Introduction to Infectious Disease Epidemiology

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Section A

History of Infectious Diseases in the 20th Century
Crude Death Rate* for Infectious Diseases: U.S., 1906–’96

*Per 100,000 population per year


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*Per 100,000 population per year


### 10 Leading Causes of U.S. Deaths: 1900 and 1997

The 10 leading causes of death as a percentage of all deaths in the United States, 1900 and 1997

<table>
<thead>
<tr>
<th>1990</th>
<th>1997</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pneumonia</td>
<td>1. Heart Disease</td>
</tr>
<tr>
<td>2. Tuberculosis</td>
<td>2. Cancer</td>
</tr>
<tr>
<td>4. Heart Disease</td>
<td>4. Chronic Lung Disease</td>
</tr>
<tr>
<td>5. Stroke</td>
<td>5. Unintentional Injury</td>
</tr>
<tr>
<td>6. Liver Disease</td>
<td>6. Pneumonia &amp; Influenza</td>
</tr>
<tr>
<td>7. Injuries</td>
<td>7. Diabetes</td>
</tr>
<tr>
<td>8. Cancer</td>
<td>8. HIV Infection</td>
</tr>
<tr>
<td>9. Senility</td>
<td>9. Suicide</td>
</tr>
<tr>
<td>10. Diptheria</td>
<td>10. Chronic Liver Disease</td>
</tr>
</tbody>
</table>

# U.S. Death Rates for Common Infectious Diseases

Death Rates for Common Infectious Diseases in the United States in 1900, 1935, and 1970

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mortality rate per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1900</td>
</tr>
<tr>
<td>Influenza and pneumonia</td>
<td>202.2</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>194.4</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>142.7</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>40.3</td>
</tr>
<tr>
<td>Typhoid fever</td>
<td>31.3</td>
</tr>
<tr>
<td>Measles</td>
<td>13.3</td>
</tr>
<tr>
<td>Dysentery</td>
<td>12.0</td>
</tr>
<tr>
<td>Whooping cough</td>
<td>12.0</td>
</tr>
<tr>
<td>Scarlet fever (including streptococcal sore throat)</td>
<td>9.6</td>
</tr>
<tr>
<td>Meningococcal infections</td>
<td>6.8</td>
</tr>
</tbody>
</table>
It is frequently assumed that the identification of the causative organisms and the development of vaccines and antibiotics are the reasons that mortality has changed, but this is not quite true for most infectious diseases.
“Because infectious diseases have been largely controlled in the United States, we can now close the book on infectious diseases.”

— William Stewart, MD
U.S. Surgeon General, 1967
Some Recent Epidemics of Emerging Infectious Diseases

- Lassa Fever (Nigeria) 1976
- Legionnaire’s Disease 1976
- Ebola Virus 1976-Present
- Toxic Shock Syndrome 1981-Present
- AIDS 1981-Present
- Hemorrhagic Enteritis, E. Coli 0157:H7 1983-Present
- Sin Nombre Virus 1993-Present
- West Nile Virus (USA) 1999-Present
- Anthrax, SARS 2001
- Monkey Pox 2003
- Influenza, H5/N1 1999-2005
Trends in Deaths Caused by Infectious Diseases

United States, 1980–1992

Multiple cause of death

Underlying cause of death

National Center for Health Statistics underlying and multiple cause-of-death data
Trends in Deaths Caused by Infectious Diseases, by Age

- United States, 1980–1992, by age group

National Center for Health Statistics underlying and multiple cause-of-death data
Death Trends Caused by Infectious Disease Syndromes

United States, 1980–1992

National Center for Health Statistics underlying and multiple cause-of-death data
Section B

Newly Emerging Infections
Trends in Death Rates from Leading Causes, Ages 25–44


Adapted from National Center for Health Statistics
National Vital Statistics System

*Preliminary 1998 data
Some Emerging AIDS-Related Infectious Diseases

1. *Pneumocystis carinii* pneumonia
2. Tuberculosis
3. Mycobacterium-avium complex
4. Kaposi’s sarcoma (HHV-8)
5. HSV-2
6. Cryptosporidium
7. Microsporidium
8. *Cryptococcus neoformans*
9. *Penicillium marneffei*
10. Disseminated salmonella
11. Bacillary angiomatosis (*Bartonella henselae*)
12. HPV
Some Emerging Non-AIDS-Related Infectious Diseases

1. SARS
2. West Nile disease
3. Variant CJD disease
4. Monkey pox
5. Ebola and Marburg viruses
6. Dengue
7. Influenza H5/N1 (?)
8. Hanta virus
9. *E. Coli* O157:H7
10. Antibiotic-resistant
    - Pneumococci
    - *Staph-aureus*
    - Gonococci
    - Salmonella
11. Cryptosporidium
12. Anthrax
The 8500 cases and 850 deaths worldwide were related to 1 case. A physician from southern China who checked into a hotel in Hong Kong was ill with pneumonia and infected 13 other people, probably through airborne transmission.

The 13 infected persons were on their way to other countries and introduced the epidemic to others upon arrival at their destinations.
- Canada
- United States
- Ireland
- Thailand
- Singapore
- Vietnam
SARS Epidemic Curve in Hong Kong, 2003
Epidemic Curve for Beijing SARS Outbreak and Timeline of Major Control Measures (March 5 to May 29, 2003)

22 Universities and 2610 schools closed
Fever checks at airports begin, Quarantine of close contacts
Outbreak announced publicly by government
HCW training in PPE and Management of patients with SARS
Joint SARS group formed, Fever clinics open
SARS made reportable, Contact tracing begins
Libraries, bars, theaters closed
Start to group patients with SARS in designated wards
New 1000-bed SARS hospital opens
MOH infection control guidelines
66 designated fever clinics
All patients with SARS in designated hospitals

Adapted by CTLT from Pang, X. et al. JAMA 2003;290:3215-3221.
Factors Leading to Emergence of Infectious Diseases

- AIDS
- Population growth
- Speed and ease of travel
- Dam building
- Global climate change
- Increased antibiotic use for humans and animals
- Encroachment of human populations on forest habitats

- Industrial commercial agriculture
- War and social disruption
- Relocation of animals
- Growth of daycare
- Aging of the population
- Human-animal contact
# Emerging Infectious Diseases Related to Direct Contact between Humans and Animals

<table>
<thead>
<tr>
<th>Disease</th>
<th>Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. HIV-1, LHIV-2</td>
<td>Primates (Africa)</td>
</tr>
<tr>
<td>2. Influenza</td>
<td>Water fowl, pigs, chickens (N5/N1)</td>
</tr>
<tr>
<td>3. Ebola</td>
<td>Primates (“bush meat”)</td>
</tr>
<tr>
<td>4. Marburg</td>
<td>Primate (“bush meat”)</td>
</tr>
<tr>
<td>5. Hanta virus</td>
<td>Deer mouse</td>
</tr>
<tr>
<td>6. Arena virus</td>
<td>Various rodents</td>
</tr>
<tr>
<td>7. Variant CJD</td>
<td>Cattle</td>
</tr>
<tr>
<td>8. Cryptosporidia</td>
<td>Cattle</td>
</tr>
<tr>
<td>9. Hendra virus</td>
<td>Fruit bats</td>
</tr>
<tr>
<td>10. Nipah virus</td>
<td>Pigs, fruit bats</td>
</tr>
<tr>
<td>11. SARS</td>
<td>Civet cats</td>
</tr>
<tr>
<td>12. Monkey pox</td>
<td>Prairie dogs</td>
</tr>
</tbody>
</table>
Over the last 150 years, there have been many global changes that have enhanced the probability of the emergence of new infectious diseases of humans and animals. This chart depicts three examples of such trends: the increase in the human population, the increased construction of large dams (over 75 meters high) built in the U.S. (1890–1975), and the decrease in time needed to circle the globe.
Cryptosporidium Infection in Milwaukee, 1993

- Reported date of the onset of illness in cases of laboratory-confirmed or clinically defined cryptosporidium infection—March 1 through April 15, 1993

Note: The clinically defined cases were identified during a telephone survey begun on April 9 of residents in the area served by Milwaukee Water Works.
Maximal turbidity of treated water in southern water-treatment plants of the Milwaukee Water Works, March 2 through April 28, 1993

*NTU = nephelometric turbidity units
Public Health Burden of Foodborne Disease

- Each year an estimated 76 million cases
  - One in four Americans gets a foodborne illness each year
  - One in 1,000 Americans is hospitalized each year
  - $6.5 billion in medical and other costs
- 3.5 million cases, 33,000 hospitalizations, and 1,600 deaths are caused by the pathogens:
  - Salmonella
  - *E. Coli* O157 and other STEC
  - *Campylobacter*
  - *Listeria*
  - *Toxoplasma*
Free radical oxidants damage DNA of microbes
Nothing becomes radioactive
At doses up to 7.5 kiloGray, minimal change on taste, texture, nutritional value
Shelf life in general is prolonged (because spoilage organisms are reduced)
Effective in meats, poultry, grains, produce
Exceptions include:
  - Sprout seeds may not sprout well if irradiated
  - Oysters die if irradiated, which shortens shelf life
  - Egg whites go milky and liquid
  - Grapefruit gets mushy
<table>
<thead>
<tr>
<th>Year</th>
<th>Food</th>
<th>Dose (kGy)</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1963</td>
<td>Wheat flour</td>
<td>0.2–0.5</td>
<td>Mold control</td>
</tr>
<tr>
<td>1964</td>
<td>White potatoes</td>
<td>0.05–0.15</td>
<td>Inhibit sprouting</td>
</tr>
<tr>
<td>1986</td>
<td>Pork</td>
<td>0.3–1.0</td>
<td>Trichinosis</td>
</tr>
<tr>
<td>1986</td>
<td>Fruit and vegetables</td>
<td>1.0</td>
<td>Shelf life and insect control</td>
</tr>
<tr>
<td>1986</td>
<td>Herbs and spices</td>
<td>30</td>
<td>Sterilization</td>
</tr>
<tr>
<td>1990 (FDA)</td>
<td>Poultry</td>
<td>3.0</td>
<td>Bacterial pathogen reduction</td>
</tr>
<tr>
<td>1992 (USDA)</td>
<td>Poultry</td>
<td>1.5–4.5</td>
<td>Bacterial pathogen reduction</td>
</tr>
<tr>
<td>1997 (FDA)</td>
<td>Fresh meat</td>
<td>4.5</td>
<td>Bacterial pathogen reduction</td>
</tr>
<tr>
<td>2000 (USDA)</td>
<td>Fresh meat</td>
<td>4.5</td>
<td>Bacterial pathogen reduction</td>
</tr>
</tbody>
</table>
Number of Outbreak-Related Cases of *Escherichia coli*

- Number of outbreak-related cases of *Escherichia coli* O157:H7 Reported to the CDC

![Bar chart showing the number of outbreaks and outbreak-related cases reported to the CDC from 1982 to 1994.](chart.png)
### E. Coli Outbreaks Reported to CDC, 1982–1994

Outbreaks of *Escherichia coli* O157:H7 Reported to the Centers for Disease Control and Prevention from 1982 to 1994 Inclusive*

<table>
<thead>
<tr>
<th>Likely vehicle or mode of spread</th>
<th>No. of outbreaks</th>
<th>No. of individuals involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>All foods†</td>
<td>38</td>
<td>1,541</td>
</tr>
<tr>
<td>Ground beef †</td>
<td>22</td>
<td>1,137</td>
</tr>
<tr>
<td>All beef products and milk †</td>
<td>26</td>
<td>1,278</td>
</tr>
<tr>
<td>Drinking water– or swimming-associated</td>
<td>3</td>
<td>276</td>
</tr>
<tr>
<td>Person-to-person (no food identified)</td>
<td>9</td>
<td>243</td>
</tr>
<tr>
<td>Unknown</td>
<td>19</td>
<td>274</td>
</tr>
<tr>
<td>All outbreaks</td>
<td>69</td>
<td>2,334</td>
</tr>
</tbody>
</table>

*Source: CDC surveillance data. Note: data from 1982–1992 are incomplete: outbreaks without clear sources or sites were not tallied by the CDC †Some of these outbreaks also involved person-to-person spread
Reservoirs and Modes of Transmission of *Escherichia coli* O157:H7

- **Bovine Reservoir**
  - Direct Transmission: Milk
  - Fecal Contamination: Meat (especially ground beef)
  - Foodborne Transmission: Humans

- **Meat (especially ground beef)**
  - Cross Contamination: Other Foods
  - Foodborne Transmission: Humans

- **Humans**
  - Person-to-Person Spread: Secondary Human Cases

- **Other Foods**
  - Fecal Contamination: Bovine Reservoir

- **Milk**
  - Direct Transmission: Bovine Reservoir

- **Secondary Human Cases**
  - Foodborne Transmission: Humans

- **Questionable Ovine or Other Animal Reservoir**
Section C

International Infectious Diseases
Climate change can have a major impact on the distribution of infectious disease vectors like mosquitoes.
Data collected by Oak Ridge National Laboratory and published in *Trends ‘93: A Compendium of Data on Global Change* shows an overall increase in global carbon dioxide emissions from fossil fuels.
Aedes aegypti (Mosquito) Is Vector for Yellow Fever

Aedes aegypti control was successfully undertaken for many years until it was discovered that yellow fever has a sylvatic cycle. That is, in addition to humans, yellow fever also infects other primates in the jungle. It was therefore decided that this was a futile effort because yellow fever would persist despite elimination of Aedes aegypti in urban areas.

Source: WHO and PAHO
Dengue and dengue hemorrhagic fever (DHF) are also spread by Aedes aegypti. Prior to 1981, there were no cases in the Western Hemisphere. After the Aedes aegypti eradication program was stopped, the mosquito reestablished itself and dengue and DHF became a major health problem throughout Latin America.
Leading Causes of Death

- 53.9 million from all causes worldwide, 1998

![Pie chart showing leading causes of death]

- Cardiovascular diseases: 31%
- Infectious diseases: 25%
- Injuries: 11%
- Cancers: 13%
- Maternal: 5%
- Other: 6%
- Respiratory and digestive: 9%

Note: Cancers, cardiovascular and respiratory/digestive deaths can also be caused by infections and raise the percentage of deaths due to infectious diseases even more.
Leading Infectious Killers

 Millions of deaths, worldwide, all ages, 1998

- Acute respiratory infections (including pneumonia and influenza)
- AIDS
- Diarrheal diseases
- TB
- Malaria
- Measles

Death in Millions

Adapted from WHO, 1999
Large Outbreaks

Selected Outbreaks of More than 10,000 Cases, 1970-1990

- **Hepatitis C**: was first identified in North America in 1989. There may now be as many as 170 million infectious carriers of the disease worldwide.

- **Rift Valley Fever**: infected 200,000 people and caused 600 deaths in Egypt in 1977.

- **Visceral Leishmaniasis**: caused 100,000 deaths in the western upper Nile of Southern Sudan in 1985-87.

- **Diphtheria**: Since 1993, diphtheria cases have skyrocketed in the Russian Federation and Newly Independent States. Over 50,000 cases were reported in 1995.

- **Hepatitis A**: 300,000 cases were reported in an outbreak in Shanghai in 1989.

- **Dengue Fever**: One out of five people in New Delhi, India became sick with this disease during a 1982 outbreak.

- **Cholera**: An outbreak of cholera in Latin America infected over 500,000 people in 1991.

- **Meningitis**: An outbreak in Sao Paulo in 1974 caused 30,000 cases. There were 187,000 cases in an outbreak in Africa in 1996.

- **Typhus**: 100,000 cases emerged in Burundi between 1996 and 1998.

- **Anthrax**: In Zimbabwe over 10,000 people became sick during the largest outbreak of anthrax ever reported in the 1970s.

Adapted from World Health Organization, 1999.
**Possible Bioterrorism Agents**

**Bacteria**

*Bacillus anthracis* (anthrax)
*Vibrio cholera* (cholera)
*Yersinia pestis* (plague)
*Francisella tularensis* (tularemia)
*Coxiella burnetii* (Q fever)

**Viruses**

Variola (small pox)
Venezuelan equine encephalomyelitis
Hemorrhagic fever viruses (e.g., Ebola, sin nombre, Hantaan)

**Toxins**

Botulinum
Staphylococcal enterotoxin B
Ricin
T-2 mycotoxins

Section D

Epidemiologic Principles and Classifications of Infectious Diseases
Microbiological Classification of Diseases

1. Bacterial diseases
2. Viral diseases
3. Fungal diseases
4. Parasitic diseases
Classification of Microorganisms

Viruses
- RNA–DNA
  - RNA viruses genetically unstable
- Lipid enveloped–nonenveloped
  - Solvent-detergent treatments virucidal only for enveloped viruses

Bacteria
- Gram-positive–gram-negative
  - Antibiotic sensitivity differs
- Diagnostic and therapeutic uses of gram-negative capsule

Fungi
- Disseminated vs. superficial
- Mold vs. biphasic

Parasites
- Complete cycle
- Larval migrans

Prions
- Pathogenesis unclear
- Resistant to disinfection
A Clinician’s View

- Diseases classified according to signs and symptoms
  1. Diarrheal diseases
  2. Respiratory diseases
  3. Cutaneous/soft tissue infection
  4. CNS diseases
  5. Septicemic diseases
  6. Fever of undetermined origin
Means of Spread of Infectious Diseases

Contact
- Direct
- Indirect
  - Fomites
  - Body secretions (blood, urine, saliva, etc.)

Vector

Airborne
- Small-particle aerosol

Food and/or water
Some Infectious Diseases Spread by Contact

1. Sexually transmitted diseases
   - Syphilis, gonorrhea, chlamydia, AIDS
2. Staphylococcal infections
3. Streptococcal infections
4. Many nosocomial infections
5. Rhinovirus colds
6. Brucellosis (slaughter house contact)
7. Hepatitis B virus infection
Some Important Food- and Waterborne Infections

1. Salmonellosis
2. Campylobacter
3. Shigellosis
4. Clostridium perfringens food poisoning
5. Staphylococcal enterotoxin food poisoning
6. Cholera
7. Giardiasis
8. Listeriosi
Some Important Airborne Infections

1. Tuberculosis
2. Influenza
3. Childhood Infections
   - Measles, mumps, rubella, pertussis
4. Parainfluenza
5. RSV
6. Legionella
Measles Transmission

Duration of pediatricians office visit by index (white bar) and secondary (gold bars) measles cases
Some Important Vectorborne Infections

1. Malaria
2. Viral encephalitis
   - SLE, WEE, EE, VE, California virus
3. Schistosomiasis
4. Tularemia
5. Dengue
6. Yellow fever
7. Rocky Mountain spotted fever
8. Leishmaniasis
9. Trypanosomiasis
Summer Infection Chains for Western Equine Encephalitis

Reservoirs of Infectious Diseases

1. Human
2. Animal (zoonoses)
3. Soil
4. Water
Some Infectious Diseases with a Human Reservoir

1. AIDS (HIV infection)
2. Syphilis
3. Gonorrhea
4. Shigellosis
5. Typhoid fever
6. Hepatitis-B virus
7. Herpes simplex virus
Some Diseases with an Animal Reservoir (Zoonoses)

1. Nontyphoidal salmonellosis
2. Brucellosis
3. Anthrax
4. Listeriosis
5. Viral encephalitis (SLE, WEE, CEE)
6. Rabies
7. Plague
Some Important Diseases with a Soil Reservoir

1. Histoplasmosis
2. Coccidioidomycosis
3. Blastomycosis
4. Tetanus
5. Botulism
Some Infectious Diseases with a Water Reservoir

1. *Pseudomonas* infections
   - Sepsis, UTI, “hot tub” folliculitis
2. Legionnaires’ disease
3. Melioidosis
Infectious Agents: 3 Important Epidemiologic Properties

1. Infectivity
   - The propensity for transmission
   - Measured by the **secondary attack rate** in a household, school, etc.

2. Pathogenicity
   - The propensity for an agent to cause disease or clinical symptoms
   - Measured by the **apparent : inapparent infection ratio**

3. Virulence
   - The propensity for an agent to cause severe disease
   - Measured by the **case fatality ratio**
Definitions of Some Relevant Terms

- Incubation period
  - The period between exposure to the agent and onset of infection (with symptoms or signs of infection)
- Secondary attack rates
  - The rates of infection among exposed susceptibles after exposure to an index case, such as in a household or school
Persistent infection
- A chronic infection with continued low-grade survival and multiplication of the agent

Latent infection
- An infection with no active multiplication of the agent, as when viral nucleic acid is integrated into the nucleus of a cell as a provirus. In contrast to a persistent infection, only the genetic message is present in the host, not viable organisms.
Definitions of Some Relevant Terms (cont.)

- Inapparent (or subclinical infection)
  - An infection with no clinical symptoms, usually diagnosed by serological (antibody) response or culture

- Immunity
  - The capacity of a person when exposed to an infectious agent to remain free of infection or clinical illness

- Herd immunity
  - The immunity of a group or community. The resistance of a group to invasion and spread of an infectious agent, based upon the resistance to infection of a high proportion of individual members of the group. The resistance is a product of the number of susceptibles and the probability that those who are susceptible will come into contact with an infected person.
Estimated Number of Cancer Cases (In Thousands) in Developed and Developing Countries, 1990

Note: A greater proportion of infection-related cancers occur in developing countries. Additional cancers of the colon, bladder, lung, and other organs may be directly attributable to infection, but no precise number can be quantified.