Acute Coronary Syndrome

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Outline

- **What** Are the ACS Types?
- **How** ACS Occurs?
- **How** Do You Approach to CP?
- **How** Do You Diagnose ACS?
- **What** is the Management of ACS?

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What are the types of ACS?

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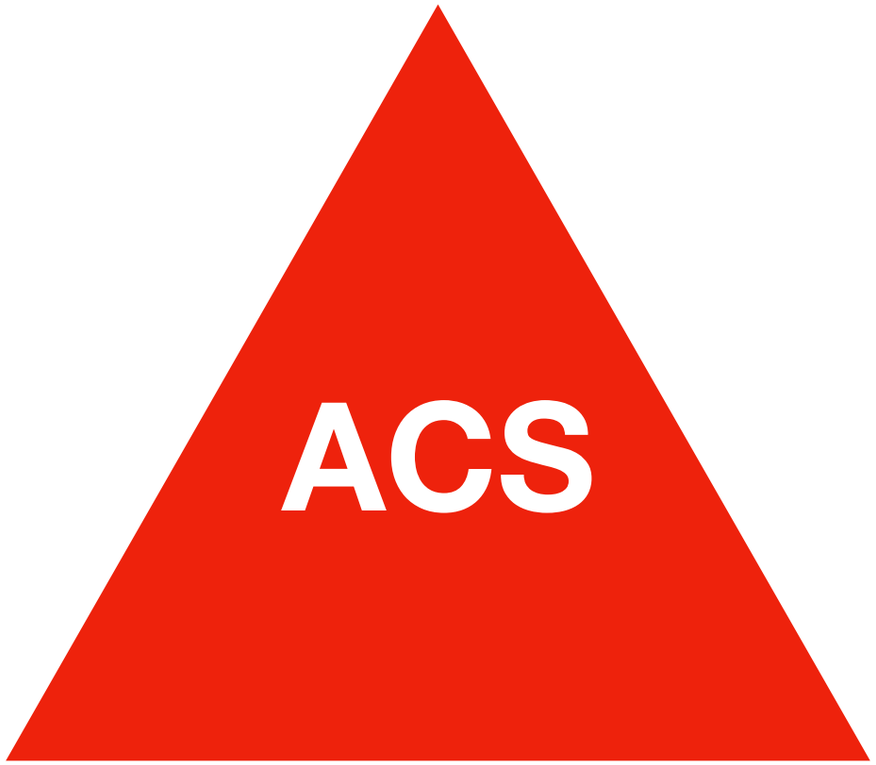
Symptoms



EKG

Troponin

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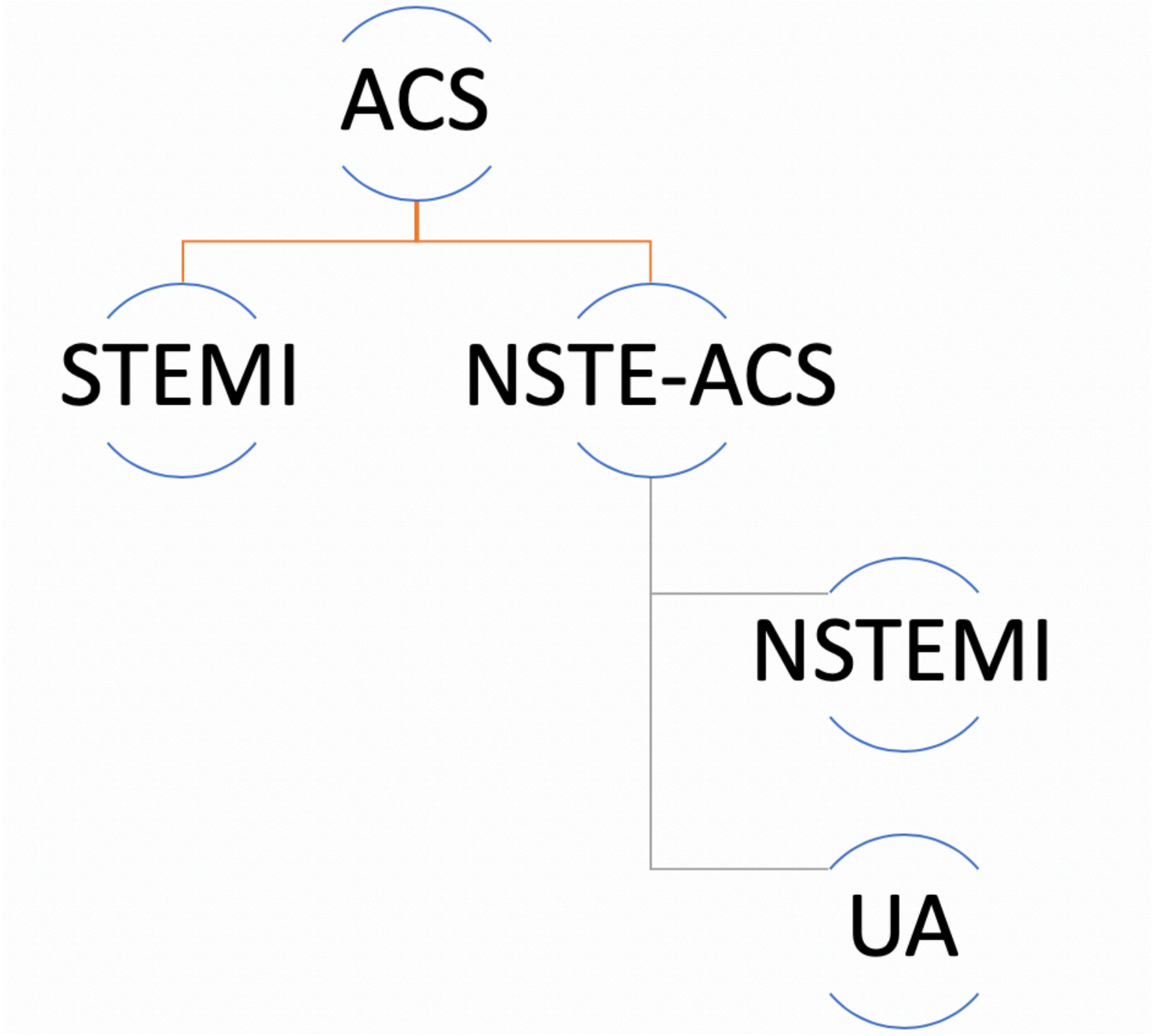

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How ACS Happens?

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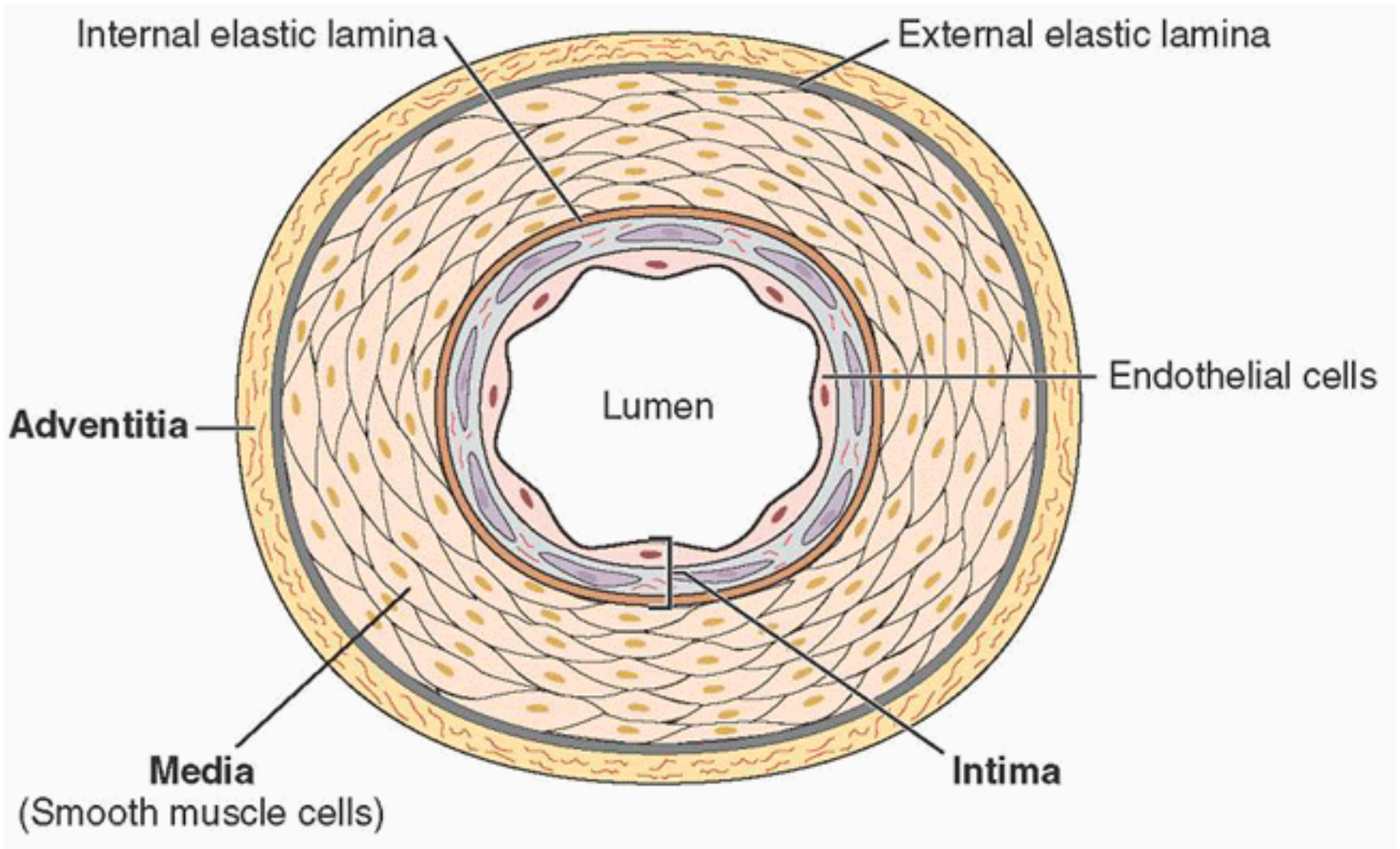

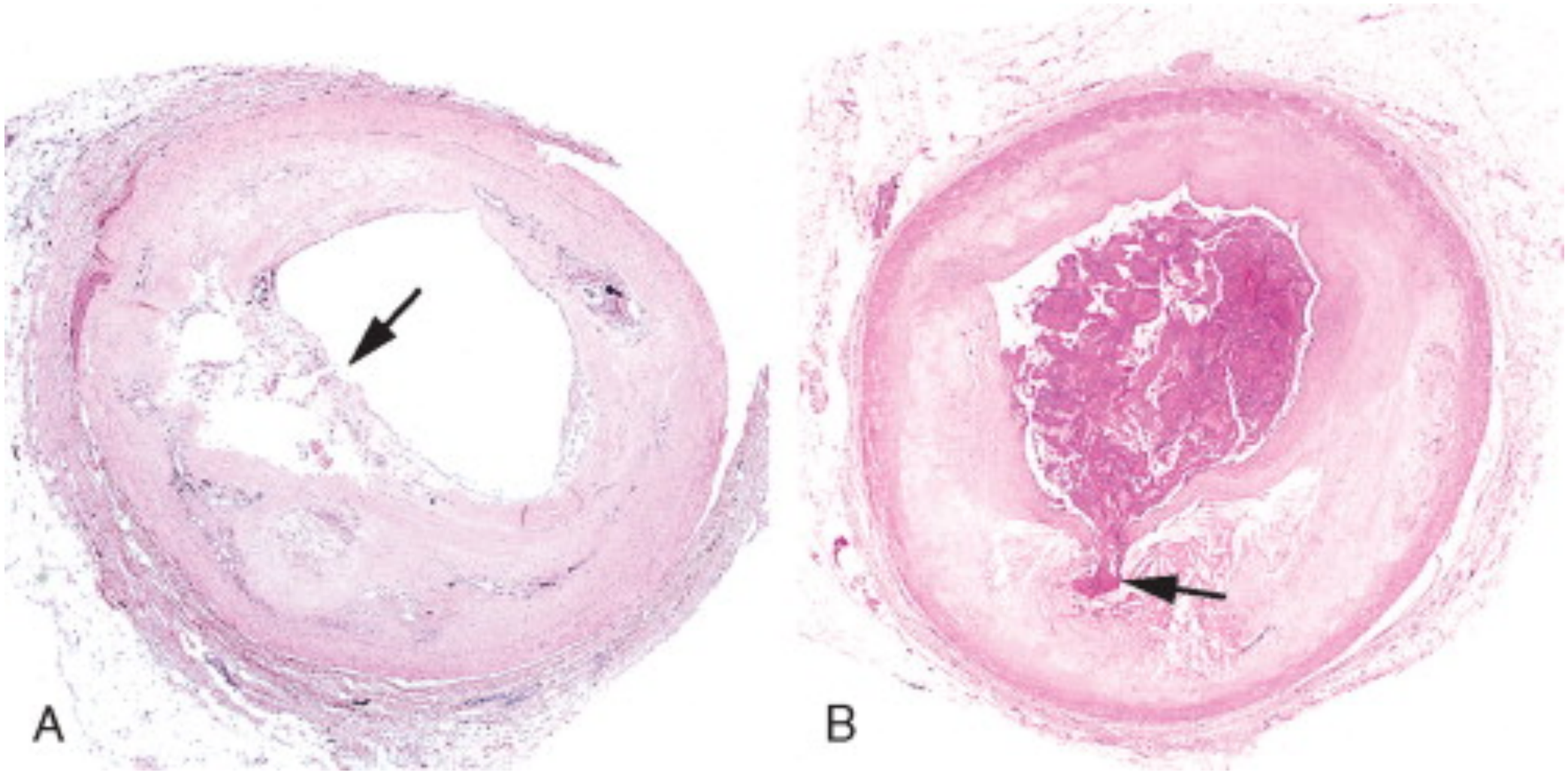

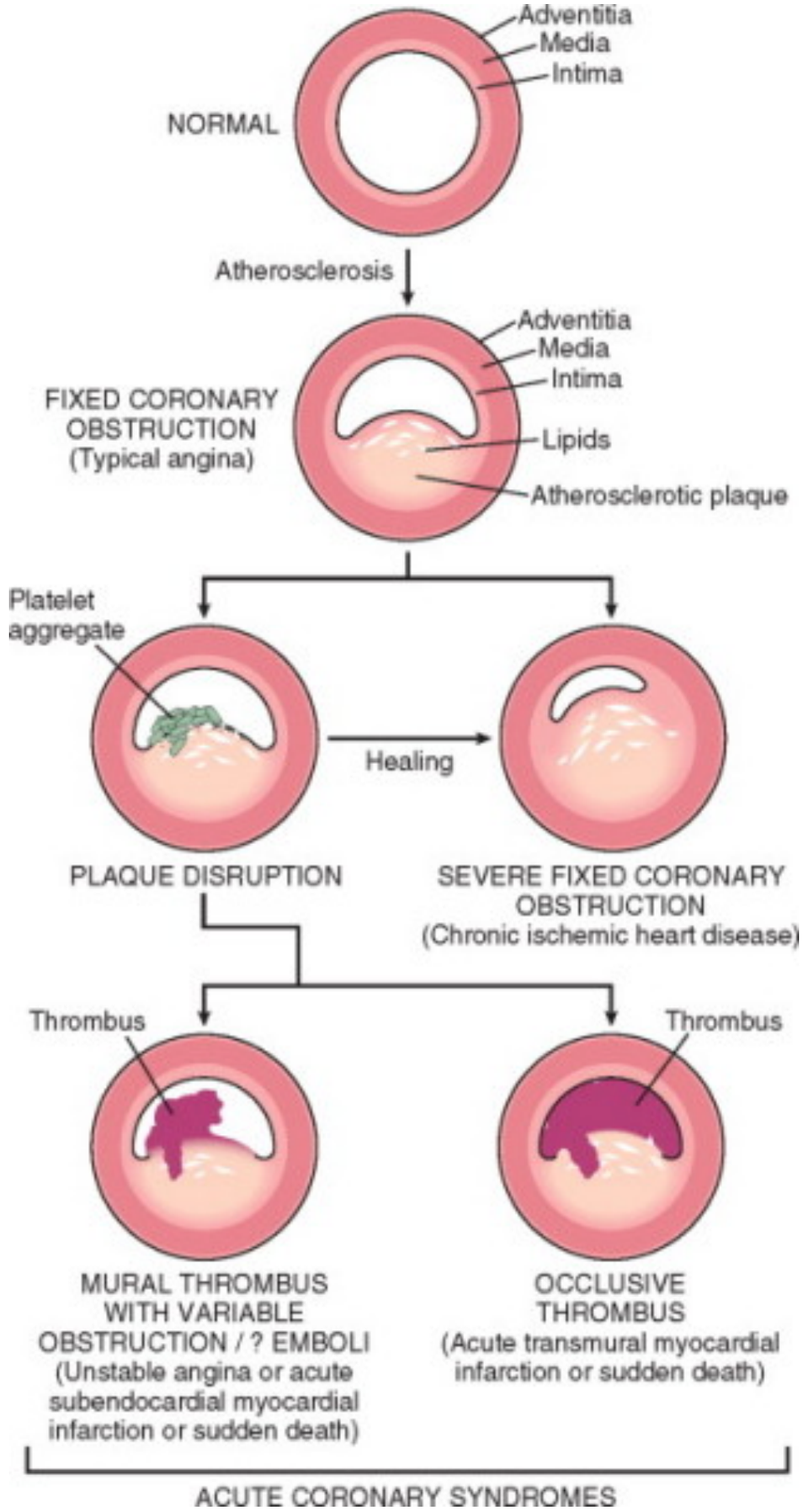

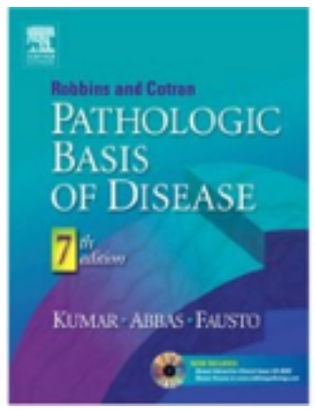

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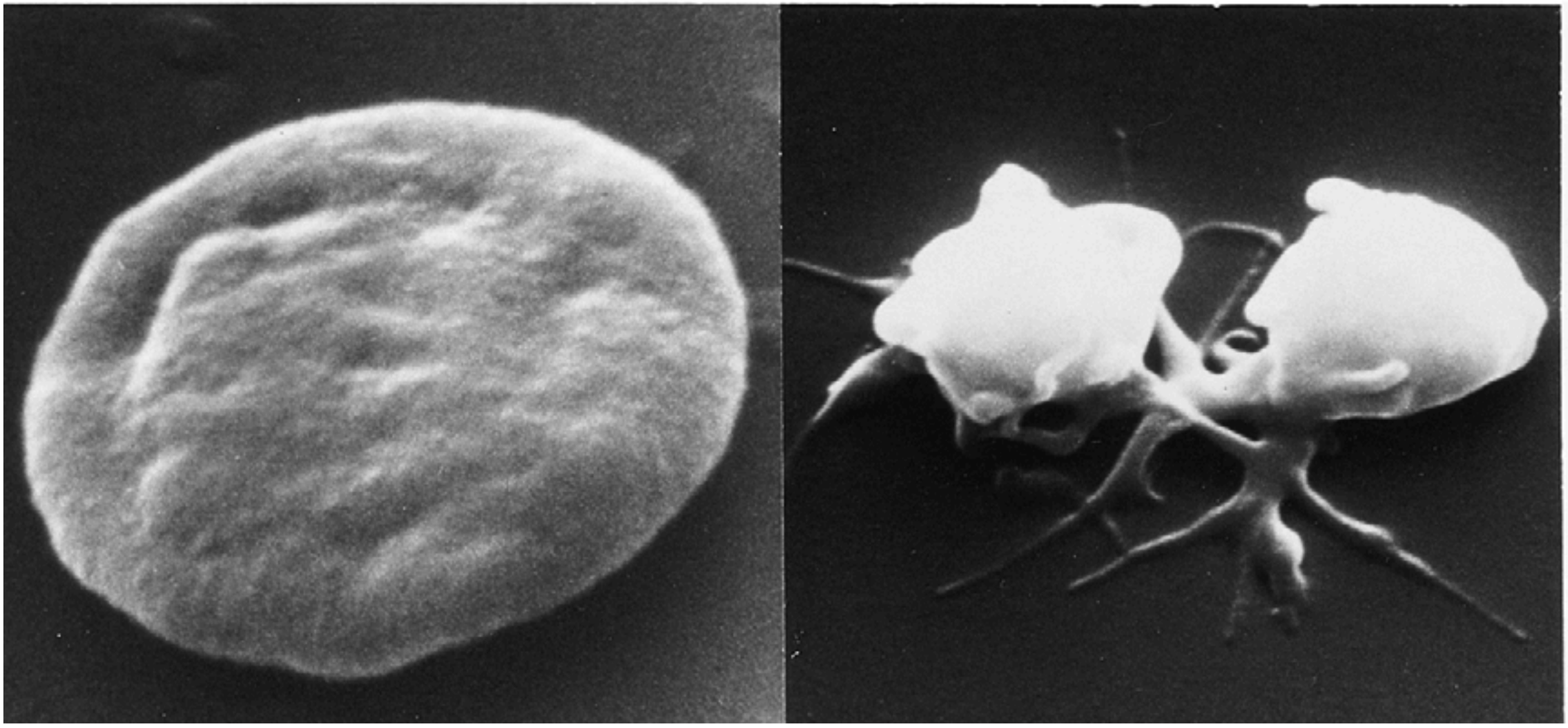


Platelet Aggregation

GP alpha IIb/Beta III

Platelet Adhesion

GP IIb/IIIa

Fibrinogen

GP IIb/IIIa

GP Ib/IX/V

vWF

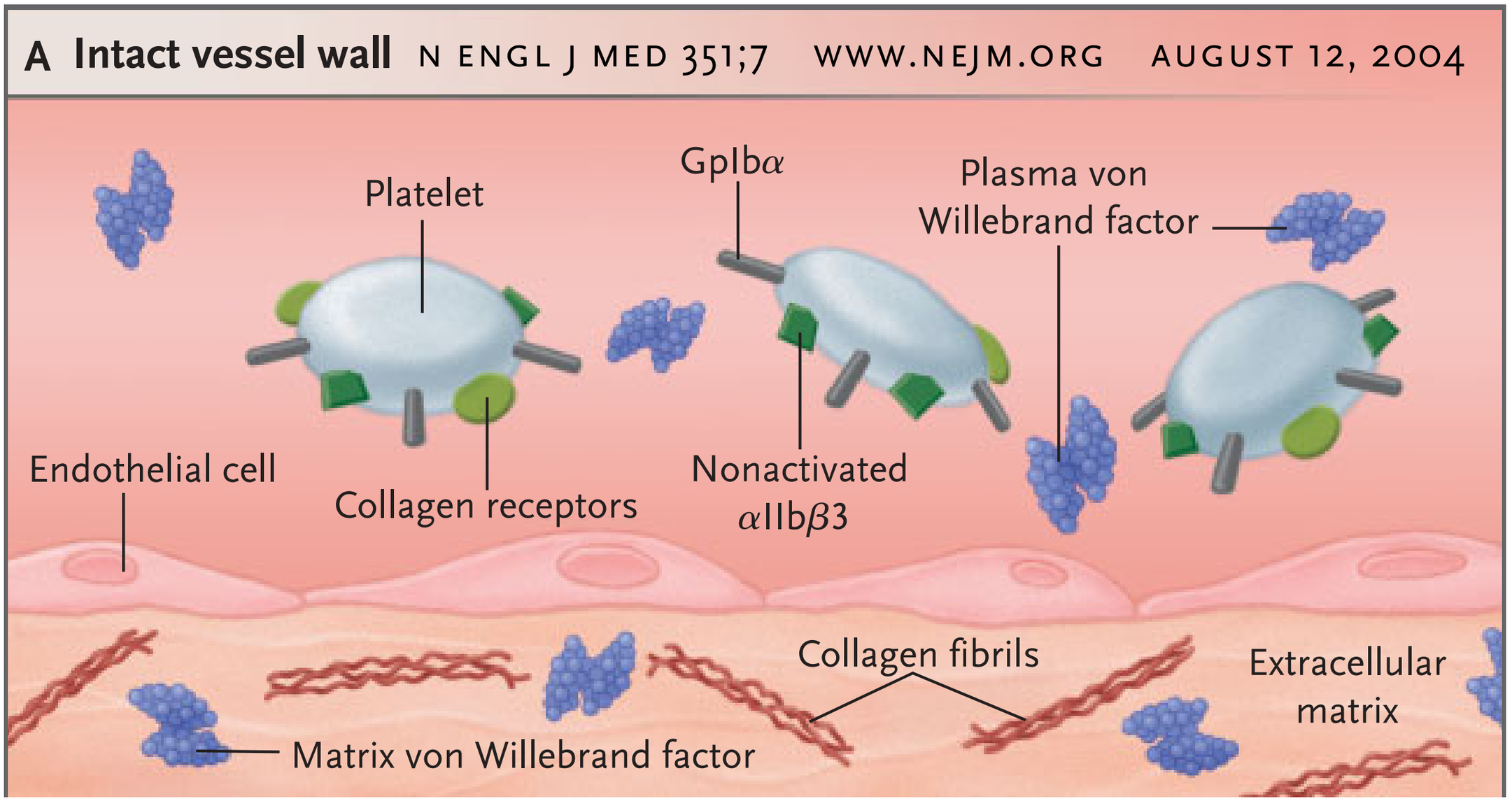
Collagen

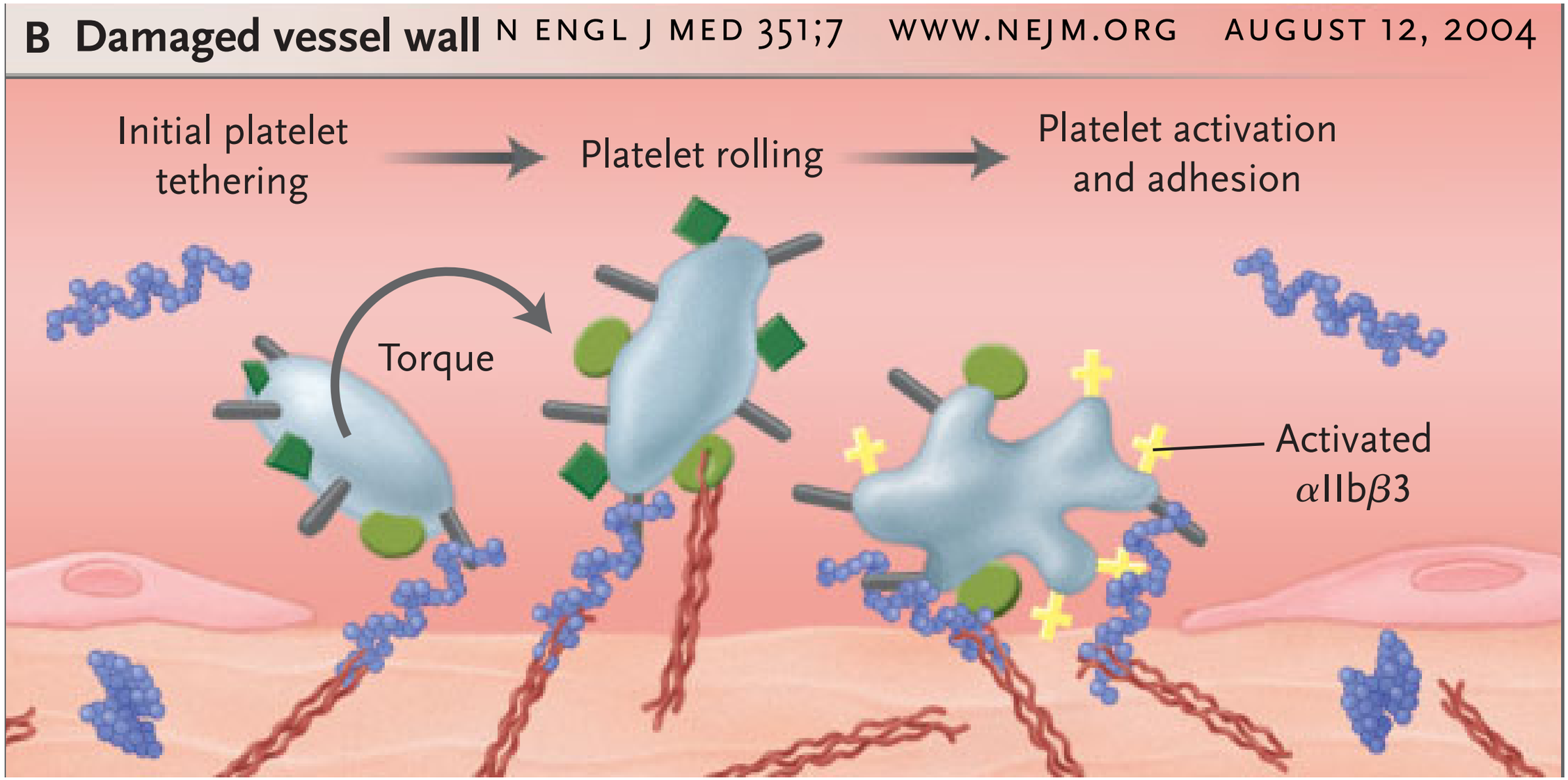
Endothelial Plaque Disruption

Coagulation cascade & Fibrin clot formation

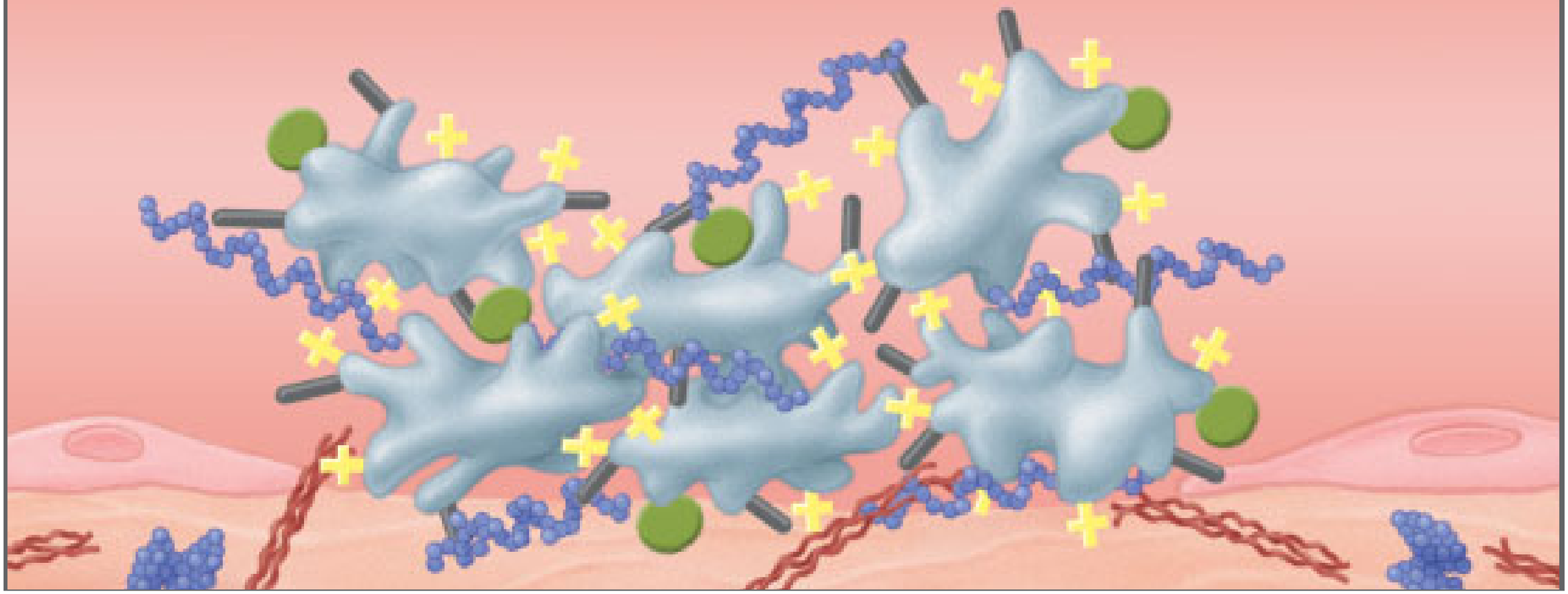
Factor VII

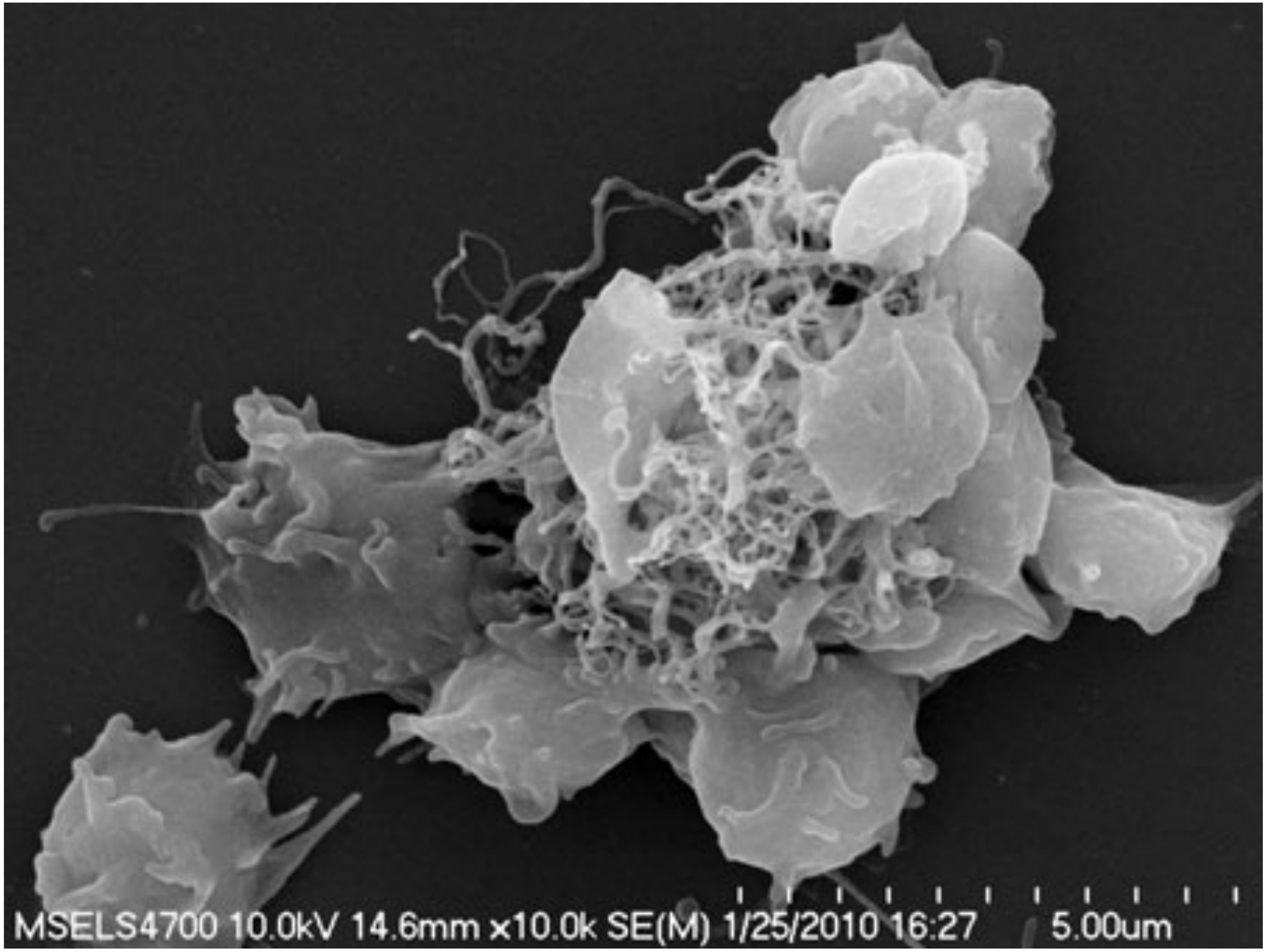
Tissue Factor





C Platelet-plug formation





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How To Approach to CP?

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S&S of ACS

1. Characteristic pain	• Severe, persistent, typically substernal
2. Sympathetic effect	• Diaphoresis • Cool and clammy skin
3. Parasympathetic (vagal effect)	• Nausea, vomiting • Weakness
4. Inflammatory response	• Mild fever
5. Cardiac findings	• S_4 (and S_3 if systolic dysfunction present) gallop • Dyskinetic bulge (in anterior wall MI) • Systolic murmur (if mitral regurgitation or VSD)
6. Other	• Pulmonary rales (if heart failure present) • Jugular venous distention (if heart failure or right ventricular MI)

What Are the Differential Diagnoses of Chest Pain in ER?

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Life-Threatening Causes of CP

CARDIAC	NON-CARDIAC
Acute coronary syndrome substernal, radiating to arm, dyspnea on exertion, diaphoresis, worse with exertion	**Acute pulmonary embolism** sudden onset, pleuritic, dyspnea, tachycardia, tachypnea, hypoxia, evidence of lower extremity deep venous thrombosis
Aortic dissection sudden onset, severe, tearing, radiating to the back (associated with neurologic deficits, AR), unequal arm BP >20 mmHg, wide mediastinum	**Tension pneumothorax** sudden onset, sharp, pleuritic, decreased breath sounds and chest excursion, hyperresonant percussion, hypoxia
Acute pericarditis & tamponade sudden onset, pleuritic, better with sitting forward, radiating to the back, pericardial rub, ± tamponade (distant heart sounds, hypotension, JVD)	**Esophageal rupture/perforation** severe, increase with swallowing, fever, abdominal pain, history of endoscopy, foreign body ingestion, trauma, vomiting

When To Call Angina Stable Vs. Unstable Symptoms?

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Unstable Anginal Symptoms

- New onset with normal activities
- Crescendo #/severity/NTG/duration
- Rest

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What is the Difference Between Typical and Atypical Angina?

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Stable Anginal Symptoms

- Substernal chest pain or discomfort
- Provoked by exertion or emotional stress
- Relieved by rest or nitroglycerine

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Bonus Q: What Symptoms Increase or Decrease the Likelihood of ACS?

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CP & LR of ACS

INCREASE THE LIKELIHOOD	LR (95 % CI)	DECREASE THE LIKELIHOOD	LR (95 % CI)
Radiates to the right arm or shoulder	4.7 (1.9–12)	Pleuritic	0.2 (0.1–0.3)
Radiates to both arms or shoulders	4.1 (2.5–6.5)	Sharp	0.3 (0.2–0.5)
Precipitated by exertion	2.4 (1.5–3.8)	Positional	0.3 (0.2–0.5)
Radiates to the left arm	2.3 (1.7–3.1)	Reproducible with palpation	0.3 (0.2–0.4)
Associated with diaphoresis	2.0 (1.9–2.2)		

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Value and Limitations of Chest Pain History in the Evaluation of Patients With Suspected Acute Coronary Syndromes

Clifford J. Swap, MD, MS
John T. Nagurney, MD, MPH

JAMA. 2005;294:2623-2629

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Box. Risk Stratification for Acute Myocardial Infarction and Acute Coronary Syndrome According to Components of the Chest Pain History

Low Risk

Pain that is pleuritic, positional, or reproducible with palpation or is described as stabbing[2,3,24,25,29]

Probable Low Risk

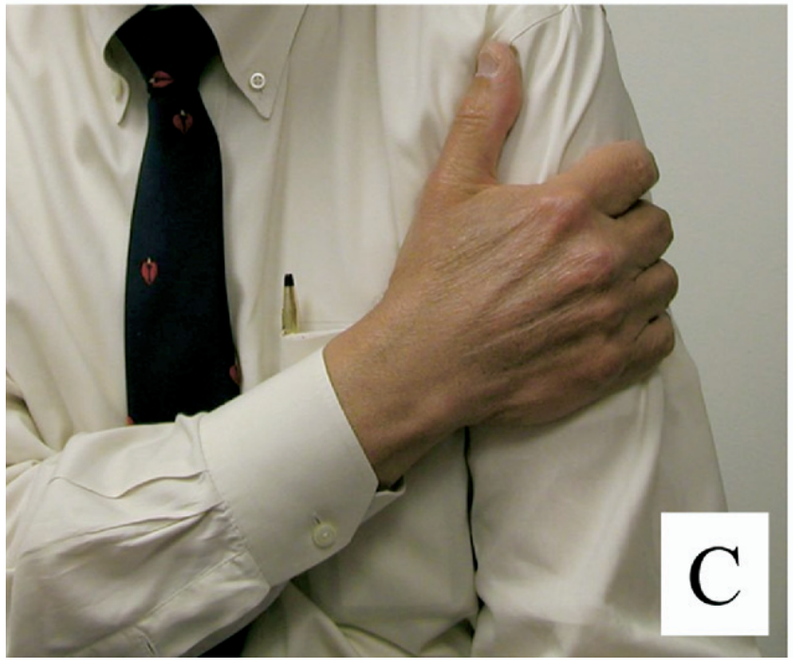
Pain not related to exertion or that occurs in a small inframammary area of the chest wall[14,31,42]

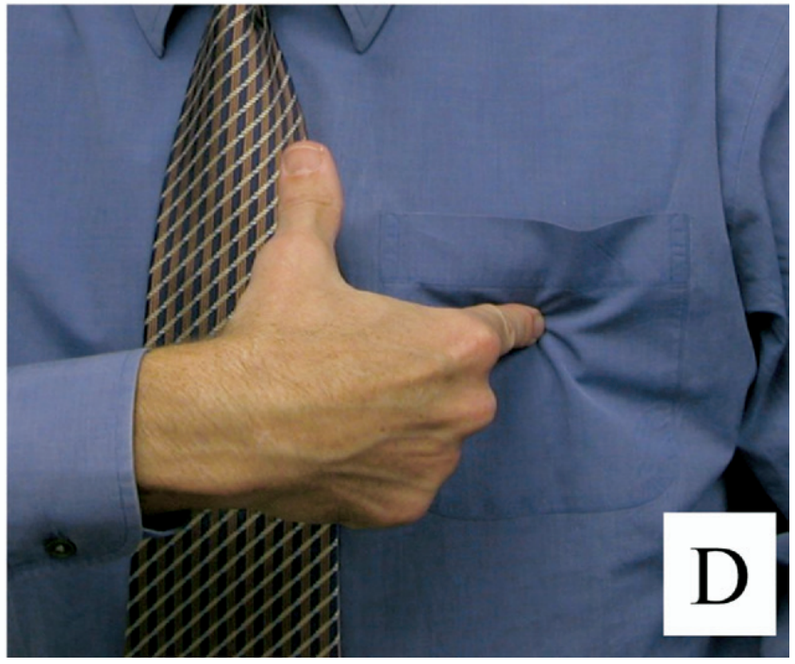
Probable High Risk

Pain described as pressure, is similar to that of prior myocardial infarction or worse than prior anginal pain, or is accompanied by nausea, vomiting, or diaphoresis[3,14,24,25,27-29]

High Risk

Pain that radiates to one or both shoulders or arms or is related to exertion[3,14,24,25,27,29]





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The American Journal of Medicine (2007) 120, 83-89

THE AMERICAN JOURNAL *of* MEDICINE®

CLINICAL RESEARCH STUDY

AJM Theme Issue: Cardiology

The Utility of Gestures in Patients with Chest Discomfort

Gregory M. Marcus, MD,[a] Joshua Cohen, MD,[a] Paul D. Varosy, MD,[a] Joshua Vessey, MD,[b] Emily Rose, MD,[c] Barry M. Massie, MD,[a,d] Kanu Chatterjee, MB,[a] David Waters, MD[a,e]

[a]Division of Cardiology, University of California, San Francisco, San Francisco, Calif; [b]Division of Cardiology, Mount Sinai Medical Center, New York, NY; [c]Department of Medicine, Brigham and Women's Hospital, Boston, Mass; [d]Division of Cardiology, San Francisco Veterans Affairs Medical Center, San Francisco, Calif; and [e]Division of Cardiology, San Francisco General Hospital, San Francisco, Calif.

Levine Sign

CLINICAL SIGNIFICANCE

- The Levine Sign has a poor sensitivity for chest pain related to myocardial ischemia or infarction.
- A patient pointing to a specific point on the chest likely does not have discomfort due to cardiac ischemia or myocardial infarction.
- Larger areas of chest discomfort correlate with a greater likelihood of cardiac ischemia or myocardial infarction.

Can ACS Present without CP?

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ACS without CP

- 33% of all ACS
- Women, DM, >70yo, prior HF
- Worse prognosis

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EKG

TABLE 2 Electrocardiographic Manifestations Suggestive of Acute Myocardial Ischaemia (in the Absence of Left Ventricular Hypertrophy and Bundle Branch Block)

ST-elevation
New ST-elevation at the J-point in 2 contiguous leads with the cut-point: ≥1 mm in all leads other than leads V_2–V_3 where the following cut-points apply: ≥2 mm in men ≥40 years; ≥2.5 mm in men <40 years, or ≥1.5 mm in women regardless of age.[a]
ST-depression and T wave changes
New horizontal or downsloping ST-depression ≥0.5 mm in 2 contiguous leads and/or T inversion >1 mm in two contiguous leads with prominent R wave or R/S ratio >1.

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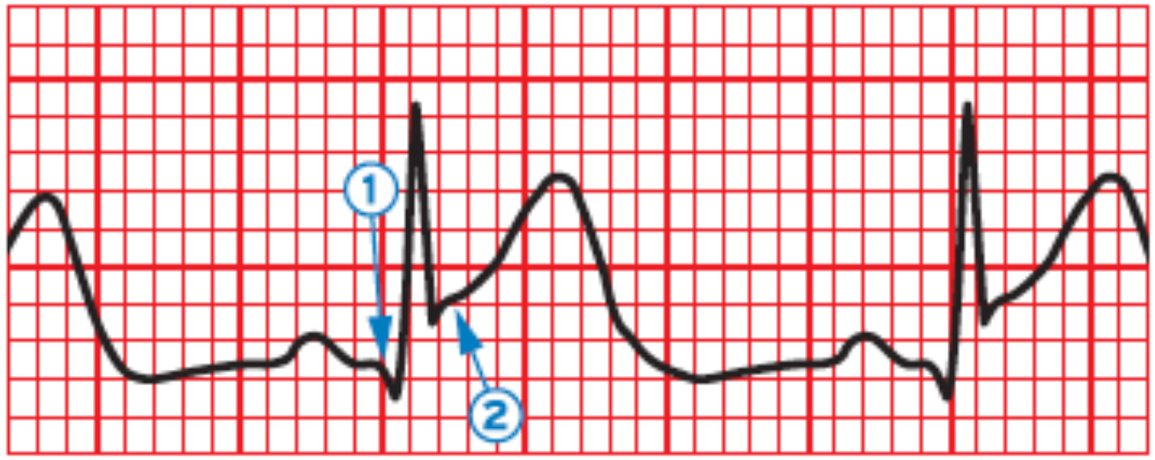
FIGURE 8 Electrocardiogram Example of ST-Segment Elevation

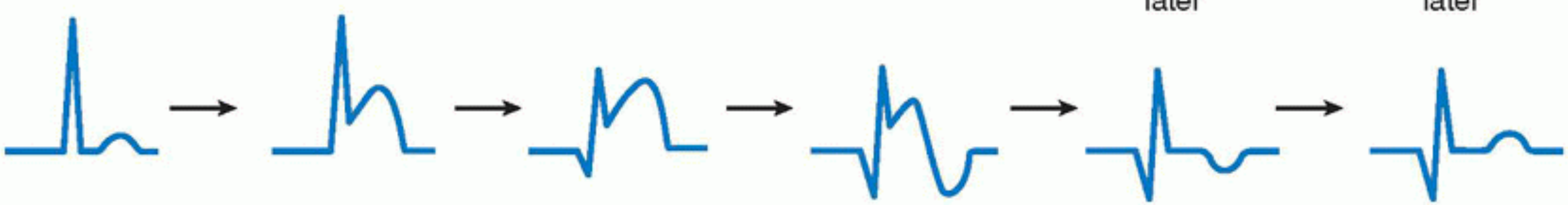


The initial onset of the Q wave shown by arrow 1 serves as the reference point and arrow 2 shows the onset of the ST-segment or J-point. The difference between the two identifies the magnitude of displacement. Measurements of both arrows should be made from the top of the electrocardiogram line tracing.

TABLE 3 **Electrocardiographic Changes Associated With Prior Myocardial Infarction (in the Absence of Left Ventricular Hypertrophy and Left Bundle Branch Block)**

Any Q wave in leads V_2–V_3 >0.02 s or QS complex in leads V_2–V_3.
Q wave ≥0.03 s and ≥ 1 mm deep or QS complex in leads I, II, aVL, aVF or V_4–V_6 in any 2 leads of a contiguous lead grouping (I, aVL; V_1–V_6; II, III, aVF).[a]
R wave >0.04 s in V_1–V_2 and R/S >1 with a concordant positive T wave in absence of conduction defect.

ST-Elevation Myocardial Infarction



- ST elevation
- ST elevation
- ↓R Wave
- Q wave begins
- T-wave inversion
- Q wave deeper
- ST normalizes
- T wave inverted
- ST & T normal
- Q wave persists

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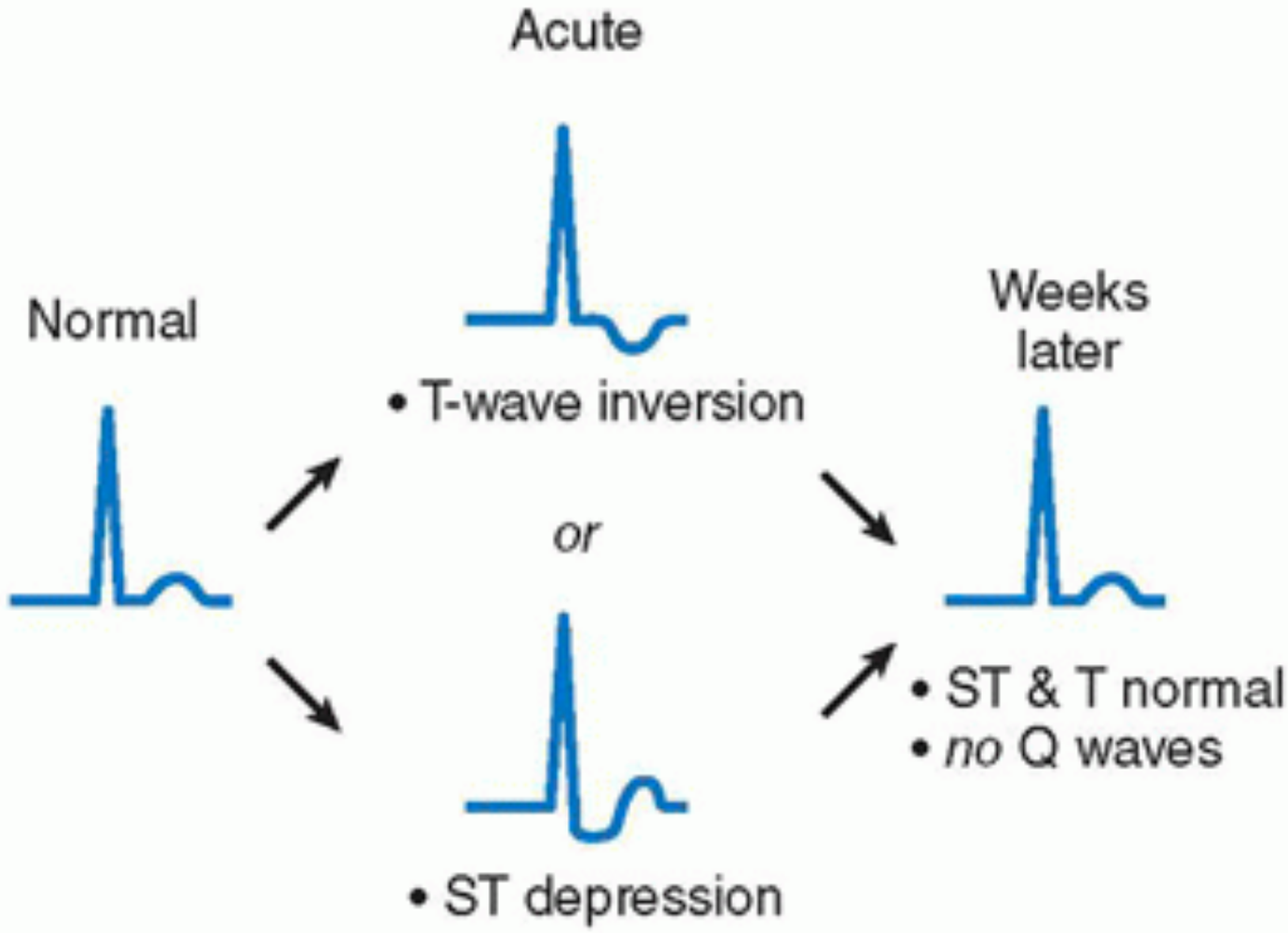
Unstable Angina/Non–ST-Elevation Myocardial Infarction



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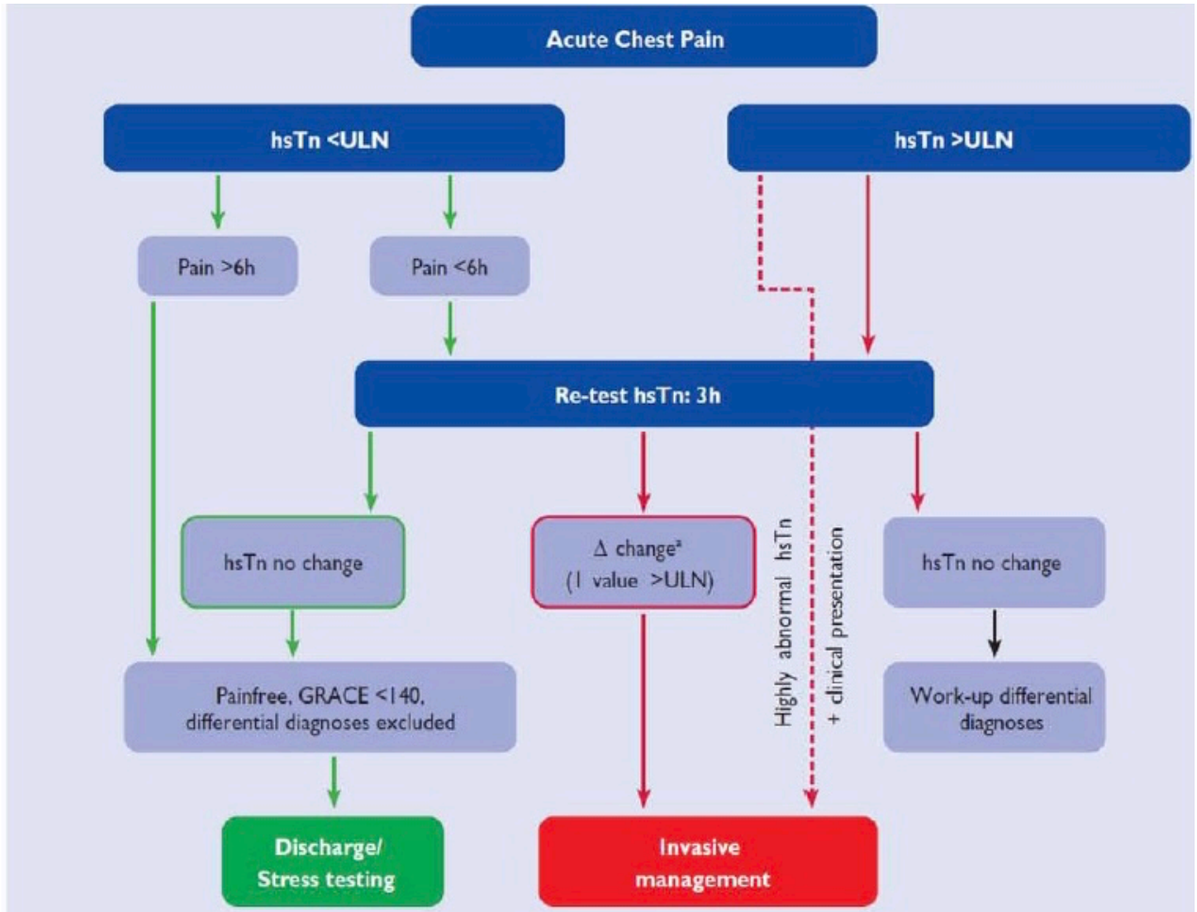
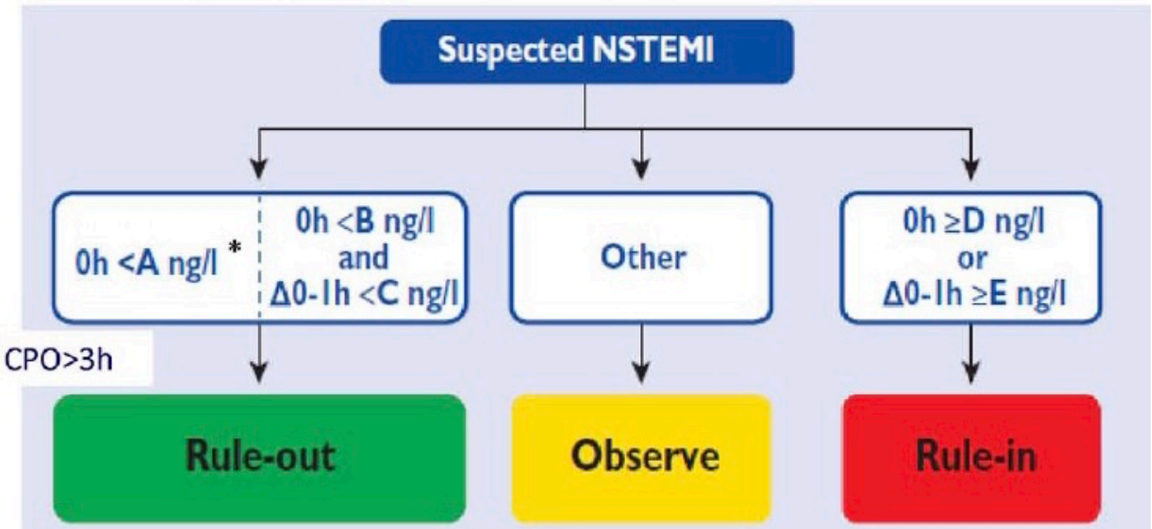


GRACE = Global Registry of Acute Coronary Events score; hsTn = high sensitivity troponin; ULN = upper limit of normal, 99th percentile of healthy controls.
*Δ change, dependent on assay. Highly abnormal hsTn defines values beyond 5-fold the upper limit of normal.



	A	B	C	D	E
Hs-cTnT (Elecsys)	5	12	3	52	5
Hs-cTnI (Architect)	2	5	2	52	6

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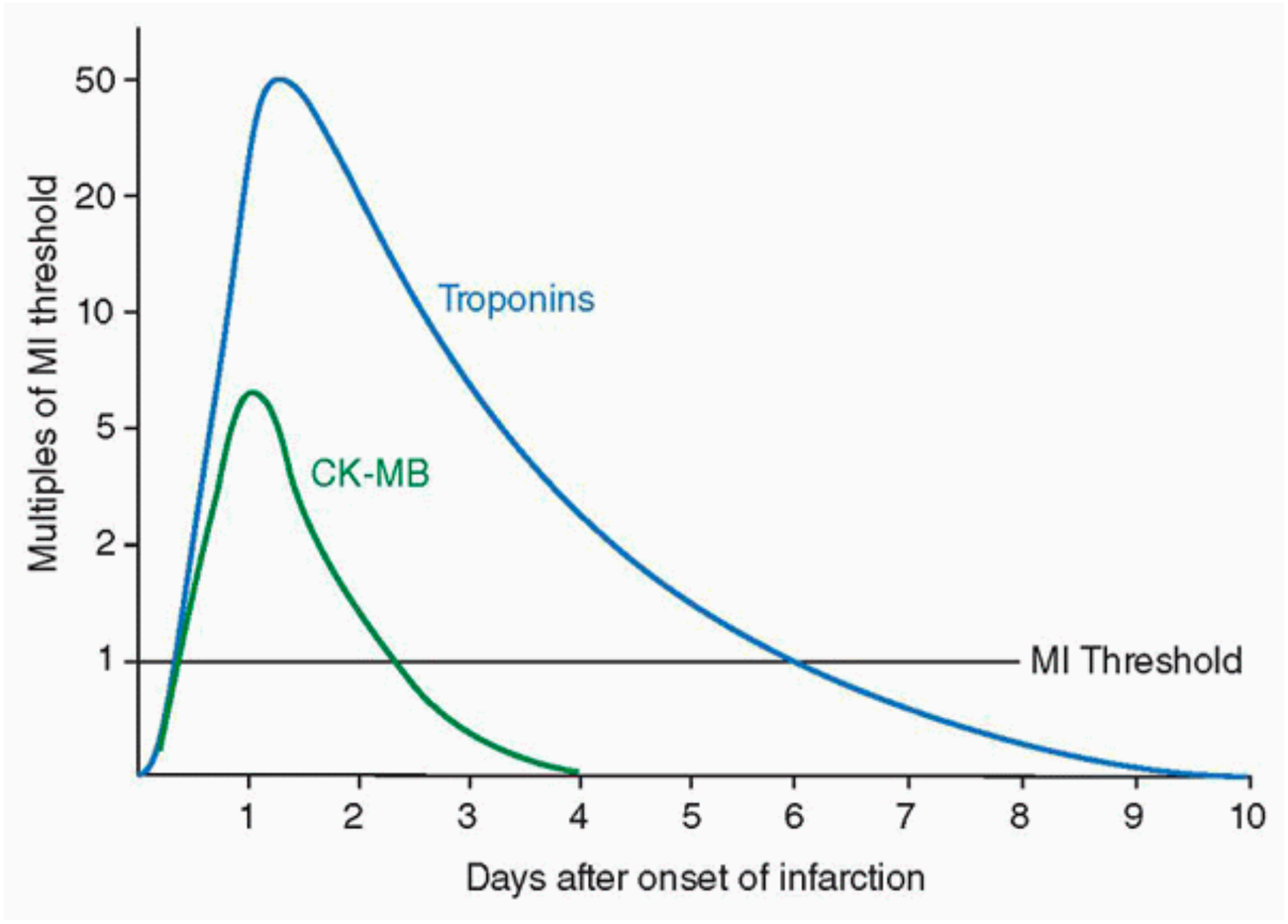
Cardiac Biomarkers



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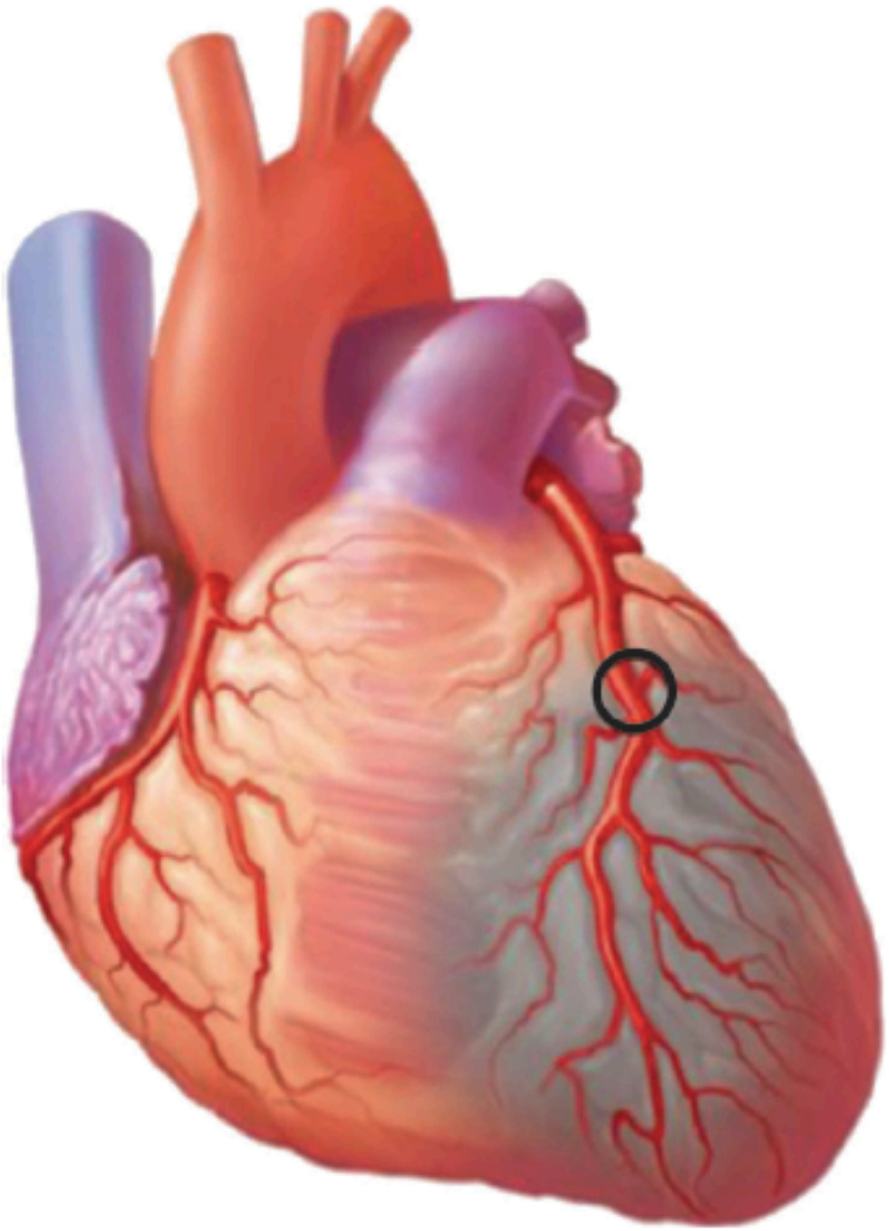
MI Type 1



Plaque rupture/erosion with occlusive thrombus

Plaque rupture/erosion with non-occlusive thrombus

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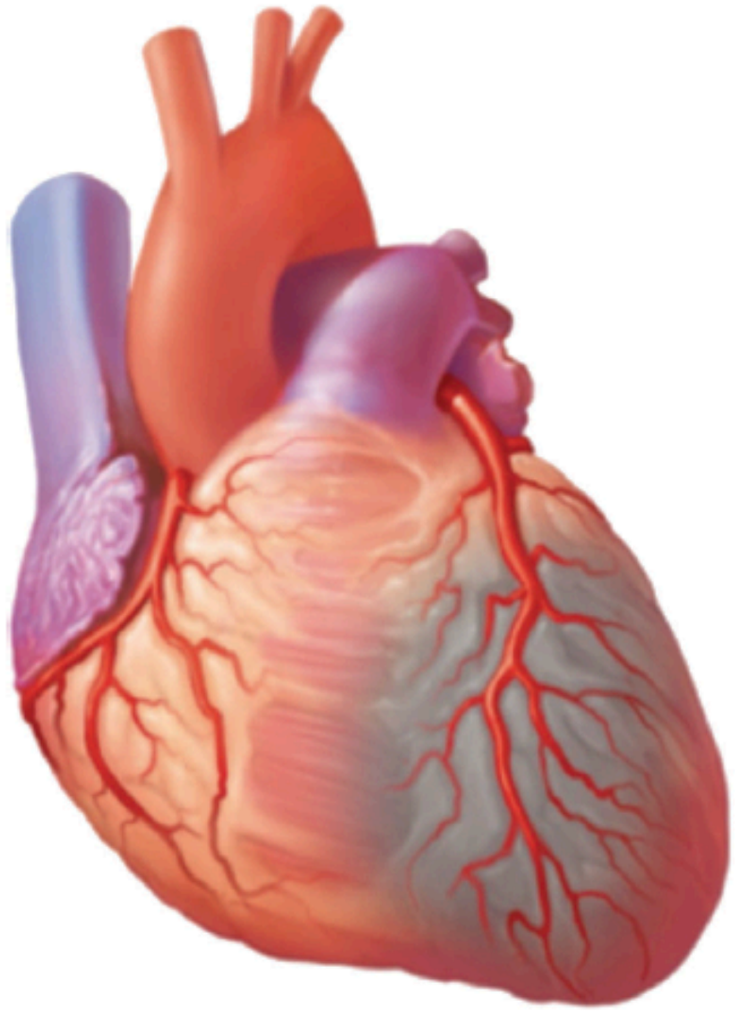
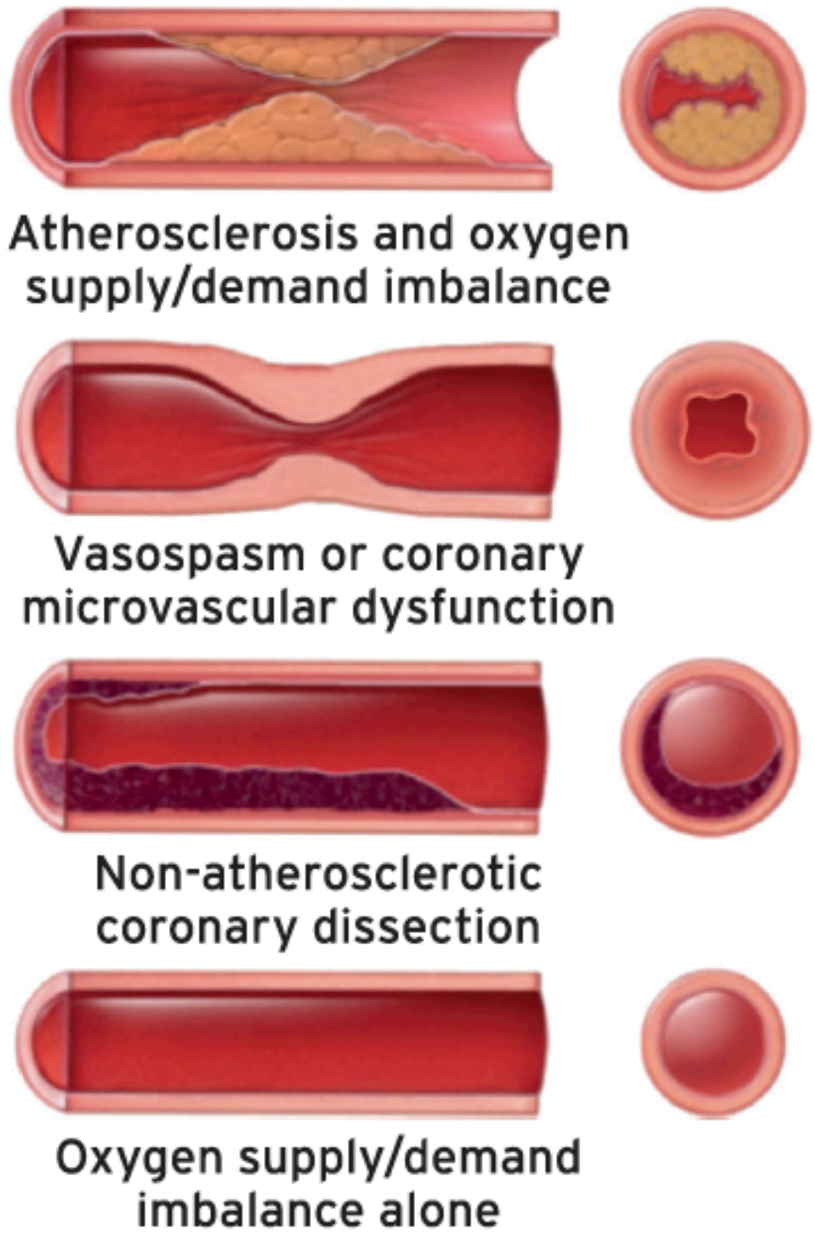
MI Type 2





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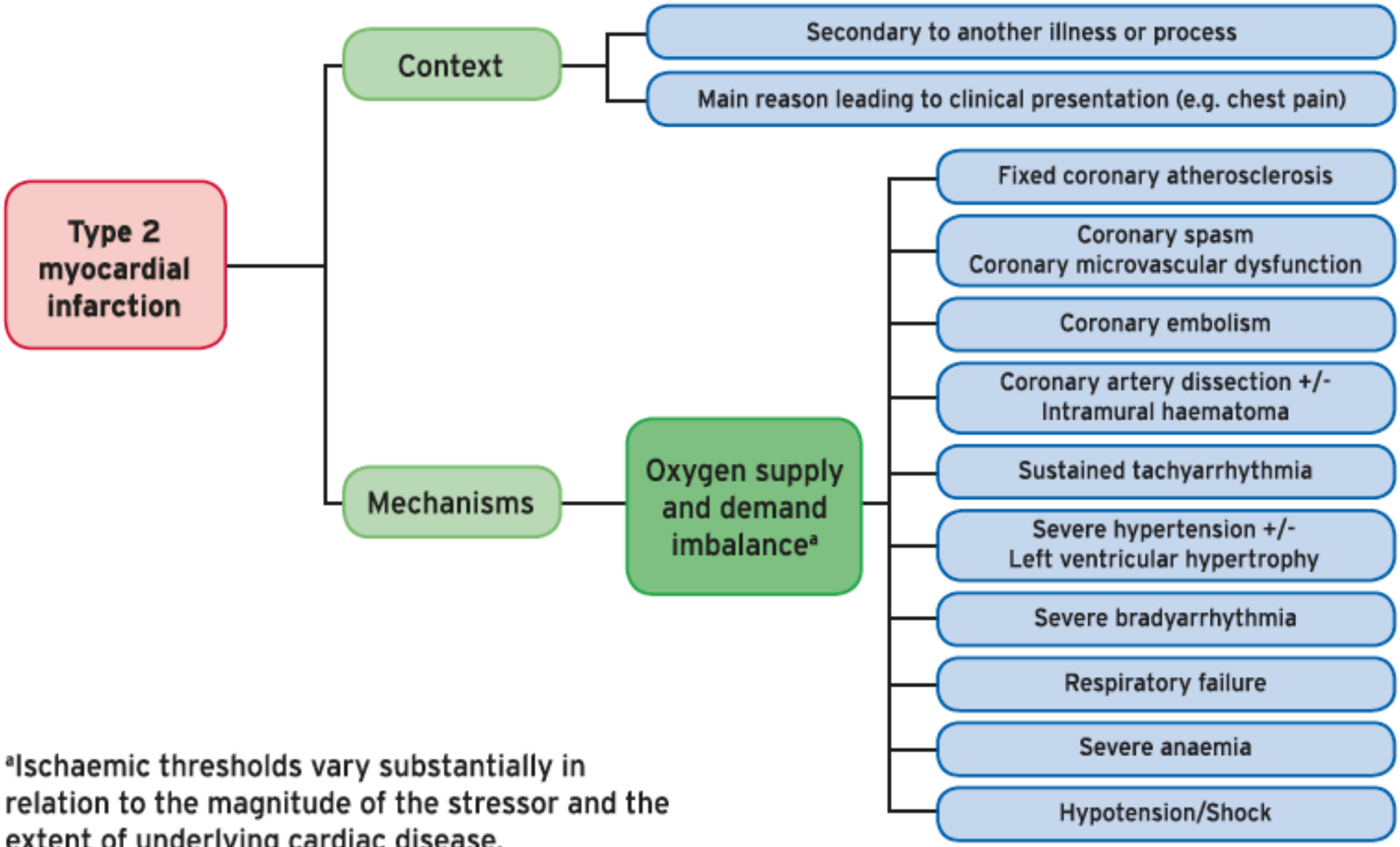

[a]Ischaemic thresholds vary substantially in relation to the magnitude of the stressor and the extent of underlying cardiac disease.

TABLE 1 Reasons for the Elevation of Cardiac Troponin Values Because of Myocardial Injury

Myocardial injury related to acute myocardial ischaemia
Atherosclerotic plaque disruption with thrombosis.
Myocardial injury related to acute myocardial ischaemia because of oxygen supply/demand imbalance
Reduced myocardial perfusion, e.g., • Coronary artery spasm, microvascular dysfunction • Coronary embolism • Coronary artery dissection • Sustained bradyarrhythmia • Hypotension or shock • Respiratory failure • Severe anaemia
Increased myocardial oxygen demand, e.g., • Sustained tachyarrhythmia • Severe hypertension with or without left ventricular hypertrophy
Other causes of myocardial injury
Cardiac conditions, e.g., • Heart failure • Myocarditis • Cardiomyopathy (any type) • Takotsubo syndrome • Coronary revascularization procedure • Cardiac procedure other than revascularization • Catheter ablation • Defibrillator shocks • Cardiac contusion
Systemic conditions, e.g., • Sepsis, infectious disease • Chronic kidney disease • Stroke, subarachnoid haemorrhage • Pulmonary embolism, pulmonary hypertension • Infiltrative diseases, e.g., amyloidosis, sarcoidosis • Chemotherapeutic agents • Critically ill patients • Strenuous exercise

ACS Facts

- ⅓ HF presentation to ER due to ACS
- ½ of all NSTE-ACS have no ischemic EKG changes
- Use TIMI score for NSTE-ACS with app

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TIMI Score

- TIMI score (Predict 30d and 1yr mortality in UA/NSTEMI)

1. **Age >= 65yo**
2. **>= 3 CAD RF HDL!!**
3. **Prior coronary stenosis >= 50%**
4. **Use of ASA in last 7d**
5. **>=2 Angina events in<24h**
6. **ST segment deviation (>= 0,5 mm)**
7. **Elevated cardiac biomarkers**

- **0-1: low risk - 2-3: mod risk - >=4:high risk**

- TIMI 0-1: **5%** all cause mortality, recurrent MI/ischemia requiring revascularization at 14d
  - 2: **8%**
  - 3: **13%**
  - 4: **20%**
  - 5: **26%**
  - 6-7: **41%**

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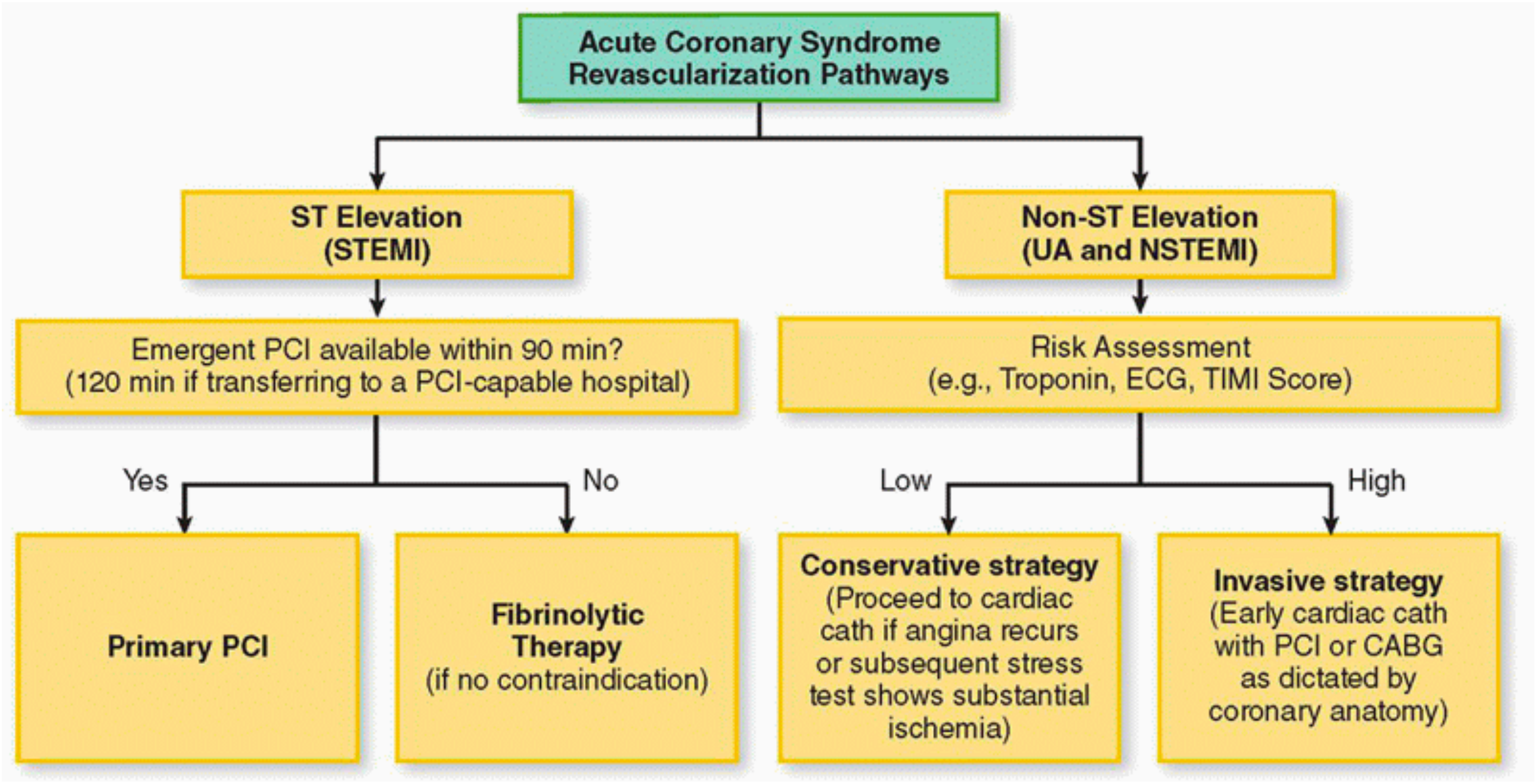

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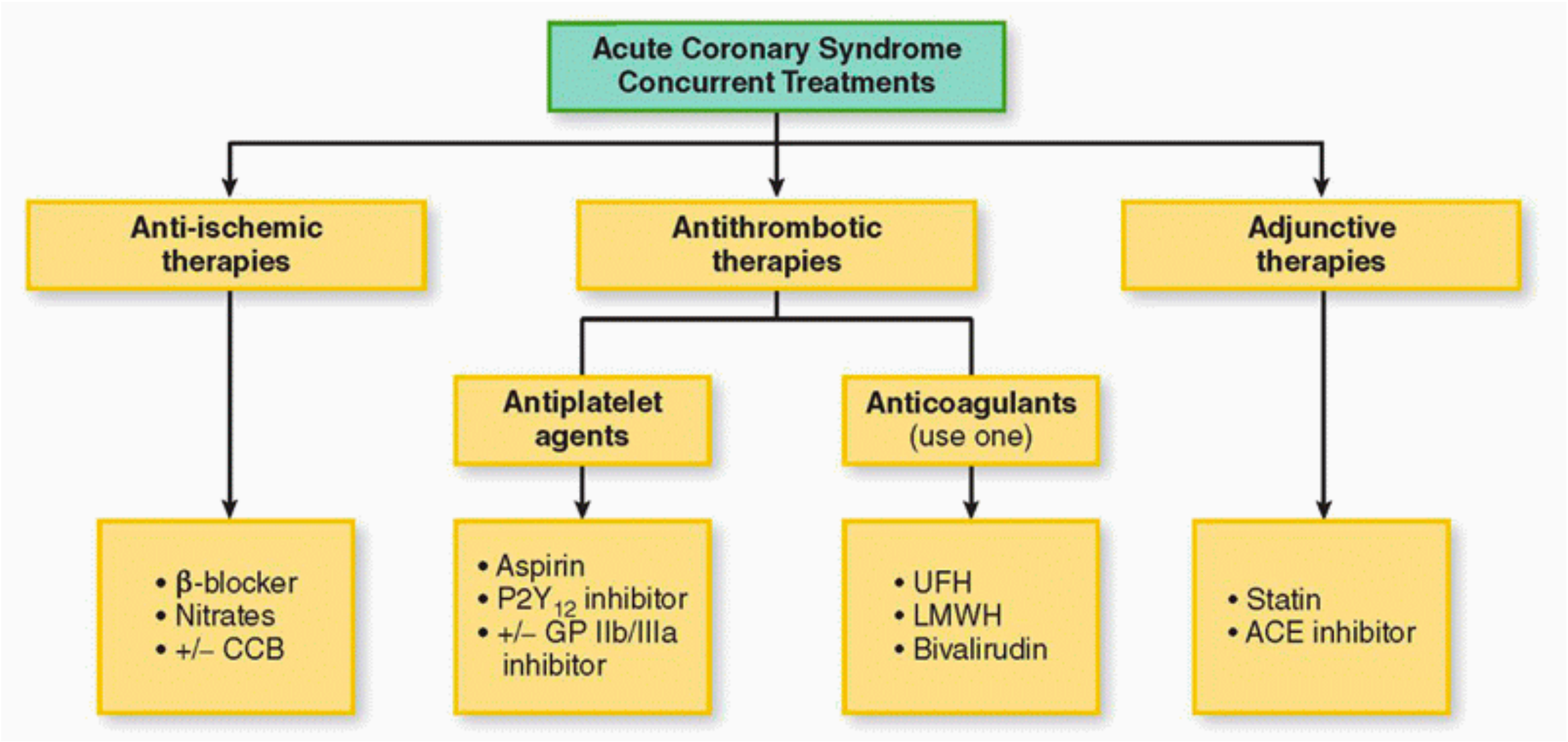
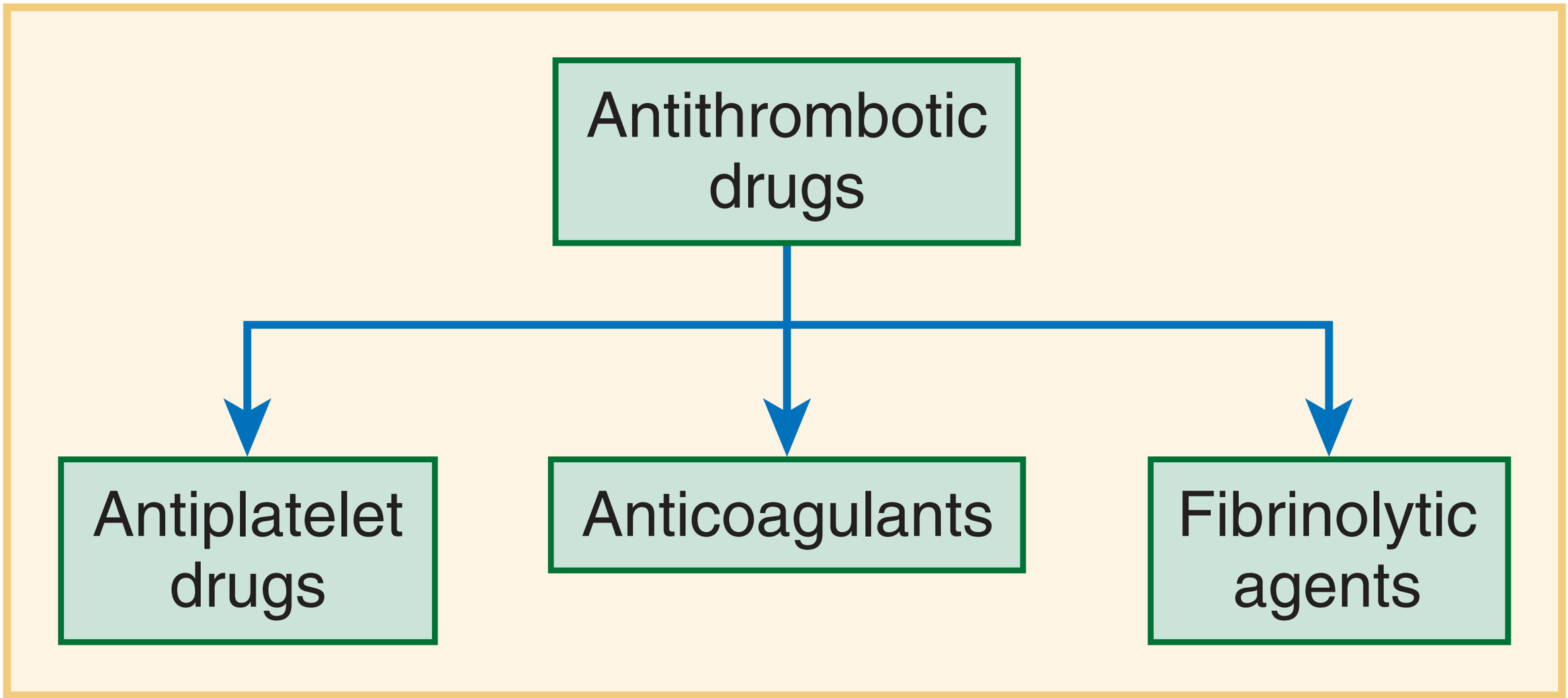

Acute Coronary Syndrome
Concurrent Treatments
Anti-ischemic therapies
Antithrombotic therapies
Adjunctive therapies
Antiplatelet agents
Anticoagulants (use one)
• β-blocker
• Nitrates
• +/– CCB
• Aspirin
• P2Y12 inhibitor
• +/– GP IIb/IIIa inhibitor
• UFH
• LMWH
• Bivalirudin
• Statin
• ACE inhibitor



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Platelet Activation

- **Activators:**
    - Collagen
    - vWF
    - Thrombin
- **Consequences of activation:**
    - AA ---COX1---> TXA2 ---> release of granule contents:
    - ADP
    - Serotonin
    - Fibrinogen

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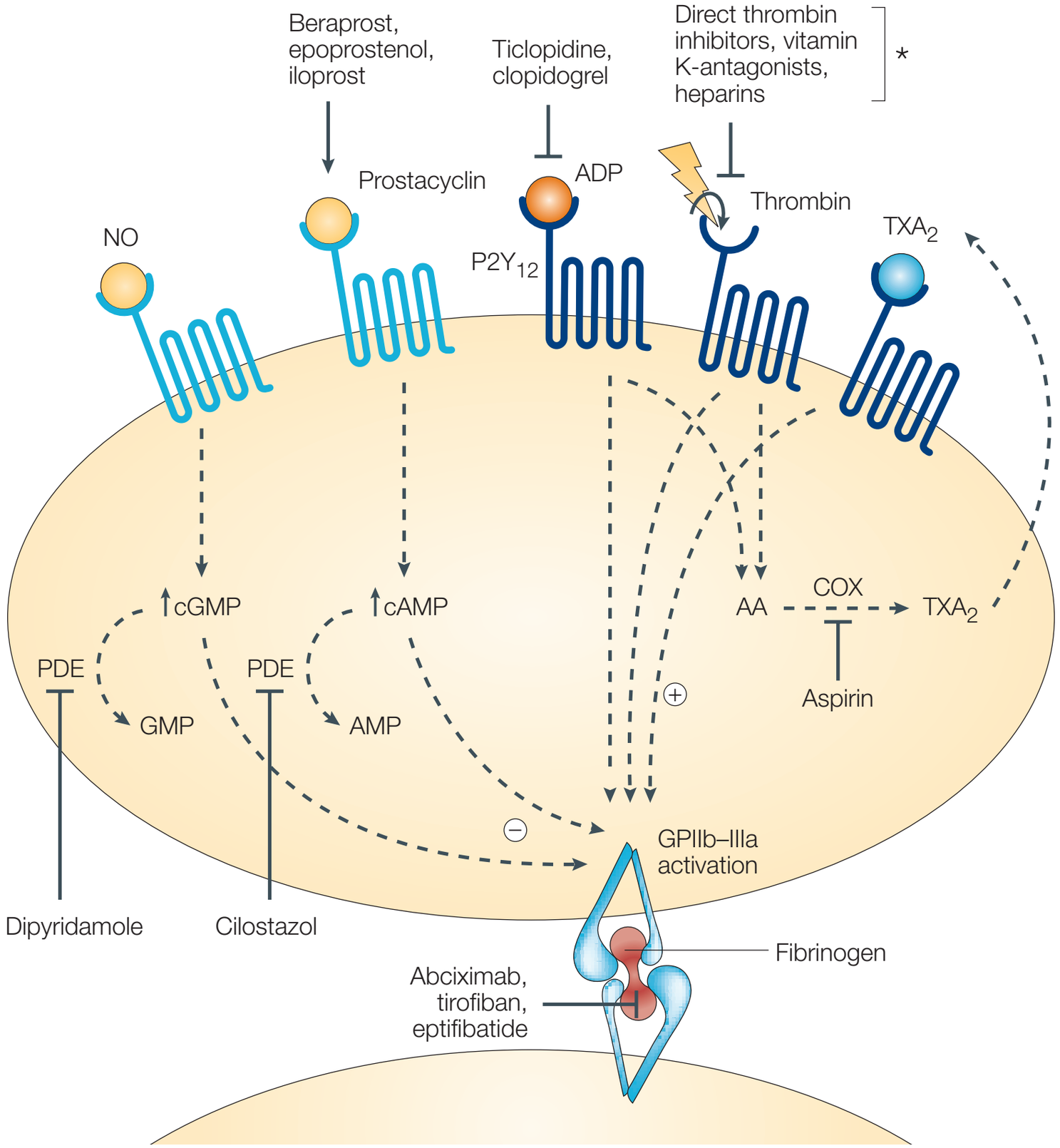

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The Lancet · Saturday 13 August 1988

RANDOMISED TRIAL OF INTRAVENOUS STREPTOKINASE, ORAL ASPIRIN, BOTH, OR NEITHER AMONG 17 187 CASES OF SUSPECTED ACUTE MYOCARDIAL INFARCTION: ISIS-2

ISIS-2 (SECOND INTERNATIONAL STUDY OF INFARCT SURVIVAL) COLLABORATIVE GROUP*

0·2%) and of confirmed cerebral haemorrhage (0·1
0·0%), but with fewer other strokes (0·6% *vs* 0·8%). T
"other" strokes may have included a few undiagı
cerebral haemorrhages, but still there was no increa
total strokes (0·7% streptokinase *vs* 0·8% placebo infu
Aspirin significantly reduced non-fatal reinfarction (
vs 2·0%) and non-fatal stroke (0·3% *vs* 0·6%), and wa
associated with any significant increase in cer
haemorrhage or in bleeds requiring transfusion. An e

ISIS-2

- Within 24hr of STEMI reduced CV mortality by 23% at 5weeks f/u
- Benefit of SK & aspirin were additive with 42% decrease mortality

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CURE Trial

EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

THE CLOPIDOGREL IN UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS TRIAL INVESTIGATORS*

N Engl J Med, Vol. 345, No. 7 · August 16, 2001 · www.nejm.org

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 10, 2009 VOL. 361 NO. 11

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Lars Wallentin, M.D., Ph.D., Richard C. Becker, M.D., Andrzej Budaj, M.D., Ph.D., Christopher P. Cannon, M.D., Håkan Emanuelsson, M.D., Ph.D., Claes Held, M.D., Ph.D., Jay Horrow, M.D., Steen Husted, M.D., D.Sc., Stefan James, M.D., Ph.D., Hugo Katus, M.D., Kenneth W. Mahaffey, M.D., Benjamin M. Scirica, M.D., M.P.H., Allan Skene, Ph.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., D.M., and Robert A. Harrington, M.D., for the PLATO Investigators*

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Canadian Journal of Cardiology 34 (2018) 214–233

Society Guidelines

2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy

PCI for STEMI or NSTEACS

DAPT for 1 year

ASA 81 mg OD +
Ticagrelor 90 mg BID **or** Prasugrel 10 mg OD
preferred over
Clopidogrel 75 mg OD

At 1 year, determine bleeding risk

Not at high risk of bleeding[1]

Continue DAPT for up to 3 years
ASA 81 mg OD +
Ticagrelor 60 mg BID or
Clopidogrel 75 mg OD[2]

High risk of bleeding[1]

SAPT
ASA 81 mg OD
or
Clopidogrel 75 mg OD

1 Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranical bleed, regular need for NSAIDS or prednisone

2 Instead of ticagrelor or clopidogrel, prasugrel 5-10 mg daily is also an option (weak recommendation)

DAPT=dual antiplatelet therapy SAPT=single antiplatelet therapy STEMI=ST segment elevation myocardial infarction NSTEMI=non-ST segment elevation myocardial infarction OD=once daily BID=twice daily

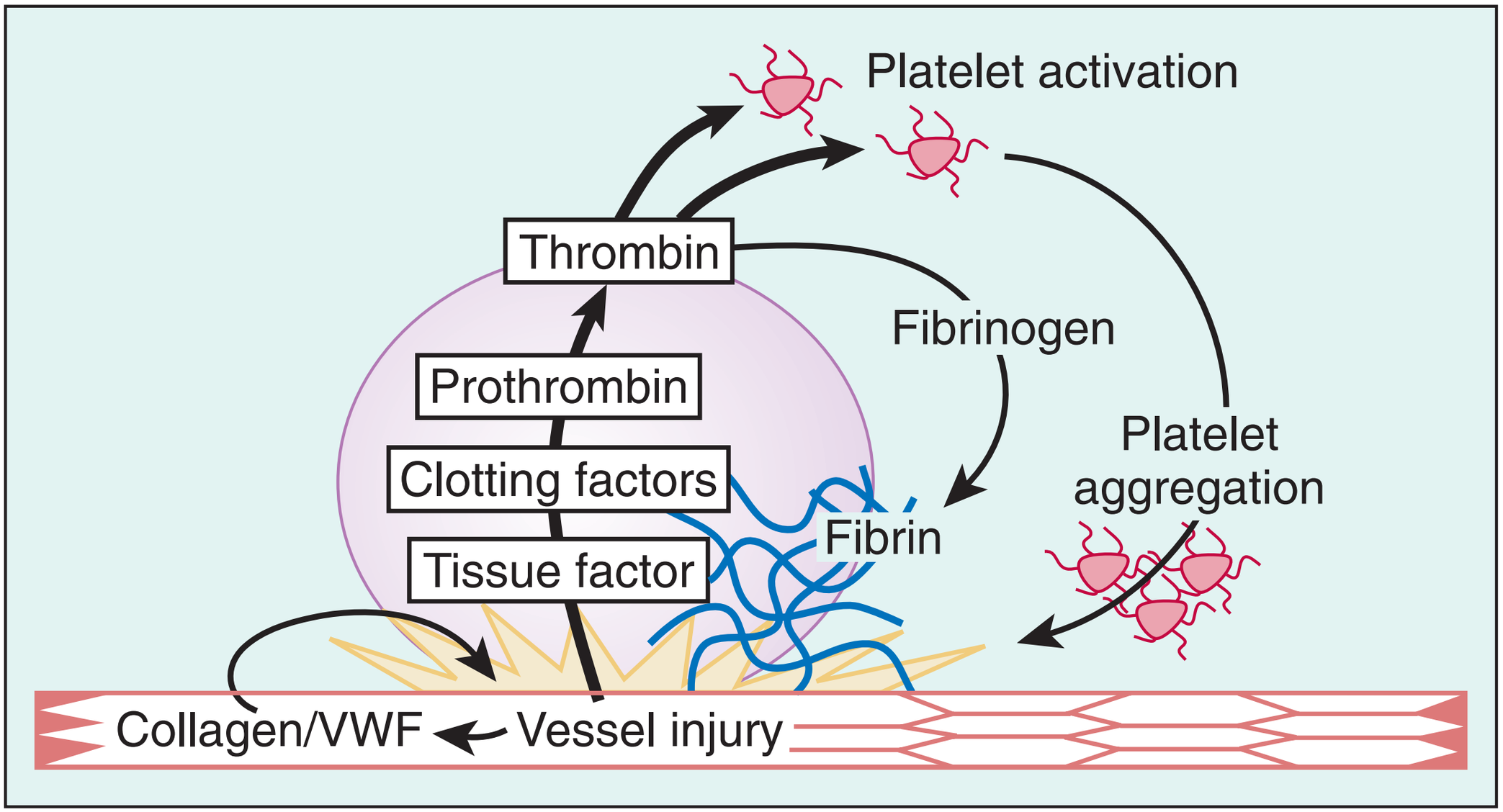
Canadian Journal of Cardiology 34 (2018) 214–233

Strong recommendation
Weak recommendation

Anticoagulants

- Anticoagulants are typically stopped after the PCI
- If PCI is not performed, anticoagulants are typically administered for at least 48 hours, and preferably longer, for the duration of hospitalization (up to 8 days)

Where All the Wars Start?



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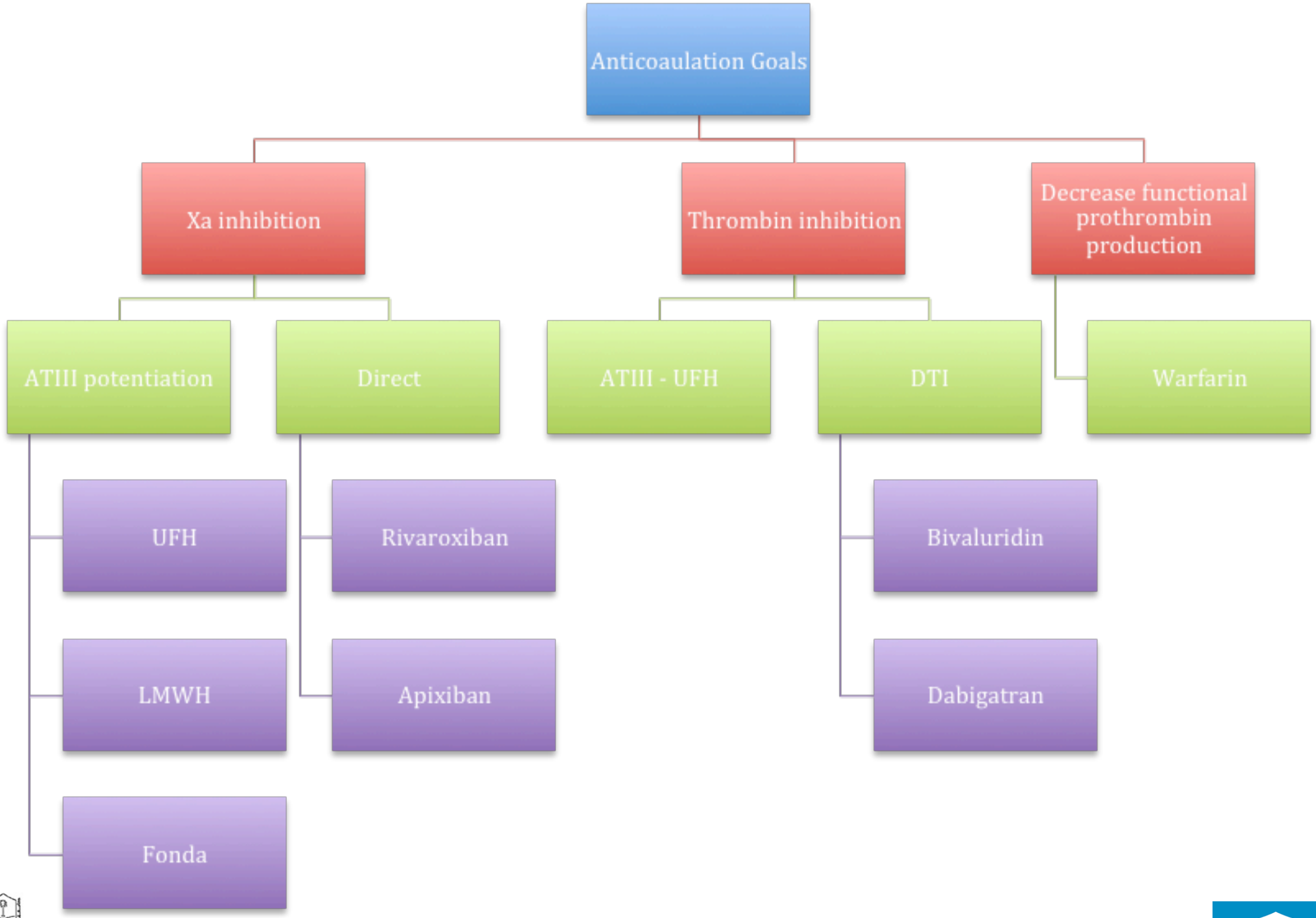

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LMWH > UFH

- Greater **anti-Xa activity** (so greater thrombin inhibition)
- Greater release of tissue factor pathway inhibitor
- Less **thrombocytopenia**
- Higher bioavailability so s/c administration
- **Less binding to plasma protein** so more **consistent effect** and **no monitoring** required

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TABLE 87-3 Comparison of the Features of Heparin, Low-Molecular-Weight Heparin, and Fondaparinux

FEATURE	HEPARIN	LMWH	FONDAPARINUX
Source	Biologic	Biologic	Synthetic
Molecular weight	15,000	5000	1728
Target	Xa and IIa	Xa and IIa	Xa
Bioavailability (%)	30	90	100
Half-life (hr)	1	4	17
Renal excretion	No	Yes	Yes
Antidote	Complete	Partial	No
HIT	<5%	<1%	Never

Thromblytics

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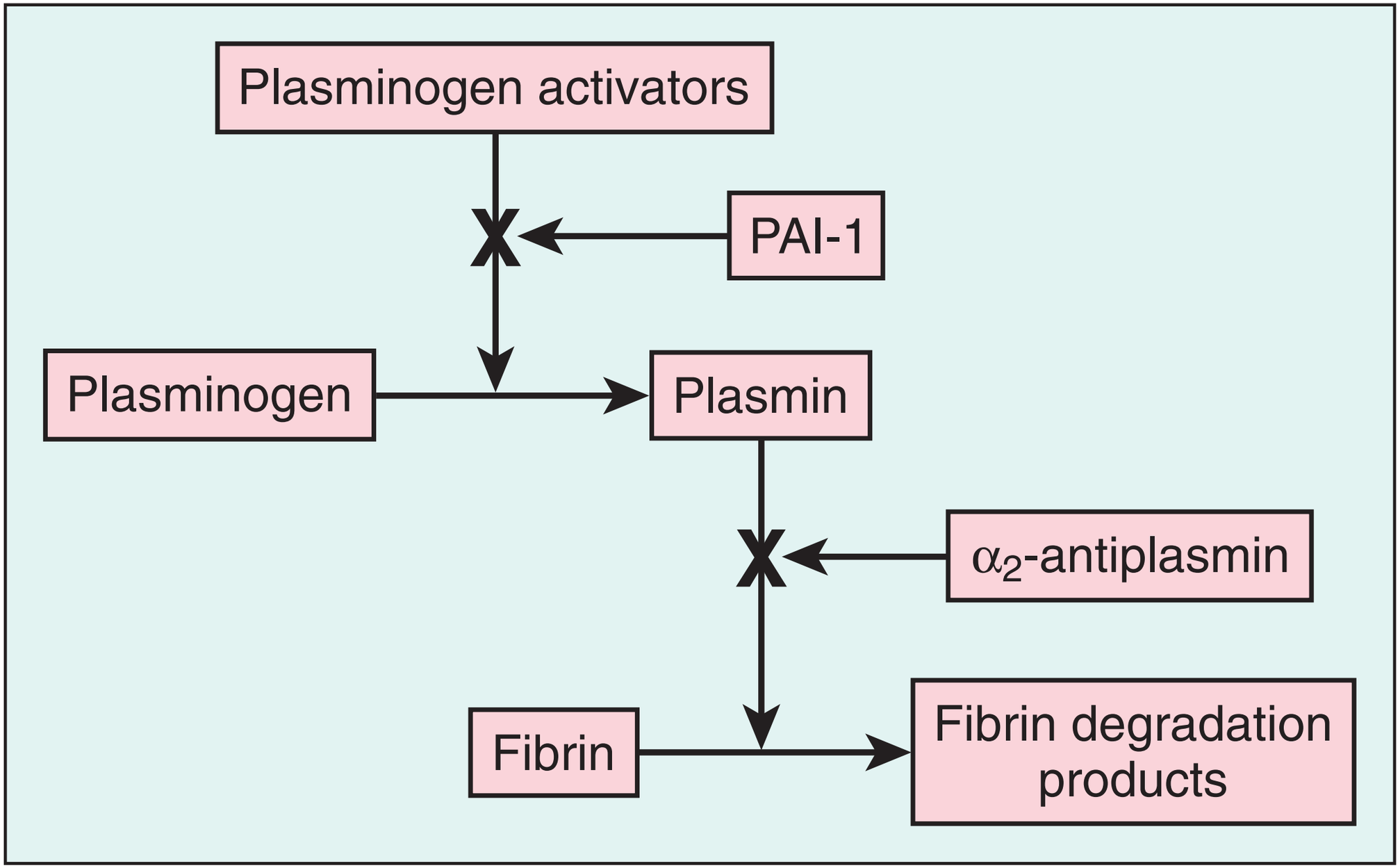
MOA



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Drug	Dosage	Add On
tPA **Accelerated regimen** **3 Doses**	**15mg** IV bolus — >**0.75mg/kg (max 50)** over 30min —>**0.5mg/kg** **(max35)** over 1hr	Better than SK (**GUSTO-1**) 100mg over 90min
rPA **2 Doses**	**10U** over 2min then 10U at 30min	=tPA
TNK **1 Dose**	Single bolus over 10sec **<60kg=30mg** **90≥50mg** **5mg increment/10kg**	=tPA (**ASSENT-2**) but less non-cerebral bleeding & Tx

All pts get ASA load/UFH 60U/Kg max 4000 then infusion 12U/Kg max 1000U/hr
PTT target 50-70 (UFH not beneficial with SK)

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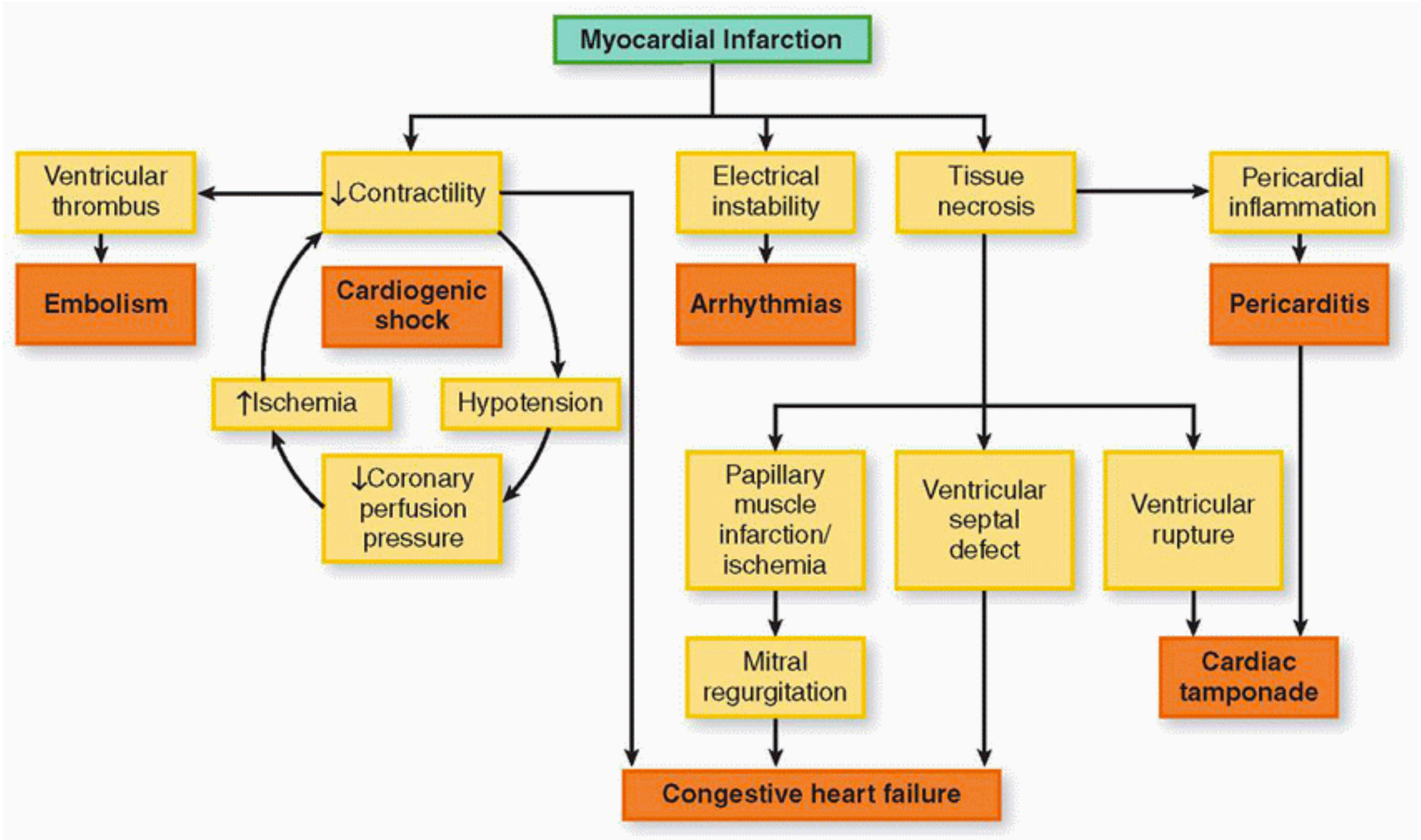
Anti-ischemic Therapy

- **BB** - COMMIT-CCS trial Day 2-15
  - Reduced the endpoint of death/ MI/ cardiac arrest
  - 1 month up to 3 year for normal LVEF
- **ACEI** - ISIS-4 6 weeks, PEACE no benefit
- **Statin** - PROVE-IT trial
  - LDL? Superior stabilization of vulnerable plaque
- **NTG**
- **PPI**
- **Regular activities** - 1 week if revascularized/ 1 month for sports

MI Complications



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Outline

- **What** Are the ACS Types?
- **How** ACS Occurs?
- **How** Do You Approach to CP?
- **How** Do You Diagnose ACS?
- **What** is the Management of ACS?

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Questions?

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