Ischaemic heart disease

- Ischaemia means literally ‘to hold back blood’.

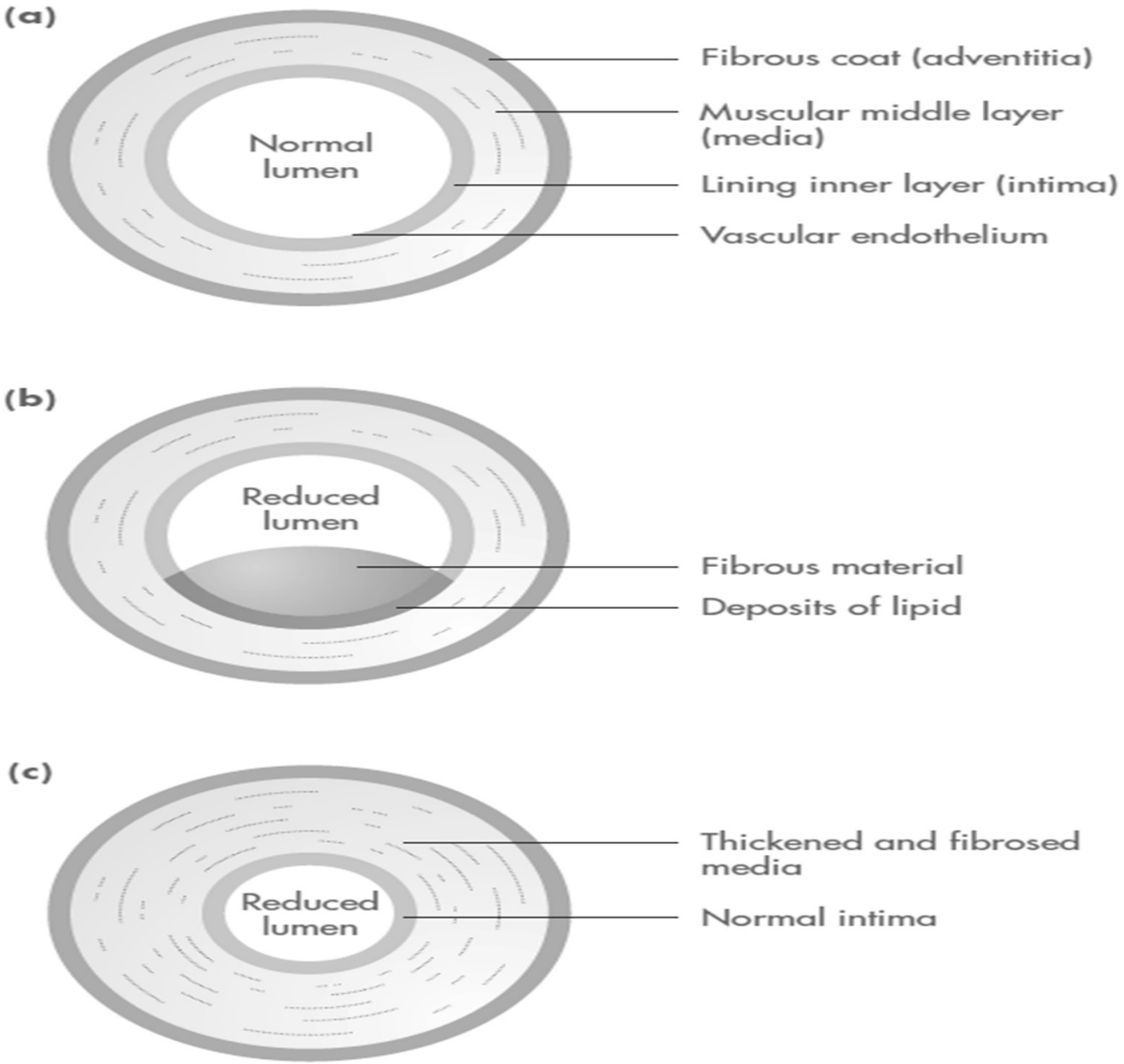
- Ischaemic heart disease (IHD) is the collective name for a number of conditions in which obstructive lesions of the coronary arteries restrict myocardial blood flow.

- The main clinical manifestations are angina pectoris and MI, but heart failure and arrhythmias also occur.

Arteriosclerosis: Although this term is commonly used to describe all degenerative or proliferative arterial lesions, it should be reserved for the symmetrical thickening of the middle muscle layer (media) of arterioles throughout the body.

- The media often becomes fibrosed and calcified, especially in the elderly. It is popularly known as ‘hardened arteries’.

- However, in the elderly there may be chronically reduced cerebral or renal perfusion.

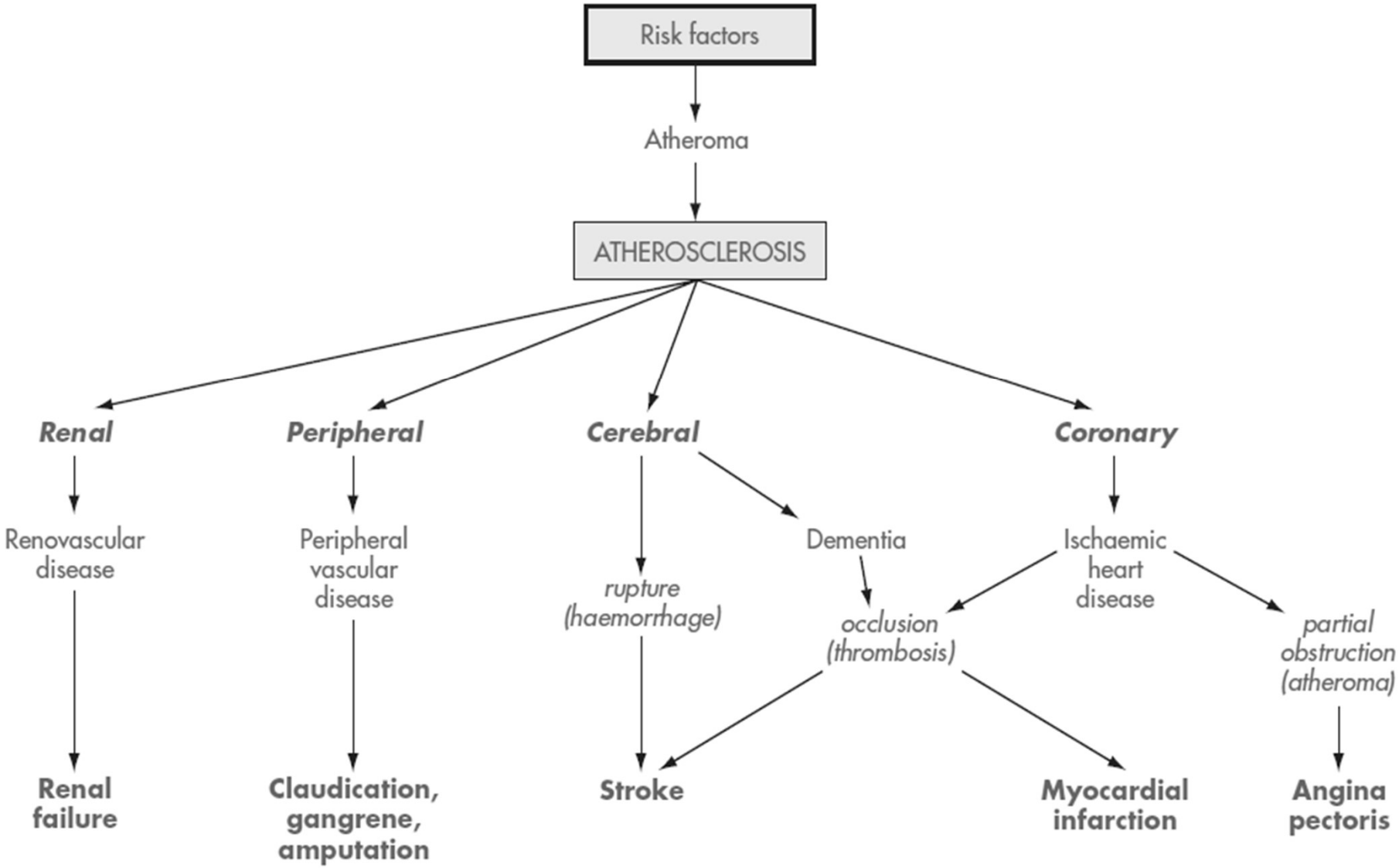

(a)
Normal lumen
Fibrous coat (adventitia)
Muscular middle layer (media)
Lining inner layer (intima)
Vascular endothelium
(b)
Reduced lumen
Fibrous material
Deposits of lipid
(c)
Reduced lumen
Thickened and fibrosed media
Normal intima

Atherosclerosis:

- Fatty-fibrous plaques or atheromas are deposited asymmetrically within the innermost layer (intima) of certain, but not all, arteries.

- Sites such as bends, branches or bifurcations seem especially prone.

Clinical manifestations of atherosclerosis



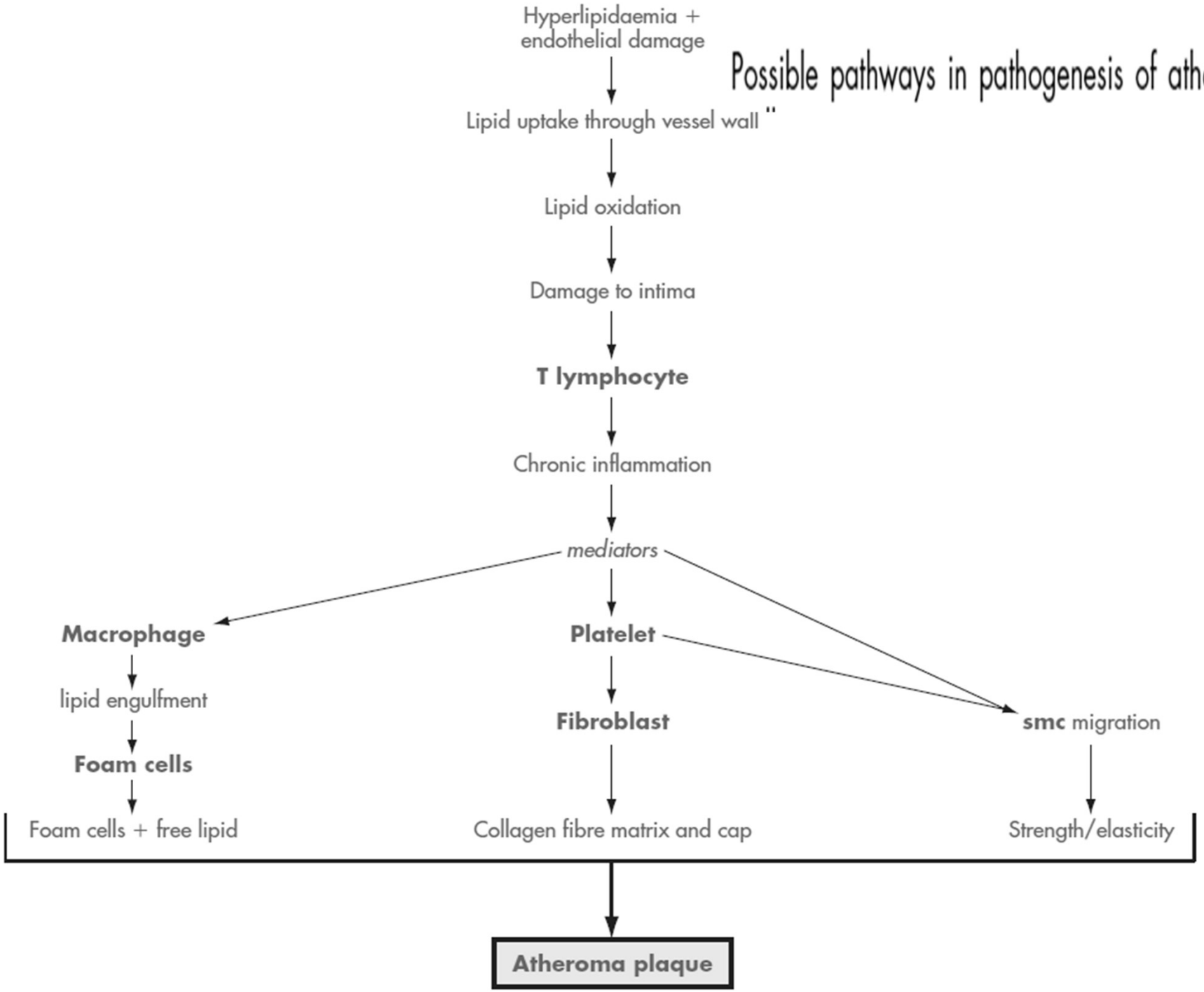
Pathological factors initiating atheroma and thrombosis

Abnormality	Arterial atheroma	Arterial thrombosis	Venous thrombosis
Histological	Chronic inflammation (? oxidized LDL, smoking) Infection (*Chlamydia*, *Helicobacter*) Hypoxia (smoking)	Ruptured atheroma? Heart valve (i) inflamed (ii) vegetation (endocarditis)	Inflamed venous valve (phlebitis)
Rheological	High pressure (i.e. HPT) High wall stress (i.e. HPT) Fast turbulent flow at bends, branches	Atrial fibrillation	Venous stasis, e.g. prolonged bedrest, recumbency
Biochemical	Dyslipidaemia (↑ LDL, ↓ HDL) Platelets (growth factors) Diabetes (dyslipidaemia) Irritants (smoking)	Clotting factors (↑ fibrinogen) Platelets (adhesiveness, growth factors)	Clotting factors Platelets Drugs, e.g oral contraceptives

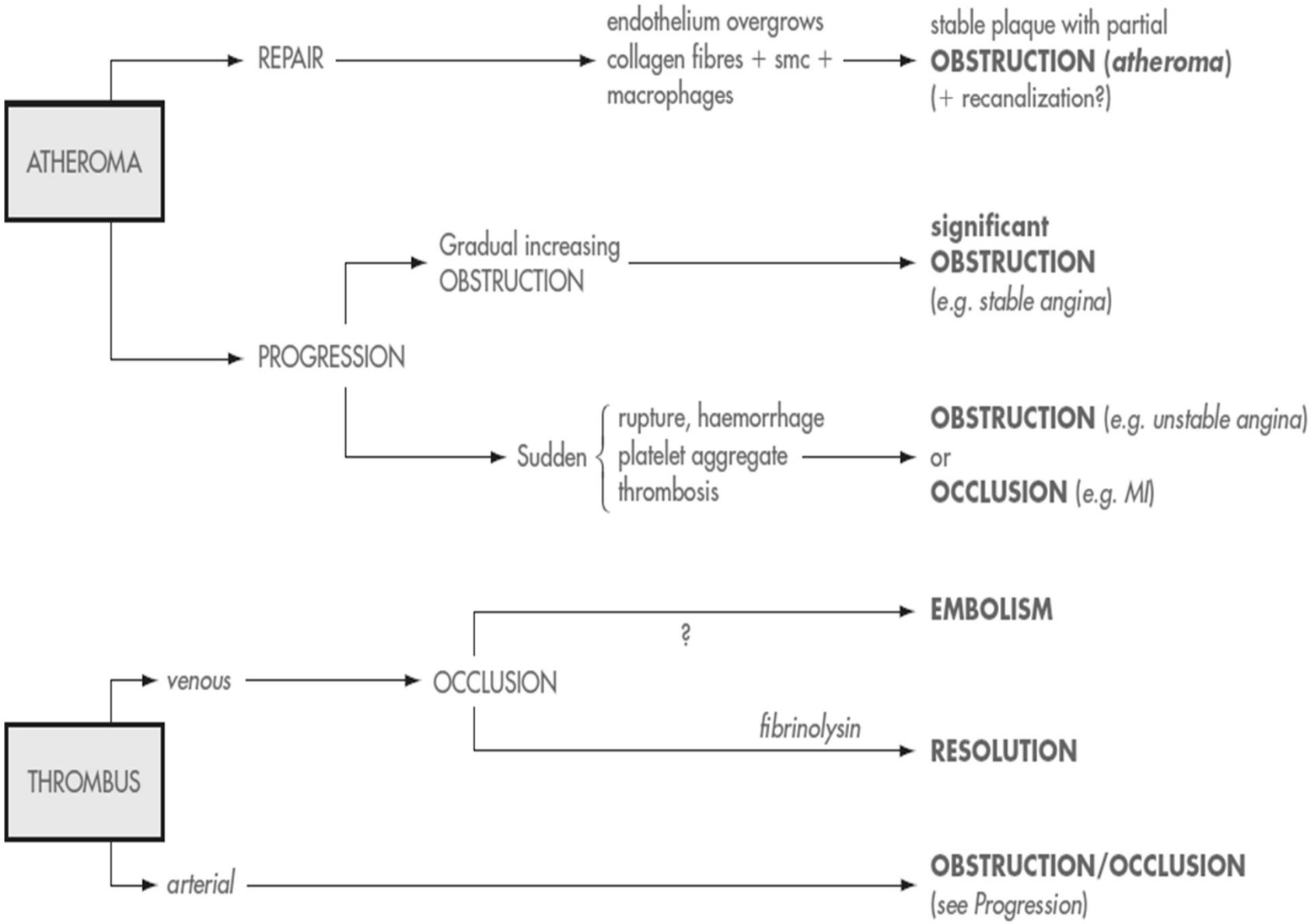
Risk factors for developing atherosclerosis

Primary modifiable	Secondary modifiable	Unmodifiable
Hyperlipidaemia[a]	Abdominal obesity[c]	Family history
Smoking	'Stress'[d]	Ethnic group
Diabetes[b]	Sedentary life/lack of exercise	Type A personality[d]
Hypertension	Diet poor in fresh fruit/vegetables	Age
	Excess or no alcohol	Male sex
		Female sex post-menopause
	Industrialized society	
	High sugar and low fibre intake	
	? Fetal deprivation due to maternal malnutrition	
	? Chronic infection[e]	
	? Raised plasma urate	
	? Raised plasma homocysteine	
	? Soft water	

Possible pathways in pathogenesis of atheroma



Progression of atheromas and thrombi and possible sequels



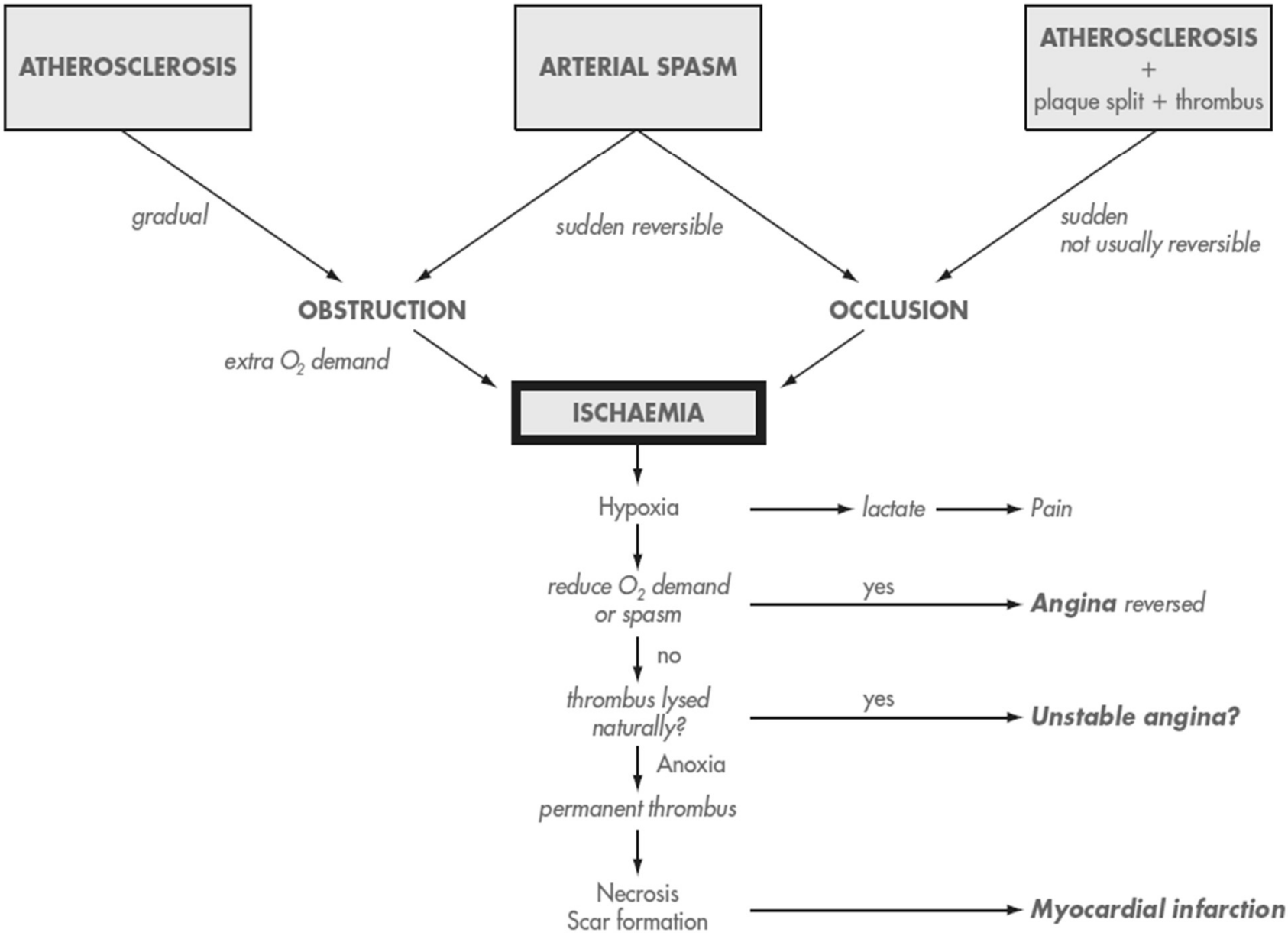
Myocardial ischaemia:

Why the heart?

The factors that make the heart particularly sensitive are:

- The myocardium has a high O2 demand and high O2 extraction.
- The heart works continuously.
- There are relatively few coronary collateral vessels.
- Myocardial cells regenerate poorly after damage.
- The heart is an integrated organ.

Pathogenesis of myocardial ischaemia



Prevention and treatment:

- Primary prevention theoretically implies preventing the atherosclerotic process from starting, whereas secondary prevention means taking measures to limit or perhaps reverse damage that is discovered subsequently, or prevent symptomatic recurrence.

Reducing risk factors for atherosclerosis

Recommendation	Rationale – pathological factor targeted
Stop smoking	Vascular endothelium, platelets
Reduce salt intake	Blood pressure
Reduce cholesterol intake	Cholesterol absorption
Reduce saturated fat[a]	Cholesterol synthesis
Increase unsaturated fat[a]	LDL level; also encourage anti-aggregatory mediators, etc.
Increase fibre intake[b]	Lipid absorption?
Increase fresh fruit and vegetable intake	Lipid level; also provide antioxidants
Moderate alcohol intake	BP; also protect against atheroma?
Moderate exercise	BP and lipid level; also encourage coronary collateral vessel development
Reduce sugar intake	Calorie intake/weight
'Reduce stress'	Reduce BP Reduce atheroma formation?
Aim for ideal body weight	Lipid level, cardiac load, blood pressure

Angina pectoris:

- Angina is both defined and diagnosed by clinical criteria. Typical ischaemic cardiac pain is retrosternal (behind the breastbone), intense, diffuse rather than sharp, and gripping, constricting or suffocating.

- Patients describe the sensation of having their chest crushed by a bearhug, or they may clench their fist over their chest.

- Yet even when it radiates to the upper arms, neck or jaw on either side it may be difficult to distinguish from severe dyspepsia, ‘heartburn’ or oesophageal pain, or even pericarditis, so other signs must also be sought.

Trigger factors, symptoms and signs of an angina attack

Trigger factors

Exertion, e.g. climbing stairs, sexual intercourse

Emotion – increased heart rate

Heavy meals – diversion of blood for increased gastrointestinal perfusion

Getting into a cold bed
Going out in cold windy weather
} peripheral vasoconstriction raises peripheral resistance

Symptoms

Onset: pain builds up over seconds or minutes (not instantaneous)

Crushing, constricting, dull central chest pain

Relieved by rest or glyceryl trinitrate

Radiation of pain into throat, left jaw and arm, occasionally into back and right arm

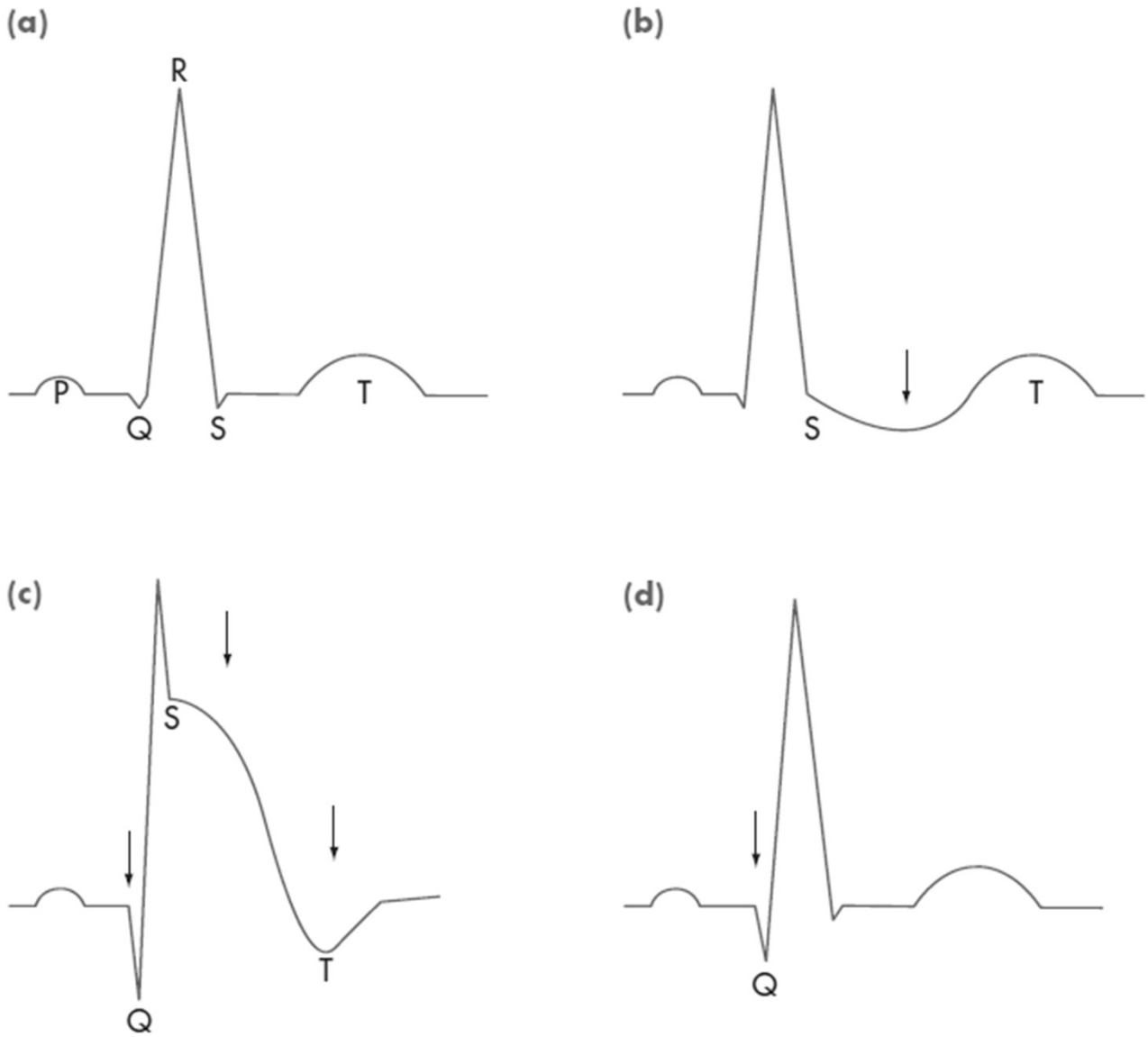
Tachycardia, sweating, anxiety

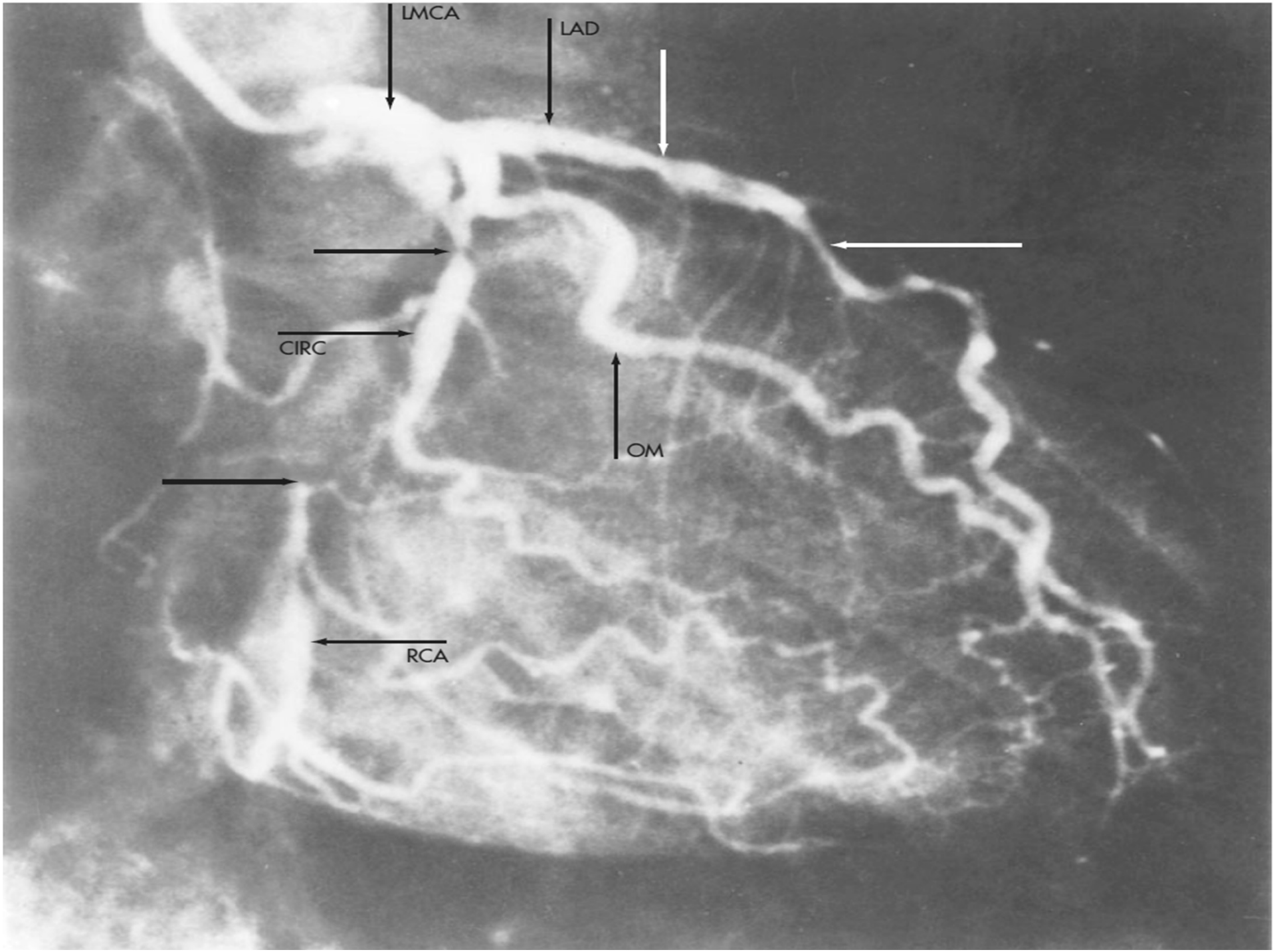
Breathlessness

Signs

ECG[a]

- between attacks – normal
- during attack – classical: ST segment depressed
  – variant: ST segment elevated


(a)
R
P
Q
S
T
(b)
S
T
(c)
S
T
Q
(d)
Q


LMCA
LAD
CIRC
OM
RCA

Management

Aims and strategy

- The overall aim in the management of angina is to minimize myocardial ischaemia.

- There are three objectives:

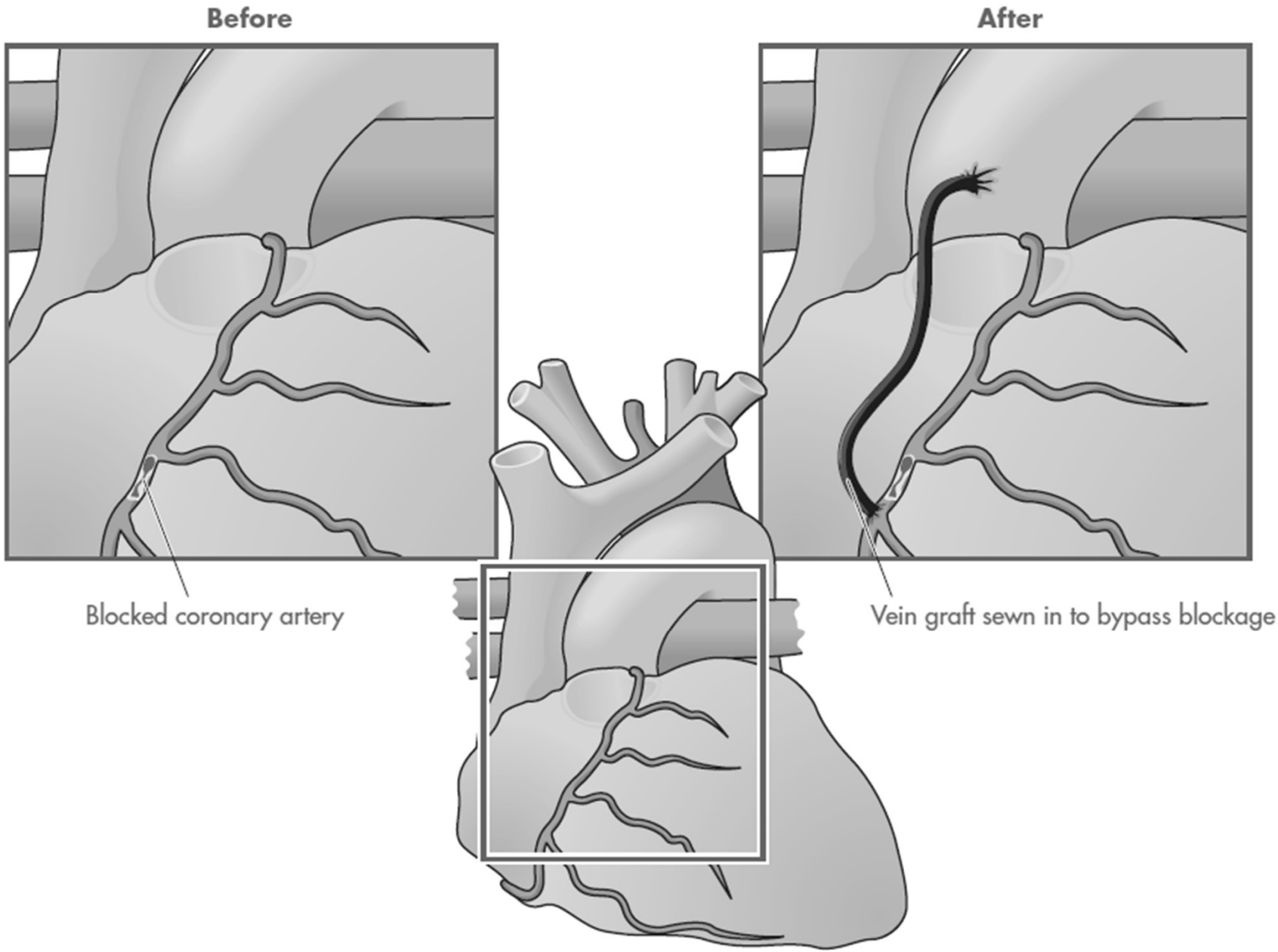
1. To abolish the symptoms of an acute attack.

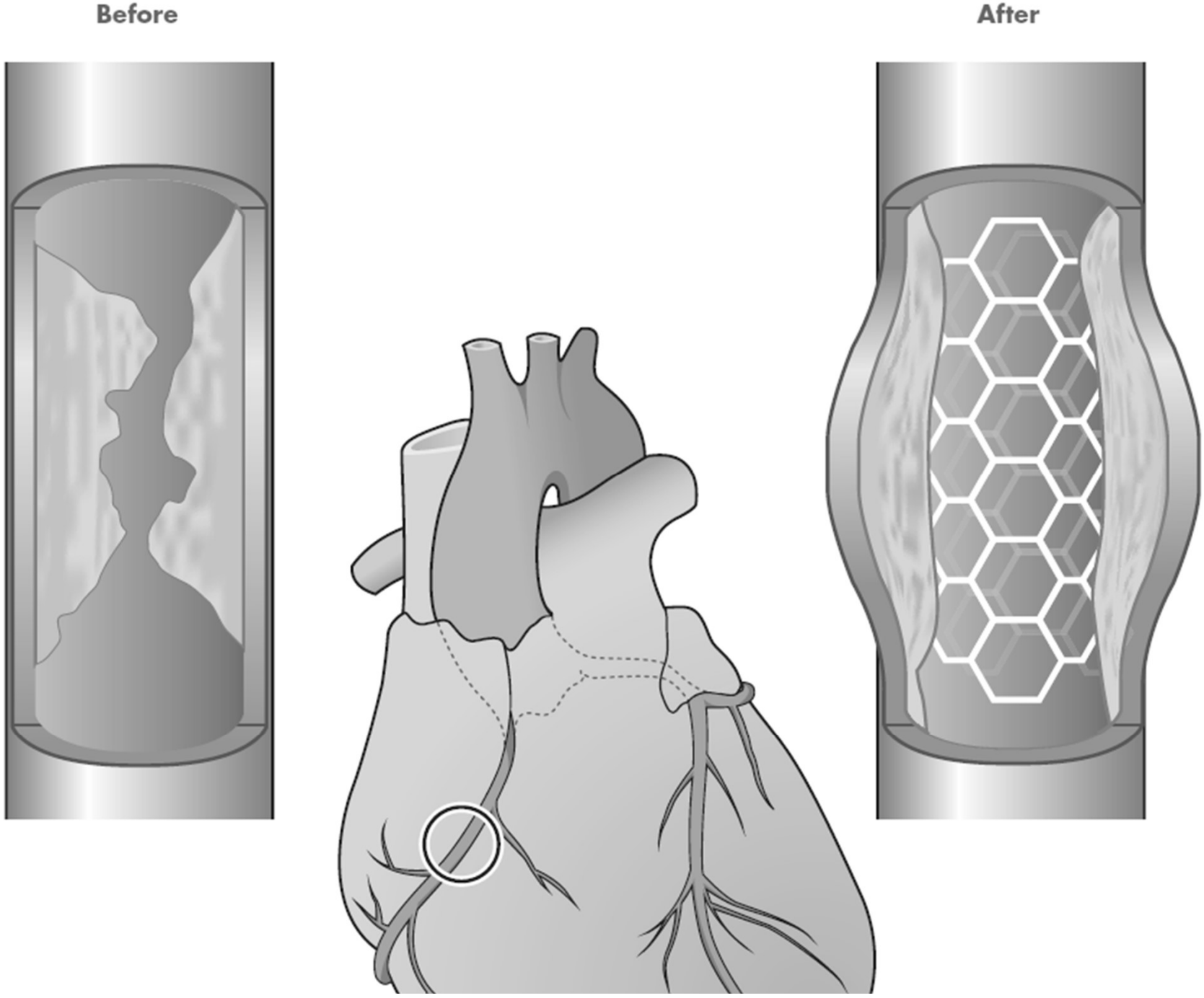
2. To prevent or minimize the frequency of symptomatic or silent myocardial ischaemia.

3. To halt or reduce the progression of the underlying atherosclerosis.

Restoring myocardial oxygen balance

Strategy	Methods	Example
Reduce oxygen demand		
Reduce cardiac workload		
Reduce perfusion demands	Rest	
	Avoid stress	
	Stop smoking	
	Reduce weight	
Reduce preload	Venodilator	Nitrate, potassium channel activator
Reduce afterload	Arterial dilator	CCB, nitrate[a], potassium channel activator
Reduce rate/contractility	Negative inotrope	Beta-blocker, CCB
Reduce rate	Sinus node inhibitor	Ivabradine
Improve cardiac efficiency	Improve fitness	Exercise, stop smoking, lose weight
Improve oxygen supply		
Increase coronary flow	Arterial dilator	CCB, nitrate[a]
	Surgery	Bypass, angioplasty
Prevent further obstruction		
Reduce progression of atherosclerosis	↓Risk factors	Diet, stop smoking, etc.
	Antiplatelet	Aspirin
	Lipid-regulating	Statin, fibrate, etc.

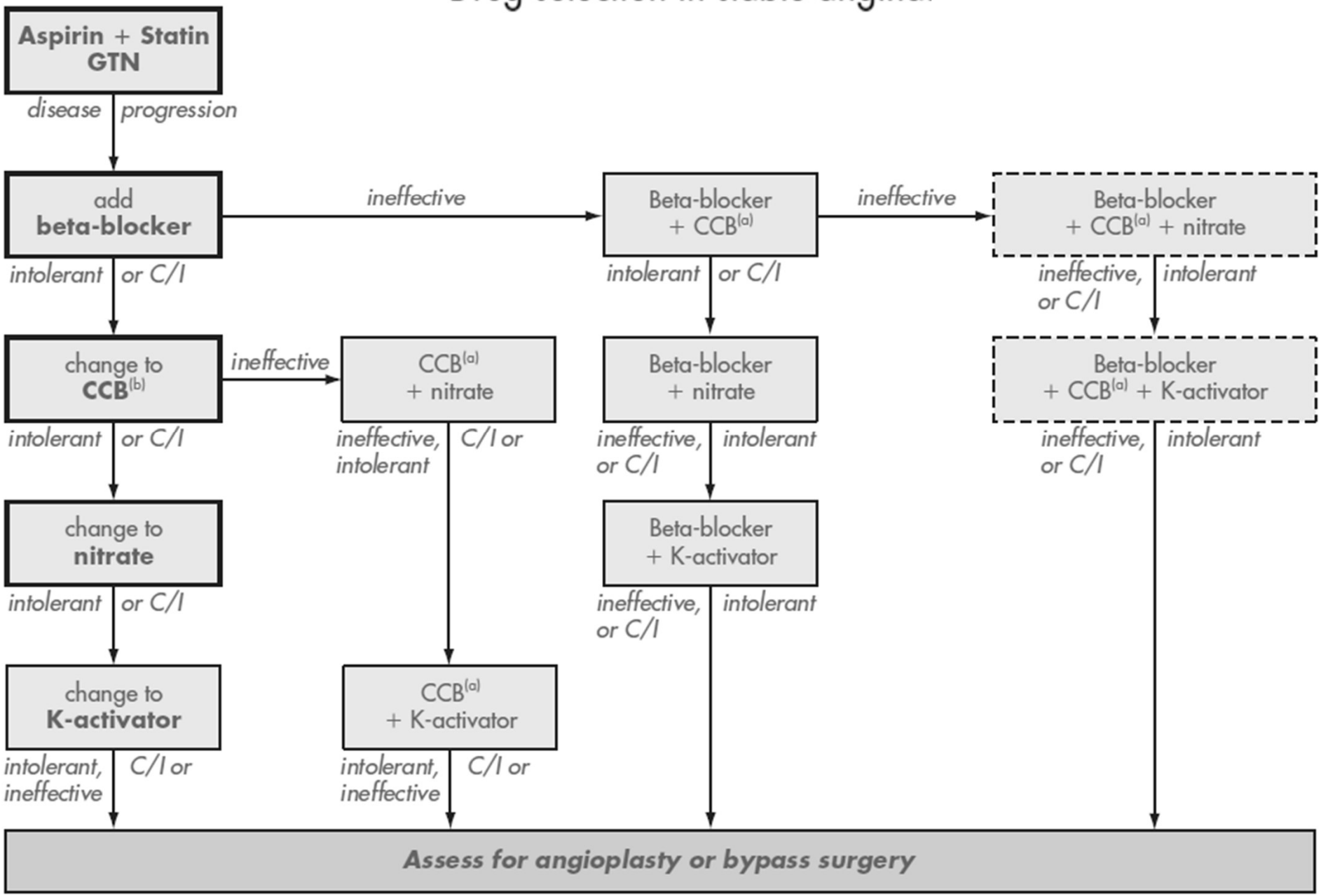

Before
After
Blocked coronary artery
Vein graft sewn in to bypass blockage


Before
After

Use of glyceryl trinitrate for acute angina attacks

Mode of action	Peripheral venodilatation → reduced preload Coronary vasodilatation?
Rapid effect	Buccal/sublingual absorption • avoids delay in absorption • effect within 1 min; lasts 30 min • may be chewed for more rapid effect • avoids hepatic first-pass metabolism • sublingual aerosol available
Side-effects (vasodilatation)	Hypotension – patients advised to sit when taking Flushing Headache (often regarded as an index of effectiveness)
Stability	Sublingual tablets are volatile, easily absorbable – use tightly sealed glass containers, with foil-lined closures To be discarded 8 weeks after dispensing Buccal modified-release and aerosol formulations more stable – longer shelf-life

Drug selection in stable angina.



Myocardial infarction:

- Myocardial infarction (MI, ‘heart attack’, ‘coronary thrombosis’) occurs when a coronary vessel becomes occluded for more than about 6 h, whether or not the occlusion is subsequently relieved.

- Unlike for angina, exertion is not a trigger for MI, and although MI is frequently associated with current stress or general ‘life events’, the patient may be unable to recall a particular precipitating event.

Comparison of classic angina and myocardial infarction

Angina	Myocardial infarction
Caused by atherosclerosis	Caused by atherosclerosis
Triggered by exertion	Triggers often unknown
Pain: severe, crushing, retrosternal, possibly radiating	Pain: severe, crushing, retrosternal, possibly radiating
Pain reversed on resting in a few minutes	Pain persistent
Pain relieved by glyceryl trinitrate	Pain unrelieved by glyceryl trinitrate
↑ Oxygen demand	↓ Oxygen supply
Partial obstruction	Complete occlusion
Myocardial hypoxia	Myocardial anoxia
Reversible	Irreversible

- Some MIs may be so mild as to be dismissed by the patient, relatives and sometimes even doctors as indigestion, especially if the patient has not experienced ischaemia before.

- On admission, patients are usually cold and pale (owing to central conservation of reduced cardiac output), clammy (due to sympathetic discharge), nauseated and breathless with rapid shallow breathing.

- Their great distress is due not only to severe pain but also to profound fear and anxiety. This heightens the perception of pain because patients are literally mortally afraid.

- There may be hypotension, tachycardia or profound bradycardia, and signs of pulmonary oedema (e.g. crackles heard through the stethoscope).

- All patients with suspected MI are closely monitored for 72 h to confirm the diagnosis and anticipate complications.

- Precise diagnostic criteria vary, but generally the diagnosis depends on significant findings in at least two of three crucial areas:
- Clinical presentation and history.
- Progressive ECG changes.
- Progressive serum cardiac marker changes.

Complications of myocardial infarction

Complication	Comment
Early	
(Left) ventricular failure	Common
Pulmonary oedema	If LV failure severe
Cardiogenic shock	10% MI patients; if ventricular damage >33%
Arrhythmias, especially ventricular fibrillation and asystole	Potentially fatal; monitoring essential
Thromboembolism	Hypercoagulable state
• further infarct, stroke	• transmural infarcts (endocardial damage)
• deep vein thrombosis	• prolonged immobilisation
Hypotension/bradycardia	Autonomic imbalance
Late	
Pericarditis	First few days
Systolic stretch, ventricular aneurysm, ventricular remodelling	Causes ventricular failure
Ventricular rupture	
• cardiac tamponade[a]	Causes 10% of hospital MI deaths
• septal defect	Rare
Post-MI autoimmune syndrome	Pericarditis, fever, effusion

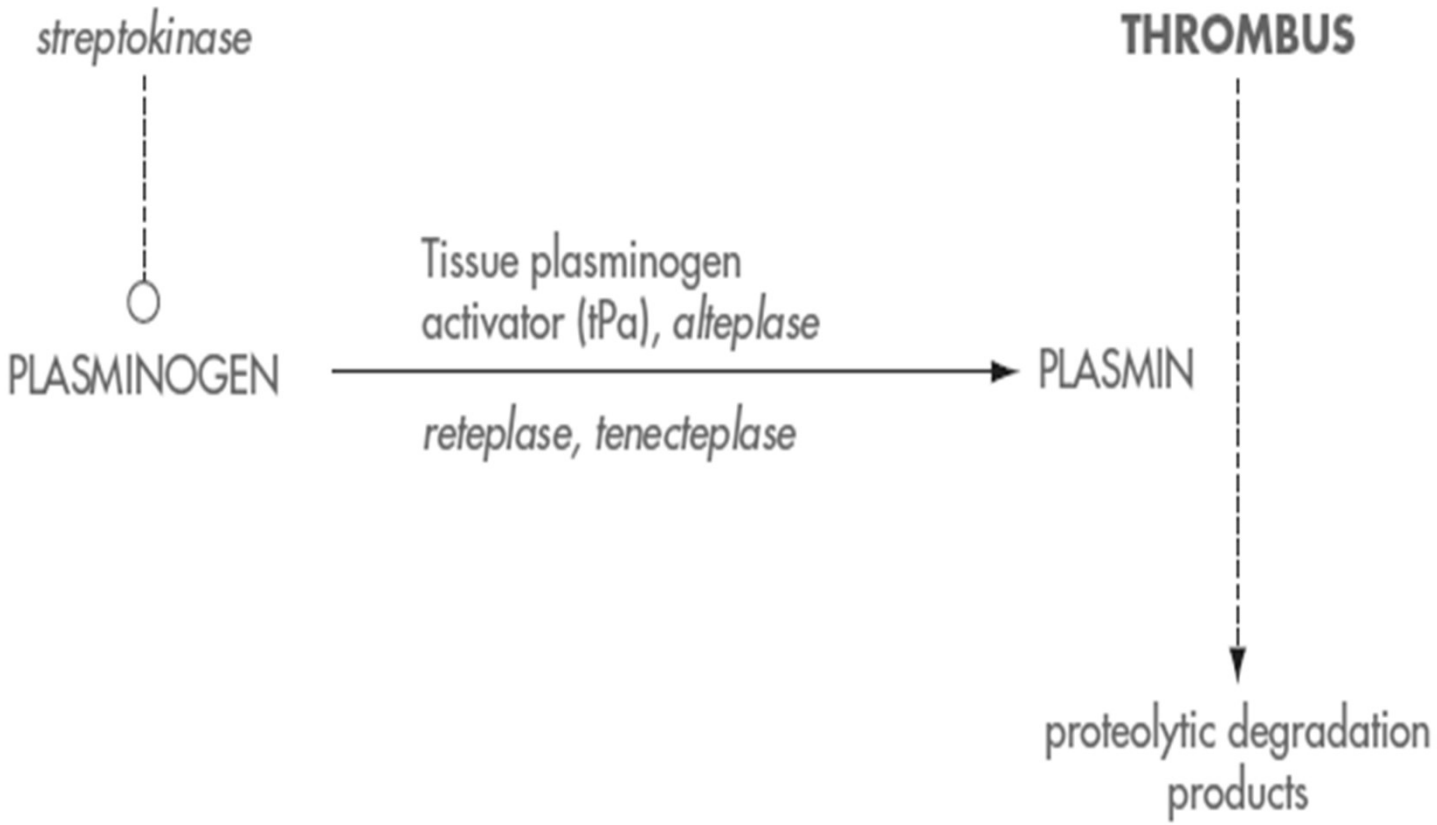
- **Management:**
- The aims in managing MI are, in sequence, to:
- act promptly to save life and reduce complications;
- treat acute symptoms;.
- restore flow through the affected artery (revascularization);
- minimize subsequent infarct size;
- treat complications;
- rehabilitate;
- ensure secondary prevention of subsequent attack.

Routine acute management of myocardial infarction symptoms

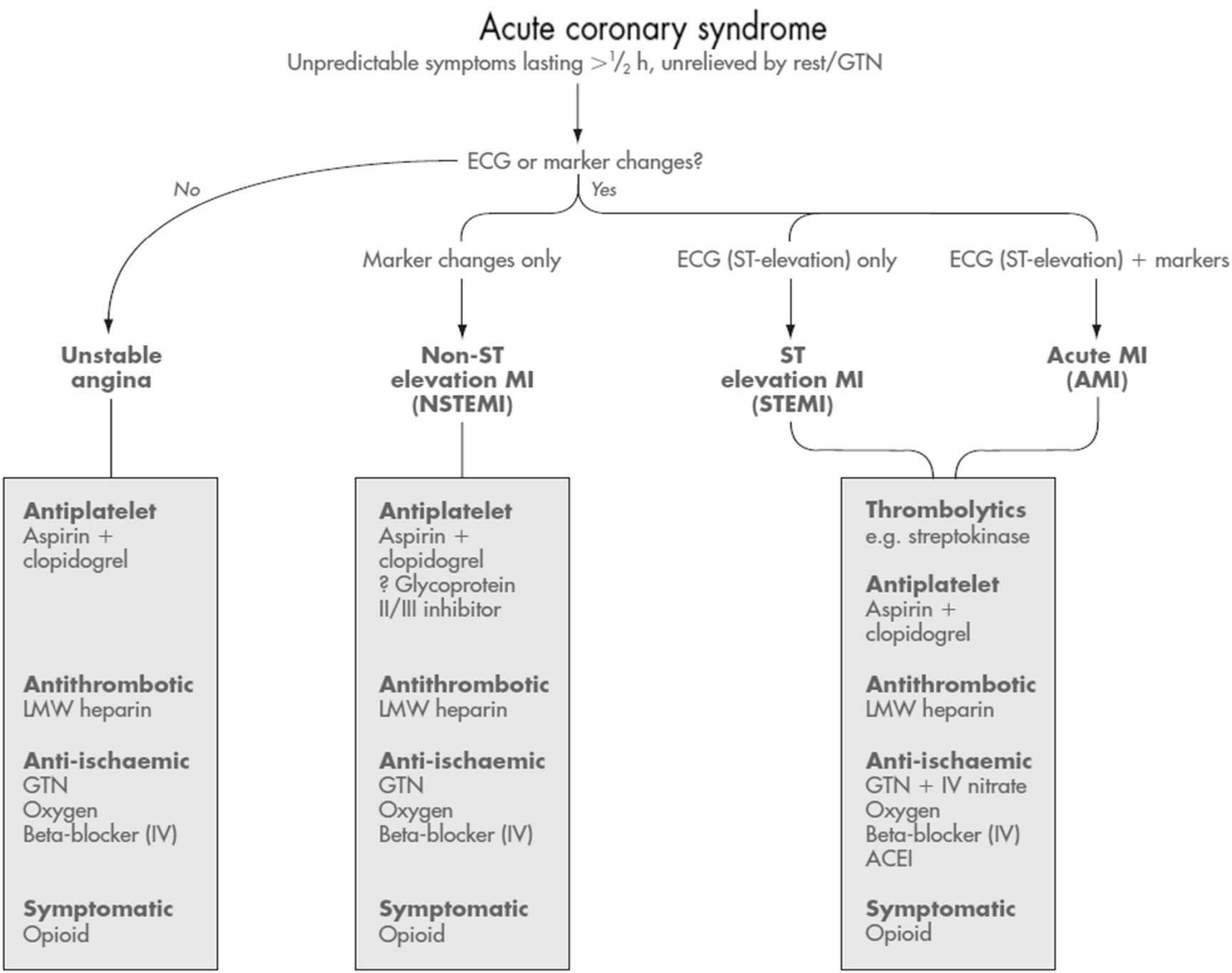
Target	Management
Pain	GTN, opioid plus anti-emetic
Distress, anxiety	Opioid
Minimize thrombus extension	Aspirin
Hypoxaemia	Oxygen
Dissolve thrombus	Thrombolytic
Heart failure	Nitrate, diuretic, ACEI
Pulmonary oedema	Diuretic, opioid

Comparison of fibrinolytic agents

	Streptokinase	Alteplase	Reteplase	Tenecteplase
Mode	Infusion	Infusion	Bolus	Bolus
Duration	1 h	3 h	30 min[a]	10 s
Antigenicity	Antigenic	Non-antigenic	Non-antigenic	Non-antigenic
Side-effect	Haemorrhagic[b]	Less haemorrhage?	Less haemorrhage?	Less haemorrhage?
Cost	Cheap	Expensive	Expensive	Expensive
Half-life	Longest half-life (25 min)	Shortest half-life (5 min)	Intermediate half-life (15 min)	Intermediate half-life (20 min)
		Better recanalization than streptokinase, but no better outcomes		


streptokinase
THROMBUS
Tissue plasminogen
activator (tPa), alteplase
PLASMINOGEN
PLASMIN
reteplase, tenecteplase
proteolytic degradation
products

Overview of management of myocardial infarction.


Acute coronary syndrome
Unpredictable symptoms lasting >½ h, unrelieved by rest/GTN
ECG or marker changes?
No
Yes
Marker changes only
ECG (ST-elevation) only
ECG (ST-elevation) + markers
Unstable angina
Non-ST elevation MI (NSTEMI)
ST elevation MI (STEMI)
Acute MI (AMI)
Antiplatelet
Aspirin + clopidogrel
Antithrombotic
LMW heparin
Anti-ischaemic
GTN
Oxygen
Beta-blocker (IV)
Symptomatic
Opioid
Antiplatelet
Aspirin + clopidogrel
? Glycoprotein II/III inhibitor
Antithrombotic
LMW heparin
Anti-ischaemic
GTN
Oxygen
Beta-blocker (IV)
Symptomatic
Opioid
Thrombolytics
e.g. streptokinase
Antiplatelet
Aspirin + clopidogrel
Antithrombotic
LMW heparin
Anti-ischaemic
GTN + IV nitrate
Oxygen
Beta-blocker (IV)
ACEI
Symptomatic
Opioid