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

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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?

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http://bayloraids.org/curriculum/

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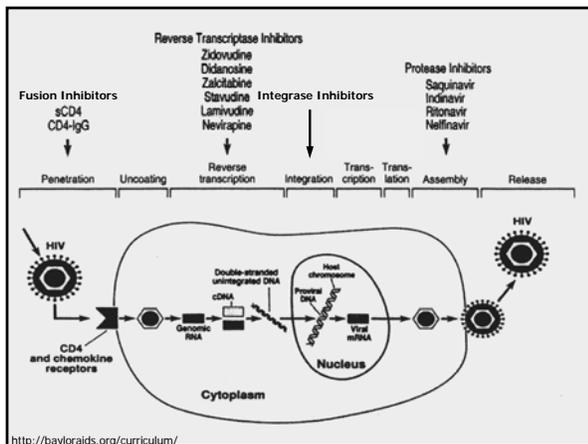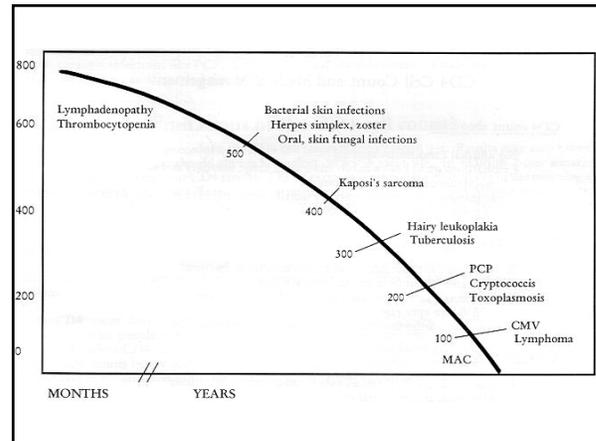
2. Unintentional Injuries

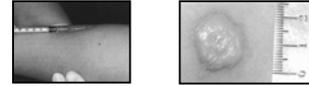- Do unintentional injuries account for more deaths in developed or developing countries? Give several reasons why.

Cancer and Cardiovascular Diseases
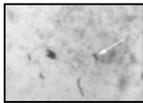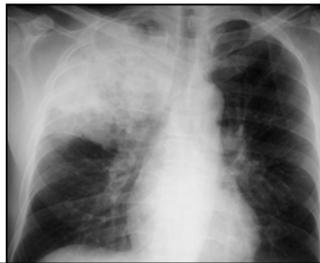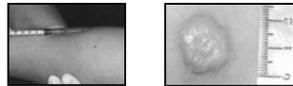
- Will be discussed today!

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)

> 13
6.5–13
<6.5
no data

http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/index.html
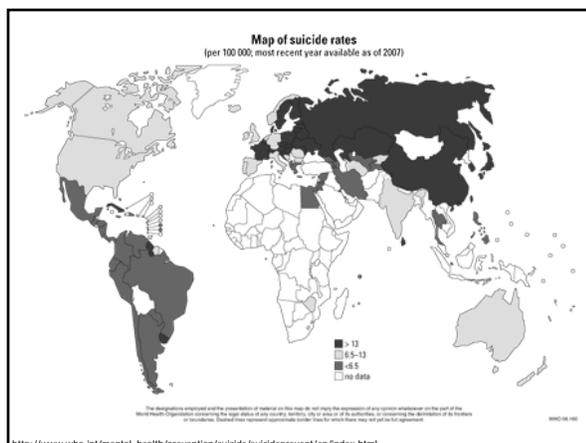
Suicide Screening and Prevention

S
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G
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C
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S

Lecture 4:
Leading Causes of Mortality Ages 45-60
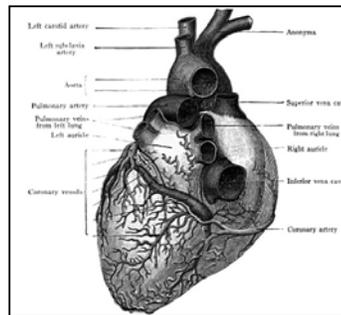
- Developing World
    1. Cardiovascular diseases
    2. Cancer (malignant neoplasms)
    3. Unintentional injuries
    4. HIV/AIDS
- Developed World
    1. Cardiovascular diseases
    2. Cancer (malignant neoplasms)
    3. Unintentional injuries
    4. Digestive Diseases

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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...

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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
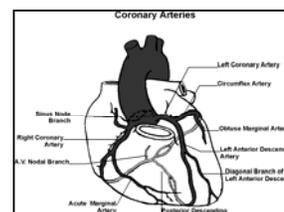
Ischemic Heart Disease: Pathogenesis

- 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

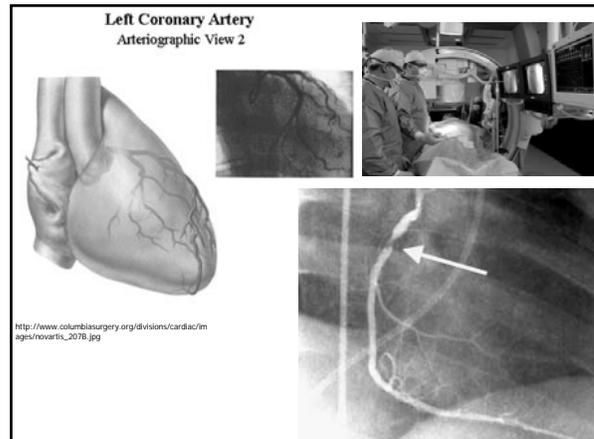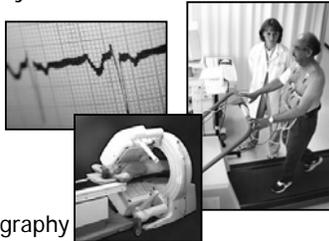# Ischemic Heart Disease: Pathogenesis
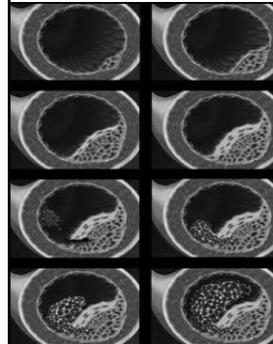
Evolution of a heart attack:
1. Endothelial injury
2. Fatty deposits
3. Fibrous cap with necrotic core
4. Unstable plaques rupture, thrombogenic core causes blood clots
5. Blood clots can lead to complete occlusion
6. Heart muscle supplied by occluded artery dies
7. If patient survives, affected heart 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

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   CABG   After

Blocked coronary artery

Vein graft sewn in to bypass blockage

ADAM.

PTCA
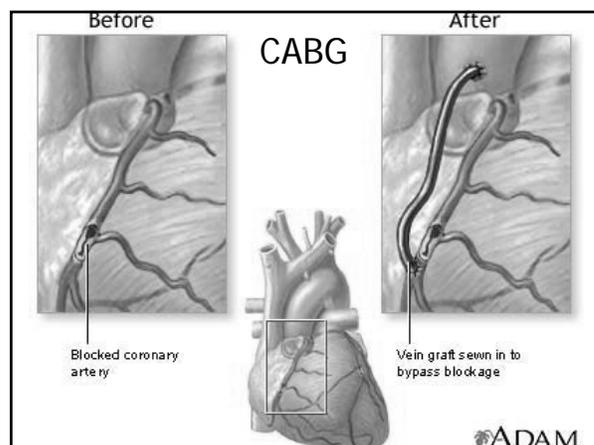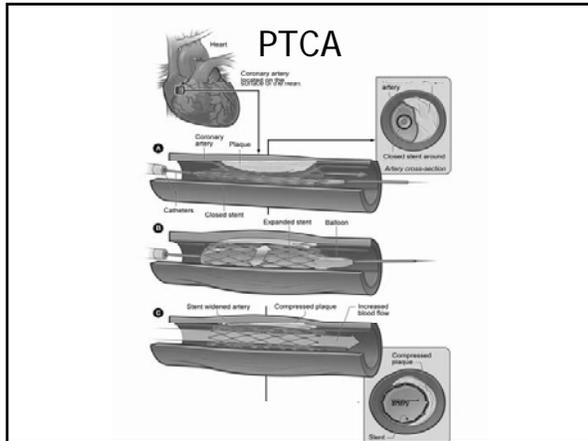
Cerebrovascular Disease: Epidemiology

- 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

	Men 294,120	Women 271,530		
Lung & bronchus	31%		26%	Lung & bronchus
Prostate	10%		15%	Breast
Colon & Rectum	8%		9%	Colon & rectum
Pancreas	6%		6%	Pancreas
Liver & intrahepatic bile duct	4%		6%	Ovary
Leukemia	4%		3%	Non-Hodgkin lymphoma
Esophagus	4%		3%	Leukemia
Urinary bladder	3%		3%	Uterine corpus
Non-Hodgkin lymphoma	3%		2%	Brain/other nervous system
Kidney	3%		2%	Myeloma
All other sites	24%		23%	All other sites

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
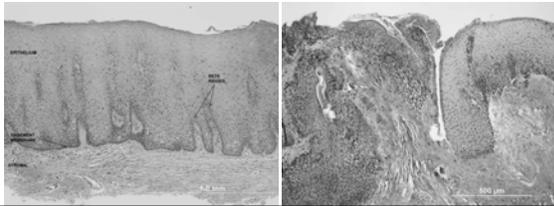
Pathogenesis of Cancer

- 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...
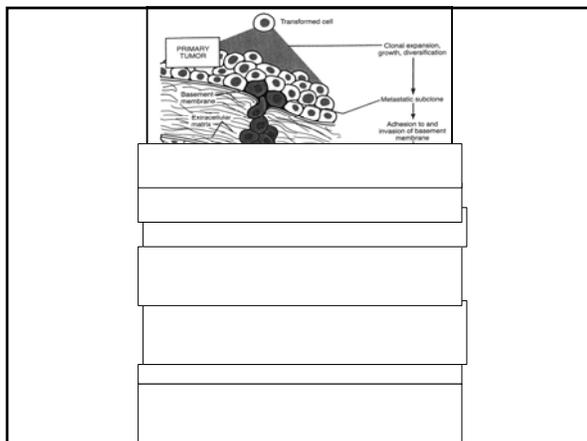
Pathogenesis of Cancer

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
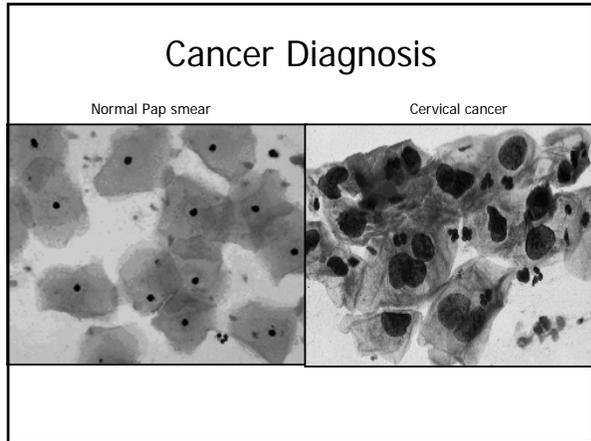
Treatment of Cancer

- 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
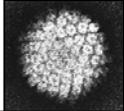

- Local
- Regional
- Distant
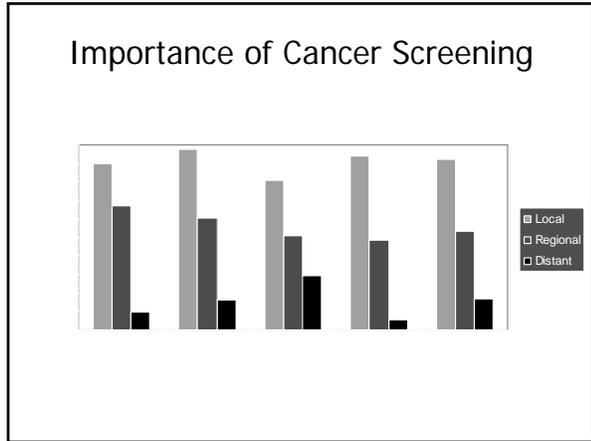
Cancer and Infectious Diseases

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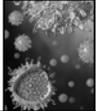
H. pylori, stomach cancer

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
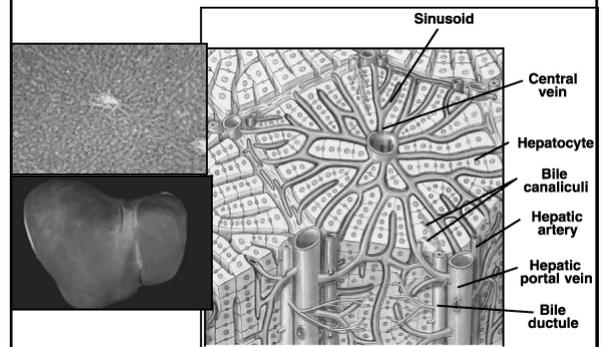- Hepatitis

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
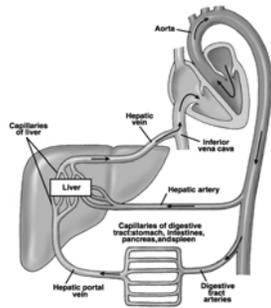
Normal Liver

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
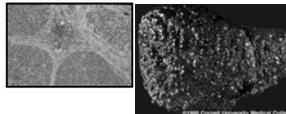
Hepatitis

- 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:	Ages 15-44:	Ages 45-59:
Perinatal conditions	HIV/AIDS	Cardiovascular diseases
Lower respiratory infections	Unintentional injuries	Cancers
Diarrheal diseases	Cardiovascular diseases	Unintentional injuries
Malaria	Tuberculosis	HIV/AIDS
Perinatal conditions	Unintentional injuries	Cardiovascular diseases
Congenital anomalies	Cardiovascular disease	Cancer
Lower respiratory infections	Cancer	Unintentional injuries
Unintentional injuries	Self-Inflicted Injuries	Digestive Diseases

Structural Violence

Structural Violence

Structural Violence

Structural Violence

Universal Declaration of Human Rights
ELEANOR ROOSEVELT et al.
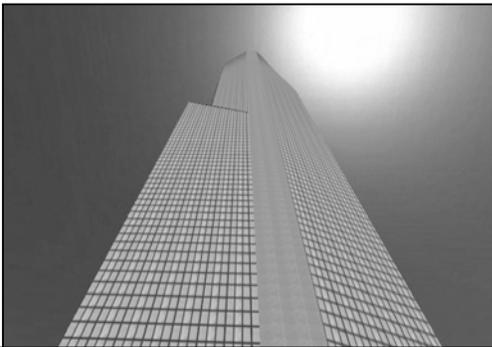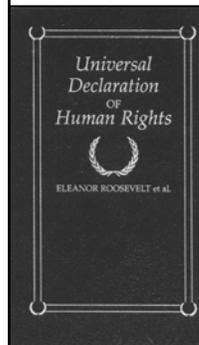
"It's not just a treaty… it may well become the international Magna Carta"
--Eleanor Roosevelt

Structural Violence

Universal Declaration OF Human Rights
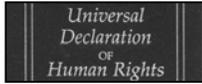
ARTICLE 25

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

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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
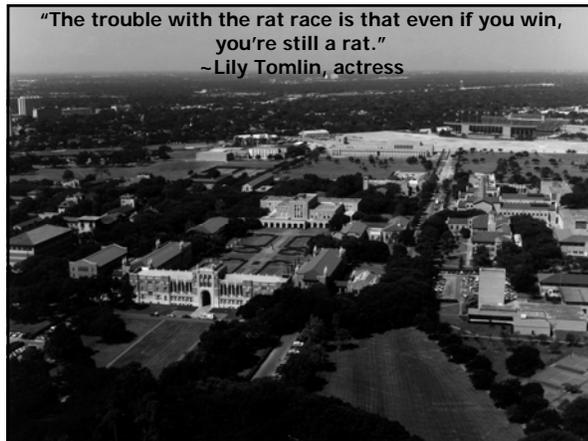GC#12 Create immunological methods that can cure chronic infections

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
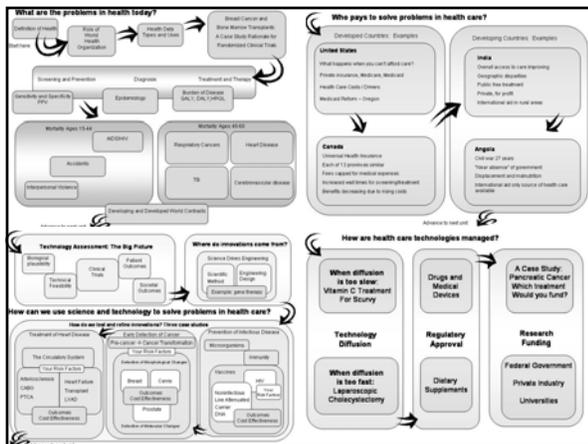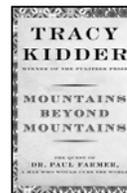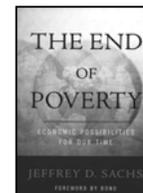

Closing Thoughts

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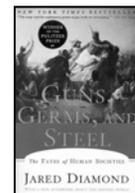
"Poverty wields its destructive influence, from the moment of conception to the grave. It conspires with the most deadly and painful diseases to bring a wretched existence to all who suffer from it." ~World Health Organization

"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	**The End of Poverty**	**Guns, Germs, and Steel**
by Tracy Kidder	by Jeffrey Sachs	by Jared Diamond

Assignment Due Next Time

- HW1