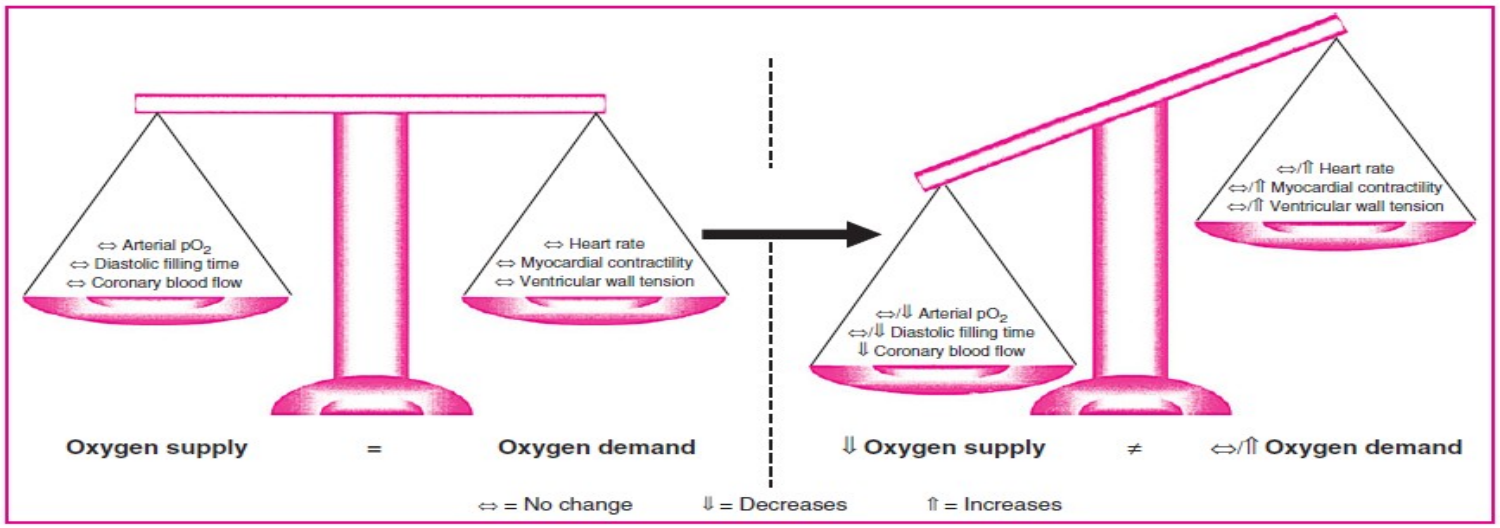
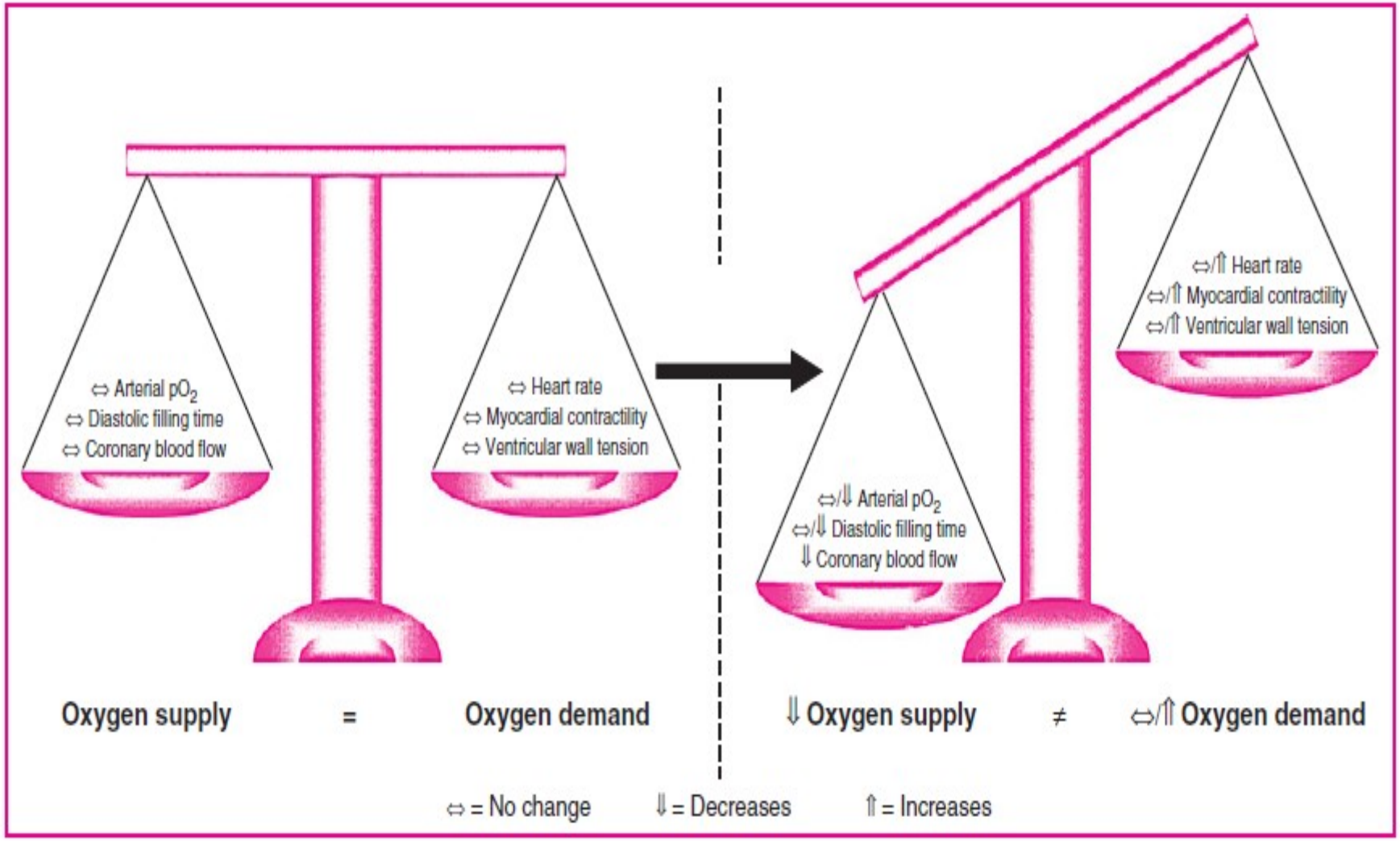
Ischemic Heart Disease



Ischemia

- Lack of oxygen due to inadequate perfusion
- Imbalance b/n supply and demand


⇔ Arterial pO_2
⇔ Diastolic filling time
⇔ Coronary blood flow
⇔ Heart rate
⇔ Myocardial contractility
⇔ Ventricular wall tension
⇔/⇓ Arterial pO_2
⇔/⇓ Diastolic filling time
⇓ Coronary blood flow
⇔/⇑ Heart rate
⇔/⇑ Myocardial contractility
⇔/⇑ Ventricular wall tension
Oxygen supply = Oxygen demand
⇓ Oxygen supply ≠ ⇔/⇑ Oxygen demand
⇔ = No change ⇓ = Decreases ⇑ = Increases

Classification

- IHD
  - Stable angina
  - Acute coronary syndrome
    - Unstable angina/ non ST elevation MI
    - ST elevation MI

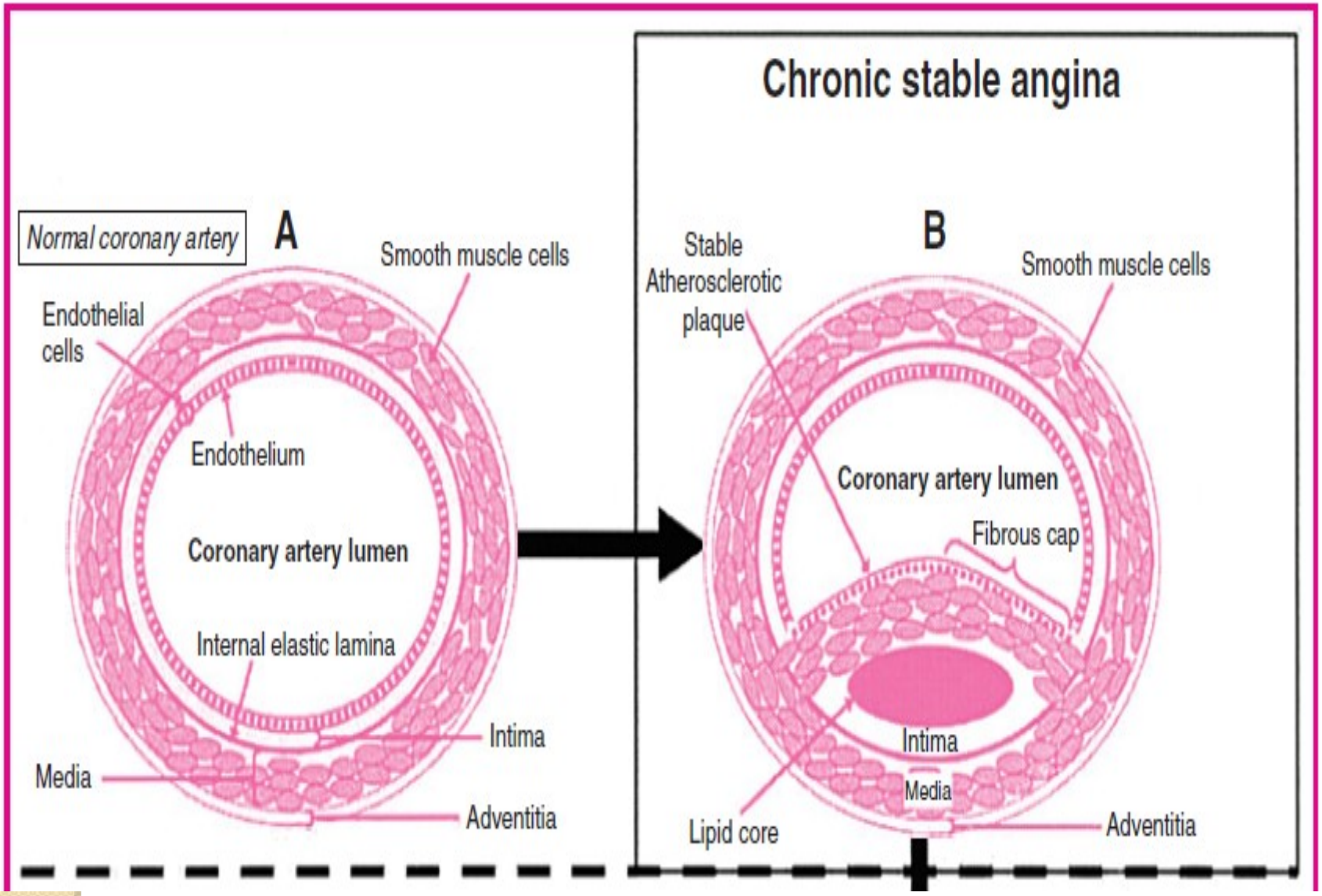
Risk factors

- Diabetes mellitus
- Obesity
- Insulin resistance
- Hypertension
- Dyslipedemia
- High fat and energy rich diet
- Smoking
- Sedentary life style
- Family history of premature(<45) death due to IHD
- Male gender

Stable angina pectoris

Pathophysiology

- Established atherosclerotic plaque that impedes coronary blood flow to the extent that myocardial oxygen supply can no longer meet increases in myocardial oxygen demand
- Over time, an established plaque may become unstable and rupture, leading to an ACS.


Chronic stable angina
Normal coronary artery
A
Smooth muscle cells
Endothelial cells
Endothelium
Coronary artery lumen
Internal elastic lamina
Intima
Media
Adventitia
B
Stable Atherosclerotic plaque
Smooth muscle cells
Coronary artery lumen
Fibrous cap
Intima
Media
Lipid core
Adventitia

Clinical Presentations

- Chest pain
- Heaviness, pressure, squeezing or choking
- Frank pain is rare
- Levine’s sign/clenched chest pain/Samuel A. levine’s (1891-1966)
- Crescendo-decrescendo in nature, lasts for 2-5 mins
- Ppted by excertion or emotion, unfamiliar tasks like meal or exposure to cold weather
- Relieved by rest or drugs

Physical examination

- Usually normal
- Look for other signs of atherosclerosis
  - Bruit/significant sound with in the body
  - Decreased arterial pulses
- Signs of heart failure

Lab

- RBS/FBS
- Lipid profile (LDL, HDL, TG, Cholesterol)
- U/A: albumin
- RFT
- CBC
- CXR
- ECG
  - 12 lead ECG normal in 50% of cases
  - Non specific ST-T changes

Cholesterol

Total <200 mg/dL

LDL 70–160 mg/dL

HDL >40 mg/dL for males and >50mg/dl for females

Triglycerides (fasting) <160 mg/dL

Treatment

- Identification & treatment of aggravating conditions
  - Anemia
  - Thyrotoxicosis
  - Aortic valve diseases
  - Obesity
  - Hypertension

Treatment

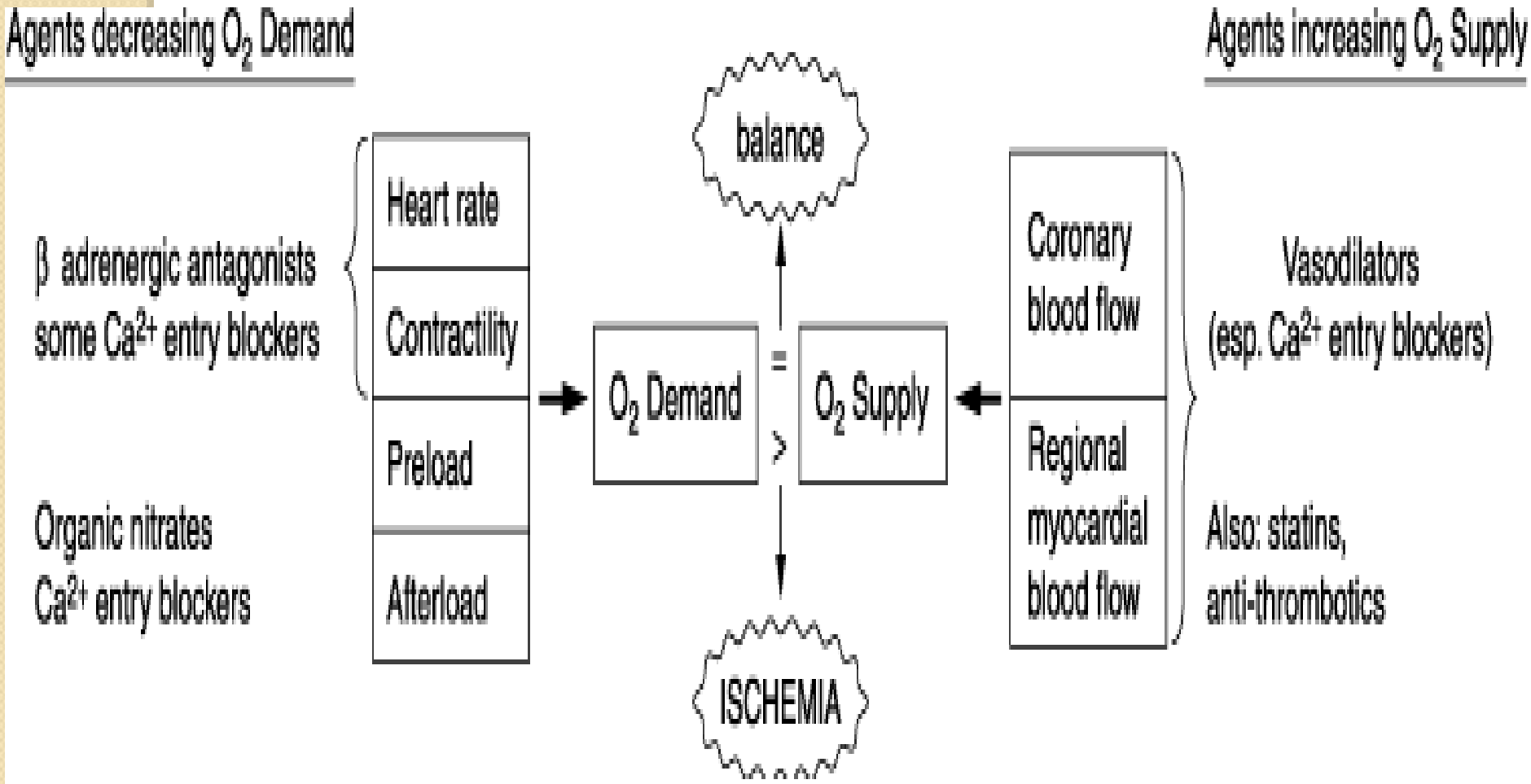
- Goals of therapy
- Prevent acute coronary syndromes and death
- Alleviate acute symptoms of myocardial ischemia
- Prevent recurrent symptoms of myocardial ischemia
- Avoid or minimize adverse treatment effects.

Treatment

- **General Approach to Treatment**

The primary strategies for preventing ACS and death are to:

- ✓ Modify cardiovascular risk factors
- ✓ Slow the progression of coronary atherosclerosis
- ✓ Stabilize existing atherosclerotic plaques.



Source: Brunton LL, Lazo JS, Parker KL: *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 11th Edition: http://www.accessmedicine.com

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Effect of Drug Therapy on Myocardial O_2 Demand

			LV Wall Tension	
	Heart Rate	Myocardial Contractility	Systolic Pressure	LV Volume
Nitrates	↓	0	↓	↓↓
β-Blockers	↓↓	↓	↓	↓
Nifedipine	↓	0 or ↓	↓↓	0 or ↓
Verapamil	↓	↓	↓	0 or ↓
Diltiazem	↓↓	0 or ↓	↓	0 or ↓

CaCBs and nitrates also may increase myocardial oxygen supply through coronary vasodilation. Diastolic function may be improved with verapamil, nifedipine, and perhaps, diltiazem. These effects may vary from those indicated in the table depending on individual patient baseline hemodynamics.

Lifestyle Modifications

- Smoking cessation,
- Dietary modifications(fruits, vegetables, grains, low-fat or non-fat dairy products, legumes, poultry, and lean meats, Fatty fish, such as salmon)
- Increased physical activity(Once drug therapy started, a low level of exercise for 20 to 30 minutes at a time, with increases in exercise duration and intensity as symptoms allow)
- weight loss(BMI >25kg/m2).

Drug therapy

- Statins
- Anti-platelet agents
- B-blockers
- Calcium channel blockers
- Nitrates
- ACE inhibitors/ARBs

Statins

- lovastatin, simvastatin, pravastatin, and atorvastatin.
- Potent lipid-lowering agents,
- Specifically lowering LDL cholesterol
- should be considered in all patients with IHD at high risk of major adverse cardiac events, regardless of baseline LDL cholesterol
- Non–lipid-lowering effects
- Provide additional benefit to patients with IHD.

Statins ---

- Shift LDL cholesterol particle size from predominantly small, dense, highly atherogenic particles to larger, less atherogenic particles.
- Improve endothelial function leading to more effective vasoactive response of the coronary arteries.
- Prevent or inhibit inflammation by lowering C-reactive protein and other inflammatory mediators thought to be involved in atherosclerosis.
- Possibly improving atherosclerotic plaque stability.

Antiplatelet Agents

- Aspirin 75-325 mg daily
- Clopidogrel 75 mg daily
- platelets adhere to the site of atherosclerotic plaque rupture
  - activated,
  - Aggregated
  - stimulate thrombus formation and ACS.
- aspirin should be considered for all patients without contraindications, particularly in patients with a history of MI.

Antiplatelet Agents

- If aspirin is contraindicated (e.g., aspirin allergy, active peptic ulcer disease, or active internal bleeding) or is not tolerated by the patient, other antiplatelet agents such as clopidogrel should be considered.
- Combination of aspirin and clopidogrel 75 mg daily for up to 9 months was more effective than aspirin alone in decreasing the risk of death, MI, and stroke.

ACE Inhibitors

- A recent meta-analysis of 22 clinical trials with ACE inhibitors in post-MI patients found that ACE inhibitors reduced 1-year mortality by 16% to 32% percent, and the mortality-reducing effects were sustained for up to 4 years.

ACE Inhibitors

If no C/I ;ACE inhibitors should be considered in IHD patients with

- ✓ Diabetes mellitus
- ✓ left ventricular dysfunction
- ✓ history of MI or
- ✓ Any combination of these

TABLE 4–5. Doses of ACE inhibitors and Angiotensin Receptor Blockers Indicated in Ischemic Heart Disease (IHD).

Drug	Indications	Usual Dosage in IHD
Angiotensin-Converting Enzyme Inhibitors		
Captopril	HTN, HF, post-MI, diabetic nephropathy	6.25–50 mg 3 times daily
Enalapril	HTN, HF	2.5–40 mg daily in 1–2 divided doses
Fosinopril	HTN, HF	10–80 mg daily in 1–2 divided doses
Lisinopril	HTN, HF, post-MI	2.5–40 mg daily
Perindopril	HTN, IHD	4–8 mg daily
Quinapril	HTN, HF, post-MI	5–20 mg twice daily
Ramipril	HTN, high-risk for IHD, HF, post-MI	2.5–10 mg daily in 1–2 divided doses
Trandolapril	HTN, HF, post-MI	1–4 mg daily
Angiotensin Receptor Blockers		
Candesartan	HTN, HF	4–32 mg daily
Valsartan	HTN, HF, post-MI	80–320 mg daily in 1–2 divided doses

HF, heart failure; HTN, hypertension; MI, myocardial infarction.

Nitroglycerin to Relieve Acute Symptoms

- Short-acting nitrates are first-line treatment to terminate acute episodes of angina.
- All patients with a history of angina should have sublingual nitroglycerin tablets or spray to relieve acute ischemic symptoms.

Nitroglycerin

- Nitrates
- ✓ Primarily cause venodilation
- ✓ Reductions in preload.
- ✓ Decrease in ventricular volume and wall tension
- ✓ Reduction in myocardial oxygen demand.
- ✓ At higher doses, nitrates may also cause arterial dilation and reduce after load.

Nitroglycerin

- Dilating the epicardial coronary arteries and collateral vessels,
- ✓ Nitrates increase myocardial oxygen supply
- ✓ Nitrates also relief vasospasm
- At the onset of an angina attack, a 0.3 to 0.4mg dose of nitroglycerin (tablet or spray) should be administered sublingually, and repeated every 5 minutes until symptoms resolve.

Long-Acting Nitrates

- Isosorbide dinitrate, in a sublingual form, has a longer half-life with anti-anginal effects lasting up to 2 hours.

- For patients with more frequent attacks, long-acting nitrates is recommended.
- The major limitation of nitrate therapy is the development of tolerance with continuous use.

Long-Acting Nitrates

- The loss of anti-anginal effects may occur within the first 24 hours of continuous nitrate therapy.

✓ Depletion of the sulfhydryl groups necessary for the conversion of nitrates to nitric oxide, and

✓ Generation of free radicals that degrade nitric oxide.

mainly contribute to the development of tolerance.

- Allow a daily nitrate-free interval of at least 8 to 12 hours possibly during the night.

Long-Acting Nitrates

- Monotherapy with nitrates for the prevention of ischemia be avoided for.
- Secondary to nitrate-induced venodilation, reflex increases in sympathetic activity and heart rate, with resultant increases in myocardial oxygen demand.
- Patients are unprotected from ischemia during the nitrate-free interval.

Long-Acting Nitrates

- Treatment with long-acting nitrates should be added to baseline therapy with either a b-blocker or calcium channel blocker or a combination of the two.
- β-Blockers attenuate the increase in sympathetic tone and heart rate that occurs during nitrate therapy
- In turn, nitrates attenuate the increase in wall tension during β-blocker therapy.

Nitrate Products

Product	Onset (min)	Duration	Initial Dose
Nitroglycerin			
IV	1 – 2	3 – 5 min	5 mcg/min
Sublingual/lingual	1 – 3	30 – 60 min	0.3 mg
Oral	40	3 – 6 h	2.5 – 9 mg tid
Ointment	20 – 60	2 – 8 h	0.5 – 1 in
Patch	40 – 60	> 8 h	1 patch
Erythritol tetranitrate	5 – 30	4 – 6 h	5 – 10 mg tid
Pentaerythritol tetranitrate	30	4 – 8 h	10 – 20 mg tid
Isosorbide dinitrate			
Sublingual/chewable	2 – 5	1 – 2 h	2.5 – 5 mg tid
Oral	20 – 40	4 – 6 h	5 – 20 mg tid
Isosorbide mononitrate	30 – 60	6 – 8 h	20 mg daily, bid[a]

[a] Product dependent

Beta-Blockers

- Stimulation of the β1-receptors in the heart increases heart rate and cardiac contractility
- β-Blockers decrease myocardial oxygen demand by
- ✓ Antagonizing β1-Stimulation
- ✓ Lowering blood pressure and ventricular wall tension.
- β-Blockers do not improve myocardial oxygen supply.

Beta-Blockers

- β-blockers may increase ventricular wall tension.
- However, the net effect of β-blockade is usually a reduction in myocardial oxygen demand
- β-Blockers with intrinsic sympathomimetic activity (ISA)
- ✓ Produce lesser reductions in myocardial oxygen demand and should be avoided in patients with IHD.
- Other β-blockers appear equally effective at controlling symptoms of angina.

Beta-Blockers

- Consider frequency of dosing and drug cost while selecting a particular drug.
- The β-blocker dose is commonly titrated to achieve the following:

✓ Resting heart rate between 50 and 60 beats per minute

✓ Maximum heart rate with exercise of 100 beats per minute or less or 20 beats per minute above the resting heart rate.

Beta-Blockers

Contraindications

- ✓ Severe bradycardia (heart rate less than 50 beats per minute)
- ✓ atrioventricular (AV) conduction defects in the absence of a pacemaker.
- ❖ Caution:-combination with other agents that depress AV conduction (e.g., digoxin, verapamil, and diltiazem) = increased risk for bradycardia and heart block.

Beta-Blockers

Relative contraindications

- ✓ Asthma
- ✓ Bronchospastic disease
- ✓ Severe depression
- ✓ Peripheral vascular disease.

Beta-Blockers

β1-Selective blockers are preferred in patients with

- Asthma or chronic obstructive pulmonary
- Diabetes Mellitus
- selectivity is dose dependent
- β1-selective agents may induce bronchospasm and slow recovery from hypoglycemia in insulin dependent diabetes at higher doses.
- β-blockers initiated in very low doses with slow up-titration to avoid worsening heart failure symptoms.
  - ejection fraction less than 35%.

Beta-Blockers

Abrupt β-blocker withdrawal may increase the

frequency and severity of angina, possibly because of

- ✓ increased receptor sensitivity to catecholamines after longterm β-blockade.
- ✓ If the decision is made to stop β-blocker therapy, the dose should be tapered over several days to weeks to avoid exacerbating angina.

Calcium Channel Blockers

- Inhibition of calcium entry into the vascular smooth muscle cells leads to systemic vasodilation and reductions in afterload.
- Inhibition of calcium entry into the cardiac cells leads to reductions in cardiac contractility.

✓ Reduction in wall tension

✓ Reduction in Cardiac contractility

✓ Reduction in myocardial oxygen demand

- The nondihydropyridine CCBs further decrease myocardial oxygen demand.

Calcium Channel Blockers

- Due to their negative **chronotropic effects**
  - **Verapamil** and diltiazem are generally more effective anti-anginal agents than the dihydropyridine CCBs.

- In addition to decreasing myocardial oxygen demand
  - All CCBs increase myocardial oxygen supply.

Calcium Channel Blockers

Calcium channel blockers are recommended as initial treatment in IHD when b-blockers are contraindicated or not tolerated.

In addition, CCBs may be used in combination with b-blockers when initial treatment is unsuccessful.

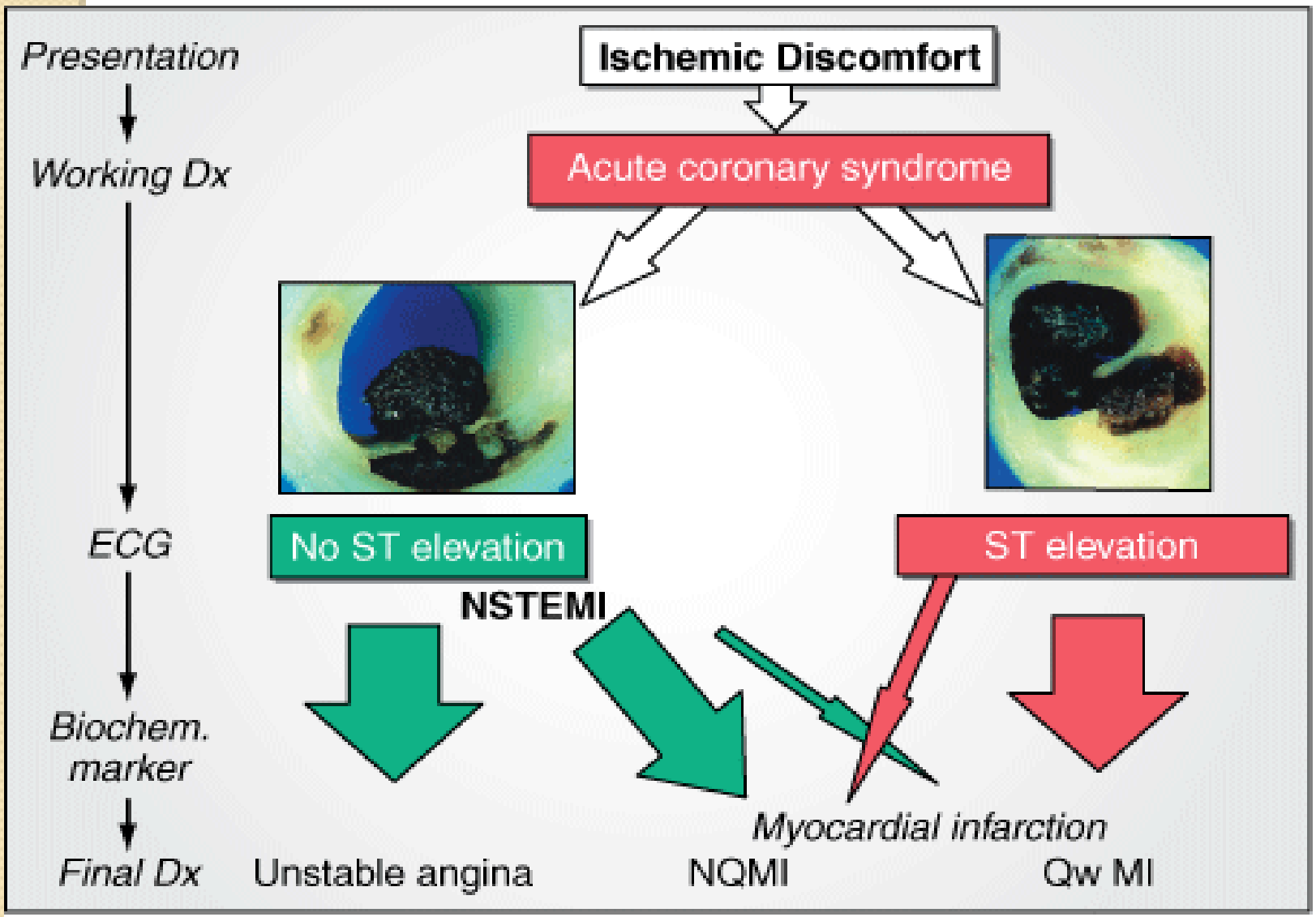
- A long-acting dihydropyridine CCB is preferred.
- Amlodipine and felodipine possess less negative inotropic effects and appear to be safe in patients with left ventricular systolic dysfunction.

Calcium Channel Blockers

- Finally, there is some evidence that short acting calcium channel blockers (particularly short acting nifedipine and nicardipine) may increase the risk of cardiovascular events
- Therefore, short-acting agents should be avoided in the management of IHD.

Acute coronary syndromes`1

- Acute coronary syndromes (ACS), including unstable angina (UA) and myocardial infarction (MI), are a form of coronary heart disease (CHD) that comprises the most common cause of CVD death.
- The cause of an acute coronary syndrome is the rupture of an atherosclerotic plaque with subsequent platelet adherence, activation, and aggregation, and the activation of the clotting cascade. Ultimately, a clot forms composed of fibrin and platelets.



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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Unstable angina & Non-ST elevation MI

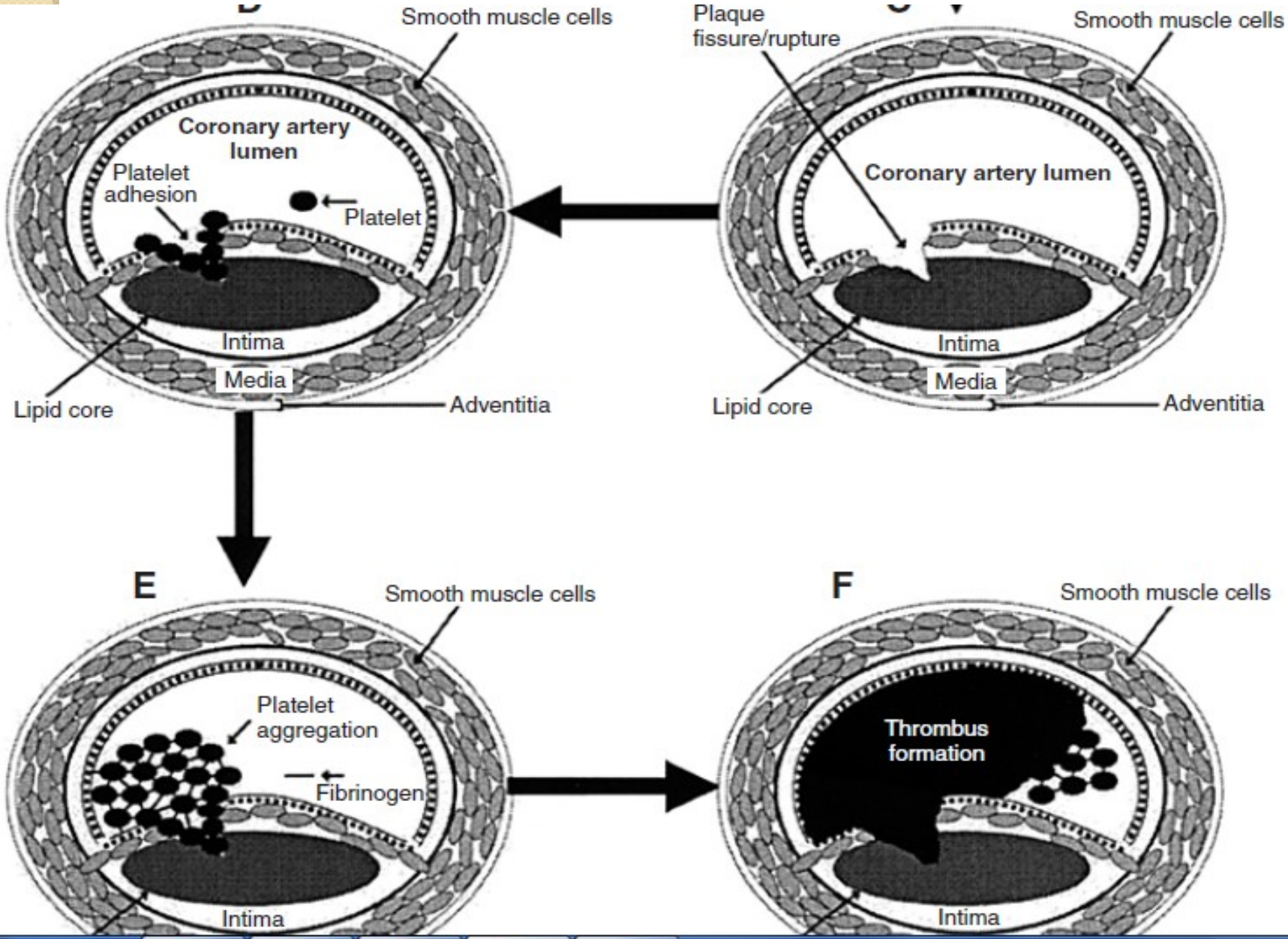
- Unstable angina
  - Angina with at least one of the three features
    - It occurs at rest, lasts >10 min
    - Severe & of new onset, with in the past 4-6 wks
    - Occurs with a crescendo pattern
- NSTEMI
  - UA + elevated cardiac biomarkers

Pathophysiology

- In contrast to stable angina:
  - An ACS results primarily from diminished myocardial blood flow secondary to:
    - An occlusive or partially occlusive coronary artery thrombus.
- Following plaque rupture, a clot (a partially occlusive or completely occlusive thrombus), forms on top of the ruptured plaque.

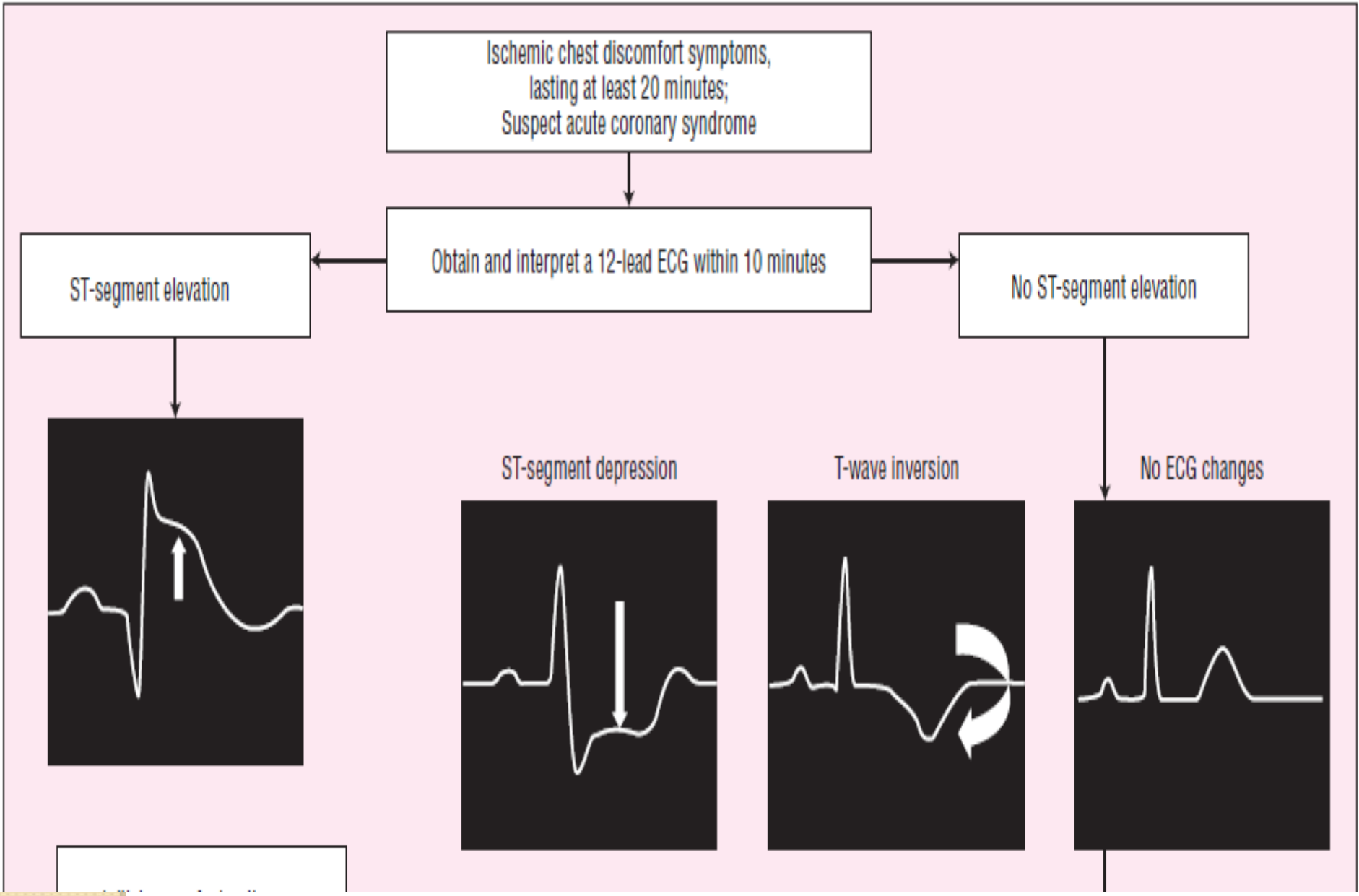
ACS, Pathophysiology

- Ventricular remodeling is a process that occurs following an MI.
- It is characterized by left ventricular dilation and reduced pumping function of the left ventricle leading to cardiac failure.
- Heart failure represents one of the principal causes of mortality and morbidity following MI
- Preventing ventricular remodeling is an important therapeutic goal.


Smooth muscle cells
Coronary artery lumen
Platelet adhesion
Platelet
Intima
Media
Lipid core
Adventitia
Plaque fissure/rupture
Smooth muscle cells
Coronary artery lumen
Intima
Media
Lipid core
Adventitia
E
Smooth muscle cells
Platelet aggregation
Fibrinogen
Intima
F
Smooth muscle cells
Thrombus formation
Intima

LAB

- ECG
  - ST segment depression
  - Transient ST-segment elevation ± T-wave inversion
- Cardiac biomarkers
- Creatine kinase
- CK is composed of M and B subunits, which are further divided into three isoenzymes: MM, BB, and MB.
  - The CK-MM isoenzyme is found predominantly in skeletal muscle
  - The CKBB isoenzyme in the brain
  - The CK-MB isoenzyme in the myocardium
- CK-MB
- Troponin_


Ischemic chest discomfort symptoms,
lasting at least 20 minutes;
Suspect acute coronary syndrome
Obtain and interpret a 12-lead ECG within 10 minutes
ST-segment elevation
No ST-segment elevation
ST-segment depression
T-wave inversion
No ECG changes

Comparison of ACSs

	Unstable Angina	NSTEMI	STEMI
Symptoms present	+	+	+
ECG changes	None	ST segment depression, T wave inversion, or no changes	ST segment elevation
Biochemical marker	No changes	Inc.Troponins & CK MB	Inc.Troponins & CK MB

ST-Segment elevation MI

- 30 day mortality rate is 30 %, ½ of it occurs before the patient reaches the hospital
- Pathophysiology
  - Acute plaque rupture→ platelet adhesion→ activation of coagulation cascade→ thrombus formation with total occlusion of arterial lumen

Clinical feature

- Pain
  - Anginal, severe, prolonged (>30 mins)
  - Could be absent in diabetes
- P/E
  - Pallor, diaphoresis/sweating, anxious patient
  - PR/BP (↑/↓)
  - S3, S4
  - Fever could be present

Lab

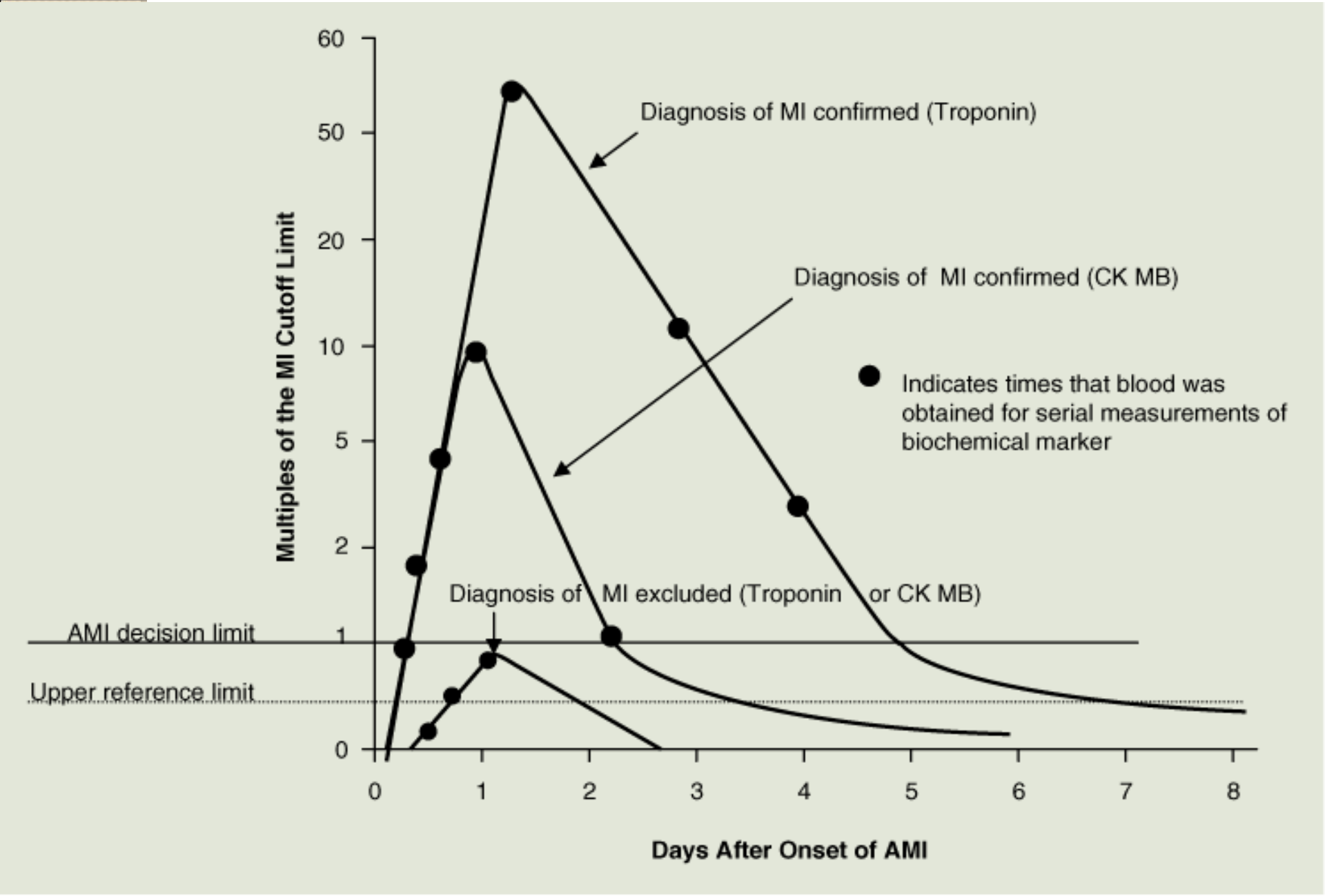
- ECG
- Biomarkers
  - CK-MB: rises within 4-8 hrs & returns to normal by 48-72 hrs
  - cTnT & cTnI: rises within 4-8 hrs but remains elevated for 7-10 days after AMI.
- Echocardiography
  - Wall motion abnormality
  - EF estimation
  - Thrombus (LV)
  - V infarction
  - Pericardial effusion

Biomarkers

CK-MB 0–12 units/L

cTnI <0.03 ng/mL

Troponin is specific than CK-MB for myocardial damage, elevated sooner and remains elevated longer than CK-MB. cTnI >2.0 suggests acute myocardial injury.



DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: *Pharmacotherapy: A pathophysiologic Approach,* 7th Edition: Http://www.accesspharmacy.com

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Acute Coronary Syndromes TREATMENT

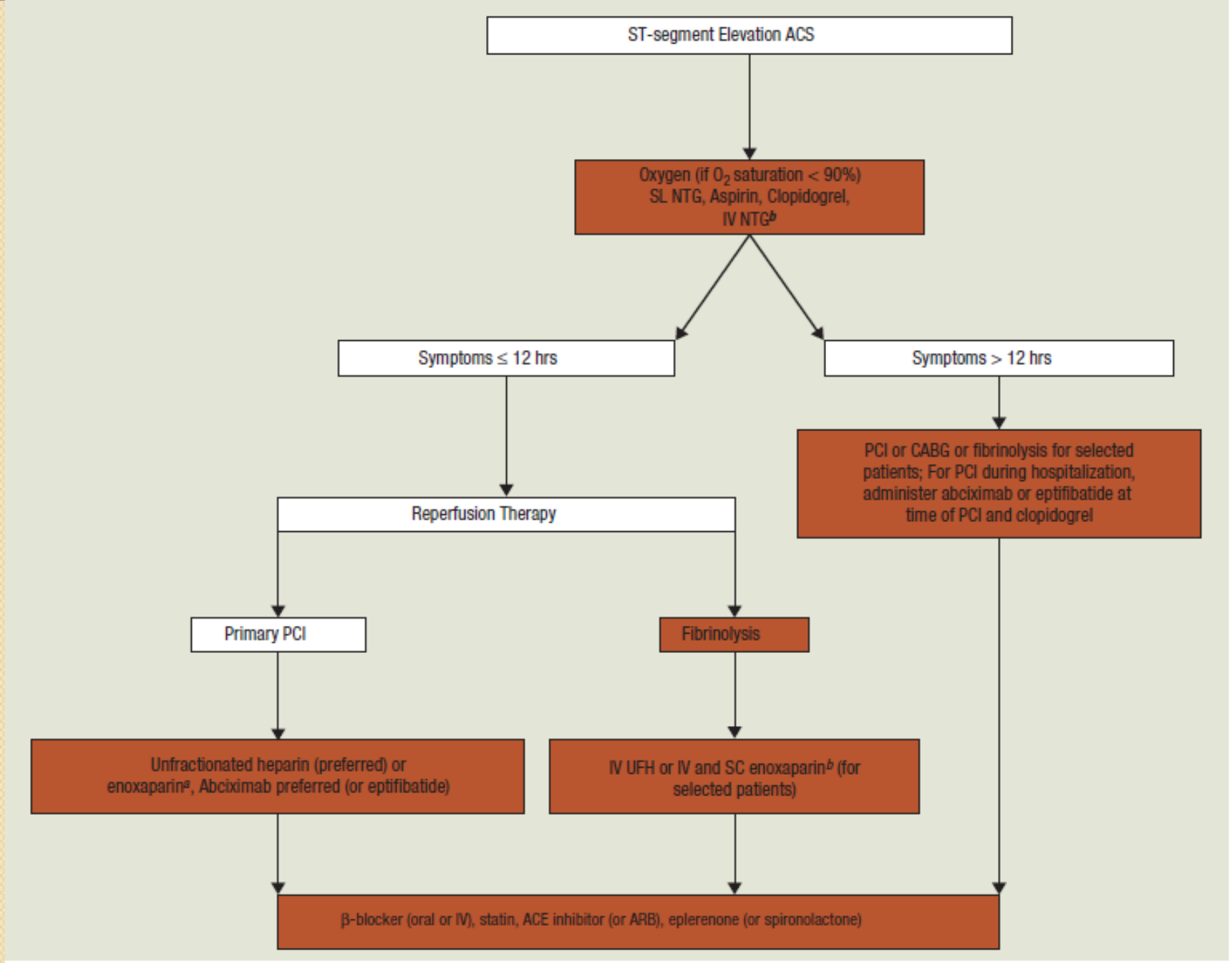
DESIRED OUTCOMES

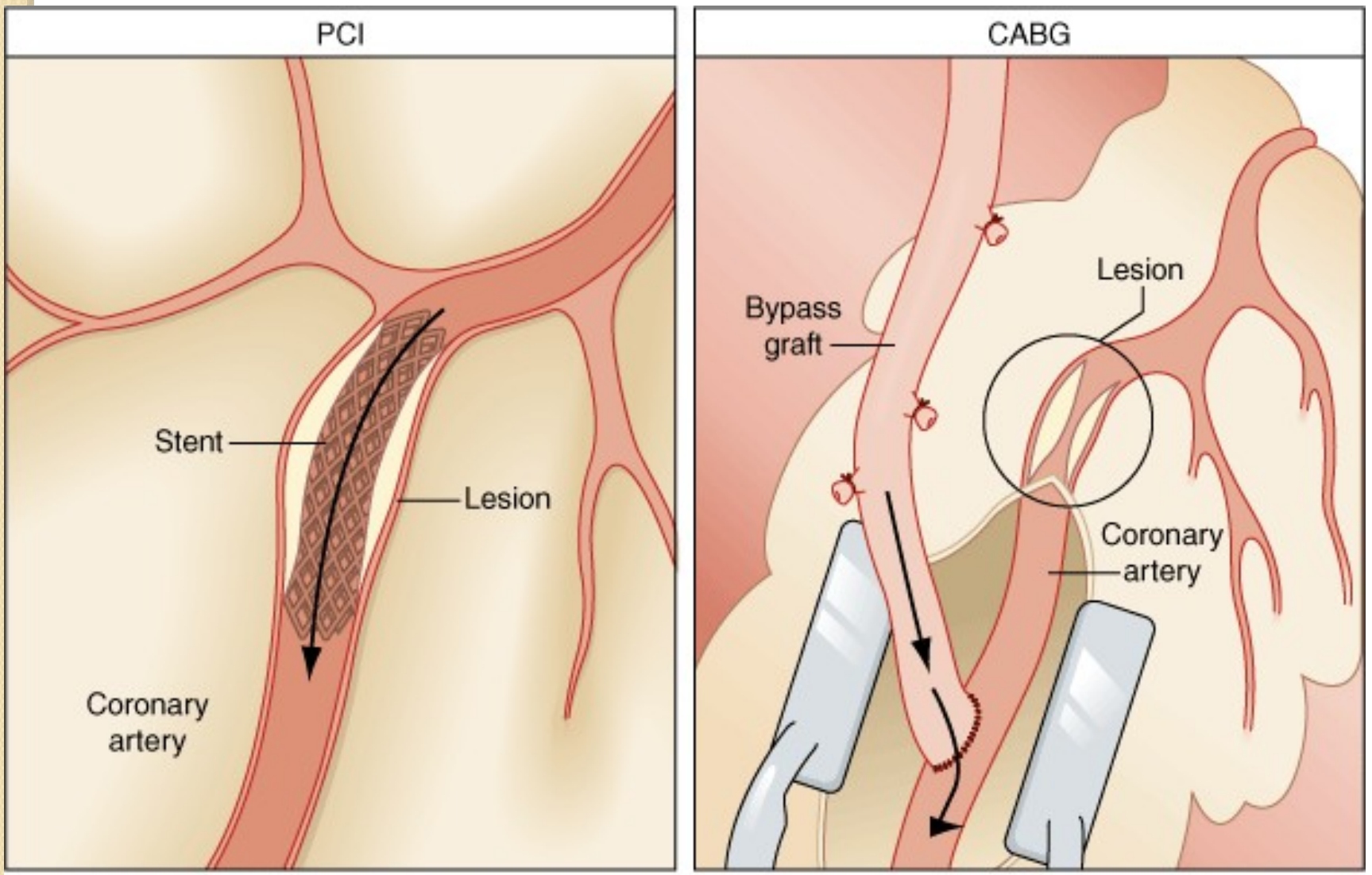
The short-term goals of treatment for the ACS patient are as follows:

- 1. Early restoration of blood flow to the infarct-related artery to prevent infarct expansion (in the case of MI) or prevent complete occlusion and MI (in unstable angina)
- 2. Prevention of death and other complications
- 3. Prevention of coronary artery reocclusion
- 4. Relief of ischemic chest discomfort

EARLY PHARMACOTHERAPY FOR STE ACS

- Early pharmacotherapy of STE ACS should include:
  - Intranasal oxygen (if oxygen saturation is <90%)
  - Sublingual (SL) nitroglycerin (NTG)
  - Aspirin
  - β-blocker
  - Unfractionated heparin (UFH)
  - Fibrinolysis in eligible candidates.
- CABG, coronary artery bypass grafting
- PCI, percutaneous coronary intervention


ST-segment Elevation ACS
Oxygen (if O_2 saturation < 90%)
SL NTG, Aspirin, Clopidogrel,
IV NTG[b]
Symptoms ≤ 12 hrs
Symptoms > 12 hrs
PCI or CABG or fibrinolysis for selected patients; For PCI during hospitalization, administer abciximab or eptifibatide at time of PCI and clopidogrel
Reperfusion Therapy
Primary PCI
Fibrinolysis
Unfractionated heparin (preferred) or enoxaparin[a], Abciximab preferred (or eptifibatide)
IV UFH or IV and SC enoxaparin[b] (for selected patients)
β-blocker (oral or IV), statin, ACE inhibitor (or ARB), eplerenone (or spironolactone)



Stent addresses the existing lesion but not future lesions.

Bypass grafting addresses the existing lesion and also future culprit lesions.

Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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Acute Coronary Syndromes TREATMENT

Morphine is administered to patients with refractory angina as an analgesic and a venodilator that lowers preload.

- These agents should be administered early, while the patient is still in the emergency department.

- An ACE inhibitor should be started within 24 hours of presentation, particularly in patients with LVEF ≤40%

Fibrinolytic Therapy

- Administration of a fibrinolytic agent is indicated in patients with STE ACS who present to the hospital within 12 hours of onset of chest discomfort and have at least 1 mm of STE .

- Fibrinolytic therapy also should be considered in patients presenting within 12–24 hours of onset of chest discomfort and have persistent symptoms of ischemia and at least 1 mm of STE in two or more contiguous leads.

Fibrinolytic Therapy

- The mortality benefit of fibrinolysis is highest with early administration and diminishes after 12 hours.
- Fibrinolytic therapy is preferred over primary PCI in patients who present within 3 hours of symptom onset.
- It is not necessary to obtain the results of biochemical markers before initiating fibrinolytic therapy.

TABLE 18-5 Indications and Contraindications to Fibrinolytic Therapy According to ACC/AHA Guidelines for Management of Patients with ST-Segment Elevation Myocardial Infarction

Indications

1. Ischemic chest discomfort at least 20 minutes in duration but ≤12 hours since symptom onset
   and
   ST-segment elevation of at least 1 mm in height in ≤2 contiguous leads or
   New or presumed new left bundle-branch block
2. Ongoing ischemic chest discomfort at least 20 minutes in duration 12–24 hours since symptom onset
   and
   ST-segment elevation of at least 1 mm in height in ≥2 contiguous leads

Absolute contraindications

Active internal bleeding (not including menses)
Previous intracranial hemorrhage at any time; ischemic stroke within 3 months
Known intracranial neoplasm
Known structural vascular lesion (e.g., arteriovenous malformation)
Suspected aortic dissection
Significant closed head or facial trauma within 3 months

TABLE 18-5 Indications and Contraindications to Fibrinolytic Therapy According to ACC/AHA Guidelines for Management of Patients with ST-Segment Elevation Myocardial Infarction

Relative contraindications

Severe, uncontrolled hypertension on presentation (blood pressure >180/110 mm Hg)

History of prior ischemic stroke >3 months, dementia, or known intracranial pathology not covered above under absolute contraindications

Current use of anticoagulants

Known bleeding diathesis

Traumatic or prolonged (>10 minutes) CPR or major surgery (<3 weeks)

Noncompressible vascular puncture (e.g., a recent liver biopsy or carotid artery puncture)

Recent (within 2–4 weeks) internal bleeding

For streptokinase administration, previous streptokinase use (>5 days) or prior allergic reactions

Pregnancy

Active peptic ulcer

History of severe, chronic poorly controlled hypertension

Fibrinolytic Therapy

- Eligible patients should be treated as soon as possible, but preferably within 30 minutes from the time they present to the emergency department, with one of the following regimens:

✓ **Alteplase: 15-mg IV bolus followed by 0.75-mg/kg infusion (maximum** 50 mg) over 30 minutes, followed by 0.5-mg/kg infusion (maximum 35 mg) over 60 minutes (maximum dose 100 mg).

Aspirin

- Early aspirin administration to all patients without contraindications within the first 24 hours of hospital admission is a quality care indicator.
- In patients undergoing PCI, aspirin prevents acute thrombotic occlusion during the procedure.
- In patients experiencing an ACS, an initial dose equal to greater than 160 mg nonenteric aspirin is necessary to achieve rapid platelet inhibition.

Aspirin

- This first dose can be chewed in order to achieve high blood concentrations and rapid platelet inhibition.

- Current data suggest that although an initial dose of 160 to 325 mg is required, long-term therapy with doses of 75 to 150 mg daily are as effective as higher doses and, therefore, a daily maintenance dose of 75 to 160 mg is recommended.

Aspirin

- although the risk of major bleeding, particularly gastrointestinal bleeding, appears to be reduced by using lower doses of aspirin,

- low-dose aspirin, taken chronically, is not free of adverse effects.
- Patients should be counseled on the potential risk of bleeding.

- Aspirin therapy should be continued indefinitely

Anticoagulants

- UFH, administered as an IV bolus followed by a continuous infusion, is a first-line anticoagulant for treatment of patients with STE ACS, both for medical therapy and for patients undergoing PCI.

- Anticoagulant therapy should be initiated in the emergency department and continued for at least 48 hours in selected patients who will be bridged over to receive chronic warfarin anticoagulation following acute MI

Anticoagulants

- If a patient undergoes PCI, UFH is discontinue immediately after the procedure.

For STEMI, administer 60 units/kg IV bolus (maximum 4000 units) followed by a constant IV infusion at 12 units/kg/h (maximum 1000 units/h)

For NSTE ACS, administer 60–70 units/kg IV bolus (maximum 5000 units) followed by a constant IV infusion at 12–15 units/kg/h (maximum 1000 units/h)

Titrated to maintain an aPTT of 1.5–2.5 times control for NSTE ACS and 50–70 seconds for STEMI

First aPTT should be measured at 4–6 hours for NSTE ACS and STE ACS in patients not treated with fibrinolytics

First aPTT should be measured at 3 hours in patients with STE ACS who are treated with fibrinolytics

Anticoagulants

- The dose of UFH infusion is adjusted frequently to a target activated partial thromboplastin time (aPTT). (20-70se)
- When coadministered with a fibrinolytic, aPTTs above the target range are associated with an increased rate of bleeding
- Whereas aPTTs below the target range are associated with increased mortality and reinfarction

Anticoagulants

- Other beneficial effects of anticoagulation in patients with ACS are prevention of cardioembolic stroke and venous thromboembolism.

- Rates of reinfarction are higher if UFH is not given in combination with fibrin-selective agents.

Nitrates

- Nitrates promote the release of nitric oxide from the endothelium, which results in venous and arterial vasodilation at higher doses.
- Venodilation lowers preload and myocardial oxygen demand.
- Arterial vasodilation relieves coronary artery vasospasm, dilating coronary arteries to improve myocardial blood flow and oxygenation.

Nitrates

- One SL NTG tablet (0.4 mg) should be administered every 5 minutes for up to three doses to relieve myocardial ischemia.

- If patients have previously been prescribed SL NTG and ischemic chest discomfort persists for more than 5 minutes after the first dose,
- The patient should be instructed to contact emergency medical services before self-administering subsequent doses in order to activate emergency care sooner

Nitrates

- ACE inhibitors or β-blockers, should not be withheld for nitrates use because the mortality benefit of nitrates is unproven.

β-Blockers

- A β-blocker should be administered early in the care of patients with STE ACS and continued indefinitely.
- Early administration of a β- blocker within the first 24 hours of hospitalization in patients lacking a contraindication is a quality care indicator.

β-Blockers

- β1- blockade produces a reduction in heart rate, myocardial contractility, and blood pressure, decreasing myocardial oxygen demand.
- The reduction in heart rate increases diastolic time, thus improving ventricular filling and coronary artery perfusion
- β-blockers reduce the risk for recurrent ischemic, infarct size, risk of reinfarction, and occurrence of ventricular arrhythmias in the hours and days following MI

β-Blockers

- Although initiating IV followed by oral β-blockers early in the course of STEMI was associated with a lower risk of reinfarction or ventricular fibrillation,

- There may be an early risk of cardiogenic shock, especially in patients presenting with pulmonary congestion or systolic blood pressure <120 mm Hg.

- The use of β- blockers, particularly when administered IV, should be limited to patients who are hemodynamically stable and who do not demonstrate any signs or symptoms of decompensated heart failure.

β-Blockers

- β-blockers is not appropriate for patients who present with decompensated heart failure,
- But initiation of β-blockers can be attempted before hospital discharge in most patients following treatment of acute heart failure.

- β-blockers with ISA may increase Myocardial oxygen demand, should be avoided.

Calcium Channel Blockers

- Administration of CCBs in the setting of STE ACS is reserved for patients who have contraindications to β-blockers and is given for relief of ischemic symptoms.

- In patients prescribed CCBs for treatment of hypertension who are not receiving β-blockers and who do not have a contraindication to β-blockers, the CCB should be discontinued and a β-blocker initiated.

Calcium Channel Blockers

- Variant (or Prinzmetal) angina caused by coronary vasospasm
- Calcium channel blockers and/or NTG generally are considered the agents of choice in these patients because they can reverse coronary spasm by inducing smooth muscle relaxation in the coronary arteries.
- β-blockers generally should be avoided in these patients unless they have uncontrolled sinus tachycardia (>100 beats/min)

Calcium Channel Blockers

- β-blockers actually may worsen vasospasm through an unopposed β2-blocking effect on the smooth muscle cells

SECONDARY PREVENTION FOLLOWING MI

- The long-term goals following MI are as follow:

1. Control modifiable CHD risk factors
2. Prevent development of systolic heart failure
3. Prevent recurrent MI and stroke
4. Prevent death, including sudden cardiac death

SECONDARY PREVENTION FOLLOWING MI

- Pharmacotherapy that has been proven to decrease mortality, heart failure, reinfarction, or stroke should be initiated prior to hospital discharge for secondary prevention.

- Following MI from either STE or NSTE ACS, patients should receive indefinite treatment with aspirin, a β-blocker, and an ACE inhibitor.

SECONDARY PREVENTION FOLLOWING MI

- Selected patients also should be treated with long-term warfarin anticoagulation.

- For all ACS patients, treatment and control of modifiable risk factors, such as hypertension, dyslipidemia, and diabetes mellitus, are essential.

Aspirin

- Aspirin decreases the risk of death, recurrent MI, and stroke following MI.
- An aspirin prescription at hospital discharge is a quality care indicator in MI patients
- Aspirin should be given indefinitely to all patients, or clopidogrel to patients with a contraindication to aspirin

Aspirin

- The risk of major bleeding from chronic aspirin therapy is approximately 2% and is dose related.

- After an initial dose of 325 mg, chronic therapy with aspirin should be 75 to 81 mg once daily.

- Other gastrointestinal disturbances, including dyspepsia and nausea, are infrequent when low-dose aspirin is used

Anticoagulants

- Anticoagulation Warfarin should be considered in selected patients following an ACS,
  - Patients with an LV thrombus
  - Patients demonstrating extensive ventricular wall-motion abnormalities on cardiac echocardiogram
  - Patients with a history of thromboembolic disease or chronic atrial fibrillation.

Anticoagulants

- Use of low, fixed-dose warfarin (mean INR 1.4) combined with aspirin or low-intensity anticoagulation (mean INR 1.8) monotherapy:
  - Provided no significant clinical benefit compared with Aspirin monotherapy
  - But significantly increased the risk of major bleeding.
- Therefore, warfarin therapy targeted to INR <2 cannot be recommended for secondary prevention of CHD events following MI.

β-Blockers, Nitrates, and Calcium Channel Blockers

- Current treatment guidelines recommend that, following an ACS, patients should receive a β-blocker indefinitely

- Because the benefit from β-blockers appears to be maintained for at least 6 years following an MI, it is recommended that all patients receive β-blockers indefinitely in the absence of contraindications or intolerance

β-*Blockers, Nitrates, and Calcium Channel Blockers*

- β-blockers with intrinsic sympathomimetic actvity(*Acebutolol , Pindolol)* are generally not recommended.

- β-blockers should be avoided in patients with decompensated heart failure

- Initiation of β-blockers prior to hospital discharge is safe in these patients once heart failure symptoms have resolved

β-Blockers, Nitrates, and Calcium Channel Blockers

- In C/n to a β- blocker, a calcium channel blocker can be used to prevent angin symptoms but should not be used routinely in the absence of such symptoms

ACE Inhibitors

- The benefit of ACE inhibitors in patients with MI most likely derives from their ability to prevent cardiac remodeling.

ACE Inhibitors

- The largest reduction in mortality is observed for patients with LV dysfunction (low LVEF) or heart failure symptoms.

- Because the benefits of ACE inhibitor administration have been documented for up to 12 years following therapy for 2 to 4 years post- MI in patients with LV dysfunction
  - Aadministration should continue indefinitely.

EVALUATION OF THERAPEUTIC OUTCOMES

Monitoring parameters for efficacy of therapy include:

- Relief of ischemic discomfort;
- Return of ECG changes to baseline; and
- Absence or resolution of heart failure signs.