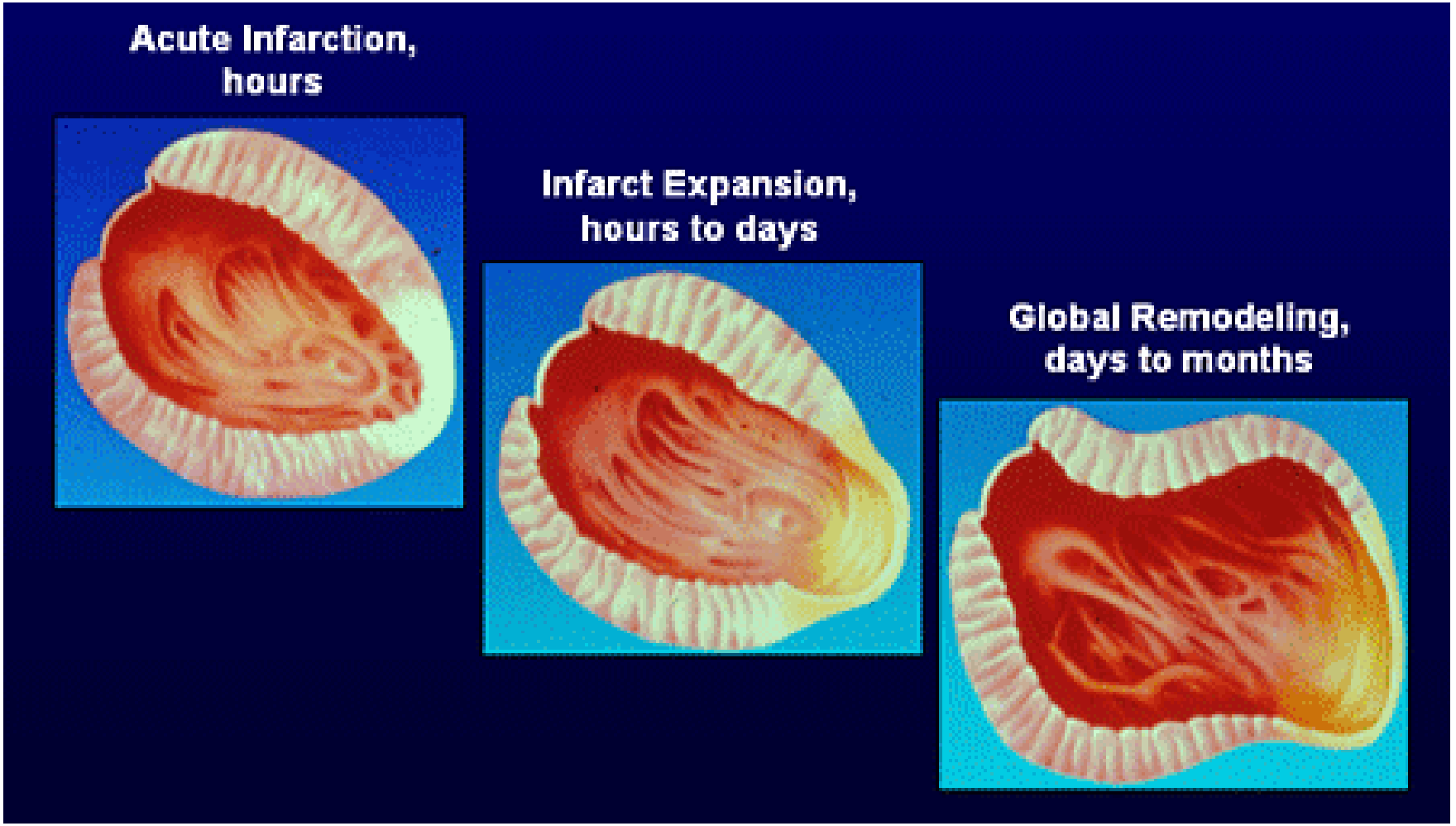


Reperfusion Injury



Yellon & Hausenloy NEJM 2007

Post-MI LV Remodelling



Mechanisms Underlying LV Remodelling

- Infarct thinning, elongation, expansion
- LV dilatation
  - reduce wall tension
  - maintains cardiac output
- Non-infarcted myocardium
  - LVH + myofilament dysfunction
  - Altered electromechanical coupling
  - Myocardial fibrosis
  - Apoptosis
  - Inflammation

Consequences of Adverse LV Remodelling

- Increased systolic wall tension/stress
- Increased MVO2
- Reduced myocyte shortening
- Increased diastolic wall tension/stress
- Reduced subendocardial perfusion
- Dysynchronous depolarization/contraction
- Mitral regurgitation
- Ventricular arrhythmias
- Ventricular fibrillation

Manage Thrombotic Burden/Risk

Acute

- Thrombectomy
- Drugs
  - Oral antiplatelets: Aspirin, clopidogrel, prasugrel, ticagrelor
  - SC anticoagulants: LMWH, fondaparinux
  - IV antiplatelets: GpIIb/IIIa inhibitors
  - IV anticaogulants: Bivalirudin,, fibrinolytics, *Factor Xa inhibitors*

Recurrent

- Oral antiplatelet drugs
- Anticoagulants
  - *Direct thrombin inhibition*
  - *Factor Xa inhibitors*

Plaque Stabilisation

Mechanical

- Stent

Drugs

- Statins (high dose)
- ACE inhibitors

Manage LV Remodelling

Non-Drug

- CRT-P/D
- Progenitor cells

Drugs

- β blockers
- ACE inhibitors
- Angiotensin receptor blockers
- Aldosterone receptor antagonists

Embolism

- An obstruction in a blood vessel due to a thrombus or other foreign matter that gets stuck while travelling through the bloodstream.
- Arterial (thrombus [ACS, TIA, stroke], air, fat, amniotic, foreign body/material)
- Venous (thrombus [DVT, PE])

TIA/Stroke

- Embolic
  - ICA plaque rupture
  - Intracardiac (e.g. AF, old MI, valve disease)
  - Intracardiac communication
- Treatment
  - Fibrinolysis
  - Clot extraction
  - Antiplatelet drugs
  - Modify atherosclerotic risk factors
  - Endarterectomy, stent
  - Hole closure
- Haemorrhagic
  - Vascular malformation
  - Hypertension
  - Tumor
  - Iatrogenic
- Treatment
  - Coil/clip aneurysm
  - Withdraw pro-haemorrhagic medication
  - Control hypertension

Venous Thromboembolism

Deep Vein Thrombosis

- Incidence: 1.6/1000/yr
- Aetiology:
  - Trauma
  - Orthopaedic surgery
  - Malignancy
  - Autoimmune disease
  - Thrombophilia
  - Immobility
- Diagnosis: Clinical (Wells Score), D-Dimer, Duplex ultrasound, CT, MRI, Venography
- Complications:
  - PE (in 50% if symptomatic DVT untreated)
  - Post-thrombotic syndrome (in ~45% within 1 year of symptomatic DVT's)
  - Venous ulcer
- Prevention
  - TEDS, sc LMWH/Anti-Xa
- Treatment
  - Anticoagulation, Fibrinolysis, Thrombectomy

Pulmonary Embolism

- Symptoms: Dyspnoea, chest pain, hypotension, shock
- Diagnosis: clinical, ECG, D-dimer, echo, CTPA, MRI, VQ scan, pulmonary arteriogram
- Complications: death, shock, pulmonary hypertension, RV failure
- Treatment: anticoagulation, fibrinolysis, mechanolysis, IVC filter

Embolism - Other

- **Air embolism**
  - Iatrogenic
  - Decompression sickness
  - Trauma
- **Fat embolism**
  - Trauma
- **Amniotic fluid embolism**
  - Pulmonary vasoconstriction, inflammation
  - ~1:54,000 deliveries, CFR 13-30%
  - Sudden CV collapse: Pulmonary HTN + RV failure -> LV failure
  - DIC
  - Rx: pulmonary vasodilators, FVIIa, ITU support
- **Cholesterol embolism**
  - Showers of microemboli from within plaque of large calibre artery
  - Plaque rupture (spontaneous, traumatic, iatrogenic)
  - Embolization of plaque debris (cholesterol crystals, platelets, fibrin)
  - Lodging of emboli in arterioles 100-200μm diam.
  - Foreign body inflammatory response
  - End-organ damage due to microvascular plugging and inflammation

Questions?

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

NHS
National Institute for Health Research