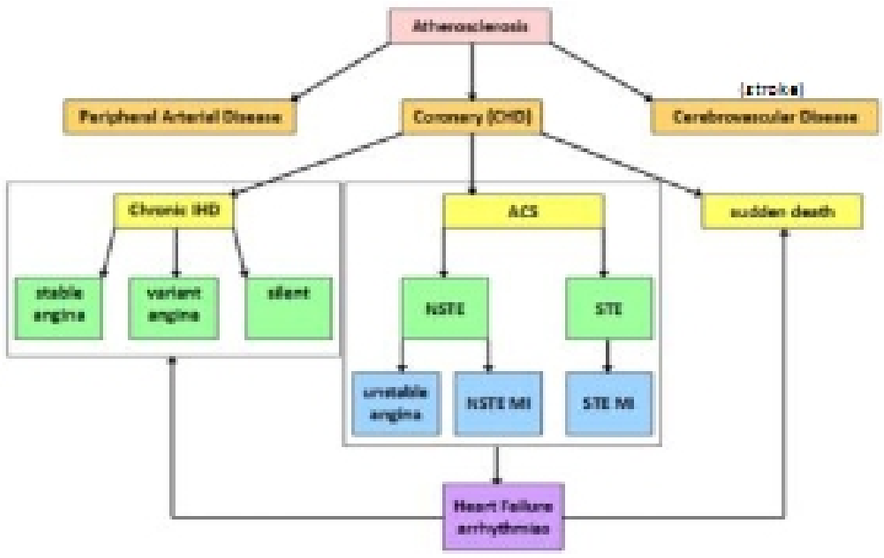
Ischemia

Saturday, November 8, 2014
8:24 PM

Learning Objectives:
- pathophysiology of atherosclerosis (fatty streak --> fibrous atheromatous plaque --> complicated lesion)
- pathophysiology of plaque rupture & thrombous formation
- myocardial O_2 supply & demand
- mod/nonmod risk factors for IHD
- diagnostic tests to evaluate IHD patient
- pathology, signs/symptoms, EKG changes, & cardiac biomarkers of:
  - chronic stable angina
  - ST-segment elevation ACS
  - non-ST-segment elevation ACS
- time frames of cardiac biomarkers after MI



Epidemiology

- CVD:
  - ↑incidence, ↓death
  - > 81 million > 1 type of CVD
- IHD: leading cause of death in US
  - ↑incidence, ↑death
  - 1/4 deaths
  - 15% MIs --> death (most ppl survive heart attacks)
  - 50%men, 64%women = IHD sudden death (no symptoms)
- black
- men
- Finland, Ireland, Scotland, Africa > France, Japan

*IHD = CHD = CAD

CVD = cardio vascular disease
IHD = coronary heart disease
MI = heart attack

*IHD (30s-40s): men (4-5x) > women
*IHD: women lag 10 years
*MI/death: women lag 20 years

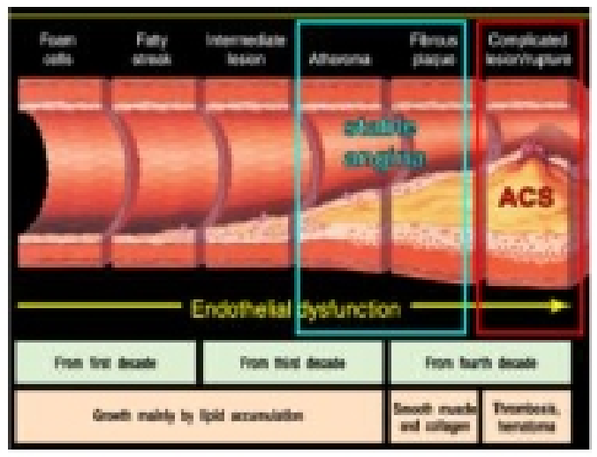
Atherosclerosis

ATHEROSCLEROSIS - fibrofatty lesions in intimal lining of med-large arteries due to underlying chronic inflammation
- aorta & branches
- coronary arteries
- large brain vessels

Pathophysiology: oxLDL --> inflammation --> Macrophage/T-Cell "foam cells" --> "foam cells" release oxLDL --> fatty streak --> inflammation --> vessel cells enlarge & form FAP --> complicated lesion

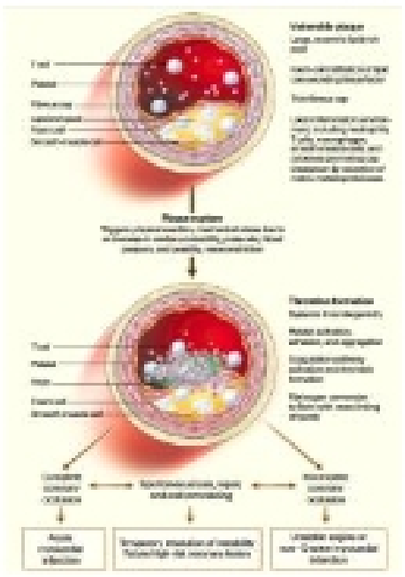
FATTY STREAK - lipids + inflammatory cells on vessel intimal wall (can occur by age 10)
ATHEROMA - beginning of lipid core
FIBROUS ATHEROMATOUS PLAQUE (FAP) - hard cover over fatty streak; IC + EC lipids, scar tissue, thickening of vessel intima
FIBROUS CAP - connective tissue + vessel cells
NON-COMPLICATED LESION - stable angina + stable plaque + NO rupture
COMPLICATED LESION - unstable angina + unstable plaque + potential RUPTURE --> exposed collagen/VWF/TF attracts platelets, coagulation, thrombus, MI (--> ACS)

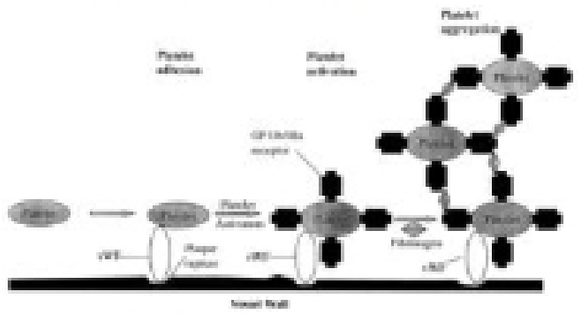
↑Plaque Rupture
- large/less solid
- thin cap
- inflammation > repair
- eccentric shape
- ↑BP, flow, contraction



THROMBUS (CLOT) - fibrin + platelets form clot on top of ruptured plaque

Platelet Aggregation:
1) Adhesion
2) Activation (ADP, TXA2, Thrombin)
3) Aggregation (GPIIb/IIIa)
   - ADENOSINE DIPHOSPHATE (ADP) - activates platelets
   - THROMBOXANE A_2 (TXA_2) - activates platelets
   - TISSUE FACTOR (TF) - in ruptured plaque; activates extrinsic coagulation pathway; forms Thrombin
   - THROMBIN - fibrinogen --> fibrin
   - VWF - normally helps endothelial cells to bind collagen in basement membrane; when exposed via rupture, lassoes & activates platelets, causing conformational change in GPIIb/IIIa receptors
   - FIBRINOGEN - links platelets via GPIIb/IIIa receptors





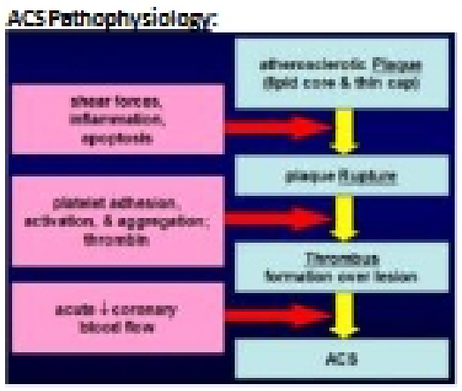
Types of Clots:

WHITE CLOT	platelets > fibrin	incomplete occlusion	NSTE ACS
RED CLOT	fibrin/RBC > platelets	complete occlusion	STE ACS

Atherosclerosis Risk Factors
- smoking
- obesity
- dyslipidemia
- DM
- HTN

Sites = high pressure vessels
- cerebral
- carotid
- coronary
- renal
- femoral

ACS Pathophysiology:



Coronary Heart Disease

CHD - coronary occlusions; "umbrella term"
  IHD - ↓heart O_2 perfusion
MI - due to chronic IHD or complete coronary occlusion; causes necrotic (dead)/nonviable/dysfunctional myocardium
ANGINA - chest pain (usually w/exercise)

*myocardium is salvageable/viable if ischemia is temporary or quickly reversed

Ischemia

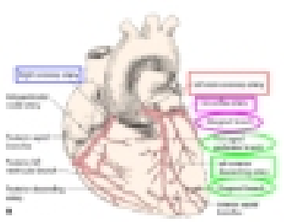
ISCHEMIA - $MVO_2 > O_2$
MVO_2 - myocardium O_2 demand

↓Supply vs. ↑Demand

*CHRONOTROPY - HR
*INOTROPY - contraction

↓O_2	↑MVO_2 (exercise)
↓Artery P_{O_2} ↓Diastolic Filling Time ↓Flow: ↓Coronary Perfusion Pressure ↑Arteriole Resistance	↑HR ↑Contraction ↑Wall Tension: ↑LV pressure/dilation ↑LV thinning

Main Coronary Arteries:
- Right (R)
- Left Main (LM)*
  - Left Anterior Descending (LA)
  - Left Circumflex (LCx)



*prognosis largely dependent on # vessels obstructed

Obstructed Vessels	12-yr Survival
0	88%
1	74%
2	59%
3	40%

Risk Factors for IHD:

Mod	Smoking	↑MI, sudden death, cerebrovascular, peripheral arterial // ↓HDL
	Obesity/sedentary (IBW+>20%)	↑BP, insulin resistance, TG // ↓HDL
	Dyslipidemia	↑non-HDL, ↓HDL
	HTN	>140/90, antihypertensives
	DM	glycemic control
	CKD	
	↑C-Reactive Protein (CRP)	serum marker for systemic inflammation
	↑Lipo A	genetic
	↑Homocysteine	related to ↓B6, B12, folate (causes vascular inflammation --> atherosclerosis)
Nonmod	Age	(Men>45, Women>55)
	Family History of early IHD (+MI/sudden death)	(Dad<55, Mom<65)

Angina

Quality	-heavy pressure, squeezing, tightness, crushing, burning, discomfort (does not change with position) -NOT sharp/stabbing
Location	-substernal/retrosternal -epigastrium, back, neck, shoulders, arms, jaw
Radiation	-neck, shoulders, arms, jaw
Duration	-stable = 3-5 mins -unstable = >20 mins *both can range 30secs-30mins
Exacerbations	-exercise -stress -cold -smoking -large meals, walking after meals
Relief	-rest -Nitroglycerin
Accompaniments (mostly women)	-dyspnea -fatigue -weakness -syncope

*may be confused with indigestion
*pain severity ≠ IHD severity

NITROGLYCERIN - (30secs-5mins)(call 911 if need 2nd dose)(re-dose every 5mins, max 3)

Types of Angina:

Chronic Stable	Variant (Prinzmetal)
- reproducible, constant intensity - caused by fixed obstruction - made worse with exercise/stress - relief w/Nitro - most have atherosclerosis	- vasospastic - ↓coronary blood flow - mostly at night&early AM, NOT caused by exercise/stress - NO relief w/Nitro - may not have atherosclerosis

SILENT ISCHEMIA - ischemia w/ NO angina: due to altered pain threshold/autonomic neuropathy in elderly/diabetics

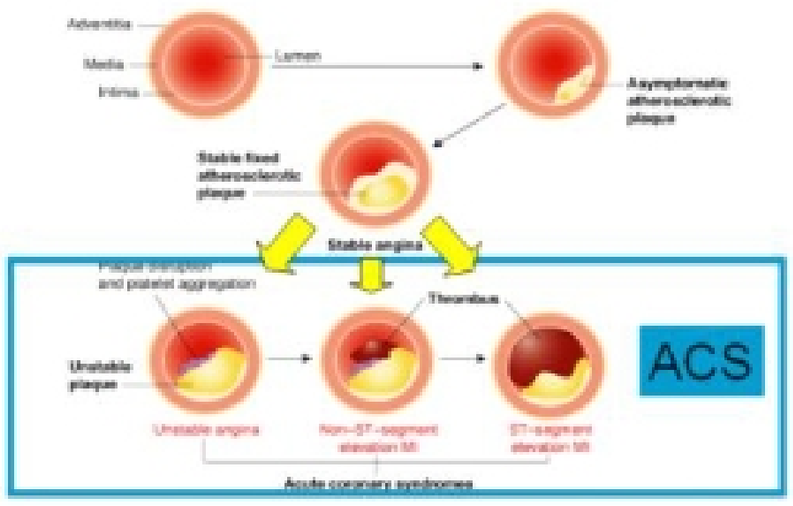
Differential Diagnosis
- pericarditis
- GERD/peptic ulcer disease
- aortic dissection
- pulmonary embolism
- biliary disease
- musculoskeletal disease

Patient History
- detailed history of chest pain
  - nature
  - precipitating factors
  - duration
  - radiation
  - response to test/nitroglycerin
- risk factors

Acute Coronary Syndrome (ACS)

ACS- ↓O_2 perfusion due to unstable angina & plaque rupture; may cause complete occlusion; sudden, unexplained chest pain

	NSTE	STE
Occlusion	incomplete	complete
EKG	- ↓ST-segment - T-wave inversion	- ↑ST-segment - Q-waves (transmural necrosis)
Biomarkers	- NSTE MI (+) - UA (-)	- STE MI (+)



Clinical Presentation	- midline anterior angina (>20mins) - if UA: (new-onset (<2 months) angina at rest, severe/worsening) - if MI: (longer & more intense angina at rest)
Accompanying Signs/Symptoms (women, elderly, diabetes = less likely to have normal symptoms)	Symptoms: - dyspnea - weakness - diaphoresis - N/V Signs: NONE - (arrhythmias) *patients may have signs of acute Heart Failure: - jugular vein distension - rales - (+) S_3
Diagnostic Tests	- EKG - biomarkers - angiography ("cardiac catheter") - echocardiogram - stress tests

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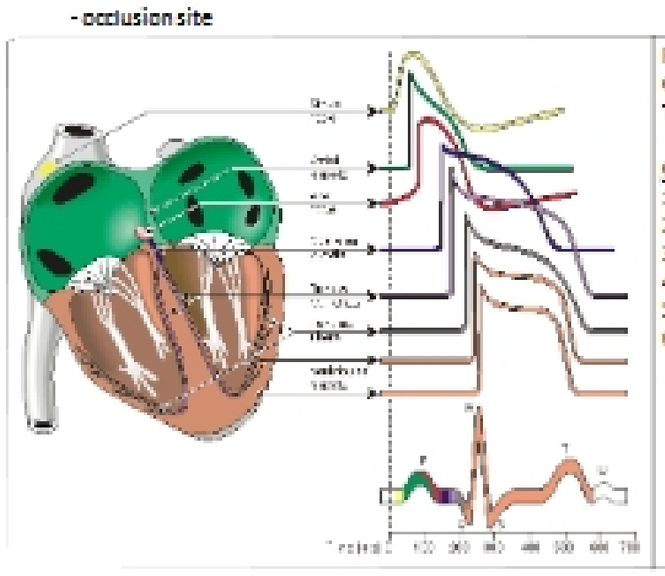
DIAGNOSTIC TESTS

Electrocardiogram (EKG)

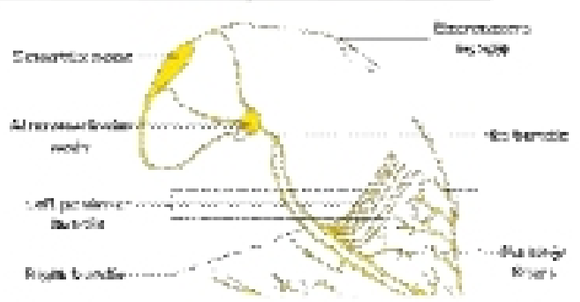
12-LEAD EKG - diagnosis, prognosis, management; used within 10 mins of ER arrival
- presence of ischemia/injury/MI
- MI location
- occlusion site



P-wave = atrial depolarization
QRS-wave = ventricle depolarization
T-wave = ventricle repolarization

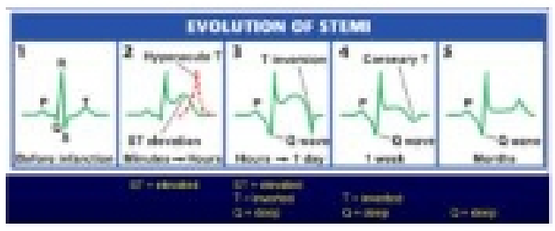
Cycle:
1) SA node
2) Bachmann's bundle
3) AV node
4) His bundle
5) Left --> Right atrial bundle branches
6) Purkinje fibers

	used for	findings
EKG	diagnosis, severity, mgmt	- IHD, injury, MI - location
Biomarkers	severity	- MI
Angiography	diagnosis, severity	- % blockage
Stress Testing (exercise/Rx)	severity	- BP, EKG
Nuclear Imaging	diagnosis	- location
Echo	diagnosis	- EF - abnormal wall motion

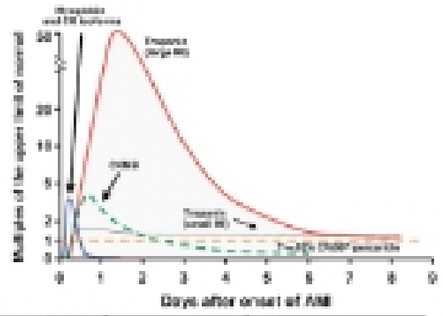


Findings:
- resting EKG> 50% normal
- may have various ST-segment/T-wave changes
  - ↑ST-segment = acute MI
  - ↓ST-segment = acute ischemia
  - T-wave inversion = acute ischemia
- Variant Angina = ↑ST-segment
- Silent Ischemia = ↑/↓ ST-segment
- Significant Ischemia = ↓ST-segment > 2mm

*MI: ↑ST-segment = earliest sign (<2 hrs after symptoms onset)
*STE MI: Q-waves appear <12 hours (sometimes <1-2 hrs) after symptoms onset



*ST & T normalize after several weeks in both NSTE & STE



BIOMARKERS - released into blood due to myocardial necrosis; indicative of MI
- Myoglobin
- CK-MB
- Troponins

	Definition	Indications	Advantages	Measurements	Elevation	Peak	Baseline
Mb	O_2-carrying protein in heart & skeletal muscle	muscle/renal damage	fastest highly sensitive		1-4 hrs	4-8 hrs	within 24 hrs
CK (-MM/-BB/-MB)	IC enzyme in muscle cells	muscle/renal damage	can detect early reinfarction	serially (base/6-12/12-24) need 2+	2-4 hrs	within 24 hrs	2-3 days
Troponins (TnI, TnT)	protein complex part of actin filaments; regulates Ca^{+2}-mediated striated muscle contractions	death risk	more sensitive/specific (than CK-MB)	serially (base/6-12/12-24) need 1+	2-12 hrs	within 24 hrs	TnI = 7 days TnT = 10-14 days

Angiography
ACS + angina + EKG(ΔST/T) + Biomarkers(+) --> CORONARY ANGIOGRAPHY (heart catheter)
ANGIOGRAPHY - "gold standard" for presence/severity of IHD; catheter + dye to assess % blockage
Significant IHD: balloon angioplasty/stent

LM	>50% stenosis
LAD/LCx/RCA	>70% stenosis

Percutaneous Intervention (PCI)
PCI - treatment; catheter + stent
Goal Times:

Fibrinolytic therapy	<30 mins
Primary PCI	<90 mins

Stress Testing
STRESS TESTING - measures BP & EKG; not diagnostic (cannot determine location); determines prognosis (future events, mortality)/probability of IHD in chronic stable angina patients
- EXERCISE TOLERANCE TEST (ETT) - treadmill w/ increasing difficulty
- PHARMA - meds that stress heart; for patients that cannot use treadmill

Dipyridamole/Adenosine	vasodilation	↑supply
Dobutamine	↑HR, contractility	↑demand

Nuclear Imaging (+ Stress Testing)
NUCLEAR IMAGING - radionuclide tracers + imaging after rest/exercise; "cold spots" (↓perfusion) determine location; used with stress testing

Reversible	Exercise
Irreversible	Exercise + Rest

Echocardiography (+ Stress Testing)
ECHO - heart ultrasound; determines EF, abnormal wall motion
TRANSESOPHAGEAL (TEE) *more sensitive/specific
TRANSTHORACIC (TTE)