ACUTE CORONARY SYNDROMES

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Course 341

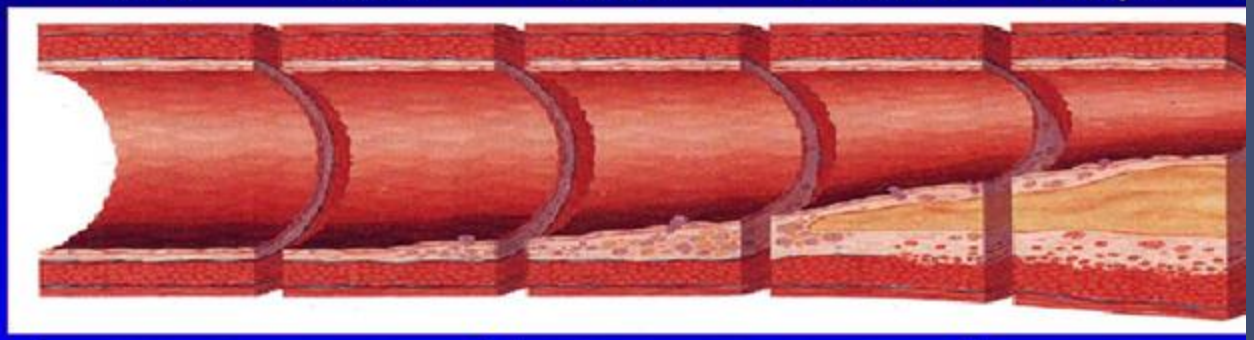
Objectives

- Understand pathophysiology of atherosclerosis.
- Classification of ACS's
- Diagnostic workup and management
- Common complications of ACS's

Resources

- Davidson or Kumar
- Lecture

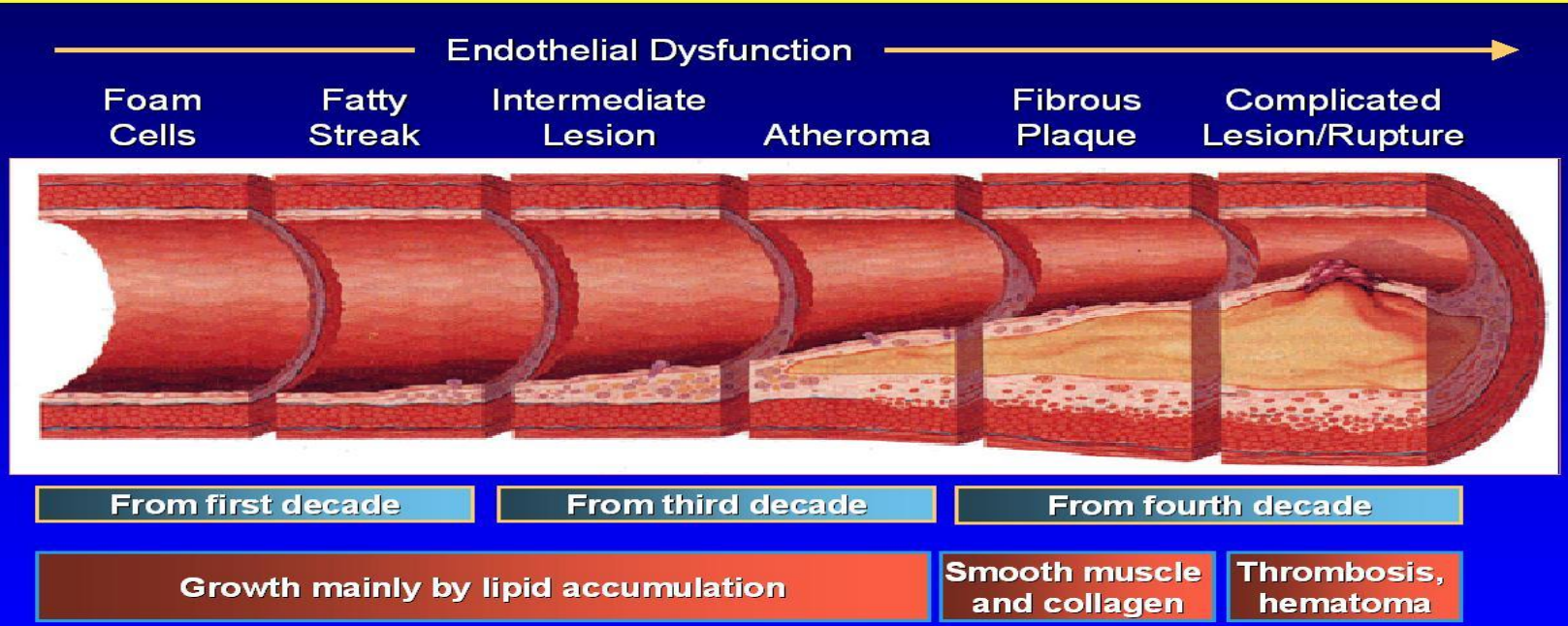
Atherosclerosis Timeline



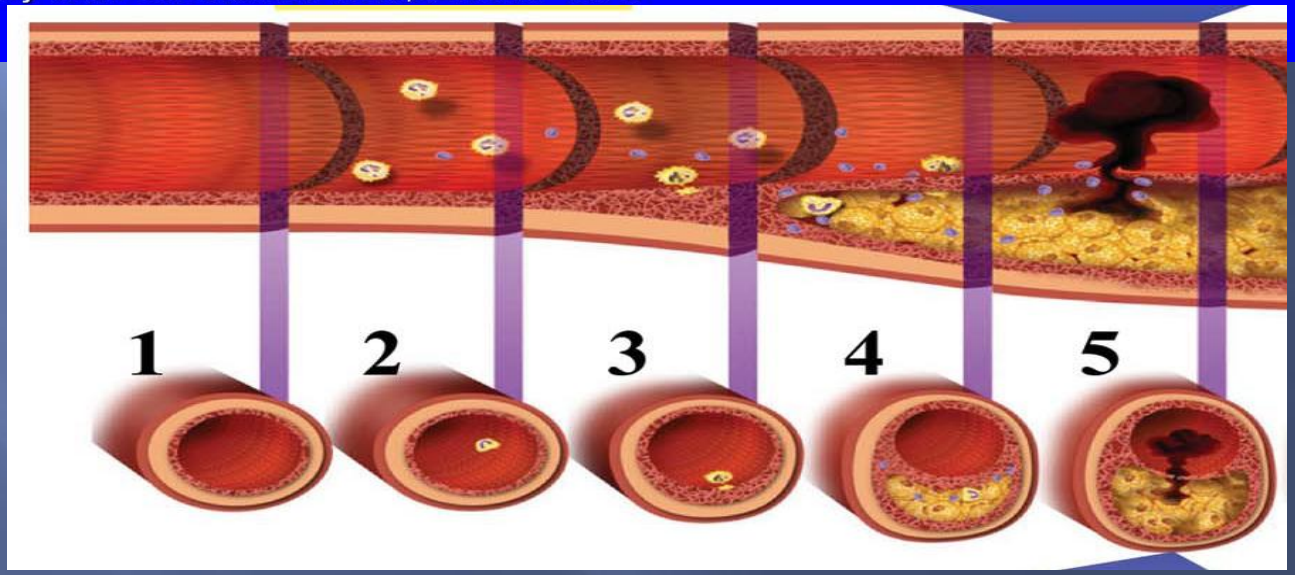
Stary et al. *Circulation*. 1995;92:1355-1374.


Tissue
Demand
O2
Supply

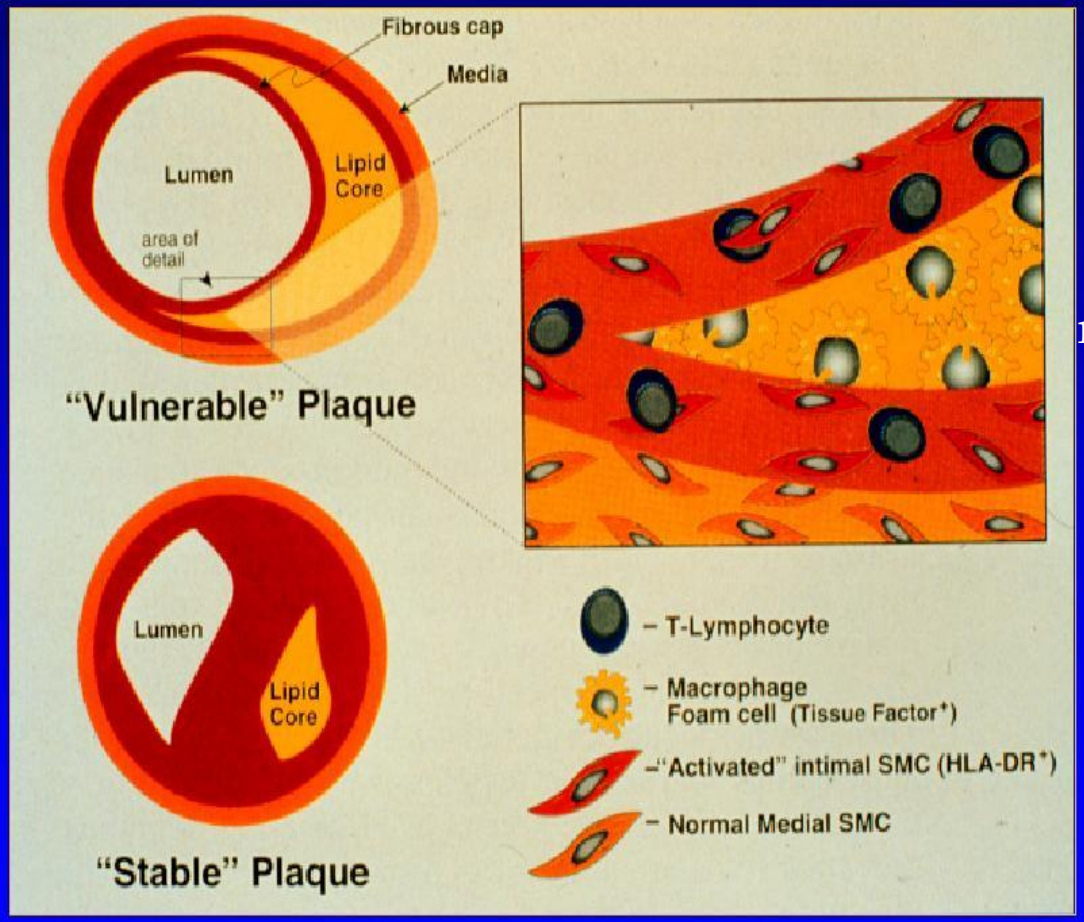
Atherosclerosis Timeline



Stary et al. *Circulation*. 1995;92:1355-1374.

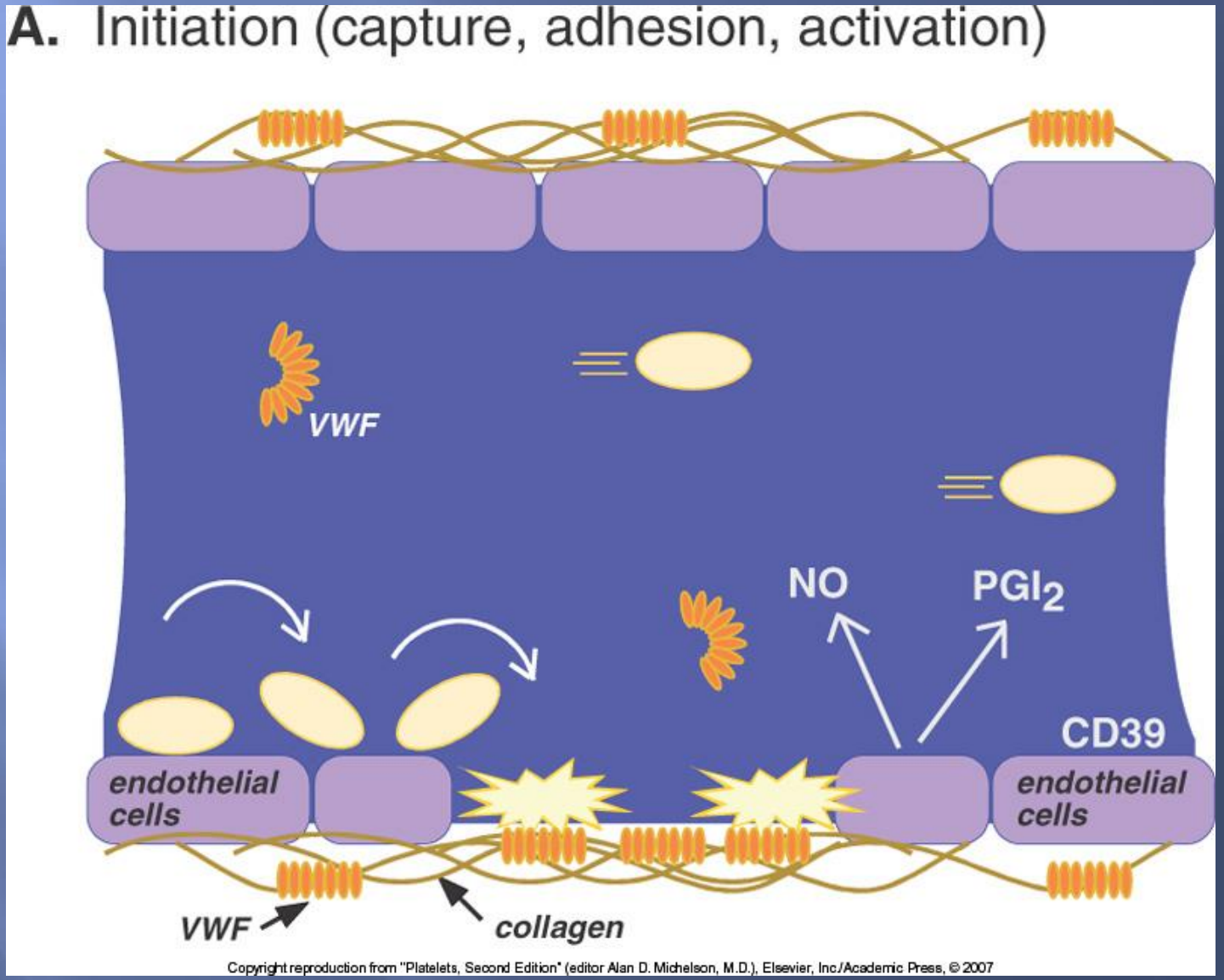


"Vulnerable" Plaque and "Stable" Plaque

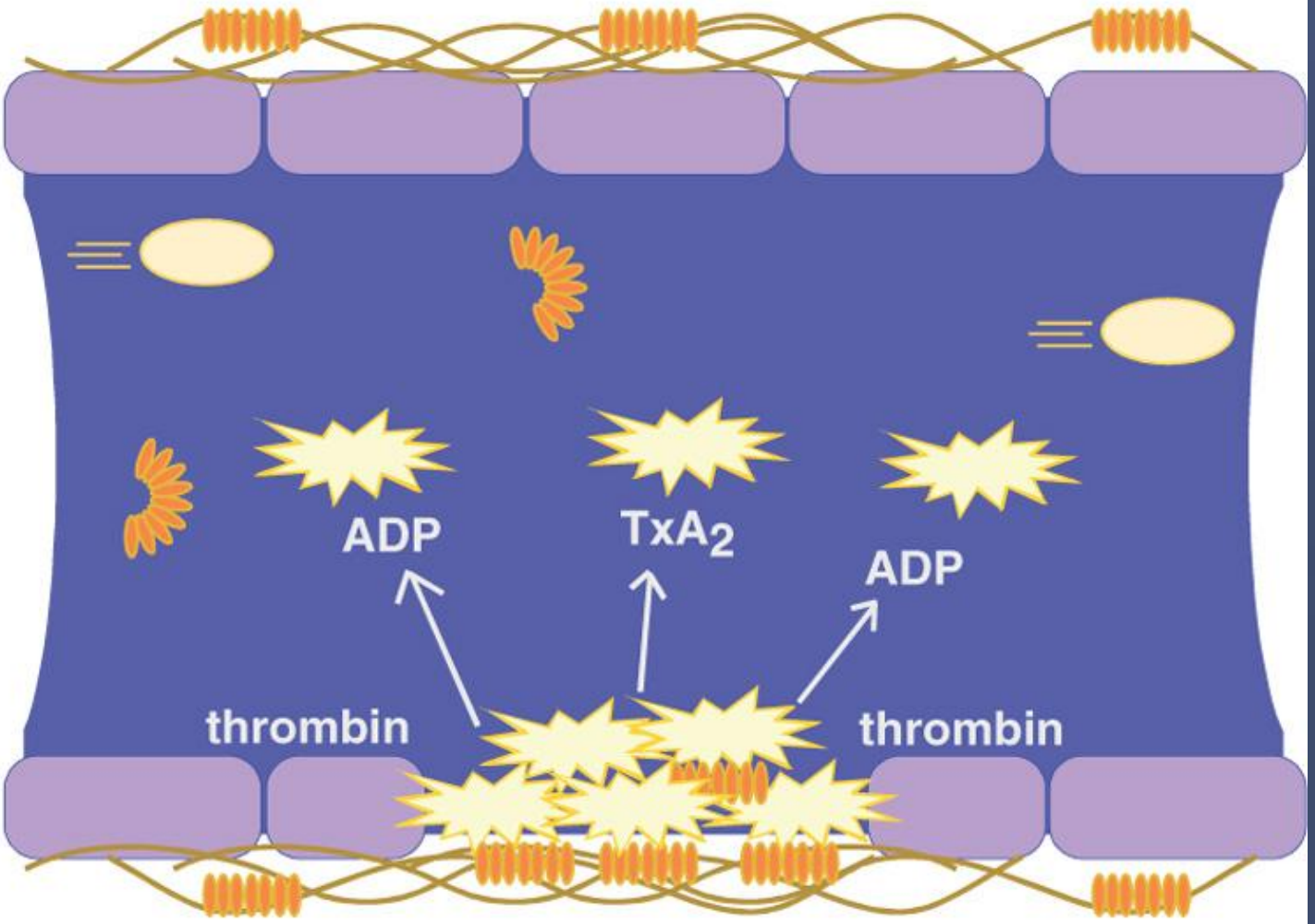


Secretion of Matrex metalloprotenases

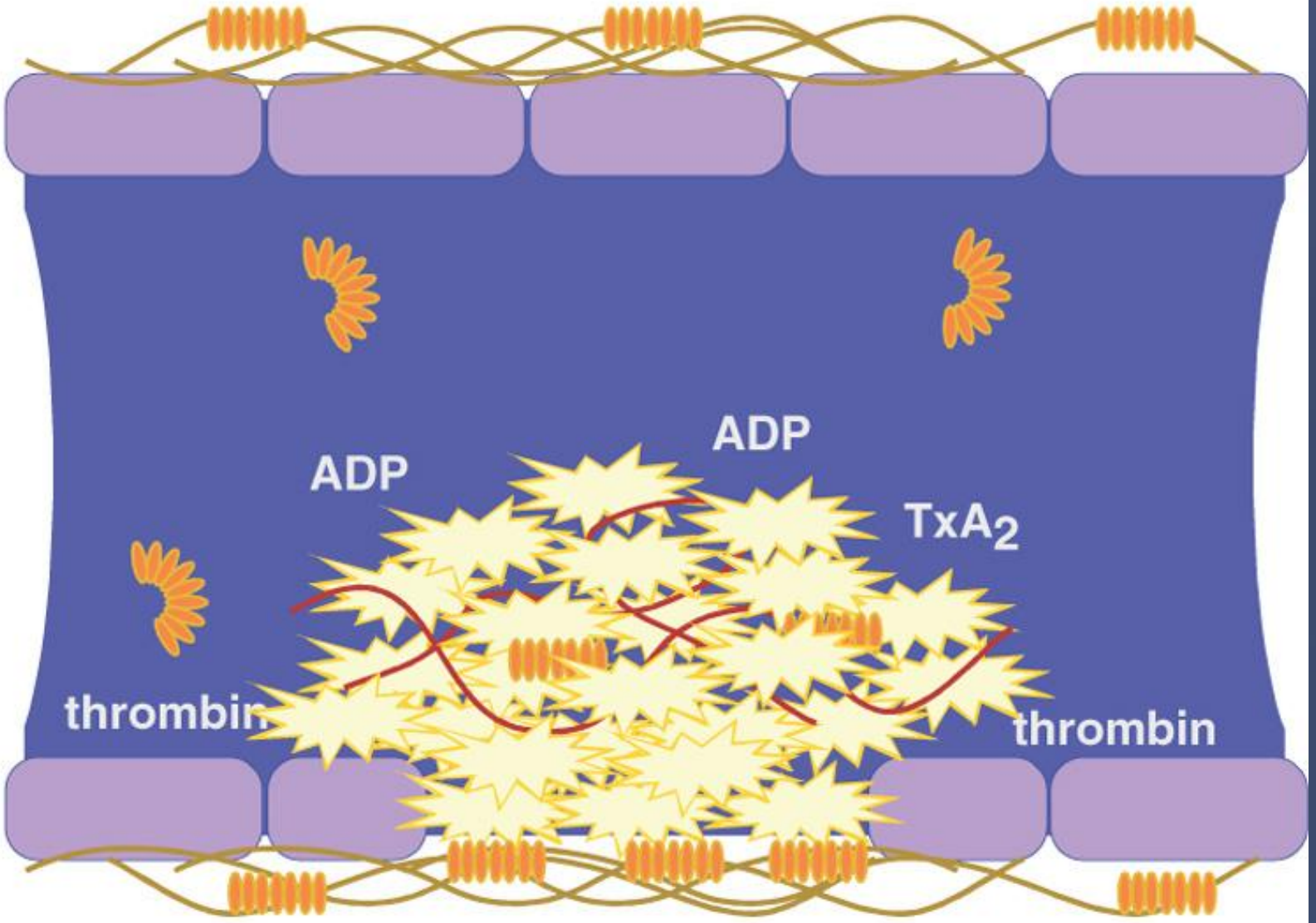
Libby. *Circulation*. 1995;91:2844-2850.

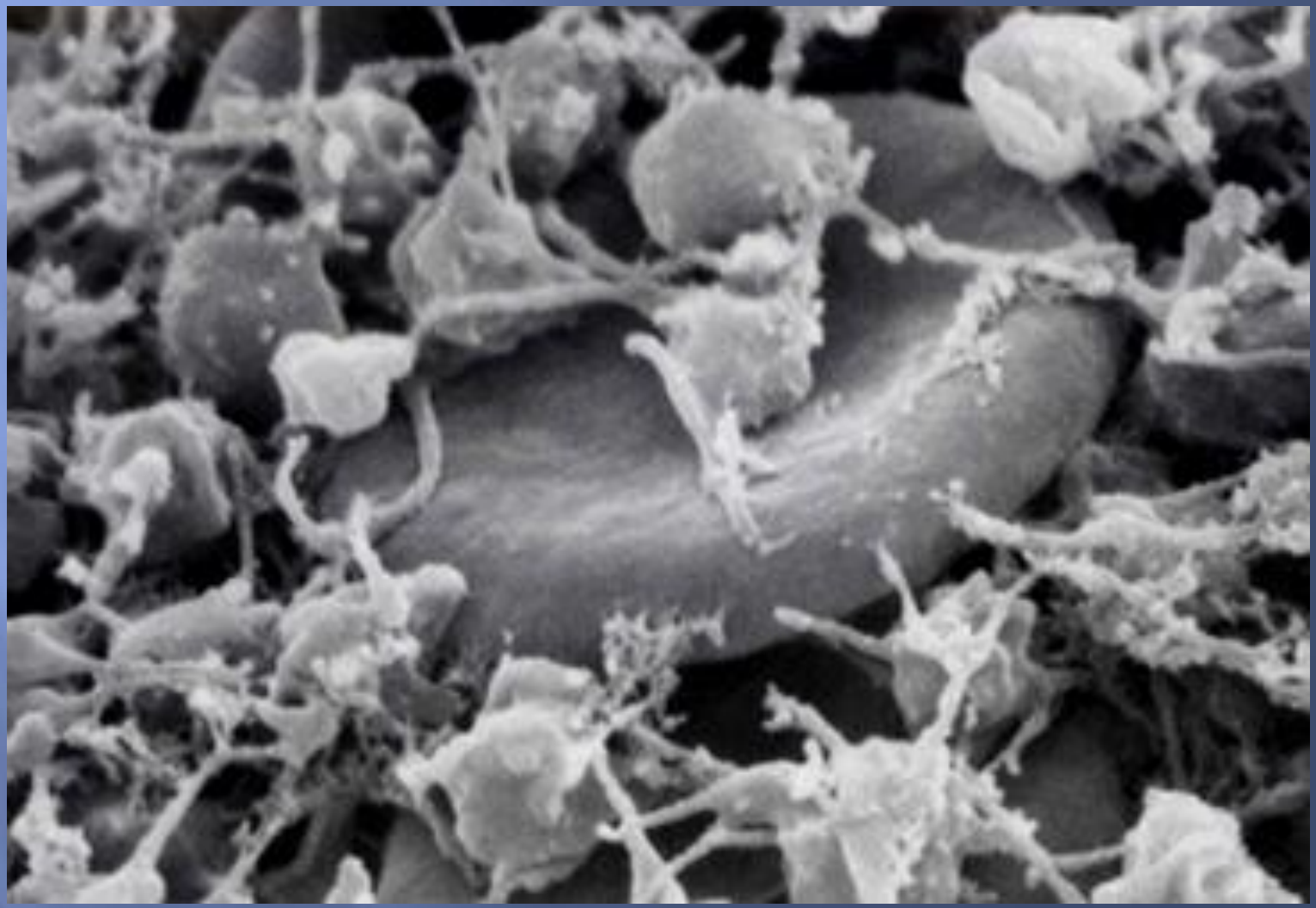


B. Extension (cohesion, secretion)

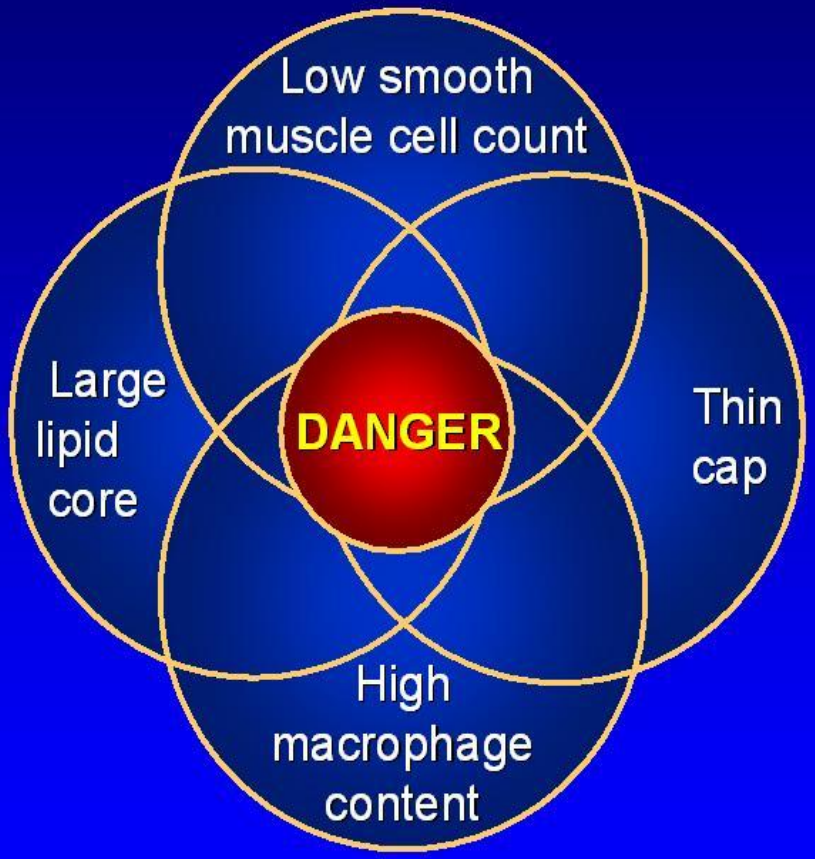


C. Perpetuation (stabilization)





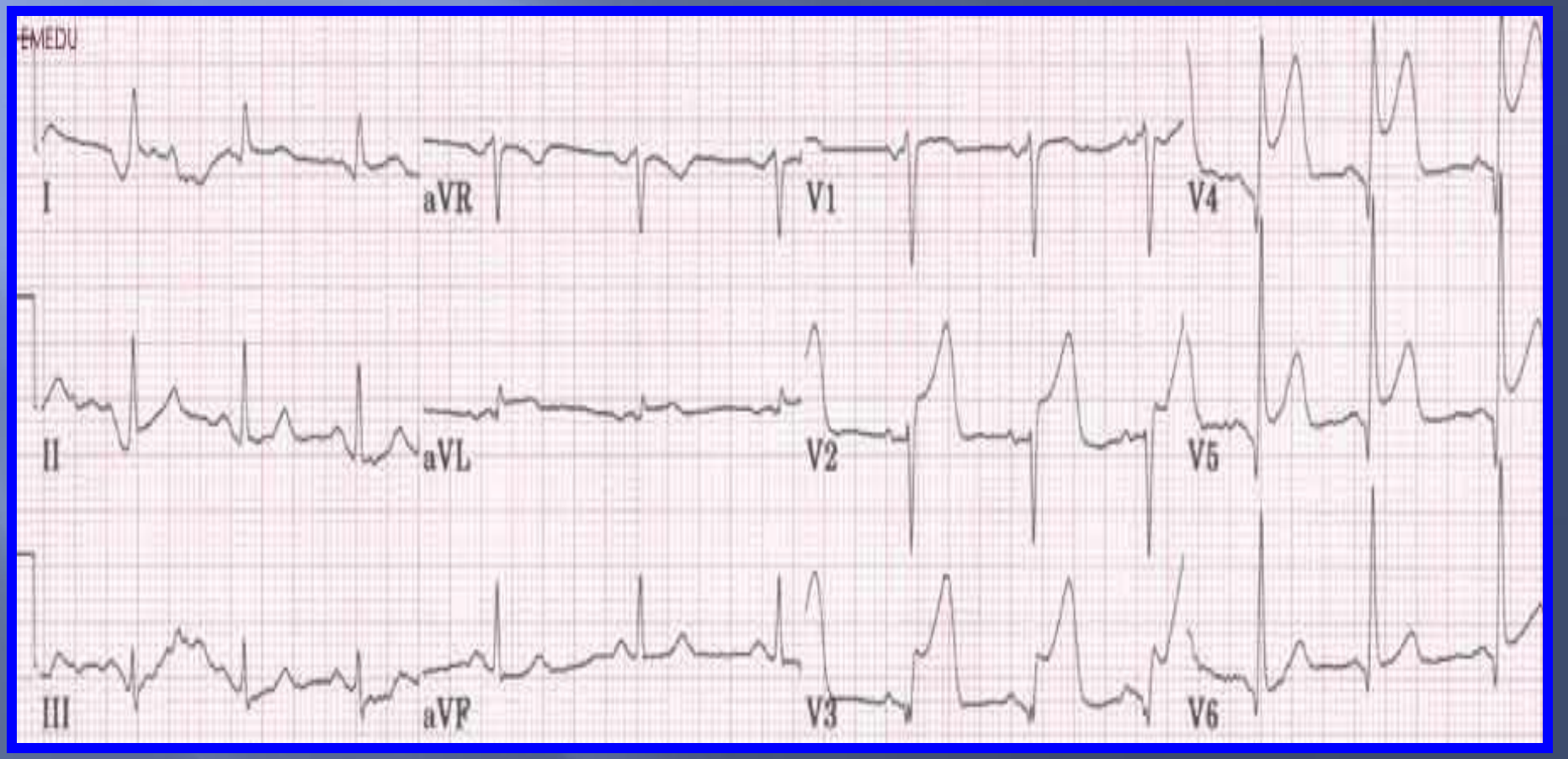
Factors Contributing to Plaque Vulnerability



Davies. *Circulation*. 1996;94:2013-2020.

Investigations in ER

12 lead ECG



What is the diagnosis?

Acute Coronary Syndroms

Unstable Angina (UA)

Non ST Elevation MI (NSTEMI)

ST Elevation MI (STEMI)

The Spectrum of acute coronary syndromes

Diagnosis of MI

- Typical rise in cardiac troponin T or I , CK-MB with at least one of the following:
    1. Ischemic symptoms
    2. Pathological Q wave on ECG
    3. Ischemic ECG changes (e.g ST elevation or depression, new LBBB)
    4. Imaging evidence of new loss of viable myocardium or a new WMA

Circulation , Oct 19 2007

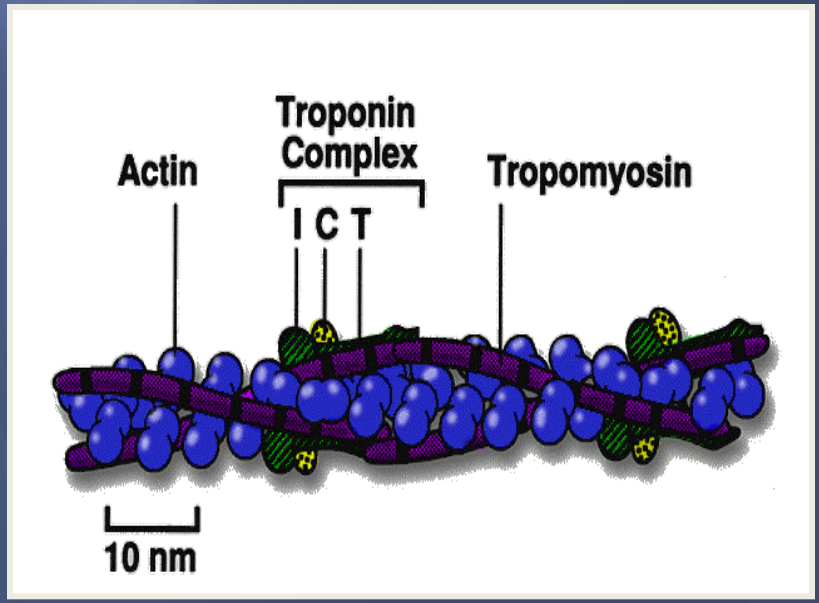
Markers for Myocardial Necrosis

Biochemical markers

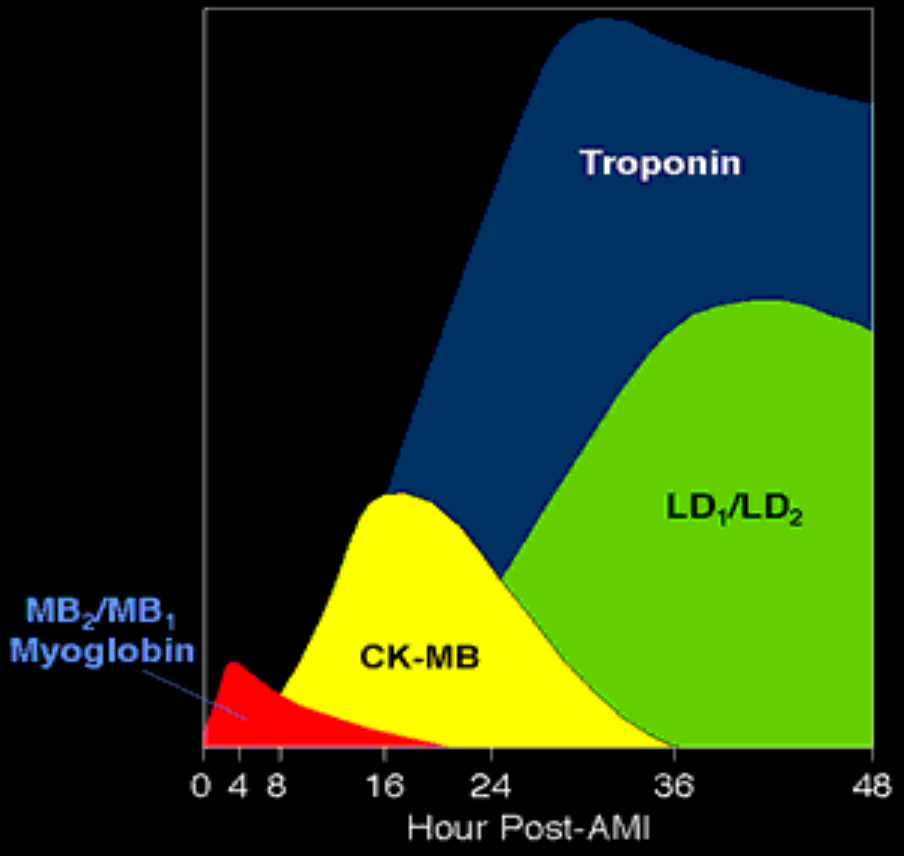
- MI causes release of certain enzymes and proteins into the blood stream.
- Creatin Kinase (CK) is released from multiple organs such as the myocardium , skeletal muscles, and the brain.
- The Iso-form CK-MB, is cardiospecific
- Starts to rise 4-6 hrs after onset of ischemia, then falls within 48-72hrs.

Biochemical markers

- Cardiospecific proteins Troponin I, and T are the most sensitive & specific markers for myonecrosis.
- Released with 4-6hrs, but can last upto 2 weeks.



Relationship between onset of MI and release of markers



Other helpful investigations

- CBC- Leucocytosis
- Elevated ESR
- Chest X-Ray (Pulmonary Edema)
- Echocardiography

  Wall motion abnormalities, Valvular dysfunction, r/o other causes of chest pain.

Aims of therapy

- Improve oxygen supply
  1. Supplemental O2
  2. Antiplatelets drugs
  3. Antithrombotics
  4. Coronary vasodilators (Nitroglycerine)
  5. Reperfusion therapy
     a. Fibrinolytic therapy
     b. Percutanous coronary intervention (PCI)

Aims of therapy

- Reduce O2 demand
  1. Beta blockers (Propranolol, Metoprolol)
  2. Analgesics (Morphine)
- Other medications
  - ACE inhibitors(Enalapril, Lisinopril)
  - Statin therapy

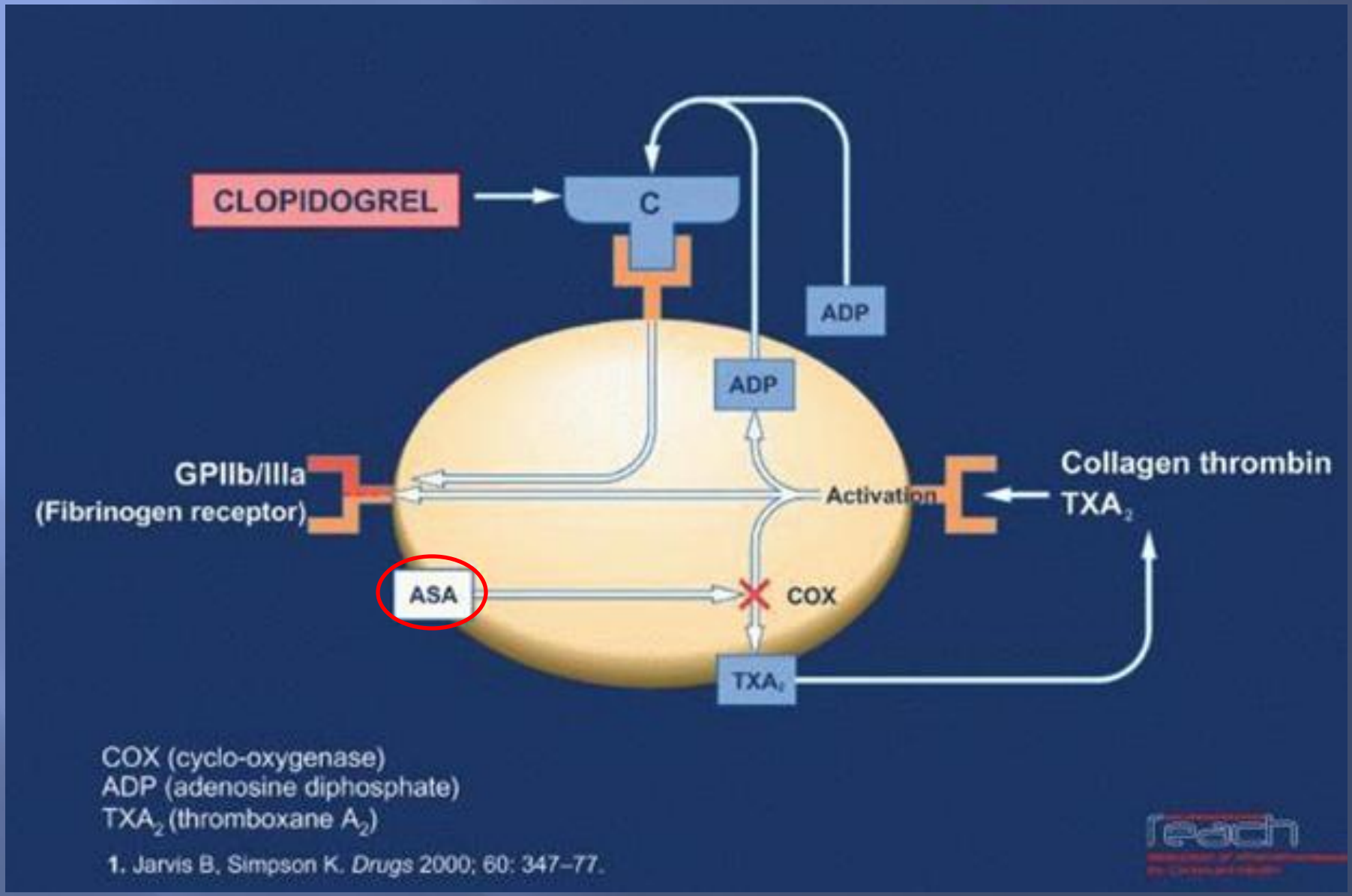
Antiplatelets

Aspirin (ASA)

- Aspirin decreases mortality in MI and should be administered as early as possible and continued indefinitely in patients with ACS.
- Chewable aspirin 160 to 325 mg at presentation, then 75 to 325 mg daily.

Clopidogrel

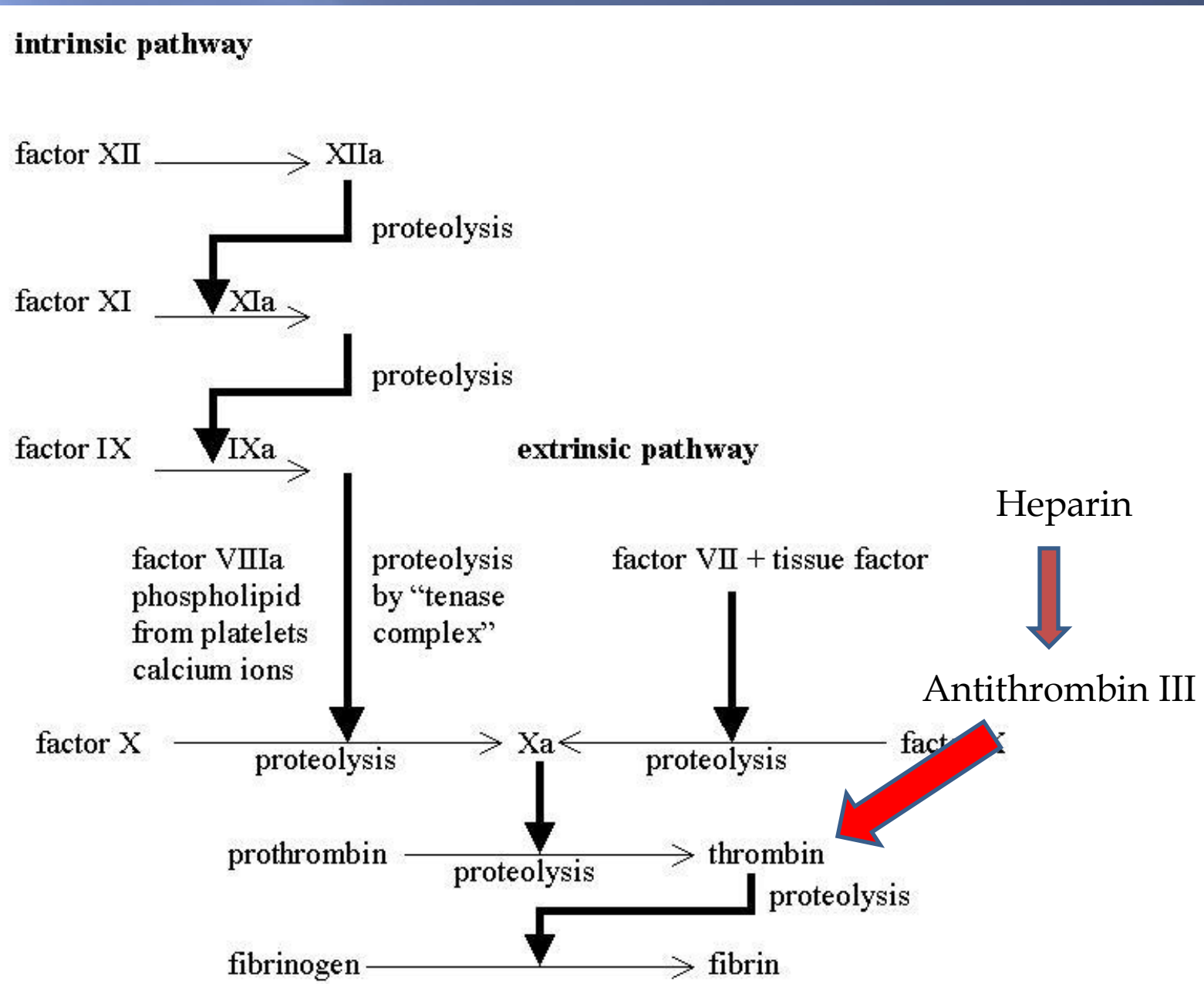
- More potent than ASA
- Irreversible ADP receptor blockers
- Adjunct to reperfusion therapy



COX (cyclo-oxygenase)
ADP (adenosine diphosphate)
TXA_2 (thromboxane A_2)

1. Jarvis B, Simpson K. *Drugs* 2000; 60: 347–77.

Antithrombotics


intrinsic pathway
factor XII
XIIa
proteolysis
factor XI
XIa
proteolysis
factor IX
IXa
extrinsic pathway
Heparin
factor VIIIa
phospholipid
from platelets
calcium ions
proteolysis
by "tenase
complex"
factor VII + tissue factor
Antithrombin III
factor X
proteolysis
Xa
proteolysis
prothrombin
proteolysis
thrombin
proteolysis
fibrinogen
fibrin

Antithrombotics

- Heparin
  - Unfractionated
  - Low molecular
- Used for patients with NSTEMI and STEMI
- Prevents further thrombosis and aids in insuring patency of the occluded artery.

REPERFUSION THERAPY

Fibrinolytics

- ONLY USED FOR STEMI (NOT NSTEMI)
- Reduces short and long term mortality
- shown to be effective in numerous randomized trials involving over 100,000 patients.
- Should be given during a 12hr window, and given ASAP.
- 2 types of fibrinolytics:
    1. Non Fibrin specific (Streptokinase)
    2. Fibrin specific

Fibrin specific agents

Characteristic	Alteplase (t-PA)	Reteplase (rPA)	Tenecteplase (TNK)	Lanoteplase (nPA)
Immunogenicity	No	No	No	?
Plasminogen activation	Direct	Direct	Direct	Direct
Fibrin specificity	++	+	+++	+
Plasma half-life	4–6 min	18 min	20 min	37 min
Dose	15-mg bolus plus 90-min infusion up to 85 mg	10+10-MU double bolus 30 min apart	±0.5 mg/kg single bolus	120 KU/kg single bolus
PAI-1 resistance	No	?	Yes	?
Genetic alteration to native t-PA	No	Yes	Yes	Yes
	Recombinant version	Finger, EGF, and kringle-1 regions deleted	2 single amino acid substitutions in kringle-1 and substitution of 4 amino acids in catalytic domain	Finger, EGF regions deleted and glycosylation sites in kringle-1 domain modified

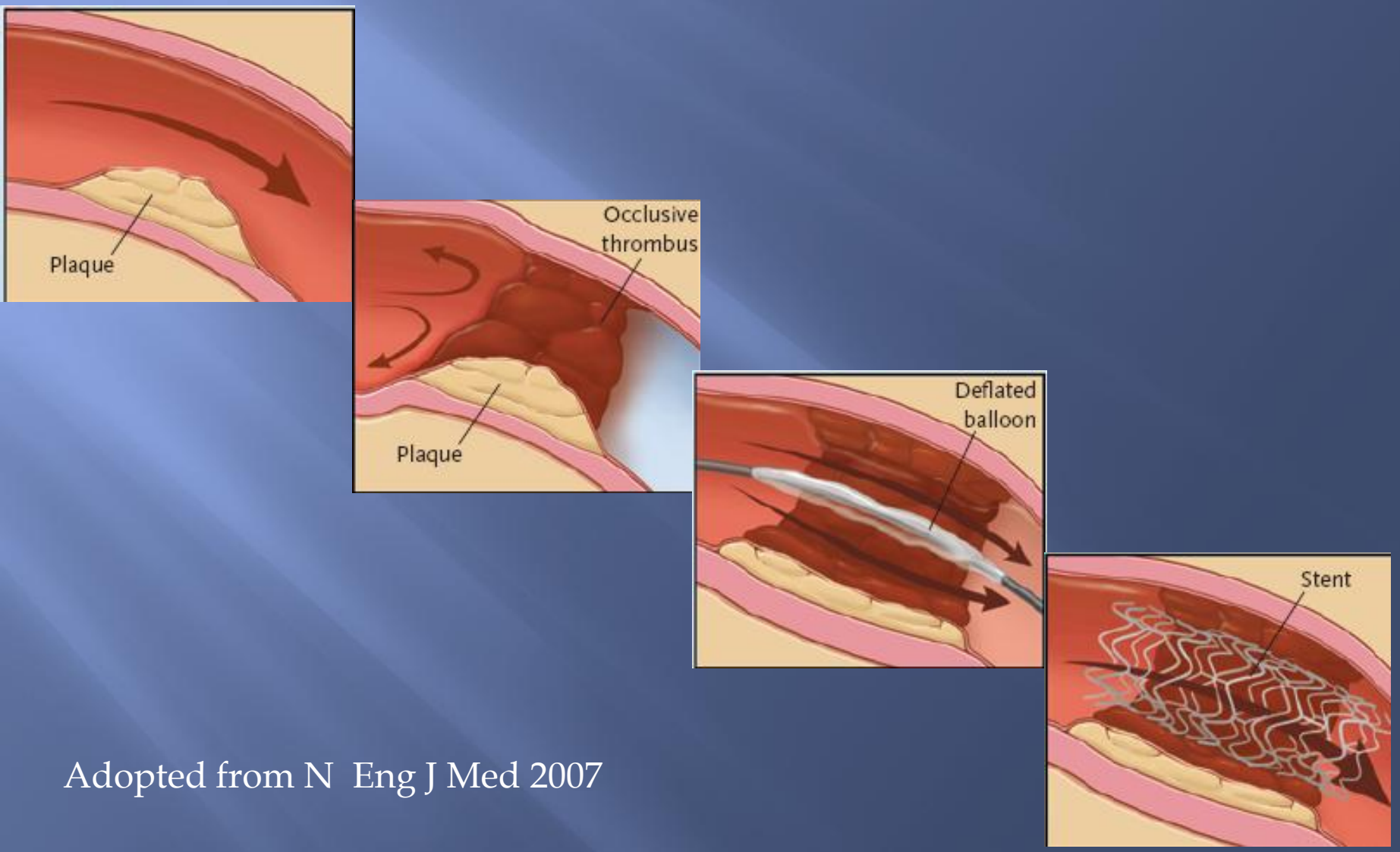
Absolute contraindications

- Any prior intracranial hemorrhage
- Known structural cerebral vascular lesion
- Known intracranial neoplasm
- Ischemic stroke within the past 3 months (except for acute stroke within 3 hours)
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 months

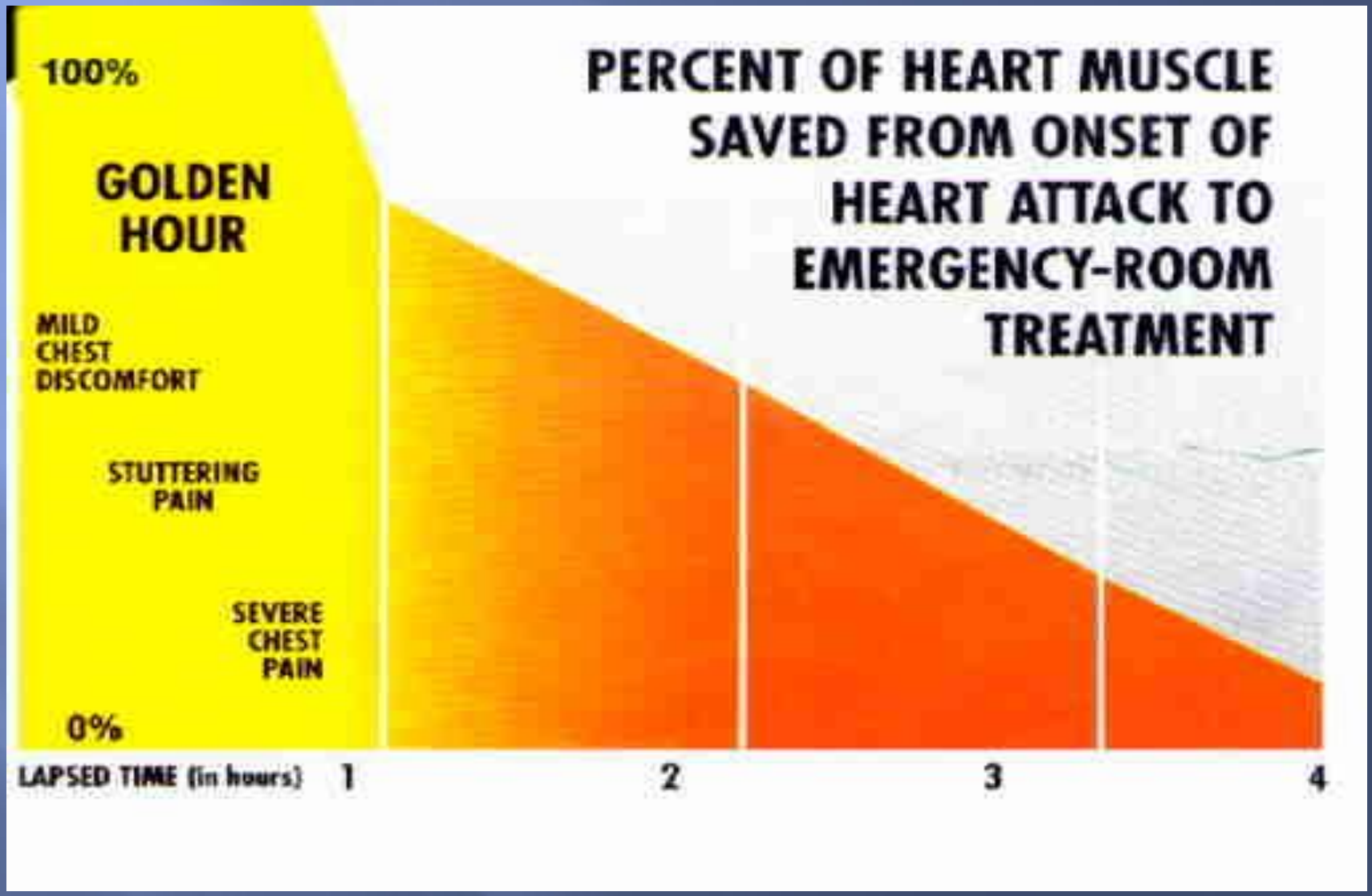
Relative contraindications

- History of chronic, sever, poorly controlled hypertension
- Systolic pressure >180 mm Hg or diastolic >110 mm Hg
- History of prior ischemic stroke >3 months previously, dementia, or known intracranial pathology not covered in absolute contraindications
- Recent (within 2–4 weeks) internal bleeding
- Noncompressible vascular punctures
- Pregnancy
- Active peptic ulcer
- Current use of anticoagulants: the higher the INR, the higher the risk of bleeding
- For streptokinase/anistreplase: prior exposure (more than 5 days previously) or prior allergic reaction to these agents

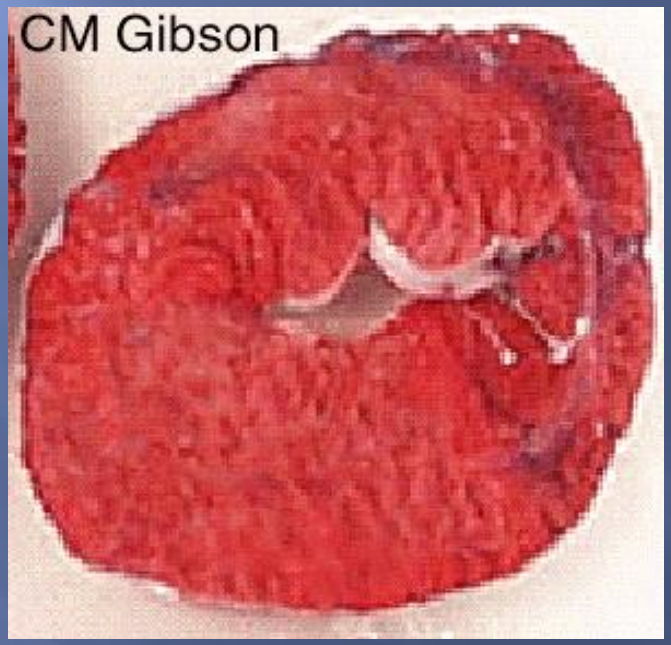
Primary PCI



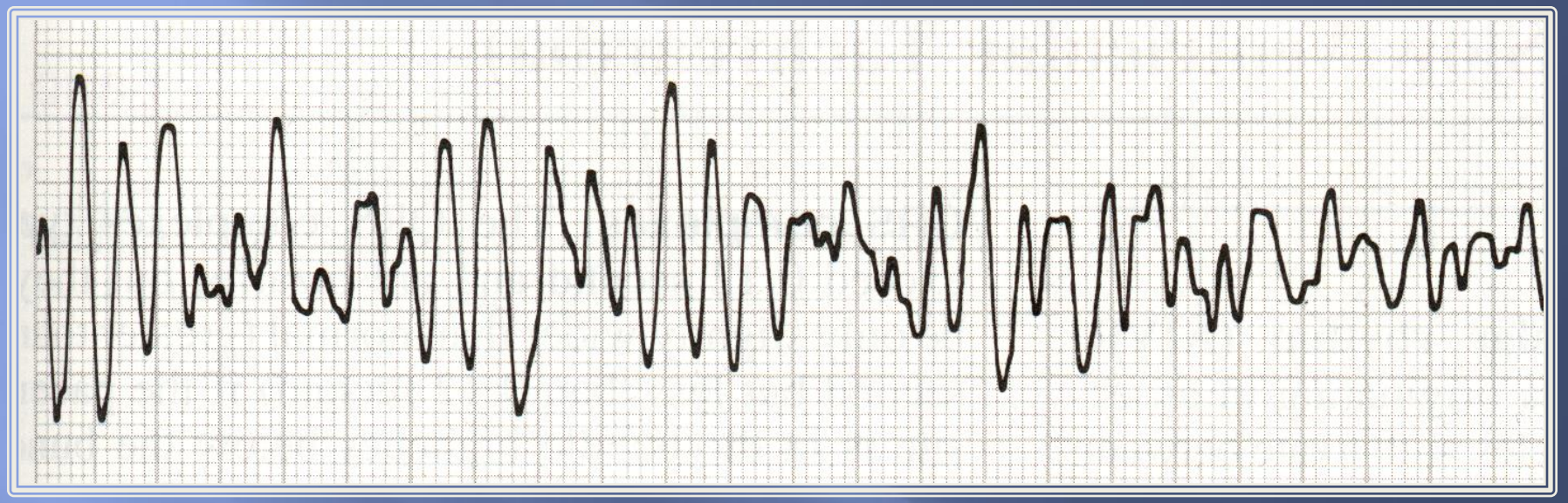
Adopted from N Eng J Med 2007


100%
GOLDEN HOUR
MILD CHEST DISCOMFORT
STUTTERING PAIN
SEVERE CHEST PAIN
0%
PERCENT OF HEART MUSCLE SAVED FROM ONSET OF HEART ATTACK TO EMERGENCY-ROOM TREATMENT
LAPSED TIME (in hours)
1
2
3
4

Myonecrosis based on duration of occlusion



Door to needle time <30min
Door to balloon time <90min



Ventricular Fibrillation

Complications of MI

- Electrical complications:

1. Tachyarrhythmias
   a. Ventricular:
      - Ventricular Tachycardia
      - Ventricular Fibrillation
   b. Supraventricular:
      - Atrial Fibrillation

2. Bradyarrhthmias
   - 1st, 2nd, and 3ed degree AV blocks
   - New LBBB, or RBBB

- Mechanical complications:
  1. Mitral regurgitation
     - (2-7 days post MI)
     - Caused by papillary muscle rupture.
  2. Free LV wall rupture
     - Rare
     - 1st 24hr upto 2 weeks
  3. Ventricular septal defect
     - 1-3%
     - Occurs with inferior and anterior MI

- Pump failure

1. Heart failure

- Bad prognostic sign
- Reflects the size of the MI
- ACE inhibitors and diuretics is cornerstone therapy.

2. Cardiogenic Shock

- Happens with major MI's
- Carries high mortality (>50% in 30 days)
- Should be rushed for cardiac cath and either PCI or Coronary bypass grafting.

Summery

- Plaque vulnerability is affected by an inflammatory process
- Acute coronary syndromes is a spectrum and is classified according to markers of Myonecrosis and ST changes.
- In STEMI , time to reperfusion is critical in myocardial salvage (time is muscle)