

Biomedical Engineering for Global Health

Lecture Three: Leading Causes of Mortality, Ages 15-44



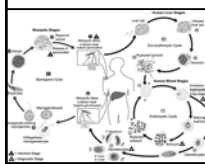
A Malaria Vaccine Breakthrough??

SANARIA

MALARIA ERADICATION THROUGH VACCINATION



<http://www.sanaria.com/>

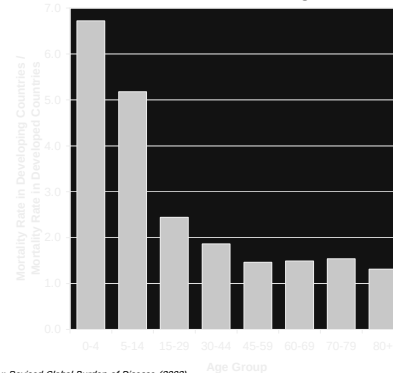


http://www.cdc.gov/malaria/images/graphs/malaria_lifecycle.gif

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



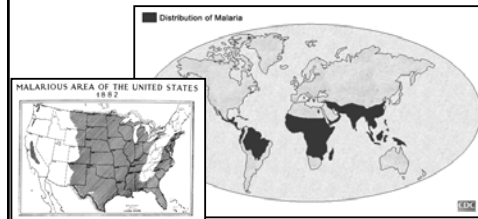
- Question: How can a busy health worker (or a parent) *quickly* screen for pneumonia in a child?

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

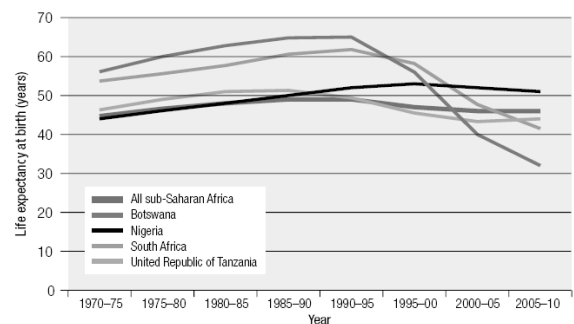
- Burden of HIV/AIDS
- Pathophysiology of HIV
- Clinical course of HIV/AIDS
- Highly Active Antiretroviral Therapy
- Prevention of Mother to Child Transmission (PMTCT)

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%)

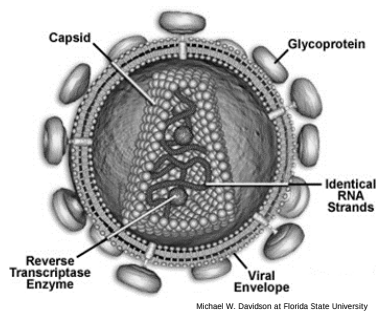
Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

Burden of HIV/AIDS in the U.S.

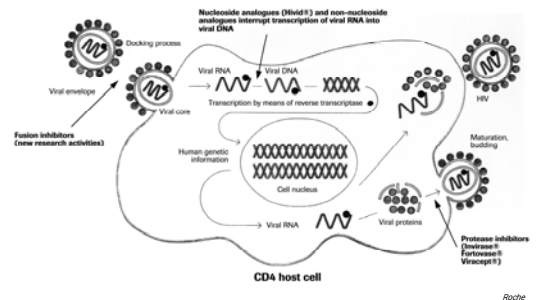
- Racial and ethnic minorities are disproportionately affected:
 - 48% of AIDS diagnoses are African-Americans (15% pop)
 - The rate of new HIV diagnoses was 21x higher in African-American women than in Caucasian women
- Women are increasingly affected:
 - The proportion of women among new HIV/AIDS diagnoses 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



Pathophysiology of HIV/AIDS



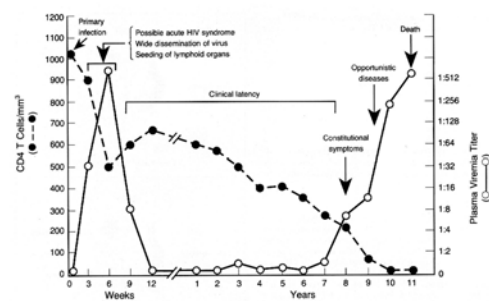
Pathophysiology of HIV/AIDS

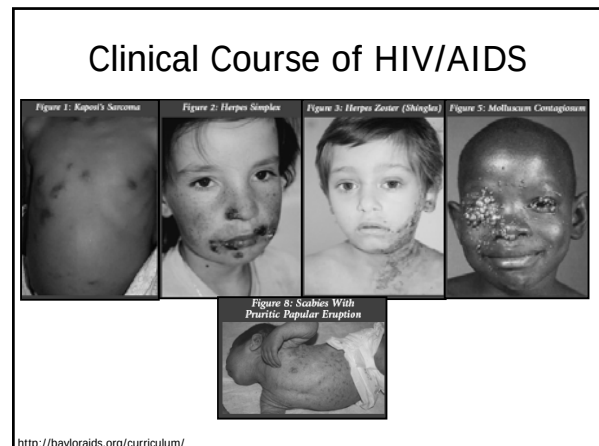
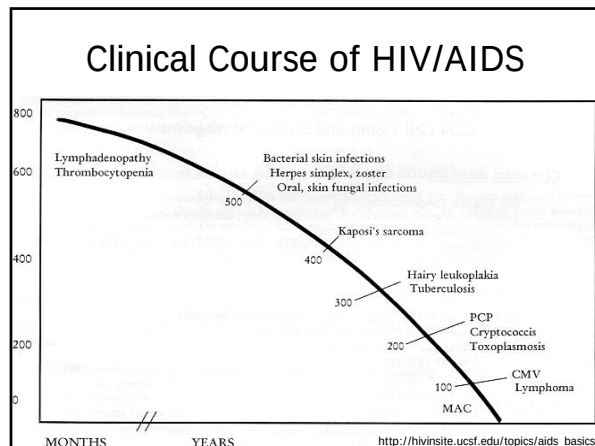
Table 1: Cells Susceptible to HIV Infection

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://bayloraid.org/curriculum/>

Clinical Course of HIV/AIDS





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%

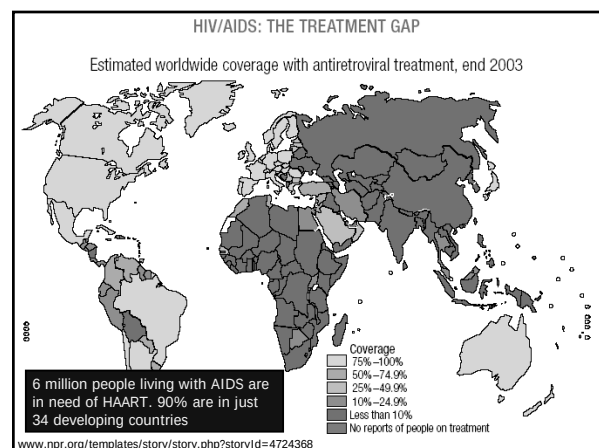
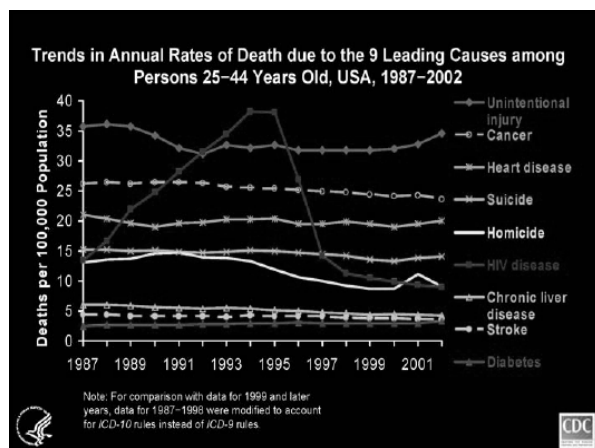
Cumulative survival probability

Time from seroconversion (years)

--- Pre-HAART period

— HAART period

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.



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

- Newton's 2nd Law:
 - $F = m a$
 - $a = dv/dt$
 - $a = \text{initial velocity} / \text{time to come to rest}$
- 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

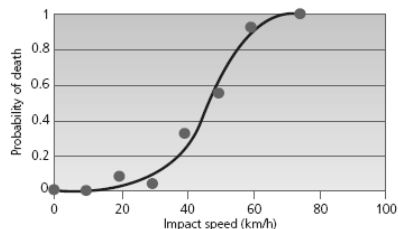


CDC/Gwinnett County Police Department.

Accident Physics

1. Reduce initial velocity of impact

- Excessive speed contributes to:
 - 30% of deaths in developed countries
 - 50% of deaths in developing countries

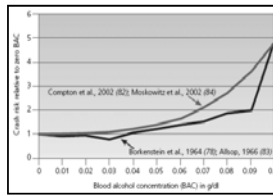


Slowed Driver Reaction Time

- 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!



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*

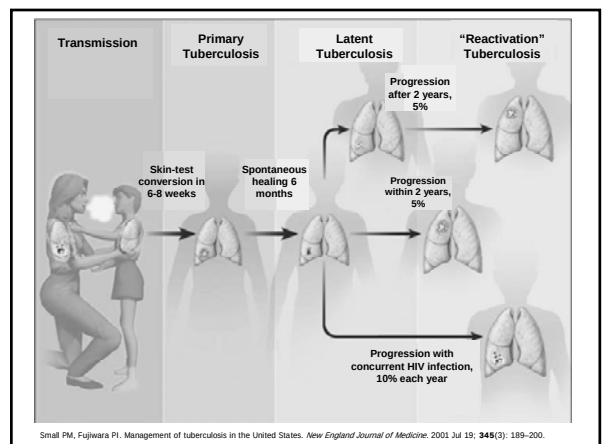
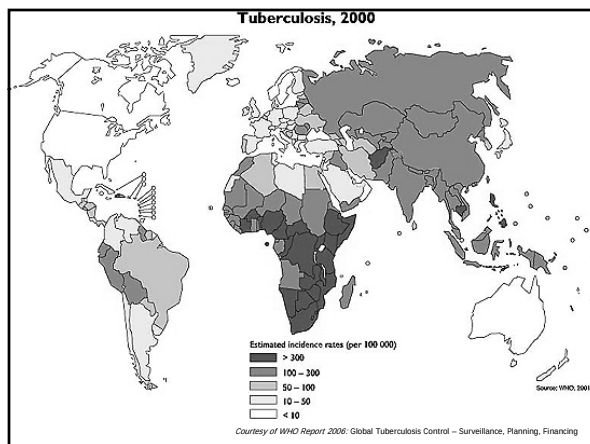
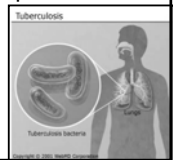


4. Tuberculosis

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

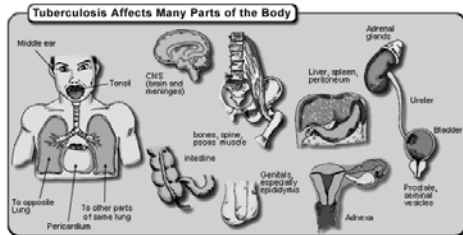
Burden of Tuberculosis

- 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



TB Pathophysiology

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



TB Pathophysiology

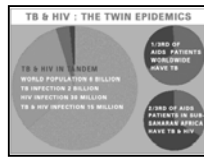
- Active TB:
 - Symptoms
 - Fever
 - Night sweats
 - Weight loss
 - Weakness
 - Coughs (productive with bloody sputum)
 - Airborne transmission
 - Left untreated, one person with active TB can cough millions of infectious droplets into the air



Andrew Dandhu, Rochester Institute of Technology.

TB Pathophysiology

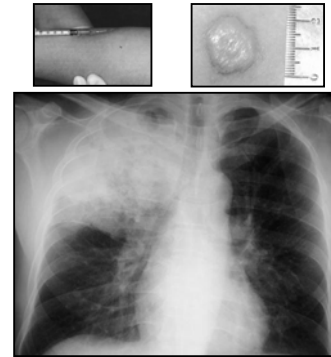
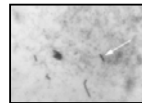
- TB and AIDS
 - People with AIDS are 10x more likely to develop active TB once infected
 - TB is the leading cause of death among HIV positive individuals, accounting for 13% of AIDS deaths worldwide



www.ourjet.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 Houston

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
- 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 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
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 4. Self-inflicted injuries