Acute Coronary Syndromes: Unstable Angina and Myocardial Infarctions Part 3

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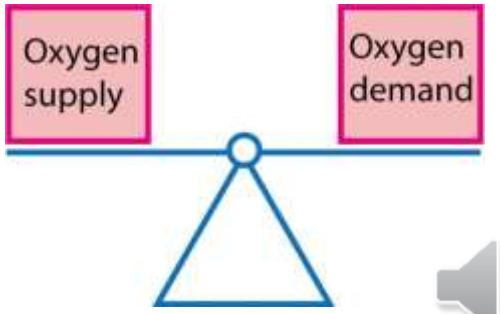
Treatment of ACS

1. Management of ACS S/Sx
2. Initial Management in ED
3. **Acute therapies during hospitalization**
    1. Non-pharmacologic Management
    2. **Pharmacologic Management**
        - **A. Anti-ischemic**
        - B. Acute Reperfusion
        - C. Anti-thrombotic
        - D. Adjunct
4. Chronic therapies after discharge

Pharmacologic Therapies During Hospitalization



Anti-ischemic therapies (for all ACS pts):

ED

- Oxygen
  - When to use:
- Analgesics
- Nitrates
- Beta-blockers (CCB as alternative)

Goals of therapy: Decrease myocardial O_2 demand, increase O_2 supply, and decrease pain

Anti-Ischemic Therapy: Analgesics

- Outcome: Relieve pain/anxiety during hospitalization only
- MOA: produce arterial and venous vasodilation by inhibiting sympathetic tone and augmenting vagal tone
- Agent: Morphine
  - Administer PRN only if there is inadequate pain relief from NTG
  - SE: Can mask ongoing pain, depress respiratory drive, cause hypotension, confusion, N/V, and constipation
  - Drug interaction: P2Y12 inhibitors
  - Recommend stool softener like docusate (to avoid Valsalva maneuver) and antiemetic (to avoid N/V)

ACC/AHA 2013 STEMI guidelines; 2014 NSTE ACS guidelines

Analgesics Continued

- NSAIDs
  - NSAIDs and COX-2 inhibitors may increase risk for mortality, re-infarction, myocardial rupture and HF!
    - Discontinue on admission
    - Do not initiate during hospitalization
    - Recommend acetaminophen, non-acetylated salicylates, tramadol, or narcotics (last resort) for treatment of chronic pain post discharge
    - <u>This recommendation does not include aspirin!</u>

ACC/AHA 2013 STEMI guidelines; 2014 NSTE ACS guidelines

Anti-Ischemic Therapy: Nitrates

- Outcome:
  - Provide relief of ongoing ischemia, relieve vasospasms, decrease infarct size and expansion, control BP (afterload), and manage pulmonary congestion (preload)
  - Decrease incidence of early death by ~30% but no effect on long-term mortality
- Dose:
  - Initiate in patients who still have CP despite 3 SL NTG tabs
  - IV infusion for first 24-48 hours, then switch to oral/topical agent if therapy is needed to prevent angina
  - Careful titration is required to prevent hypotension that prohibits the use of BB and ACEI

Circ 1988;78:906-19, Lancet 1988;1:1088-92; Lancet 1994;343:1115-22, Lancet 1995;345:669-85

Nitroglycerin Dosing

- IV NTG: Start at 5-10 mcg/minute
  - Increase by 5 mcg/min every 5 minutes based on pain and BP to max rate of 200 mcg/min
  - Monitor HR, BP, EKG, pain intensity
  - Avoid SBP<90 mmHg or decrease of SBP >30% from baseline
  - Avoid in patients with right ventricular infarcts
  - Tolerance may develop in 7-8 hours
- Contraindication: phosphodiesterase inhibitors
- **Common side effect is severe HA**
  - May be dose limiting
  - Other SE: hypotension, tachycardia, paradoxical bradycardia

Anti-Ischemic Therapy: BB

- Outcome: ~50% decrease in incidence of recurrent infarction with early IV therapy
- Dose: See following slides, initiate within 24 hrs of admission
- MOA:
  - Slow HR to allow for longer diastolic filling time and decrease incidence of arrhythmias
  - Lower BP to reduce risk of intracranial hemorrhage (ICH) with fibrinolytic therapy
- Short term SE: bradycardia, hypotension, AV block

Prog Cardiovasc Dis 1993;36:261-6

Beta Blocker Dosing for ACS

- Carvedilol: 6.25mg po q12hr, titrate to 25mg BID as tolerated
- Metoprolol tartrate used the most:
  - 12.5-50 mg po q6hrs, titrate as tolerated (max dose 200mg/day?)
  - IV load if hypertensive, tachycardic, or has ongoing ischemia:
    - Dose: 5mg administered over 1-2 min q5min for 3 doses
    - Start oral therapy (doses above) within 1-2 hours of last IV dose

ACC/AHA 2013 STEMI guidelines; 2014 NSTE ACS guidelines; Goldberger JJ et al. JACC 2015;66:1431-41

Contraindications to Acute BB

- Symptomatic bradycardia (use with caution if HR < 60)
- 2nd or 3rd degree AV block
- PR interval > 0.24 sec
- SBP < 80 mmHg
- Moderate or severe LV dysfunction
- Signs of peripheral hypoperfusion or cardiogenic shock
- Active asthma or COPD
- (relative contraindication: ACS due to cocaine or meth-amphetamine use, vasospastic angina)
- If contraindications prohibit early BB therapy, patient should be re-evaluated for BB therapy once stabilized

Anti-Ischemic Therapy: CCBs

- Diltiazem or verapamil may be tried when BB are ineffective, contraindicated, or cause side effects
  - ACS due to cocaine/amphetamine or vasospasm
- Nifedipine IR contraindicated
- Only use in absence of heart failure, LV dysfunction, or AV block

NEJM 1988;319:385-92; Am J Cardiol 1990;66:779-85, Am J Cardiol 1996;77:365-9; Am J Cardiol 1987;60:A18-25, Arch Intern Med 1993;153:345-53

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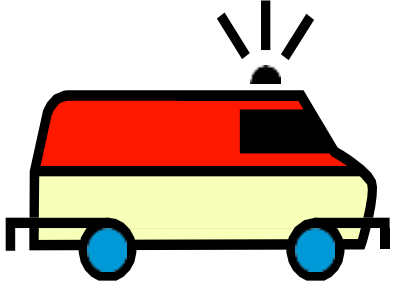


Acute Reperfusion Therapies

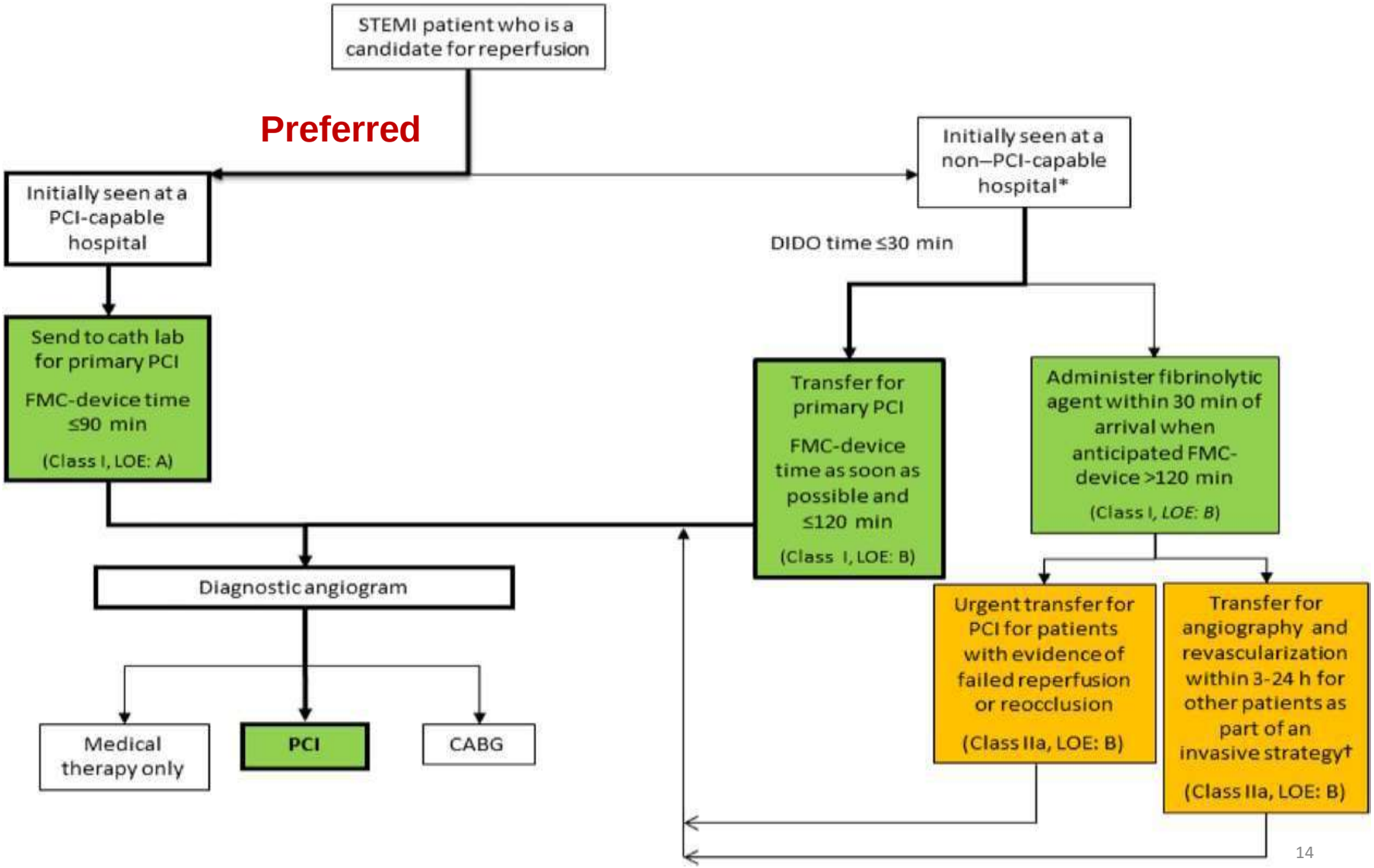
Acute Reperfusion within 12 hours of symptoms – for STEMI patients only!

1. Fibrinolytics
2. **Percutaneous Coronary Intervention (PCI)**
3. Emergent CABG

Goals of treatment: restore blood flow to reverse ischemia, salvage ischemic tissue before infarction, and minimize infarction size

Selection based on: time from onset, bleeding risk with fibrinolytics, presence of shock or severe HF, and time to skilled PCI center

Options for Patients With STEMI



Reperfusion Therapy: Fibrinolytics

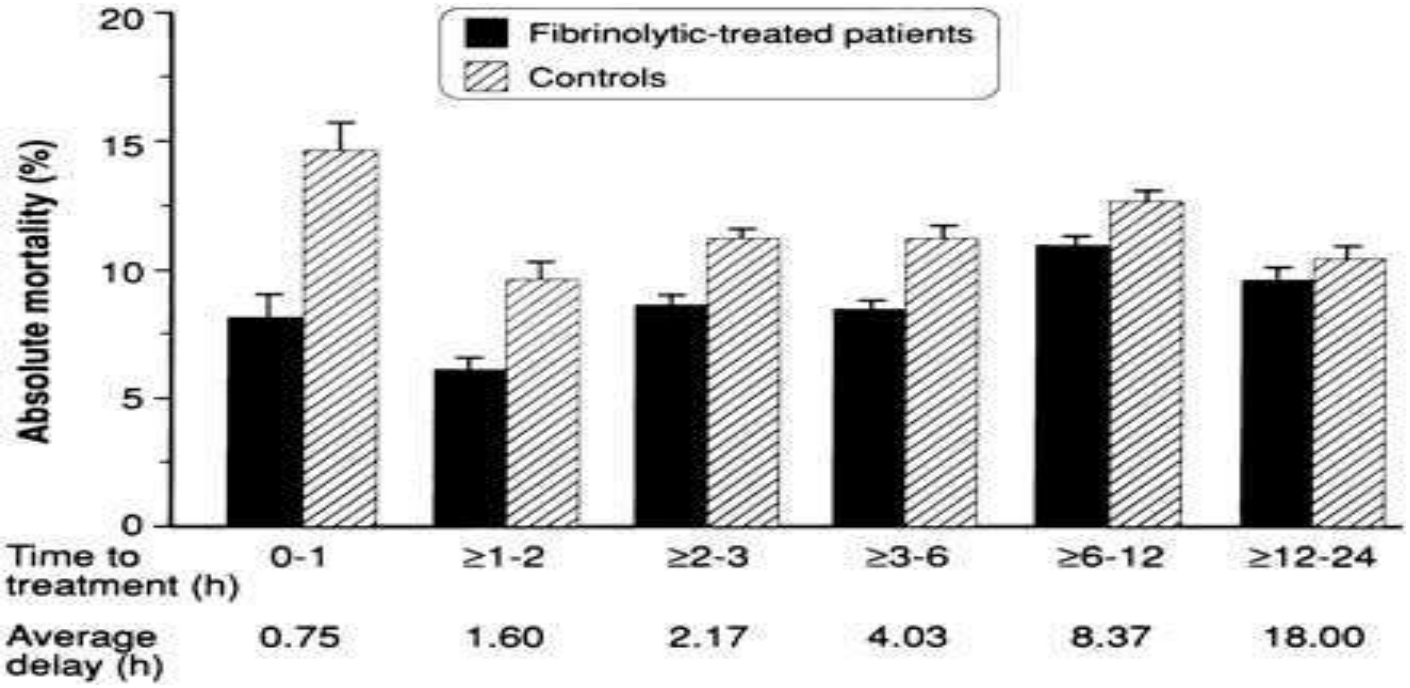
- Outcome: Up to 50% reduction in mortality, sustained up to 10-12 years post MI
- MOA: see coagulation cascade
- Dosing: See following slides
- **Anti-thrombotic therapies are required with fibrinolytic treatment:**
  - **Anti-platelet:** ASA (clopidogrel if ASA allergic)
  - **Anti-coagulant:** UFH or LMWH

Candidates for Fibrinolytics

1. **Patients with STEMI:**
   - Who present within 12 hours of onset of ischemia
   - Who present within 12-24 hours and have s/sx of ongoing ischemia
   - Who do not have any absolute contraindications to therapy (at risk for ICH)
2. **Time to receiving hospital for PCI > 120 min vs immediate administration of fibrinolytic**
3. Patients with NSTEMI are not candidates unless they develop ST-segment elevation
4. PCI preferred in patients at higher risk for bleeding

ACC/AHA STEMI Guidelines 2013

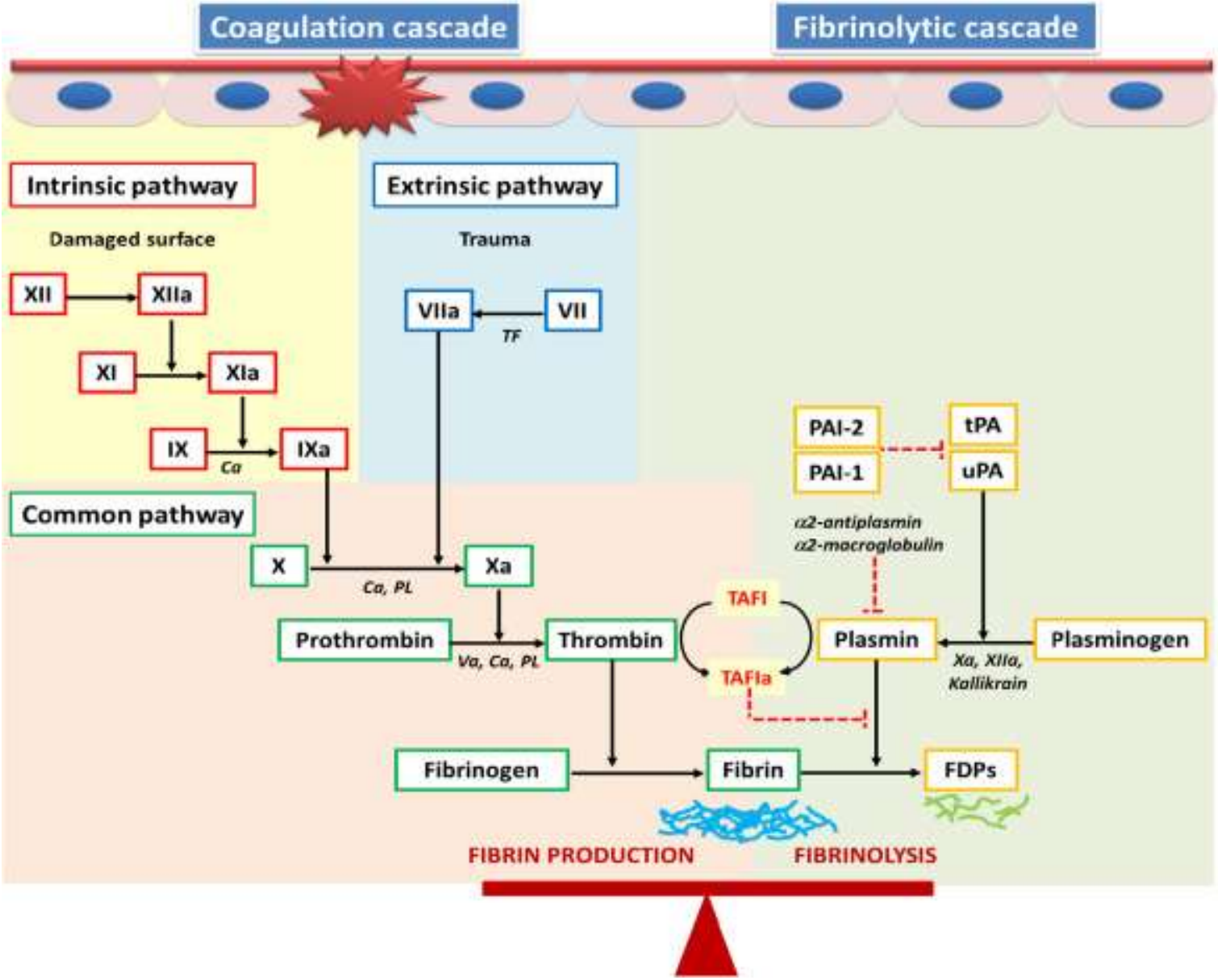
Time is Tissue!



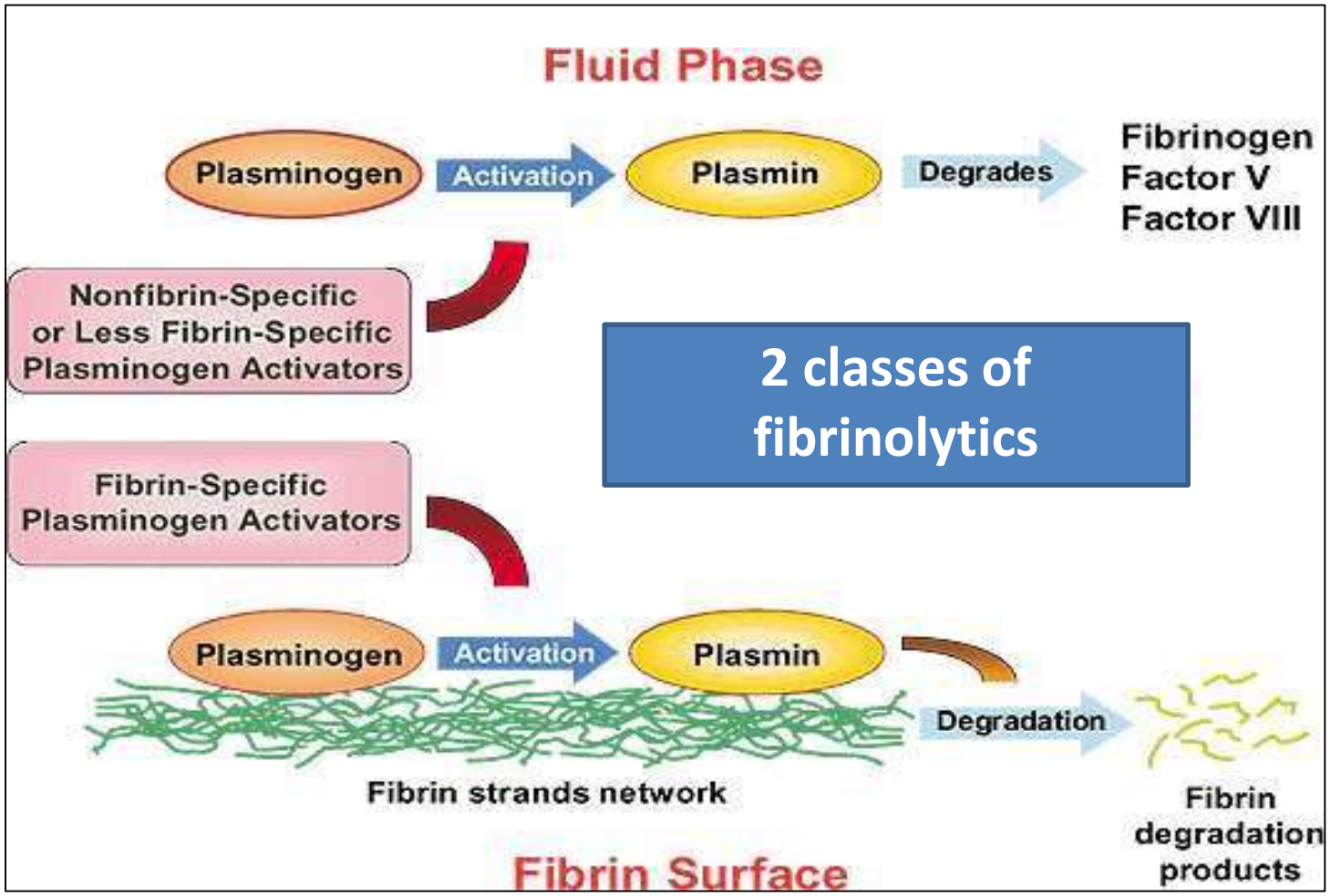
If used within the first hour of MI onset, fibrinolytics can save 50 lives per 1000 patients treated.

Circulation 1998;97:1632-1646

Coagulation and Fibrinolytic Cascades



Fibrinolytics and the Coagulation Cascade



- Fibrinolytics enhance the conversion of plasminogen to plasmin
- Plasmin dissolves the stable, fibrin-rich clots associated w/STEMI

Fibrinolytic Options

1. Non-fibrin specific: Streptokinase, Urokinase, and Anistreplase
2. **Fibrin specific:**
   - **Alteplase:** 15mg IV bolus, 0.75mg/kg IV over 30 min (max 50mg), then 0.5 mg/kg IV (max 35mg) over 60 min (max total dose 100mg)
   - **Reteplase:** 10 units IV x 2 doses 30 min apart
   - **Tenecteplase:** 30mg (< 60kg), 35mg (60-69kg), 40mg (70-79kg), 45 mg (80-89mg), or 50mg (>/= 90 kg) IV x 1 dose

Comparison of Fibrin-Specific Fibrinolytics

	Alteplase	Tenecteplase	Reteplase
Human TPA Derivation	Recombinant DNA of tPA	Mutant of human wild-type	Mutant of human wild-type
Dosing	Bolus and infusion	Single bolus	Double bolus
Fibrin specific	**++**	**++++**	**++**
90 min TIMI 2 or 3 flow rate achieved	**73-84%**	**85%**	**84%**
ICH (%)	0.62-0.94	0.93	0.77-1.2

Clev Clinic J of Med 2004;71:20-37; Circulation 2001;103:2862-6; 2013 STEMI guidelines

Efficacy of Fibrinolytic Therapy

- **Resolution of symptoms**
- **Restoration of hemodynamic stability**
- **Reduction in cardiac marker levels**
- **Resolution of ST-segment elevation**
  - 50% or more reduction in elevated ST-segment within 60-90 minutes
- Characterization of flow (TIMI grading)
  - Grade 0: complete blockage of infarct-related artery
  - Grade 3: complete perfusion of artery with normal flow

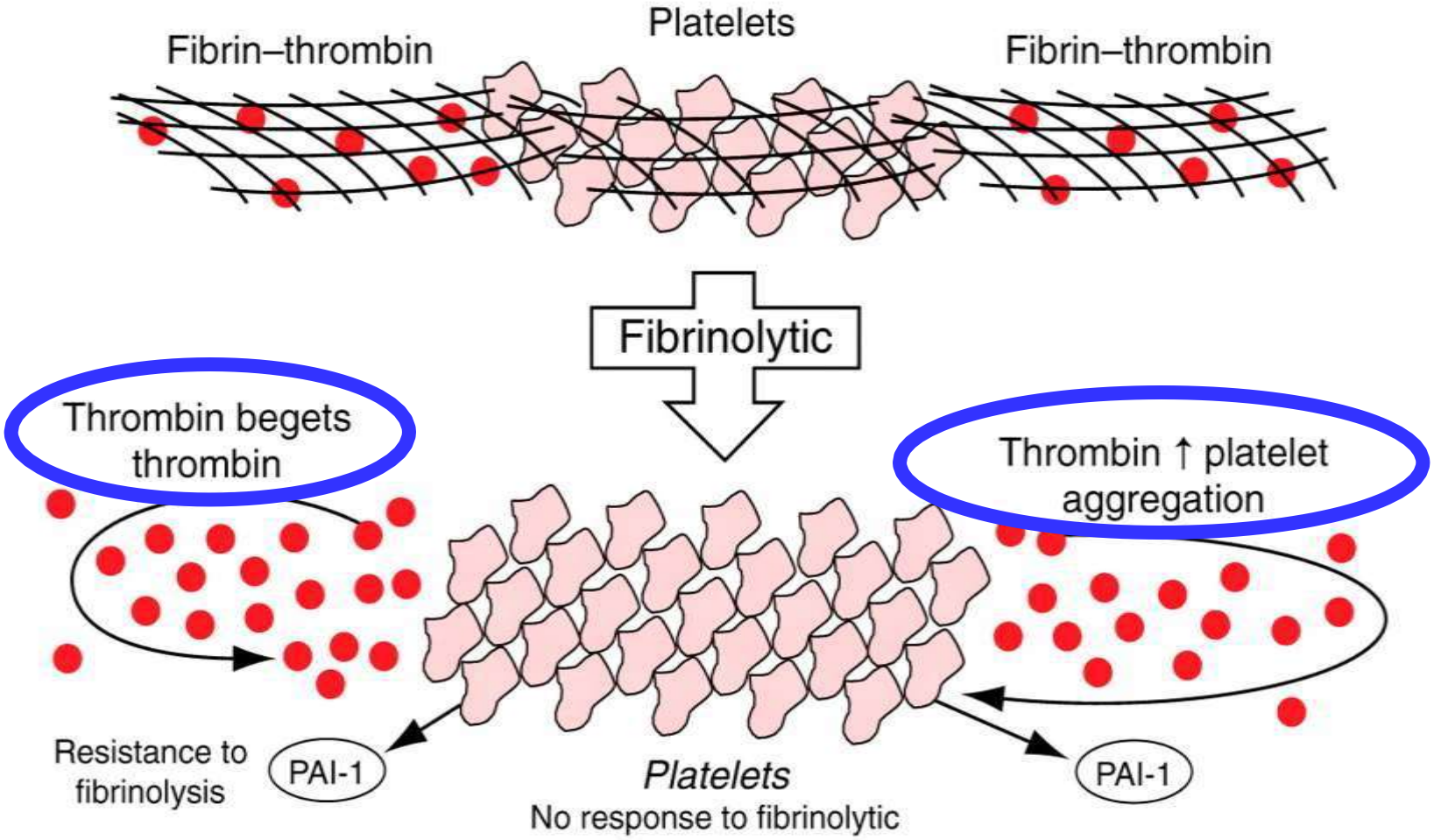
Fibrinolytic Side Effects

- Hypotension
- Bleeding
- Intracranial hemorrhage- Who's at risk?
  - Female gender
  - Black ethnicity
  - Elderly
  - Low body weight
  - H/O cerebrovascular disease, stroke, or TIA
  - Elevated BP

Fibrinolytic Side Effects Continued

- Re-occlusion
  1. Distal micro-embolization of plaque content
  2. Fibrinolytic therapy has pro-coagulant potential
     - Exposure of clot-bound thrombin (factor II) is a potent platelet activator
     - Activated platelets secrete plasminogen activator inhibitor-1 (PAI-1) and alpha-2 antiplasmin
  - **Fibrinolytic therapy mandates concomitant anti-platelet and anti-coagulant therapies**
    - Aspirin or clopidogrel if ASA allergic (target platelets)
    - UFH, enoxaparin, fondaparinux (target thrombin)

Prothrombotic Effects of Fibrinolytics



Topol E J Heart 2000;83:122-122

Post-Fibrinolytic Monitoring

- **Monitoring Efficacy:**
  - Pain
  - Hemodynamic stability
  - EKG
  - Biomarkers
  - ❖ **Reperfusion arrhythmias**
- **Monitoring SE:**
  - BP
  - H/H
  - Platelet count
  - aPTT
  - Fibrinogen level
  - Fibrin degradation products level
  - ❖ **Reperfusion arrhythmias**

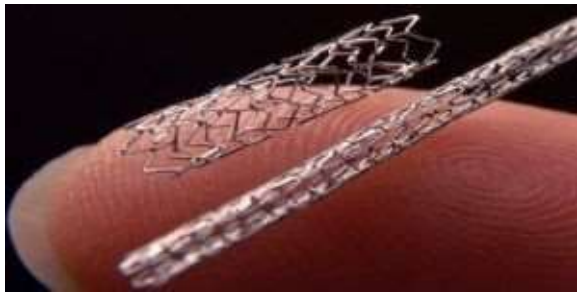
Reperfusion Therapy: Primary PCI

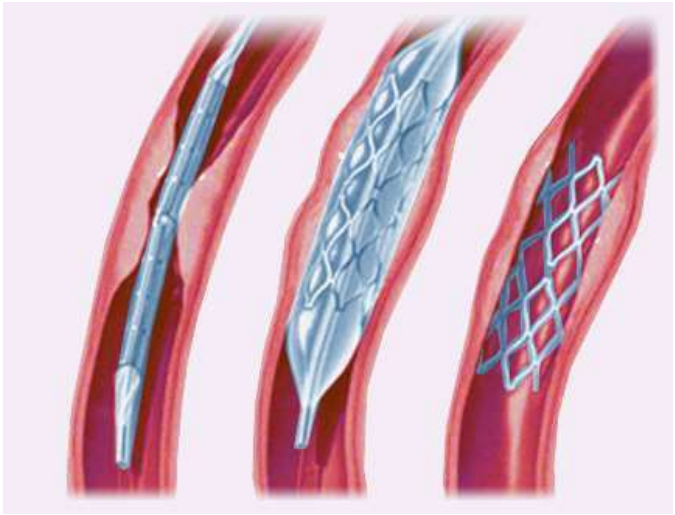
- **PCI is superior to fibrinolytic therapy for STEMI patients in facilities that can perform it**
  - Goal: PCI within 90 minutes of admission (or < 120 min FMC-device time)

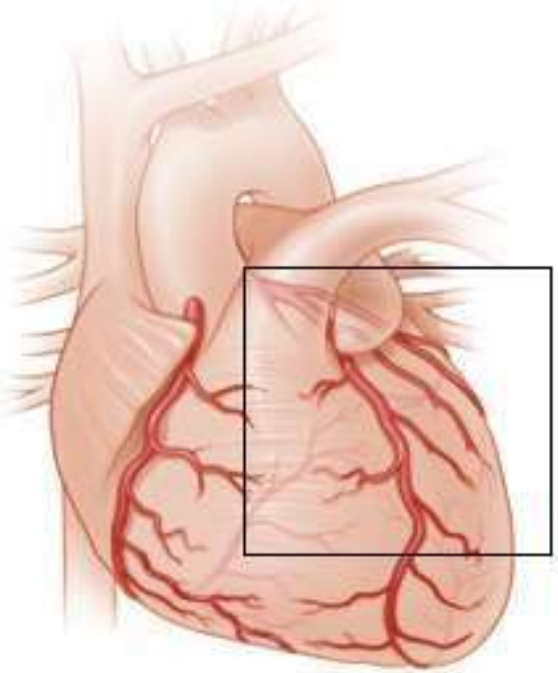
- **Timing for UA/NSTEMI- depends on risk**
  - High risk = early intervention for hemodynamically unstable patients, those with refractory angina, s/sx of HF, sustained VT, PCI within 6 months, prior CABG
  - Low risk = conservative treatment first (meds) then intervention for stabilized patients

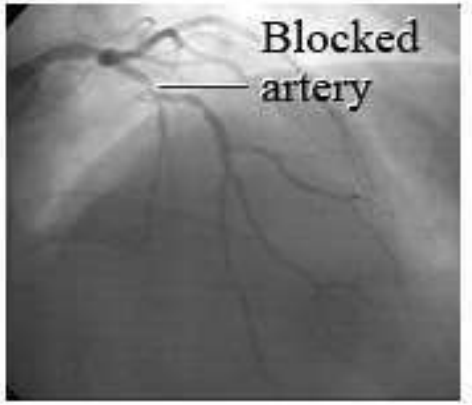
2013 STEMI Guidelines, 2014 NSTE ACS Guidelines

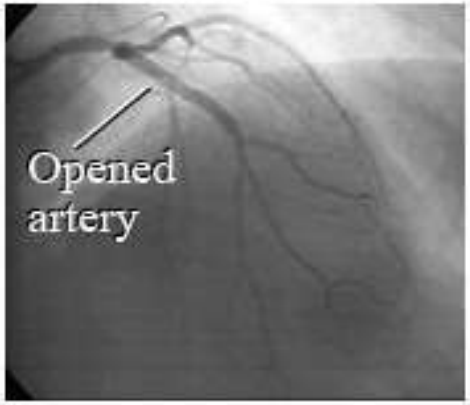
PCI = Angioplasty with Stent Placement







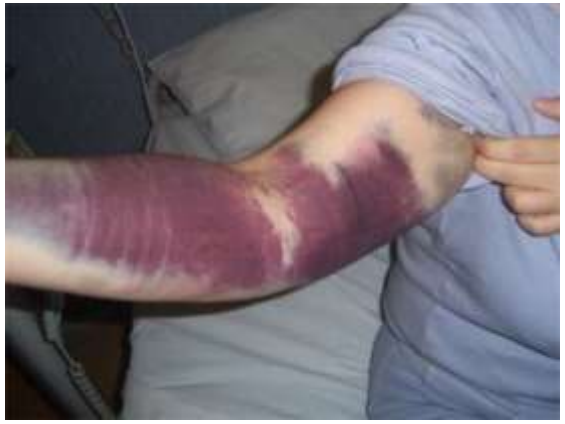




Two types of stents: BMS, DES

Complications with PCI

- Coronary artery complications:
  - dissection, periprocedural MI, perforation, thrombosis, restenosis
- Vascular access complications:
  - Bleeding, limb ischemia
- Contrast dye exposure:
  - Allergic reaction, acute kidney injury



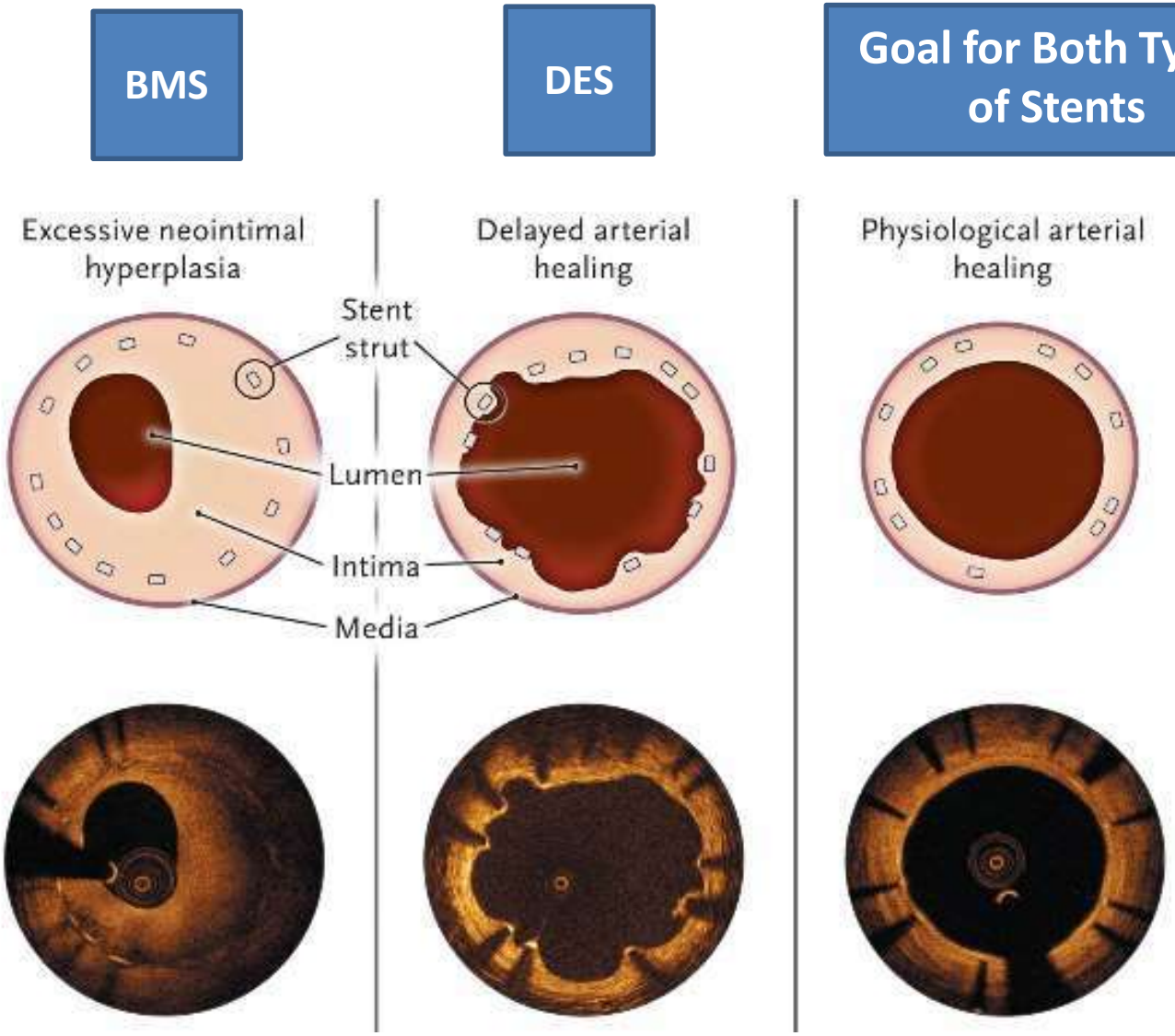
PCI Complications Continued

- **Thrombosis:**
  - Anti-thrombotic therapies are required before, during and after PCI to inactivate platelets and prevent re-occlusion of previously blocked coronary artery:

    1. Anti-platelet (before, during, & after): ASA in combo with a P2Y12 inh and/or glycoprotein IIb/IIIa inhibitor

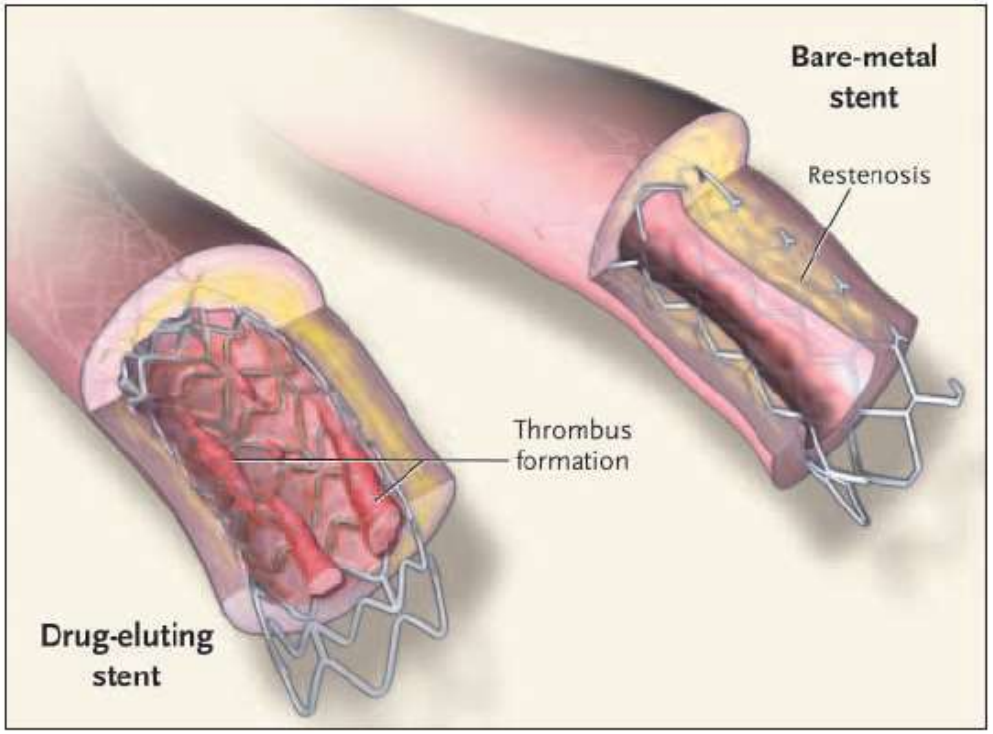
    1. Anti-coagulant (before & during PCI): UFH, LMWH, DTI, or Factor Xa inh (before PCI only)

Stent Complications- Restenosis



NEJM 2013;368:254-65

Stent Complications Summary



Contrasting Mechanisms of Obstruction of Bare-Metal Stents and Drug-Eluting Stents.

Bare-metal stents may be narrowed or obstructed by ingrowth of tissue. With drug-eluting stents, this process is inhibited, but since the struts remain uncovered, they may be prone to thrombosis after antiplatelet therapy is discontinued.

Complications Summary:

- Stent restenosis risk: BMS > DES
- Stent thrombosis risk: DES > BMS

JAMA 2008;532-539

Selection of stent type is dependent on patient's ability to take DAPT!

Thank-you!