

# BIOE 301/362

## Lecture Four:

### Leading Causes of Mortality, Ages 45-60 Global Health Challenges

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

## ■ Developing World

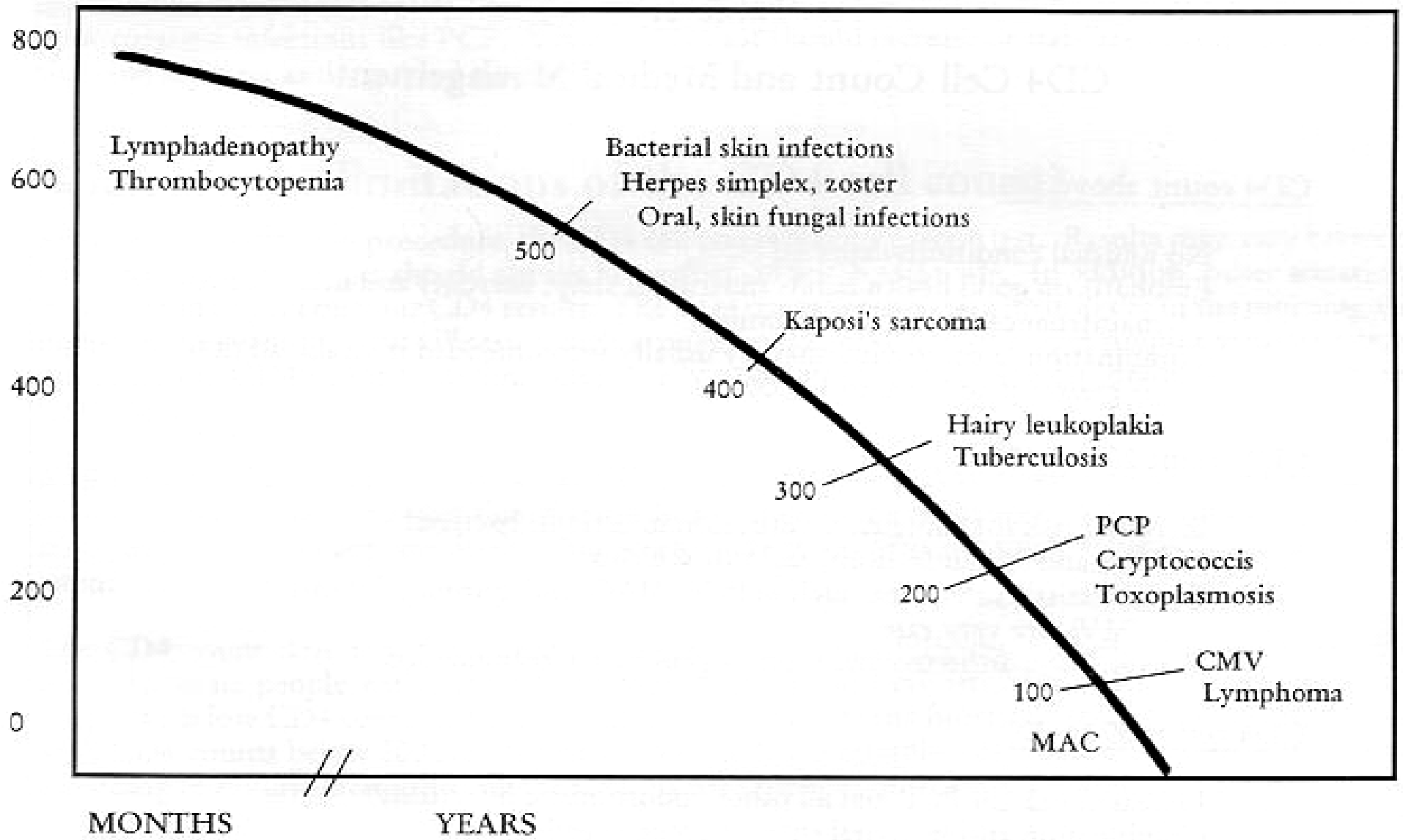
1. HIV/AIDS
2. Unintentional injuries
3. Cardiovascular diseases
4. Tuberculosis

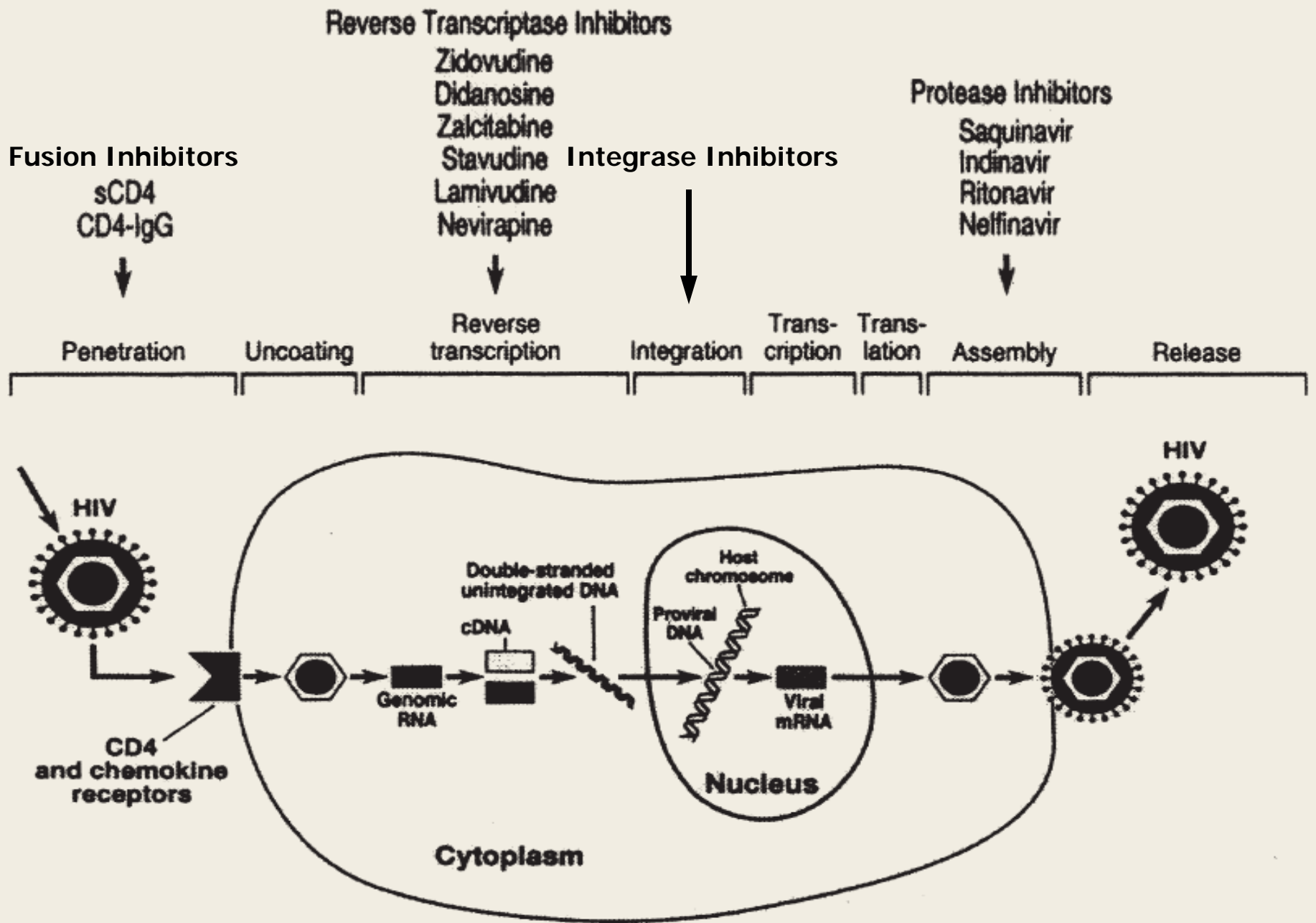
## ■ Developed World

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.



# Cancer and Cardiovascular Diseases

- Will be discussed today!

## 4. Tuberculosis

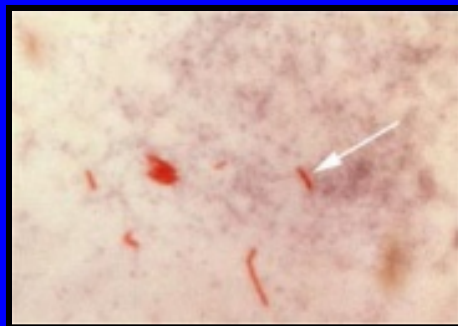
- If your next PPD skin test is positive, what will your doctor do next?





# Diagnosis of Tuberculosis

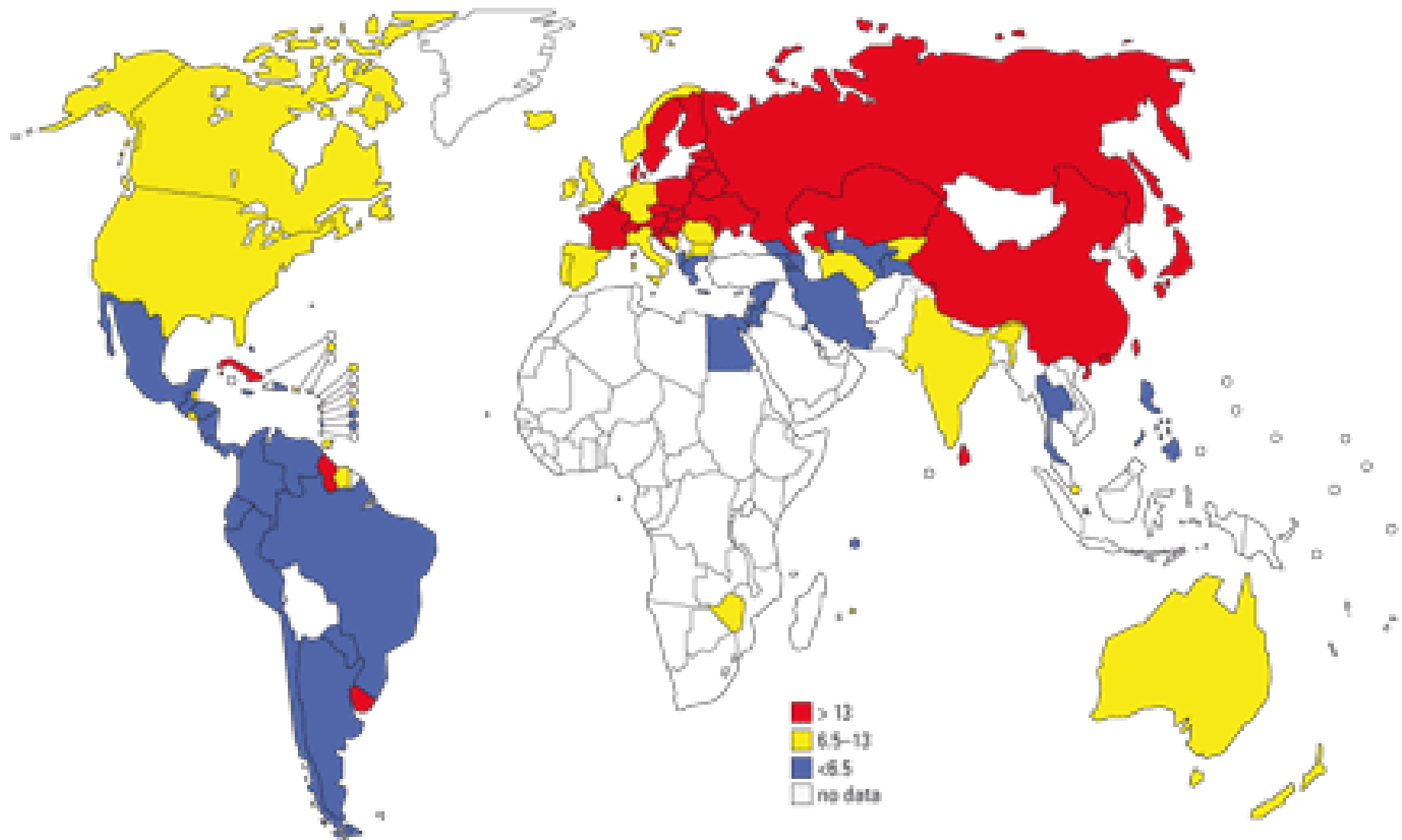
- Skin test (PPD)
- Serum test
- Chest X-ray
  - Shows nodules in active TB
- Sputum
  - Acid-fast bacilli



## 4. Self-Inflicted Injuries

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

### Map of suicide rates (per 100 000; most recent year available as of 2007)



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dashed lines represent approximate border lines for which there may not yet be full agreement.

WHO/06.100

# Suicide Screening and Prevention

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## Lecture 4:

# Leading Causes of Mortality Ages 45-60

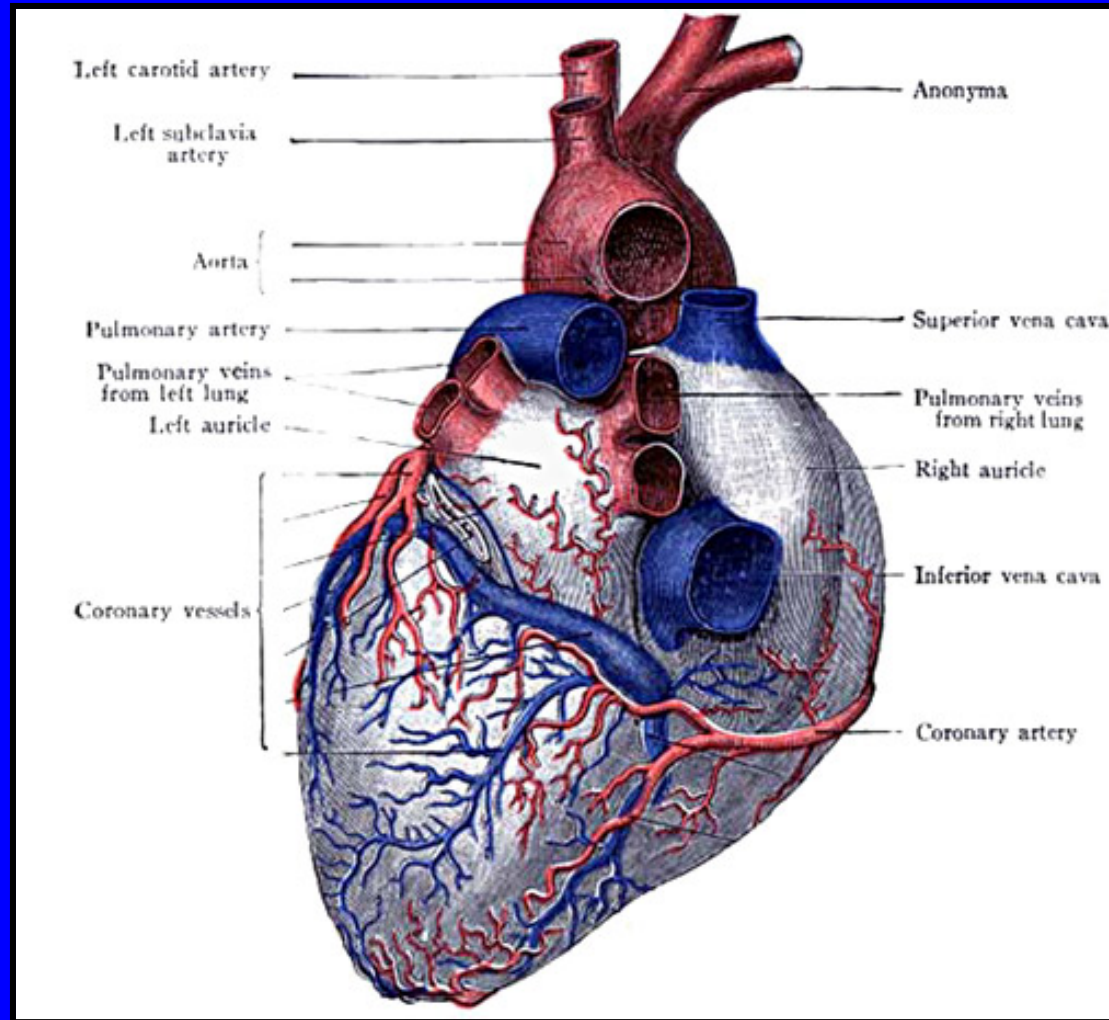
### ■ Developing World

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)

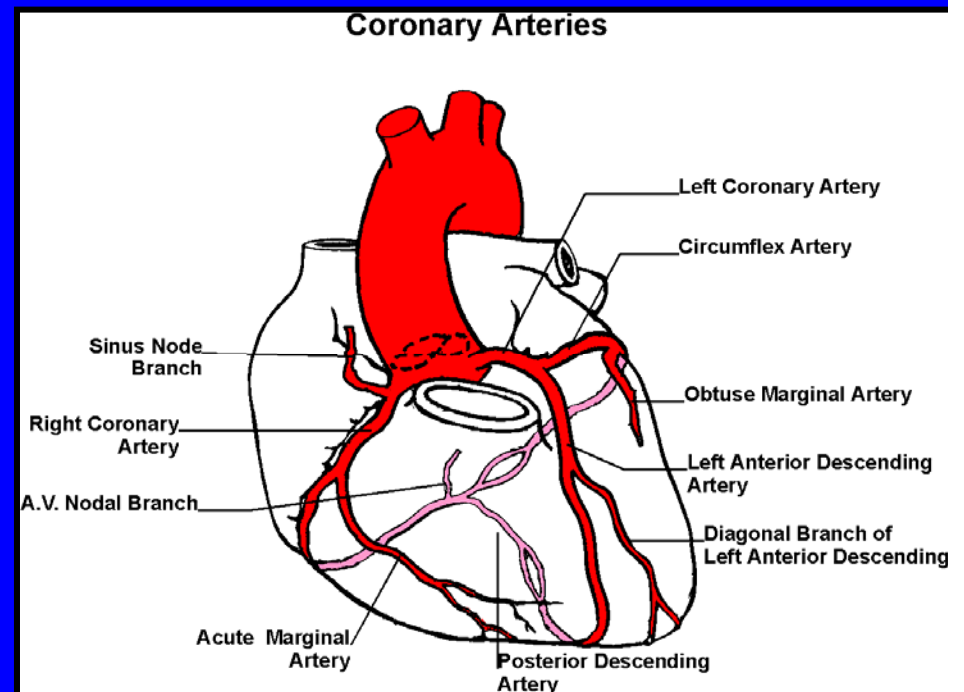
# Ischemic Heart Disease: Epidemiology

## ■ 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

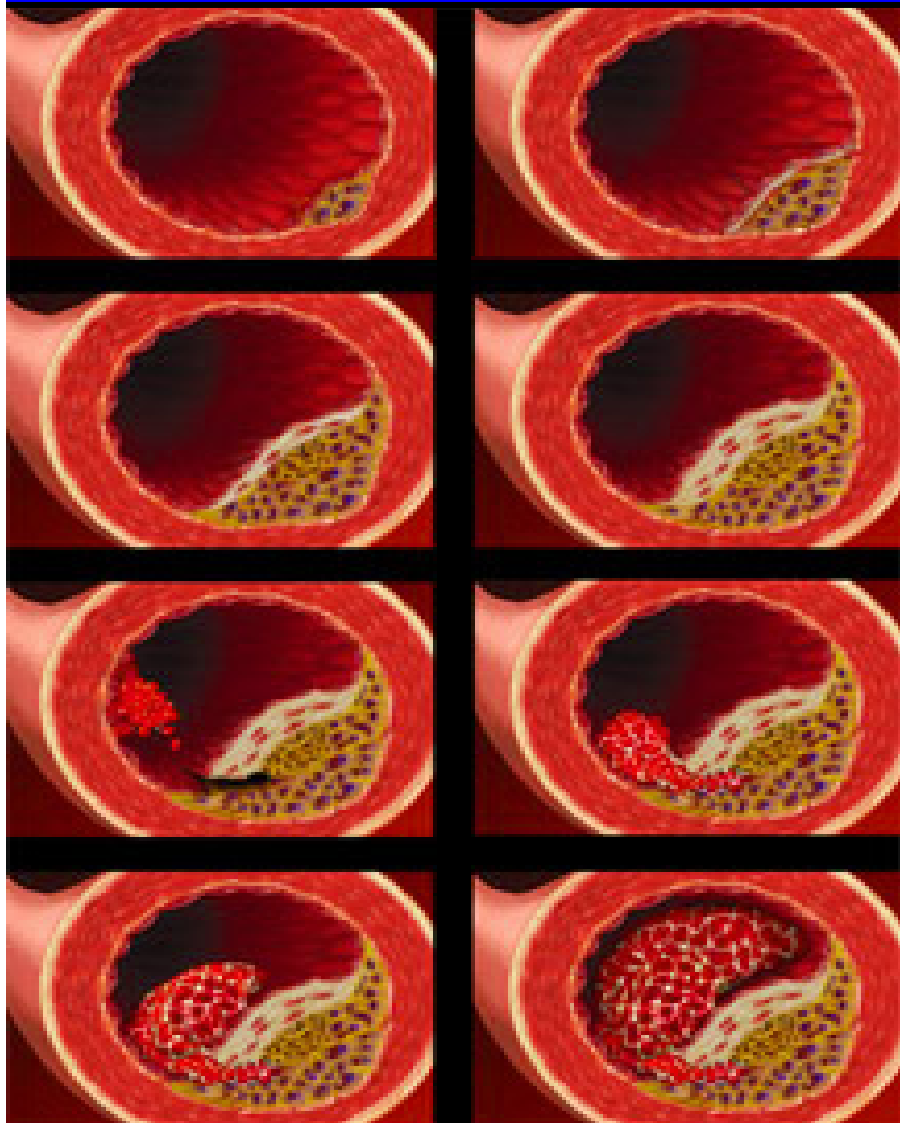


# Ischemic Heart Disease: Pathogenesis

## ■ 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



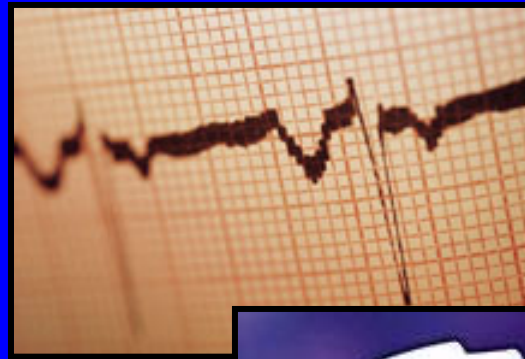
## Evolution of a heart attack:

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

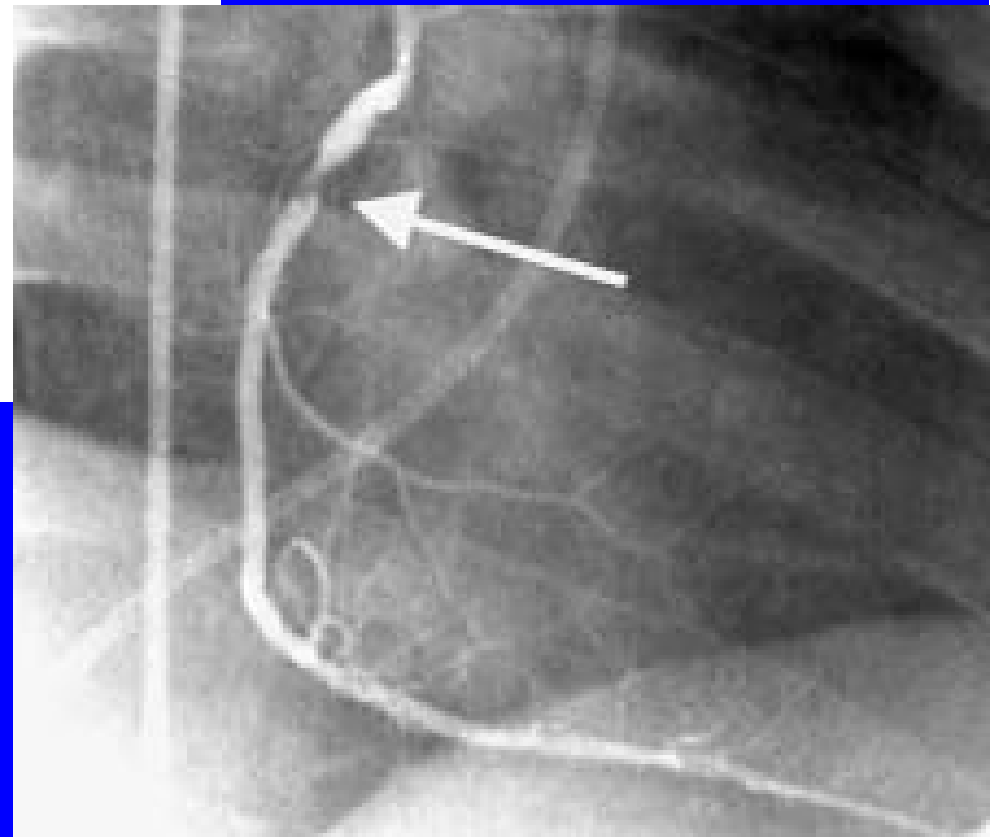
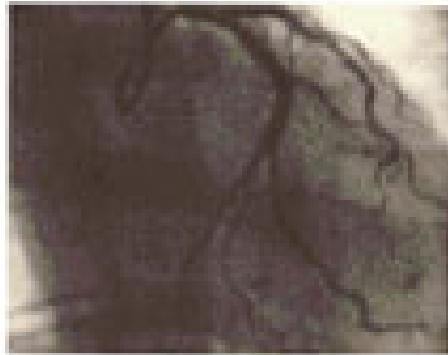
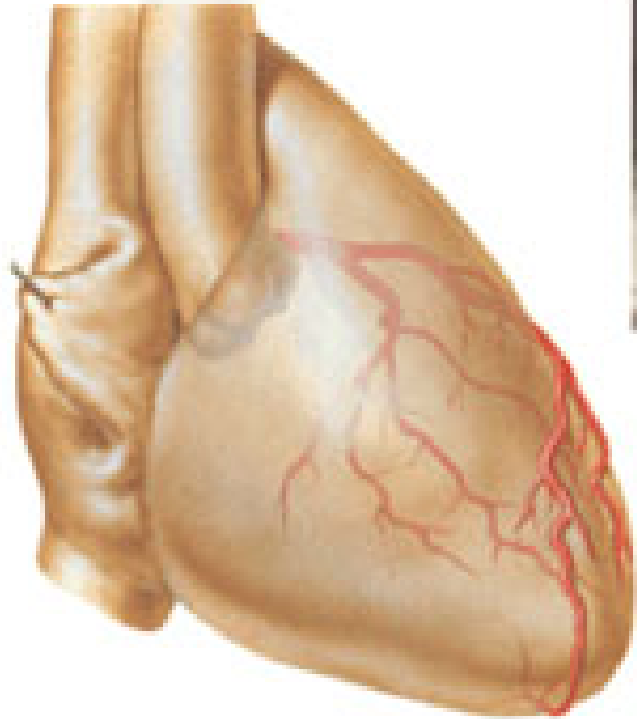
- *In the US, 30% of patients do not survive a first heart attack*
- *For 50% of CAD patients, their first symptom is a heart attack*

# 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

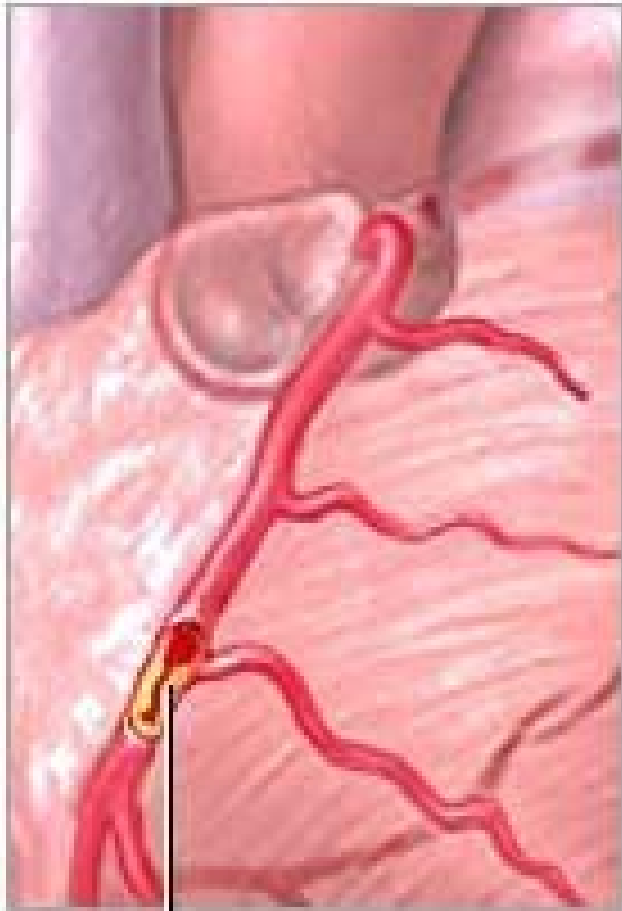


[http://www.columbiasurgery.org/divisions/cardiac/images/novartis\\_207B.jpg](http://www.columbiasurgery.org/divisions/cardiac/images/novartis_207B.jpg)

# Ischemic Heart Disease: Treatment

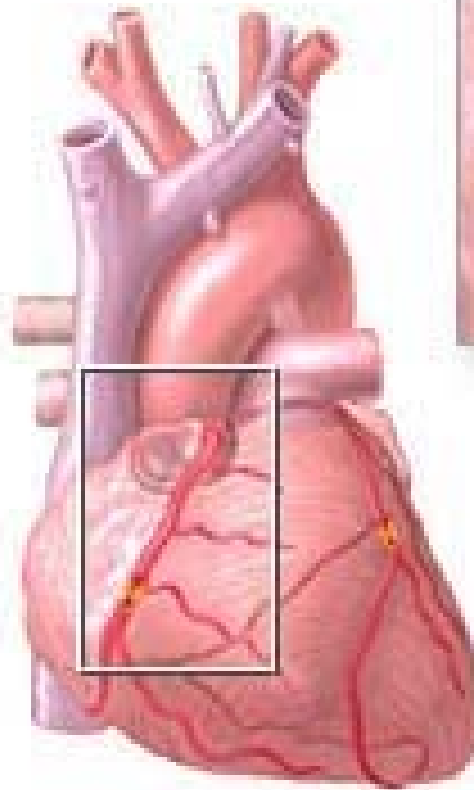
- Medical management (may relieve symptoms of CAD, but does not reduce coronary blockage)
  - Nitrates
    - Increase myocardial oxygen supply, systemic vasodilation
  - Beta blockers
    - Inhibit increases in heart rate and contractility
    - Decrease myocardial oxygen demand
  - Calcium channel antagonists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

Before

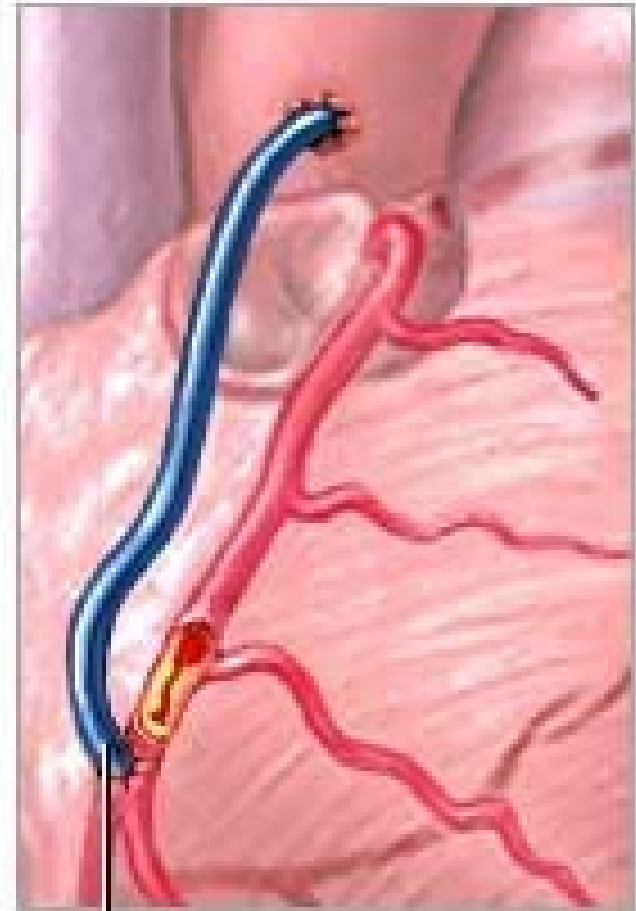


Blocked coronary artery

# CABG



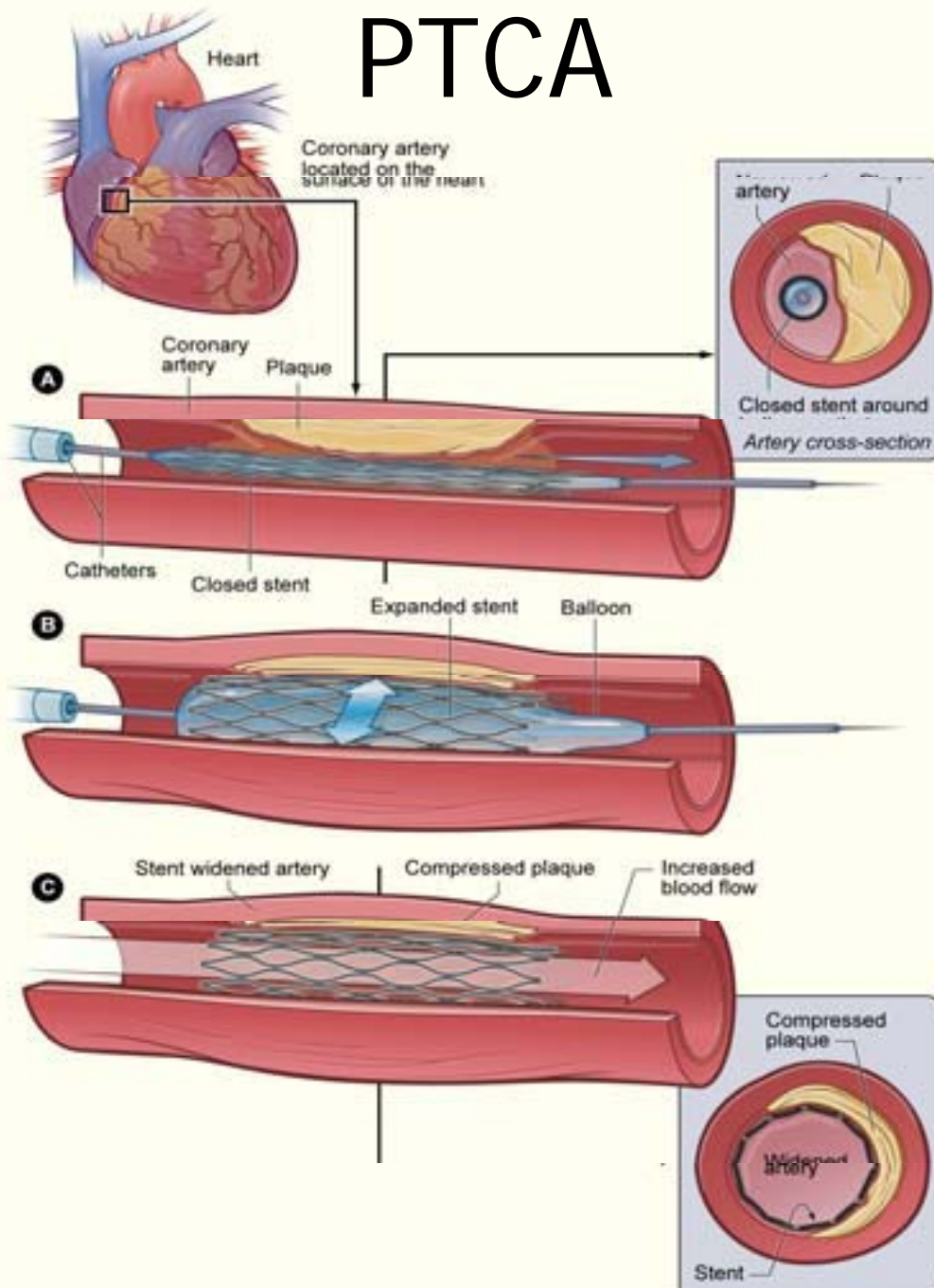
After



Vein graft sewn in to bypass blockage

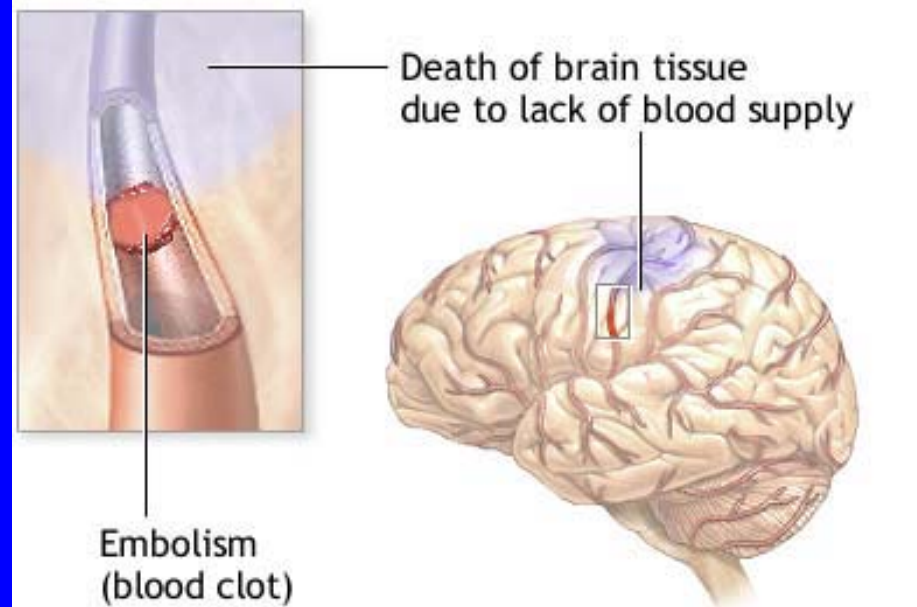


# PTCA



# 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

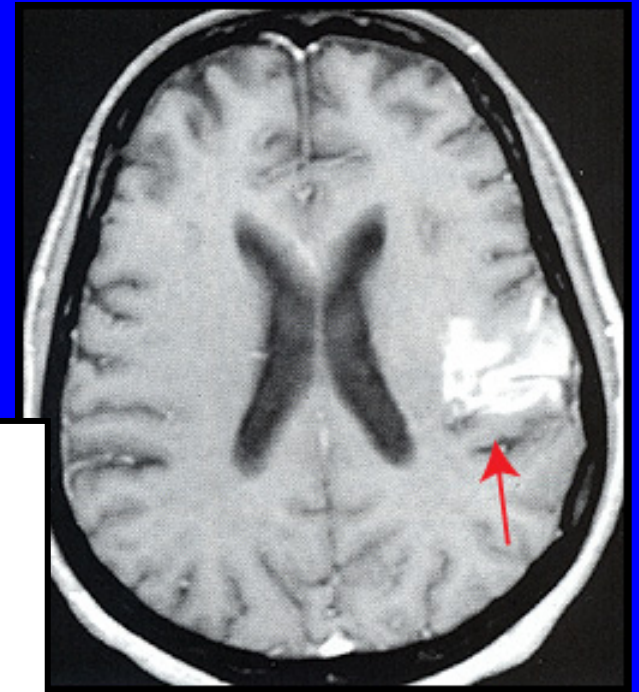
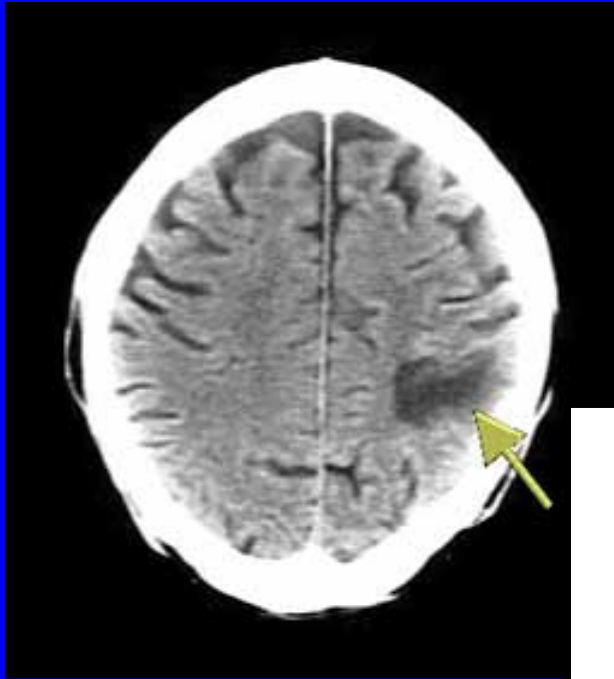
- Abrupt onset with focal neurologic deficit
- Usually mini-event or warning signs
  - 15% Transient Ischemic Attacks (TIAs)
- Reversible ischemia
  - Some lasting 24-72 hours
- Completed stroke
  - Maximal deficit within hours
  - Often patient awakens with completed stroke
  - Usually preceded by TIA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

# Cerebrovascular Disease: Diagnosis

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

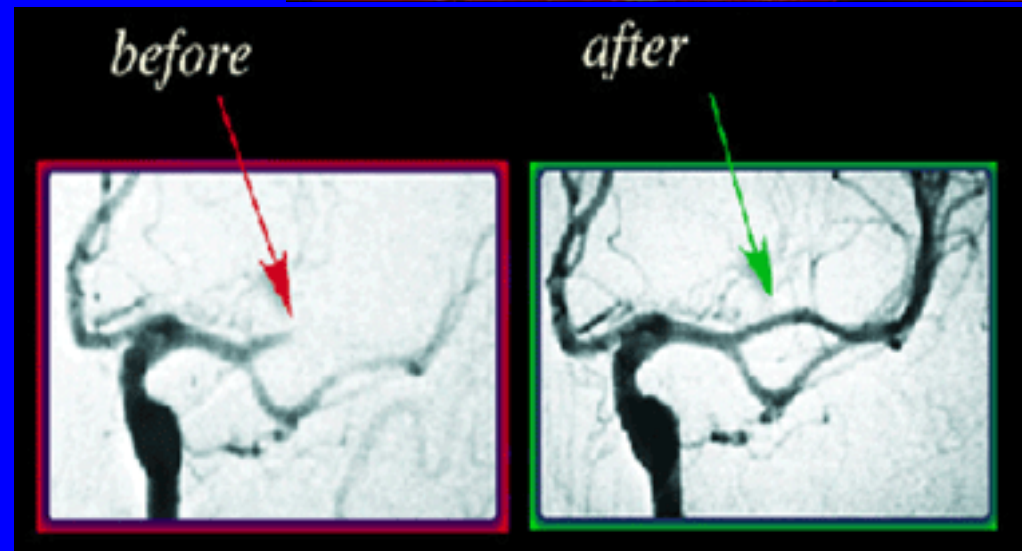


# Cerebrovascular Disease: Diagnosis



# Cerebrovascular Disease: Treatment

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



## 2. Cancer

- Burden
- Pathogenesis
- Diagnosis
- Treatment
- Cancer and Infectious Diseases



# 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)

# 2008 Estimated US Cancer Deaths



Source: American Cancer Society, 2009.

# Pathogenesis of Cancer

- 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

# Pathogenesis of Cancer

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

# Pathogenesis of Cancer

## 1) Malignant Transformation, AKA Carcinogenesis:

- Result of non-lethal genetic damage
  - Carcinogens, hereditary defects, or both

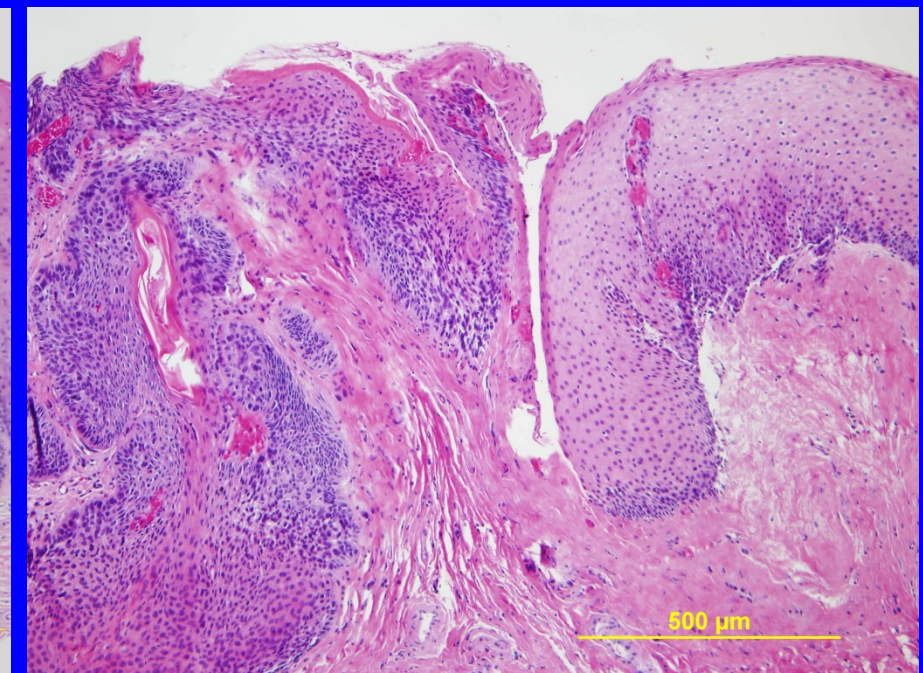
## 2) Growth of Transformed Cells

- 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

## 3) Local Invasion

- Detach from primary tumor
- Degrade surrounding matrix
- Migrate via blood or lymphatic vessels

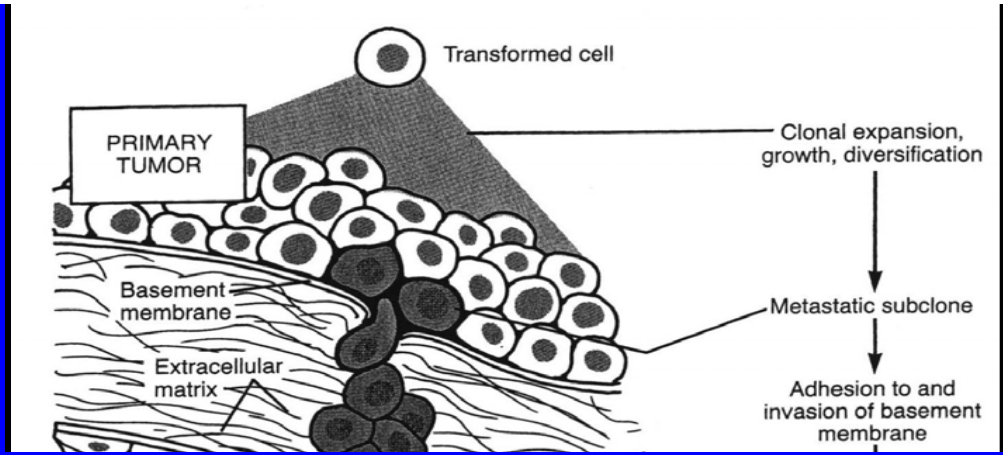


# Pathogenesis of Cancer

## 4) Metastasis

- Causes 90% of cancer death
- Series of sequential steps/mutations





# Cancer Diagnosis

## ■ Benign tumors

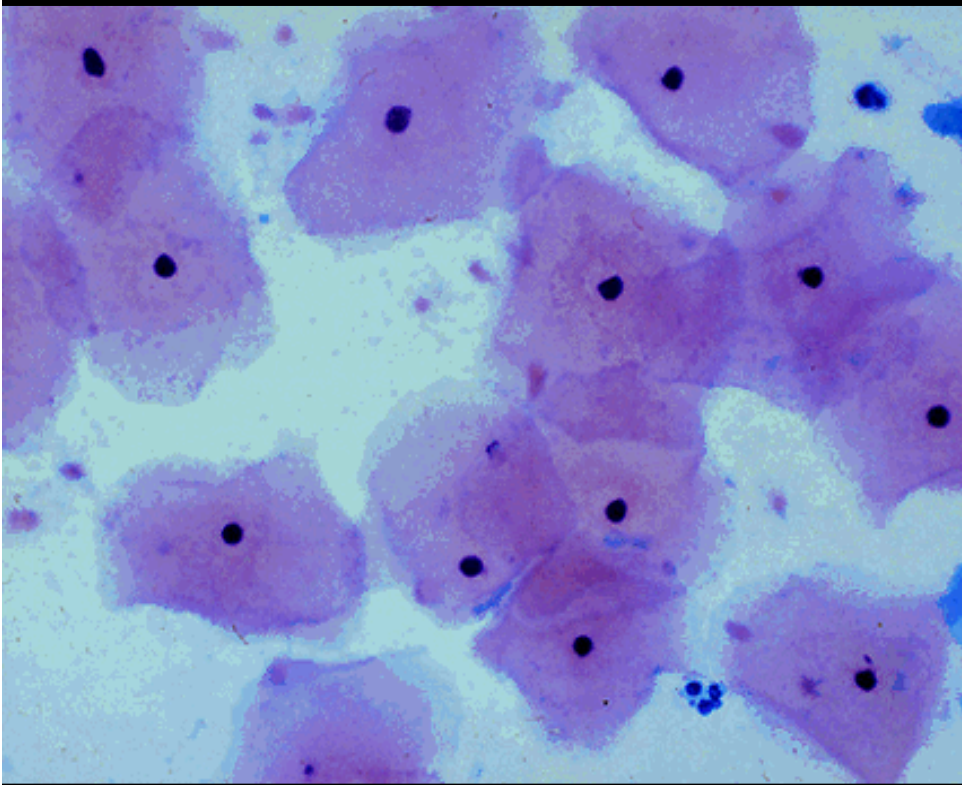
- Well differentiated
- Dysplasia
  - Precancerous condition in epithelial tissue
  - Anaplastic cells in epithelium
  - Dysplasia does not always progress to cancer

## ■ Malignant tumors

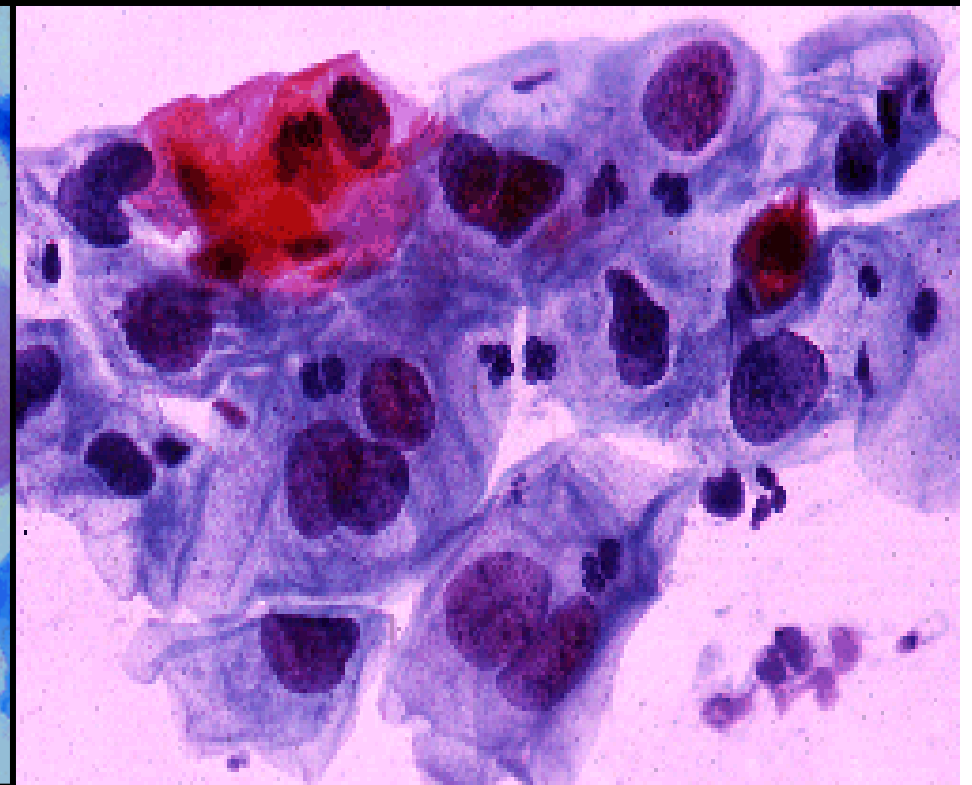
- Range from well to poorly differentiated
- Anaplasia:
  - Cells and nuclei show pleomorphism
  - Cells contain abundant DNA, coarse, clumped chromatin
  - Large NC ratio (1:1) rather than 1:4 or less
  - Large nucleoli
  - Large # of mitoses

# Cancer Diagnosis

Normal Pap smear



Cervical cancer



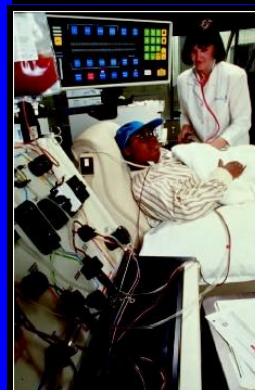
# Treatment of Cancer

## ■ Surgical excision

- The most effective therapy, IF the entire tumor can be resected
- 90% 5-year survival
- Often, metastasis has already occurred

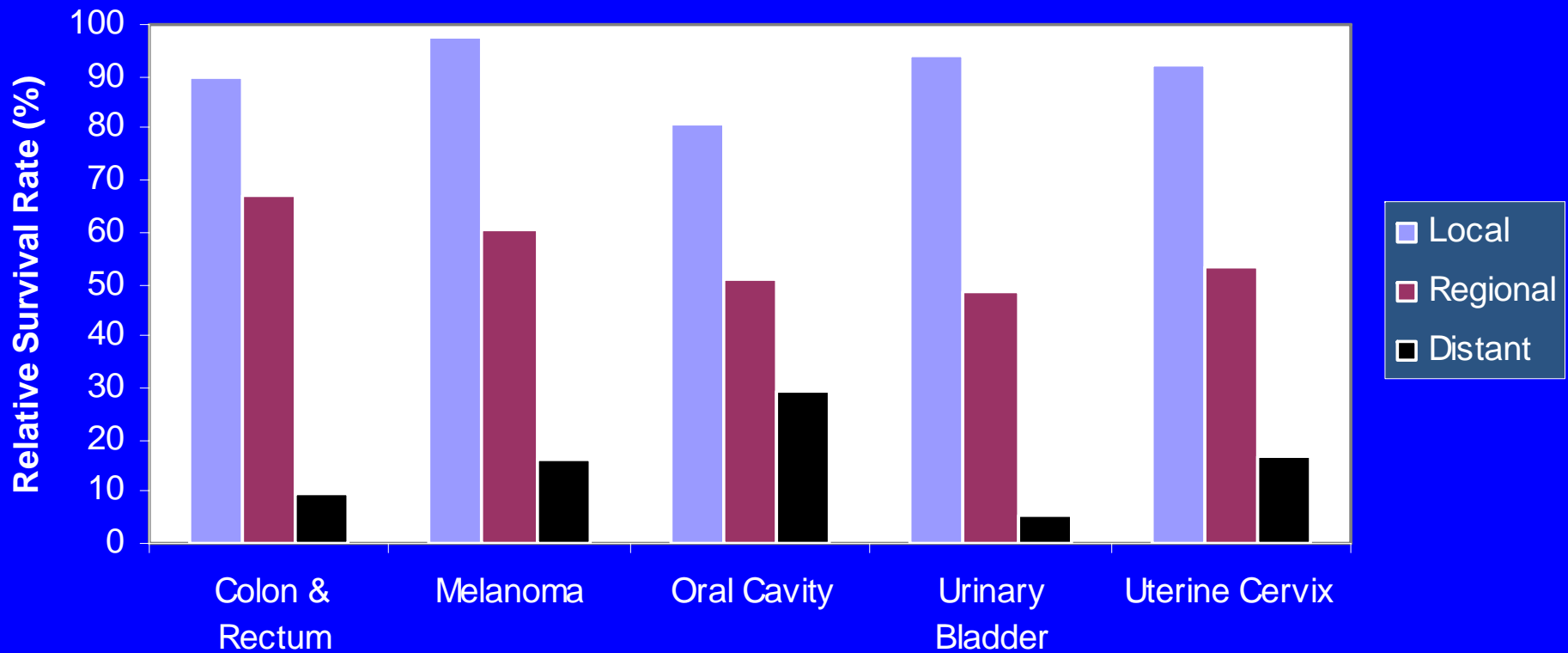
## ■ Radiation/Chemotherapy

- Side effects



# Importance of Cancer Screening

Five-Year Relative Survival Rates by Stage at Diagnosis

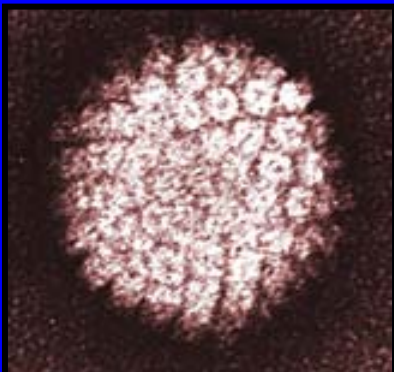


# Cancer and Infectious Diseases

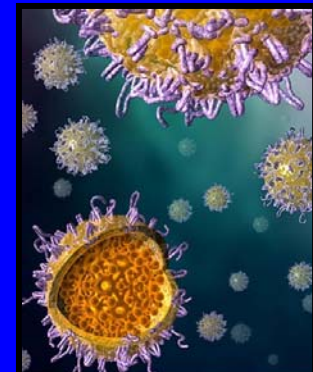
- Worldwide, 15-20% of cancers are linked to infectious diseases
- These cancers can be avoided by preventing the infection associated with them

*H. pylori*, stomach cancer

HPV, cervical 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

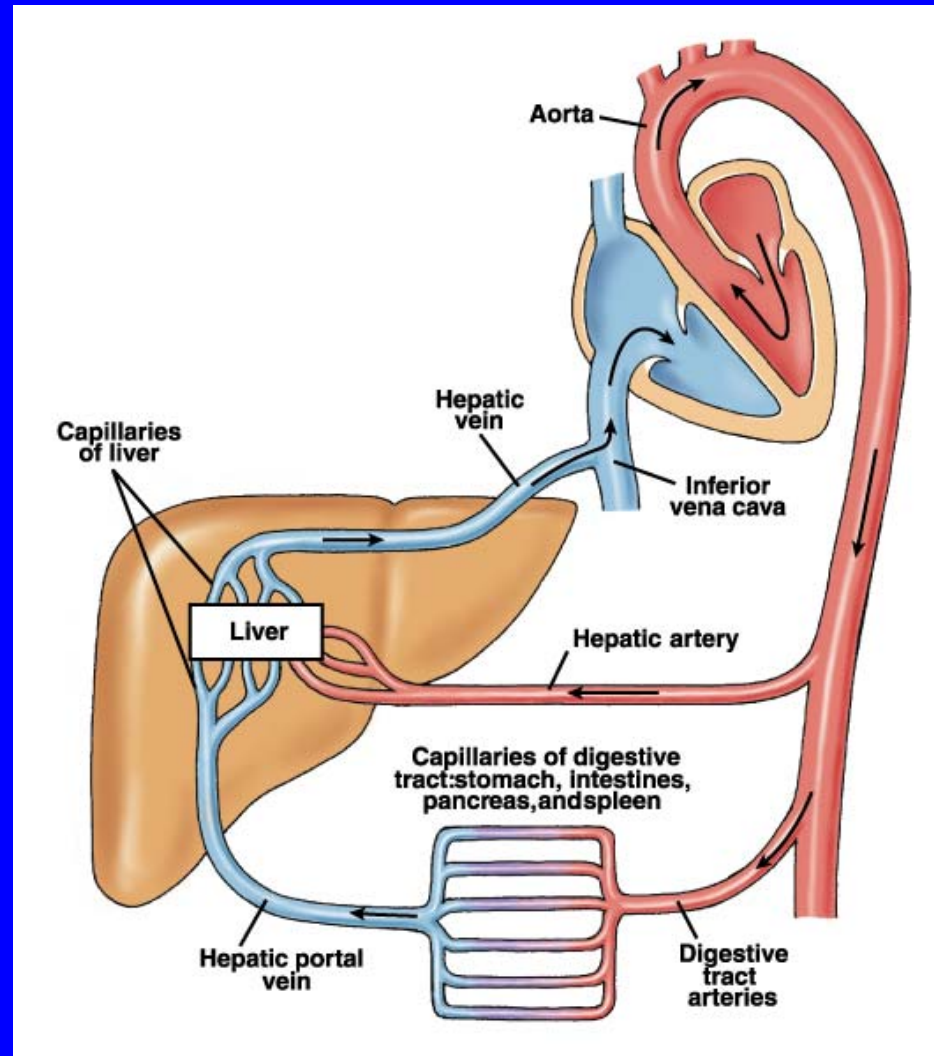
- Burden of digestive diseases
- Normal liver
- Cirrhosis
- Hepatitis

# Burden of Digestive Diseases

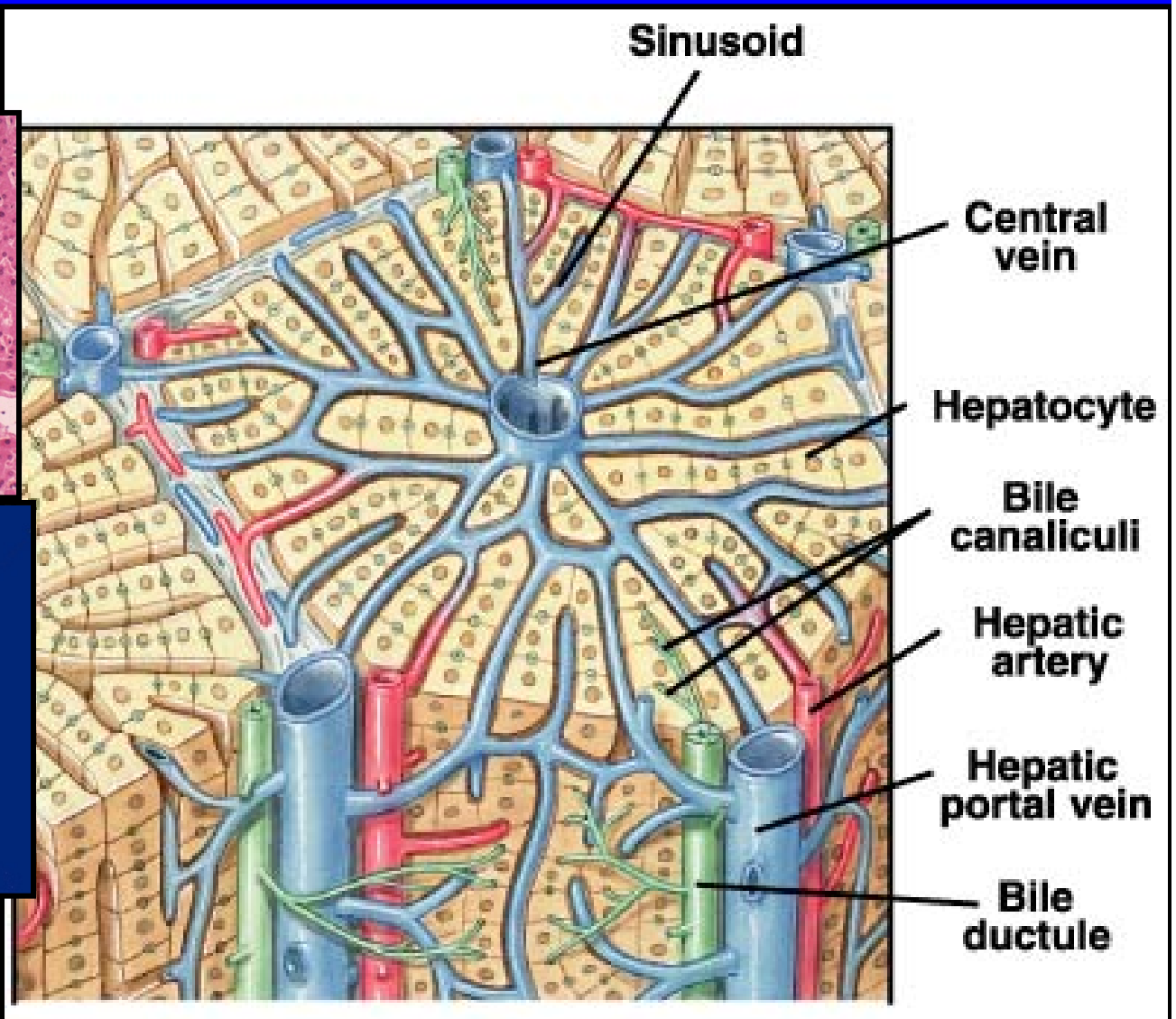
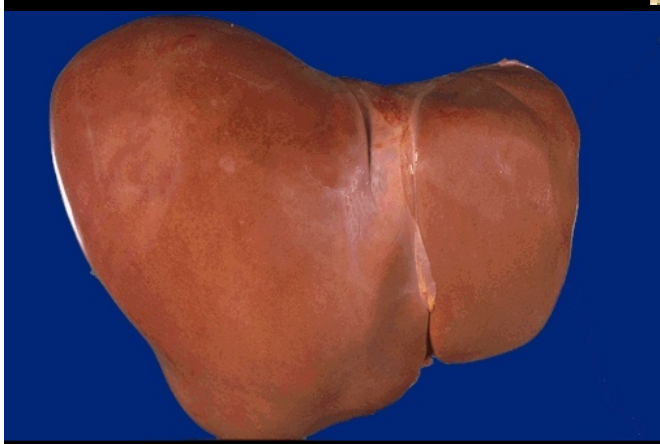
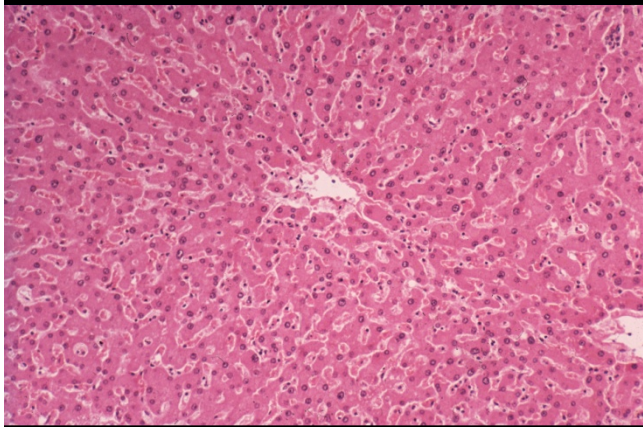
- Worldwide, 456,000 people aged 45-60 die each year from digestive diseases
- Cirrhosis of the liver
  - Kills 250,000 people each year between the ages of 45 and 60

# 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

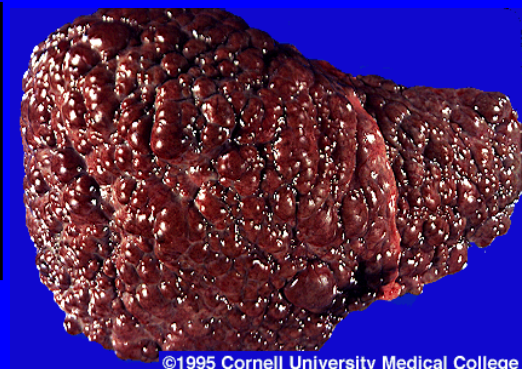
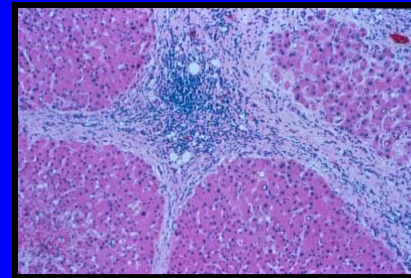


# Normal Liver



# 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

# Leading Causes of Death

## **Ages 0-4:**

Perinatal conditions  
Lower respiratory infections  
Diarrheal diseases  
Malaria

Perinatal conditions  
Congenital anomalies  
Lower respiratory infections  
Unintentional injuries

## **Ages 15-44:**

HIV/AIDS  
Unintentional injuries  
Cardiovascular diseases  
Tuberculosis

Unintentional injuries  
Cardiovascular disease  
Cancer  
Self-Inflicted Injuries

## **Ages 45-59:**

Cardiovascular diseases  
Cancers  
Unintentional injuries  
HIV/AIDS

Cardiovascular diseases  
Cancer  
Unintentional injuries  
Digestive Diseases



# Structural Violence



# Structural Violence

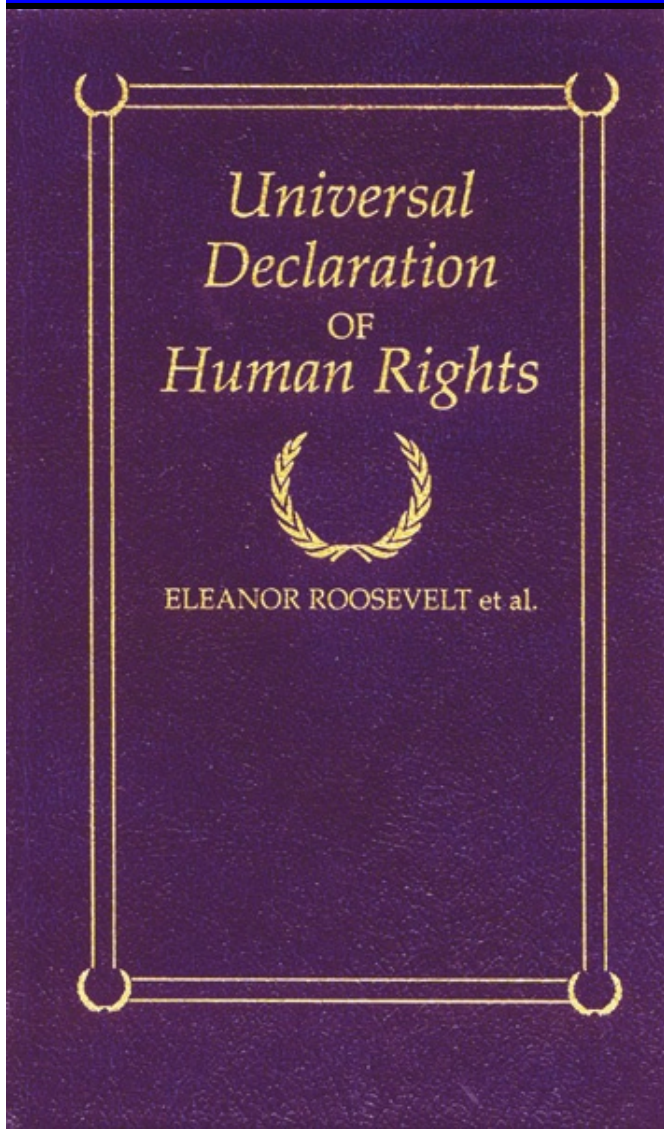


# Structural Violence





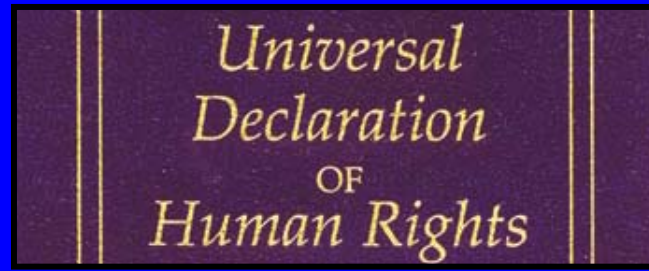
# Structural Violence



**“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.

# Grand Challenges in Global Health

- <http://www.gcgh.org>
- 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
- Meant to:
  - Direct investigators across scientific disciplines to work on solutions that could provide breakthrough advances for those in the developing world
- \$436 M initiative launched in 2003
  - Bill & Melinda Gates Foundation; National Institutes of Health (NIH); Canadian Institutes of Health Research (CIHR); Wellcome Trust
- \$100 M Grand Challenge Explorations launched in 2008
  - Accelerated grant initiative: 2 pages, online, no prelim data required
  - \$100K initial grants, renewable for \$1M or more
  - Currently funding 180 researchers in 29 countries

# 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



**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

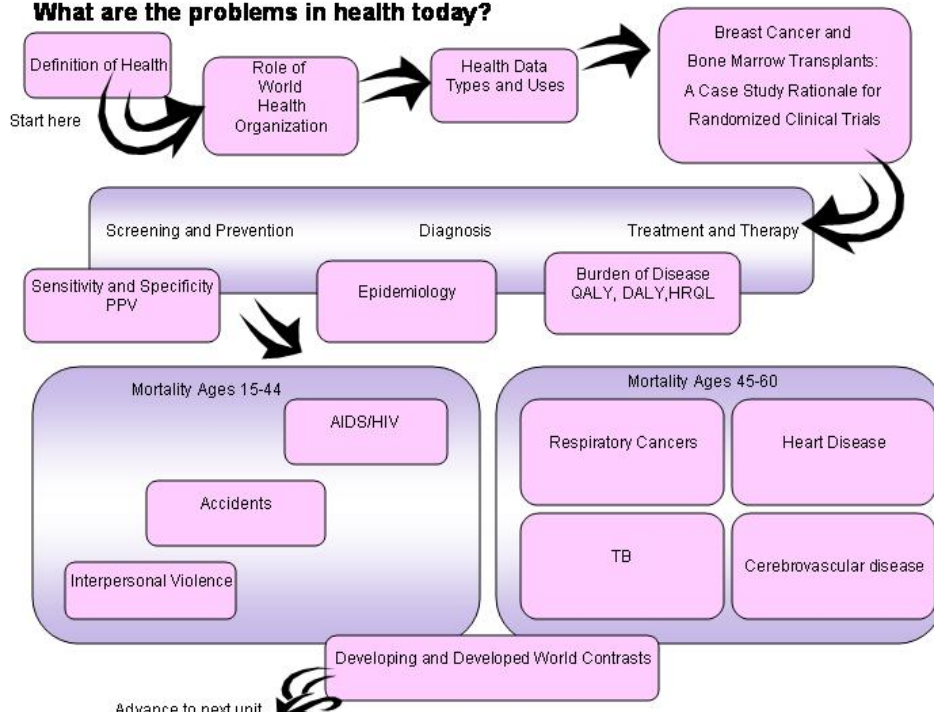
**GOAL: To measure disease and health status accurately and economically in developing countries:**

GC#13 Develop technologies that permit quantitative assessment of population health status

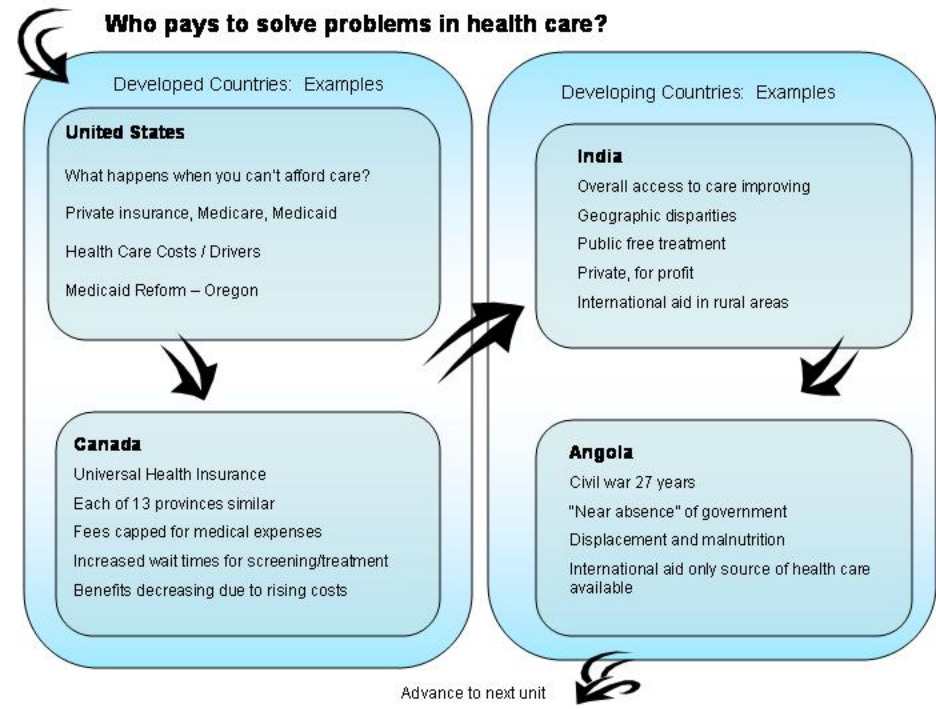
GC#14 Develop technologies that allow assessment of individuals for multiple conditions or pathogens at point-of-care



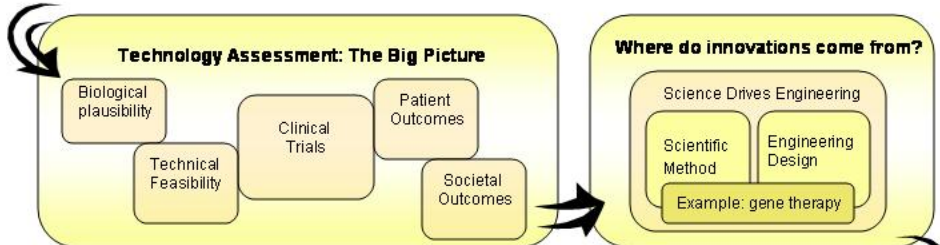
## What are the problems in health today?



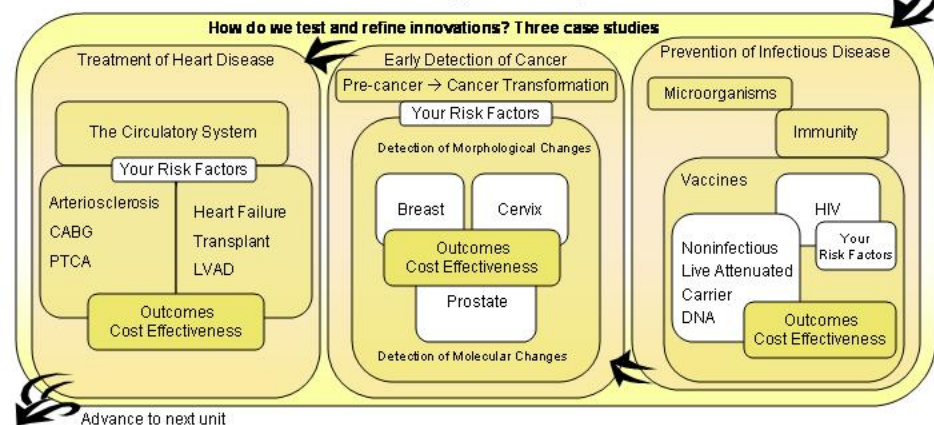
## Who pays to solve problems in health care?



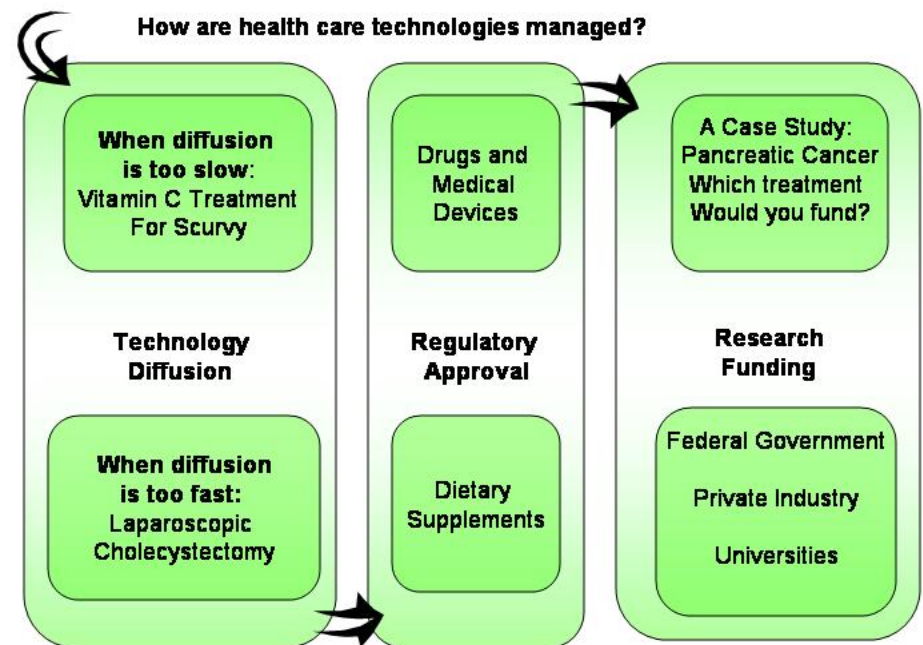
## Technology Assessment: The Big Picture



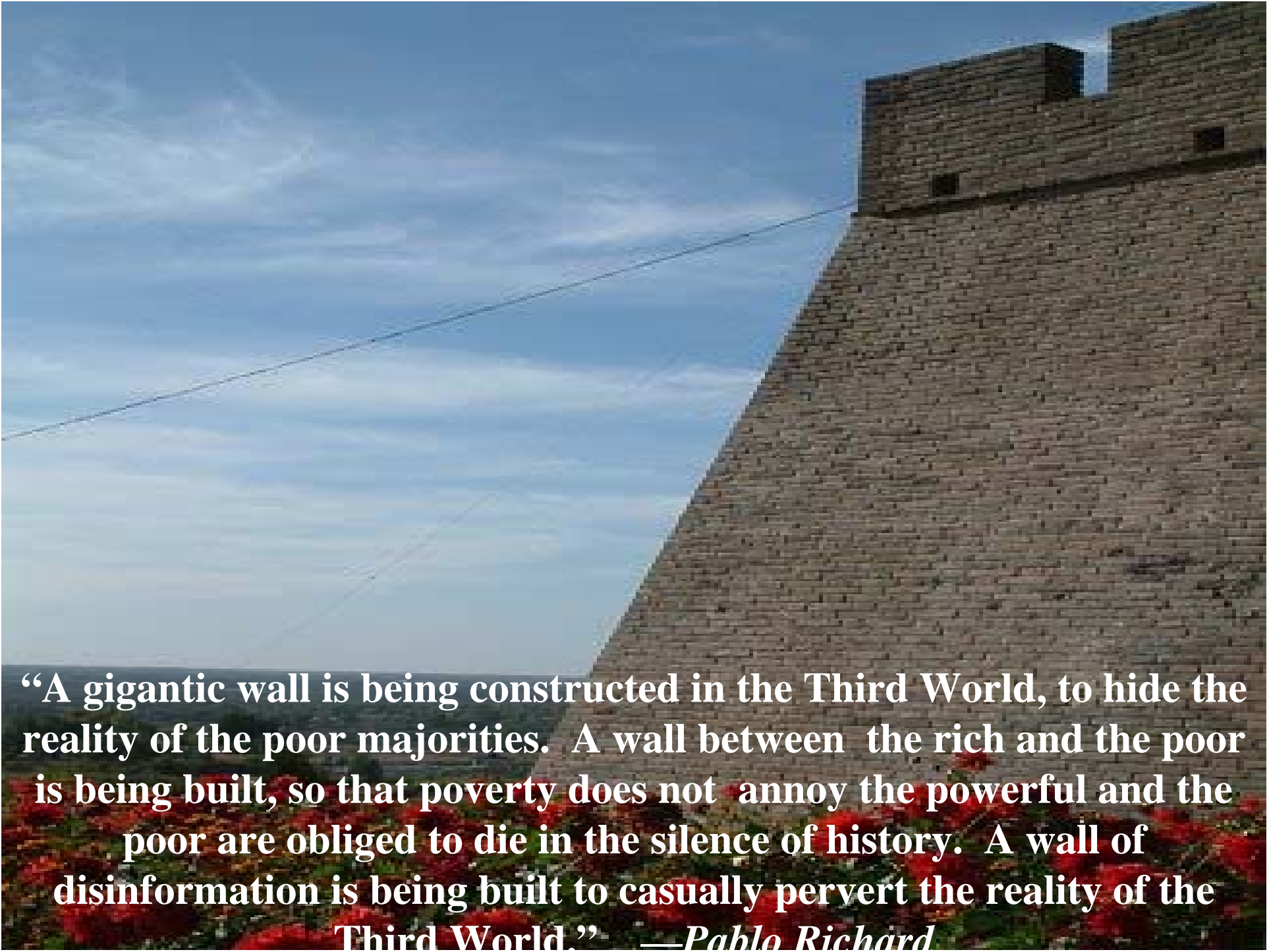
## How can we use science and technology to solve problems in health care?



## How are health care technologies managed?



# Closing Thoughts



**“A gigantic wall is being constructed in the Third World, to hide the reality of the poor majorities. A wall between the rich and the poor is being built, so that poverty does not annoy the powerful and the poor are obliged to die in the silence of history. A wall of disinformation is being built to casually pervert the reality of the Third World.” —Pablo Richard**



"Poverty wields its destructive influence, from the moment of conception to the grave. It conspires with the most deadly and painful diseases to bring a wretched existence to all who suffer from it." ~World Health Organization

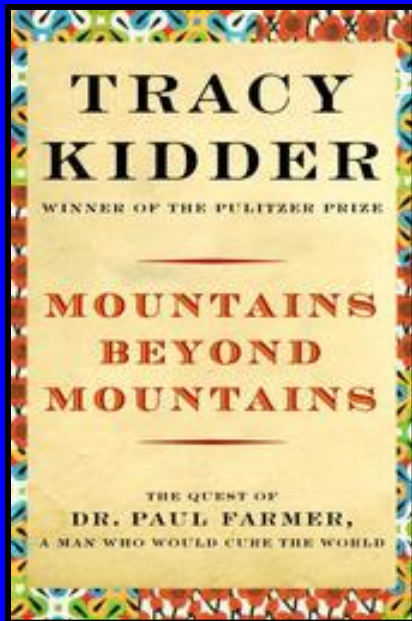


**“The trouble with the rat race is that even if you win,  
you’re still a rat.”  
~ Lily Tomlin, actress**

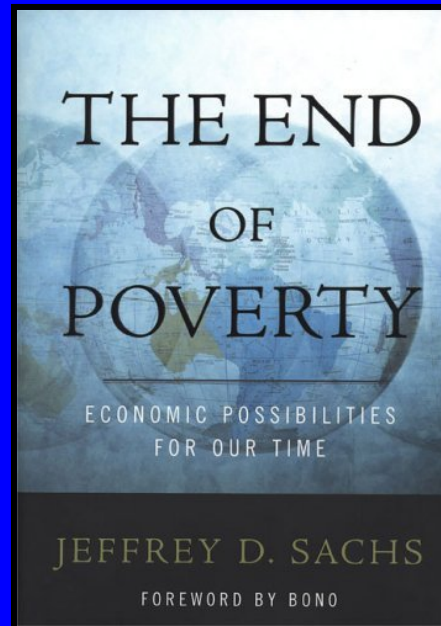




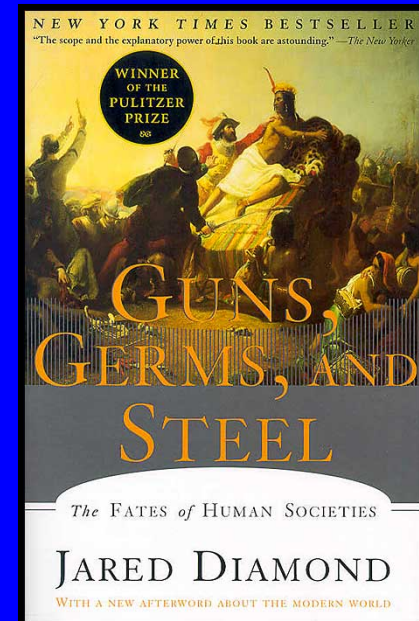
# Warmly Recommended Reading



**Mountains Beyond Mountains**  
by Tracy Kidder



**The End of Poverty**  
by Jeffrey Sachs



**Guns, Germs, and Steel**  
by Jared Diamond

# Assignment Due Next Time

- HW1