Technologies for Treatment of Heart Disease

Lectures 17-19

3.18.08
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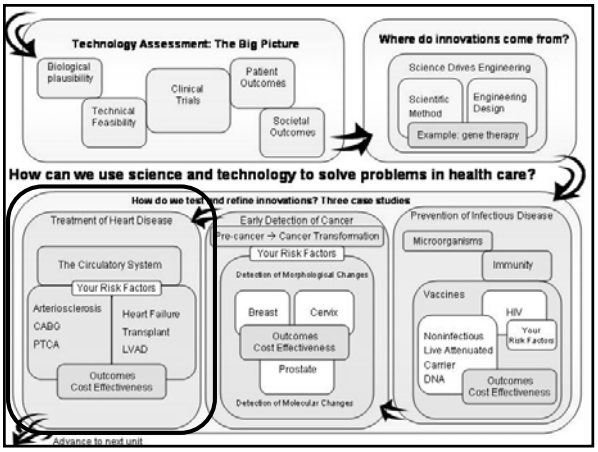
From Last Tuesday 3/11

- Cost-effectiveness of new technologies
- Advantages and disadvantages
  - Balancing effectiveness with cost-effectiveness
    - What's a good sell?
    - What's ethical?
    - Variations between developed and developing countries

Four Questions

- What are the major health problems worldwide?
- Who pays to solve problems in health care?
- How can technology solve health care problems?
- How are health care technologies managed?



Outline: Treatment of Heart Disease

- Burden of cardiovascular disease (CVD)
- Cardiovascular system
- Measuring cardiovascular health
- Valve diseases
- Atherosclerosis and treatments
  - Stroke
  - Heart attack
- Heart failure and treatments

Muddiest point/Clearest point

Burden of Cardiovascular Disease (CVD)

What is Cardiovascular Disease (CVD)

- Generally: all diseases that involve the heart and blood vessels
  - Valve diseases
- Typically: those diseases related to atherosclerosis
  - Cerebrovascular disease
    - Stroke
  - Ischemic heart disease
    - Coronary artery disease (CAD)

Global Burden of CVD

- In 1999: CVD contributed to a third of global deaths
  - 80% are in low and middle income countries
- By 2010: CVD is estimated to be the leading cause of death in developing countries
  - General improvements in health make CVD a factor in overall mortality rates
- In 2003: 16.7 million deaths due to CVD
  - Cost of care for these conditions is high

2002 Worldwide Mortality

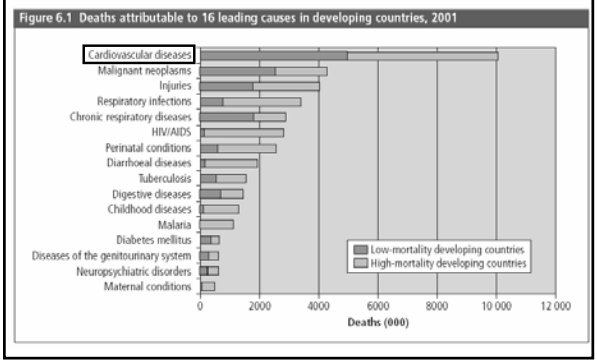
Mortality – adults aged 15–59

Rank	Cause	Deaths (000)
1	HIV/AIDS	2279
2	Ischaemic heart disease	1332
3	Tuberculosis	1036
4	Road traffic injuries	814
5	Cerebrovascular disease	783
6	Self-inflicted injuries	672
7	Violence	473
8	Cirrhosis of the liver	382
9	Lower respiratory infections	352
10	Chronic obstructive pulmonary disease	343

Mortality – adults aged 60+

Rank	Cause	Deaths (000)
1	Ischaemic heart disease	5825
2	Cerebrovascular disease	4689
3	Chronic obstructive pulmonary disease	2399
4	Lower respiratory infections	1396
5	Trachea, bronchus, lung cancers	928
6	Diabetes mellitus	754
7	Hypertensive heart disease	735
8	Stomach cancer	605
9	Tuberculosis	495
10	Colon and rectum cancers	477

Mortality in Developing Countries



US Burden of CVD

- CVD:
  - 61 million Americans (≈ 25% of population)
  - Accounts for > 40% of all deaths -- 950,000/year
- Cost of CVD disease:
  - $351 billion
    - $209 billion for health care expenditures
    - $142 billion for lost productivity from death and disability
- Stroke
  - Third leading cause of death in the US
- Ischemic Heart/CAD
  - Leading cause of death in US
  - Coronary heart disease is a leading cause of premature, permanent disability among working adults

US Burden of CVD: Heart Attack

- Consequences of ischemic heart disease
  - Narrowing of the coronary arteries that supply blood to the heart
- Each year:
  - 1.3 million Americans suffer a heart attack
  - 460,000 (≈ 40%) are fatal
  - Half of those deaths occur within 1 hour of symptom onset, before person reaches hospital
- Onset is often sudden
  - Importance of prevention

Risk Factors of CVD

- Risk Factors:
  - Tobacco use
  - Low levels of physical activity
  - Inappropriate diet and obesity
  - High blood pressure
  - High cholesterol

<u>For almost all individuals these are modifiable!!!</u>

Early Detection of CVD

- Screening for CVD:
  - Measure blood pressure (BP) annually
    - 12-13 point reduction in blood pressure can reduce heart attacks by 21%
  - Check cholesterol every 5 years
    - 10% drop in cholesterol can reduce heart attacks by 30%
- Patient compliance
  - High BP: not under control in 70% of patients
  - High cholesterol: not under control in 80% of patients

The Cardiovascular System

Cardiovascular System

- Anatomy and Physiology
  - Vessels
  - Heart
  - Valves
- How to we assess our risk factors?
  - Measure BP and cholesterol levels
- How to we measure the health and functionality of our cardiovascular system?
  - Listen to heart sounds
  - Quantitative parameters for heart function

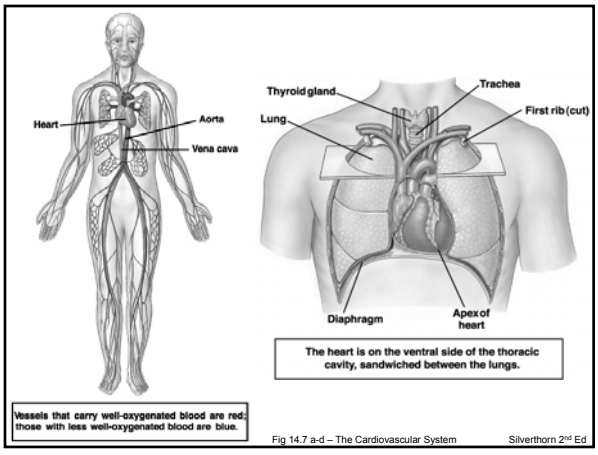


Fig 14.7 a-d – The Cardiovascular System Silverthorn 2nd Ed

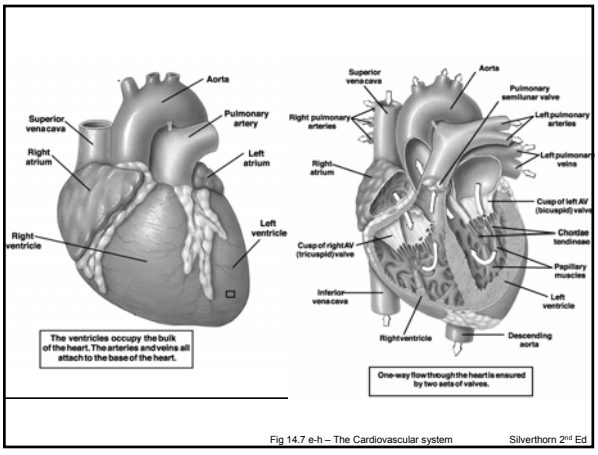


Fig 14.7 e-h – The Cardiovascular system Silverthorn 2nd Ed

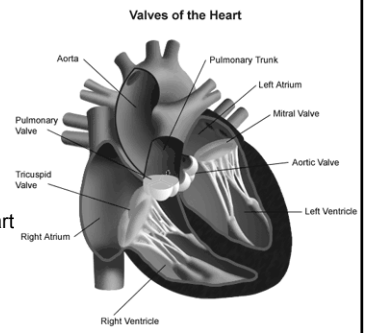
The Heart as a Pump

- The right atria fills with blood returning to heart from the vena cava
  - Tricuspid valve separates right ventricle
- Right ventricle pumps blood to lungs to be oxygenated
  - Pulmonary valve separates pulmonary artery
- Left atria fills with oxygen rich blood from pulmonary vein
  - Mitral (bicuspid) valve separates the left ventricle
- Left ventricle pumps blood to body
  - Aortic value separates the aorta
- Filling is the "resting" state -- diastole
- Pumping/contraction

http://www.pbs.org/wgbh/nova/eheart/human.html

Four Heart Valves

- Two types
  - AV
    - Atria/ventricle
    - 2 or 3 flaps
    - Right: tricuspid
    - Left: mitral/bicuspid
  - Semilunar
    - Blood leaves the heart
    - 3 cusps
    - Right: pulmonary
    - Left: aortic



http://www.uabhealth.org/14549/

Measuring CV Health

Measuring CV Health

- Heart sounds
- Blood Pressure (BP)
- Serum cholesterol levels/lipid panel
- Echocardiogram
- Electrocardiogram

Measuring CV Health: Heart Sounds

- Heart sounds are produced by valve closure
- Normal heart sound is "lub-dup"
  - Lub: AV valves close
  - Dup: Semilunar valves close
- Abnormalities can produce heart murmurs
  - Not always though
  - Echocardiography

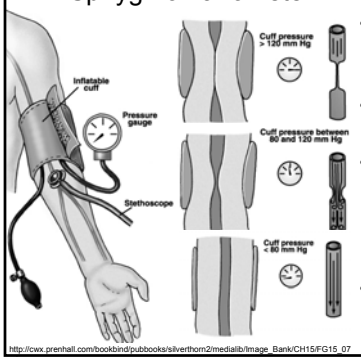
Measuring CV Health: Blood Pressure

- Normal blood pressure:
  - Varies from minute to minute
  - Varies with changes in posture
  - Should be < 120/80 mm Hg for an adult
    - The higher/top number + systolic
    - The lower/bottom number =diastolic
- Pre-hypertension:
  - Blood pressure that stays between 120-139/80-89
- Hypertension:
  - Blood pressure above 140/90 mm Hg
- My blood pressure = 108/64

http://www.medicaldiscoverynews.com/shows/bloodpressure.

How Do We Measure Blood Pressure?

Sphygmomanometer



http://cwx.prenhall.com/bookbind/pubbooks/silverthorn2/medialib/Image_Bank/CH15/FG15_07

- Increase cuff pressure > systolic
  - No blood flow in arm
- Gradually release pressure
- Cuff pressure = systolic
  - Turbulent rush of blood gives Korotkoff sounds
- Cuff pressure = diastolic
  - No compression of

Blood Pressure Activity

- Groups of 6
  - Even numbers since you'll need a partner
- Measure each person's blood pressure twice
- Write down the results each time
- Get an average BP for each person
- Get an average for your entire group
- We'll make a class average and compare

Measuring CV Health: Serum Cholesterol

- LDL (low-density)
  - "bad" cholesterol
  - Cholesterol builds up inside blood vessels
- HDL (high-density)
  - "good" cholesterol
  - Removes cholesterol from vessels to liver for excretion

Interpretation of Serum Lipid Levels				
	Total Cholesterol	LDL	HDL	Triglycerides
Optimal		Under 100	Above 60	
Desirable	Under 200	Under 130		Below 150
Borderline	200-239	130-159		150-199
Abnormal	Over 240	Over 160	Below 40	Above 200

http://www.medicaldiscoverynews.com/shows/transfats.html

Serum Cholesterol Levels: Case Study

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Borderline	200-239	130-159		150-199
Abnormal	Over 240	Over 160	Below 40	Above 200

Patient A				Patient C			
Total cholesterol	LDL	HDL	Triglycerides	Total cholesterol	LDL	HDL	Triglycerides
192	135	44	67	235	136	63	182
Patient B				**Patient D**			
Total cholesterol	LDL	HDL	Triglycerides	Total cholesterol	LDL	HDL	Triglycerides
197	97	77	116	195	109	66	99

Serum Cholesterol Levels: Case Study

Patient A				Patient C			
Total cholesterol	LDL	HDL	Triglycerides	Total cholesterol	LDL	HDL	Triglycerides
192	135	44	67	235	136	63	182
Patient B				**Patient D**			
Total cholesterol	LDL	HDL	Triglycerides	Total cholesterol	LDL	HDL	Triglycerides
197	97	77	116	195	109	66	99

Serum Cholesterol levels: Case Study

- Physiologic measurements vary a lot!
  - Let's see with your BP values
- What's important is to monitor over time
  - Start young
  - Be consistent
  - Take responsibility for your health

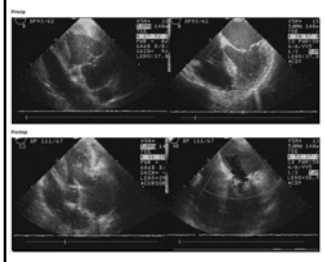
Quantifying Heart Performance

- Heart Rate (HR)
  - Number of heartbeats per minute
  - Normal value is 60-90 bpm at rest
  - Can drop as low as 20 bpm when sleeping
- Stroke Volume (SV)
  - Amount of blood pumped by ventricle with each heartbeat
  - Normal value is 60-80 mL
- Cardiac output (CO)
  - Total volume of blood pumped by ventricle per minute
  - CO = HR x SV
  - Normal value is 4-8 L/min

Quantifying Heart Performance

- Blood volume
  - Total volume of blood in circulatory system
  - Normal value is ≈ 5 L
  - Total volume of blood is pumped through our heart each minute!!
- Ejection Fraction (EF)
  - Fraction of blood pumped out of ventricle relative to total volume (at end diastole)
    - End diastolic volume (EDV)
  - EF = SV/EDV
  - Normal value > 60%
  - So no one's heart is a "perfect" pump

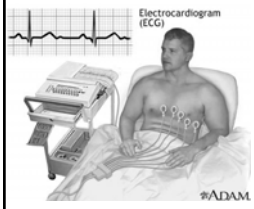
Advanced Measures of CV Performance: Echocardiogram



- Sound waves produce images
  - Ultrasound
- Visualize complex movements within the heart
  - Ventricles squeezing and relaxing
  - Opening and closing of valves in time with heartbeat
- Identify and confirm abnormalities in muscle and valves

http://www.heartsite.com/html/echocardiogram.html#
http://dir.nhlbi.nih.gov/labs/cs/image_gallery/echocardiography.asp

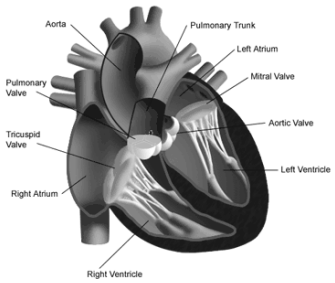
Advanced Measures of CV Performance: Electrocardiogram



- Electrical activity (ECG or EKG)
- Records the electric waves generated by heart activity
  - Electric signal measured in mV
  - Different waveform is seen based on location of the electrode
- Normal heartbeat is initiated by a small pulse of current
- Electrical activity starts at the top of the heart, spreads downward and then up again
  - Excites the muscles in optimal way for pumping blood
- Pacemaker Cells
  - Specialize in producing electrical signal

http://nobelprize.org/educational_games/medicine/ecg/

Valve Diseases



http://www.uabhealth.org/14549/

Valve Diseases: Etiology

- Two main types of valve dysfunction
  - Regurgitation
    - Improper valve closing allows backwards leakage
  - Stenosis
    - Narrowing of opening does not let enough blood through
- Common causes
  - Congenital birth defect
  - Infective endocarditis
  - Rhuematic fever
  - Myxomatous degeneration

Valve Diseases: Detection and Treatment

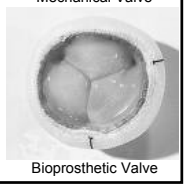
- May be detectable through heart sounds
- Diagnosis with Doppler echocardiogram
  - Doppler assesses blow flow
    - Direction and velocity
- Treatment is usually surgically repairing or replacing the affected valve(s)
- > 100,000 valve replacements and repairs in the US each year

http://www.youtube.com/watch?v=IBBCu3x_TKo

Artificial Heart Valves

- Surgical Repair or Reconstruction
  - Common for mitral valve dysfunction
  - Use pulmonary in place of aortic
- Mechanical
  - Last for 10-12 years
  - Require anticoagulation therapy
- Bioprosthetic
  - Glutaraldehyde fixed pericardium and valves
  - Calcification
  - Some can last for up to 20 years
- Xenografts
  - Porcine valves; good mimic
  - Immunogenic
- Allografts
  - Good for children
  - Scarce supply

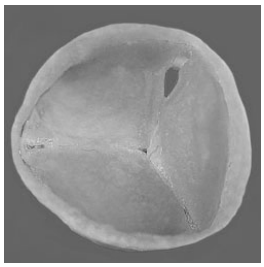
Mechanical Valve



Bioprosthetic Valve

Tissue Engineered Heart Valves

- Primarily targeted for use in pediatric patients
  - No other option works well here
- Need of successful tissue-engineered living valve, which can grow with patients and last for lifetime
- Regeneration
  - Implanted matrix remodels in vivo
- Repopulation
  - Implant acellular porcine valve which fills in with patient cells



Tissue-engineered heart valve
Hoerstrup et al., *Circulation* 2002

Valve Diseases: Final Thoughts

- Early concerns have been addressed
  - Replacement valve longevity
  - Surgical mortality
- Repeated use of bioprosthetic valves is common
  - Risk of second surgery is ≈ risk of thromboembolism associated with mechanical valves
- Edwards pericardial valve may last 20 years
  - Equivalent to an allograft

http://circres.ahajournals.org/cgi/content/full/97/8/74

Valve Diseases: Final Thoughts

- The status quo seems to be acceptable
- Does this affect the field of engineering new replacement valve products?
  - A number of new innovations have failed in clinical trials
    - Physicians don't want to try new things
  - Should we spend money and resources on tissue engineering valves?
  - Still no effective therapy for children
    - Only 10% of adult market
    - First clinical tissue engineered product tested failed

http://circres.ahajournals.org/cgi/content/full/97/8/74

Outline: Treatment of Heart Disease

- ~~Burden of cardiovascular disease (CVD)~~
- ~~Cardiovascular system~~
- ~~Measuring cardiovascular health~~
- ~~Valve diseases~~
- Atherosclerosis and treatments
  - Stroke
  - Heart attack
- Heart failure and treatments

For Thursday…

- No homework is due next class
- Muddiest point & clearest point
- And thanks again to Vishal for material and expertise on heart valves!