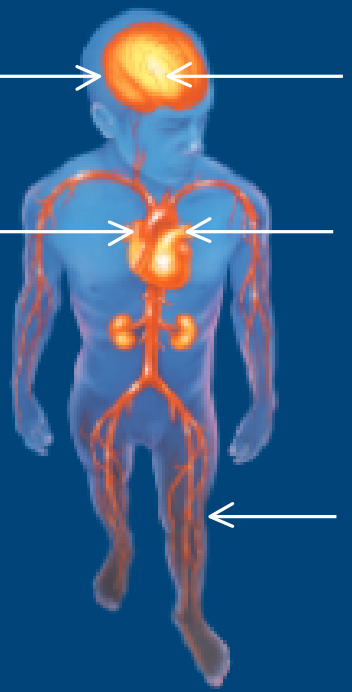
ATHEROTHROMBOSIS

Major Vascular Manifestations of Atherothrombosis



Ischemic stroke

Transient ischemic attack

Myocardial infarction

Angina:
- Stable
- Unstable

Peripheral arterial disease:
- Intermittent claudication
- Rest pain
- Gangrene
- Necrosis

Adapted from: Drouet L. *Cerebrovasc Dis* 2002; 13(suppl 1): 1-6

Atherothrombosis Will Remain the Leading Cause of Disease Burden

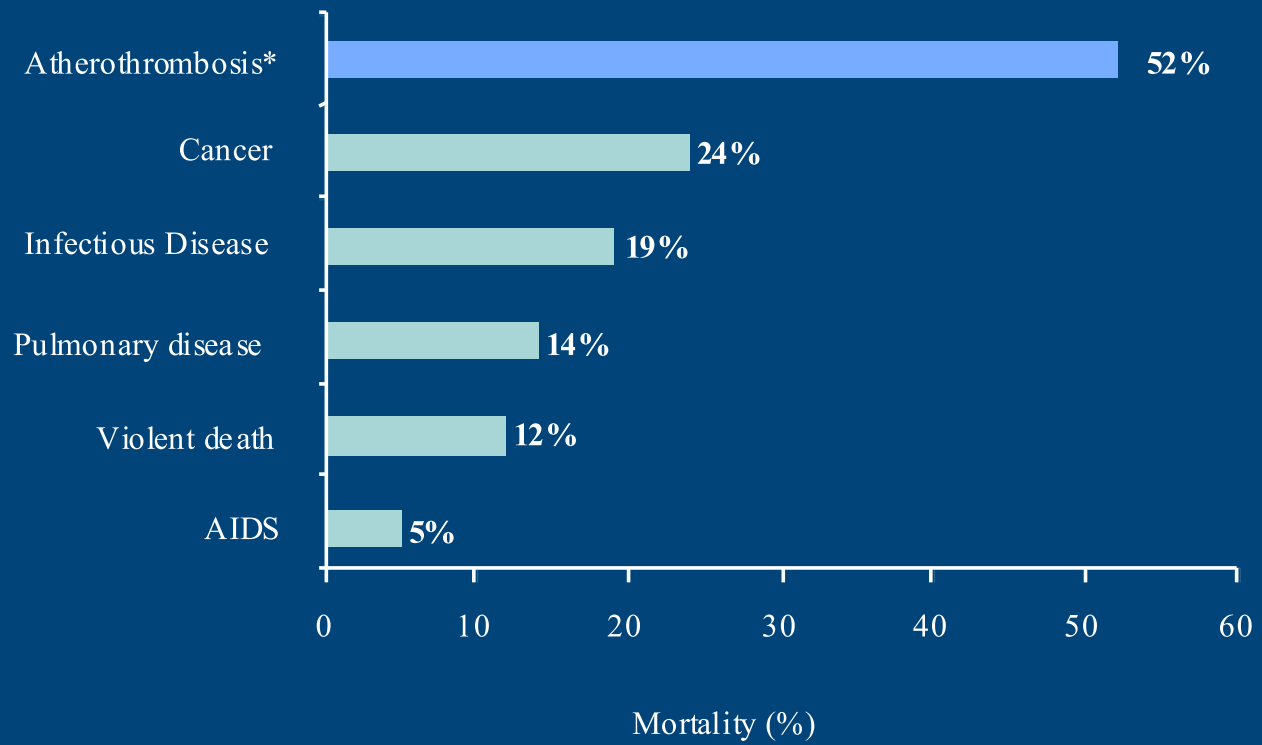
The ten leading causes of disease burden in developed countries 1990–2020

1990 disease or injury[1]	Rank order	2020 disease or injury[2]
Ischemic heart disease	**1**	**Ischemic heart disease**
Cerebrovascular disease	**2**	**Cerebrovascular disease**
Road traffic accidents	3	Unipolar major depression
Trachea bronchus and lung cancers	4	Trachea bronchus & lung cancers
Self-inflicted injuries	5	Road traffic accidents
Conditions arising during perinatal period	6	Alcohol use
Lower respiratory infections	7	Osteoarthritis
Congenital anomalies	8	Dementia and other CNS disorders
Colon and rectal cancers	9	Chronic obstructive pulmonary disease
Stomach cancer	10	Self-inflicted Injuries

Note: Disease burden is measured in disability-adjusted life years (DALYs), a measure that combines the impact on health of years lost due to premature death and years lived with a disability. One DALY is equivalent to one lost year of healthy life

1. Murray and Lopez. *Global Burden of Disease Study*. 1996
2. Murray and Lopez. *Global Burden of Disease Study*. 1997

Atherothrombosis* is the Leading Cause of Death Worldwide†1



*Cardiovascular disease, ischemic heart disease and cerebrovascular disease

†Worldwide defined as Member States by WHO Region (African, Americas, Eastern Mediterranean, European, South-East Asia and Western Pacific).

1. World Health Organization. The World Health Report 2001. Geneva: WHO; 2001.

ATHEROSCLEROSIS

* PROGRESSIVE (AND COMPLEX) PROCESS

* GENERALISED
  - CEREBRAL
  - CARDIAC
  - PERIPHERAL

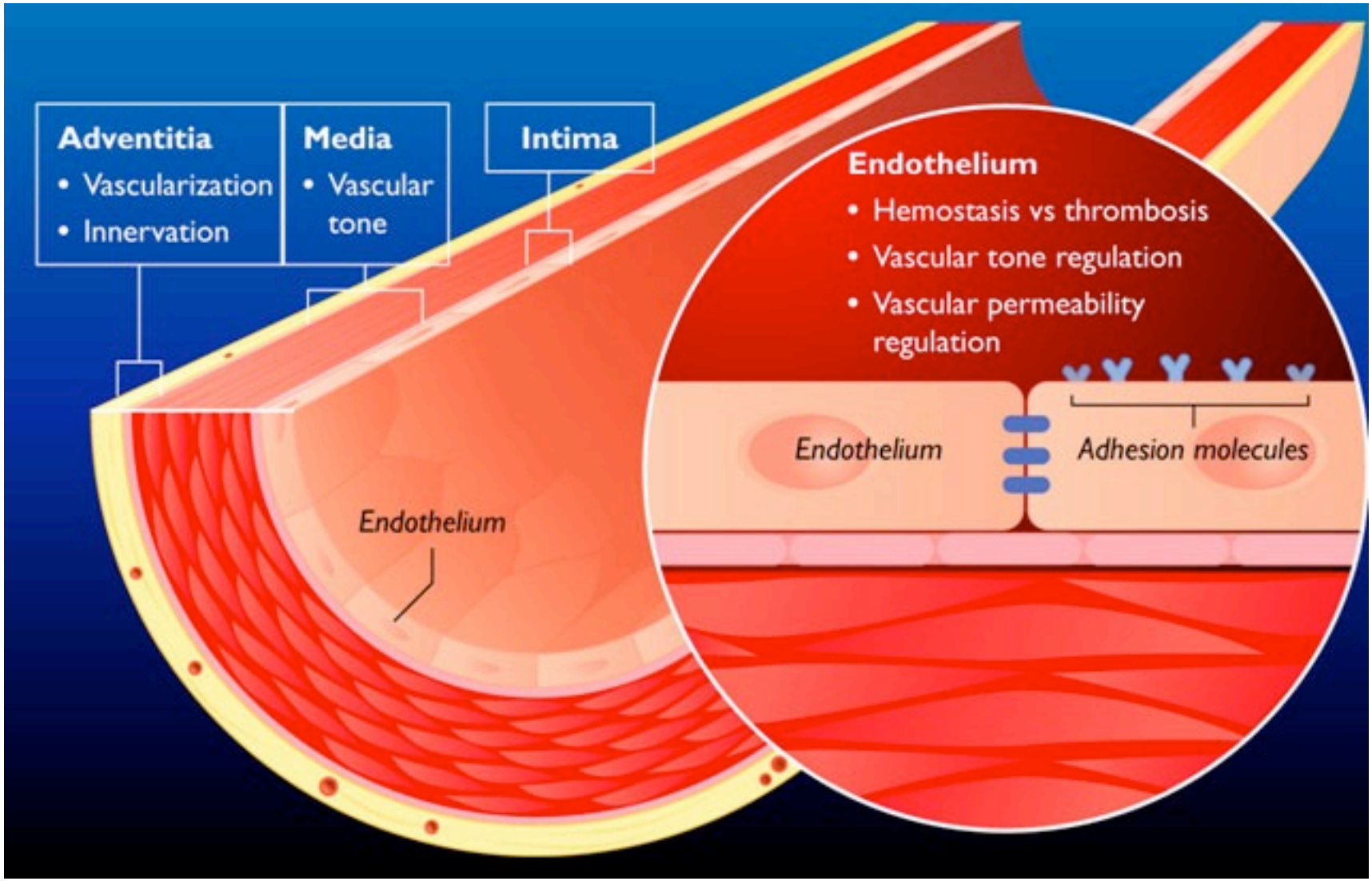
“HOW DOES IT START?”

??????

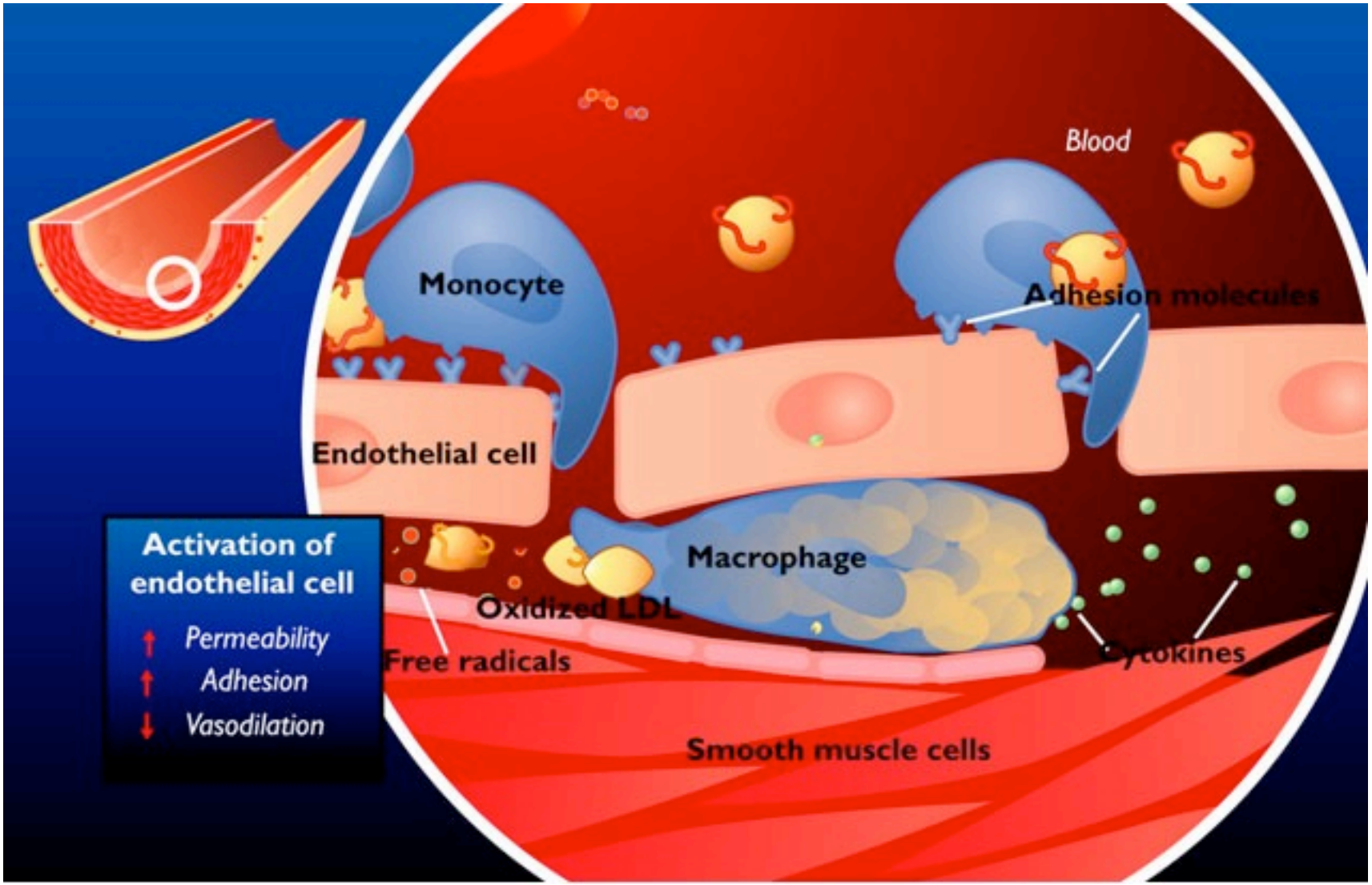
DAMAGE TO ENDOTHELIUM

- HYPERCHOL
- HYPERTENSION
- SMOKING

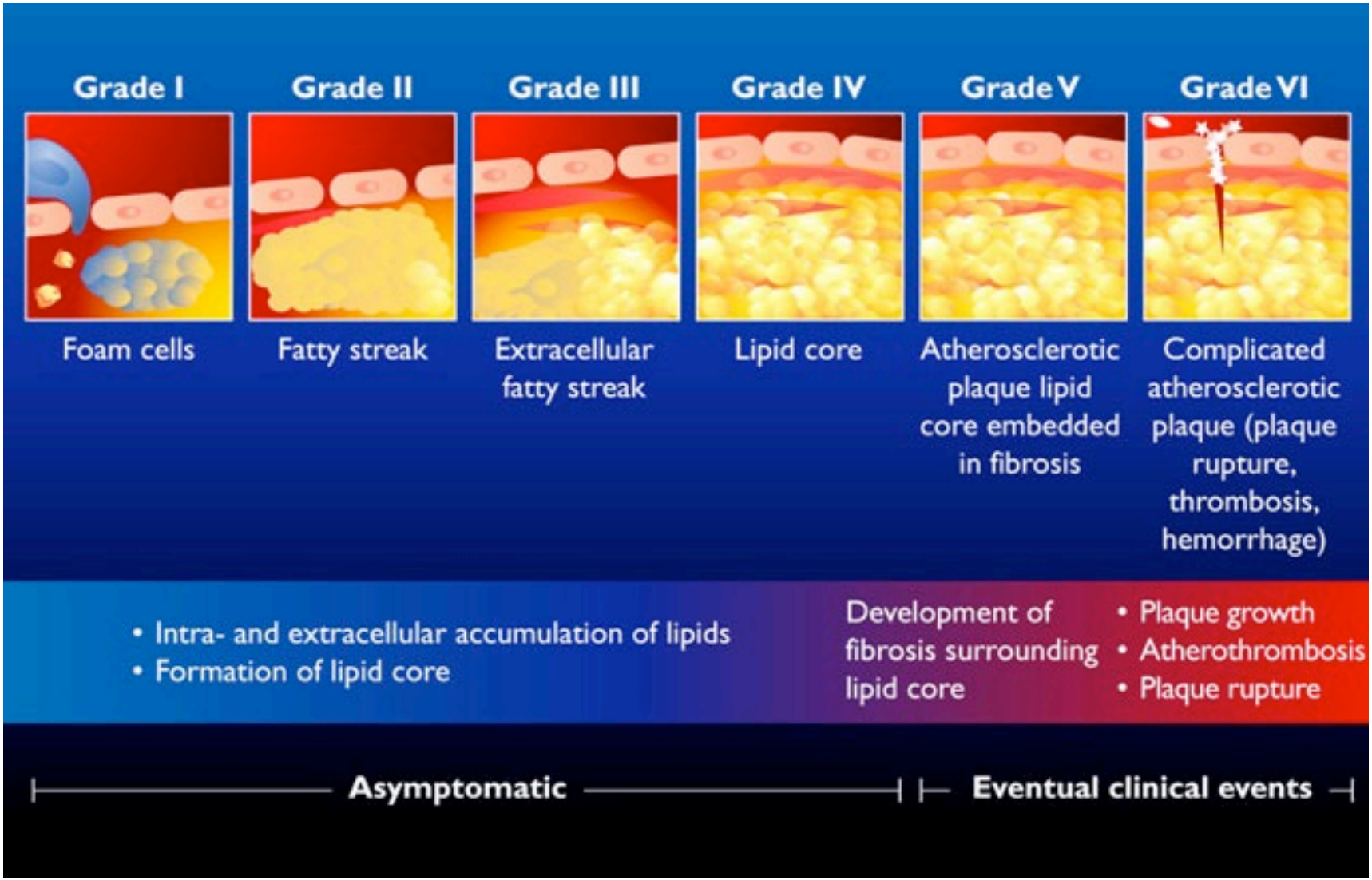
BAD NEWS: START IN YOUR TEENS!


Adventitia
• Vascularization
• Innervation
Media
• Vascular tone
Intima
Endothelium
• Hemostasis vs thrombosis
• Vascular tone regulation
• Vascular permeability regulation
Endothelium
Endothelium
Adhesion molecules

Vascular endothelium modification in atherosclerosis

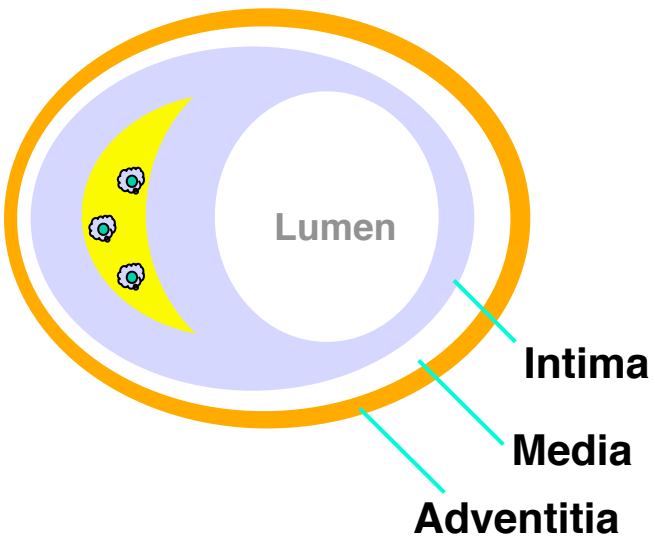


Different stages of atherosclerotic plaque development



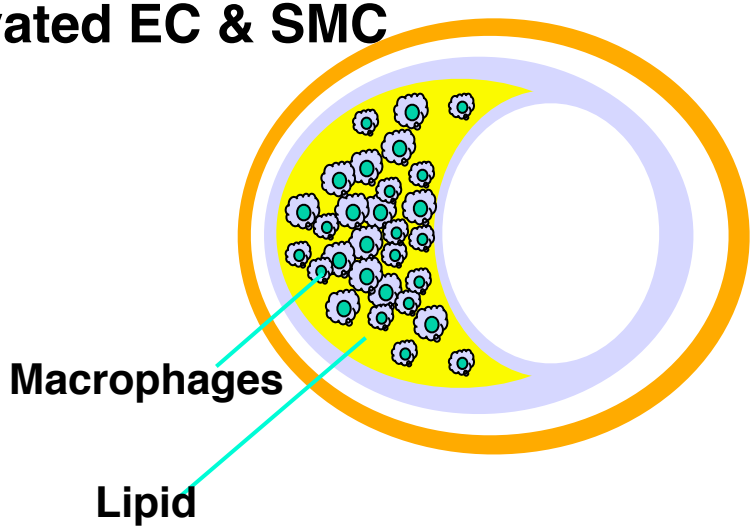
‘Stable’

Collagen-rich, thick fibrous cap
Few macrophages

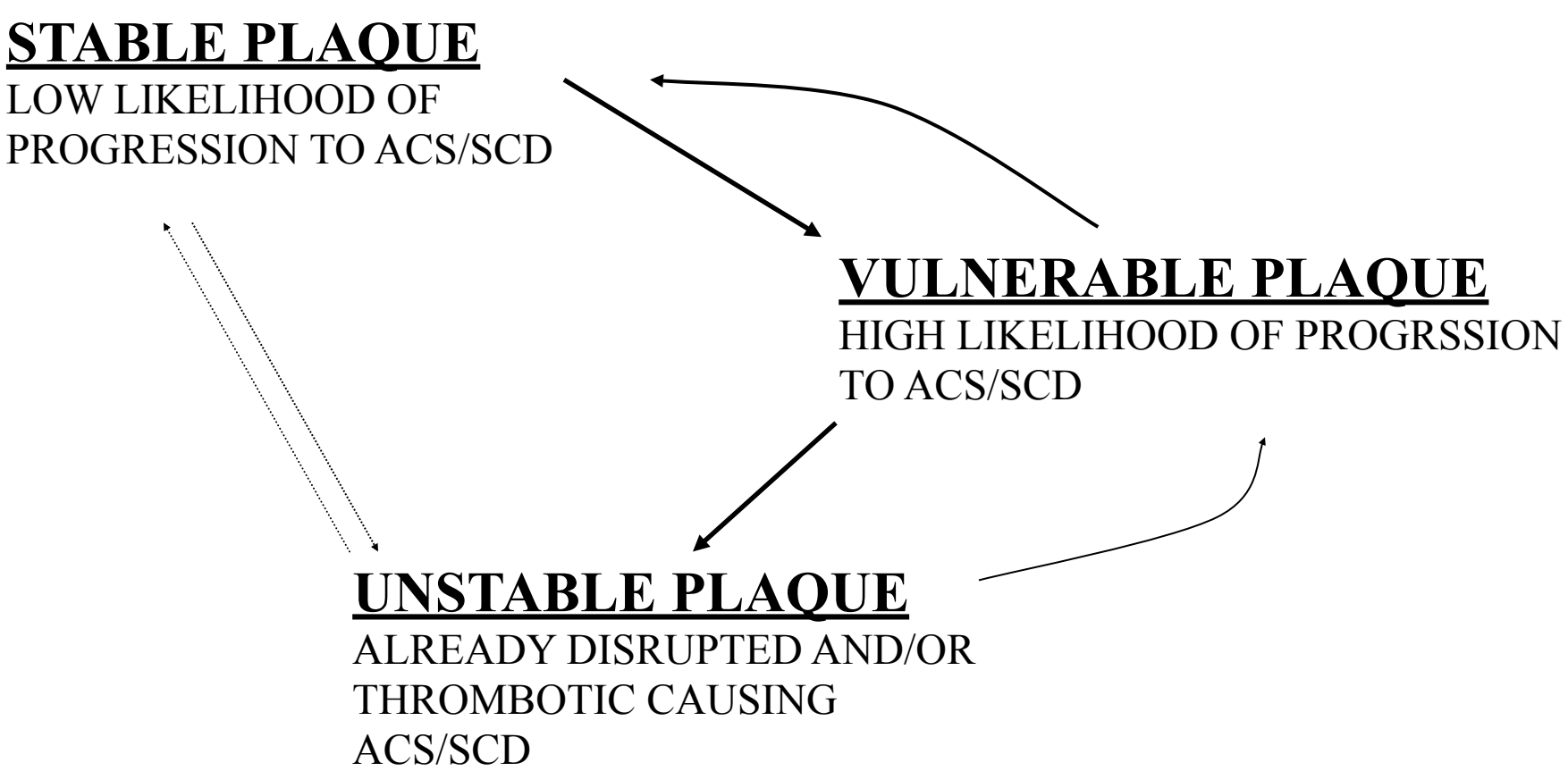


‘Vulnerable’

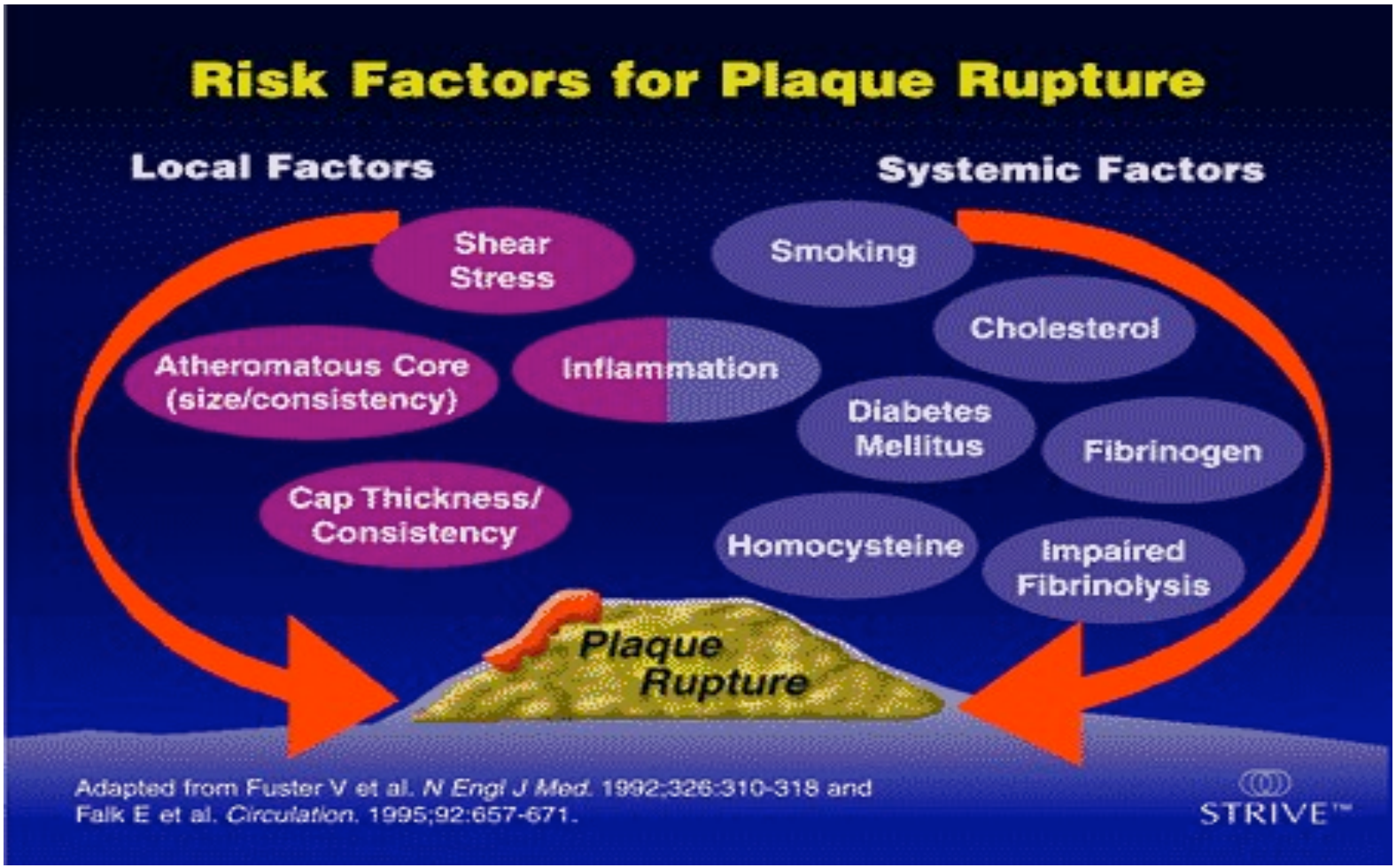
Collagen-poor, thin fibrous cap
Many macrophages (collagenases, TF, PAI-1)
Activated EC & SMC



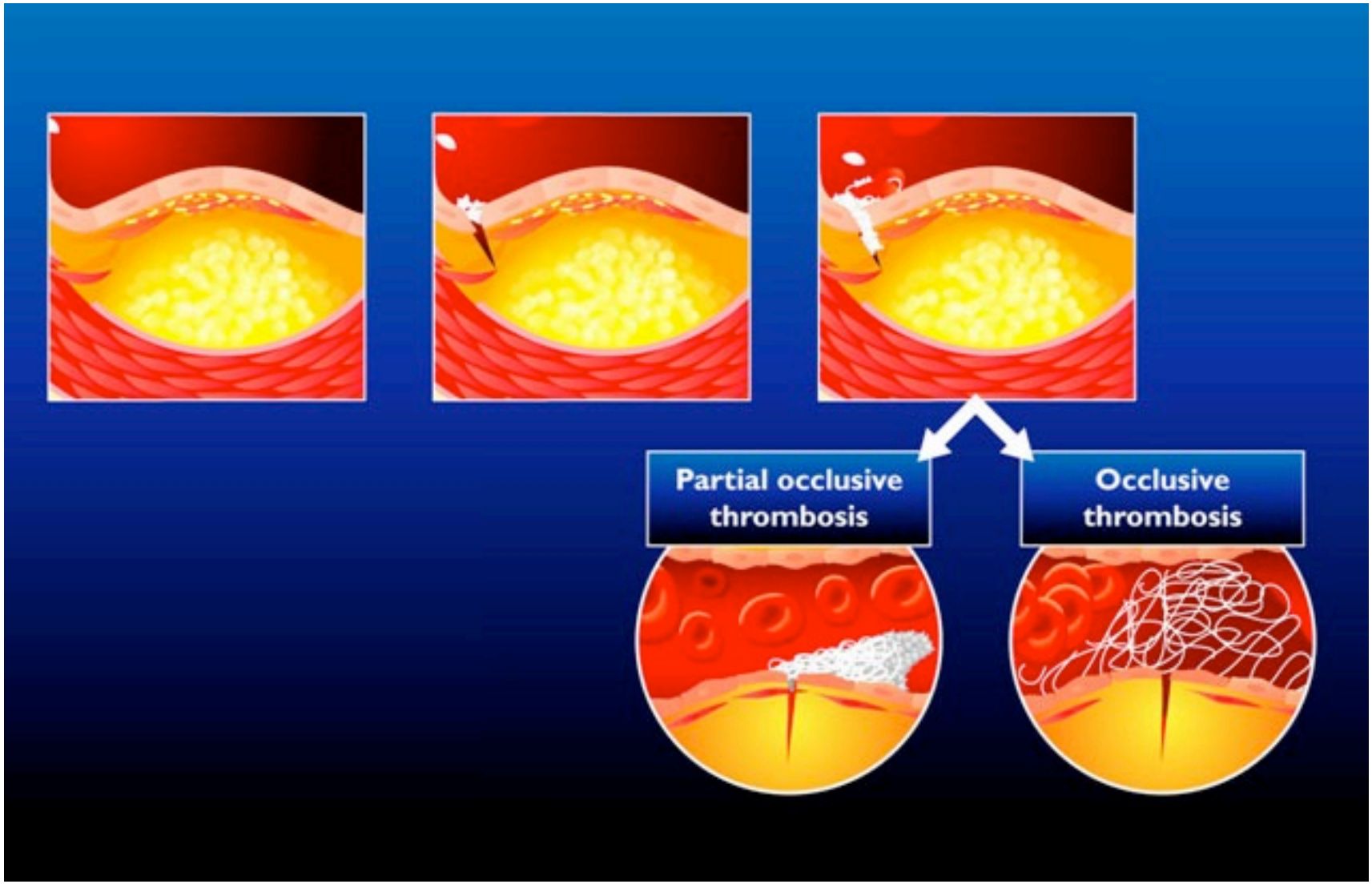
CLINICAL PATHOLOGICAL SPECTRUM OF CORONARY ATHEROSCLEROTIC DISEASE



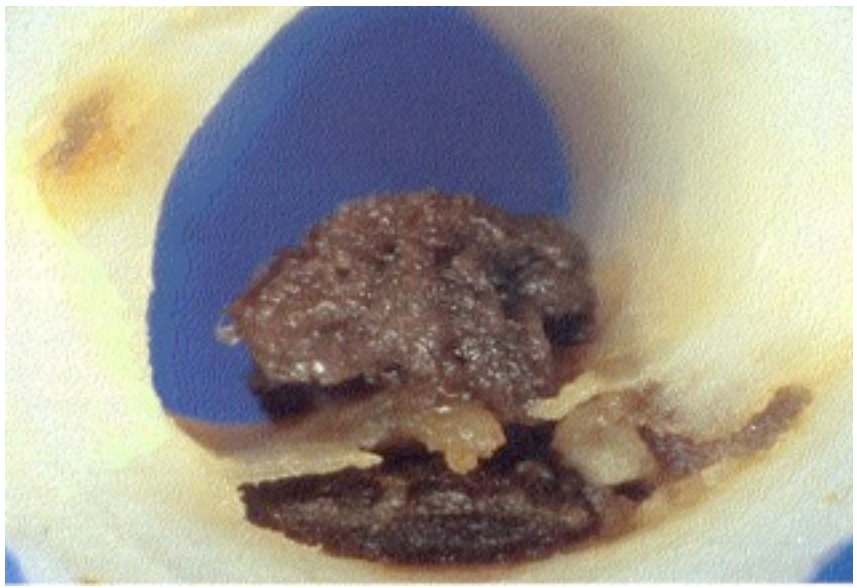
PLAQUE RUPTURE

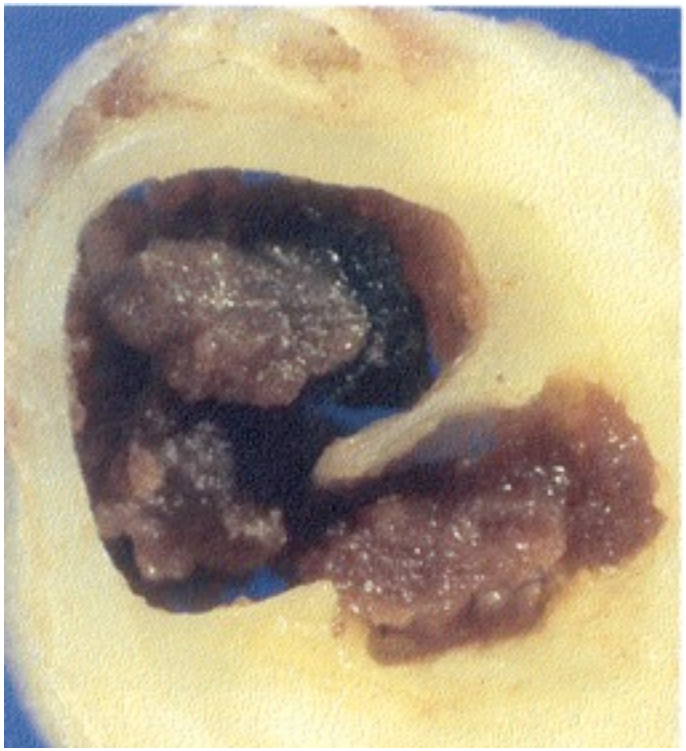


From plaque to thrombosis, key event: plaque rupture

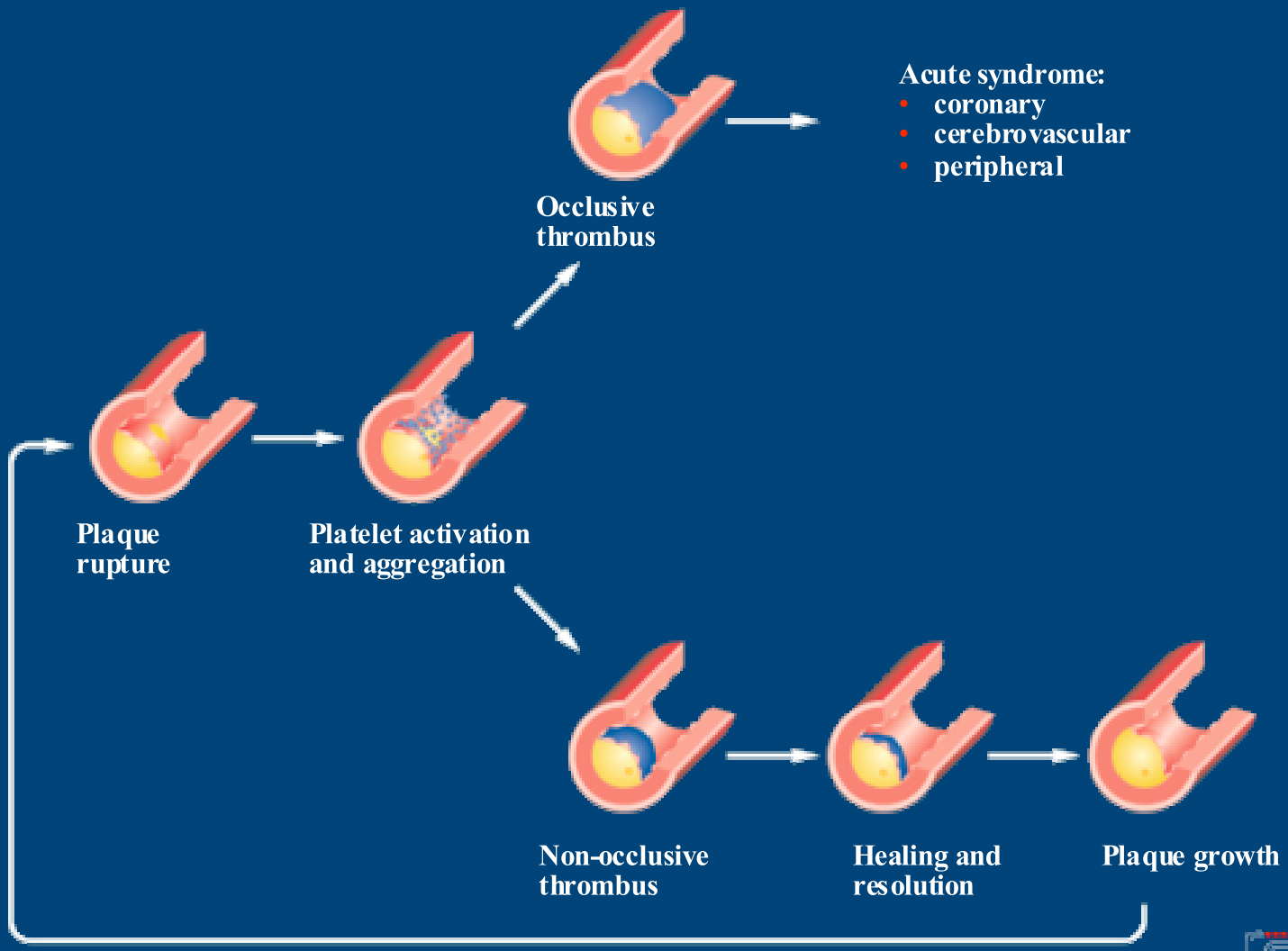


PLAQUE RUPTURE





The Development of Atherothrombosis – a Generalized and Progressive Process



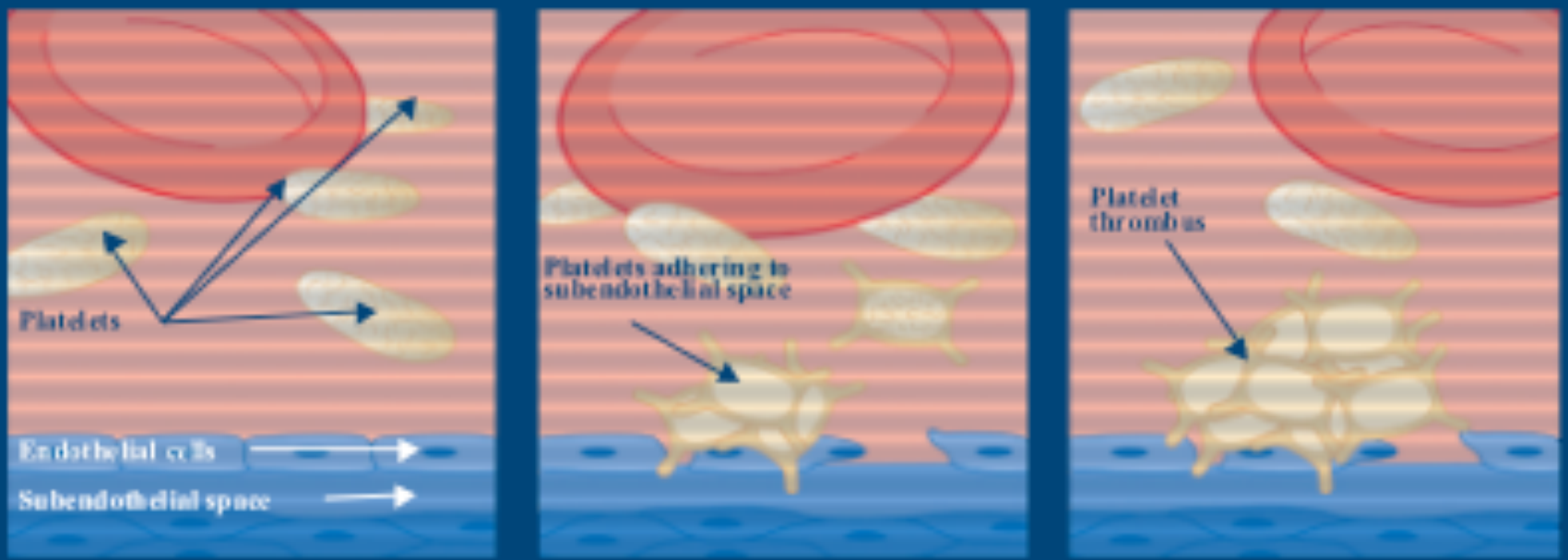
Adapted from: Drouet L. *Cerebrovasc Dis* 2002; 13(suppl 1): 1–6.

Platelet Adhesion and Activation

Normal platelets in flowing blood

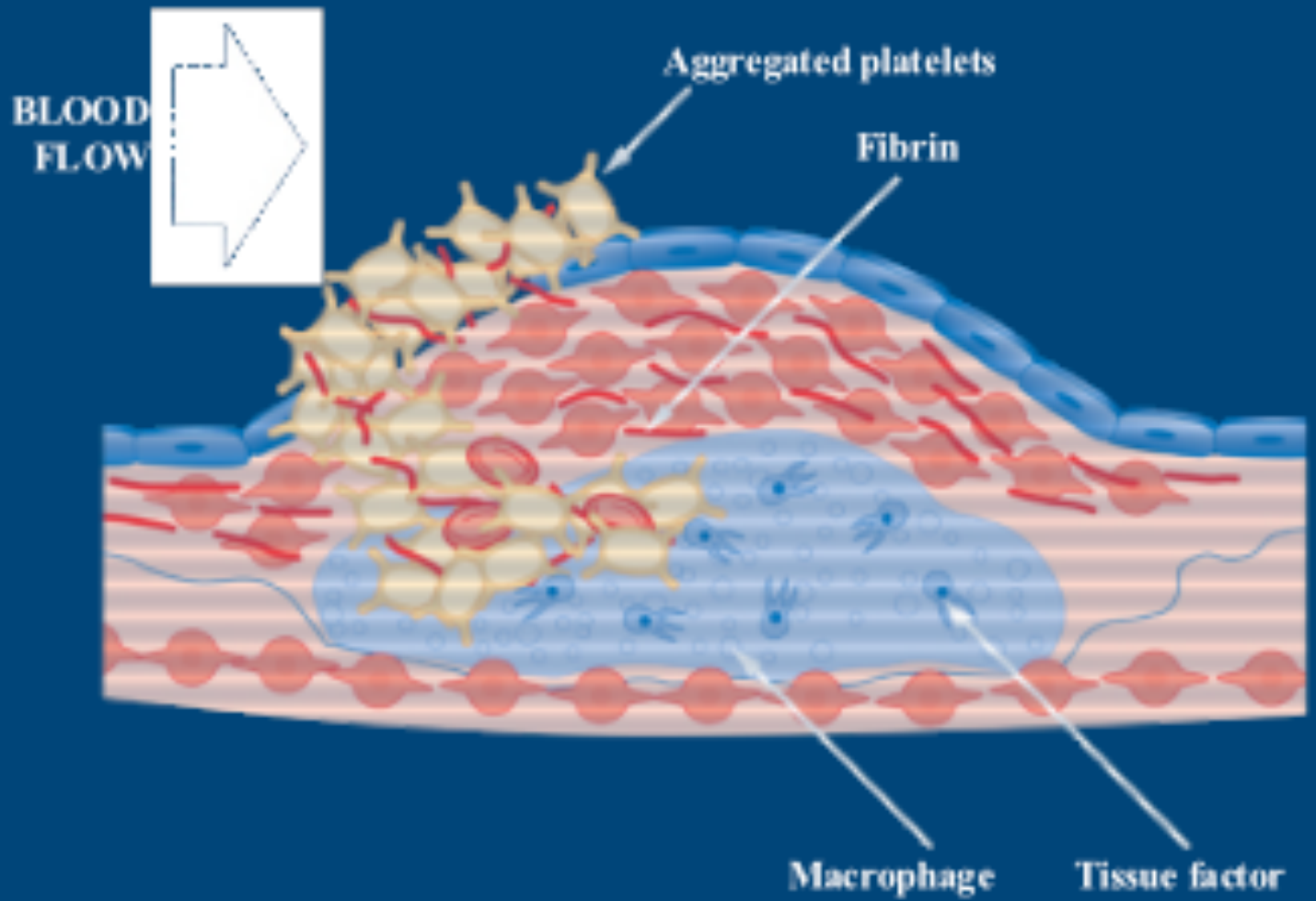
Platelets adhering to damaged endothelium and undergoing activation

Aggregation of platelets into a thrombus



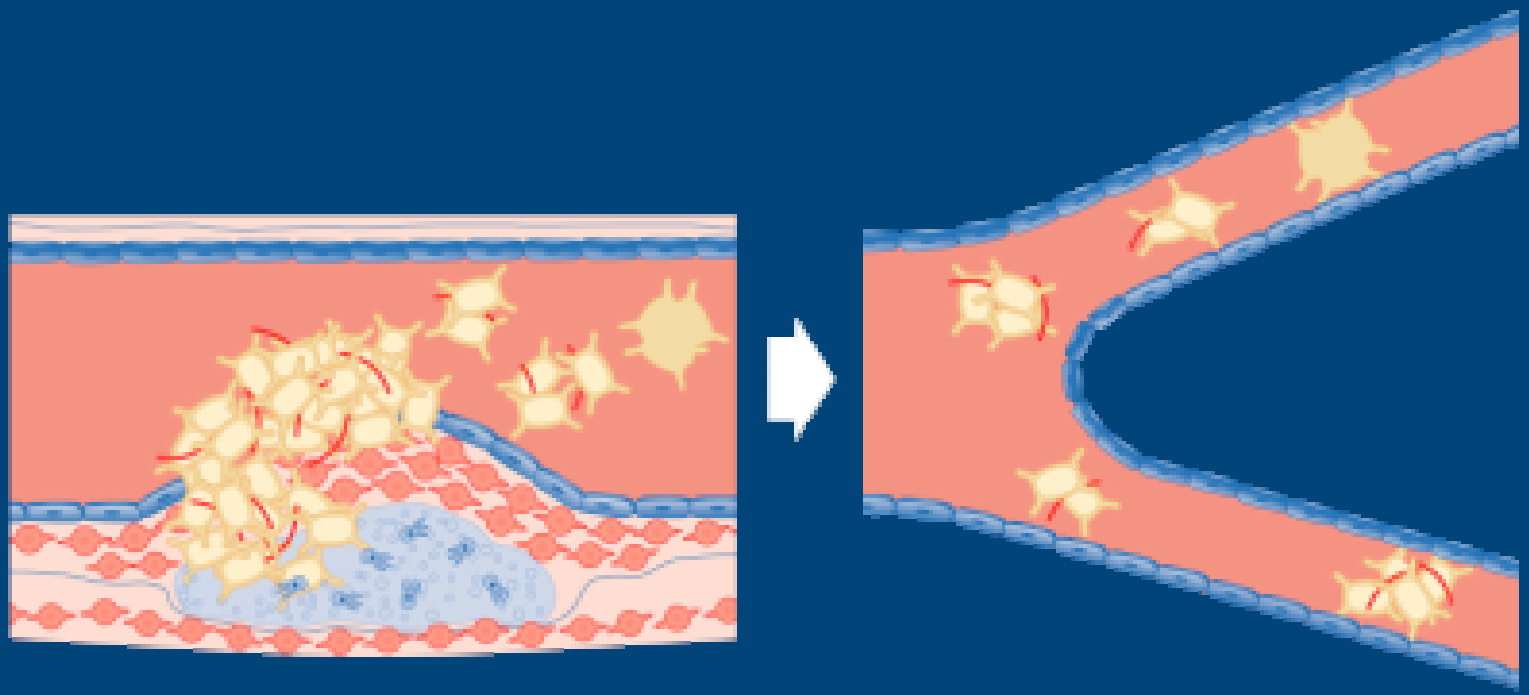
Adapted from: Ferguson JJ. *The Physiology of Normal Platelet Function*. In: Ferguson JJ, Chronos N, Harrington RA (Eds). *Antiplatelet Therapy in Clinical Practice*. London: Martin Dunitz; 2000: pp.15–35.

Plaque Disruption Leading to Atherothrombosis Formation



Adapted from: Falk E *et al. Circulation* 1995; 92: 657–71.

Atherothrombosis and Microcirculation



Plaque rupture

Embolization

Microvascular obstruction

Adapted from: Topol EJ, Yadav JS. *Circulation* 2000; 101: 570–80, and Falk E *et al.* *Circulation* 1995; 92: 657–71.

The consequences of ACS are not benign. Among those who survive to reach hospital alive, approximately

~ 12% of patients with STEMI

~ 13% of those with NSTE-ACS

~ 8% with unstable angina

die in the succeeding 6 months

(JUST AS MANY ARE READMITTED WITH FURTHERCARDIAC PROBLEMS)

RISK STRATIFICATION IN NSTE-ACS

HIGH RISK

INTERMEDIATE RISK

LOW RISK

RISK STRATIFICATION IN NSTE-ACS

- **High-risk patients include those with:**
  - **Recurrent ischaemia**
  - **Recurrent chest pain**
  - **Dynamic ST-segment depression or transient ST-segment elevation**
  - **Elevated troponin levels**
  - **Diabetes**
  - **Previous MI**
  - **Major arrhythmias**
- **High-risk patients should be referred immediately to a cardiologist for their assessment and intervention**

TIMI risk score for UA/NSTEMI

HISTORICAL	POINTS
Age ≥ 65	1
≥ 3 CAD risk factors (FHx, HTN, ↑ chol, DM, active smoker)	1
Known CAD (stenosis ≥ 50%)	1
ASA use in past 7 days	1
PRESENTATION	
Recent (≤ 24H) severe angina	1
↑ Cardiac markers	1
ST deviation ≥ 0.5 mm	1

RISK SCORE = Total Points (0-7)

RISK OF CARDIAC EVENTS (%) BY 14 DAYS IN TIMI 11B*

RISK SCORE	DEATH OR MI	DEATH, MI OR URGENT REVASC
0/1	3	5
2	3	8
3	5	13
4	7	20
5	12	26
6/7	19	41

*Entry criteria: UA or NSTEMII defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or positive marker)

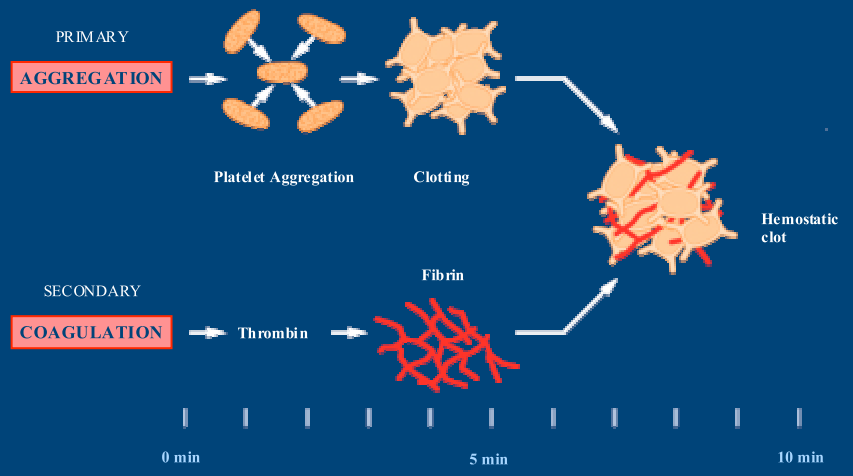
Antman et al *JAMA 2000*; 284: 835-842

Drug therapies in NSTE-ACS management

- **Aspirin**
- **Clopidogrel**
- **LMWH**
- **GPIIb/IIIa receptor antagonists**

- Beta blockers, High-dose Statin, ?ACE-I
- Nitrates (if ongoing pain/LVD)

Hemostatic Plug Formation



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