Biomedical Engineering for Global Health

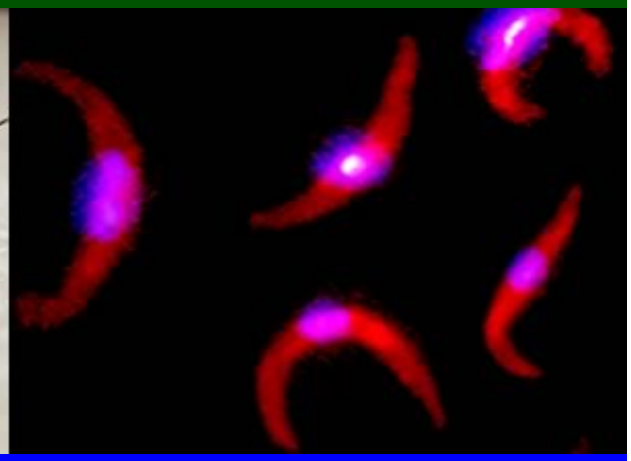
Lecture Three:

Leading Causes of Mortality, Ages 15-44

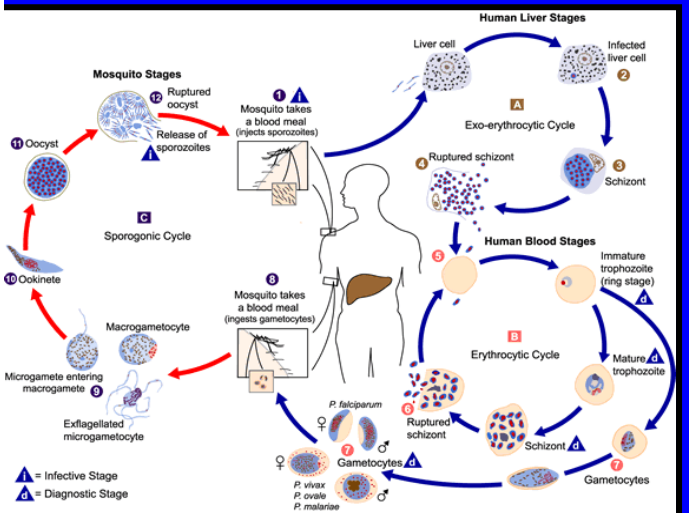
A Malaria Vaccine Breakthrough??

SANARIA

MALARIA ERADICATION THROUGH VACCINATION



http://www.sanaria.com/

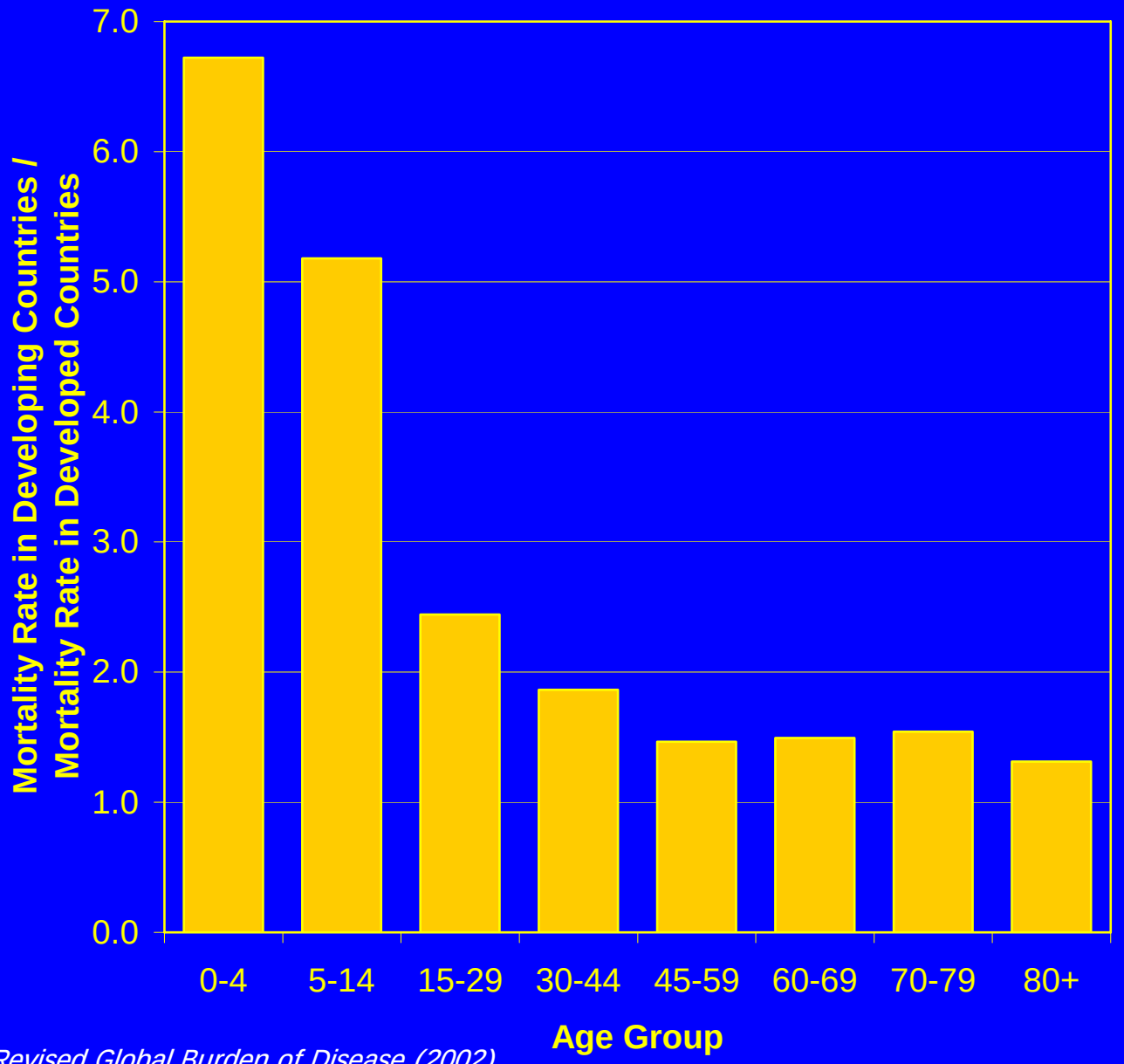


http://www.cdc.gov/malaria/images/graphs/malaria_lifecycle.gif

Review of Lecture Two:
Leading Causes of Mortality, Birth-Age 4

- Developing world
  1. Perinatal conditions
  2. Lower respiratory infections
  3. Diarrheal diseases
  4. Malaria
- Developed world
  1. Perinatal conditions
  2. Congenital anomalies
  3. Lower respiratory infections
  4. Unintentional injuries

Ratio of Mortality Rate



WHO. *Mortality: Revised Global Burden of Disease (2002)*

1. Perinatal Conditions

- Question: What is the #1 way to prevent septicemia in a newborn in the developing world?

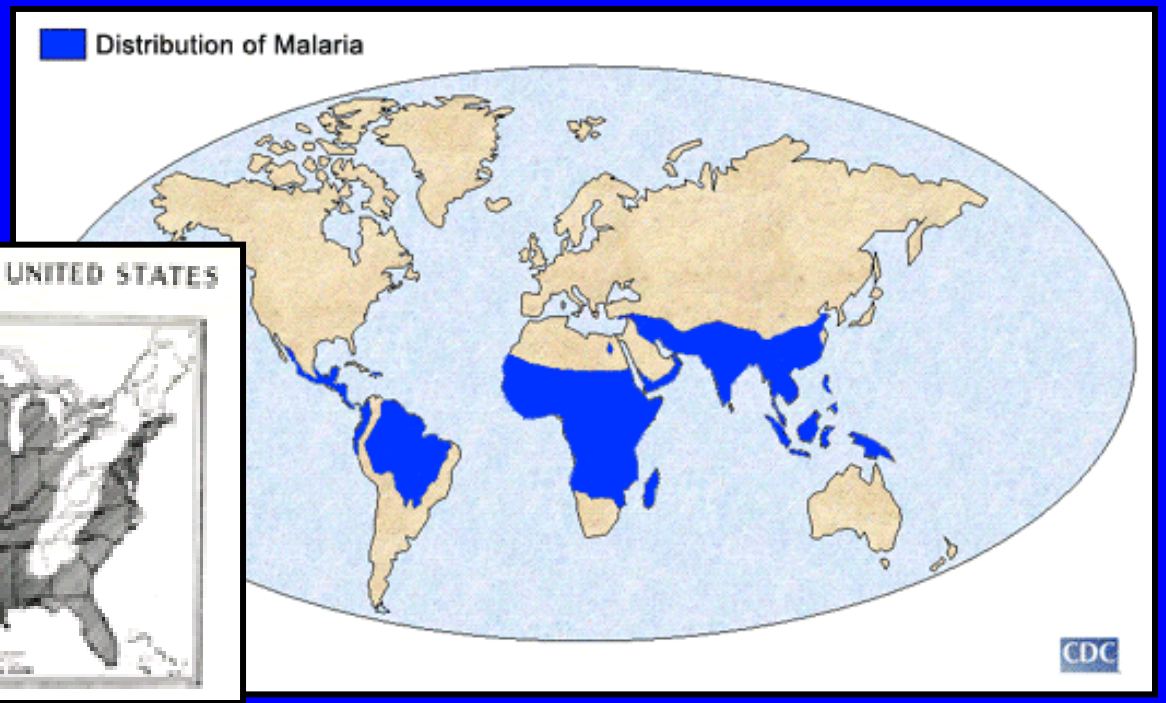
2. Lower Respiratory Infections

- Question: How can a busy health worker (or a parent) *quickly* screen for pneumonia in a child?

3. Diarrheal Diseases

- Question: What is the #1 way to prevent diarrheal illness in a newborn?

4. Malaria



- Question: How was malaria eradicated from the southern U.S.? What are the challenges with implementing this technology in less developed countries?

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

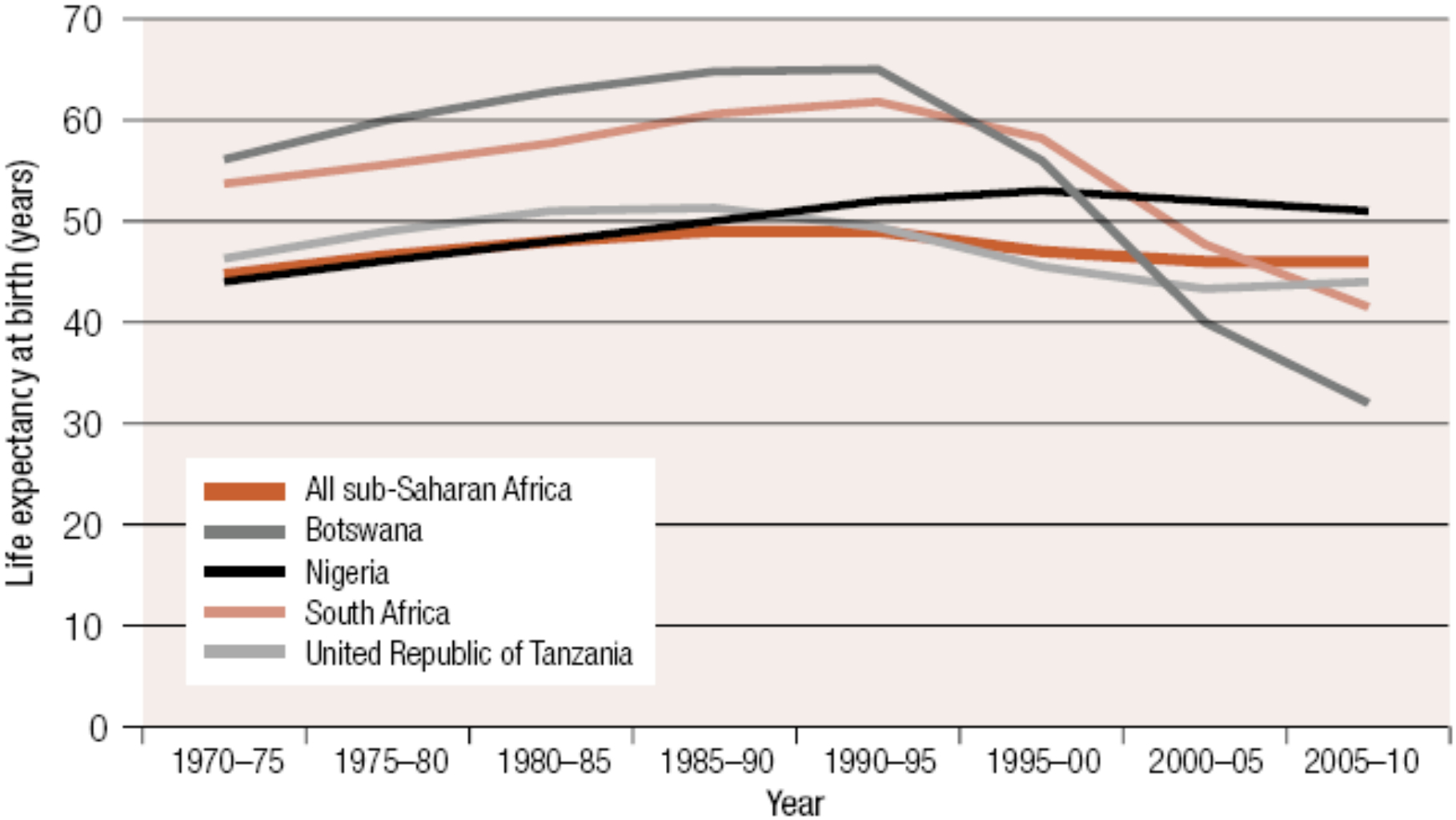
- Burden of HIV/AIDS
- Pathophysiology of HIV
- Clinical course of HIV/AIDS
- Highly Active Antiretroviral Therapy
- Prevention of Mother to Child Transmission (PMTCT)

Burden of HIV/AIDS

- Worldwide
  - 33.2 million people are living with HIV/AIDS
  - 20 million people have been killed by the disease
  - 2007:
    - 2.1 million deaths
    - 2.5 million new HIV infections
    - 17% of new infections occurred in children (<15 yrs)
  - 2/3 of those with AIDS and 3/4 of all AIDS deaths are in sub-Saharan Africa
  - 6800 new infections per day
    - 96% in low- and middle-income countries
    - 1200 children

Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

AIDS has Reduced Life Expectancy



Beaglehole R, Irwin A, Prentice T. *The World Health Report 2004: Changing History.*

Burden of HIV/AIDS in the U.S.

- 1.2 million people have HIV/AIDS (prevalence)
- 30,000-40,000 new infections per year (incidence)
- Only 7 countries in the world have more people living with HIV than the U.S.
- Routes of transmission:
  - Unsafe sex between men (53%)
  - Unprotected heterosexual intercourse (32%)
  - Non-sterile drug injection equipment (18%)

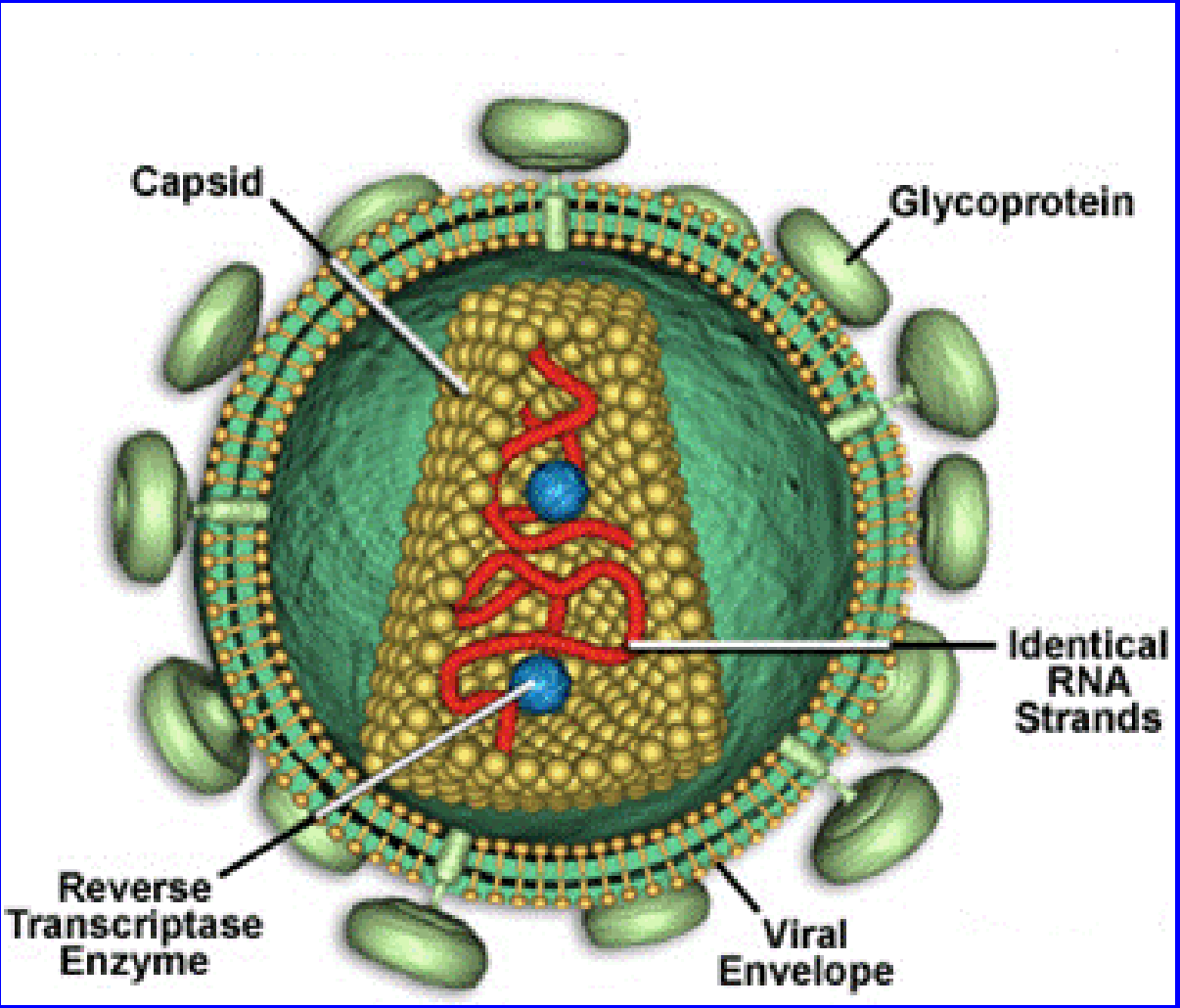
Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

Burden of HIV/AIDS in the U.S.

- Racial and ethnic minorities are disproportionately affected:
  - 48% of AIDS diagnoses are African-Americans (15% pop)
  - The rate of new HIV diagnoses was 21x higher in African-American women than in Caucasian women
- Women are increasingly affected:
  - The proportion of women among new HIV/AIDS diagnoses have risen from 15% to 26% in 10 years
- Question: Why is the prevalence of HIV in the U.S. continuing to increase?

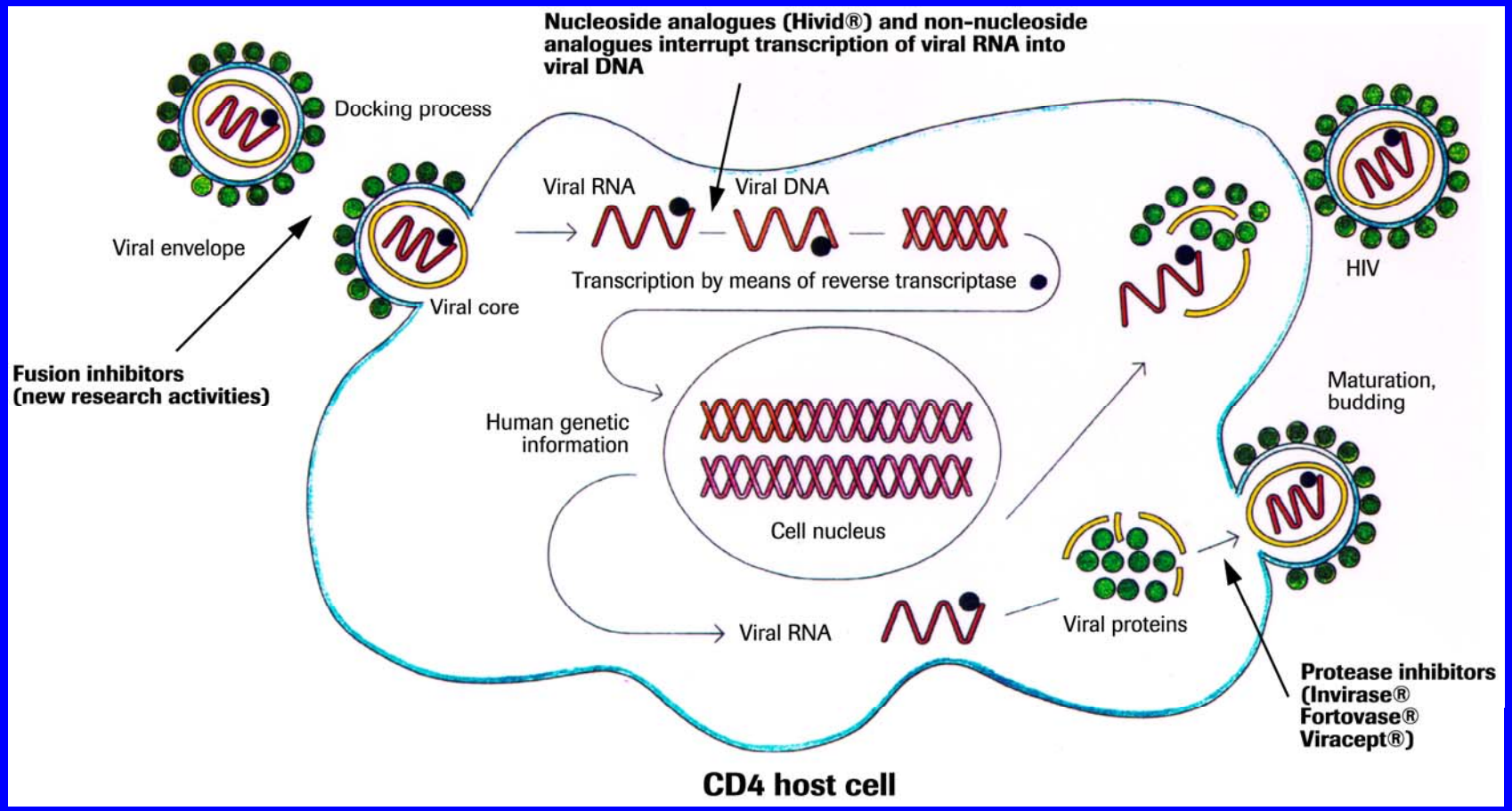
Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

Pathophysiology of HIV/AIDS



Michael W. Davidson at Florida State University

Pathophysiology of HIV/AIDS



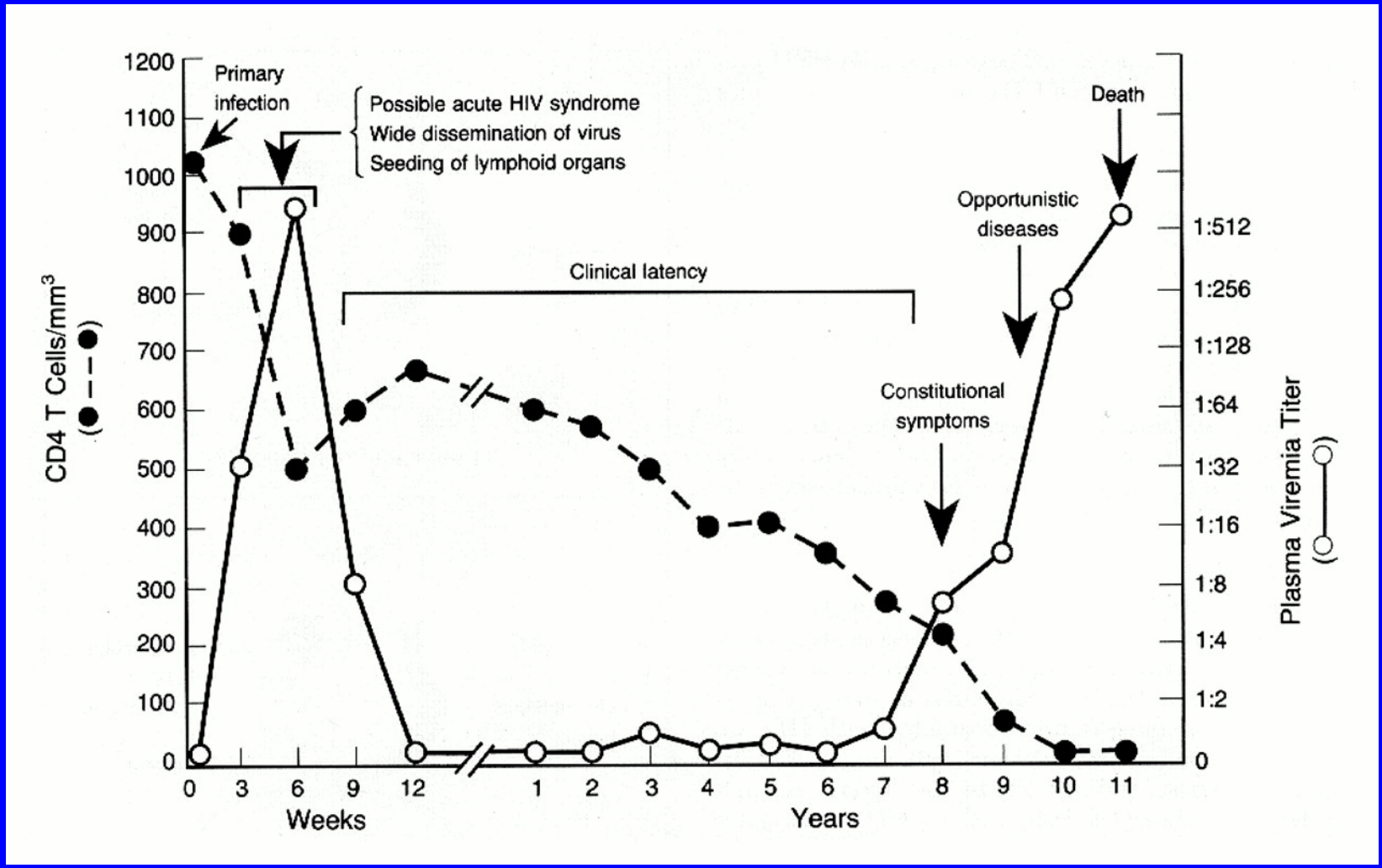
Roche

Pathophysiology of HIV/AIDS

Table 1: Cells Susceptible to HIV Infection	
System	Cell
Hematopoietic	• T-cells (CD4+ or CD8+) • Macrophages/monocytes • Dendritic cells • Fetal thymocytes and thymic epithelium • B-cells • NK cells • Megakaryotic cells • Stem cells
Central Nervous	• Microglia • Capillary endothelial cells • Astrocytes • Oligodendrocytes
Large Intestine	• Columnar epithelium
Other	• Kupfer cells (liver) • Synovial cells • Placental trophoblast cells

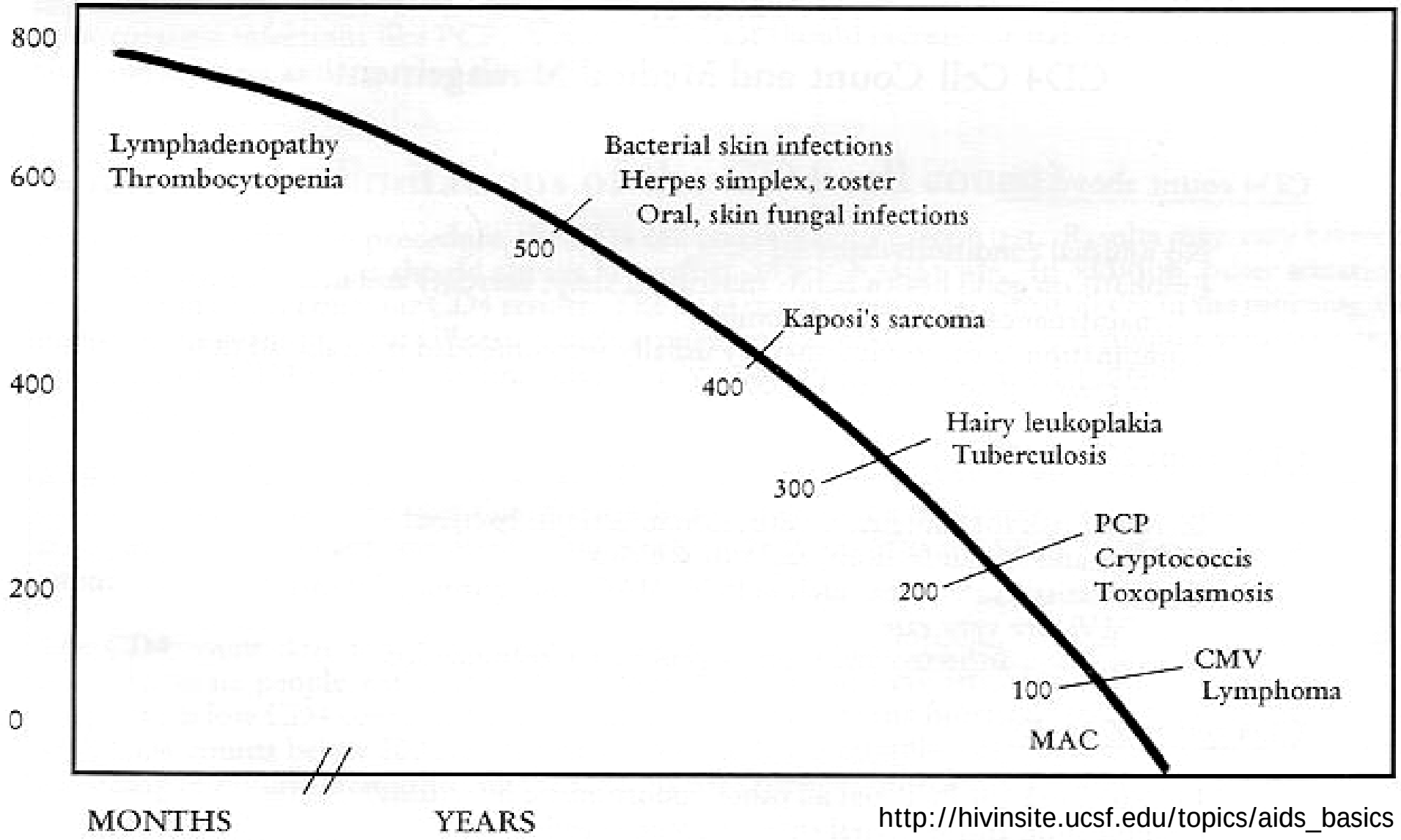
http://bayloraids.org/curriculum/

Clinical Course of HIV/AIDS



Pantaleo, G., Graziosi, C., Fauci, A. (1993) The Immunopathogenesis of Human Immunodeficiency Virus Infection. Mechanisms of Disease. 328 (S): 327–335.

Clinical Course of HIV/AIDS



http://hivinsite.ucsf.edu/topics/aids_basics

Clinical Course of HIV/AIDS


Figure 1: Kaposi's Sarcoma


Figure 2: Herpes Simplex


Figure 3: Herpes Zoster (Shingles)


Figure 5: Molluscum Contagiosum


Figure 8: Scabies With Pruritic Papular Eruption

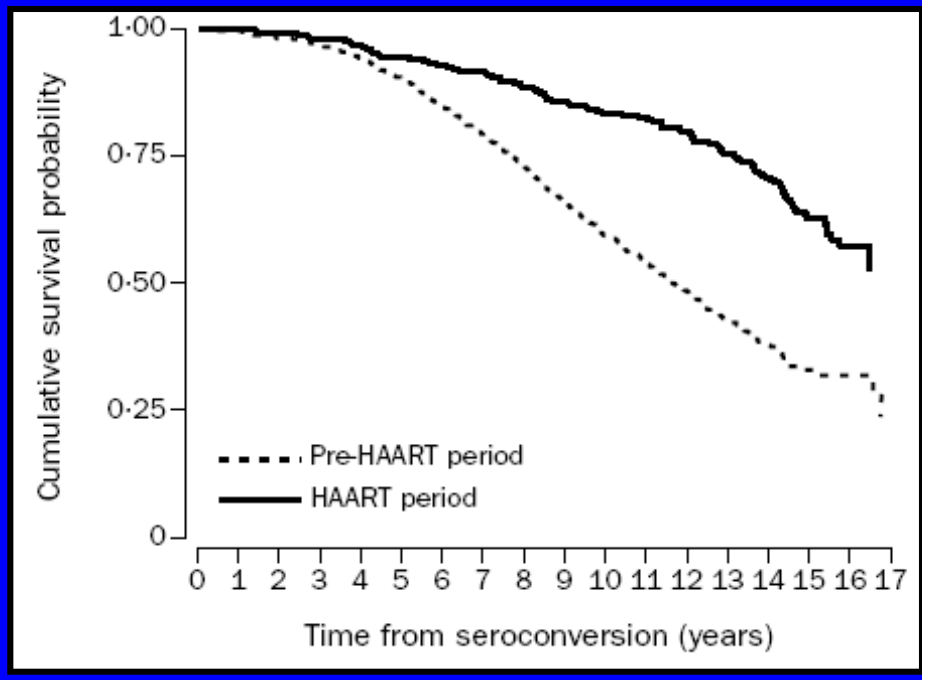
http://bayloraids.org/curriculum/

HIV/AIDS Therapy

- Reverse Transcriptase Inhibitors (1987)
  - Enzyme is specific to HIV
  - Combinations of RTIs appear effective
- HIV Protease Inhibitors (1995)
  - HIV proteases are distinct from mammalian proteases
  - Most significant advance in HIV therapy yet
- Highly Active Antiretroviral Therapy (HAART)
  - Combination of three or more drugs
- Fusion inhibitor (2003)
- Integrase inhibitor (2007)

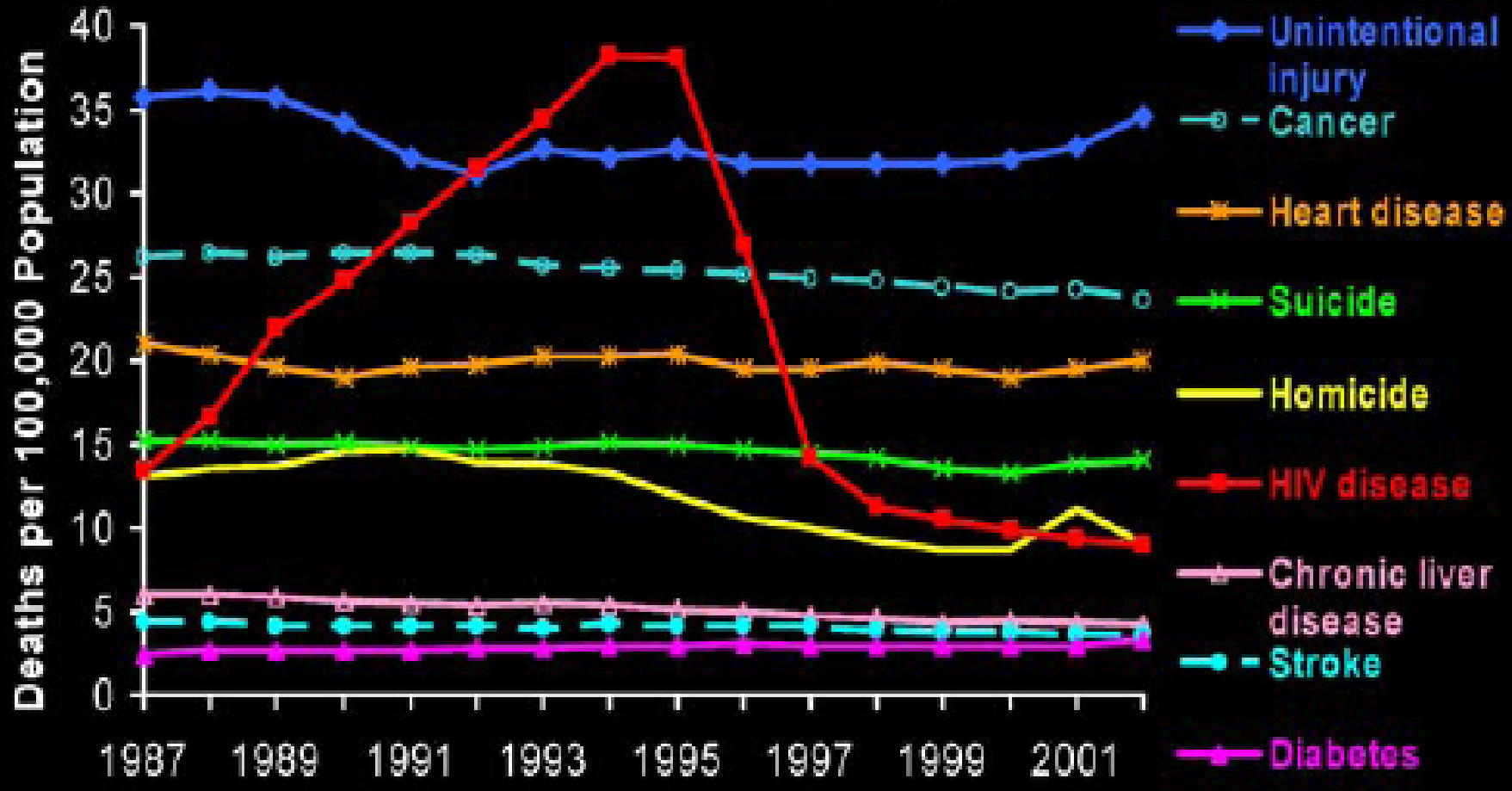
HIV/AIDS Therapy

- HIV can rapidly mutate to quickly develop resistance to a single drug
- Resistance develops much more slowly to drug combinations
- Goal of HAART:
  - Reduce viral levels to undetectable levels
  - Has reduced death rate in US and Europe by 80%



The Lancet, *Vol.* ***355****, The CASCADE Collaboration, Survival after introduction of HAART in people with known duration of HIV-1 infection, page 1, 2000, with permission from Elsevier.*

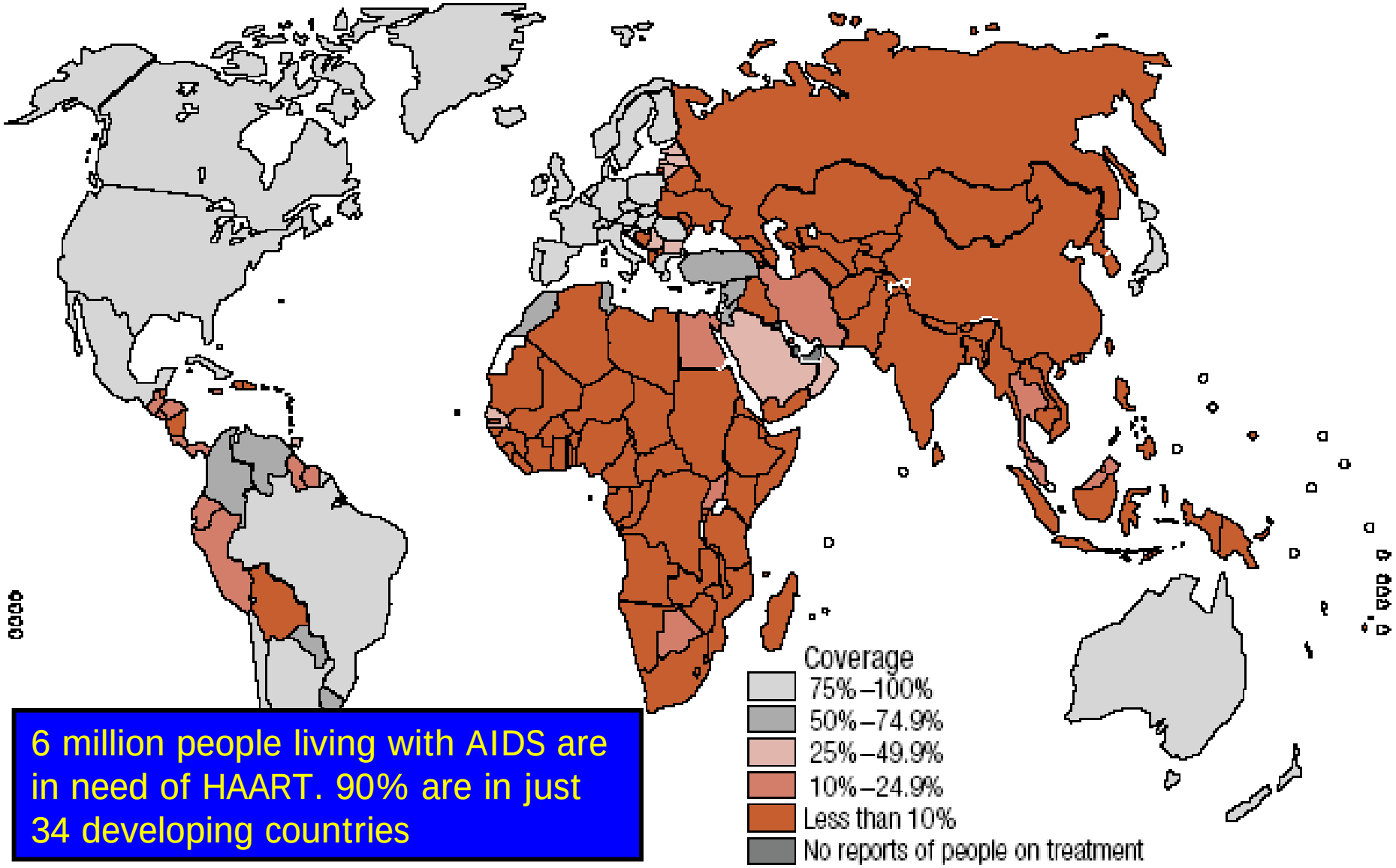
Trends in Annual Rates of Death due to the 9 Leading Causes among Persons 25–44 Years Old, USA, 1987–2002



Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for *ICD-10* rules instead of *ICD-9* rules.

HIV/AIDS: THE TREATMENT GAP

Estimated worldwide coverage with antiretroviral treatment, end 2003



6 million people living with AIDS are in need of HAART. 90% are in just 34 developing countries

www.npr.org/templates/story/story.php?storyId=4724368

Prevention of Mother to Child Transmission (PMTCT)

- 3 routes of transmission:
  - Parentally (during pregnancy)
  - Perinatally (during delivery)
  - Breast feeding (through milk)
- 4 Core interventions:
  - HIV testing and counseling
  - ARV prophylaxis (ZDV, NVP)
  - Safer delivery practices
  - Safer infant-feeding practices
- Reduces transmission from 30-40% to 4-6%

2. Unintentional Injuries

2. Unintentional Injuries

- Burden of Unintentional Injuries
- Accident Physics
- Slowed Driver Reaction Time
- Prevention of Road Accidents

Burden of Unintentional Injuries

- More than 1.25 million people ages 15-44 die from unintentional injuries each year
- 1 million deaths in developing countries, 1/4 million in developed countries
- 40x this number are injured
- Major cause of disability
- Leading cause is *road accidents*:
  - 500,000 deaths per year in this age group
  - 90% of these deaths occur in developing countries

Burden of Unintentional Injuries

- Road Accidents in the U.S.
  - Rates declining steadily
  - A leading cause of potential years of life lost
  - 2006:
    - 42,642 Americans killed
    - 2,699,000 Americans injured
    - Fatal accident rates 3X higher for males than for females
    - Motorcycles: 40X higher death rate per mile traveled
  - 39% of fatalities related to alcohol use

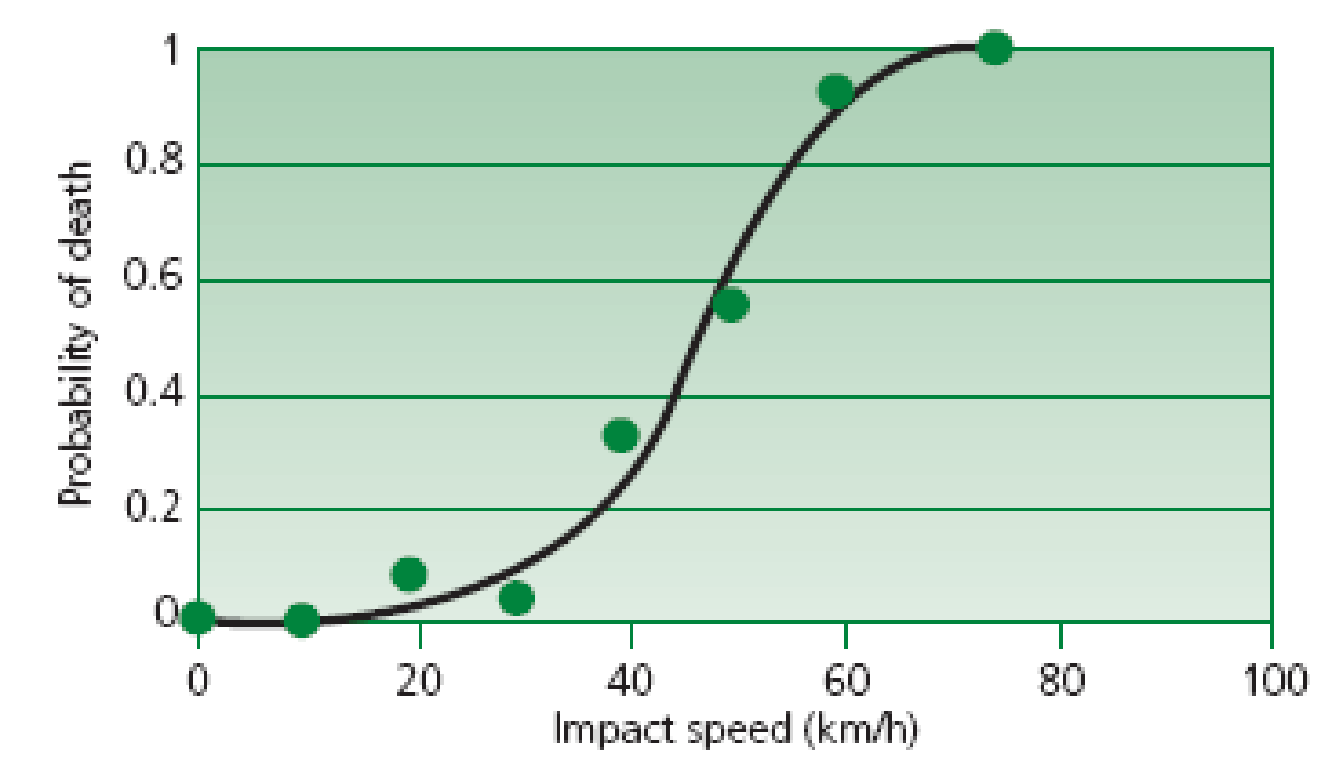
Accident Physics

CDC/Gwinnett Country Police Department.

- Newton's 2nd Law:
  - F = m a
  - a = dv/dt
  - a = initial velocity/time to come to rest
- In a crash:
  - Velocity slows to zero in a very short time
  - Generates large forces
- How can we reduce these forces?
  1. Reduce initial velocity of impact
  2. Extend time that it takes passengers to come to rest

Accident Physics

1. Reduce initial velocity of impact
   - Excessive speed contributes to:
     - 30% of deaths in developed countries
     - 50% of deaths in developing countries

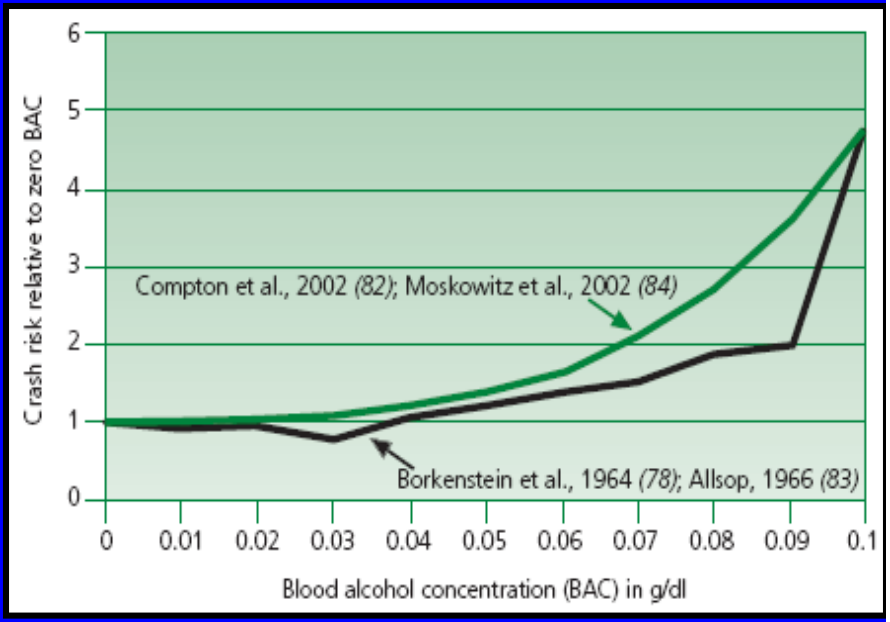


Slowed Driver Reaction Time

- When drivers anticipate a crash, they have time to brake and reduce initial velocity
- Factors which slow driver reaction time:
  - Alcohol use
  - Mobile phone use
  - Poor visibility
  - Driver inexperience

Slowed Driver Reaction Time

- Alcohol impaired drivers have 17X increased risk of being in fatal crash
- Alcohol use increases risk more in younger drivers
- 1 in 5 Americans will be involved in an alcohol-related crash at some time in their lives
- TX BAC limit:
  - 0.08+ g/dl is illegal
  - Approx 3 drinks in a 140 lb individual
  - Significant driving impairment at just 0.04 BAC!



World Report on Road Traffic Injury Prebention, *2004*

Slowed Driver Reaction Time

- Mobile phone use:
  - At any given daylight moment in US:
    - 10% of drivers are using a cell phone
  - Increases driver reaction time by 0.5-1.5 seconds
  - Risk of crash is 4X higher when using a mobile phone
  - Same as driving with a BAC of 0.09 g/ dl
- 4 states and D.C. have banned use of hand held phones while driving (NY, NJ, CT, CA)
  - Partial bans in AR, AZ, FL, GA, IL, ME, MA, MN, NH, NM, OH, PA, TN, VA, WA

Prevention of Road Accidents

2. Extending Time to Come to Rest:

- Crumple zones
  - Allow passengers additional time to decelerate
- Seat belts
  - Keep occupants in the passenger compartment
  - Stretch during impact
  - Reduce risk of death in crash by 40-60%
- Air bags
  - When combined with seat belts, reduce risk of serious and fatal injuries by 40-65%
- Child restraints:
  - Reduce risk of infant death by 71% and toddler death by 54%

Prevention of Road Accidents

- Legislation:
  - Speed
  - Seat belts, Car seats, Air Bags
  - Alcohol use
  - Motorcycle helmets
- Engineering:
  - Restraints
  - Safety standards
- Education:
  - Seat belts, Car seats, Air Bags
  - Alcohol use

3. Cardiovascular Diseases

- 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)
- Will be covered in depth in *Lecture 4*

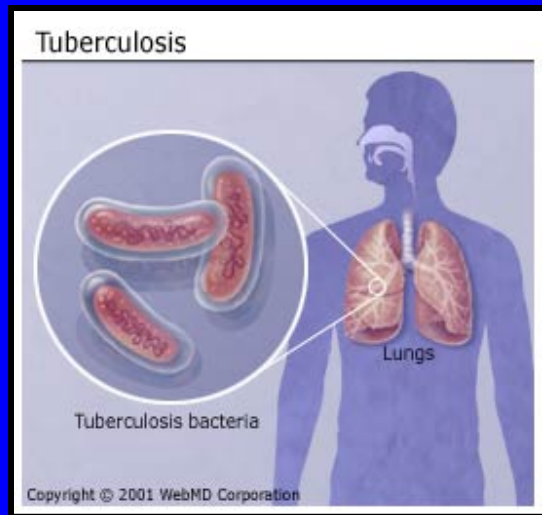

www.ohsu.edu/library/hom/exhibits/exhimages/200501tb/openair_pavilions.jpg

4. Tuberculosis

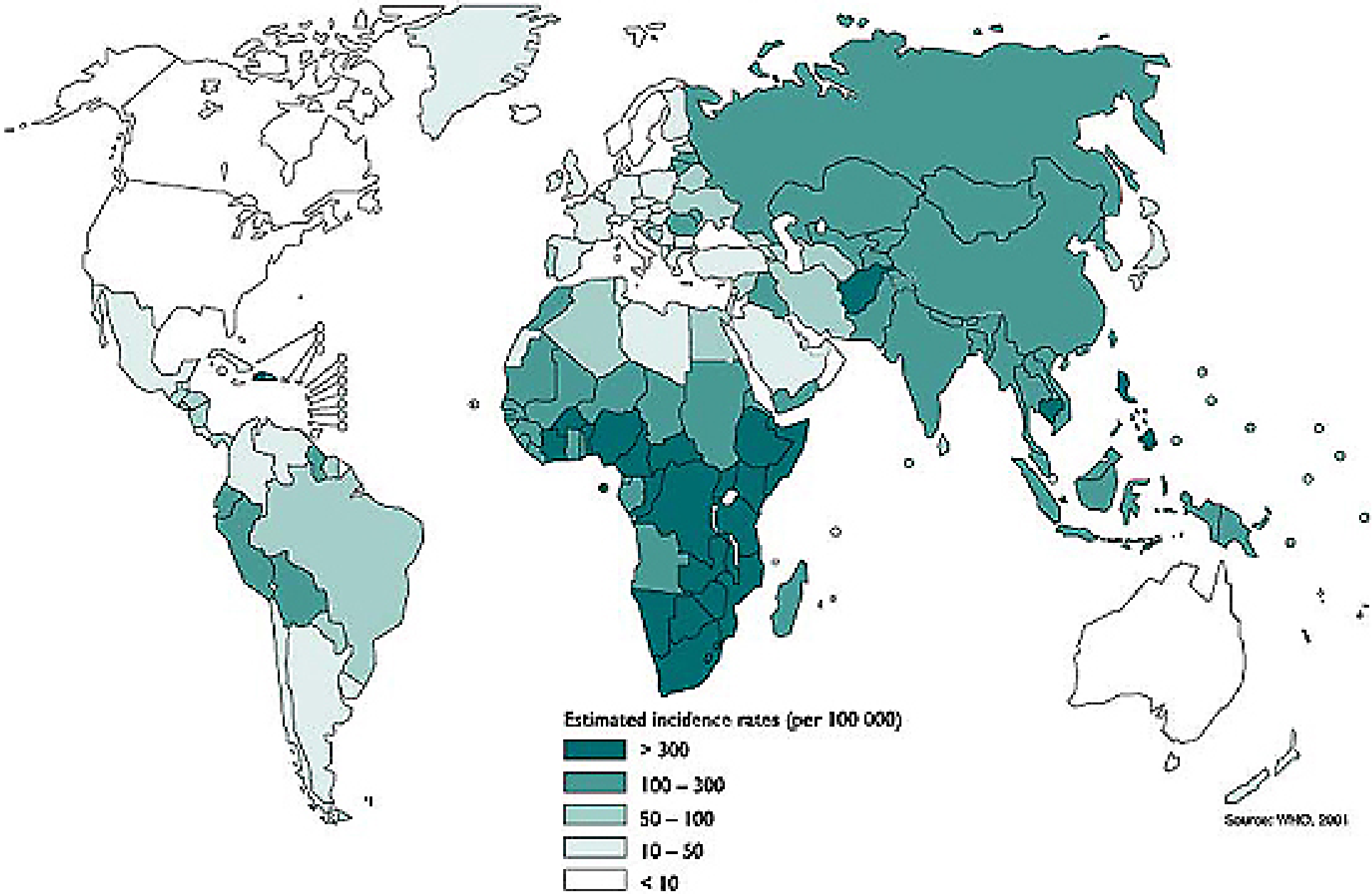
- Burden of Tuberculosis
- TB Pathophysiology
- Diagnosis of Tuberculosis
- Directly Observed Therapy

Burden of Tuberculosis

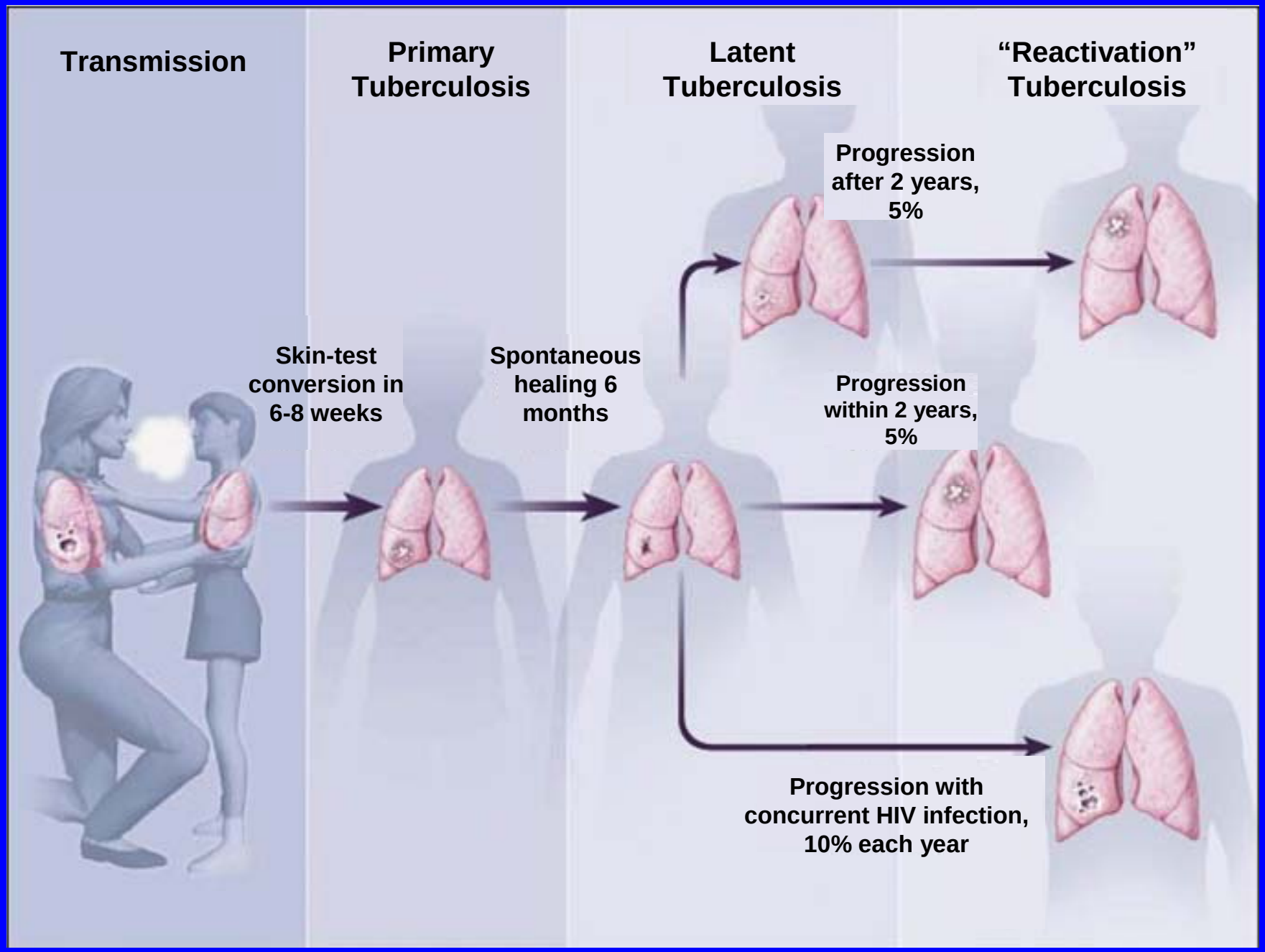
- Bacterial infection of the lungs caused by *Mycobacterium tuberculosis*
- Bacterium infects 1 in 3 people on the planet
- Drugs that cure TB were discovered in 1940s
- Results in death in 5 years in half of cases if untreated
- Kills 600,000 people ages 15-44 each year
- Estimated that TB will kill 35 million people in next 20 years if situation does not change
- 2005:
  - 8.8 million new cases (incidence)
  - Growing 1%/year
  - 1.6 million deaths
  - 98% of deaths occur in developing world



Tuberculosis, 2000



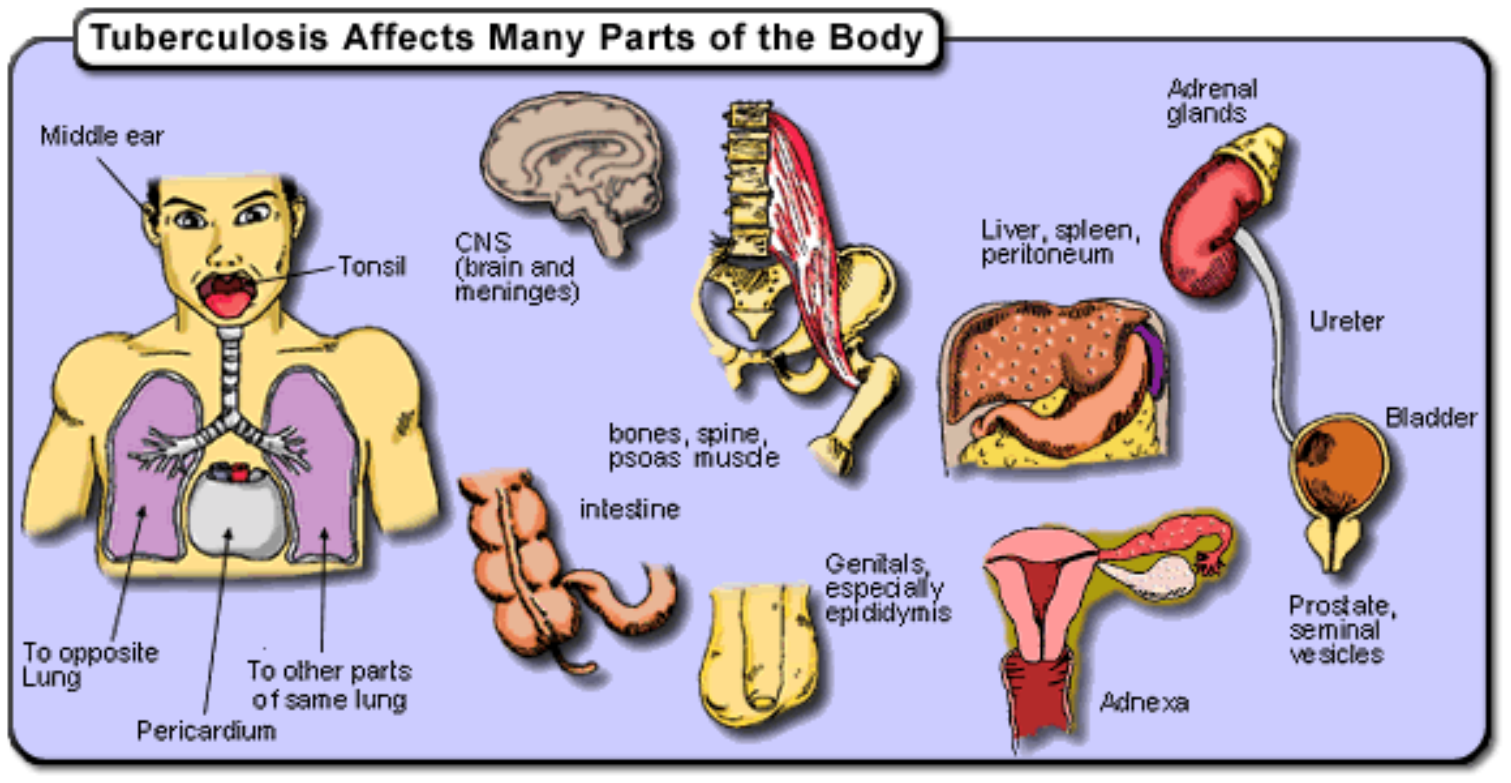
Courtesy of WHO Report 2006: Global Tuberculosis Control – Surveillance, Planning, Financing



Small PM, Fujiwara PI. Management of tuberculosis in the United States. *New England Journal of Medicine*. 2001 Jul 19; **345**(3): 189–200.

TB Pathophysiology

- Primary TB
- Latent TB
- Secondary, or reactivation, TB



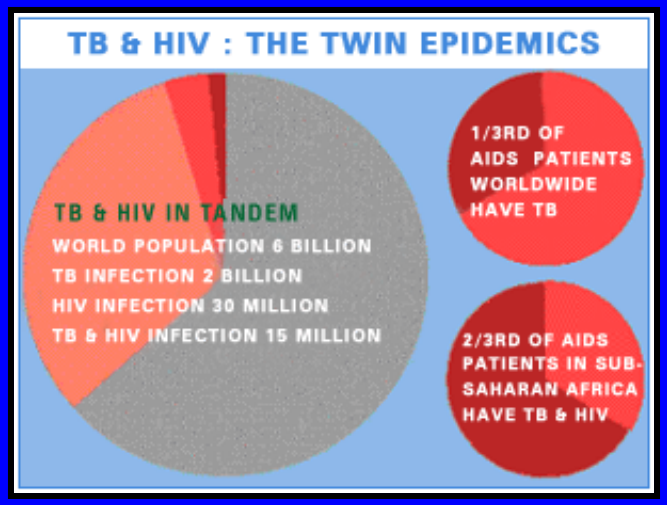
TB Pathophysiology

- Active TB:
  - Symptoms
    - Fever
    - Night sweats
    - Weight loss
    - Weakness
    - Coughs (productive with bloody sputum)
  - Airborne transmission
  - Left untreated, one person with active TB can cough millions of infectious droplets into the air

Andrew Dandhazy, Rochester Institute of Technology.

TB Pathophysiology

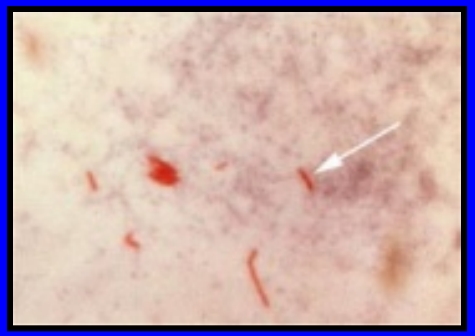
- TB and AIDS
  - People with AIDS are 10x more likely to develop active TB once infected
  - TB is the leading cause of death among HIV positive individuals, accounting for 13% of AIDS deaths worldwide

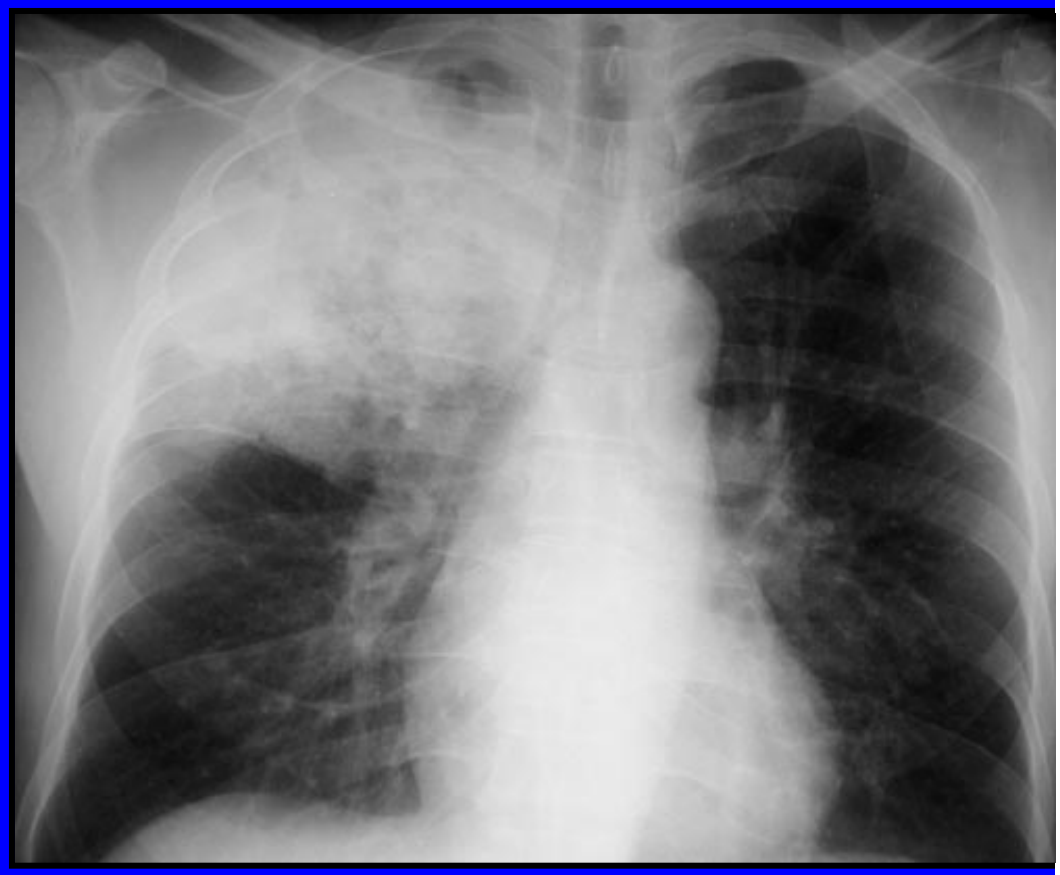


www.ourjeet.com/images/twinepidemics.gif

Diagnosis of Tuberculosis

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





CDC/Dr. Thomas Hooten.

Directly Observed Therapy (DOT)

- A health care worker watches and helps as the patient swallows anti-TB medicines in his/her presence.
- DOT shifts responsibility for cure from patient to health care system
- Requires political commitment, accurate diagnosis, quality drugs, observation, follow up
- DOT works well in many developing countries

Directly Observed Therapy (DOT)

- 6 month supply is $10
- Cure rates of up to 95% even in poorest countries
- 17 million patients worldwide have been treated with DOT since 1995
- 25% of world's population does not have access to DOT.

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

3. Cancer

- 580,000 people ages 15-44 die as a result of cancer every year
- Most common causes:
  - Liver Cancer (68,000 deaths per year)
  - Leukemias (65,000)
  - Stomach Cancer (58,000)
  - Breast Cancer (57,000)
- Will be covered in depth in *Lecture 4*

4. Self-Inflicted Injuries

- Burden of Self-Inflicted Injuries
- Risk Factors Associated with Suicide
- Methods of Suicide
- Screening and Prevention

Burden of Self-Inflicted Injuries

- 480,000 people ages 15-44 take their own lives each year (4th leading cause of death)
- Unipolar depressive disorder ranks #1 for DALYs in this age group in developed countries
  - Second to HIV/AIDS in developing countries
- Highest rate of completed suicides
  - Men >65 years old
- Highest rate of attempted suicides
  - Men and women ages 20-24

Risk Factors Associated with Suicide

- Psychiatric illness
  - Affective, substance abuse, personality, other mental disorders
- Other risk factors
  - Social adjustment problems
  - Serious medical illness
  - Living alone
  - Recent bereavement
  - Personal history of suicide attempt or completion
  - Divorce or separation
  - Unemployment

Methods of Suicide

- Most common:
  - Firearms are used in 60% of suicides
- 2nd leading cause:
  - Men: Hanging
  - Women: Drug overdose or poison
- Alcohol is involved in 25-40% of suicides
- Women attempt suicide more often; men are more often successful

Screening and Prevention

- 50-66% of all suicide victims visit physician <1 month before event
- 10-40% in the preceding week
- Hard to identify who is at risk
  - Direct questioning has low yield
  - General questions about sleep disturbance, depressed mood, guilt and hopelessness
  - Survey instruments aren't good at predicting what will happen

Screening and Prevention

- How do we quantify the efficacy of such questionnaires?
  - Goal of screening:
    - Catch as many positives as possible, even at the risk of some false positives
  - Sensitivity:
    - Se = probability of testing positive if you will commit suicide

$$Se = \frac{\#\text{ who test positive}}{\#\text{ who commit suicide}}$$

  - Sensitivity of best questionnaires: 56% (low)

Screening and Prevention

- How many false positives result?
  - Positive predictive value:
    - PPV=probability of committing suicide if you test positive

$$PPV = \frac{\#\text{ who test positive and commit suicide}}{\#\text{ who test positive}}$$

  - PPV of best questionnaires: 3% (pathetic)

Summary of Lecture 3

- 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