Coronary Artery Disease, Angina and MI

Coronary Artery Disease

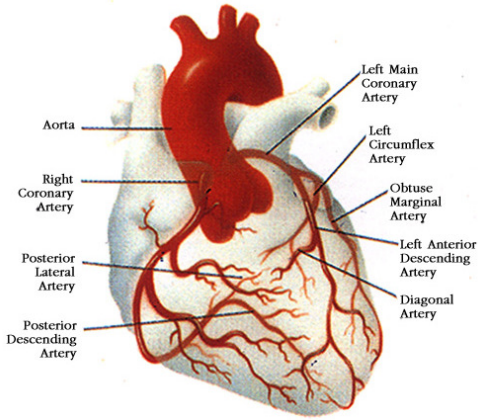
- Most CAD nothing more than Atherosclerosis in the coronary arteries
- Chronic leads to angina pectoris
- Acute is MI
  - 700,000 new MIs in U.S.
  - 500,000 recurrent MIs in U.S.

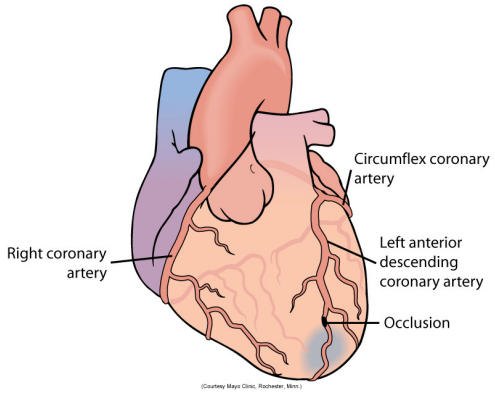
Risk Factors

- Major nonmodifiable
  - Age/gender
  - Family hx
- Major modifiable
  - Dyslipidemia
  - Hypertension
  - Smoking
  - DM, insulin resistance
  - Obesity
  - Sedentary
  - Atherogenic diet
- Nonconventional
  - HS CRP
  - Homocysteine
  - Lp(a)

Coronary Arteries

- Coronary Arteries surround and then penetrate the heart muscle
  - Right coronary artery (RCA) (back of heart)
  - Left (Main) coronary artery
    - Left circumflex (Side)
    - Left anterior descending (Front)





Myocardial Ischemia

- Blood flow must be impeded before heart metabolism is affected
  - Absolute
  - Relative
- Causes
  - Atherosclerosis, Vasospasm
  - Hypotension, Arrythmias, Anemia, V/Q

Supply/Demand Considerations

- Oxygen supply
  - Cardiac output
  - Hemoglobin levels
  - Respiratory function
  - Fitness of muscle
- Oxygen demand
  - Work of the heart
    - Contractility
    - HR
  - Hypertrophy of the heart

Myocardial Ischemia

- Myocardium becomes ischemic within 10 seconds of coronary occlusion
- ***Working*** cells remain viable for up to 20 minutes
  - Anaerobic mechanisms kick in
    - Lactic acid
    - Free radical damage, esp after reperfusion

Cardiac Ischemia Manifestation

- Stable angina
  - Chronic obstruction
  - Chest pain with exertion
  - May radiate, may have diaphoresis, SOB, pallor
  - Relief with rest or nitrates
- Prinzmetal angina
- Silent ischemia
- Unstable angina
  - May become a myocardial infarction

Evaluation

- H&P
- Lipids, BP, risk factor assessment
- ECG
- Stress test
- Angiography
- Unstable angina
  - Cardiac enzymes (rule in/out for MI)

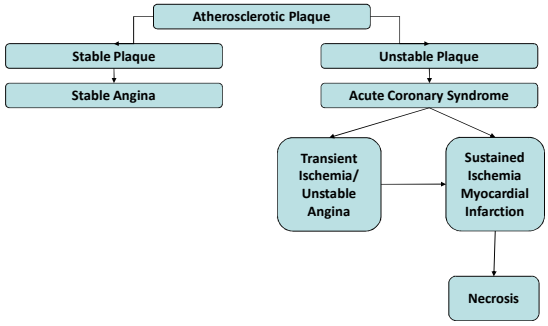
Treatment for Stable Angina

- Drug
  - Nitrates
  - Beta blockers
  - Calcium Channel Blockers
  - Atherosclerotic disease tx (HTN, Lipids)
- Surgery
  - Bypass
  - PCI (PTCA, Stent)
  - Experimental

Acute Coronary Syndrome

- Unstable Angina – reversible ischemia
  - Rupture of an unstable plaque
  - Clots spontaneously resolve over time
  - Damage depends on size of clot and rate of dissolution vs. rate of clot formation
  - Myocardial infarction

Acute Coronary Syndrome



MI Pathophysiology

- Plaque rupture --> Clotting cascade active
- Thrombus occludes vessel
- Myocardium becomes hypoxic
  - Shift to Anaerobic Respiration
  - Waste products release/hypoxic injury
  - Cardiac output impaired
    - Norepinephrine/Epinephrine Release
    - Renin release

Myocardial Changes

- Myocardial stunning
  - Temporary loss of contractility that persists for hours to days
- Myocardial hibernation
  - Chronically ischemic; myocytes are hibernating to preserve function until perfusion can be restored
- Myocardial remodeling
  - Loss of contractility mediated by Ang II, catecholamines, and inflammatory cytokines

Ischemic Morphology

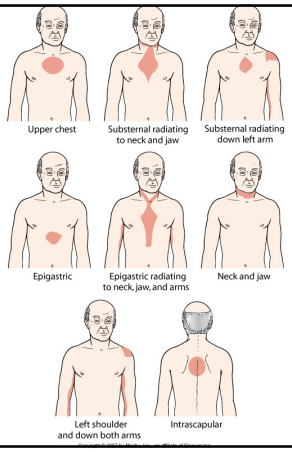
- Increased O2 demand: epinephrine, RAAS
- Hypoactive wall/Necrosis
  - Transmural
  - Subendocardial
- Conductile problems
  - PVCs
  - Dysrhythmias

ECG changes

- Conductile cells of heart are most sensitive to hypoxia
- Classic: T-wave inversion, ST-elevation, Q waves
- Non-Q wave MI: no Q waves, possibly normal ST segment
- R/O CANNOT be made with ECG alone!!!

MI Manifestations

- Prodromal
  - Symptoms usually appear 24-72 hours before
  - Malaise, Tiredness, Weakness fatigue
  - Visual disturbance
- Acute Phase
  - Symptoms: Chest Pain, Dyspnea, Nausea, Diaphoresis, weakness, fatigue, anxiety
  - Signs: Gray/ashen, gasping, clutching, loss of consciousness, confused, ECG changes, tachycardia, tachypnea



Eval & Tx

- ECG
- Cardiac Enzymes X 4
  - If Ruled in
    - Anticoagulation, antiplatelet
    - Thrombolytic Therapy
    - Cath lab, Emergency bypass
  - If Ruled out
    - Stress test
    - Angiogram
- MONA: Morphine, O_2, Nitrates, ASA

Nitroglycerine

- Vasodilating actions
  - Primarily acts on veins and large arteries
  - Uptake by VSM cells and converts to active form: NO
- Therapeutic uses: Stable Angina
  - Decreases preload → decreases contraction → oxygen demand
  - Does **not** dilate coronary arteries

Nitrates

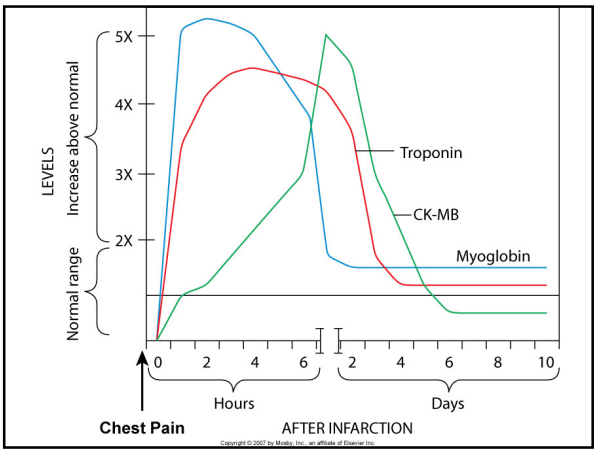
- Kinetics
  - Highly lipid soluble: can be given PO, IV, SL, transdermal
  - Rapid inactivation by organic nitrate reductases
  - Half-life 5 – 7 minutes
  - PO: most drug is destroyed in liver before reaching systemic circulation
- Adverse Effects
  - Headache
  - Orthostatic Hypotension
  - Reflex tachycardia

Nitrates

- Interactions
  - Other hypotensive drugs
  - Beta blockers, verapamil, diltiazem
  - Sildenafil (Viagra) – life threatenening: 25 mmHg drop
- Tolerance
  - Most common in high dose, continuous therapy
  - Prevent by using lower dose intermittent therapy: 8 hour drug free time

Nitrates

- Preparations
  - Sublingual: works in 1 – 3 minutes; lasts an hour; expires within 6 months of opening
  - Translingual spray
  - Topical Ointment
  - Transdermal patch
  - PO Sustained release capsules or tablets: higher doses d/t first pass effect (isosorbide mononitrate, dinitrate)
  - IV infusion: glass bottle, special (vented) tubing
- Nursing implications
  - Check BP before and after administering
  - Assess for headache
  - Discontinue slowly if patient has been on it for a while



Immediate Post MI Tx

- Most common cause of death within 72 hours of MI is _____
  - Must be monitored
- Reduce myocardial workload
- Prevent Remodeling
- Reduce chances of reocclusion
- Reduce oxidative stress (reperfusion injury)

Post MI Treatment

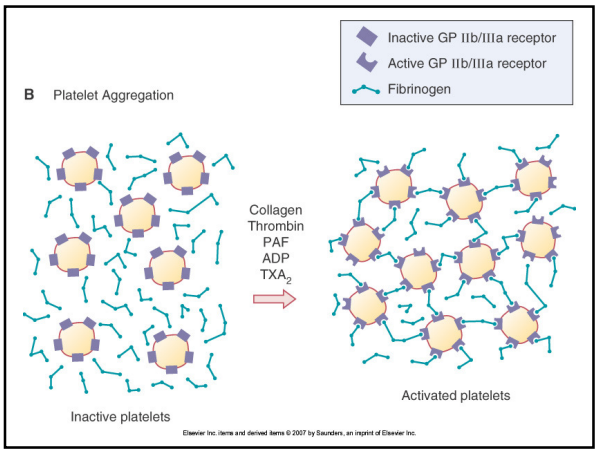
- Lifestyle
  - Diet
  - Exercise – Cardiac Rehab
  - Stress management
- Drugs
  - Antiplatelet: ASA, clopidogrel, persantine
  - Beta blocker
  - Statin medication
  - Treat risk factors (HTN, lipid, smoke, etc.)
  - Sometimes coumadin

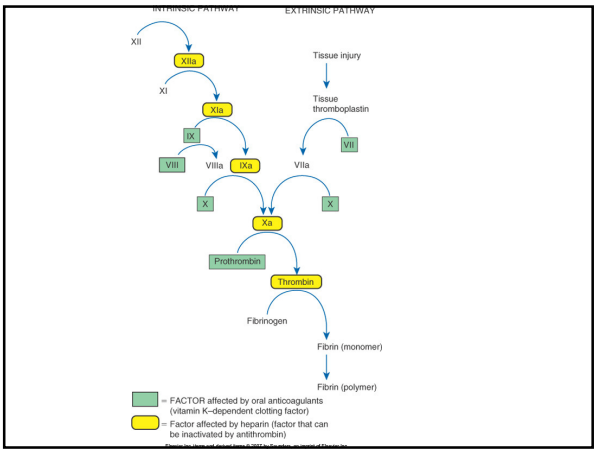
Post MI Evaluation

- Stress test
- Angiography
- Symptoms

Clot Review

- Platelet aggregation
  - Become sticky
  - Activate GP IIb/IIIa receptors
  - Chemicals
    - Prostaglandins
    - Thromboxanes
    - ADP
- Clot Stabilization
  - Activation of fibrinogen
  - Binds to GP IIb/IIIa
  - Chemicals
    - Clotting cascade → Thrombin → Fibrinogen activation





Drugs

- Antiplatelet
  - ASA (prostaglandin)
  - Clopidogrel (ADP)
  - Integrilin (GP IIb/IIIa)
- Anti Clotting factors
  - Heparins (intrinsic)
    - UF Heparin
    - LMWH
  - Fondaparinux (intrinsic)
  - Warfarin (extrinsic)

Anticoagulant Monitoring

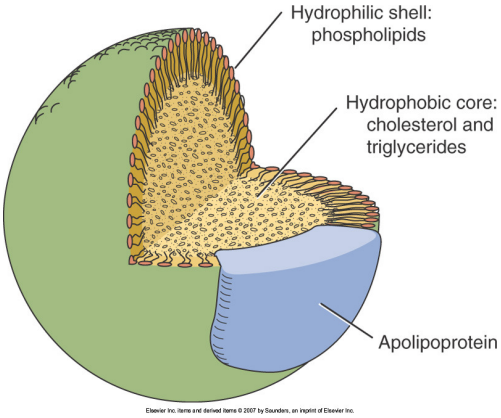
- Intrinsic → PTT
  - IV Unfractionated heparin only
  - Measure in seconds
- Extrinsic → PT/INR
  - Warfarin only
  - PT: Measure seconds (ignore it: worthless, useless, stupid!)
  - INR: Ratio
    - 1:1 = 1 = Normal
    - INR 2 – 3 therapeutic
    - > 4 toxic
    - Exception: mech heart valves 3.5 – 4.5

Dyslipidemia

- Half of all heart attacks occur in persons with elevated cholesterol
- Lipoprotein
  - Lipids, Phospholipids, Cholesterol, Tryglycerides
- Needed for
  - plasma membrane maintenance
  - Sterol hormones
  - Bile acids
  - Skin (water resistance)

Cholesterols

- Sources of cholesterol
  - Dietary absorption (exogenous)
  - Synthesis of new cholesterol (endogenous)
  - Increased dietary consumption inhibits synthesis
  - Fat substrates
- Triglycerides
  - Storage form of lipids long term storage
  - Adipose tissue



Plasma Lipoproteins

- Function: carrier molecules
- Structure
  - Hydrophobic Core
  - Hydrophillic shell
    - Phospholipids
    - Apolipoproteins
      - Recognition sites for receptors
      - Activate enzymes
      - Increase structural stability
      - A-I, A-II, B-100

Cholesterol Cycle

- Chylomicrons
  - Lipid packages absorbed from intestine
  - Transported to liver
- Liver manufactures
  - VLDL: triglycerides + protein
  - LDL: cholesterol + protein
  - HDL: phospholipids + protein
  - Lipoprotein(a) [Lp(a)]

VLDL

- one B-100 apolipoprotein
- triglyceride core
- deliver triglycerides to muscle and adipose
- Clinical significance
  - Accounts for nearly all triglycerides in blood
  - Normal triglyceride level is <150 mg/dl
  - >150 associated with Metabolic syndrome
  - >400 - 500 associated with pancreatitis

LDL

- One B-100 apolipoprotein
- Cholesterol core
- Deliver cholesterol to nonhepatic tissues
  - Cells that need cholesterol endocytose the LDL molecule
  - If more cholesterol is needed more LDL receptors are produced
- Clinical significance
  - Direct correlation with heart disease
  - 25% reduction of elevated LDL corelated with up to 50% reduction in MI risk

HDL

- Contain apolipoprotein A-I, or A-I and A-II
- Cholesterol core
- Transport cholesterol back to liver
- Clinical Significance
  - Promote cholesterol removal
  - Low cholesterol is associated with increased risk of atherosclerosis
  - Apparently only A-I HDL is cardioprotective
  - Subtype analysis

Role of Cholesterol in Atherosclerosis

- LDL is benign until oxidized in subendothelial (intimal) space
- Oxidized LDL
  - Attract monocytes and promote differentiation to macrophages
  - Inhibit macrophage mobility: chronic inflammation
  - Promote uptake by macrophages
  - Are cytotoxic: damage endothelial cells and contribute to inflammation

Dyslipidemia

- Imbalance in proportion of lipoproteins
- Primary
- Secondary
  - DM
  - Hypothyroidism
  - Pancreatitis
  - Renal nephrosis

Dyslipidemia Tx Goals

- Total cholesterol
  - >240 high
  - 200 – 240 gray zone
- LDL
  - <160 high
  - <130 depending on risk factors
  - <100 depending on risk factors
- HDL
  - > 40 for men; 50 for women low
- Triglycerides
  - < 150 high

Determinants of Treatment Goals

- Several schemes
  - Number of CAD risk factors
  - Ten year Framingham risk score
  - CHD equivalent
    - Diabetes
    - Other atherosclerotic diseases (PAD, AAA, carotid atherosclerosis

Treatment

- TLC
  - Diet
  - Weight Control
  - Exercise
  - Smoking Cessation (also helps HDL)
- Drug Therapy
  - Primary goal is lower LDL
  - Secondary targets
    - Metabolic syndrome
    - Lower Triglycerides
    - Raise HDL

Cholesterol Medications

- See table 48-7
- Statins
- Bile Acid sequestrants
- Fibrates
- Niacin (Nicotinic acid)
- Zetia

Statins

- Mechanism of action
  - Inhibits HMG-CoA reductase
  - Cause increase in hepatocyte LDL receptors
- Therapeutic effects
  - LDL, HDL, VLDL
  - Nonlipid effects
    - Plaque stabilization
    - Reduction of plaque inflammation
    - Slow coronary artery calcification
    - Improve endothelial function
    - Enhance vasodilation
    - Reduce risk of A fib
    - Reduce risk of thrombosis
- Treating Heart Disease or treating Cholesterol
  - Secondary prevention
  - Primary Prevention
  - Patients who have normal cholesterol

Statins

- Indications
  - Dyslipidemia
  - CHD
  - DM
- Kinetics
  - 30 – 90% absorption depending on agent
  - Most statins are completed sequestered in the liver
  - Hepatic metabolism followed by bile secretion
  - CYP3A4 Microzomal: atorvastatin, lovastatin, simvastatin (interactions)
  - Renal excretion: only lovastatin, pravastatin, simvastatin (10-20%)
  - Timing of dose: at night

Statins

- Adverse Effects
  - Hepatotoxicity 0.5 – 2% of patients treated > 1 year
  - Myopathy 1 – 5% --> Myositis -->**Rhabdomyolysis** 0.15/million prescriptions
  - Risk: age, small frame, frailty, DM/renal dz, high dose statins, fibrates, hypothyroid
- Interactions
  - Fibrates: myopathy
  - Agents that inhibit CYP3A4: cyclosporine, macrolides, azol fungicides, HIV protease inhibitors, grape fruit juice
  - Pregnancy: CatX
- Administration considerations
  - Timing
  - Meal or snack: lovastatin

Nicotinic Acid (Niacin)

- Raises HDL better than anything else to date
- Mechanism: Decresed production of VLDLs, HDL?
- Therapeutic effects
  - LDL, HDL, Triglyceride
- Uses
  - Risk for pancreatitis
  - Low HDL
  - Niacin deficiency (much lower doses)
- Adverse effects
  - Flushing/Itching
  - GI upset
  - Hepatotoxic
    - Fast release
    - Sustained release (slo-niacin)
    - Extended release (Niaspan)
  - Raises homocysteine
  - Rarer: hyperglycemia, gouty arthropathy

Bile Acid Sequestrants

- Older: Cholestyramine and Cholestipol
- Mechanism of Action
  - Bind to Bile acids in intestine
  - Prevents reabsorption of cholesterol
  - Body needs to increase synthesis
  - Increase of LDL hepatocytes
- Uses
  - High LDL
  - Usually in combo with statin
- Adverse effects
  - GI complaints: constipation, bloating, nausea
- Interactions
  - May bind to other drugs and prevent their absorption
  - Vitamins A,D,E, K
  - Thiazides, digoxin, warfarin, some antibiotics
- Newer: Cholesvelam (Welchol)
  - Better tolerated
  - Less interaction with Vitamins and drugs

Fibrates

- Mechanism mostly not understood
- Therapeutic effects
  - HDL
  - LDL
  - Triglycerides
- Adverse effects
  - Gallstones
  - Myopathy --> rhabdomyolysis
  - Liver damage
- Interactions
  - Increased risk of rhabdo when combined with statins

Ezetimibe (Zetia-no class)

- Mechanism
  - Blocks cholesterol uptake at the brush border of intestine
- Therapeutic effects
  - LDL, HDL, Triglycerides
- Uses
  - Lower LDL
  - Adjunct to statins
- Adverse effects
  - none?
- Interactions
  - Statins
  - Fibrates
- NO BENEFIT IN PREVENTING CAD