



**Acute Coronary Syndrome**



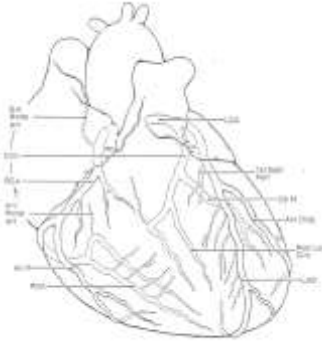
STEMI  
NSTEMI  
Unstable Angina

*Cherry Hermitage*  
Pharmaceutical Consultant  
LIFE TO LIVE



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Quick Review



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## Acute Coronary Syndrome (ACS)

- Umbrella term for a group of thrombotic coronary artery disease conditions that cause myocardial ischemia
- These syndromes represent progression of occlusion in the involved coronary artery
  - **STEMI** (ST segment Elevation Myocardial Infarction)
  - **NSTEMI** (Non-ST Segment Elevation Myocardial Infarction)
  - **Unstable Angina**

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## ♥ Heart Attack Signs & Symptoms for Males

- ♥ **Chest Pain**
- ♥ **Pain radiating down arms**
- ♥ **Jaw Pain**
- ♥ **Sweating**
- ♥ **Nausea**



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## Heart Attack Signs & Symptoms for Women

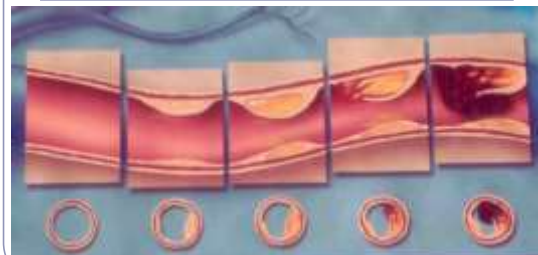
- ♥ **“Atypical” Chest Pain**
- ♥ **Shortness of Breath/ Trouble Breathing**
- ♥ **Tingling of Fingers**
- ♥ **Extreme Fatigue**
- ♥ **Heartburn / Nausea**
- ♥ **Sweating**
- ♥ **Dizziness**
- ♥ **Feeling of Apprehension or Impending Doom**



Even if they recognize the symptoms, women hesitate to call 911, and get to the hospital **40 to 60 minutes later** than men

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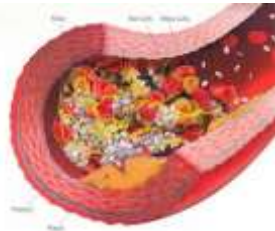
## Atherosclerosis



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### Cascade effects of atherosclerotic plaque rupture


- Platelet aggregation
- Fibrin accumulation
- Thrombus formation
- Bleeding into the plaque
- Vasospasm




ARTERY OCCLUSION

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### STEMI ST Segment Elevation Myocardial Infarction



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### Time Is Muscle

Muscle is Ejection Fraction

Ejection Fraction is Quality of Life

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### We Can STOP Heart Attacks!



• Goal: OPEN THE ARTERY!

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### Target

**Door to Balloon < 90 minutes**  
(Class 1, Level A)

or

**Door to Needle < 30 minutes**  
(Class 1, Level B)

ACC/AHA 2013 Guidelines for Management of STEMI

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### Fibrinolytic Therapy When There Is an Anticipated Delay to Performing Primary PCI Within 120 Minutes of FMC

**I IIa IIb III**  
A


In the absence of contraindications, fibrinolytic therapy should be given to patients with STEMI and onset of ischemic symptoms within the previous 12 hours when it is anticipated that primary PCI cannot be performed within 120 minutes of FMC.

**I IIa IIb III**  
C

In the absence of contraindications and when PCI is not available, fibrinolytic therapy is reasonable for patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia within 12 to 24 hours of symptom onset and a large area of myocardium at risk or hemodynamic instability.

**I IIa IIb III**  
B  
Harm

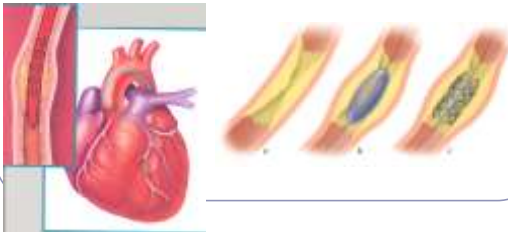
Fibrinolytic therapy **should not be administered** to patients with ST depression except when a true posterior (inferobasal) MI is suspected or when associated with ST elevation in lead aVR.



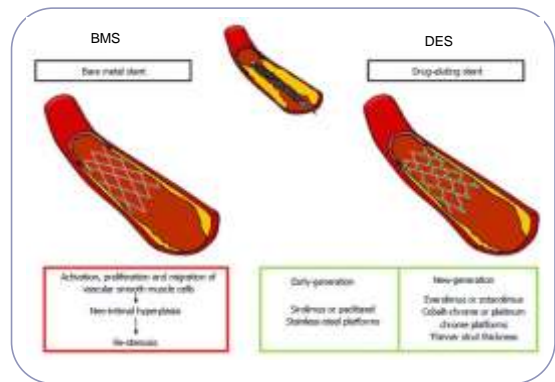
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## Open the Artery STEMI

- Goal: Have artery open < 90 minutes after arrive at ED



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Reference: www.wjnet.com/1949-8462/full/v9/i3/207.htm

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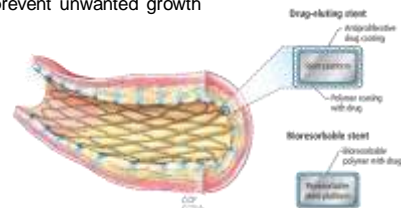
## Bare Metal Stents (BMS)

- Early bare metal stents showed a high rate of in-stent re-stenosis.
  - Stent-mediated arterial injury elicited neointimal hyperplasia, leading to restenosis and the need for repeat revascularization in up to one third of patients
- Used in patients
  - With high bleeding risk
  - Inability to comply with 1 year of DAPT (dual antiplatelet therapy)
  - With anticipated invasive or surgical procedures in the next year (Class I, Level C)

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## Drug Eluting Stents (DES)

- DES deliver medicine into the arterial tissue and prevent unwanted growth



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## Drug Eluting Stents



Harm

DES should not be used in primary PCI for patients with STEMI who are unable to tolerate or comply with a prolonged course of DAPT because of the increased risk of stent thrombosis with premature discontinuation of one or both agents.

## Adjunctive Antithrombotic Therapy to Support Reperfusion With Primary PCI

	OR	LR
<b>Antiplatelet therapy</b>		
<b>Aspirin</b>		
• 162- to 325-mg load before procedure	✓	✓
• 81- to 325-mg daily maintenance dose (indicated)	✓	✓
• 81 mg daily to the preferred maintenance dose*	✓	✓
<b>P2Y<sub>12</sub> inhibitors</b>		
<b>Loading doses</b>		
• Clopidogrel 600 mg as early as possible or at time of PCI	✓	✓
• Prasugrel 60 mg as early as possible or at time of PCI	✓	✓
• Ticagrelor 180 mg as early as possible or at time of PCI	✓	✓

\*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.



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Adjunctive Antithrombotic Therapy to Support Reperfusion With Primary PCI (cont.)

**P2Y<sub>12</sub> Inhibitor**

Maintenance doses and duration of therapy

DES placed: Continue therapy for 1 yr with

- Clopidogrel, 75 mg daily
- Prasugrel, 10 mg daily
- Ticagrelor, 90 mg twice a day\*

BMS placed: Continue therapy for 1 yr with:

- Clopidogrel, 75 mg daily
- Prasugrel, 10 mg daily
- Ticagrelor, 90 mg twice a day\*

DRY patient

\*Clopidogrel, prasugrel, or ticagrelor continued beyond 1 yr

\*Patients with 0-100% restenosis after 1 yr prasugrel

DES and BMS need DAPT for one year -- ASA and P2Y12 Inhibitor

	DES	BMS
1	1	1
2	1	1
3	1	1
4	1	1
5	1	1
6	1	1
7	1	1
8	1	1
9	1	1
10	1	1

\*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

\*Balloon angioplasty without stent placement may be used in selected patients. It might be reasonable to provide P2Y<sub>12</sub> inhibitor therapy to patients with STEMI undergoing balloon angioplasty alone according to the recommendations listed for BMS. (LOE C).

Helping Cardiovascular Professionals Learn, Advance, Thrive

American Heart Association

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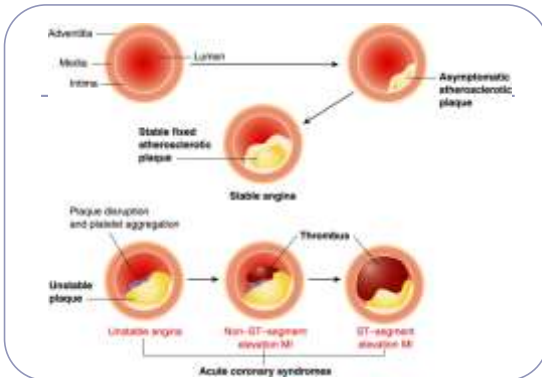
**NSTEMI**

Non ST Segment Elevation MI



- No ST segment Elevation
- ST segment depression

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**STEMI**

Both elevated Troponins

PCI < 90 minutes

**NSTEMI**

PCI within 24 - 48 hours

Inversion of the T wave

Depression of ST segment

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Differentiating MIs

**Non-STEMI**

- T wave inversion (ischemia)
- ST depression (injury)
- Laboratory values are diagnostic

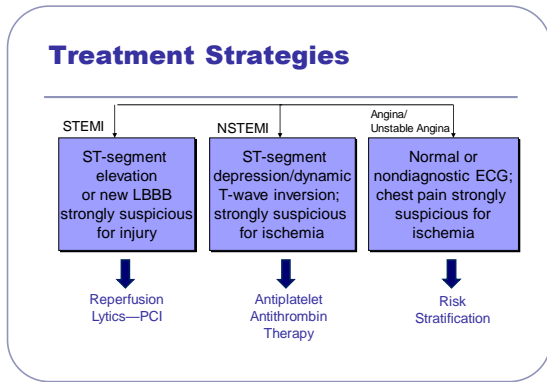
**STEMI**

- T wave inversion (ischemia)
- ST elevation (injury)
- Q wave (infarct)
- Laboratory values are diagnostic

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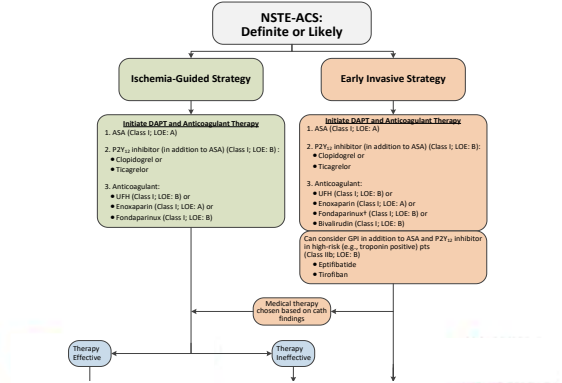
Types of Angina	Definition
Angina	Myocardial Anoxia
Exertional Angina (4 Es) (usually sign of atherosclerosis)	Pain with increased myocardial oxygen demand <ul style="list-style-type: none"> <li>• Exertion</li> <li>• Eating</li> <li>• Extreme Emotions</li> <li>• Exposure to Cold</li> </ul>
Prinzmetal's Angina or Variant Angina (thought to be a coronary spasm)	Pain at rest, during sleep or without evidence of provocation
Stable Angina	Exertional angina with consistent symptoms –typically relieved with rest or cessation of cause and possibly NTG
Unstable Angina (crescendo or preinfarction angina) Partially occluding thrombus	Recent onset (within 2 months) Severely limits activity Differs from the person's "typical exertional angina" May occur at rest RX with Anti-platelets Fibrinolytic therapy <i>is not</i> effective

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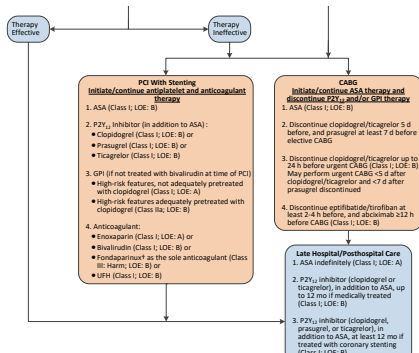


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Algorithm for Management of Patients With Definite or Likely NSTEMI-ACS



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<sup>1</sup>In patients who have been treated with fondaparinux (as upfront therapy) who are undergoing PCI, an additional anticoagulant with anti-IIa activity should be administered at the time of PCI because of the risk of catheter thrombosis.

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### Nitrates

- Cause vascular smooth muscle relaxation to increase coronary blood flow
- Reduce preload
  - Decrease cardiac wall tension
  - Decrease myocardial oxygen demand
- Short acting
  - IV
  - SL or spray
  - Ointment
- Long acting
  - Isosorbide Dinitrate
  - Isosorbide Mononitrate
  - Calcium channel blockers can be an alternative especially if uncontrolled HTN

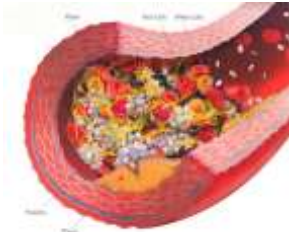
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### Nitrate contraindications

- Hypotension
- Severe aortic stenosis
- Right ventricular infarction
- Hypertrophic obstructive cardiomyopathy
- Patients who recently received a phosphodiesterase inhibitor
  - Within 24 hours of sildenafil or vardenafil or within 48 hours of tadalafil

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### Anticoagulation Pharmacology



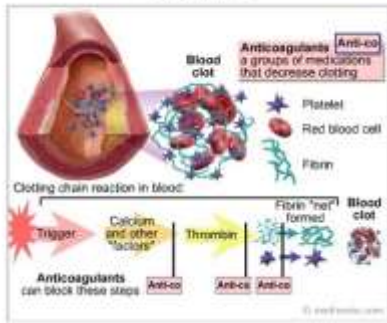
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### Clotting Cascade is like a freeway with multiple entrances



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### Anticoagulants



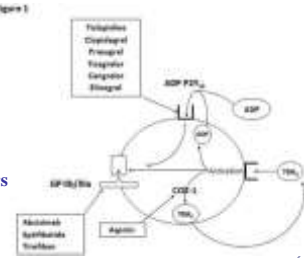
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### Antiplatelets

#### P2Y12 (ADP) platelet inhibitor

- Clopidogrel (Plavix®)
- Prasugrel (Effient®)
- Ticagrelor (Brilinta®)

Figure 1



#### Inhibition of platelet COX-1

- ASA

#### IIb/IIIa Receptor Inhibitors

- Abciximab (Repro)
- Eptifibatid (Integrilin)
- Tirofiban (Aggrastat)

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### Oral Anticoagulants Used for Atrial Fibrillation, PE, DVT

#### Direct thrombin inhibitor

- Dabigatran (Pradaxa) \*
- Praxbind for reversal

#### Factor Xa inhibitor

- Rivaroxaban (Xarelto)\*
- Apixaban (Eliquis)\*
- Edoxaban (Savaysa™)

#### Vitamin K Antagonist

- Warfarin (Coumadin)
- Vitamin K, FFP for reversal



\* = NOAC or Novel oral anticoagulants

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### Stent patient who has Afib

- Dual platelet therapy for stent
  - ASA for one month
  - Plavix, Brilinta, or Effient
- Anticoagulation for Afib, PE, DVT
  - Coumadin
  - Xarelto
  - Eliquis
  - Pradaxa

Question if they should be on triple anticoagulation therapy.... Very, Very High risk for bleeding

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## What's the common complication of all the anticoagulants?

Bleeding!

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**Table 8. CAMs That Increase Bleeding Risk With Anticoagulants via Platelet and/or Clotting Factor Effects<sup>20a</sup>**

Antiplatelet Effects	Anticoagulant Effects
Dan Shen	Dong quai
Ginkgo	Motherwort
Ginkgo	Liquorice
Motherwort	
Saw palmetto	
Hawthorn	
Liquorice	

CAM indicates complementary and alternative medicine.

Reference: AHA Scientific Statement: *Drugs that may Cause or Exacerbate Heart Failure*. *Circulation* 2016; 632 – e 69. :

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## What Happens after MI?



### Ventricular Remodeling

Alterations in the heart's size, shape, structure, and function brought about by the chronic hemodynamic stresses experienced by the failing heart.

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## Ventricular remodeling in the infarcted area

- Dilation & ventricular wall thinning
- Increased wall stress on the healthy myocardium
- Sets the stage for Heart Failure
- ACE Inhibitors reduce remodeling & prevent the progression of heart failure

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## Heart Failure is the nation's most rapidly growing cardiac problem.

- About 22% males & 46% female MI patients will be disabled with Heart Failure within 6 years.

50% Heart Failure Patients die within 5 years of HF diagnosis



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## AMI Medications

- ASA
- ACE inhibitor if EF < 40%
- Beta blocker
- Statin
- Antiplatelet if stent
- Smoking Cessation Counseling

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## Goals After Myocardial Infarction

### Reducing the risk of another heart attack

- ASA
- Antithrombotic therapy
- Beta-blockers
- Statins
- ACE inhibitors

### Reducing the risk of heart failure

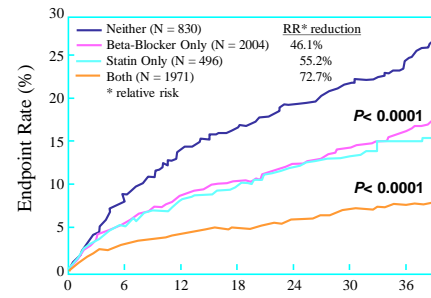
- ACE inhibitors
- Aldosterone antagonists
- Beta-blockers

### Reducing the risk of sudden cardiac death

- Life vest
- ICD therapy

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## Statins and Beta-blockers: 1-yr Mortality after Acute MI with HF



OPTIMAAL study

Hogstad et al. Am J Cardiol. 2004;93:603

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## β-Blockers

Limit the donkey's speed, thus saving energy



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## Beta Blockers STEMI & NSTEMI

- Initiate in the first 24 hours (Class I, Level B)
- Continue during & after hospitalization (Class I, Level B)
- Patients with initial contraindications to the use of beta blockers in the first 24 hours after MI should be reevaluated to determine their subsequent eligibility (Class I, Level C)
- Initiate EBP BB for stabilized HF with EF < 40% (Class I, Level C)
  - Sustained-release metoprolol succinate, carvedilol, or bisoprolol.

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## Beta Blocker "Olois"

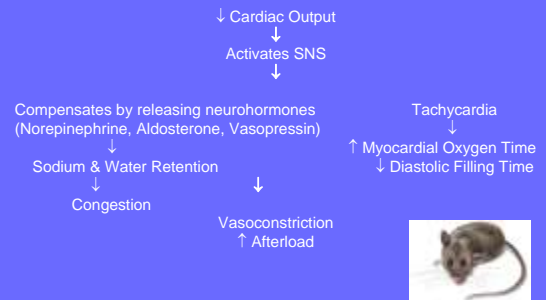
### Beta Blockade of the Sympathetic Nervous System

- Decrease oxygen demand
  - ↓ HR & contractility
  - Vasodilate
  - ↓ Afterload
  - ↓ O<sub>2</sub> wastage
- Antiarrhythmic effect
- Increase oxygen supply
  - Increased diastolic perfusion
  - Less exercise vasoconstriction

Side effect: May promote spasm in vasospastic angina

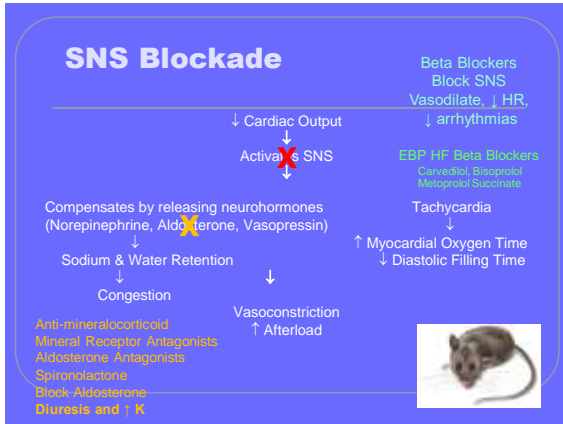
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## SNS Activation



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### Beta Blockers "Olois"

•Acebutolol	Sectral
•Atenolol	Tenormin
•Betaxolol	Kerlone
•Bisoprolol*	Zebeta
•Carvedilol*	Coreg
•Metoprolol Tartrate	Lopressor
•Metoprolol Succinate*	Toprol XL
•Nadolol	Corgard
•Pindolol	Visken
•Propranolol	Inderal
•Timolol	Blocadren

\* EBP HF BB

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### Beta Blocker

Side Effects	Contraindications
<ul style="list-style-type: none"> <li>• Bradycardia</li> <li>• Hypotension</li> <li>• Erectile Dysfunction</li> <li>• Fatigue</li> </ul>	<ul style="list-style-type: none"> <li>• Signs of heart failure</li> <li>• Low output state</li> <li>• Risk of cardiogenic shock</li> <li>• Hypotension</li> <li>• Bradycardia</li> <li>• PR interval &gt;0.24</li> <li>• Second or third-degree heart block without a pacemaker</li> <li>• Active asthma or reactive airway disease</li> </ul>

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### Cocaine and Methamphetamine Users

Recommendations	COR	LOE
Patients with NSTEMI-ACS and a recent history of cocaine or methamphetamine use should be treated in the same manner as patients without cocaine- or methamphetamine-related NSTEMI-ACS. The only exception is in patients with signs of acute intoxication (e.g., euphoria, tachycardia, and/or hypertension) and beta-blocker use, unless patients are receiving coronary vasodilator therapy.	I	C
Benzodiazepines alone or in combination with nitroglycerin are reasonable for management of hypertension and tachycardia in patients with NSTEMI-ACS and signs of acute cocaine or methamphetamine intoxication.	IIa	C
Beta blockers should not be administered to patients with ACS with a recent history of cocaine or methamphetamine use who demonstrate signs of acute intoxication due to the risk of potentiating coronary spasm.	III: Harm	C

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- ### Renin-Angiotensin-Aldosterone System Inhibitors
- ACEI: initiate within the first 24 hours (Class I a)
    - STEMI with anterior location
    - HF with EF < 40% (STEMI and NSTEMI)
  - ARB if intolerant to ACEI (Class I b)
  - ACE inhibitors are reasonable for all patients with MI and no CI to their use (Class II a)
  - Aldosterone antagonist: Initiate on patients who are already receiving an ACE inhibitor and beta blocker and who have an EF <40% and either symptomatic HF or diabetes mellitus (Class I b)

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- ### Statins help prevent recurrent MI
- Statins have pleiotropic effects (more than one benefit)
  - Anti-inflammatory and antithrombotic properties and antioxidant effects help prevent recurrent MI
  - Also lower cholesterol
  - High-intensity statin therapy should be initiated or continued in all MI patients (Class I b)

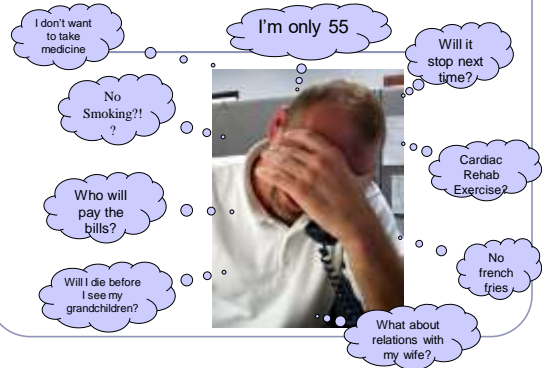
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## Lipid – Lowering Agents

- Statins
  - atorvastatin (Lipitor)
  - cerivastatin (Baychol)
  - fluvastatin (Lescol)
  - lovastatin (Mevacor)
  - pravastatin (Pravachol)
  - simvastatin (Zocor)
- Fibric Acid Derivatives
  - gemfibrozil (Lopid)
  - micronized fenofibrate (Tricor)
  - clofibrate (Atromid-S)
- Bile Acid Resins
  - colestipol (Colestid)
  - cholestyramine (Questran, Questran Light, Prevalite, LoCholest)
  - colesvelam (Welchol)
- Niacin (Niaspan and other various brands)

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## Psychosocial Aspect AMI



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## Cardiac Testing



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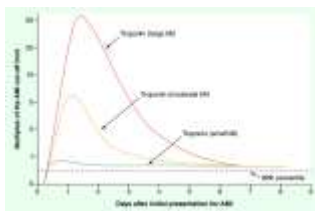
## Elevated Troponin 0.40 ng/mL and higher



### Ischemic Heart Disease

STEMI, NSTEMI

- Elevates in 4 hours and stays elevated for days
- New ischemic EKG changes
- Clinical history suggests ischemia
- New wall motion abnormality



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## Elevated Troponins Is it ischemic heart disease ????

	1	2	3	4	5
	6/20/2018	6/21/2018	6/24/2018	6/26/2018	6/27/2018
CARDIAC PROFILE					
Troponin I	0.007	0.425 *	1.020 *	1.721 *	1.085 *

- EKG changes???
- Clinical history
  - Symptoms – what's their story???
  - Family history
- What else is going on???

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**What would you do if this was the EKG?**

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	5	4	3	2	1
	6/28/2018	6/28/2018	6/28/2018	6/28/2018	6/28/2018
	1:00	1:07	1:05	1:15	1:02
CARDIAC PROFILE	<0.01	0.42*	1.00*	1.22*	1.86*
Troponin I					

Sinus Tachycardia  
 Probable Left Atrial Enlargement  
 Repolarization abnormalities, probable ischemia, anterolateral leads  
 Prolonged QT

Treat as NSTEMI – will need cardiac cath

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**What would you do if this was the EKG?**

	5	4	3	2	1
	6/28/2018	6/28/2018	6/28/2018	6/28/2018	6/28/2018
	1:00	1:07	1:05	1:15	1:02
CARDIAC PROFILE	<0.01	0.42*	1.00*	1.22*	1.86*
Troponin I					

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**Other Causes Elevated Troponins**

	5	4	3	2	1
	6/28/2018	6/28/2018	6/28/2018	6/28/2018	6/28/2018
	1:00	1:07	1:05	1:15	1:02
CARDIAC PROFILE	<0.01	0.42*	1.00*	1.22*	1.86*
Troponin I					

- Demand Ischemia
  - Mismatch between myocardial oxygen demand and supply
  - Ischemia with no critical CAD

Troponin concentrations of **0.04-0.39 ng/mL** require serial troponin measurements and clinical correlation to interpret

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**Causes Demand Ischemia**

- Tachycardia, bradycardia or heart block
  - Atrial Fibrillation with rapid ventricular response
- Critically ill
  - Sepsis, diabetes, respiratory failure
- Heart Failure Exacerbation
- Acute and Chronic Kidney Disease
- Hypoxia
- Rhabdomyolysis
- Cardiac contusion or other trauma
  - Cardioversion or Defibrillation
- Acute Stroke

Be especially concerned if elevated troponin and EKG changes

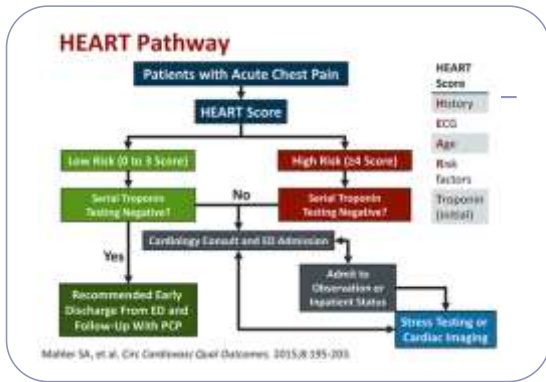
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**Chest Pain Approach to Evaluation**

	ECG	Troponin	Diagnosis
Low Likelihood	⊖	⊖	• Non-cardiac
	⊖	+	• UA
	⊖	++	• Other cardiac
	+	+	• NSTEMI
	+	++	• STEMI

Antzerden EA, et al. Circulation. 2014;130:e344-e426.

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[https://www.medscape.org/viewarticle/862168\\_2](https://www.medscape.org/viewarticle/862168_2)

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### Before ordering stress test

- Get 12 Lead EKG
- Is the appropriate stress test ordered?
  - Identify what test is indicated for what you want to know.
  - Why are we doing the test? What question/symptom are we trying to answer?
  - Is the stress test appropriate for the patient – can they walk?
  - What are the contraindications for the test you ordered?
- Nuclear Medicine tests
  - Pregnancy test prior on all women < 55y/O

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### Pre Stress: Questions to ask patient

- What brought you in?
- Can you walk on a treadmill – how far can you walk?
- Chest pain with exertion?
- Identify Cardiac Risk Factors
  - Previous heart history
  - High blood pressure
  - High Cholesterol
  - Diabetes
  - Smoke
  - Family history
- Listen to lung sounds (wheezes or crackles) and for a murmur
- Check H & H – don't do if < 9
- If come in with chest pain, need 2 negative troponins at least 6 hours apart, ideally 8 hours apart before doing stress test.
- Hold beta blockers or NTG because masks effects.

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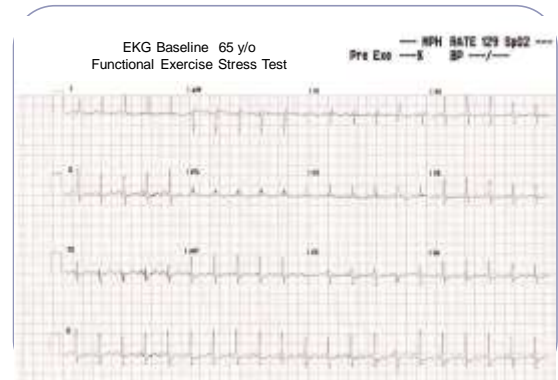
### Exercise Stress Test (EST) Functional Stress

- Initial test to evaluate for suspected or known heart disease
- Indicated for stable, low and intermediate risk patients
- Exercise stress protocols (Bruce) to exercise to target heart rate
  - $(220 - \text{age}) \times .85$  for minimum
- 70 – 80% sensitivity & 60 – 75% specificity for identification of ischemic heart disease
- High risk findings
  - ST depression > 3 mm
  - SBP > 220
  - Significant angina

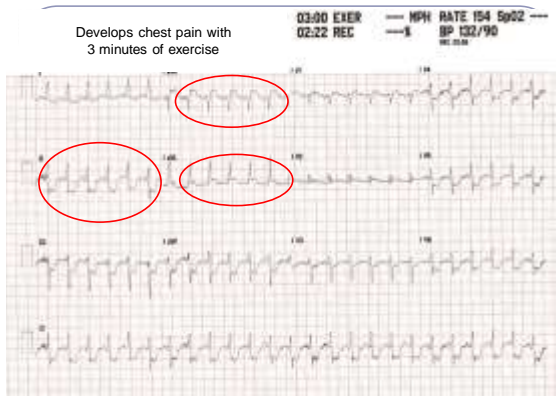
#### Contraindications

- Ischemic changes – MI in past 2 days
- Severe Aortic Stenosis
- LBBB
- Uncontrollable arrhythmias
- Hypertension
- Syncope
- Afib – need to do chemical
- PE – If lung scan is ordered, make sure it is negative before doing a stress test.
- Acute aortic dissection
- Pacing may be CI – if can't get HR up.

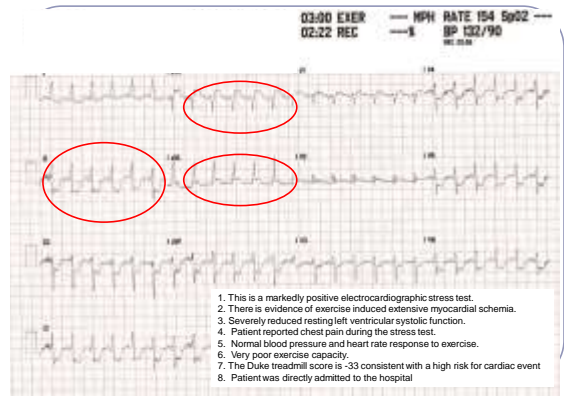
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### Sent for Coronary Angiogram

#### CONCLUSION

- Ischemic cardiomyopathy, left ventricular ejection fraction 35%.
- Severe coronary artery disease involving the left main and left anterior descending.
- Percutaneous transluminal coronary angioplasty of the left anterior descending was performed.
- Unable to cross the stent due to the short left main and acute angulation of the left anterior descending and the left main.
- Coronary bypass surgery recommended.

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### Stress Echocardiogram

- EST or pharmacological stress test + echocardiogram to assess stress-induced changes in cardiac or pulmonary vascular function
- Indicated for patients with baseline EKG changes (ie repolarization) that limit interpretation of ischemic changes on EKG.
- Baseline echo images are obtained and then at maximal tolerated exercise
- Resting and post stress images are compared
- Exercise stress protocols (Bruce) or pharmacological agents (Dobutamine) to exercise to target heart rate
  - (220 - age) x .85 for minimum
  - Get Heart rate to 100 - 110% for at least 30 seconds because it will drop really fast. Need to get echo while HR is at least 85%.
- Contraindications similar to EST
- Positive Test
  - Worsening of regional wall motion on stress images when compared to resting images
- 85% sensitivity, 77% specificity to detect CHD

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### Stress SPECT MPI (Single Photon Emission Computed Tomography Myocardial Imaging)

- Radionuclide tracers detect blood flow to the myocardium under rest and stress conditions.
- Stress induced with exercise or pharmacologically (Adenosine or Lexiscan/Regadenoson)
  - Vasodilators produce maximal coronary hyperemia
  - Causes greater increase in blood flow in normal coronary arteries than arteries with flow-limiting stenosis
- EST to 85% target heart rate, then inject tracer, exercise at least one minute more
- If unable to exercise or get to target HR, use vasodilator
- Resting and post stress images are compared
- Confirms the diagnosis and estimates the severity of CHD
- Measures size, shape and EF of heart
- Indications
  - Patients in who CHD is suspected based on symptoms and history
  - To determine progression of known CHD
- Avoid caffeine 12 hours prior
- Caffeine used to reverse effects of vasodilators
- Contraindications similar to EST +
  - Active Bronchospasm
  - Restrictive airway disease
  - 2<sup>nd</sup> or 3<sup>rd</sup> degree heart block
  - Severe bradycardia

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## Application Time



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### CASE # 1

73 y/o scheduled for functional exercise stress test for evaluation of exertional dyspnea. PMH of CAD/myocardial bridging of the distal LAD with nonobstructive disease  
Is the appropriate test ordered?



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### CASE # 2

Patient scheduled for functional exercise stress test for abnormal EKG and murmur.  
What's abnormal on EKG?  
Is the appropriate stress test ordered?



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### Case #3

Admission EKG  
What's the Rhythm?  
What's your EKG interpretation?  
What's your action?



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## Discharged on Day 2

Troponin = 24  
Creatinine = 1.41  
LDL = 95  
BP 148/78, HR 68

- ASA 81 mg
- Atorvastatin (Lipitor) 80 mg
- Hydralazine 50 mg every eight hours
- Lisinopril 20 mg daily
- NTG SL 0.4 mg SL prn
- Brilinta 90 mg bid

Are these appropriate medications and doses?

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