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Author(s): Jeffrey Smith, M.D., George Washington University Medical Center; Jim Holliman, M.D., Pennsylvania State University

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Acute Coronary Syndromes

Jeffrey Smith, M.D., M.P.H.
George Washington University Medical Center
Jim Holliman, M.D.
Pennsylvania State University

Epidemiology

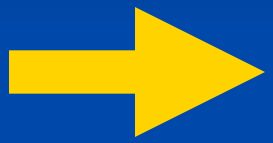
- Ischemic Heart Disease (IHD) is the leading cause of morbidity and mortality worldwide
- Over the next 10 years, IHD will become the leading cause of death and disability in most developing countries
- IHD is the leading cause of death in USA ; 1 million annually
- 50 % of all cardiovascular deaths occur in women
- Despite educational efforts, patients with Acute Myocardial Infarction (AMI) delay an average of 2 to 6 hours before seeking health care

Diagnosis remains a challenge

- Of the 1.25 million AMI's in the USA yearly, over 80 % present to the Emergency Department (ED)
- The history, exam and ECG can be nondiagnostic
- Past studies : 5 to 8% of AMI's are sent home
- Recent studies : 2 to 5% of AMI's are sent home
- Mortality doubles when AMI's are sent home

Acute Coronary Syndromes (ACS)

- Maintain high clinical suspicion
- Early recognition
- Early risk stratification



Optimize therapy

4 Areas of Delay

- Patient seeking care
- Early triage with ECG
- Delay in clinical decision to treat
- Treatment
  - Aspirin, oxygen, beta-blocker, Unfractionated heparin or Low Molecular Weight Heparin
  - Thrombolytics (door to drug in under 60 minutes)
  - Intervention (door to cath lab in under 2.2 hours)

ACS : Clinical Syndromes

- Angina
  - Class I (severe exertion) to IV (with any activity or at rest)
  - Fixed stenotic lesion ; stable precipitating and relieving factors
- Unstable Angina Pectoris (USAP)
  - Increasing frequency, transition to a higher class, pain at rest
- Variant (Prinzmetal's) angina
- AMI
  - 2 of 3 W.H.O. criteria :
    - clinical history or setting, ECG changes, positive cardiac markers
  - Non-ST Elevation (NSTE) ACS versus ST Elevation Myocardial Infarction (STEMI)
  - Various reperfusion and adjunctive therapies are based on the presence of ST segment elevation in the appropriate clinical setting

Pathophysiology of ACS

- Endothelial damage occurs by plaque disruption, irregular luminal lesions or shear injury
- Platelet aggregation is followed by thrombus formation
- Ischemia causing local mediator release and vasospasm
- Reperfusion injury
- In USAP spontaneous thrombolysis occurs rapidly.
- Persistence of occlusive thrombus for 60 to 90 minutes before spontaneous lysis results in a non-STE AMI.
- Transmural AMI occurs when the thrombus occlusion lasts for 2 to 3 hours.

History & Physical……and Atypical Presentations

- History is essential … but not diagnostic of ACS
  - only 20 to 30 % report crushing or pressure pain
- Beware of atypical presentations
  - Up to 20 % of ACS present with pain in other areas (arm, back, abdomen)
  - No pain in 25 % of diabetics
  - Burning pain in 15 % of USAP or AMI (may get relief with antacids)
  - Right sided radiation in up to 30 %
  - Chest wall tenderness in 15 % of AMI's
  - Anginal equivalent symptoms in 30 % of AMI's
    - Dyspnea, nausea, diaphoresis, back pain, jaw pain
    - Altered mental status (especially if > 85 y/o)
    - Mortality 3-fold greater (50 % vs 18 %)
  - High risk groups : young, elderly, diabetic
- Physical Exam most helpful in excluding noncardiac causes

Differential Diagnosis

- Causes of chest pain
  - Most are noncardiac and not serious
  - Acute coronary syndrome
  - Pulmonary embolism
  - Aortic dissection
  - Pericarditis / tamponade
  - Pneumothorax / tension pneumothorax
  - Pulmonary parenchymal process : pneumonia, inflammatory process, benign and malignant processes

Diagnostic Studies

- ECG
- Serial ECG's
- Cardiac enzymes

- Risk Stratify for other studies based on history, ECG, and above studies

The Electrocardiogram

- Advantages:
  - select appropriate therapy
  - determine response to treatment
  - determine inpatient disposition
  - predict complications / death

The Electrocardiogram

- Beware that the 12-lead ECG is diagnostic of transmural AMI in only 25 to 50 % of cases
- Non-specific ST / T-wave abnormalities
  - 6 % of transmural AMI's
  - 30 % of NSTE-AMI
  - 20 % of cases of unstable angina
- Completely normal in 3 to 4 % of transmural AMIs
- Serial ECGs may increase sensitivity by 10 to 20 %

The Electrocardiogram

- Nondiagnostic ECG seen in 50 %
  - Nonspecific ST-Twave (NSSTTW) changes
    - Less than 1 mm ST depression
    - Blunted, flattened or biphasic T waves
  - Low risk of AMI (4 %) yet 20 % risk of USAP
    - If good story & NSSTTW changes : ADMIT
- LVH, LBBB, VPR may mask signs of acute ischemia

The Electrocardiogram

- **Low-risk criteria**

  (14 % AMI, 0.6 % Cardiac events, 0 % mortality)

  - **Normal ECG**
  - **NSSTTW changes**
  - **Unchanged ECG**

- **High-risk criteria**

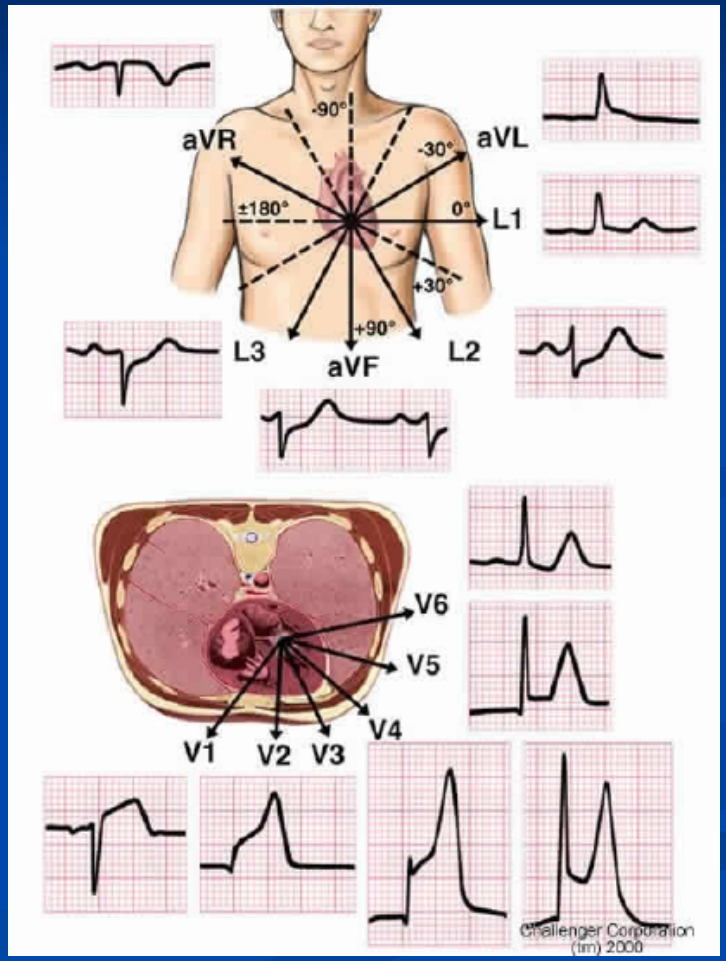
  (42 % AMI, 14 % Cardiac events, 10 % mortality)

  - **Ischemic ST segment or T wave changes**
  - **LVH, LBBB, VPR**

Q : ECG manifestation of STE- AMI

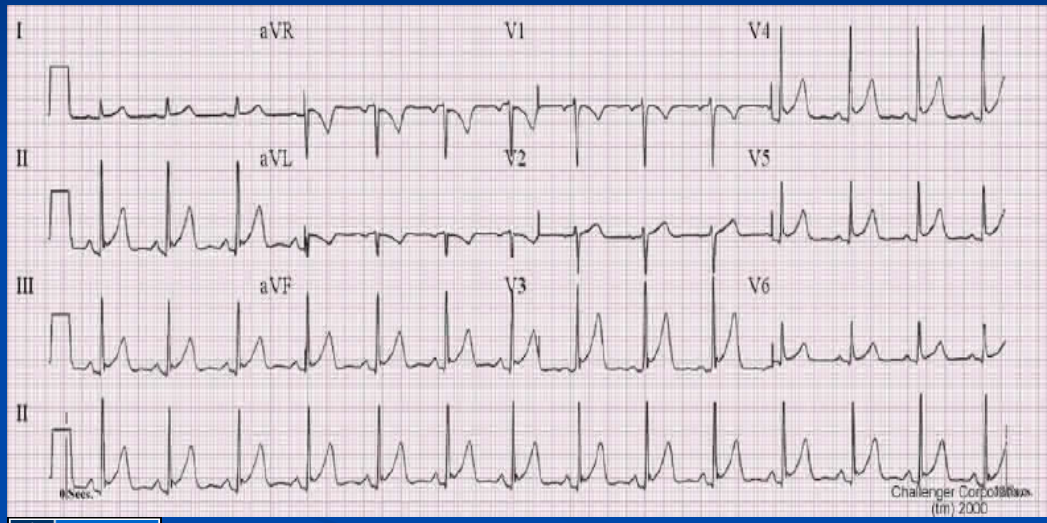
- Increase R wave voltage
- Hyperacute T wave evolves to STE over the next 30 minutes
- Pathologic Q waves :
  - Commonly develop 24 hours after infarct

  May not occur in up to 50 % of patients with an acute myocardial infarction.
- Serial ECG if persistent pain, atypical symptoms or change in VS. (or ST segment trend monitoring)



Differential diagnosis of this ECG tracing

- Acute myocardial infarction
- Hyperkalemia
- Subarachnoid hemorrhage
- Benign Early Repolarization (BER)
- LVH
- Hypertrophic cardiomyopathy
- Acute pericarditis



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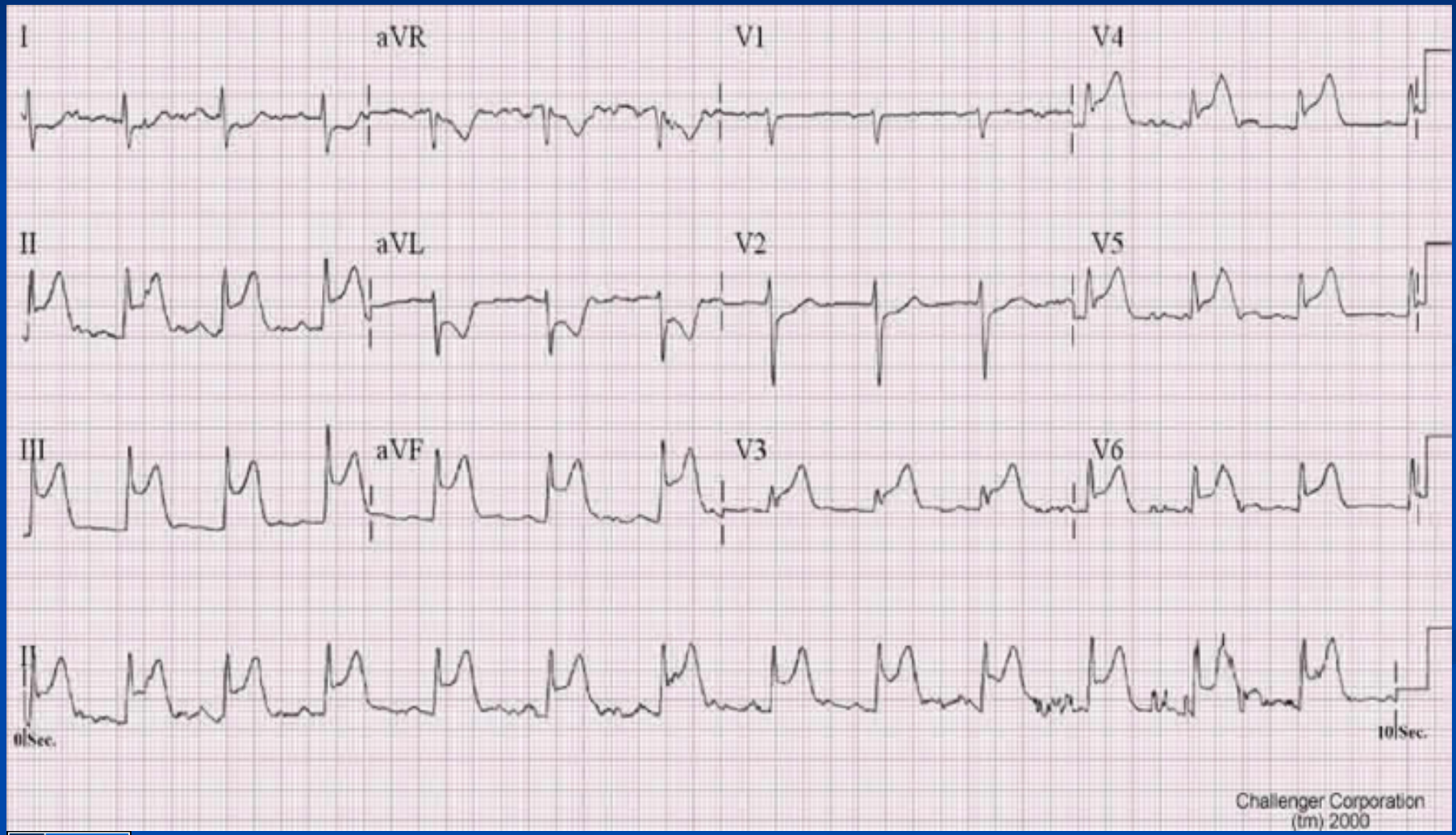
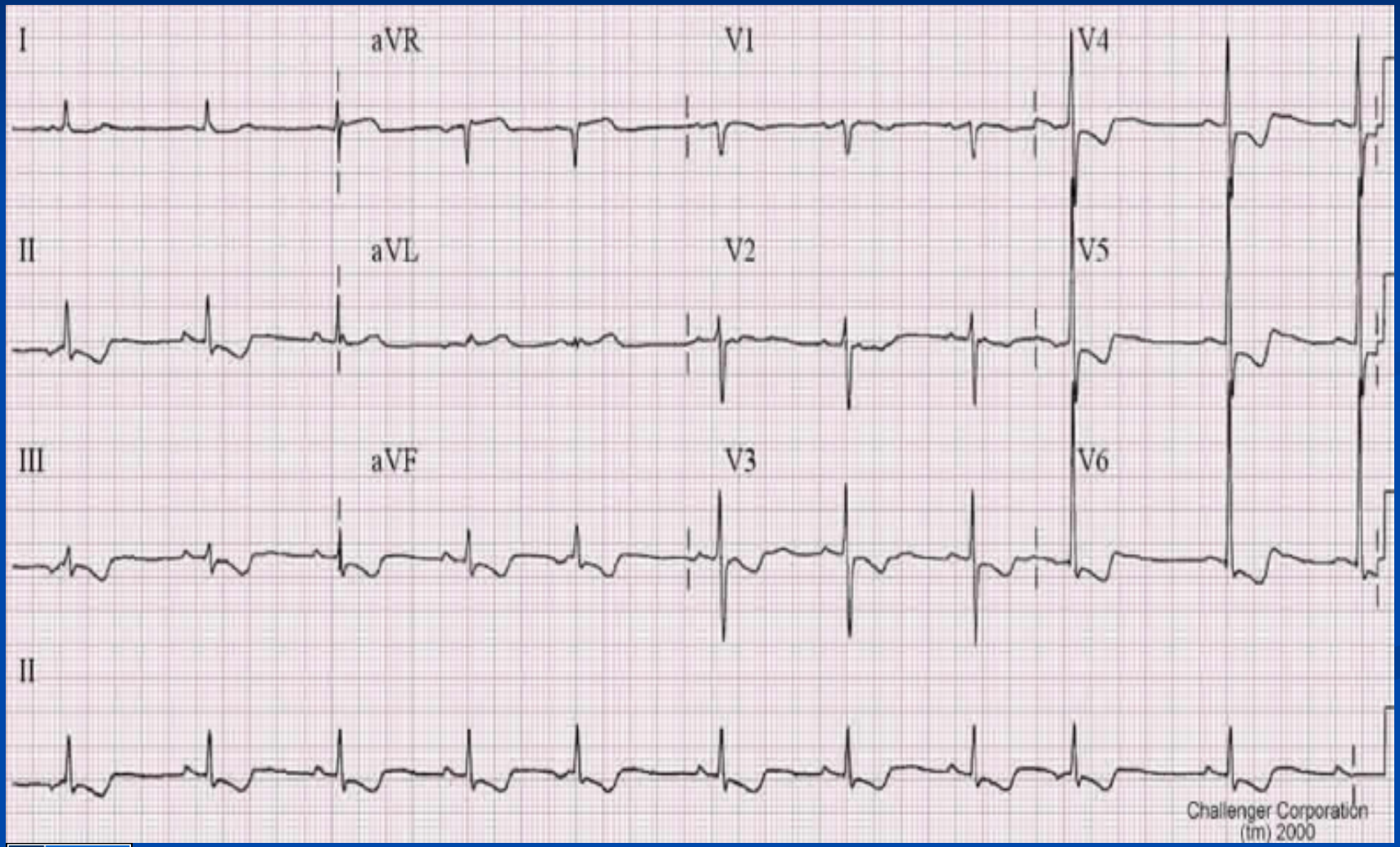
Inferolateral MI



Subendocardial / non-transmural MI



Source Undetermined

Cardiac Markers

- Cardiac Panel
  - Myoglobin
  - CPK
  - CPK-MB
  - Troponin (T and I)
- Rapid bedside assays available

Cardiac Enzymes

- Myogobin
  - Increased levels within 2 to 4 hours
  - Peaks at 6 to18 hours
  - Returns to baseline by 24 hours
  - Elevated levels also found in skeletal muscle injury (e.g. rhabdomyolysis)

Cardiac Enzymes

- CPK
  - Increased levels within 6 to 8 hours
  - Peaks at 12 to 24 hours
  - Returns to baseline by 36 to 48 hours
  - Elevated levels also found in cases of skeletal muscle injury (e.g. rhabdomyolysis)
- CPK-MB
  - Similar time course as for total CPK
  - More specific for cardiac muscle
  - Most specific if elevated and 5 % of total CPK

Cardiac Enzymes

- Troponin T and I
  - Increased levels within 6 to 8 hours
  - Peaks at 18 to 24 hours
    - Troponin T remains elevated for 5 to7 days
    - Troponin I remains elevated for up to 10 to 14 days
  - More specific for cardiac muscle (troponin I is most specific)
  - Mild elevations seen in up to 1/3 of cases of unstable angina (“microinfarcts”)
  - Prognostic value for cardiovascular complications
  - By 12 hours after onset of symptoms, CPK-MB and Troponin I have a 100 % sensitivity for detecting AMI

Additional studies for diagnosing AICS

- 2-D echocardiogram
  - Useful with a nondiagnostic ECG or difficult ECG's
  - Sensitivity 85 % ; specificity 50 %
  - Can't distinguish ischemia, AMI or previous infarction
  - Less sensitive for nontransmural.
- Radionuclide scanning : thalium 201, technetium-99
  - Decreased uptake in ischemic tissues
  - Normal perfusion and stress nuclide scans carry very low risk
- ETT
  - The more abnormal the baseline ECG, the less useful the test
  - Useful in low and intermediate risk groups stratification and discharge

Management

- Risk Stratification
- TIMI risk Score
  - Age > 65
  - Documented coronary stenosis > 50 %
  - Three or more risk factors
  - Two or more anginal equivalents within 24 hours
  - ST segment changes
  - Increased cardiac biomarkers

- High risk features :
  - Elevated cardiac biomarkers
  - Diabetes
  - TIMI score > 5
  - Refractory symptoms despite medical management
  - Elevated C reactive protein

- Relative risk features :
  - Prior CABG
  - Prior MI
  - LV dysfunction
  - CHF

AHA 2002 Guidelines

- STEMI :
  - Aspirin 162 mg
  - LMWH or UFH
  - Clopidgrel 300 mg load
  - Nitroglycerin
  - Morphine
  - Metaprolol
  - Lytic therapy
- If PCI :
  - Abciximab
  - Revascularization (PCA / stent)
- NSTE-ACS
  - If No high-risk features :
    - Aspirin
    - LMWH
    - Clopidrgrel
  - If Positive high risk features :
    - Add IIb-IIIa GP inhibitor

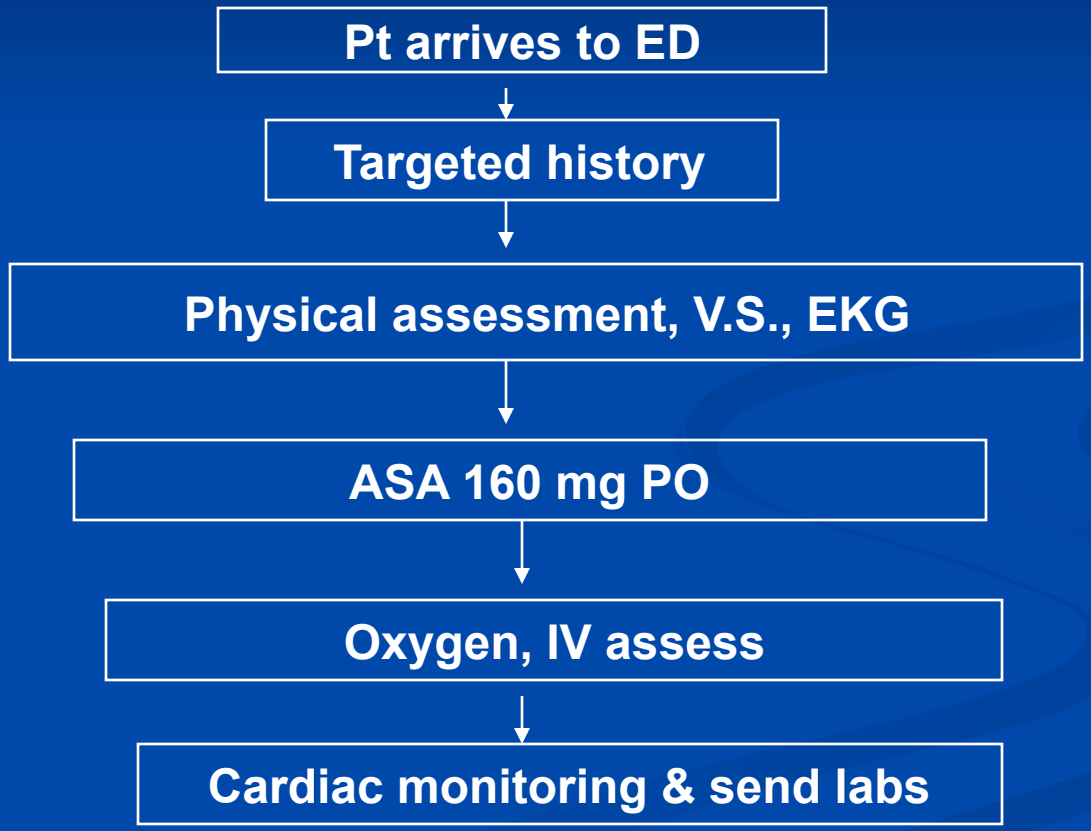
Other Treatments

- Ticlopidine
  - Inhibits tranformation of IIB-IIIa glycoprotein receptor
  - Good for USAP : takes 8 to 10 days to reach maximal benefit.
  - Recommend to load with 300 mg initially (unless CABG anticipated)
- LMW heparin
  - Better than unfractionated heparin for USAP
  - Better inactivation of Factor Xa
  - Less nonspecific binding
  - Longer half-life, predictable response
  - Less bleeding complications

Glycoprotein IIb-IIIa receptor inhibitors

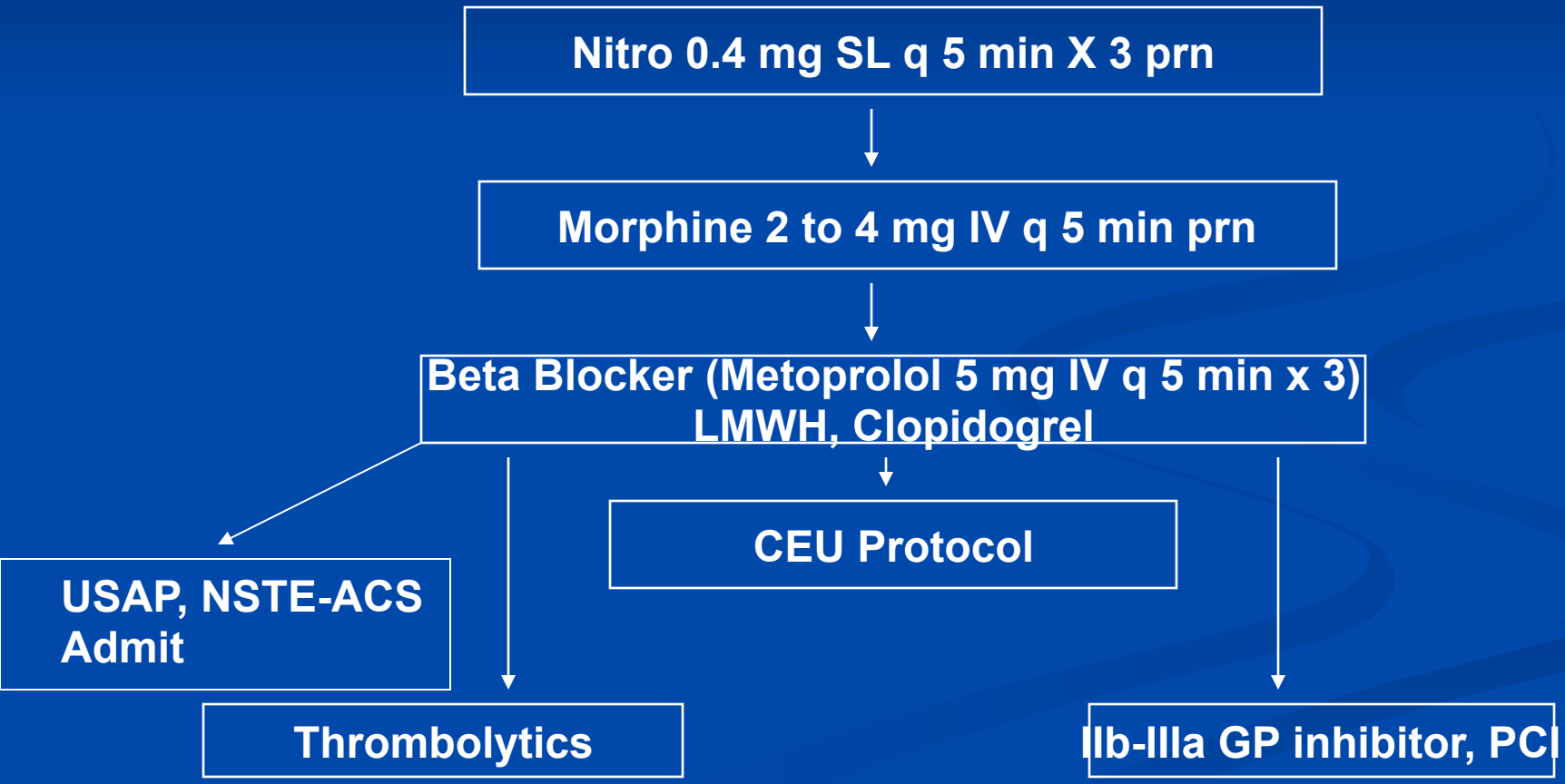
- Monoclonal antibodies that more effectively inhibit platelet function than aspirin.
- Completely inhibit platelet adhesion
- Proven additive benefit in patients undergoing percutaneous intracoronary vascular procedures (abciximab).
- Increasing evidence that these agents may be helpful in ischemic episodes not responsive to other agents.
- ACC / AHA 2002 guidelines for management of NSTE ACS :
  - Level 2A recommendation for patients without intended early cath / PCI

Management Sequence for ACS



Management of Chest Pain (CP)

If patient continues with CP and not hypotensive :



Thrombolytics

- Reduce short-term mortality by 18 to 25 %
- Overall :
  - All agents are effective and should be combined with antithrombin agents
  - Larger the infarct, the greater the mortality reduction with thrombolytics
  - Accelerated t-PA results in better flow at 90 minutes and 15 % reduction in 30 day mortality
  - TNK (mutant form of t-PA) is as effective as accelerated t-PA and single bolus dosing. TNK is 14 x more fibrin specific, 80 x more resistant to PAI-1

Thrombolytics : eligibility criteria

- Consistent history and physical exam
- STE ≥ 1 mm in two or more contiguous limb leads or ≥ 2 mm in two or more contiguous precordial leads (not ST depression : not ischemic syndromes !)
- New LBBB
- Therapeutic window is 12 hours from symptom onset.

Contraindications (CI) to Thrombolytics

- **Absolute CI :**
  - Prolonged CPR
  - Major surgery or trauma within the last 10 days
  - Significant coagulopathy
  - Diabetic hemorrhagic retinopathy
  - Left heart thrombus, SBE, pericarditis
  - Oral anticoagulant use
  - Septic thrombophlebitis
  - Previous CVA
- **Relative CI :**
  - > 12 hours after onset of symptoms
  - Age > 75 ???
  - Poorly controlled hypertension (> 180 to 200 / 110 to 120)

Additional reperfusion strategies

- PCI (percutaneous coronary interventions)
  - Lower risk of intracranial bleeding
  - Higher reperfusion rates
  - Rapid evaluation of patients not eligible for thrombolytics
  - Better risk stratification, earlier discharge
  - Early identification of surgical candidates
  - Prior CABG patients (grafts thrombose, larger burden of clot)
  - Superior to thrombolytics if intervention within 90 minutes
  - Recommended for patients in shock if PCI in 90 to 120 minutes.
- Rescue PCI if poor response to thrombolytics
- Grab bag of various strategies with no clear conclusions : i.e. lose dose thrombolytics prior to immediate PCI (facilitated PCI), glycoprotein inhibitor plus thrombolytics, etc. : Long term benefit yet to be proven.
- Radioactive implants

Who to transfer ?

- Transfer to a tertiary care facility with interventional and cardiac surgery capabilities is indicated :
  - CI to thrombolytics and may benefit from PCI, CABG
  - Persistent hemodynamic instability or ventricular arrhythmias
  - Ongoing ischemia following infarction or thrombolytics

  - Patients SHOULD receive the initial standard ED therapy including thrombolytics.

Final Thoughts

- Rapid history, rapid ECG with interpretation, rapid treatment
- Maintain a high clinical suspicion : 2 to 10 % of patients with CP and AMI are released from ED
  - Young, atypical presentations, nondiagnostic ECG's
- Single ECG and single set of enzymes can give a false sense of security
- ED cocktail : ASA, MSO_4, β-blocker, clopidogrel, LMWH, IIb-IIIa agents
- Target goal of thrombolytics within 30 minutes for STEMI
- Strongly advocate for PCI when appropriate

A Comprehensive Approach : Goals of the ED Cardiac Evaluation Unit (CEU)

1. **Early Systematic Evaluation of All Chest Pain Patients**
   - Identification of all reperfusion candidates
   - Reduction of delays in initiation of reperfusion therapy
   - Improved diagnosis and treatment of other dangerous pathology
   - Early (primary) risk stratification

ED Evaluation of Chest Pain

- 5,000,000 visits / year in U.S.
- 5 % of all ED visits
- 5 to 15 Chest Pain patients / day per ED
- Lengthy Differential Diagnosis

Identifying the Problem :

Need for a More Aggressive Approach to Acute MI :

- "Time is Myocardium"
- Dramatic Mortality Reduction in STEMI with Early Reperfusion
  - Thrombolytics
  - Immediate PTCA / stenting
- Increasing number of other treatments available for ACS
  - Require early risk assessment

Team Members

- Cardiologist : specialist, algorithm
- ED Physician : team leader
  - algorithm, educate & motivate staff
- Senior triage nurse : team facilitator
  - algorithm, educate & motivate staff
- Clinical technician : algorithm, educate & motivate staff
- Patient Service Coordinator : algorithm
- Research coordinator : data collection

CEU Goals (Continued)

2. Accelerated Rule-out of MI among low risk patients
   - Reduce LOS
   - Improve cost-effectiveness
   - Improve patient satisfaction
   - Eliminate “missed MI”
3. Secondary Risk stratification
4. Comprehensive Diagnosis and Treatment Center
5. Education and Community Outreach
6. Multidisciplinary approach

Implementation : Goal 1 : Early Diagnosis of MI

- ALL chest pain patients receive immediate, aggressive evaluation
  - Vital signs
  - Cardiac monitor
  - Intravenous "lifeline" placed
  - Oxygen and/or pulse oxymetry
- ECG performed under standing orders within 10 minutes of arrival
  - ECG handed directly to physician for interpretation

Goal 1 : Early Diagnosis of MI

- Early focused history and physical exam
- Blood drawn upon arrival for initial myocardial markers (Cardiac Panel)
  - CK-MB
  - Troponin
  - Myoglobin
- “Reperfusion Checklist”

Goal 2 : Evaluation of Low Risk Patients

- "Zero tolerance" for missed MI
- MI can not be excluded by history, exam alone
- Hospitalization for "Rule-Out MI" expensive, inefficient
- Several alternative approaches now exist

Goal 2 : Evaluation of Low Risk Patients

Initial Risk Stratification within 1 to 3 hours :

1. ST segment elevation MI :
   - Thrombolytics or cath lab
2. High Probability for ACS and / or High Risk :
   - Ischemic ECG, positive marker, etc.
   - ICU vs in-patient unit, anti-ischemic therapy, ? cath
3. Low Risk for ACS :
   - No high risk clinical features
   - Non-diagnostic ECG
   - Initial myocardial markers negative
   - Hold for further workup or go to CEU
4. Negligible Risk :
   - Atypical history, no risk factors, normal ECG and markers, other cause identified
   - Discharge home

Goal 2 : Evaluation of Low Risk Patients

- Continuous observation on cardiac monitor
  - 12 to 24 hours
- Accelerated “rule-out” of MI
  - Serial ECGs
  - Serial Myocardial Marker Measurements
    - 0, 3, 6, 9 hours
    - CK-MB, troponin
- MI definitively excluded within 12 hours

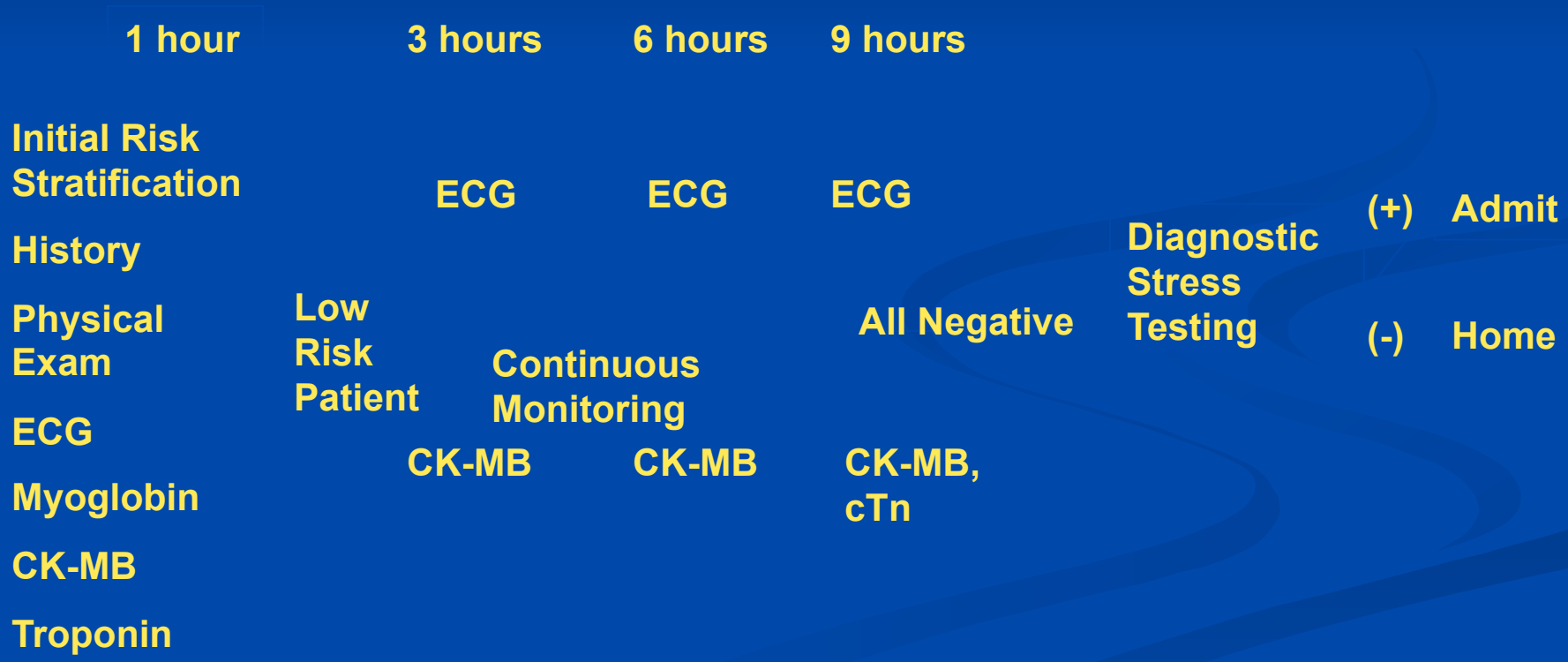
Goal 3 : Secondary Risk Stratification

- MI rule-out does not exclude other ACS (Unstable Angina)
- Further evaluation often needed prior to discharge
- Stress testing
  - Screening test for CAD
  - Accurate predictor of short and long term risk of death, adverse events
  - Reduces need for repeated evaluations

Stress Testing

- Standard (Bruce protocol) exercise (treadmill) stress testing
- Stress echocardiography
- Radionucleotide scanning
  - Thallium
  - Sestamibi
  - Dual isotope
- Pharmacologic stress testing

Low Risk Chest Pain Evaluation Protocol



Impact of CEU Approach : Low Risk Chest Pain Patients

Problems : “Unnecessary” admission of low risk patients, “Missed” MI’s

Measure : length of stay, % MI’s discharged

Interventions : accelerated rule-out protocol

Impact : Missed MI’s reduced from 4.5 to 0.4 %*

Length of stay reduced ~ 2.5 days to 1 day

* Graff et al. Am J Cardiol 1997; 80 : 563-8

Growth of Chest Pain Units in the U.S.