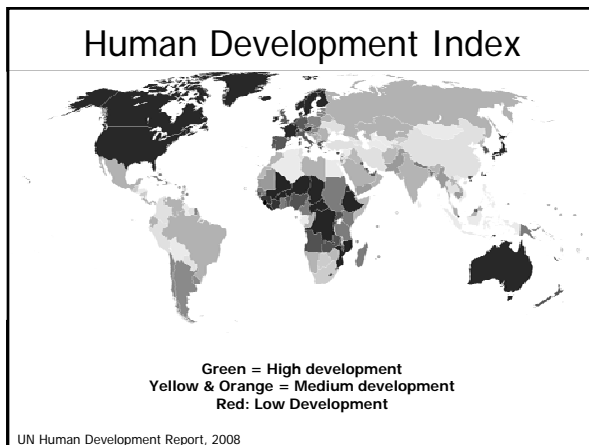


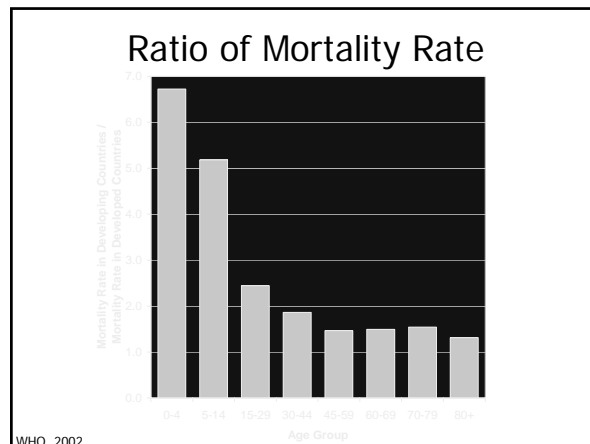
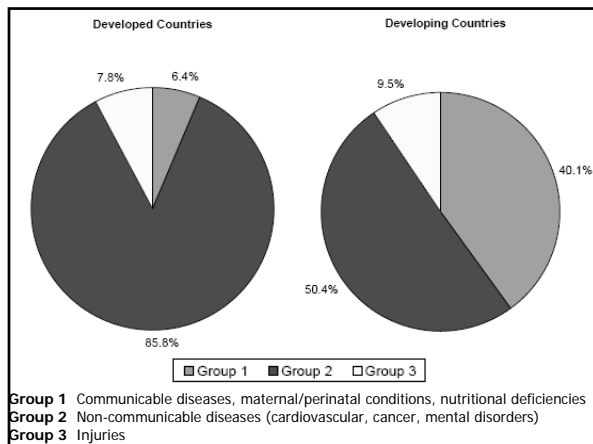
- ## Economic Data
- Per capita GDP
  - Per capita health spending
  - Purchasing power parity
    - Take into account true costs of goods and services
    - How much does a loaf of bread cost?
  - Human Development Index
    - Average achievements in health, education and income.



- ## One View of The World
- Developed vs. Developing Countries
    - There is no universally accepted definition of what a developing country is
    - Usually categorized by a per capita income criterion
      - Low income developing countries: <\$400
      - Middle income developing countries: \$400-\$4,000
    - WTO members decide for themselves if they are a developing country; brings certain rights

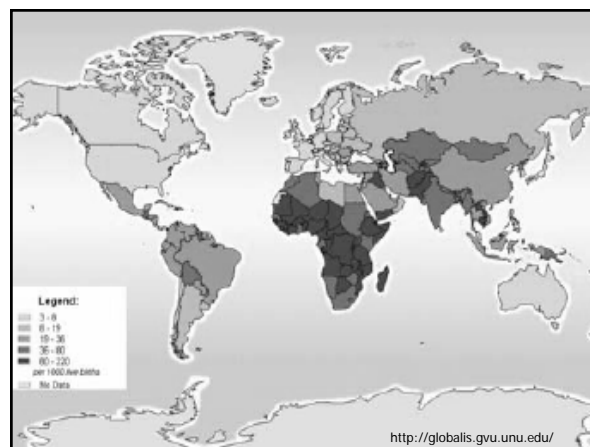
- ## Least Developed Countries
- In 1971, the UN created a Least Developed Country member category
    - Countries apply for this status
    - Low national income (<\$900 per capita GDP)
    - Low levels of human capital development
    - Economic vulnerability
    - Originally 25 LDCs
  - As of 2005, 637 million people live in world's 50 least developed countries
    - Population growth expected to triple by 2050





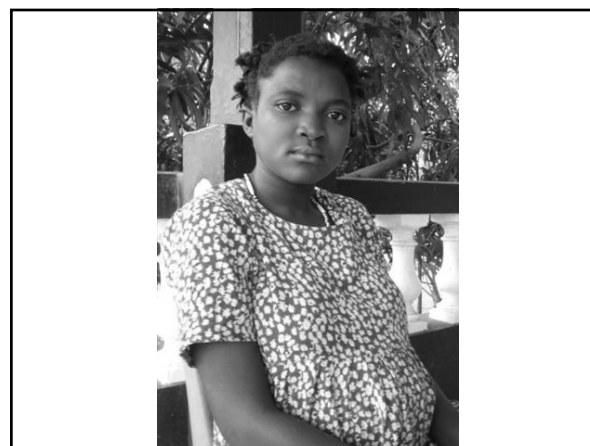
### Child Mortality

- 10 million children under the age of 5 die every year
  - 98% of these deaths occur in developing countries
  - Number of children who die each year in developing countries is more than two times the number of children born each year in the US and Canada
  - 2/3 of deaths could be prevented today with available technology feasible for low income countries
- 40% of deaths in this age group occur in first month of life (neonatal period)
- 25% of deaths occur in childbirth and first week of life (perinatal period)



### Leading Causes of Mortality: Ages 0-4

- Developing world
  - Perinatal conditions
  - Lower respiratory infections
  - Diarrheal diseases
  - Malaria
- Developed world
  - Perinatal conditions
  - Congenital anomalies
  - Lower respiratory infections
  - Unintentional injuries



## 1. Perinatal Conditions

- Burden of Perinatal Conditions
- Common Perinatal Conditions
- Preventing Perinatal Mortality
  
- Maternal Morbidity and Mortality
- Obstetric Fistula

## Burden of Perinatal Conditions

- 2.5 million children each year die in perinatal period (birth through first week of life)
- Most perinatal deaths are a result of inadequate access to healthcare
  - Poor maternal health and nutrition
  - No health care during pregnancy and delivery
  - Low birth weight
- Many cultures...
  - Don't celebrate child's birth until weeks have passed
  - Mother and child isolated during this period
  - Can reduce incidence of infection
  - Can result in delays in seeking healthcare

## Common Perinatal Conditions

### 1) Infections

- Acquired during exposure to the maternal genital tract
- Acquired using non-sterile technique to cut the umbilical cord
- "ToRCHeS"

## Common Perinatal Conditions



### 2) Birth Asphyxia

- Baby does not breathe at birth
- Umbilical cord wrapped around baby's neck

### 3) Birth Trauma

- Mechanical forces in obstructed labor prevent descent through birth canal (e.g. cephalopelvic disproportion)
- Can result in intracranial hemorrhage, blunt trauma to internal organs, injury to spinal cord or peripheral nerves

## Preventing Perinatal Conditions

- No good screening tests to indicate who will need emergency care
  - All births should be attended by a skilled health care worker
- Fetal Ultrasound



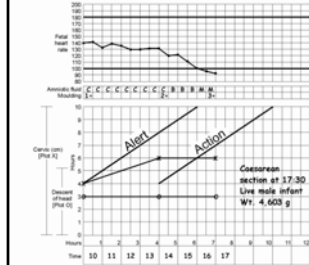
## Preventing Perinatal Conditions



## Preventing Perinatal Conditions

### Simple technologies

Name: Mrs. H      Gravidity: 4      Para: 3-0      Hospital number: 6639  
 Date of admission: 20.5.2000      Time of admission: 10:00 A.M.      Ruptured membranes: 1      hours



PATH Delivery Kit

Partograph

## Maternal Morbidity and Mortality

- >500,000 women die from complications due to childbirth
  - Severe bleeding
  - Infections
  - Hypertension (pre-eclampsia, eclampsia)
  - Unsafe abortions
  - Obstructed delivery
- 50 million women suffer from acute pregnancy-related conditions
  - Permanent incontinence, chronic pain, nerve and muscle damage, infertility

## Obstetric Fistula



view

<http://www.endfistula.org/index.htm>

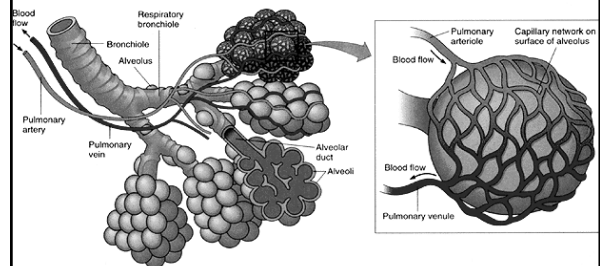
## 2. Lower Respiratory Infections

- Burden of LRIs
- Pathophysiology of Pneumonia
- Diagnosis of Pneumonia
  - Direct Fluorescence Assay
- Vaccines for Lower Respiratory Infections

## Burden of Lower Respiratory Infections

- One million children each year die from lower respiratory tract infections, mostly pneumonia
- Until 1936, was #1 cause of death in US
- Can be cured with antibiotics

## Pathophysiology of Pneumonia



## Pathophysiology of Pneumonia

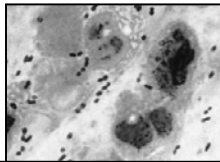
- Infection of the lungs
  - Multiple organisms cause pneumonia
- Bacterial Infection
  - Causes about 1/2 of all cases
  - *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and pertussis
  - Treated with antibiotics
- Viral Infection
  - Causes about 1/2 of all cases
  - Respiratory syncytial virus (RSV), influenza virus, parainfluenza virus, and measles
  - Usually resolve on their own
  - Serious cases: Use oxygen and antiviral drugs

## Pathophysiology of Pneumonia

- Newborns: acquire from maternal genital tract
- Older children: acquire from community
- Interferes with ability to oxygenate blood in lungs
- Symptoms:
  - Fever, cough, chest pain, breathlessness
  - Can be fatal

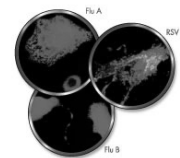
## Diagnosis of Pneumonia

- Chest X-ray
- Viral vs. Bacterial:
  - Complete blood count (CBC)
  - Sputum stain
  - Fluid from lungs
- Developing Countries:
  - Treat all pneumonias in children with antibiotics
  - Has reduced mortality
  - May encourage antibiotic resistance



## Direct Fluorescence Assay (DFA)

- Collect nasal secretions
- Spin down cells
- Place cells on slide
- Immerse in alcohol
- Apply solution containing antibodies which bind to viruses
- Antibodies are coupled to fluorescent dye
- Examine with fluorescence microscope



## Vaccines for Lower Respiratory Infections

- *Haemophilus influenzae* (Hib)
- *Streptococcus pneumoniae*
- Influenza virus

## 3. Diarrheal Disease

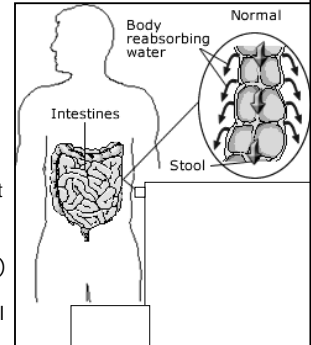
- Burden of Diarrheal Disease
- Normal Gastrointestinal Physiology
- Pathophysiology of Diarrhea
- Oral Rehydration Therapy
- Vaccines for Diarrhea

## Burden of Diarrheal Disease

- 2.2 million deaths per year
- Almost all of these deaths occur in children in developing countries
- Usually related to unsafe drinking water
- Less common in neonates

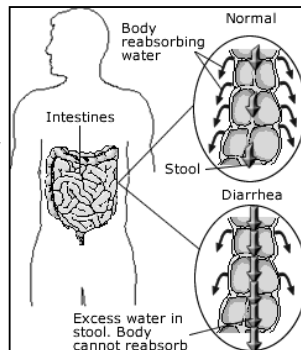
## Normal Gastrointestinal Physiology

- 8-9 L fluids enter the small intestine daily (1-2 L from dietary intake)
- Epithelial cells lining the GI tract actively reabsorb nutrients and salts; water follows by osmosis
- Small intestine absorbs most of this fluid, so only 1-1.5 L pass into colon
- Further water salvage (98%) in colon, with just 100-200 ml H<sub>2</sub>O/day excreted in stool



## Causes of Diarrhea

- Diarrhea = failure of fluid reabsorption
- Can rapidly lead to dehydration
- Loss of 10% of bodily fluids → death
- 4 types of diarrhea:
  - Osmotic
  - Secretory
  - Inflammatory
  - Motility



## Causes of Diarrhea

- 1) **Osmotic Diarrhea**  
Inadequate absorption of solutes
  - Ex: Lactose Intolerance, Ingestion of Sorbitol



- 2) **Secretory Diarrhea**  
Excess water secretion into the lumen
  - Ex: Cholera, *E. coli*



[www.vivo.colostate.edu/hbooks/pathphys](http://www.vivo.colostate.edu/hbooks/pathphys)

## Causes of Diarrhea

- 3) **Inflammatory Diarrhea**  
Usually caused by infection
  - Bacteria: *E. coli*, *Salmonella*
  - Viruses: Rotavirus, Norwalk
  - Protozoa: *Giardia*
- 4) **Motility Diarrhea**  
Accelerated GI transit time
  - Ex: Diabetes, nerve damage



[www.vivo.colostate.edu/hbooks/pathphys](http://www.vivo.colostate.edu/hbooks/pathphys)

## "Malnutrition is an Infectious Disease"

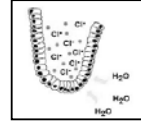


## Oral Rehydration Therapy

- 1 liter of water, 1 teaspoon of salt, 8 teaspoons of sugar
- Reduced mortality to diarrhea from 4.6 million deaths per year to 1.8 million deaths per year in 2000
- Developed in 1960s
- "The most significant medical advance of the century." *The Lancet*, 1978

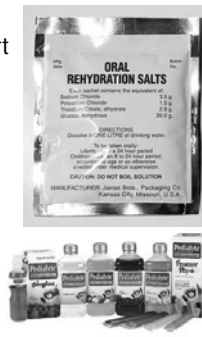
## How Does ORT Work?

- Epithelial cells which line colon are responsible for fluid reabsorption
  - They reabsorb osmotically active products of digestion, sodium
  - Water follows
- Toxins produced by bacteria bind to epithelial cells in gut and cause cells to secrete chloride and interfere with ability to absorb sodium → secretory diarrhea
- What if you give patients more water to drink?



## How Does ORT Work?

- Discovery in 1950s:
  - New method of sodium transport which depends on glucose, not affected by bacteria which produce diarrhea
- Hypothesis:
  - Provide glucose to increase sodium transport
- Packet of ORT: 10 cents
- ORT in the U.S.



## Vaccines to Prevent Diarrhea

- Rotavirus alone kills 600,000 children per year
- Found in every country, highly contagious
- Almost every child will have a rotavirus infection before age 3
- 1998: Rotashield approved by FDA
  - 80%-100% effective
  - Post-licensure surveillance: 1/12,000 fatal complication rate
  - Ethical Dilemma
- 2006: two new vaccines, safe and effective

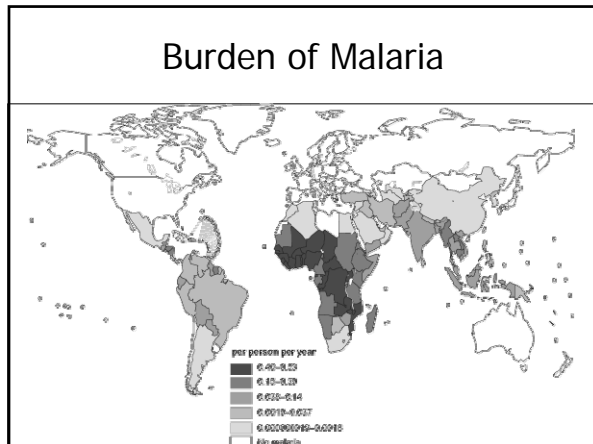
## 4. Malaria

- Burden of Malaria
- Malaria Pathogenesis
- Diagnosis of Malaria
- Preventing Malaria

## Burden of Malaria

- 40% of world's population live in malaria endemic countries
- 300 million cases of malaria per year
- African children average 1.6-5.4 episodes/yr
- 1-2 million children under the age of 5 die each year from malaria
- Pregnant women:
  - Increased susceptibility to malaria
  - Anemia can result in low birth weight babies





### Malaria Pathogenesis

- Mosquitos transmit parasite
- Parasites evade immune system
- Multiply inside liver cells
- Travel to blood, attach to red blood cells, consume hemoglobin
- Symptoms:
  - Fever, headache, vomiting, anemia
- Fatal disease:
  - Anemia: destruction of RBCs' O<sub>2</sub> carrying capacity
  - Cerebral malaria: Permanent neurologic damage

<http://sickle.bwh.harvard.edu>

### Diagnosis of Malaria

### Preventing Malaria

- Spread by *Anopheles* mosquito carrying a parasite
  - Mosquitoes only bite from dusk until dawn
- Reduced human/insect contact
  - Prevent mosquito breeding
  - Use insect repellents, mats, coils
  - Wear long sleeves/pants
  - Residual treatment of interior walls
  - Insecticide-treated mosquito bed nets
  - Treatment of those who have malaria prevent its spread!

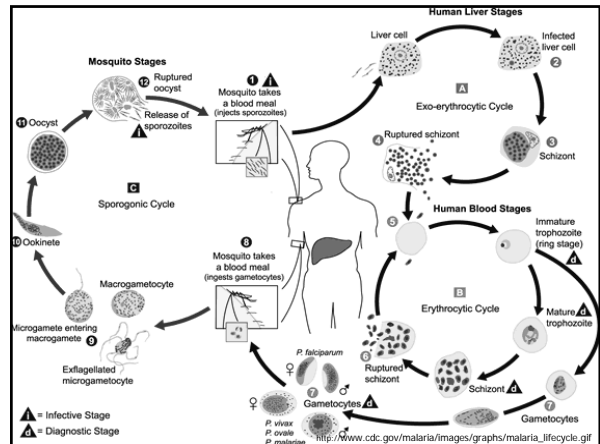
### Preventing Malaria

- Pregnant women and infants should sleep under insecticide treated nets
  - 25% reduction in low birth weight babies
  - 20% reduction in infant deaths
  - Cost: \$1.70 (Retreatment: 3-6 cents)

### Preventing Malaria

## Preventing Malaria

- Where is the malaria vaccine?
  - Funding
  - Thousands of antigens presented to the human immune system -> which ones are useful targets?
  - Plasmodium has many life stages -> different antigens at each stage
  - Plasmodium has several strategies to confuse, hide, and misdirect the human immune system
  - Multiple malaria infections of the different species and different strains of the same species may occur in one host!



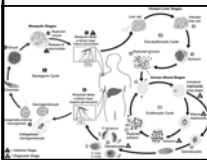
## A Malaria Vaccine Breakthrough??

### SANARIA

MALARIA ERADICATION THROUGH VACCINATION



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



[http://www.cdc.gov/malaria/images/graphs/malaria\\_lifecycle.gif](http://www.cdc.gov/malaria/images/graphs/malaria_lifecycle.gif)

## Leading Causes of Mortality: Ages 0-4

- 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

## 2. Congenital Anomalies

- Burden of Congenital Anomalies
- Common Congenital Anomalies

## Burden of Congenital Anomalies

- 2-3% of children are born with a birth defect
- 400,000 children die each year as a result
- Accounts for a higher fraction of childhood deaths in developed countries (16.9%) than in developing countries (4%)

## Common Congenital Anomalies

Cause	Classification	Example
Genetic	Chromosomal	Down syndrome
	Single gene	Cystic fibrosis
Environmental	Infectious disease	Congenital rubella syndrome
	Maternal nutritional deficiency—folic acid	Neural tube defects
Complex	Congenital malformations involving single organ system	Congenital heart disease

## 4. Unintentional Injuries

- Result in the deaths of:
  - 15,000 children per year in developed countries (4<sup>th</sup> leading cause of death)
  - 273,000 children per year in developing countries (9<sup>th</sup> leading cause of death)
- Causes:
  - Drownings (82,000 deaths)
  - Road traffic injuries (58,000 deaths)
- Covered in depth in *Lecture 3*

## Summary of Lecture Two

- 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