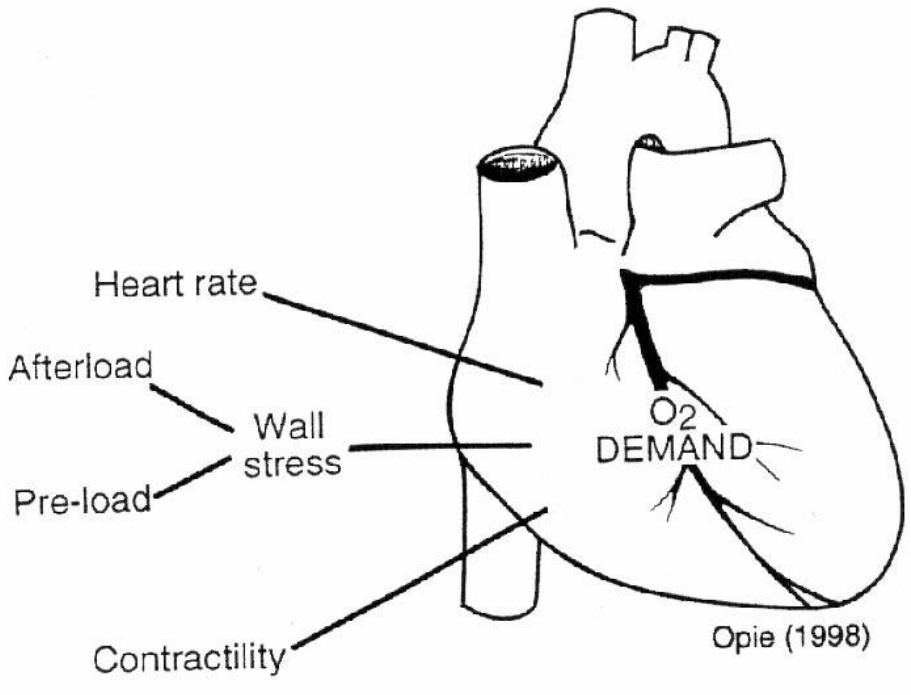
Myocardial ischaemia, myocardial infarction, and new ischaemic syndromes

Dr. Zoltán Papp
UD Department of Cardiology
Division of Clinical Physiology

Determinants of myocardial O_2 demand

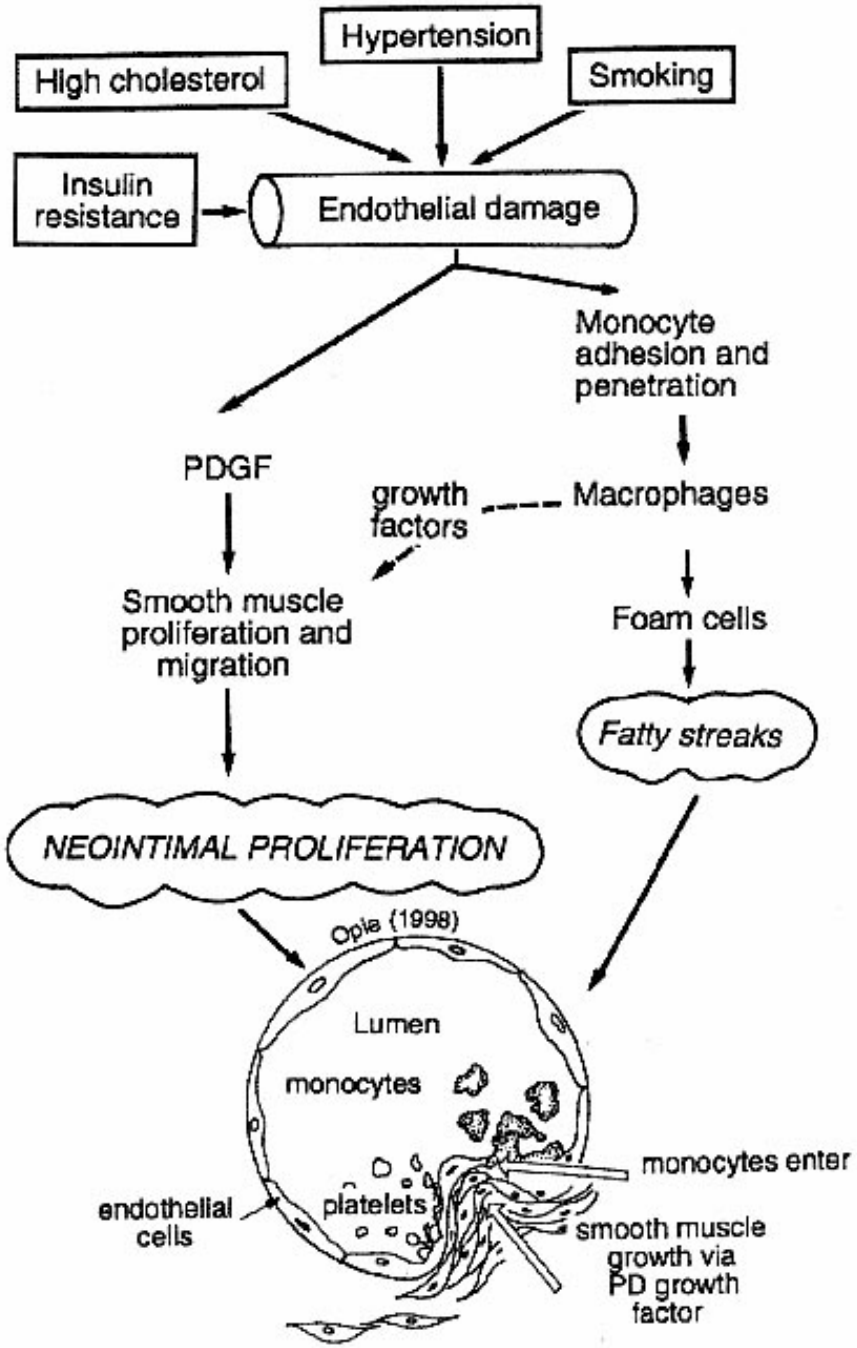


O_2 Demand determinants:
- **Heart rate (HR) - most important!**
- **Contractility (inotropy)**
- **Wall stress (preload, afterload)**

O_2 Supply determinants:
- **Coronary blood flow - O_2 content (Hb, saturation)**
- **O_2 extraction (already maximal at rest!)**

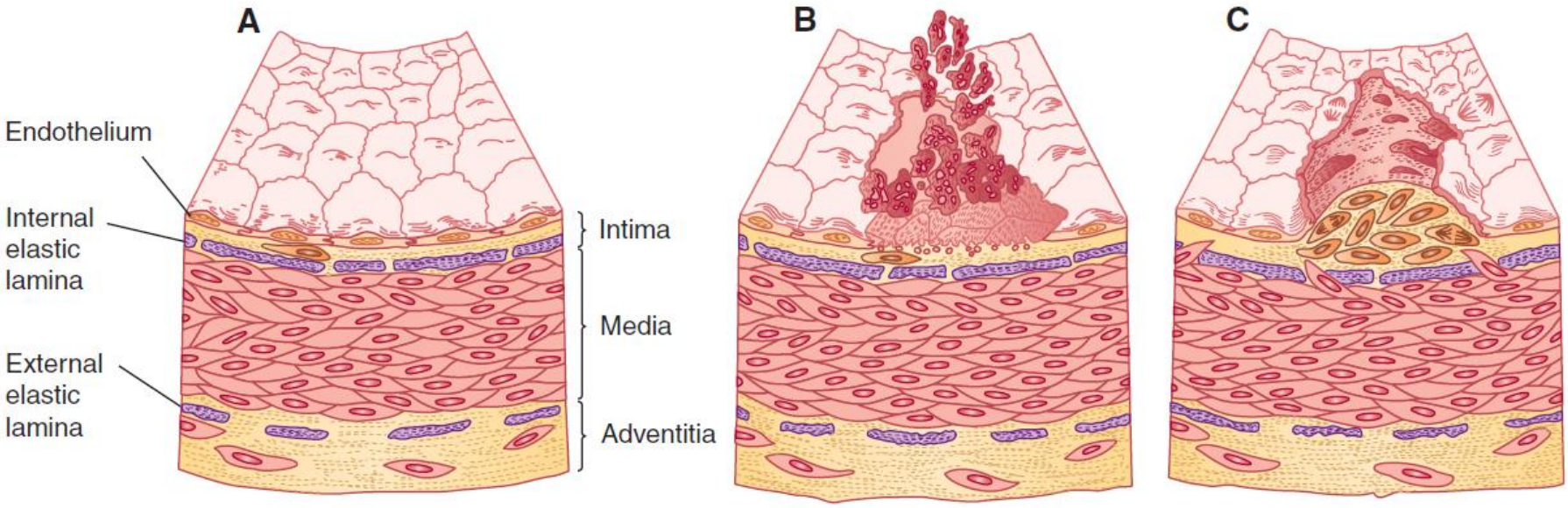
Critical concept: The heart cannot increase O_2 extraction significantly → O_2 uptake is flow-dependent!

Coronary artery disease and plaque formation

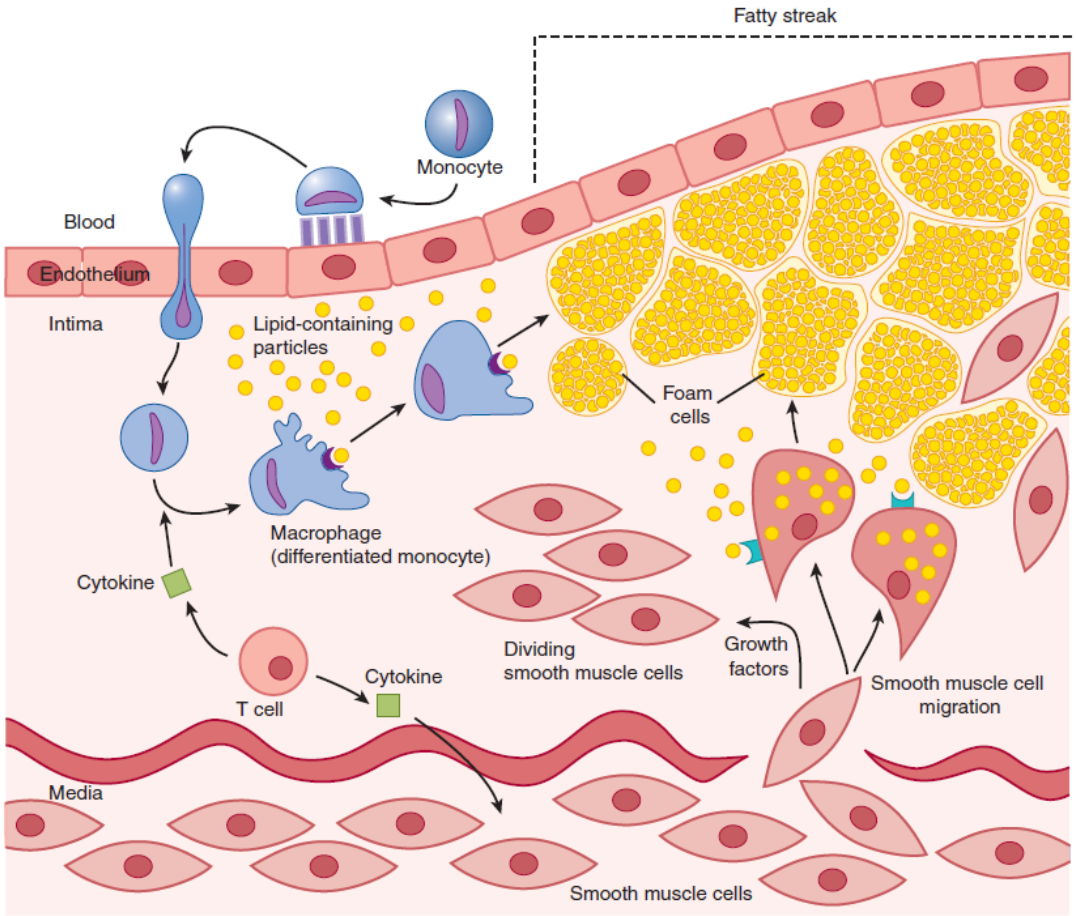


Atherosclerosis progression: - endothelial dysfunction → LDL oxidation → inflammation → plaque - stable vs unstable plaque: determined by fibrous cap thickness

Mechanisms of production of atheroma



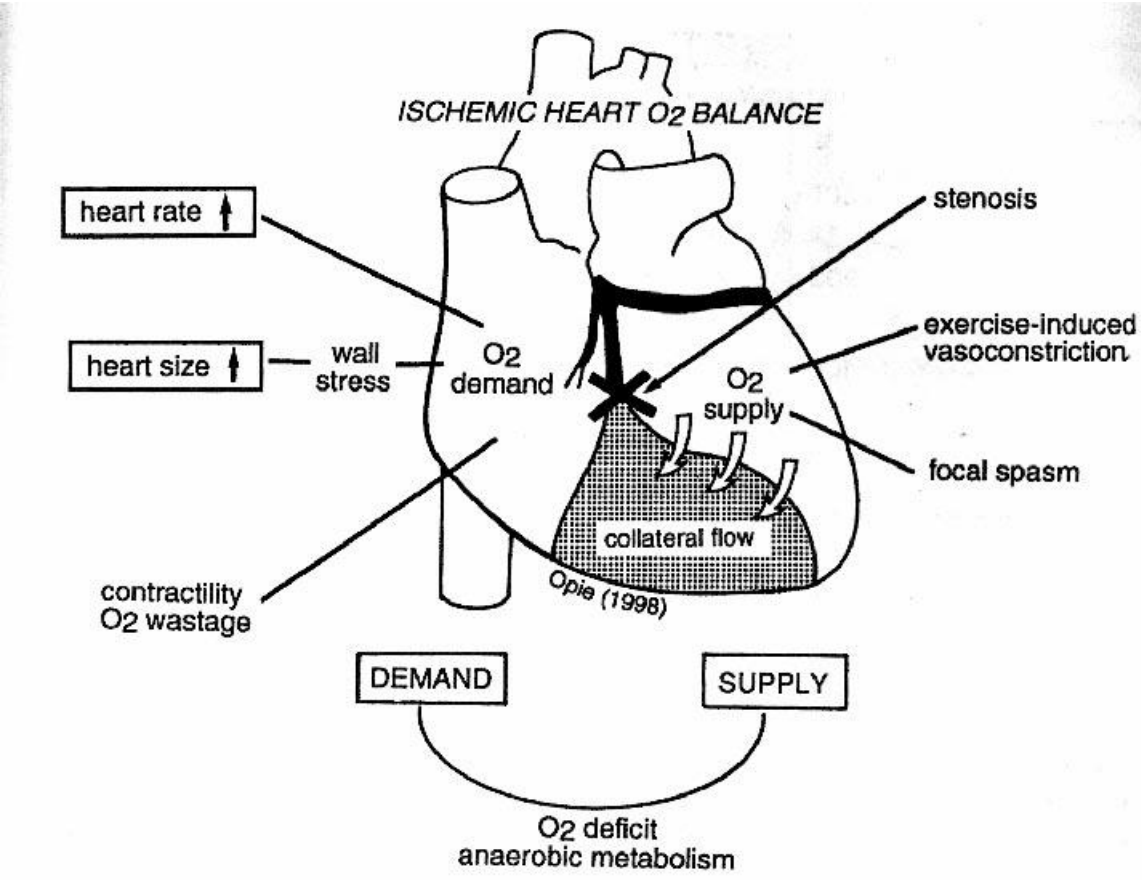
Formation of a fatty streak in an artery



Fatty streak formation:

- **Begins in childhood!**
- **But: clinical symptoms appear decades later**
- **This is why prevention is crucial**

Determinants of myocardial O_2 demand during coronary stenosis



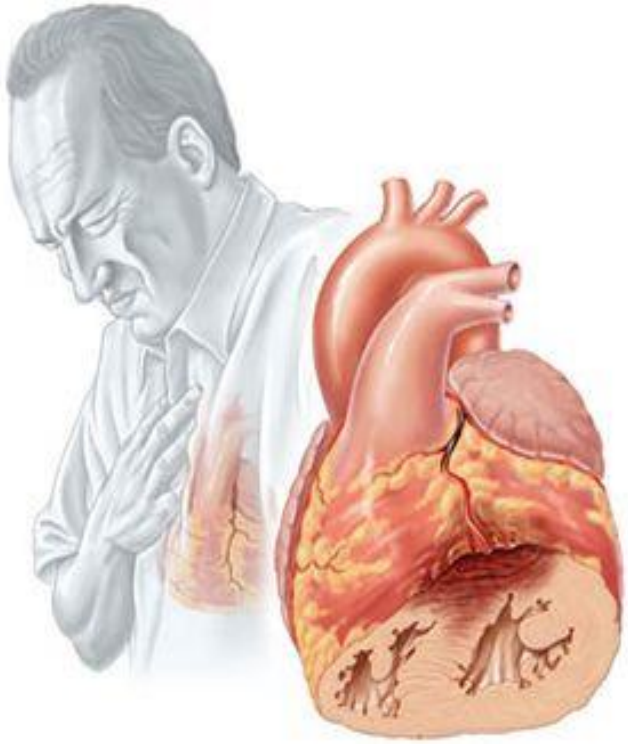
Normal heart:
- **Coronary flow reserve:**
- **4-5X increase possible**
- **During exercise: vasodilation → ↑ flow**

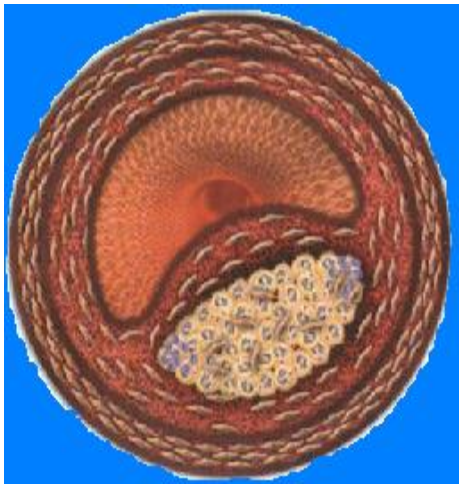
Stenosis (<70%):
- **At rest: compensated**
- **During exercise: no reserve → ischemia**

Critical stenosis (>90%):
- **Rest ischemia develops!**

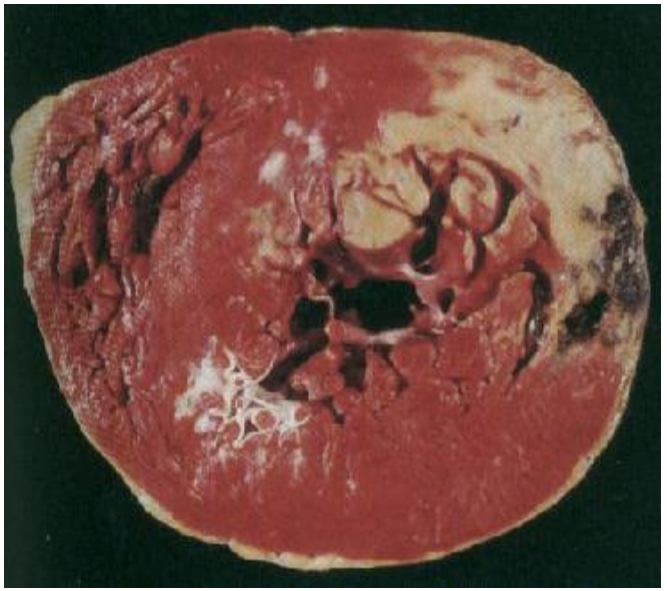
Clinical example:
This is why stable angina occurs only on exertion, but rest angina indicates critical stenosis

PATHOPHYSIOLOGY OF MYOCARDIAL ISCHAEMIA





Atherosclerotic plaque



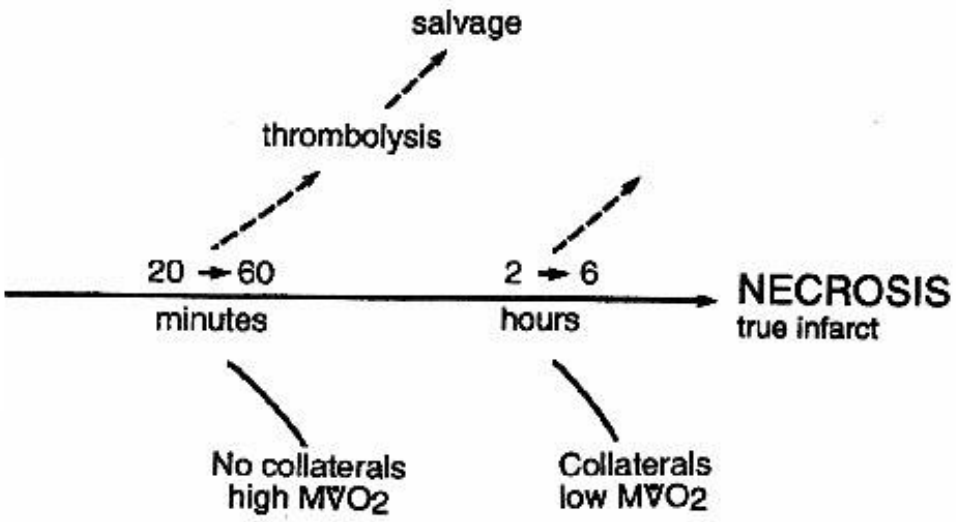
Myocardial necrosis (infarction)

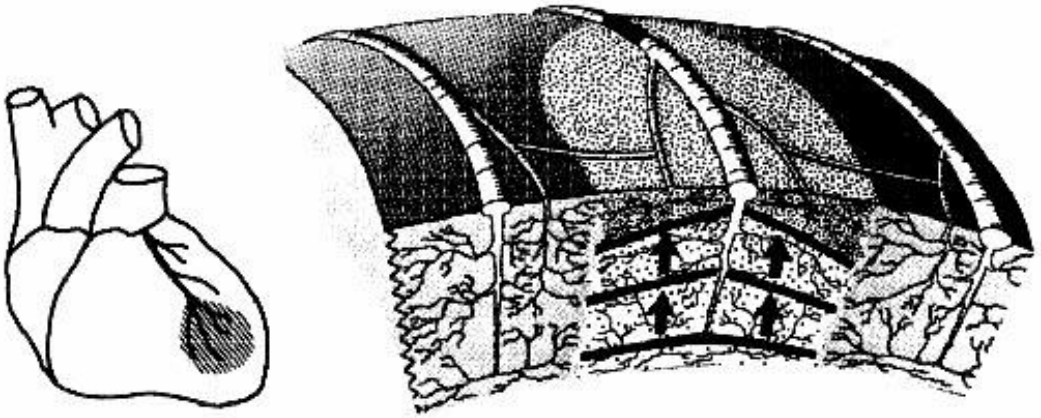
Atherosclerosis progression: Chronic stable CAD → ACS → STEMI

The key event: PLAQUE RUPTURE
→ Triggers acute coronary syndrome
→ Determines clinical presentation

Possible outcomes of myocardial ischaemia

Acute Coronary Syndrome (ACS)





ACS spectrum:

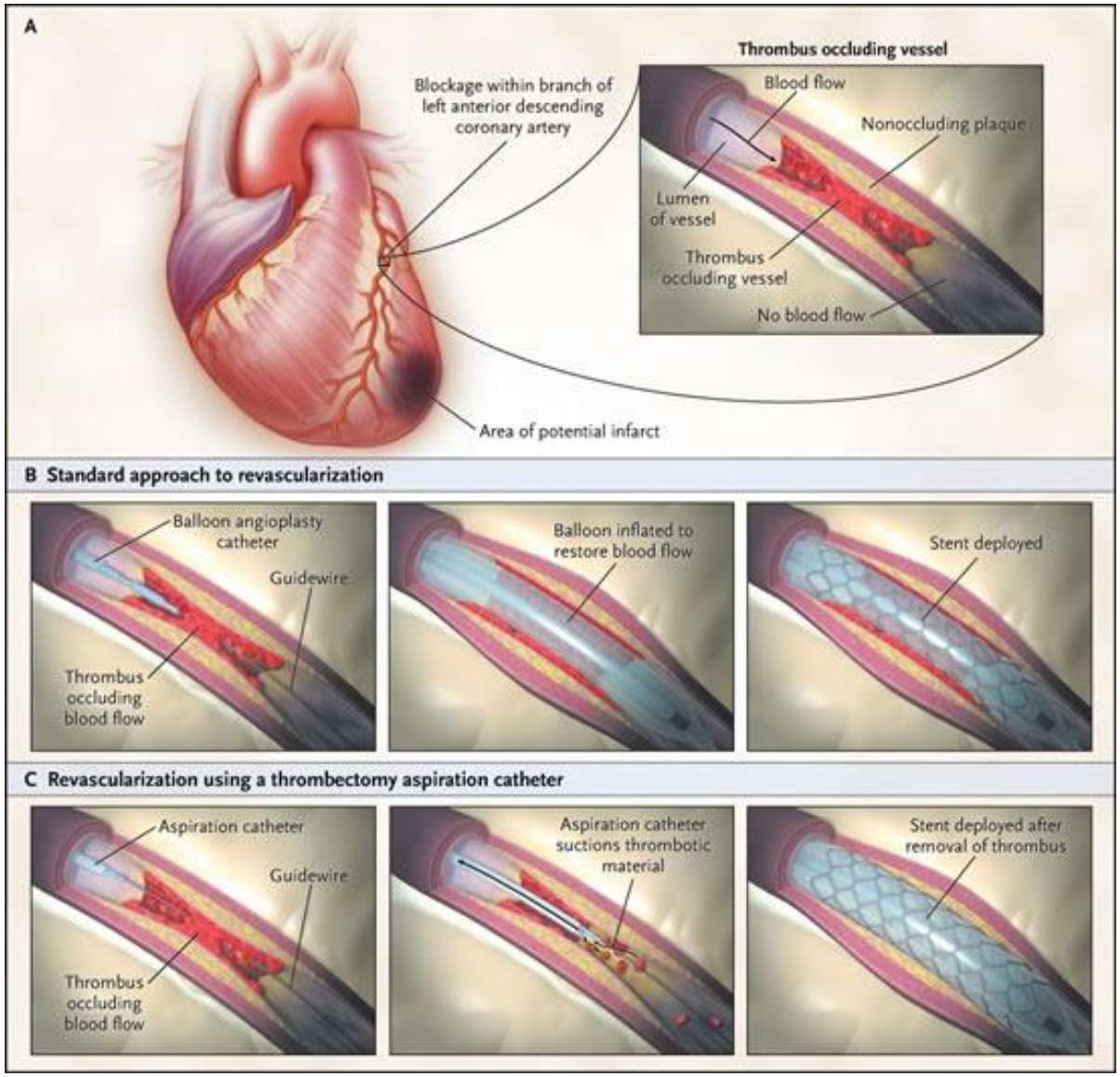
1. Unstable Angina (UA):
- **Ischemia present**
- **No necrosis (troponin negative)**

2. NSTEMI:
- **Non-ST elevation MI**
- **Necrosis present (troponin positive)**
- **No ST elevation**

3. STEMI:
- **ST elevation MI**
- **Necrosis present (troponin positive)**
- **ST elevation on ECG**

Why does this matter?
- **Different treatment strategies**
- **STEMI: immediate reperfusion (PCI <90 minutes!)**

Improving Reperfusion in Patients with Myocardial Infarction



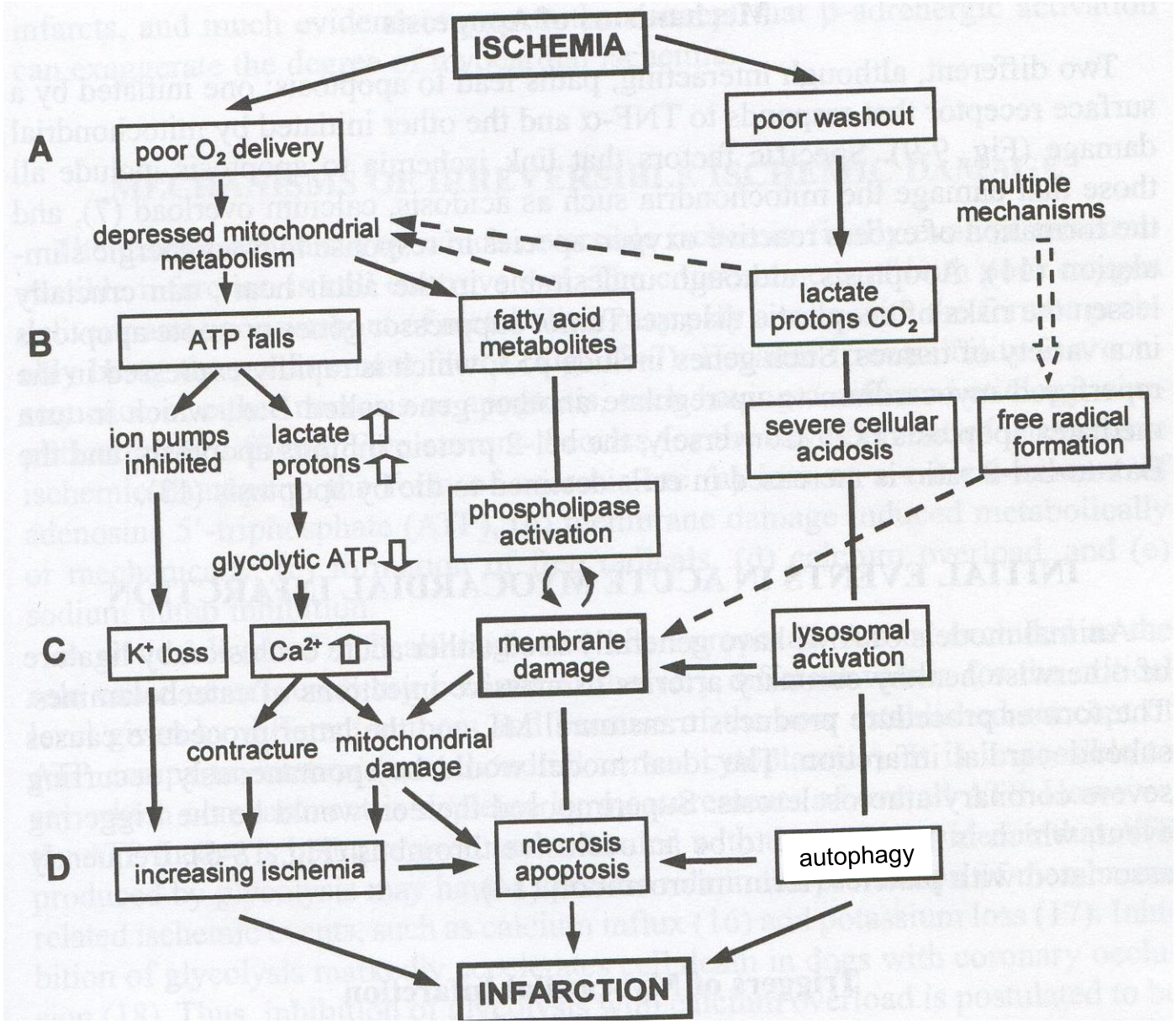
"Time is myocardium!"

- **First 1-2 hours: CRITICAL window**
- **3-6 hours: tissue still salvageable**
- **>12 hours: mostly necrosis**

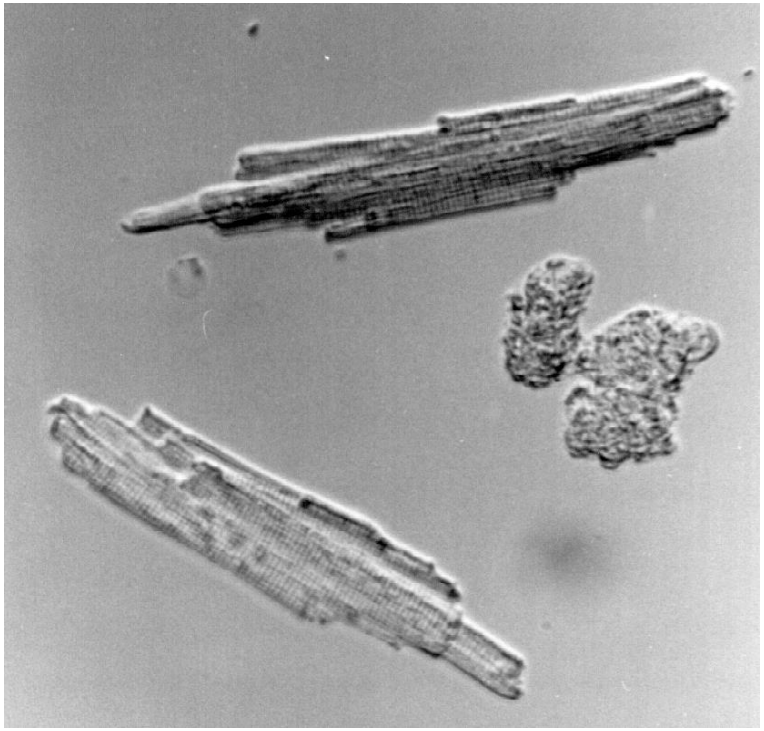
Reperfusion strategies:

- **Primary PCI (preferred)**
- **Fibrinolysis (if PCI not available within 120 minutes)**

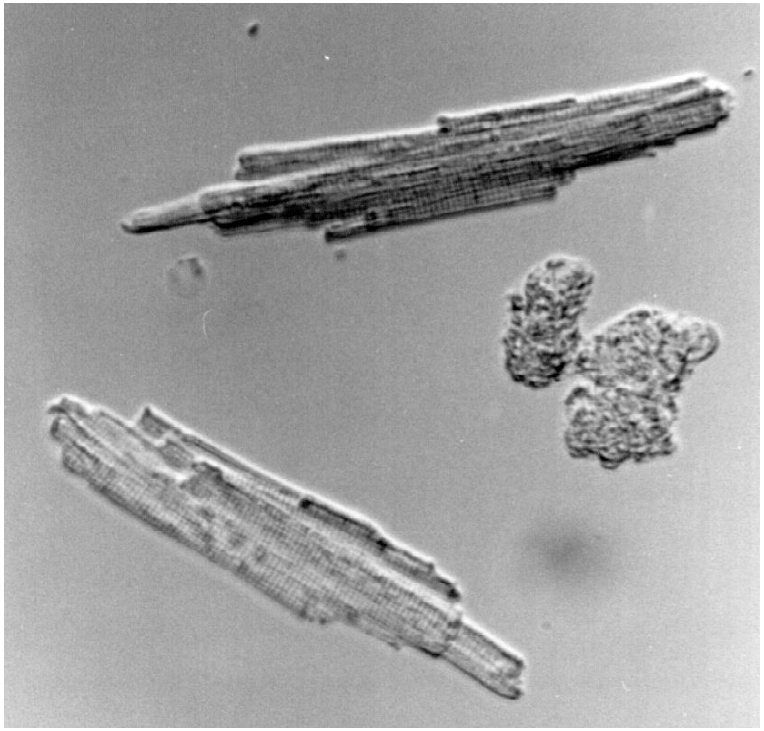
Ischaemia and infarction



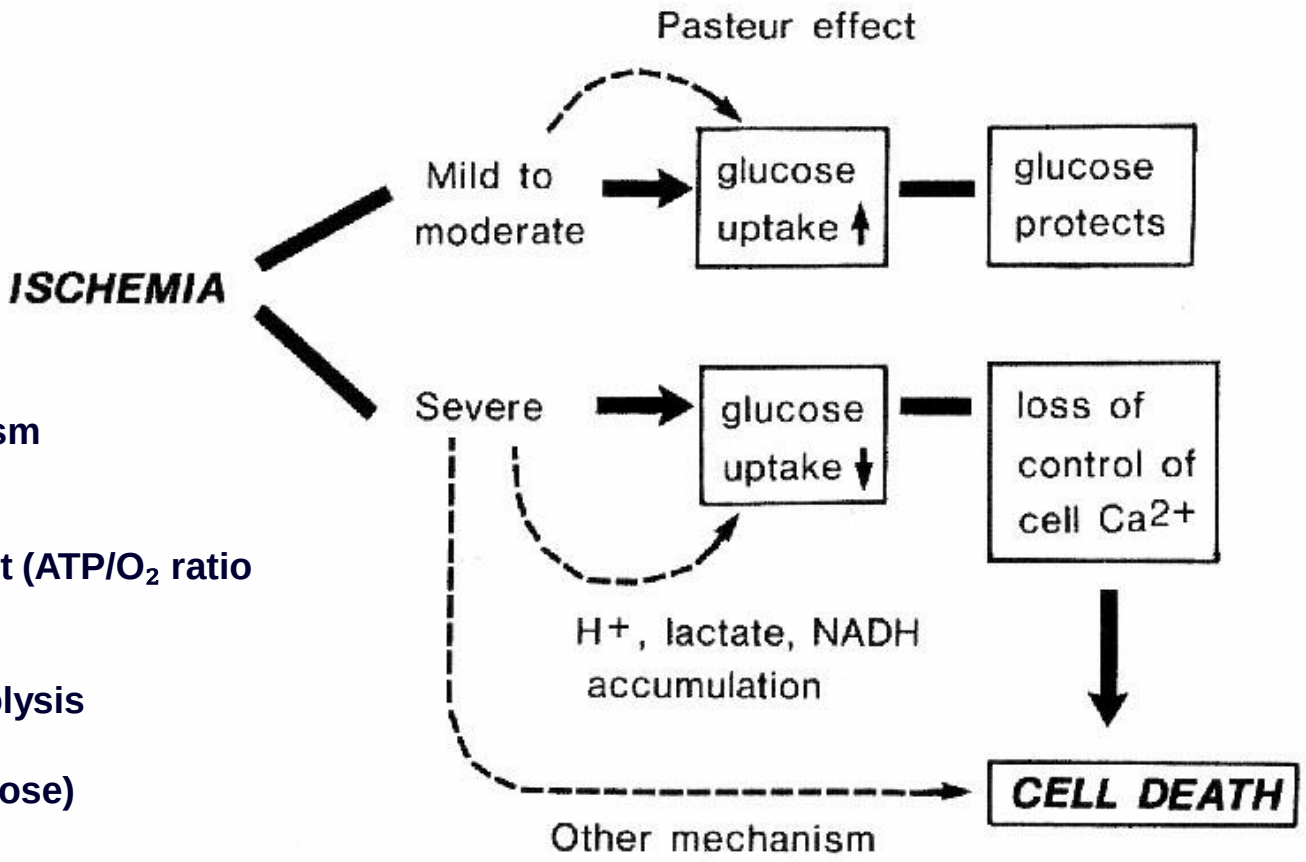
How many cardiomyocytes do you see?



How many cardiomyocytes do you see?



Ischaemic tolerance and glucose homeostasis



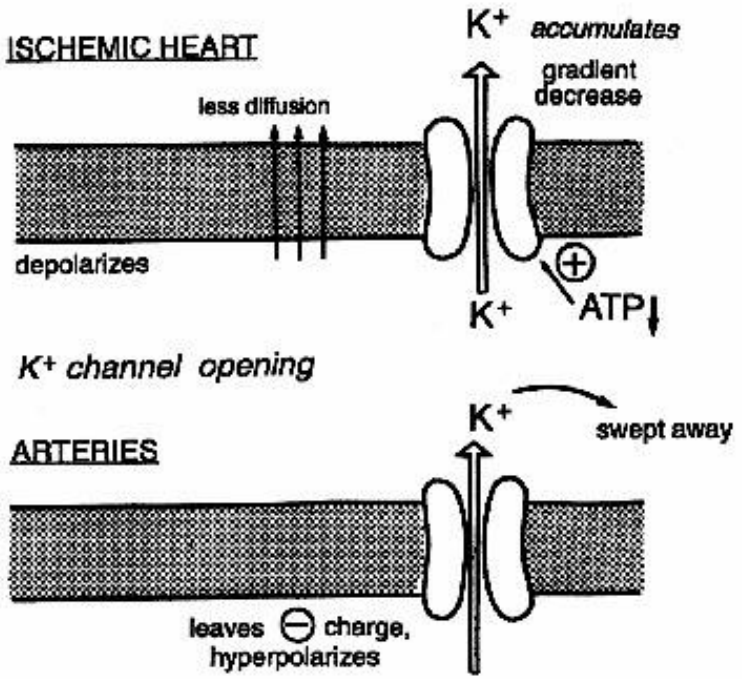
Metabolic switch:

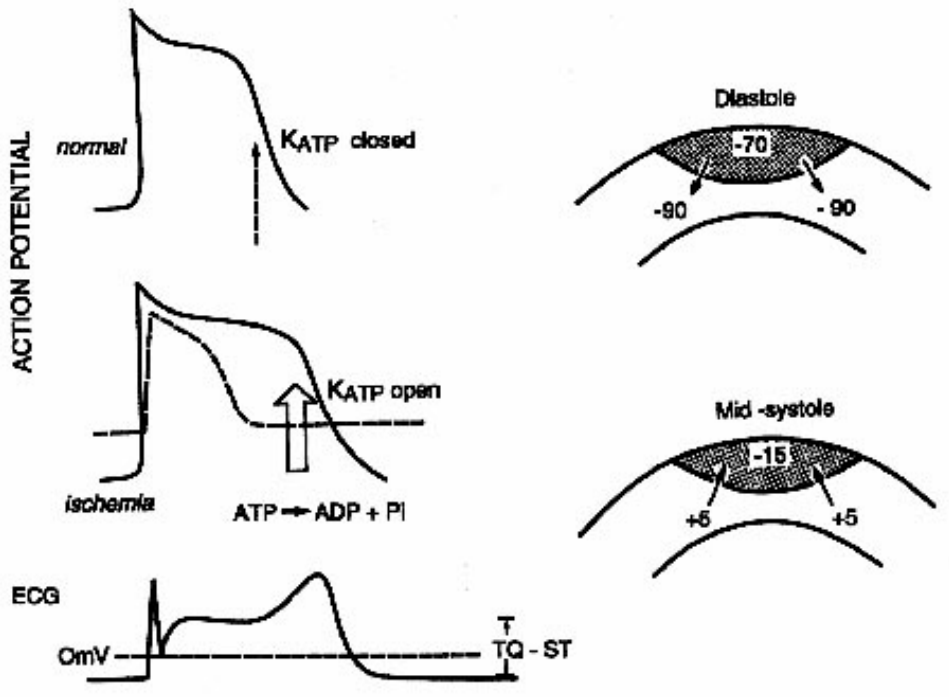
Normal: Aerobic metabolism
- **Fatty acids (60-70%)**
- **Glucose (30-40%)**
- **O_2-demanding, efficient (ATP/O_2 ratio high)**

Ischemia: Anaerobic glycolysis
- **Only glucose**
- **ATP↓ (2 vs 36 ATP/glucose)**
- **Lactate↑ → acidosis**
- **But: less O_2-demanding**

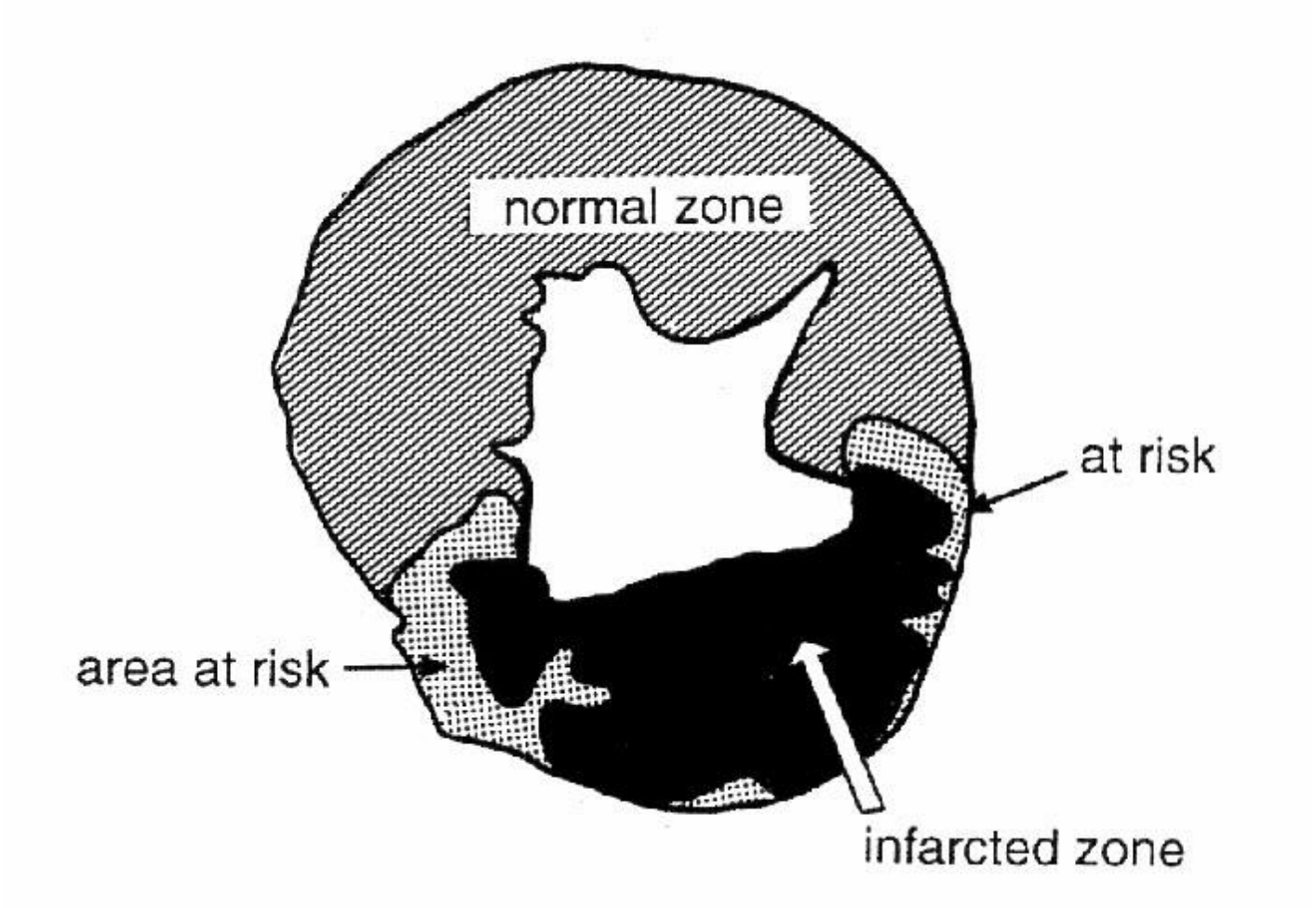
The "glucose paradox": During ischemia, glucose metabolism can be protective (requires less O_2), but acidosis is harmful.

Electrical changes during ischaemia



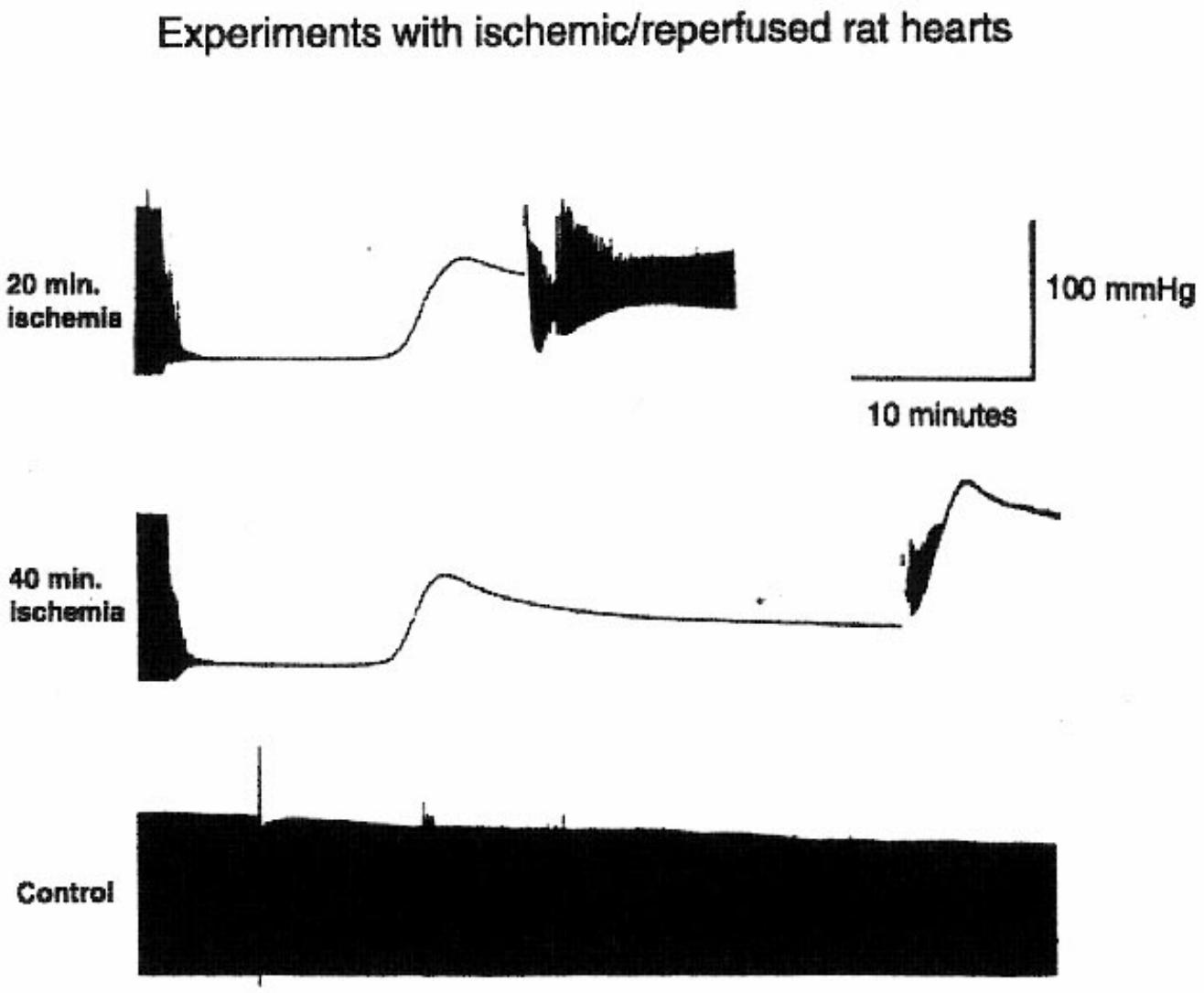


Area at risk

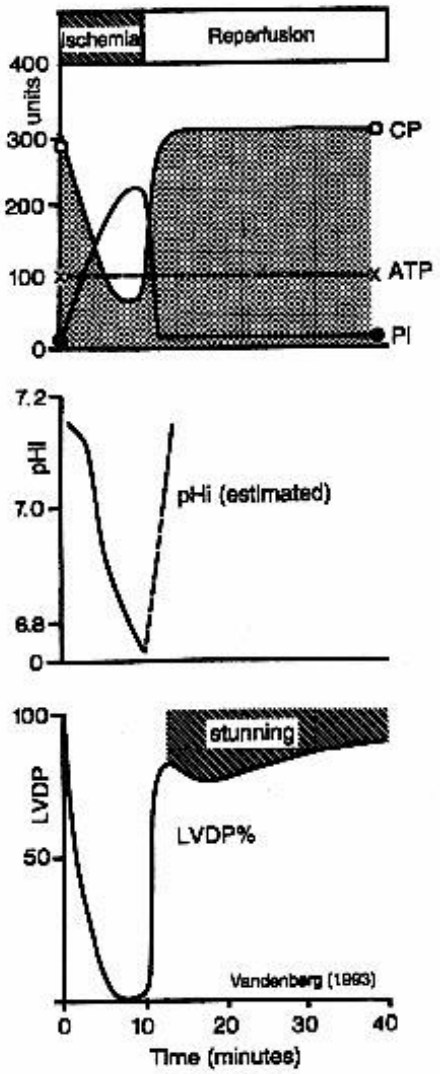


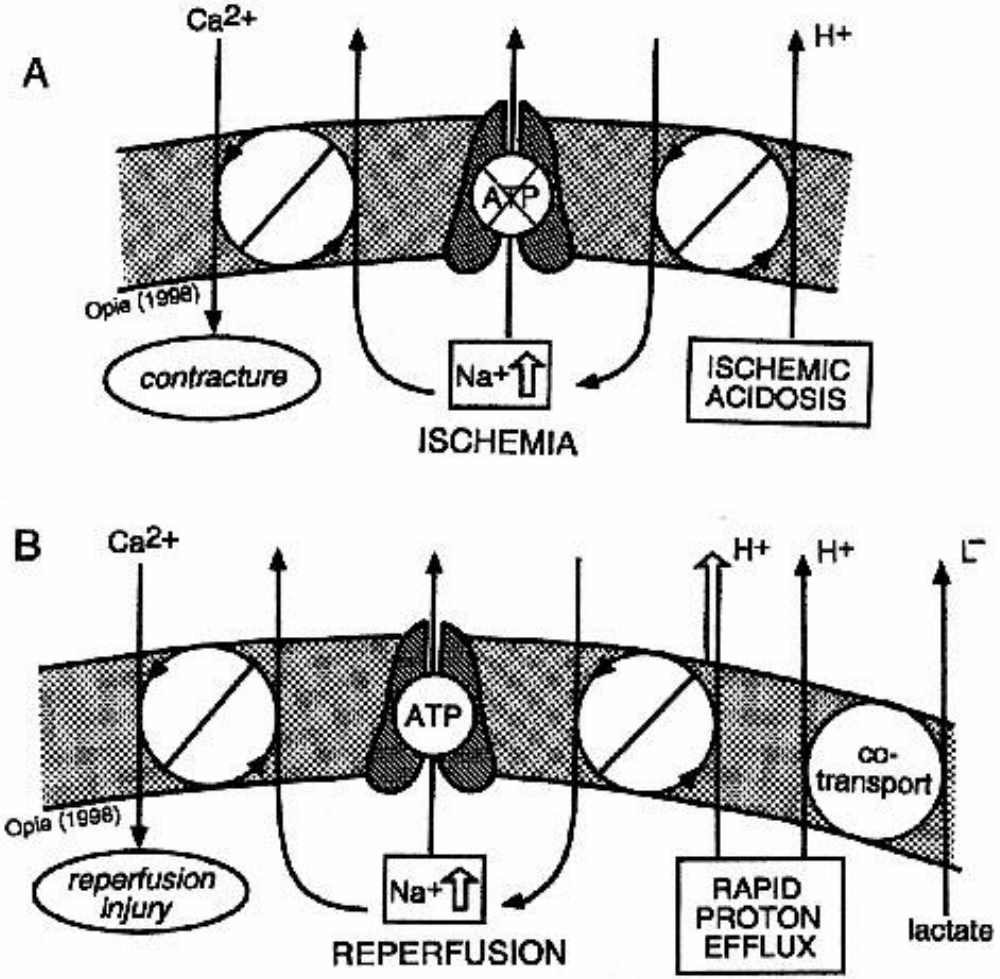
Area at risk = territory supplied by the occluded artery
Influencing factors: - Which artery is occluded (LAD > RCA > LCx typically)
- Collateral circulation
- Time to reperfusion
Goal: Minimize infarct size relative to the area at risk
→ Early reperfusion!
→ Cardioprotection (preconditioning, postconditioning)

Ischaemia and reperfusion

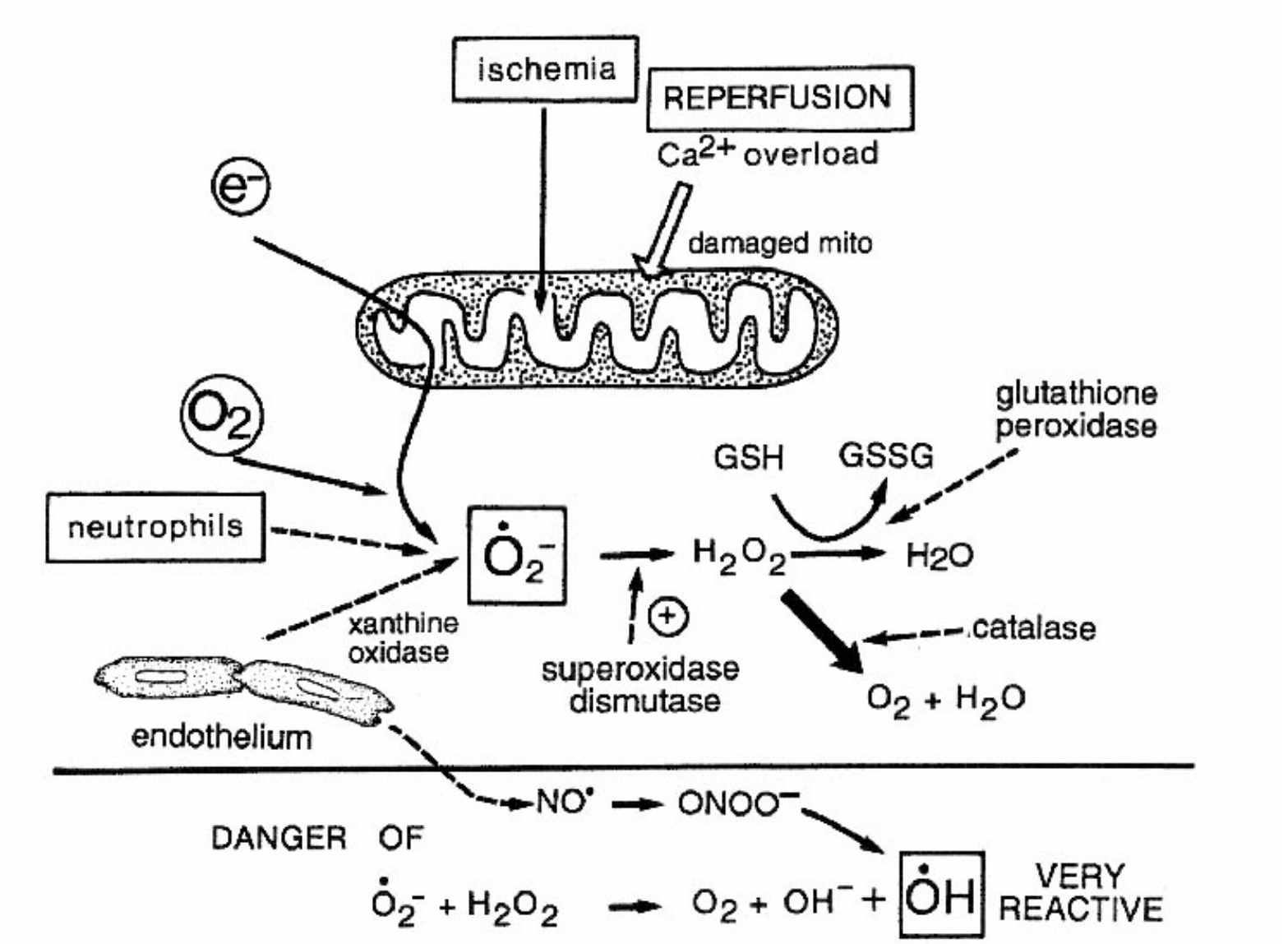


Metabolic changes during ischaemia and reperfusion

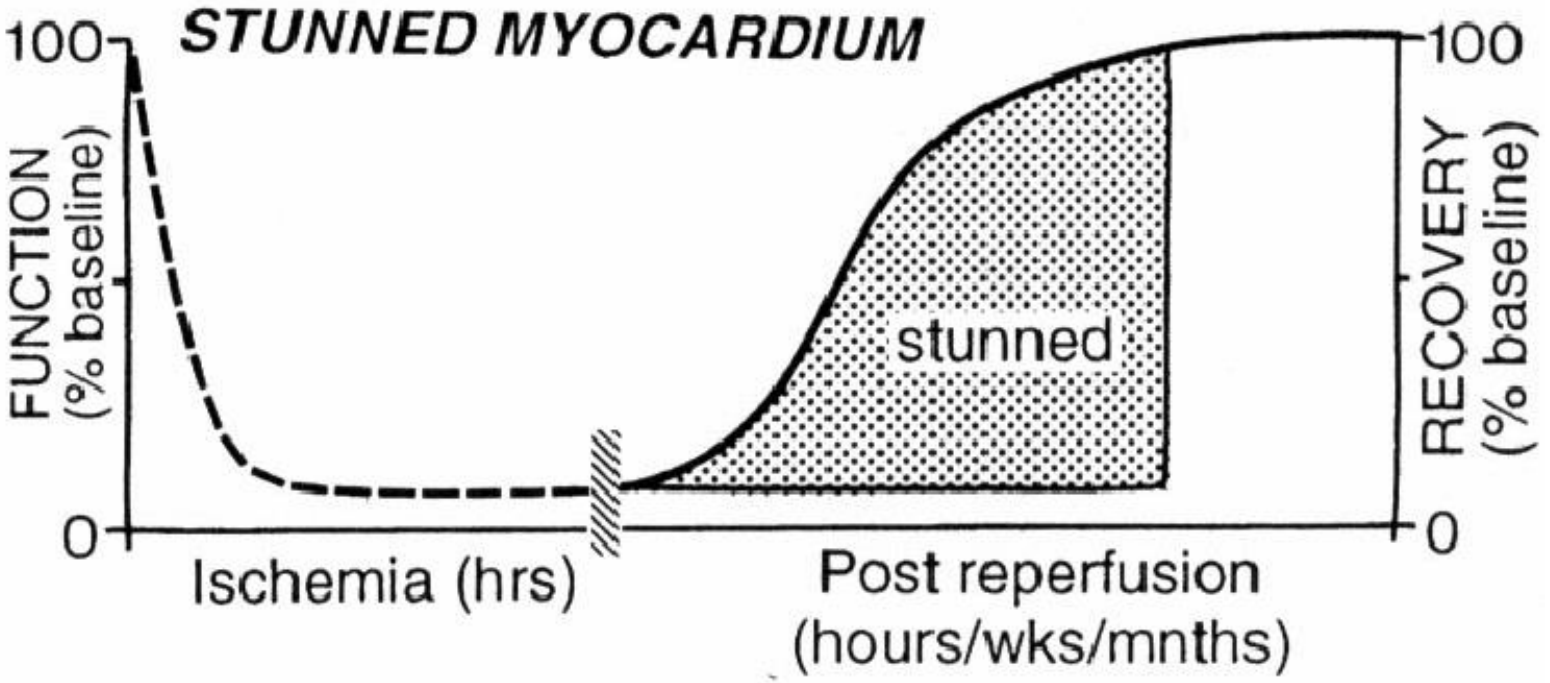




Free radical damage



Myocardial stunning

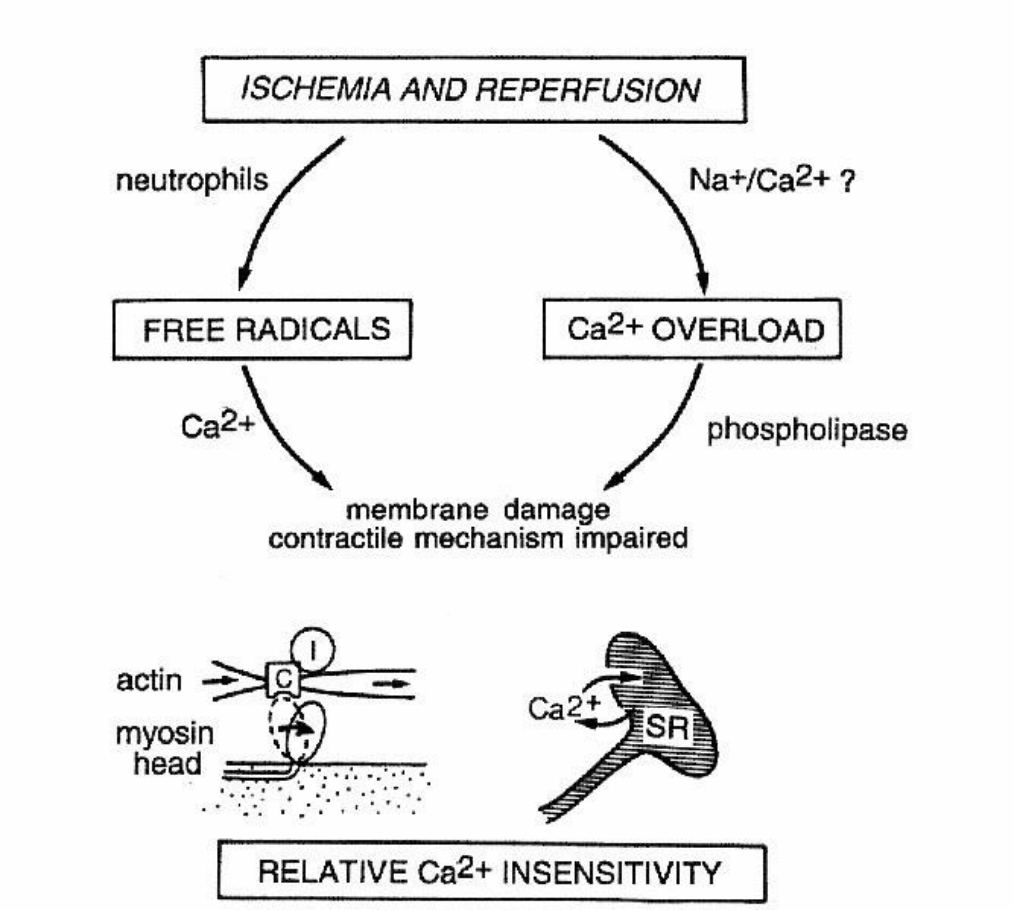


Stunning definition:

- **Prolonged contractile dysfunction**
- **AFTER successful reperfusion**
- **REVERSIBLE (hours to days)**
- **No new necrosis**

Clinical example: Post-PCI, LV function may worsen initially, then gradually improves.

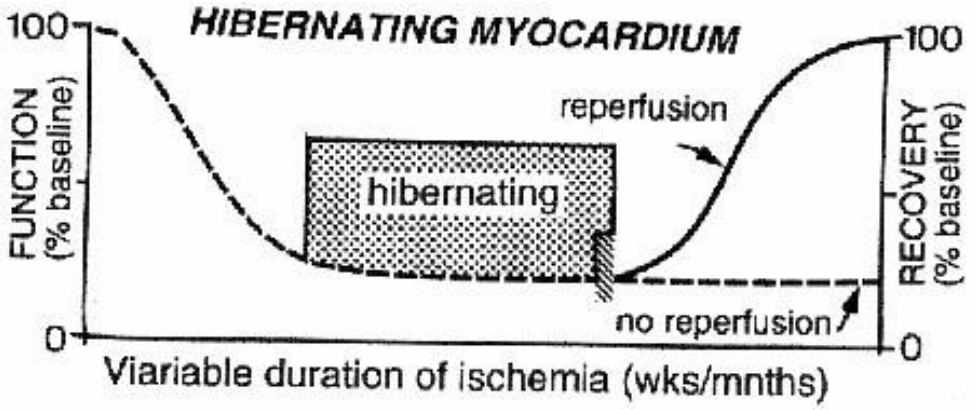
The mechanism of myocardial stunning

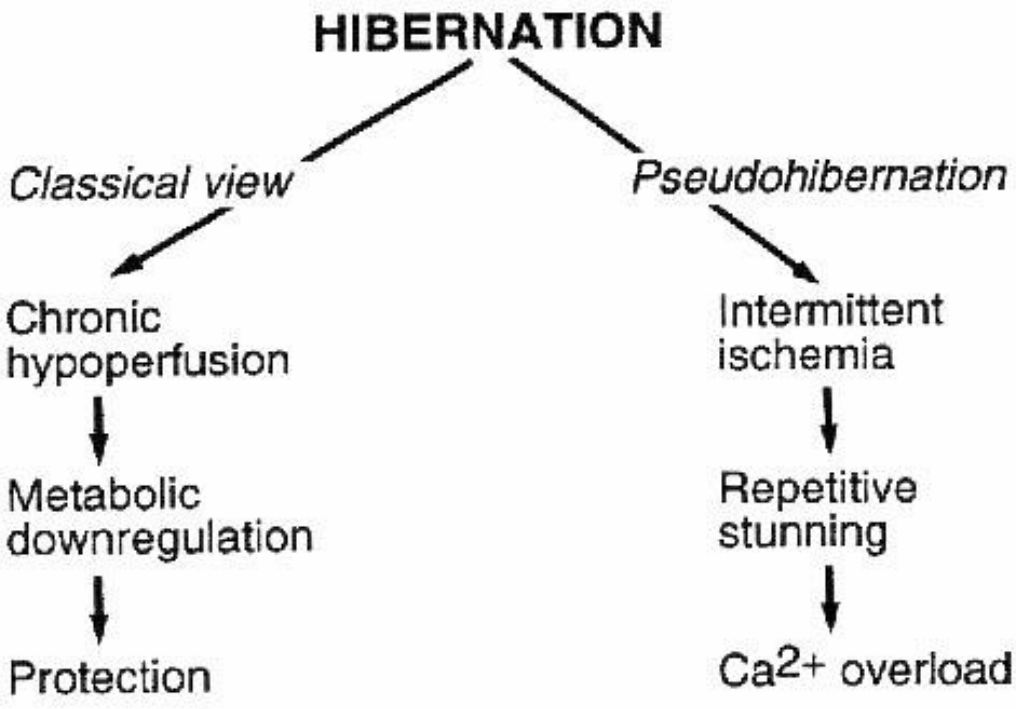


Myocardial Stunning mechanism:

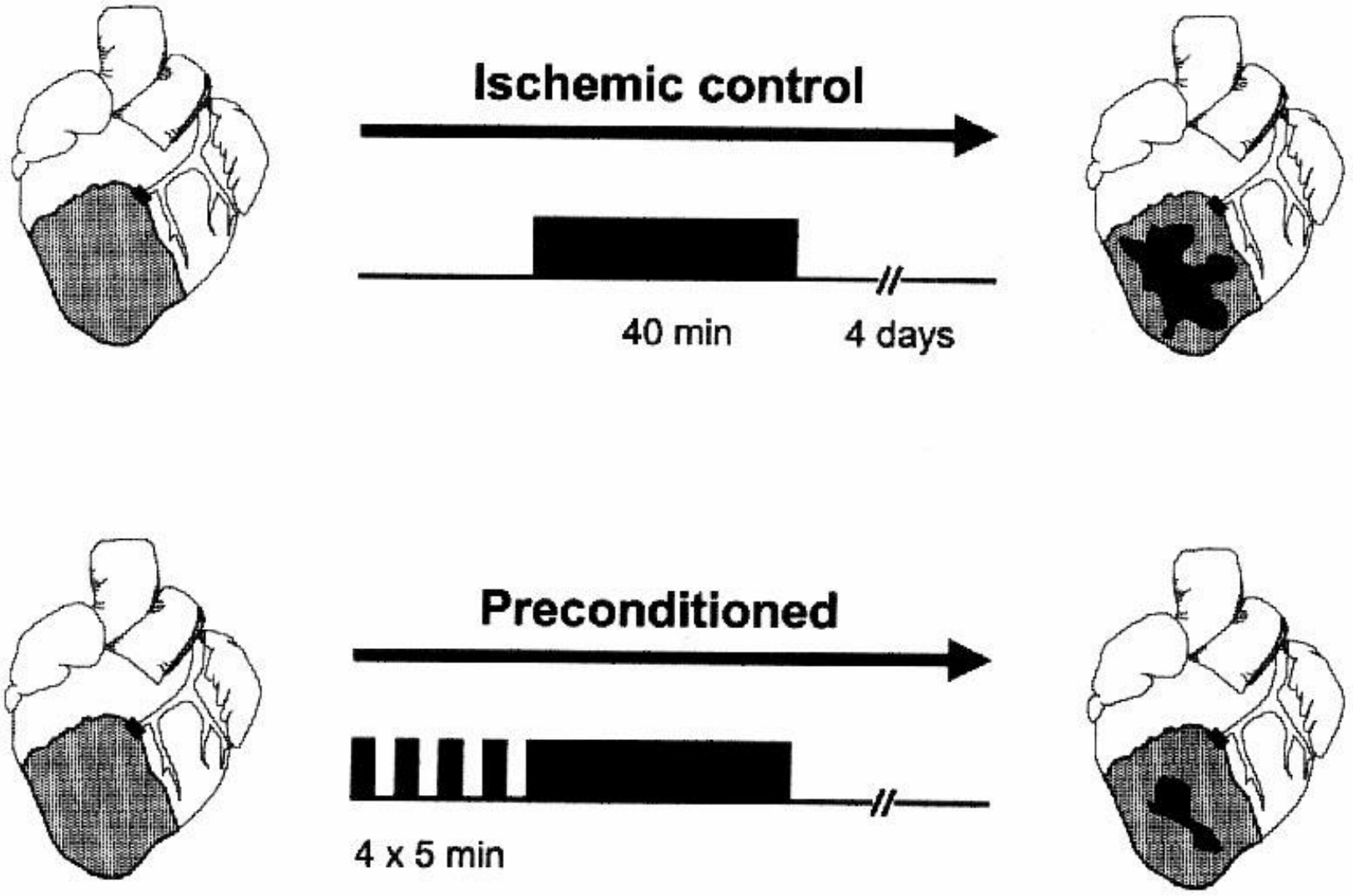
- **Ca^{2+} handling dysfunction (SERCA dysfunction)**
- **Troponin damage (↓ Ca^{2+} sensitivity)**
- **Energetic dysfunction (mitochondrial dysfunction)**

Myocardial hybernation

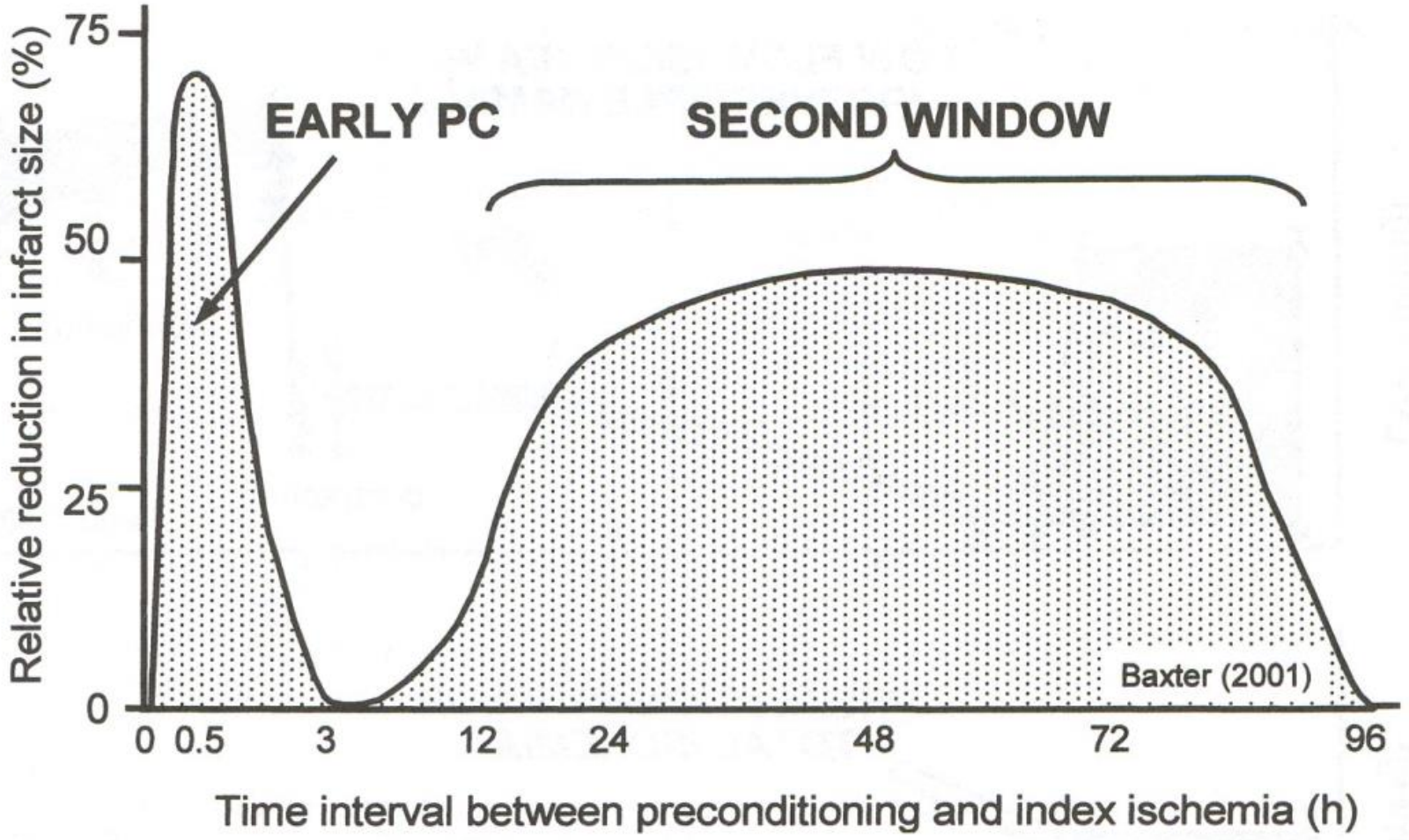




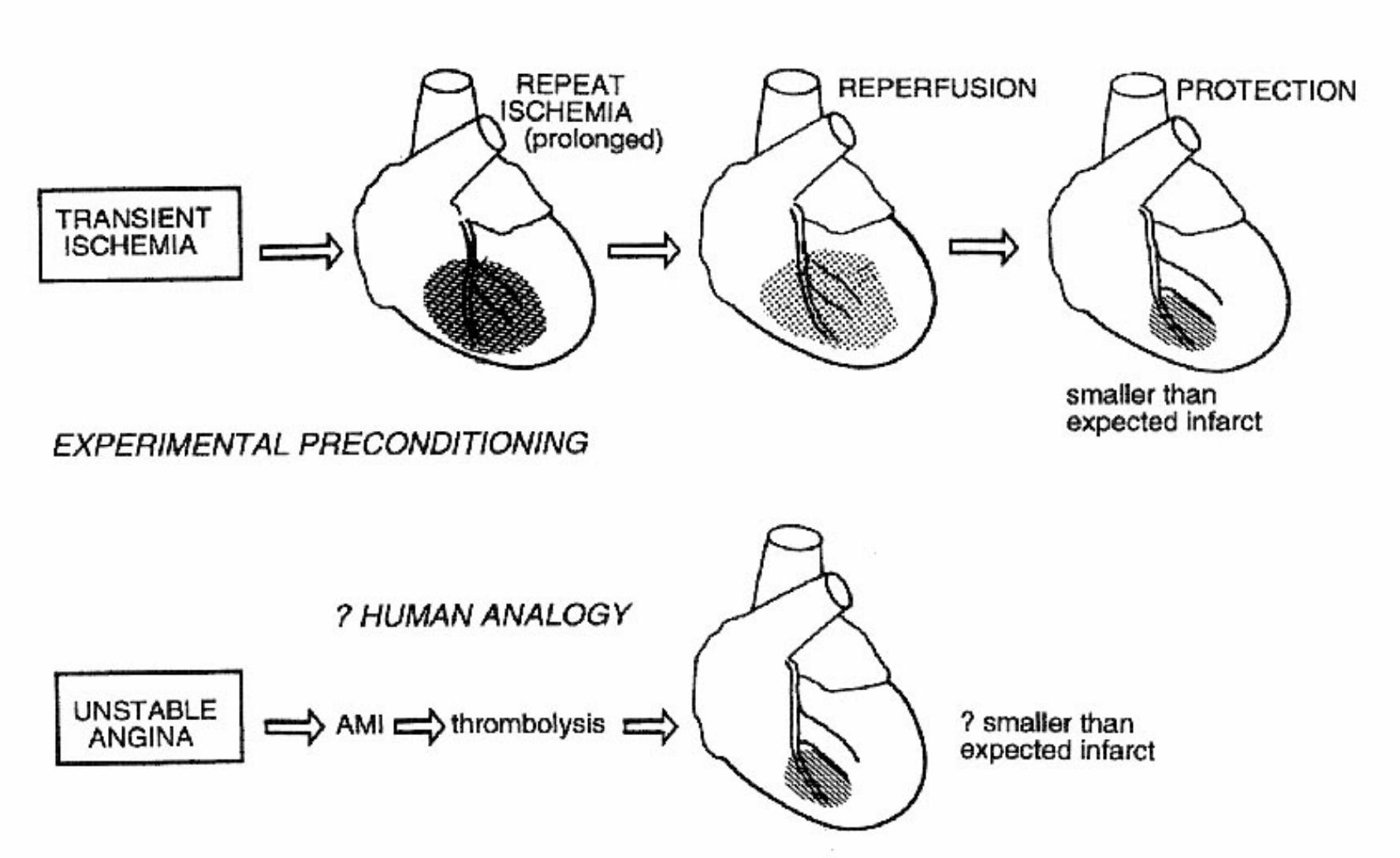
Ischaemic preconditioning



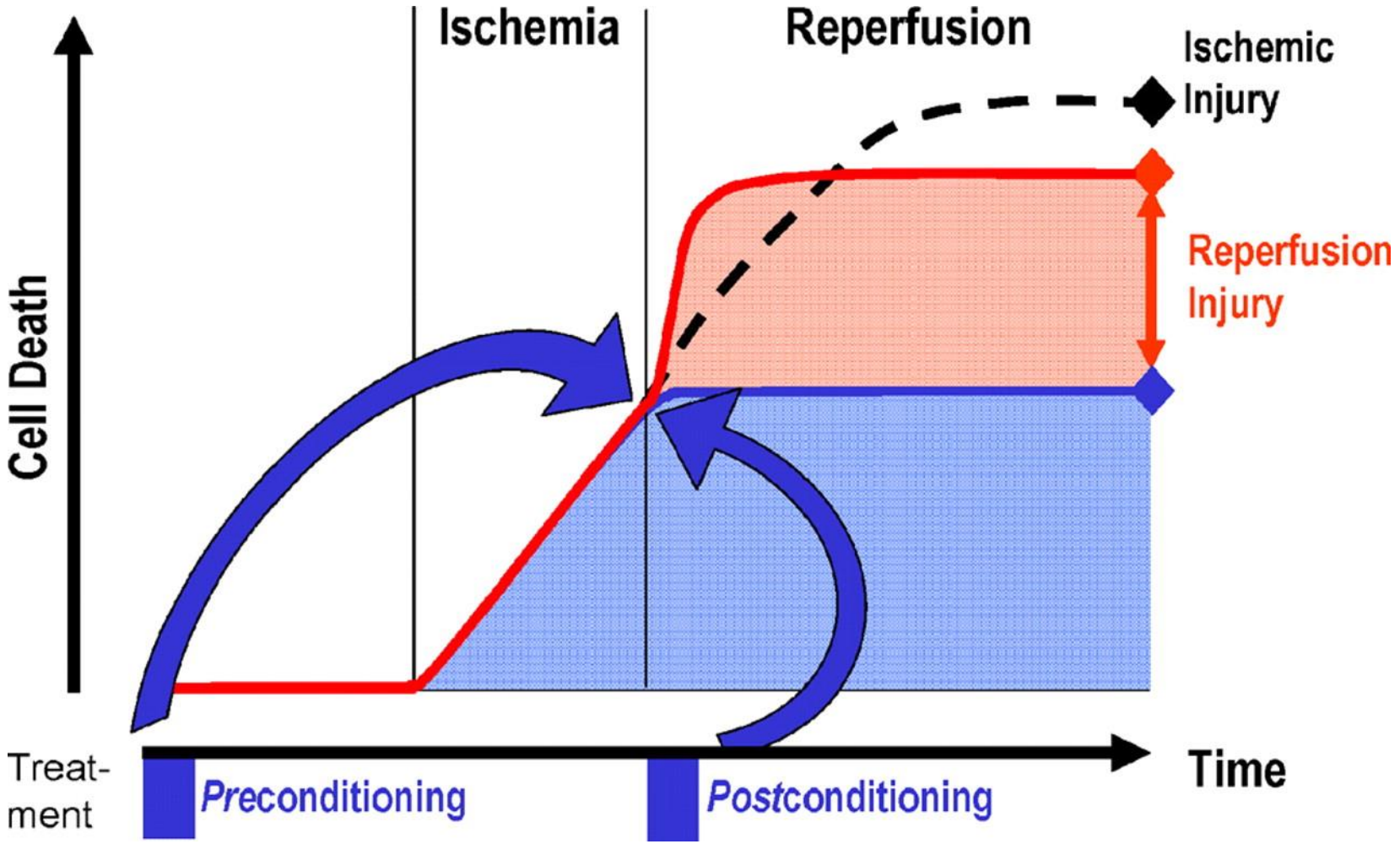
Two phases of preconditioning (PC) early and late



Preconditioning at the clinical settings



Cardioprotection *vs.* ischemia/reperfusion injury



Cardiovascular Research

David Garcia-Dorado, and Hans Michael Piper Cardiovasc Res 2006;69:1-3

The mechanism of ischaemic preconditioning