Biomedical Engineering for Global Health

Lecture Four:

Leading Causes of Mortality, Ages 45-60

Global Health Challenges

Summary of Lecture 3: Leading Causes of Mortality Ages 15-44

- Developing World
  1. HIV/AIDS
  2. Unintentional injuries
  3. Cardiovascular diseases
  4. Tuberculosis
- Developed World
  1. Unintentional injuries
  2. Cardiovascular diseases
  3. Cancer
  4. Self-inflicted injuries

1. HIV/AIDS

- While working at an outreach clinic in Africa, you encounter a critically ill adolescent who tests positive for HIV.
  - How can you estimate the severity of this patient's disease?
  - What classes of pharmaceuticals are available to treat this patient?

2. Unintentional Injuries

- Do unintentional injuries account for more deaths in developed or developing countries? Give several reasons why.

3. Cancer and Cardiovascular Diseases

- Will be discussed today!

4. Tuberculosis

- If your next PPD skin test is positive, what will your doctor do next?

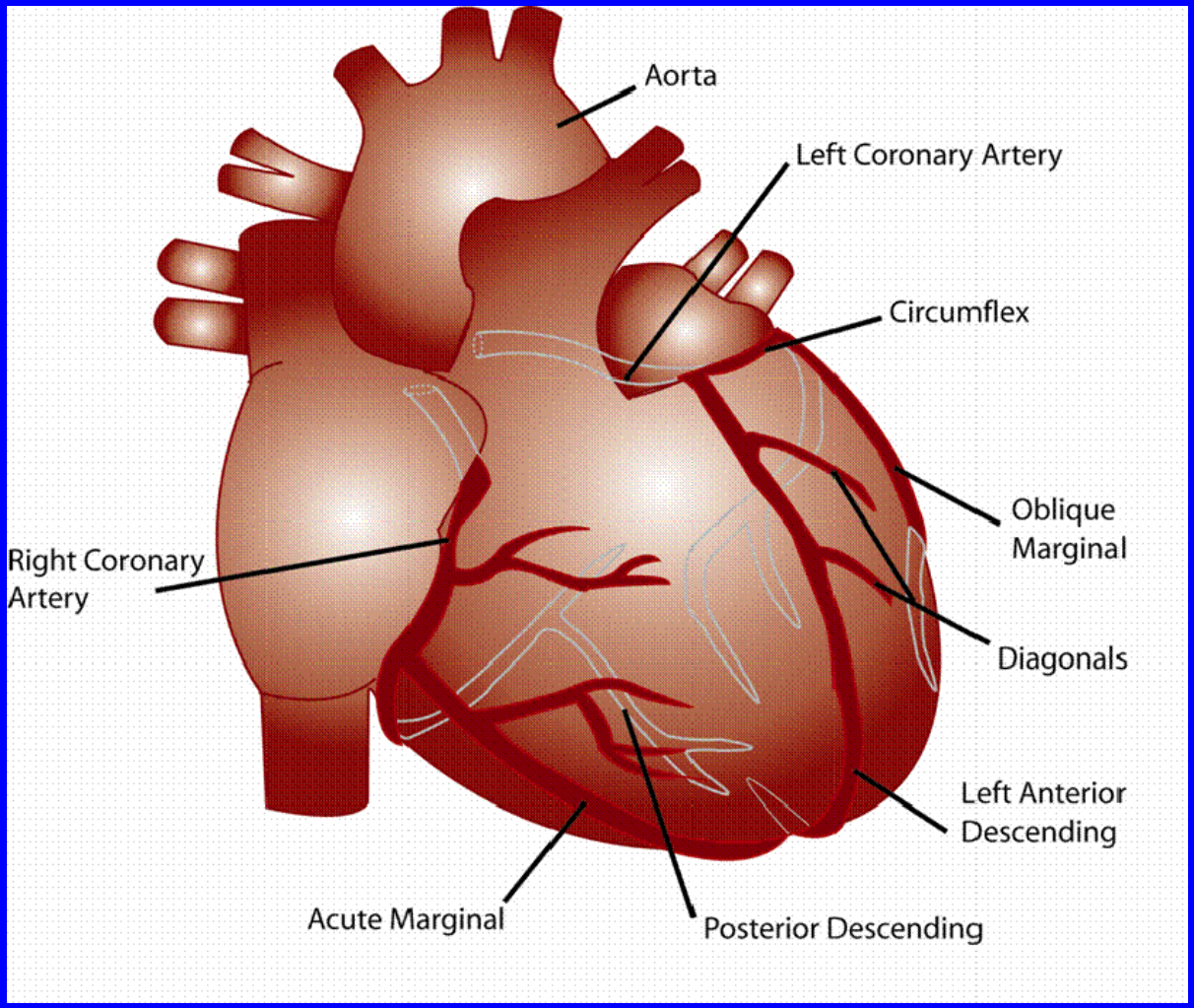
4. Self-Inflicted Injuries

- What disease ranks #1 in DALYs in developed countries?
- How can we prevent these injuries?

Lecture 4:
Leading Causes of Mortality Ages 45-60

- Developing World
  1. Cardiovascular diseases
  2. Cancer (malignant neoplasms)
  3. Unintentional injuries
  4. HIV/AIDS
- Developed World
  1. Cardiovascular diseases
  2. Cancer (malignant neoplasms)
  3. Unintentional injuries
  4. Digestive Diseases

1. Cardiovascular Diseases



70ml per beat... 1.3 gallons per minute... 1,900 gallons per day... 700,000 gallons per year... 48 million gallons by age 70...

1. Cardiovascular Diseases

- Burden of Cardiovascular Diseases
- Ischemic Heart Disease
  - Epidemiology
  - Pathogenesis
  - Diagnosis
  - Treatment
- Cerebrovascular Disease
  - Epidemiology
  - Pathogenesis
  - Diagnosis
  - Treatment

Burden of Cardiovascular Diseases: Ages 15-44

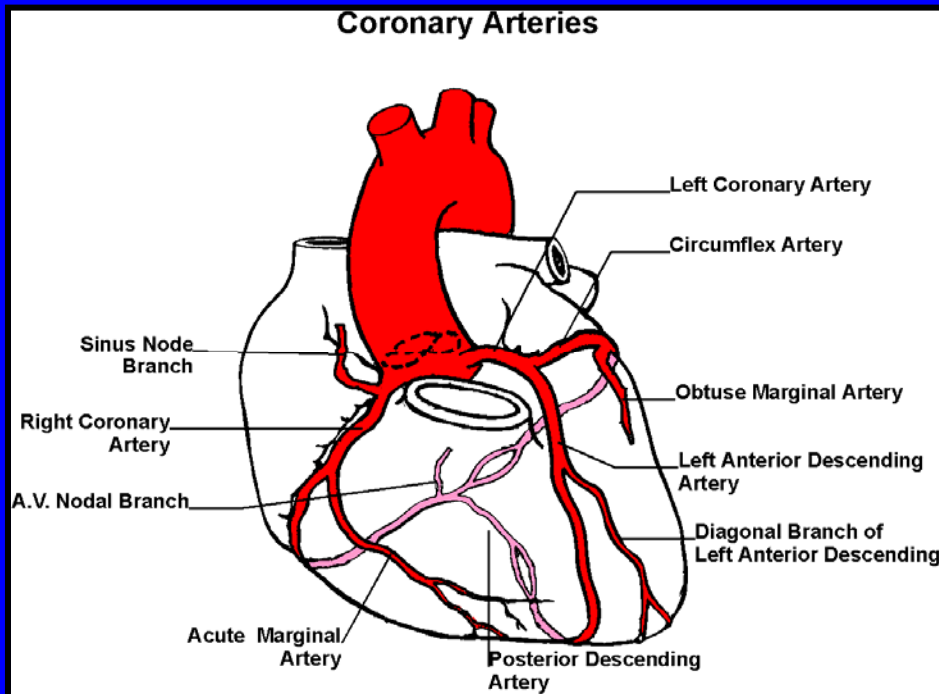
- 768,000 people ages 15-44 die as a result of cardiovascular disease every year
- Most common causes:
  - Ischemic heart disease (286,000 deaths)
  - Cerebrovascular disease (159,000 deaths)

Burden of Cardiovascular Diseases: Ages 45-60

- 2 million people ages 45-60 die as a result of cardiovascular disease every year
- Most common causes:
  - Ischemic heart disease (1 million deaths)
  - Cerebrovascular disease (625,000 deaths)

Ischemic Heart Disease: Epidemiology

- United States
  - 12 million people have coronary artery disease
  - Causes more deaths, disability and economic cost than any other illness
- Risk factors
  - Positive family history
  - Diabetes
  - Hyperlipidemia
  - Hypertension
  - Smoking



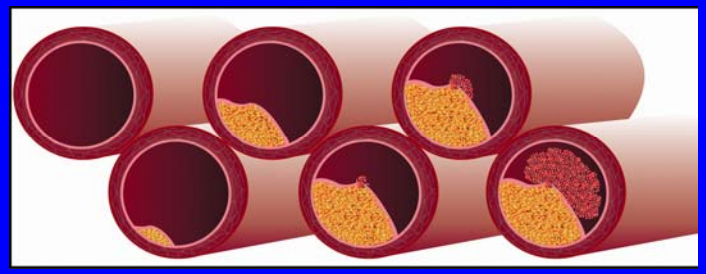
Ischemic Heart Disease: Pathogenesis

- Atherosclerosis
  - Causes decrease in myocardial perfusion
  - Most common symptom is angina
    - Stable angina (75% lumen blockage)
      - Typically a 50-60 yo man or 65-75 yo woman
      - Heaviness, pressure, squeezing, smothering or choking
      - Localized to chest, may radiate to left shoulder and arms
      - Lasts 1-5 minutes
    - Unstable angina (more than 80% blockage)
      - Patients with angina that is:
        - New onset and severe and frequent
        - Accelerating
        - Angina at rest

Ischemic Heart Disease: Pathogenesis

Evolution of a heart attack:

1. Endothelial injury
2. Fatty deposits
3. Fibrous cap with necrotic core
4. Unstable plaques rupture, thrombogenic core causes blood clots
5. Blood clots can lead to complete occlusion
6. Heart muscle supplied by occluded artery dies
7. If patient survives, affected heart muscle is replaced by scar tissue



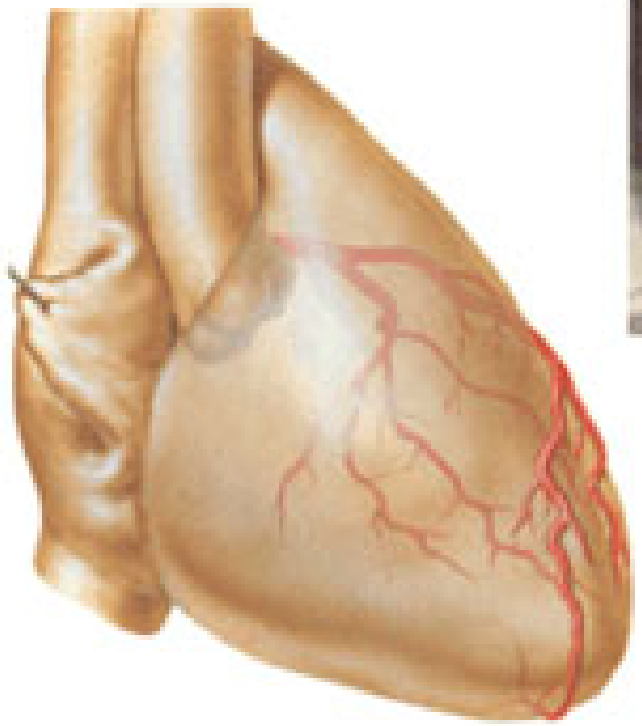
- ***In the US, 30% of patients do not survive a first heart attack***
- ***For 50% of CAD patients, their first symptom is a heart attack***

Ischemic Heart Disease: Diagnosis

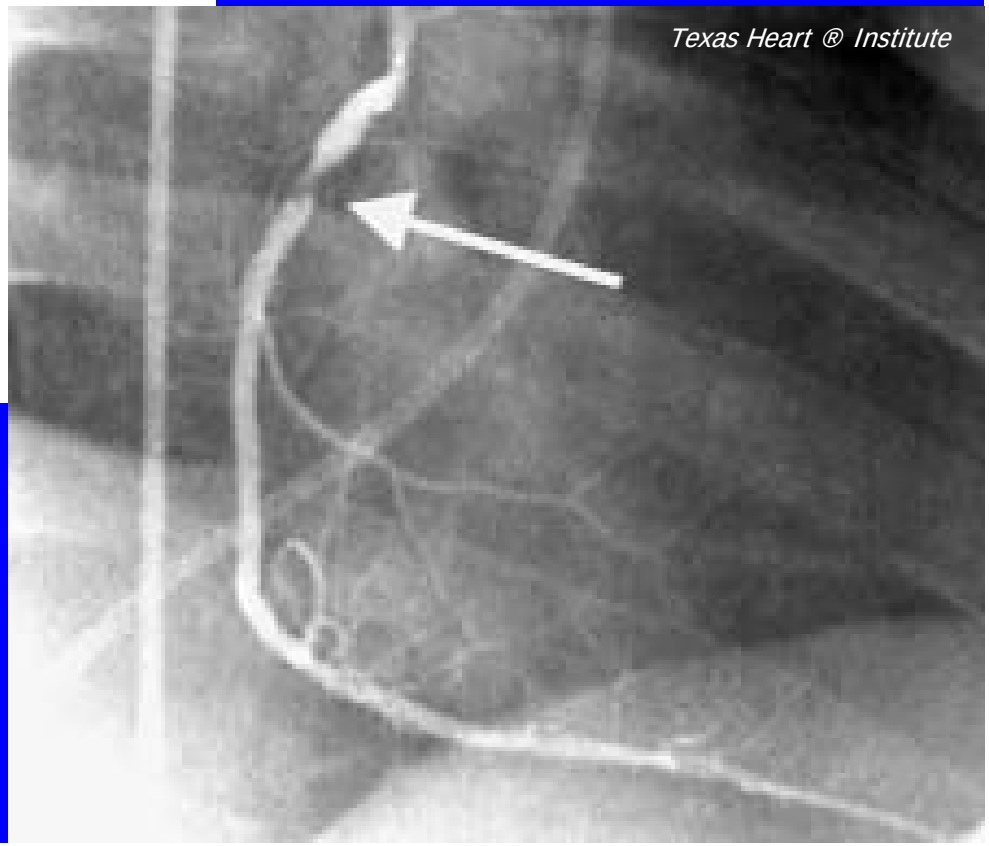
- Usually made by history
- Physical exam may reveal other disorders
  - Lipid disorders
  - Hypertension
  - Diabetes
- Testing
  - EKG
  - Stress Testing
  - Coronary arteriography

Left Coronary Artery

Arteriographic View 2



Ozarks Medical Center



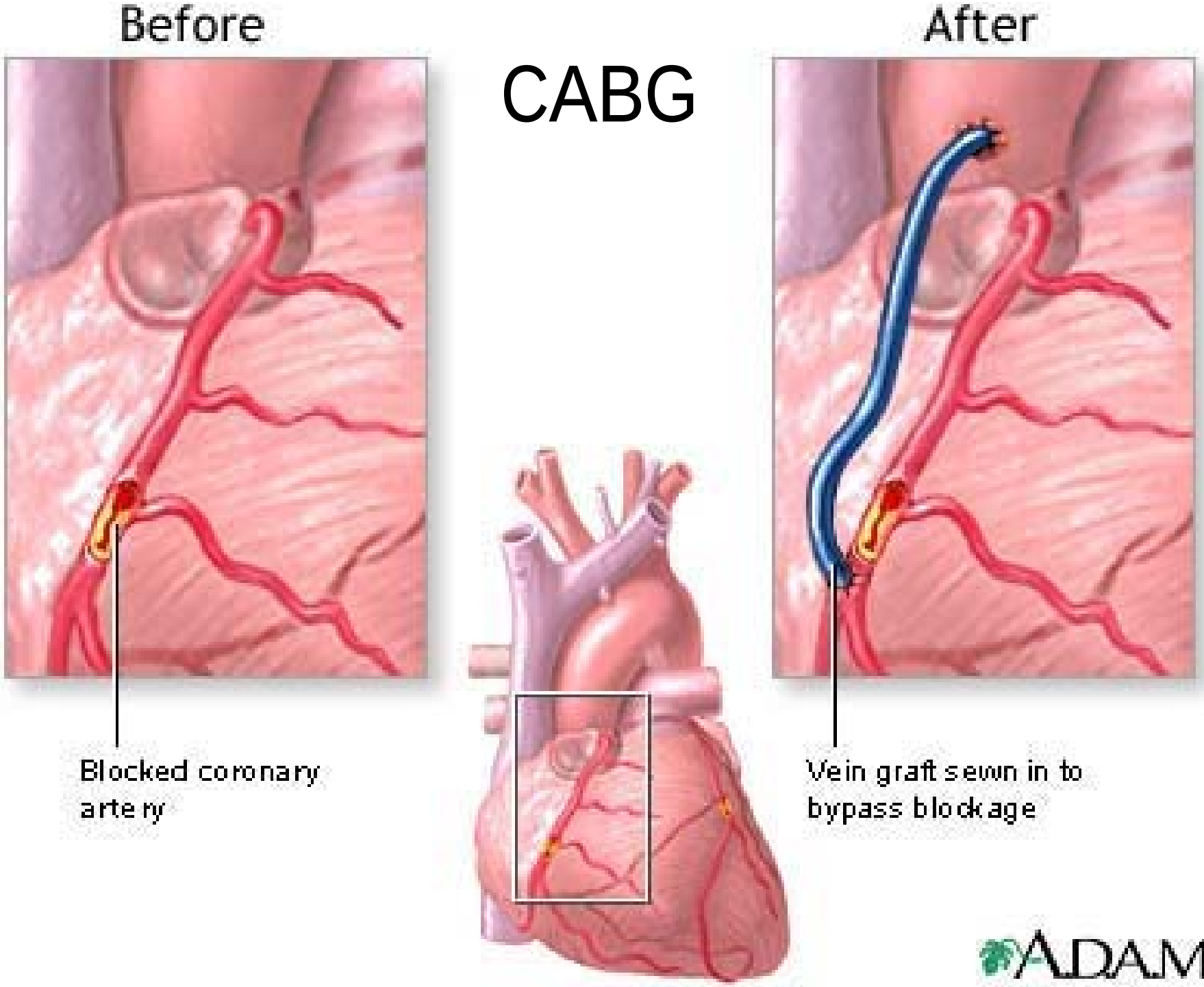
Texas Heart ® Institute

http://www.columbiasurgery.org/divisions/cardiac/images/novartis_207B.jpg

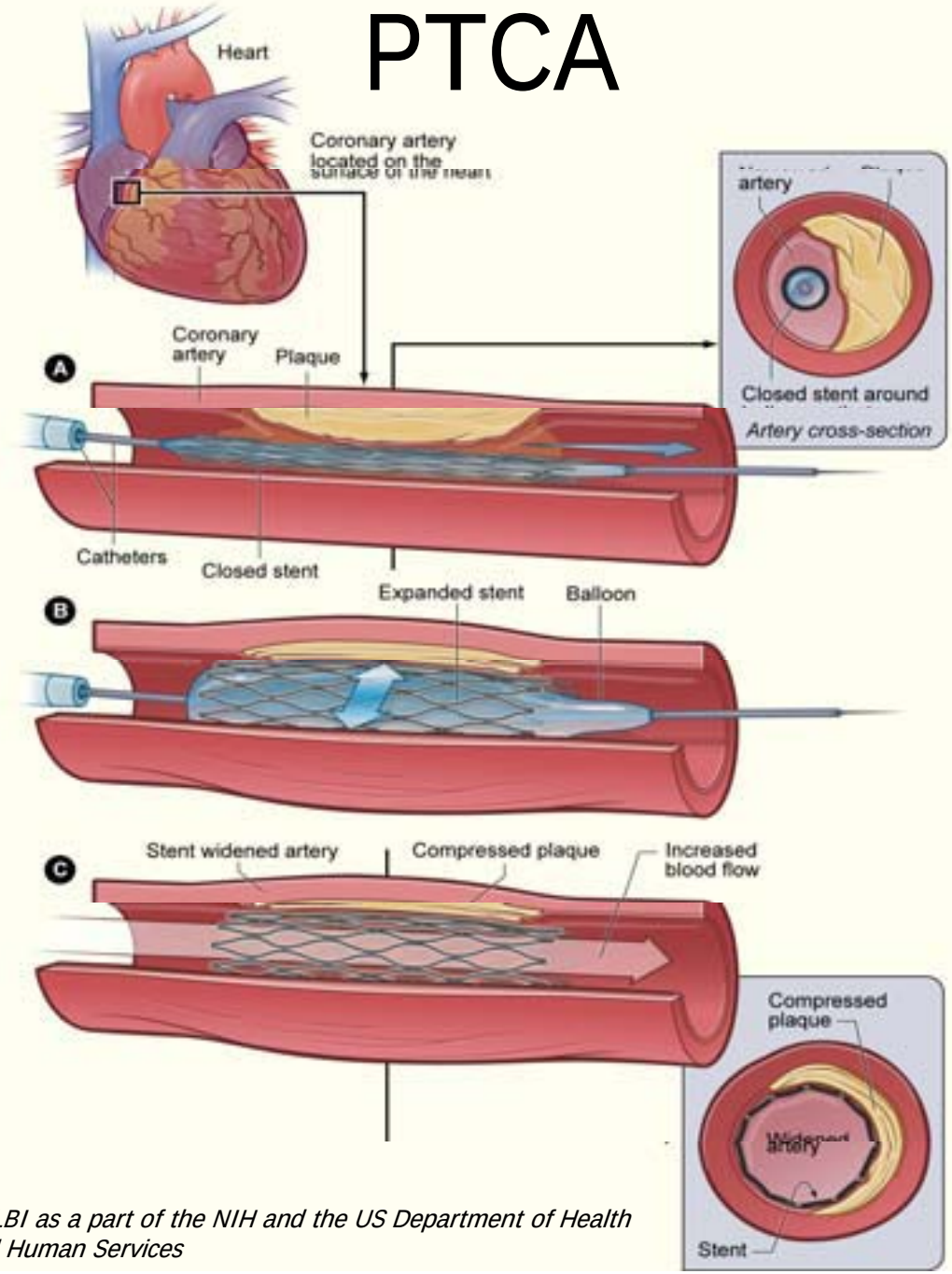
Ischemic Heart Disease: Treatment

- Medical management (may relieve symptoms of CAD, but does not reduce coronary blockage)
  - Nitrates
    - Increase myocardial oxygen supply, systemic vasodilation
  - Beta blockers
    - Inhibit increases in heart rate and contractility
    - Decrease myocardial oxygen demand
  - Calcium channel antagonists
    - Coronary vasodilators
- Thrombolysis
- CABG (Coronary Artery Bypass Grafting)
- PTCA (Percutaneous Transluminal Coronary Angioplasty)

CABG


Before
After
Blocked coronary artery
Vein graft sewn in to bypass blockage
A.D.A.M.

PTCA



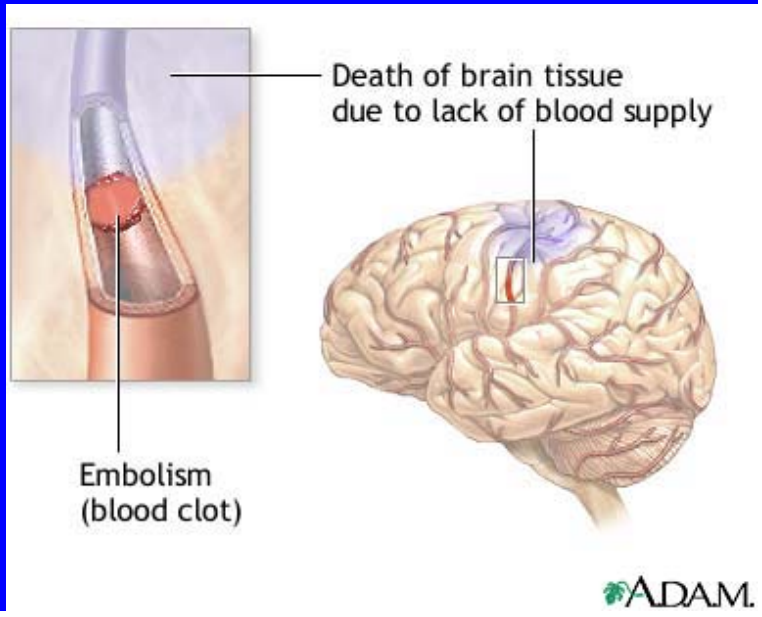
NHLBI as a part of the NIH and the US Department of Health and Human Services

Cerebrovascular Disease: Epidemiology

- Third leading cause of death in the US
- Most prevalent neurologic disorder
- 87% caused by ischemia and resulting infarction

Cerebrovascular Disease: Pathogenesis

- Causes of stroke:
  - Blood vessel supplying the brain is blocked
  - Thrombosis (clot in vessel)
  - Embolism (clot breaks off and lodges in blood vessel in brain)
  - Vasoconstriction or spasm
  - Venous collapse



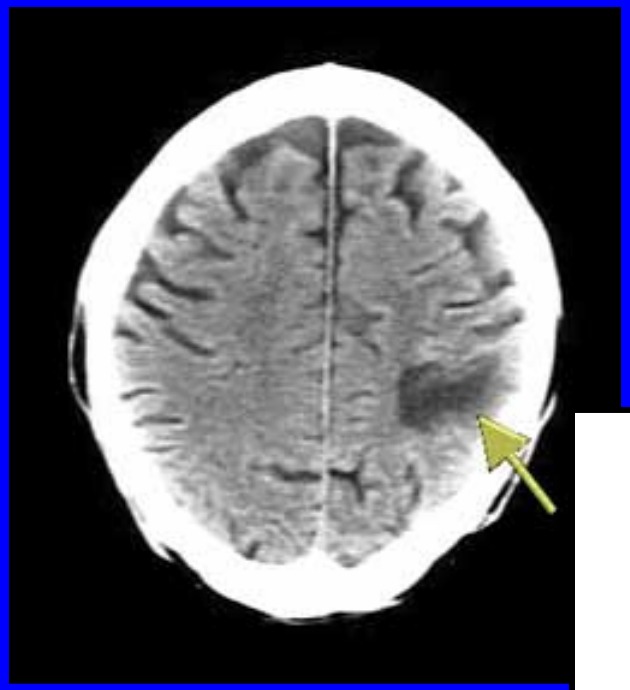
Cerebrovascular Disease: Pathogenesis

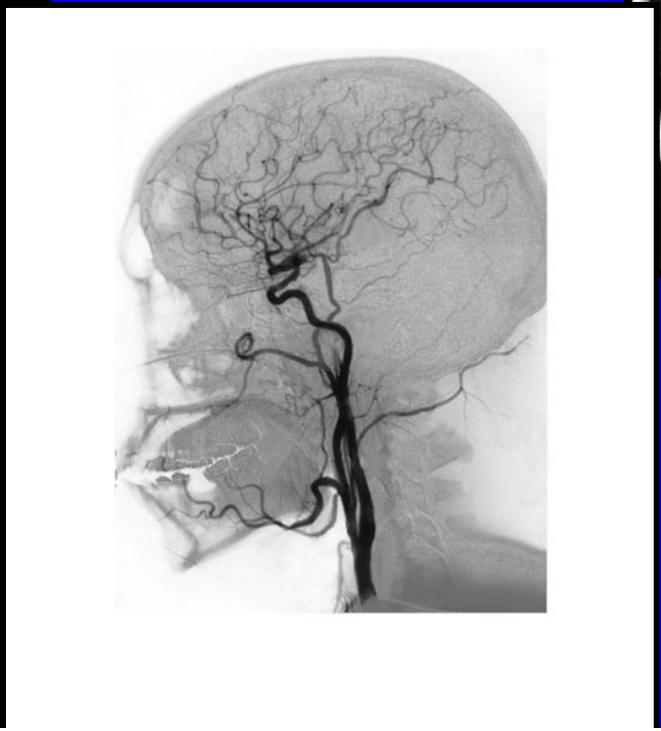
- Abrupt onset with focal neurologic deficit
  - Usually mini-event or warning signs
    - 15% Transient Ischemic Attacks (TIAs)
  - Reversible ischemia
    - Some lasting 24-72 hours
  - Completed stroke
    - Maximal deficit within hours
    - Often patient awakens with completed stroke
    - Usually preceded by TIA Progressive stroke
    - Ischemia worsens min. to min. or hour to hour

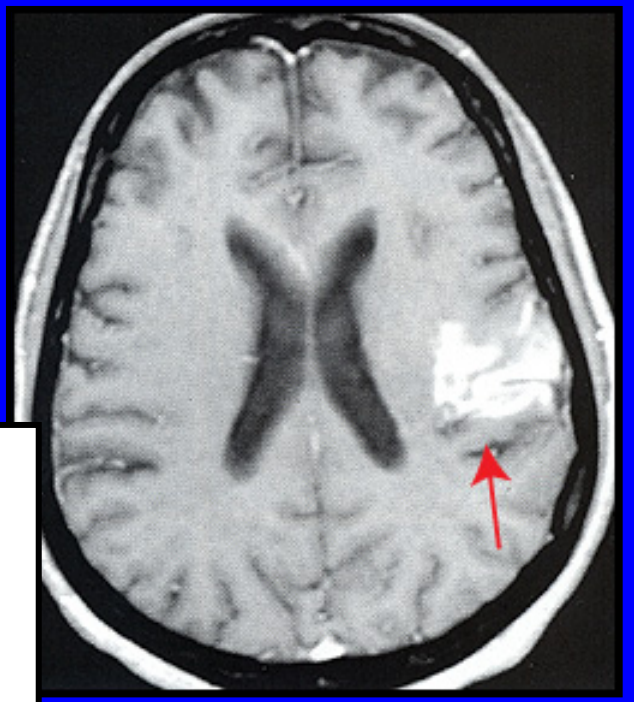
Cerebrovascular Disease: Diagnosis

- History
- Exam
- Imaging
  - CT Scan
  - MRI
  - MR Angiography

Cerebrovascular Disease: Diagnosis



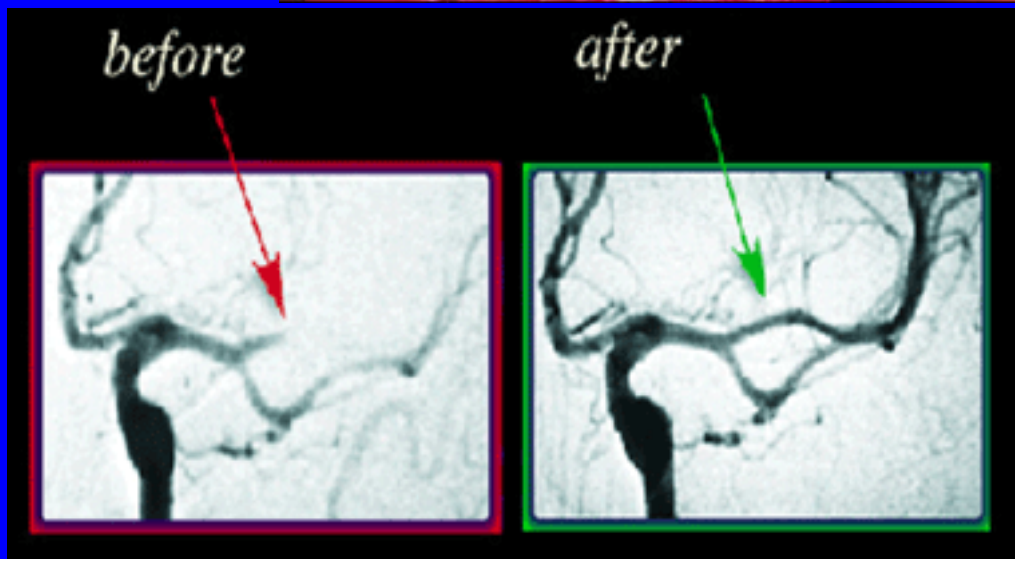




http://www.strokecenter.org/

Cerebrovascular Disease: Treatment

- Thrombolysis
- Rehabilitation
- Experimental
  - Angioplasty
  - Heparin
  - Coumarin
  - Aspirin



2. Cancer

- Cancer Overview
- Burden of Cancer
- Pathogenesis of Cancer
- Cancer Diagnosis
- Treatment of Cancer
- Cancer and Infectious Diseases
- Lung Cancer
  - Epidemiology
  - Clinical Manifestations
  - Treatment

Cancer Overview

- Cancer is a group of diseases characterized by uncontrolled cell growth
- Cancer cells usually form a tumor
  - Abnormal mass of tissue
  - Growth exceeds that of normal tissue
  - Purposeless and preys on host
  - Two types of tumors: Benign, Malignant
- Disease results from:
  - Abnormal growth, loss of normal function
  - Invasion, compression of adjacent tissues
  - Metastases to distant sites in the body

Burden of Cancer

- 2nd leading cause of death in US
- 1 of every 4 deaths is from cancer
- Nearly 1/2 of all men and 1/3 of all women will develop cancer at some point in their lives
- 5-year survival rate: 59%
- Annual costs: $107 billion

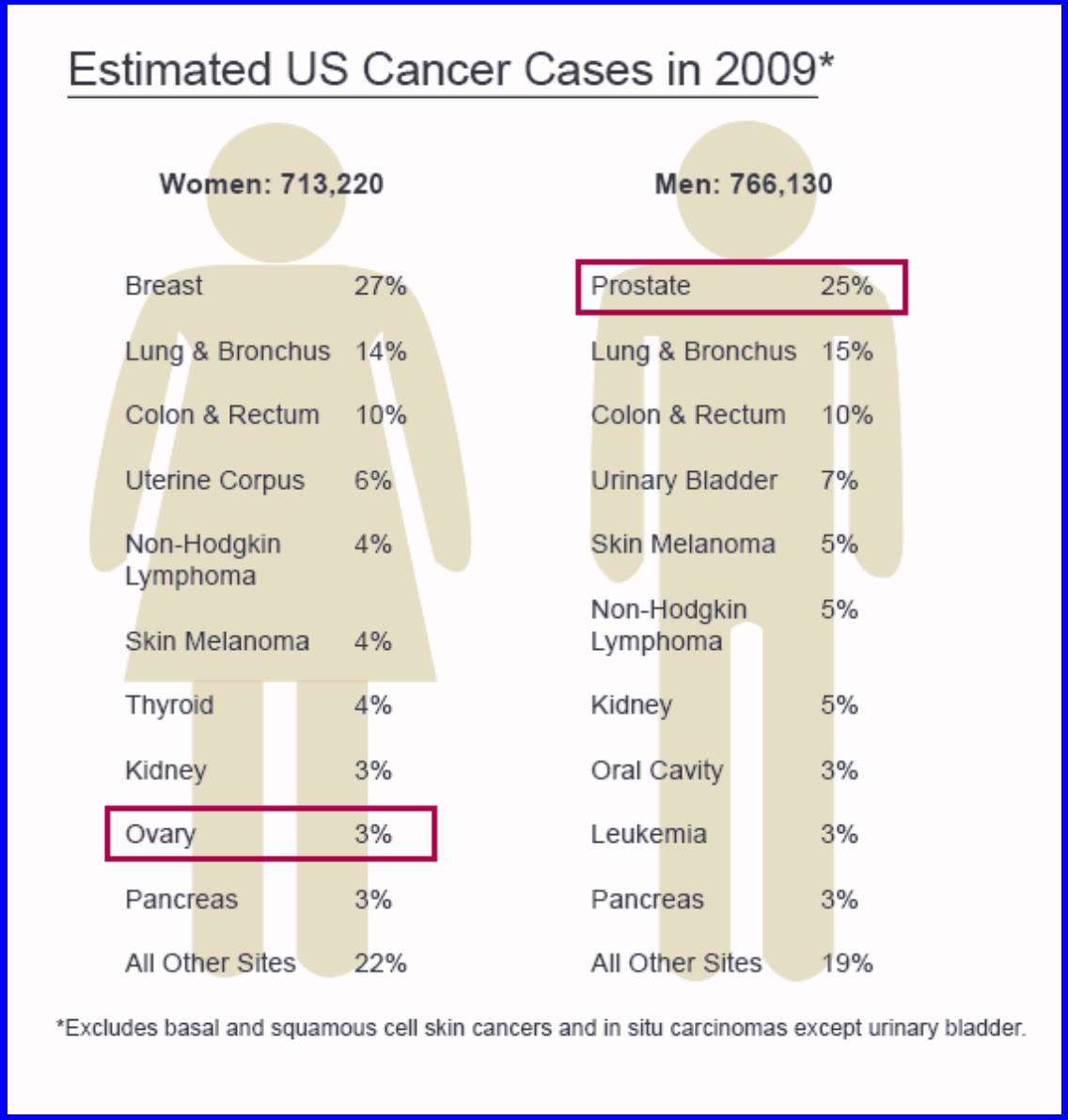
Burden of Cancer, Ages 15-44

- Cancer kills 580,000 people ages 15-44 each year throughout the world
- Most common causes, ages 15-44:
  - Liver Cancer (68,000 deaths per year)
  - Leukemias (65,000)
  - Stomach Cancer (58,000)
  - Breast Cancer (57,000)

Burden of Cancer, Ages 45-60

- Cancer kills 1.5 million people ages 45-60 each year throughout the world
- Most common causes, ages 45-60:
  - Lung cancer (263,000 deaths per year)
  - Stomach cancer (185,000)
  - Liver cancer (179,000)
  - Breast cancer (148,000)

2009 Estimated US Cancer Deaths



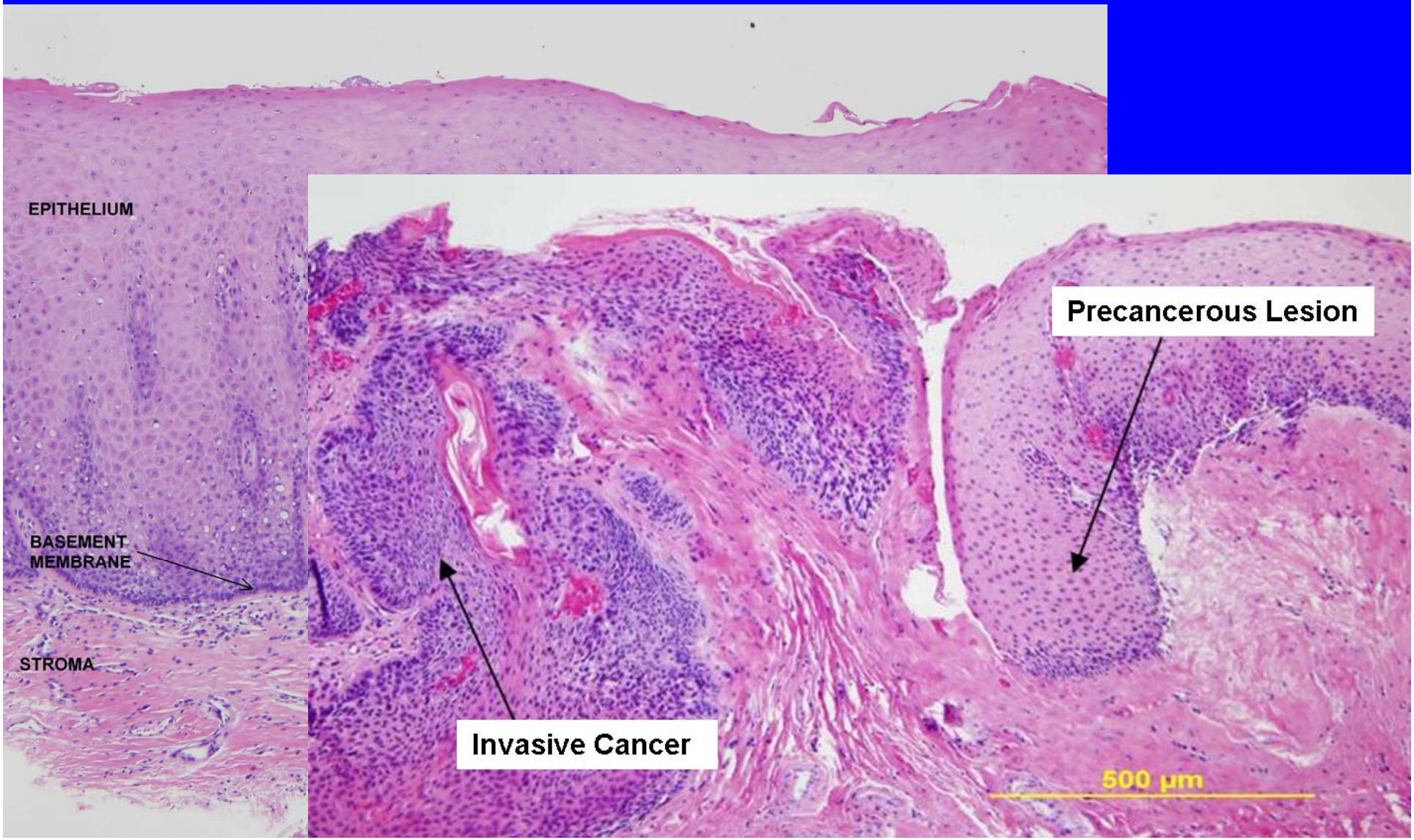
Pathogenesis of Cancer

- Natural history of most cancers include sequential phases:
  - Malignant transformation in target cell
  - Growth of transformed cells
  - Local invasion
  - Distant metastases

Pathogenesis of Cancer

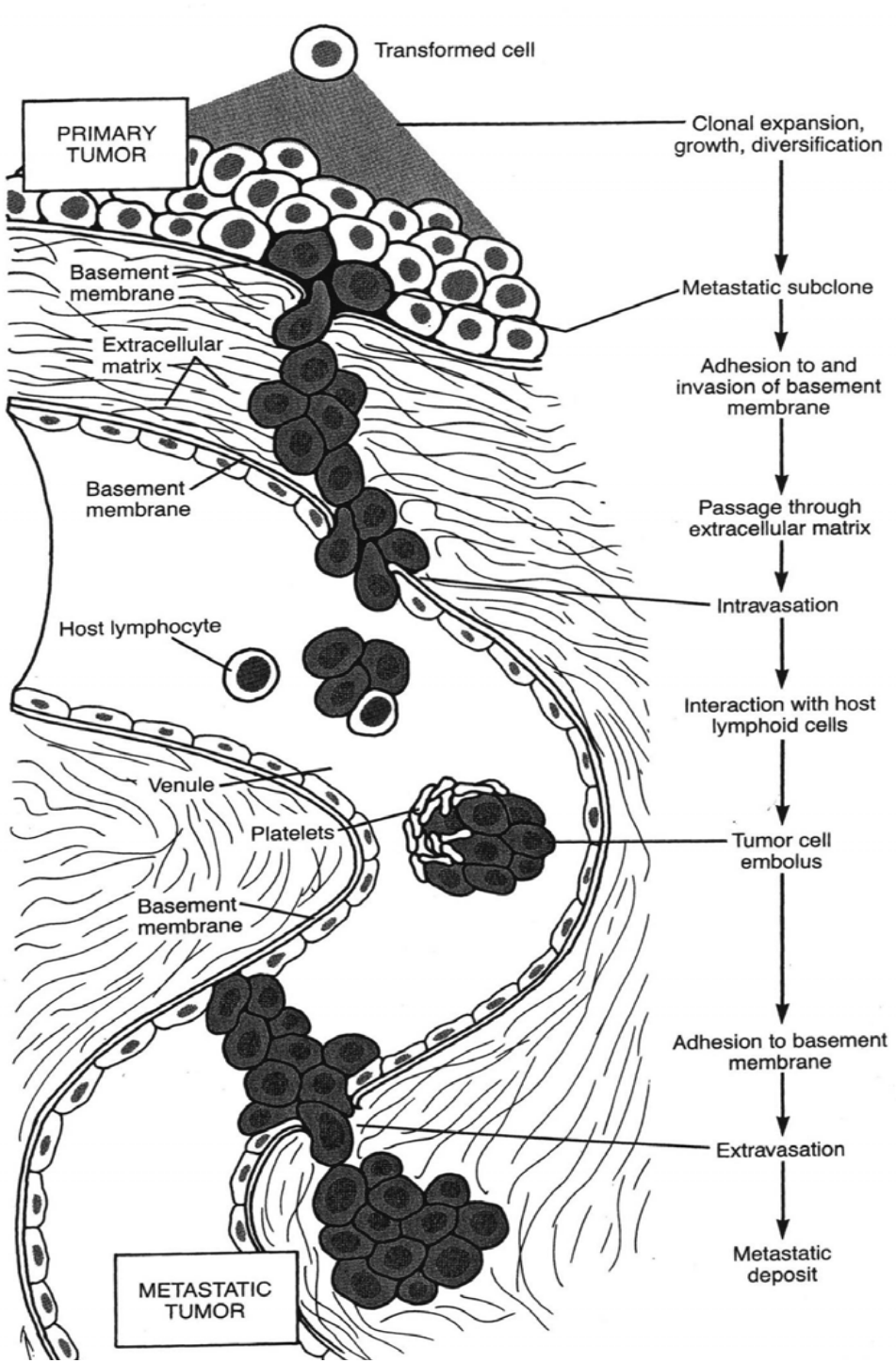
- Malignant Transformation, AKA Carcinogenesis:
  - Result of non-lethal genetic damage
    - Carcinogens, hereditary defects, or both
  - Tumor masses result from the clonal expansion of a single progenitor cell that has incurred genetic damage
  - Often, the host immune system is able to detect and eliminate the abnormally proliferating cells. But when these cells escape destruction...

Pathogenesis of Cancer



Pathogenesis of Cancer

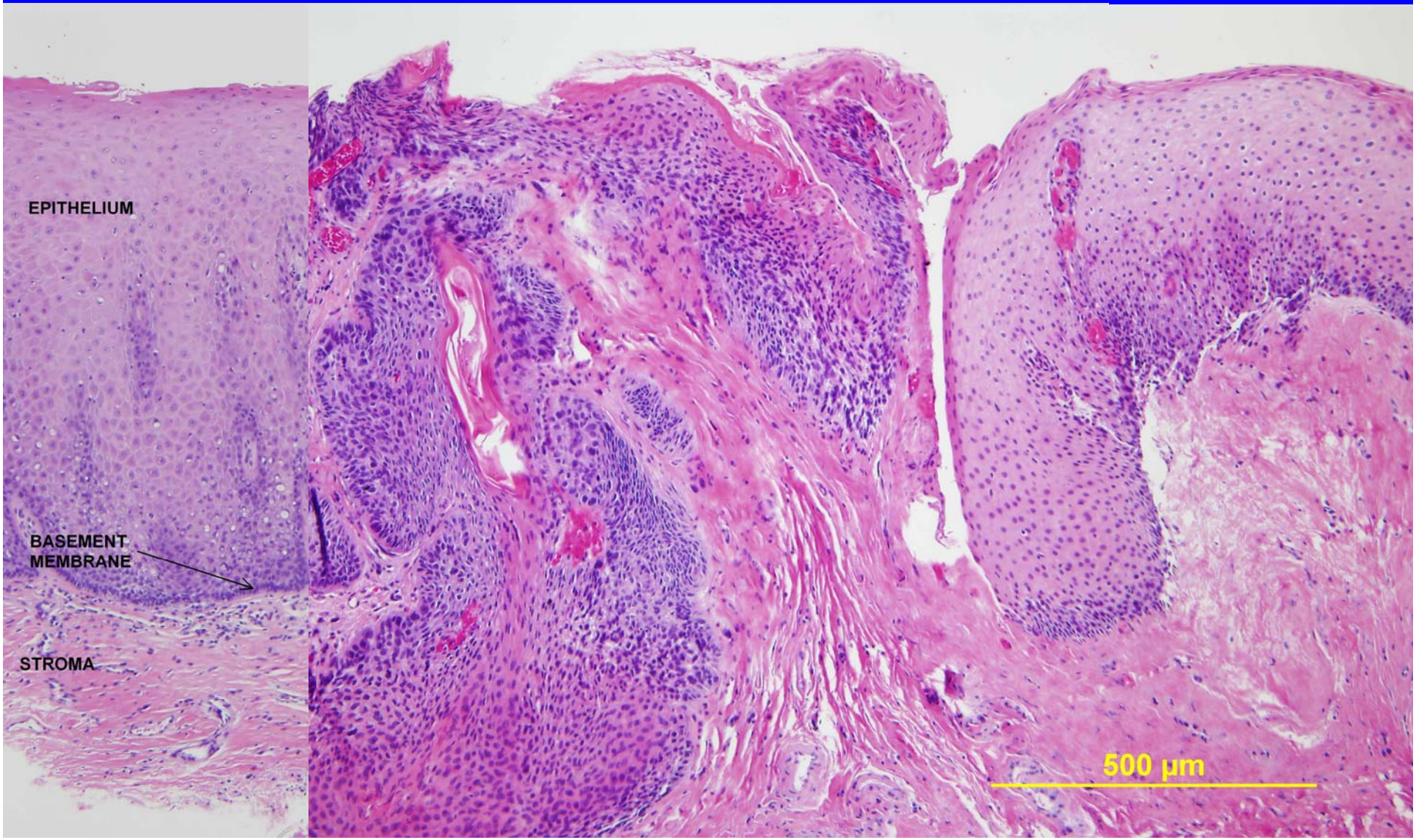
- How do tumors invade?
  - Detach from primary tumor
  - Degrade surrounding matrix
  - Migrate via blood or lymphatic vessels
- Metastasis causes 90% of cancer death


Transformed cell
PRIMARY TUMOR
Clonal expansion, growth, diversification
Basement membrane
Metastatic subclone
Extracellular matrix
Adhesion to and invasion of basement membrane
Basement membrane
Passage through extracellular matrix
Intravasation
Host lymphocyte
Interaction with host lymphoid cells
Venule
Platelets
Tumor cell embolus
Basement membrane
Adhesion to basement membrane
Extravasation
Metastatic deposit
METASTATIC TUMOR

Cancer Diagnosis

- Benign tumors
  - Well differentiated
  - Dysplasia
    - Precancerous condition in epithelial tissue
    - Anaplastic cells in epithelium
    - Dysplasia does not always progress to cancer
- Malignant tumors
  - Range from well to poorly differentiated
  - Anaplasia:
    - Cells and nuclei show pleomorphism
    - Cells contain abundant DNA, coarse, clumped chromatin
    - Large NC ratio (1:1) rather than 1:4 or less
    - Large nucleoli
    - Large # of mitoses

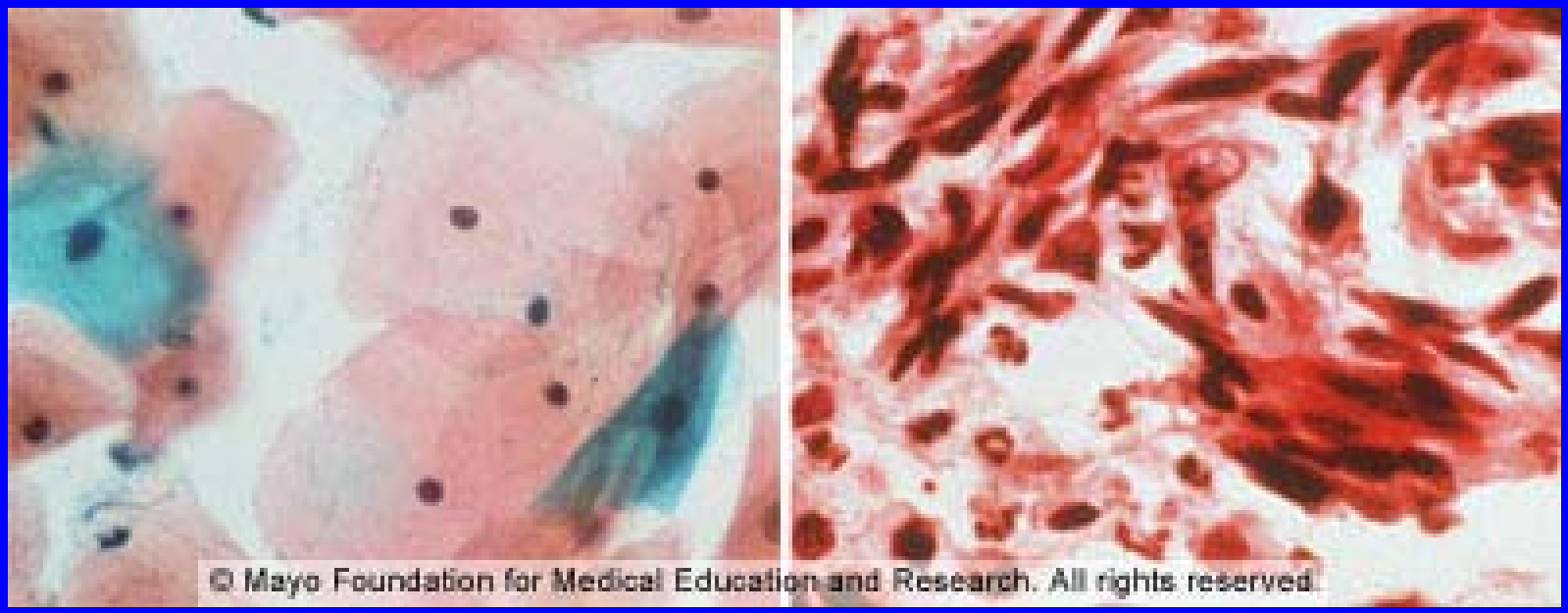
Cancer Diagnosis



Cancer Diagnosis

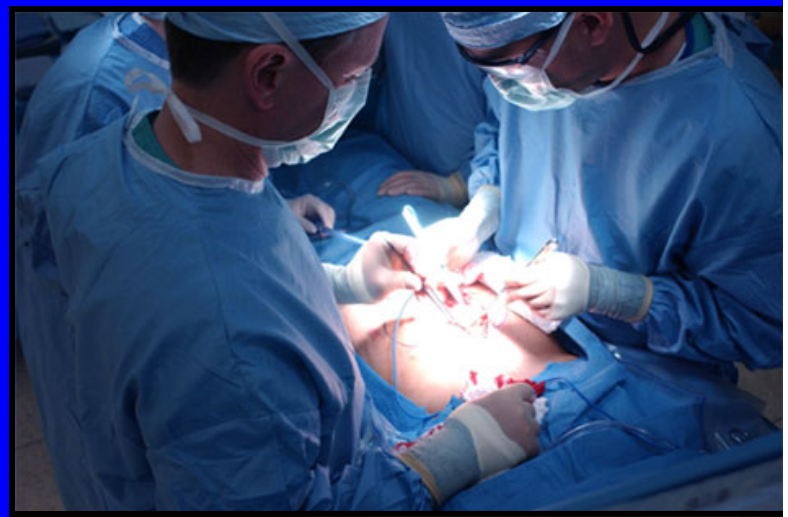
Normal Pap smear

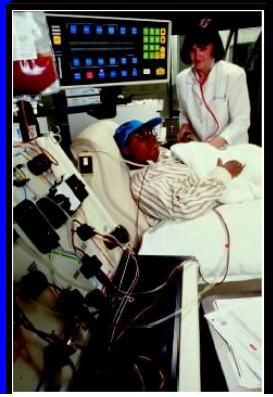
Cervial cancer



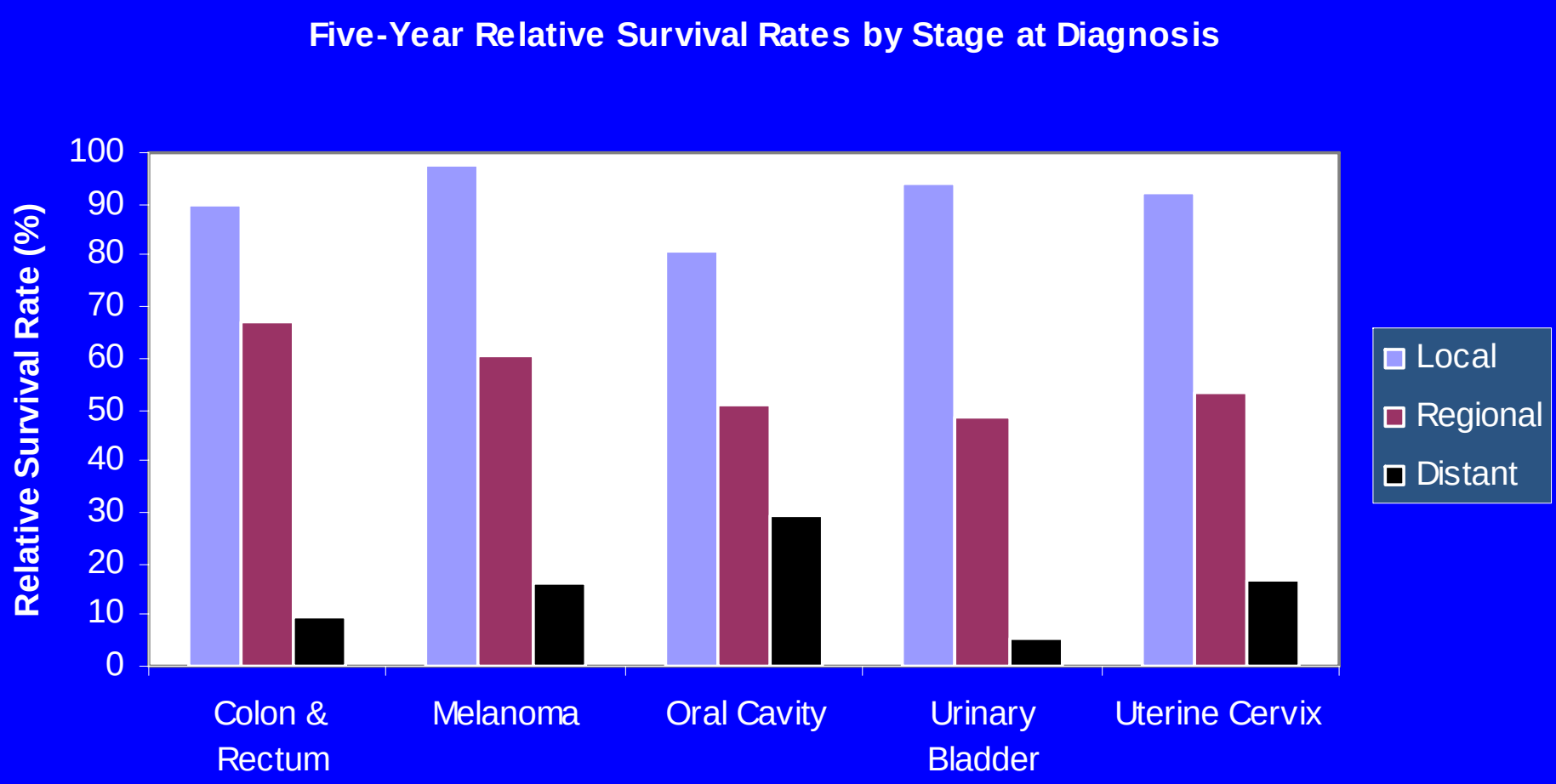
Treatment of Cancer

- Surgical excision
  - The most effective therapy, IF the entire tumor can be resected
  - 90% 5-year survival
  - Often, metastasis has already occurred
- Radiation/Chemotherapy
  - Side effects





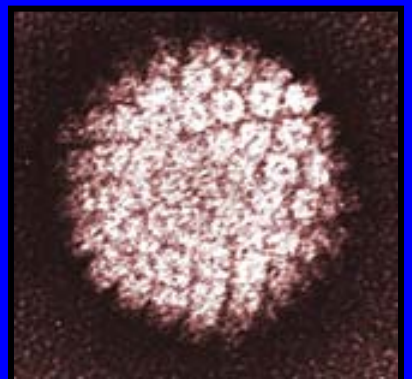
Importance of Cancer Screening



Cancer and Infectious Diseases

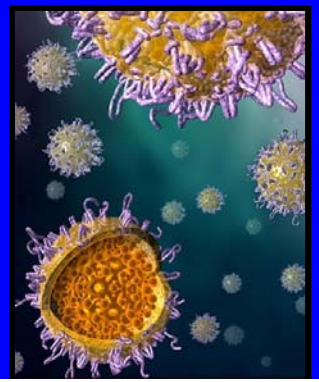
- Worldwide 15-20% of cancers are linked to infectious diseases
- These cancers can be avoided by preventing the infection associated with them

HPV, cervical cancer



H. pylori, stomach cancer

HBV, liver cancer



3. Unintentional Injuries

- More than 618,000 people ages 45-60 die from unintentional injuries each year
- Leading cause is *road accidents*:
  - 222,000 deaths per year in this age group
- Covered in *Lecture 3*

4. HIV/AIDS

- In the developing world, causes 386,000 deaths in people ages 45-60 per year
- Covered in *Lecture 3*

4. Digestive Diseases

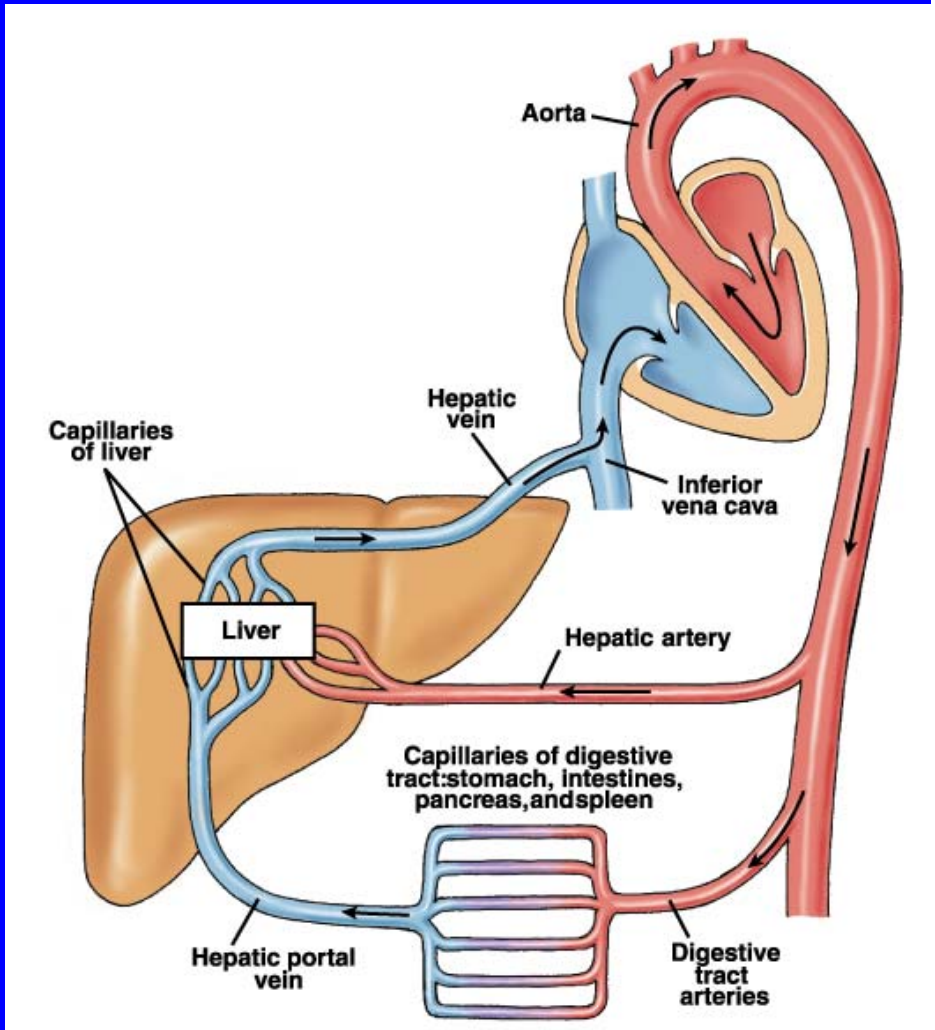
- Burden of digestive diseases
- Normal liver
- Cirrhosis
- Hepatitis

Burden of Digestive Diseases

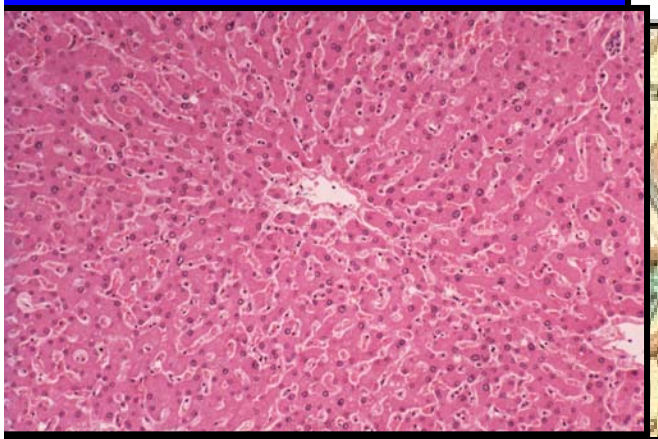
- Worldwide, 456,000 people aged 45-60 die each year from digestive diseases
- Cirrhosis of the liver
  - Kills 250,000 people each year between the ages of 45 and 60

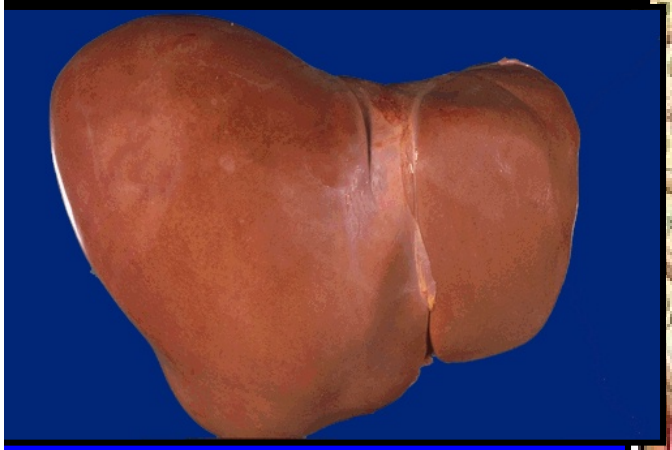
Normal Liver

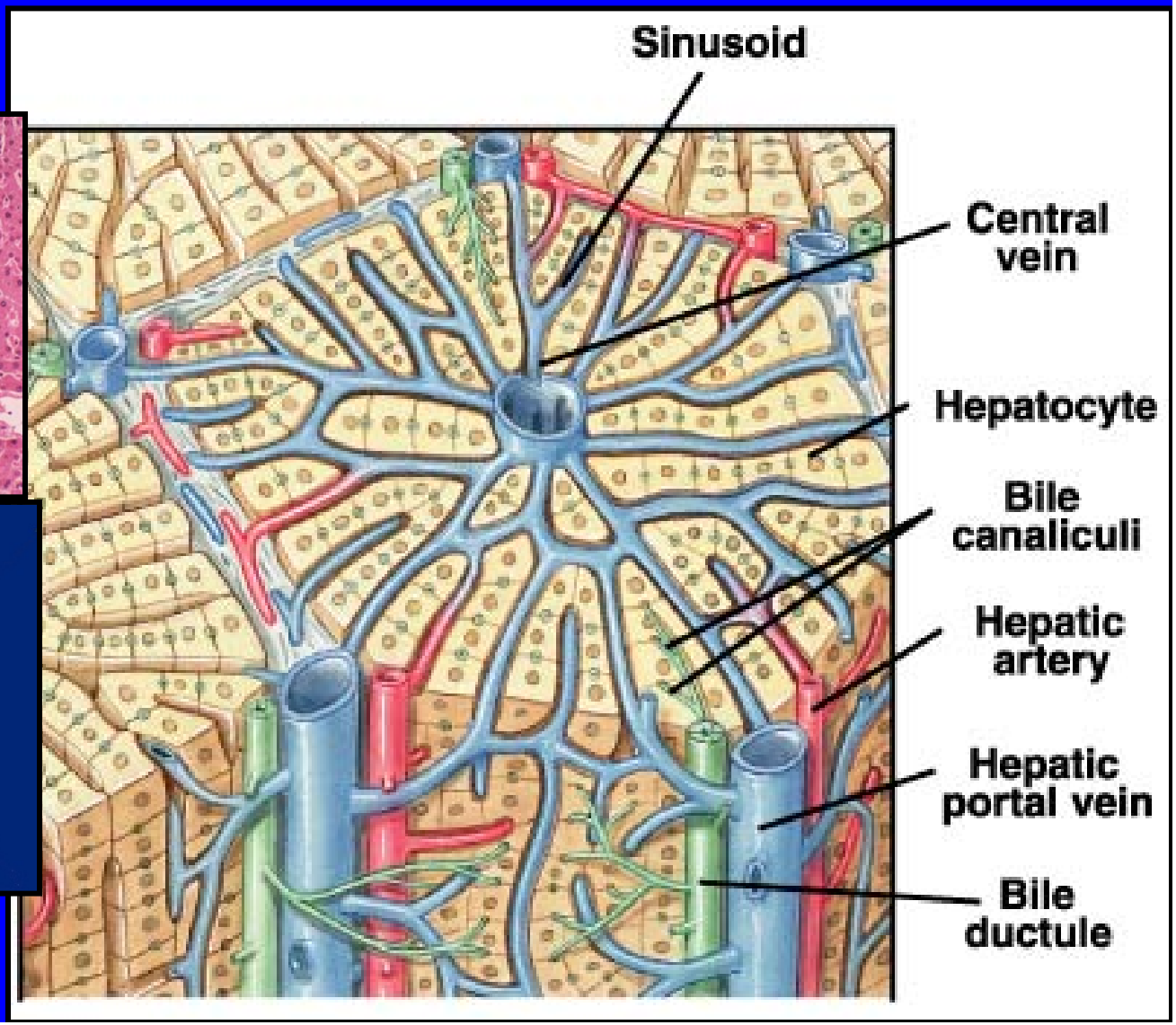
- Largest organ in the body
  - Metabolizes fat and glucose
  - Helps remove toxic substances from blood
  - Produces:
    - Bile to help absorb fats
    - Proteins that regulate blood clotting
    - Immune agents
- Loss of liver function can produce severe disease and death



Normal Liver

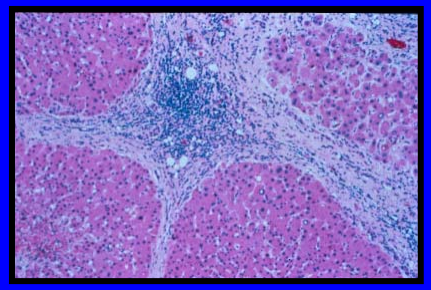


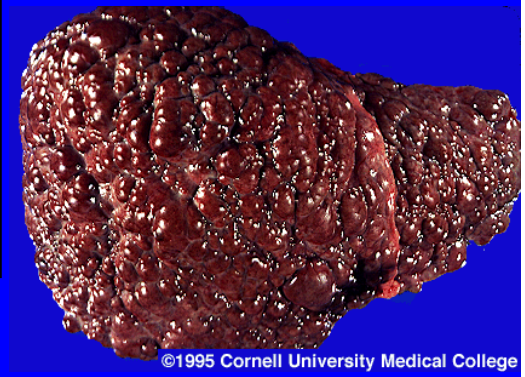




Cirrhosis

- Normal liver is replaced with scar tissue as a result of chronic injury, interfering with liver function
- Causes of cirrhosis:
  - Chronic alcoholism
  - Viral hepatitis infection





- Symptoms of cirrhosis:
  - Exhaustion, loss of appetite, nausea, vomiting blood, weakness, weight loss, and abdominal pain.
  - Patients bruise and bleed easily and become highly sensitive to medicines with increasing loss of liver functions.
- Diagnosis: needle biopsy

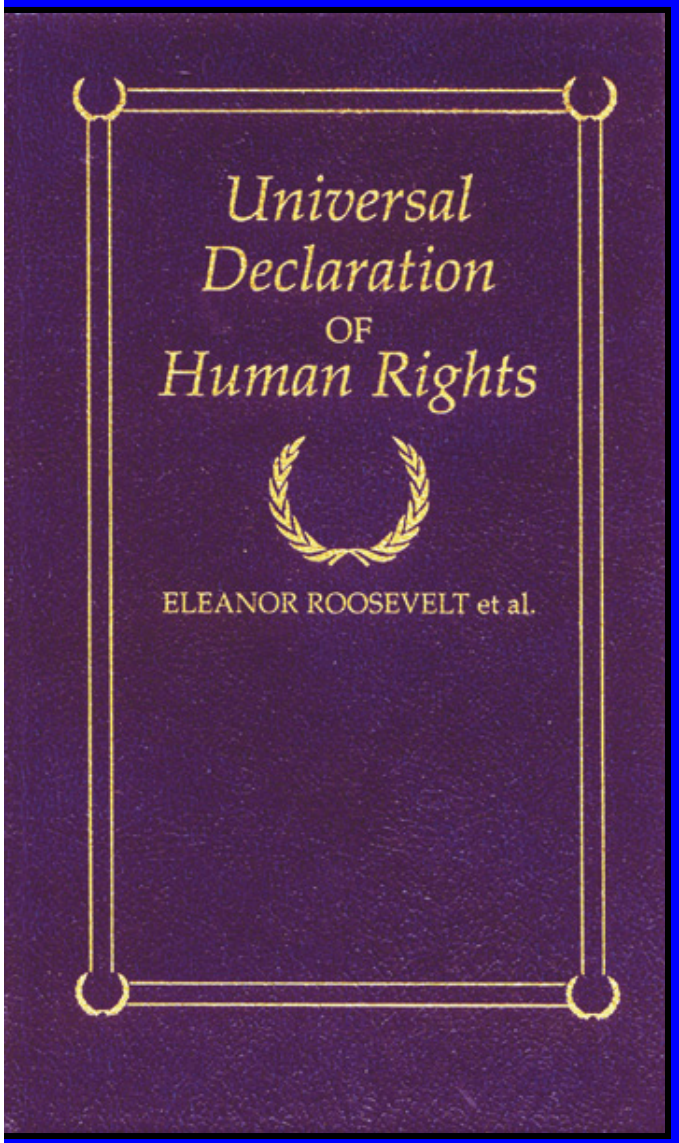
Hepatitis

- Infection which can also lead to cirrhosis
- Caused by hepatitis viruses A, B, C, D, and E
  - HBV most common worldwide
  - HCV most common in the US
- Acute HBV infection leads to chronic hepatitis in 5%, some of whom will develop cirrhosis
- Acute HCV infection leads to chronic hepatitis in 80%, 30% of whom will develop cirrhosis
- Vaccines available for HAV, HBV

Summary of Lecture Four

- Developing World
  1. Cardiovascular diseases
  2. Cancer (malignant neoplasms)
  3. Unintentional injuries
  4. HIV/AIDS
- Developed World
  1. Cardiovascular diseases
  2. Cancer (malignant neoplasms)
  3. Unintentional injuries
  4. Digestive Diseases

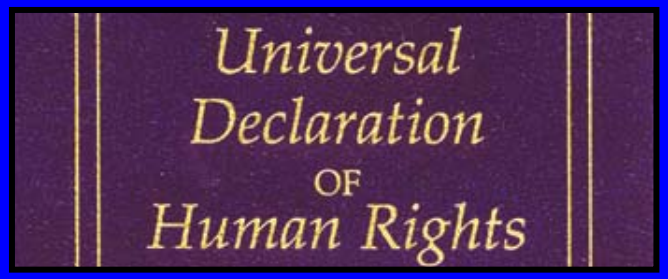
Structural Violence



“It’s not just a treaty… it may well become the international Magna Carta”

--Eleanor Roosevelt

Structural Violence



ARTICLE 25

Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care, and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control.

ARTICLE 27

Everyone has the right freely to participate in the cultural life of the community, to enjoy the arts and to share in scientific advancement and its benefits. Everyone has the right to the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author.

New World of Global Health

- Bill and Melinda Gates Foundation
  - $14.4 billion since 1999 to global health issues
  - August 24, 2006 gift from Warren Buffett
  - Exceeds the WHO budget during the same time
- Global Fund to Fight AIDS, TB and Malaria
  - $10 billion to 136 countries since 2002
- President's Emergency Plan for HIV/AIDS Relief (PEPFAR)
  - $18.8 billion since 2004

Challenges Faced

- Countries struggle with procurement policies, hard to convert $$ to drugs
- Shortages of trained health care workers
  - See *The World Health Report 2006*, WHO
- Corruption
- Lack of coherent approach

What is a Grand Challenge in Global Health?

- Scientific or technical innovation that:
  - Removes a critical barrier to solving an important health problem in developing world
  - High likelihood of global impact and feasibility
- Different than:
  - Simple statement of a “big problem” in global health
    - HIV/AIDS, malnutrition, lack of access to medical care, lack of resources
- Meant to:
  - Direct investigators to specific breakthrough that provides solution to a significant health problem(s)
- See http://www.gcgh.org/

Grand Challenges in Global Health

- $200 million medical research initiative
  - Bill and Melinda Gates Foundation
  - National Institutes of Health (NIH)
  - Encourage scientific and technological solutions to diseases that disproportionately affect the developing world
  - Announced in January 2003

Call for Grand Challenges

- Call For Ideas I (May 2003)
  - 1048 submissions from scientists and institutions in 75 countries
- Scientific Board heard proposals (August 2004)
  - Problem
  - Roadblock (obstacle to progress)
  - Challenge
  - List of potential benefits
- Funding increased to $450 million

Goals and Grand Challenges

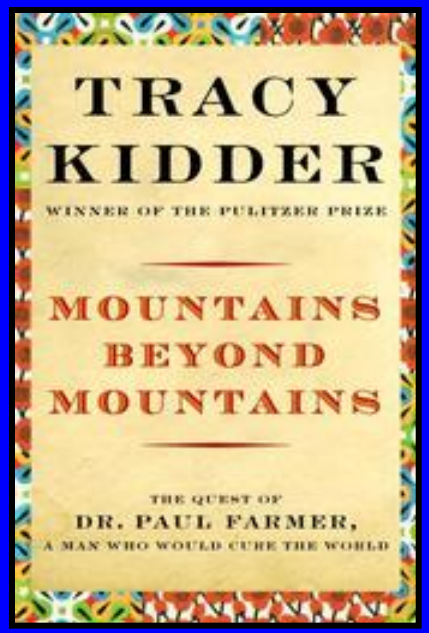
- Seven Long Range Goals
- 14 Grand Challenges
- Heavily oriented toward infectious disease
  - Infectious diseases account for the most profound discrepancies between advanced and developing economies
  - Causes of infectious diseases are well-known
  - Can more easily formulate technical and scientific obstacles to progress

Grand Challenge Proposals

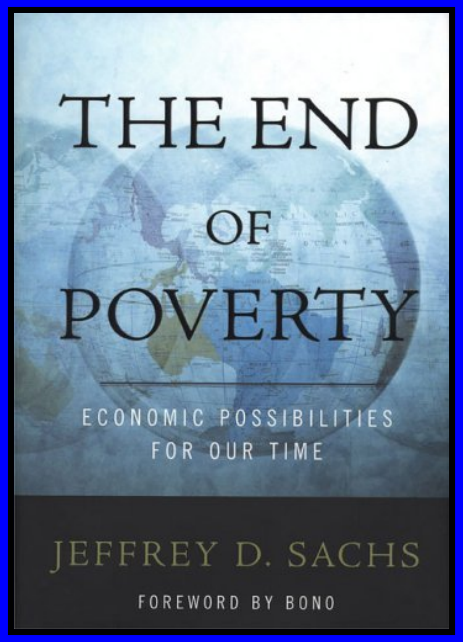
- NIH issued request for proposals to address challenges
  - Grants of up to $20M over five years or less
- http://www.gcgh.org/
- Results reported in Science (Oct 17, 2003)

GOAL: To improve childhood vaccines:
GC #1 Create effective single-dose vaccines that can be used soon after birth
GC#2 Prepare vaccines that do not require refrigeration
GC#3 Develop needle-free delivery systems for vaccines
GOAL: To create new vaccines:
GC#4 Devise reliable tests in model systems to evaluate live attenuated vaccines
GC#5 Solve how to design antigens for effective, protective immunity
GC#6 Learn which immunological responses provide protective immunity
GOAL: To control insects that transmit agents of disease:
GC#7 Develop a genetic strategy to deplete or incapacitate a disease-transmitting insect population
GC#8 Develop a chemical strategy to deplete or incapacitate a disease-transmitting insect population
GOAL: To improve nutrition to promote health:
GC#9 Create a full range of optimal, bioavailable nutrients in a single staple plant species
GOAL: To improve drug treatment of infectious diseases:
GC#10 Discover drugs and delivery systems that minimize the likelihood of drug resistant micro-organisms
GOAL: To cure latent and chronic infections:
GC#11 Create therapies that can cure latent infections
GC#12 Create immunological methods that can cure chronic infections
GOAL: To measure disease and health status accurately and economically in developing countries:
GC#13 Develop technologies that permit quantitative assessment of population health status
GC#14 Develop technologies that allow assessment of individuals for multiple conditions or pathogens at point-of-care

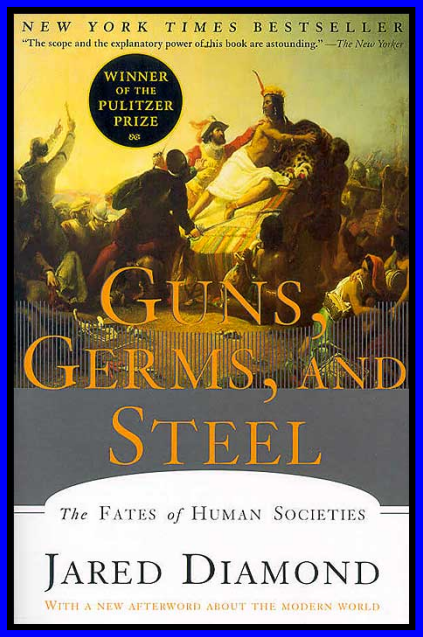
Warmly Recommended Reading



Mountains Beyond Mountains
by Tracy Kidder



The End of Poverty
by Jeffrey Sachs



Guns, Germs, and Steel
by Jared Diamond