Humans have always been interested in infectious diseases even before they knew their cause. In this course we will examine the development of the Germ Theory of Disease and the impact that discovery has had on human health.
Human population growth over the millennia
Life expectancy for males and females

Life expectancy at birth for both sexes has increased dramatically in the last century, but since 1900—when, because of the high rate of deaths from childbirth, male life expectancy actually exceeded that of females—there has been an ever widening divergence, peaking in 1979 at 7.8 years.
Causes of Death, 1900-1984

- Influenza and pneumonia
- Tuberculosis, all forms
- Gastroenteritis
- Diseases of heart
- Vascular lesions of central nervous system (stroke)
- Chronic nephritis
- All accidents
- Malignant neoplasms (cancer)
- Certain diseases of early infancy
- Diphtheria

Deaths per 100,000 population in 1900

- Diseases of heart
- Malignant neoplasms (cancer)
- Vascular lesions of central nervous system (stroke)
- All accidents
- Influenza and pneumonia
- Diabetes
- Cirrhosis of liver
- Suicide
- Atherosclerosis
- Homicide

Deaths per 100,000 population in 1984
A decreasing proportion of deaths occur among the very young.
Increasing life expectancy.

A decreasing proportion among older persons.

Illinois - 1860 to 1939.

Under 5 years of Age:
- 1860: 51% (4 crosses)
- 1880: 44% (4 crosses)
- 1900: 30% (3 crosses)
- 1920: 20% (2 crosses)
- 1939: 7% (7 crosses)

50 Years of Age and Over:
- 1860: 12% (1 cross)
- 1880: 20% (2 crosses)
- 1900: 30% (3 crosses)
- 1920: 45% (4 crosses)
- 1939: 67% (6 crosses)

Each symbol represents 10% of the deaths occurring at all ages.
Again, more data comparing 1900 with 2000

- **1900**
  - Influenza and pneumonia
  - Tuberculosis
  - Gastroenteritis
  - Heart disease
  - Stroke
  - Kidney disease
  - Accidents
  - Cancer
  - Infant diseases
  - Diphtheria

- **2000**
  - Heart disease
  - Cancer
  - Stroke
  - Pulmonary disease
  - Accidents
  - Influenza and pneumonia
  - Diabetes
  - AIDS
  - Suicide
  - Cirrhosis of the liver
  - Homicide

Deaths per 100,000 population
“The Triumph of Death”; Depictions of plague or ‘The Black Death’ from the mid-sixteenth century.
Girolamo Fracastoro

- Fracastoro, a careful observer of disease transmission
  - obvious that some diseases were the same regardless of patient
  - specific diseases passed person to person had same symptoms
- “On Contagion”, 1546
  - mentions “seminaria” or seeds of disease.
  - before microbial world
- Three general patterns:
  - Direct contact only
  - Fomes (fomites)
  - At a distance

Fracastoro’s “Incurable Wound” on rabies, humans not the only ones, but they always die
Anton van Leeuwenhoek and his microscope (1632-1723)
Recipe for making mice

J.B. van Helmont ~ 1620 AD

“If a dirty undergarment is squeezed into the mouth of a vessel containing wheat, within a few days (say 21) a ferment drained from the garments and transformed by the smell of the grain, encrusts the wheat itself with its own skin and turns it into mice. And what is more remarkable, the mice from the grain and undergarments are neither weanlings or sucklings nor premature but they jump out fully formed.”
6. Pasteur’s Experiment with the Swan-necked Flask

Nonsterile liquid poured into flask

Dust and microorganisms trapped in bend

(a) Liquid cooled slowly
(b) Flask tipped so sterile liquid contacts microorganism-laden dust

Neck of flask drawn out in flame

Open end

Long Time

Air forced out open end

Liquid sterilized by heating

(a) Liquid remains sterile for many years

(b) Microorganisms grow in liquid
Fermentation

- Sugar metabolism:
  - with $O_2 = CO_2 + \text{water}$
  - W/O $O_2 = \text{organic acids or alcohol}$
  - was considered a chemical process due to unstable molecules
  - The “ferment”
  - Schwann, yeast = Etoh
  - L. Pasteur took up the work
    - fermentation, a living process
    - Saved the French wine industry
    - “Pasteurization”
Henle’s Views

• If diseased wines were due to living organisms, then…what about disease in humans? (referring to Pasteur’s work)

• The cause of disease must be the seed of the disease or the “germ” (disease germinator, from the idea of biogenesis)

• Needed to isolate into pure culture the seeds or germs of disease—but he stated that he did not know how this could be done
Ignaz Semmelweis, 1850

- Hospital administrator in Vienna
  - Problem of Puerperal Fever, child-bed fever
  - Used hospital records
  - Two obstetric clinics
    - One for MDs, the other a midwife clinic
    - 4X as many deaths in the Drs clinic
  - Role of dissection and teaching in Drs clinic
  - Washing with chloride of lime
    - Major drop in deaths
    - The fallout!!

Dr. , Wash your hands!
Decreases in child-bed fever mortality
Putrefaction and Microorganisms

- The link between the growth of microorganisms and decay was known, but the work of Semmelweis underscored the relationship with regard to child-bed fever, but not until much later

- If micro-organisms caused putrefaction and putrefaction caused child-bed fever---
  - now we know that hemolytic *Streptococcus* sp cause puerperal fever, can still be a problem
  - the key was fermentation and putrefaction were caused by living organisms
Setting the stage

- Davaine’s work on Anthrax
- Ferdinand Cohn’s work on Endospores
Other discoveries:

The Bacillus endospore

- Henle, 1840—a professor of medicine in Berlin.
- “the contagium was the "germ" or seed of disease
- If sick wines were due to bacteria contamination, why could not bacteria also cause sickness in humans?
- But admitted he could not prove this…
- Dasimir Davaine’s work on Bacillus anthracis
- Problems with his work
- Ferdinand Cohn discovers the endospore
- The stage was set for Robert Koch
Robert Koch, 1881

- Work on Anthrax
  - experiments with mice
  - 20 different mice
  - all died the same way
  - natural history of anthrax
  - “in a cow’s eye”
  - potatoes and pure cultures
  - the definitive proof, anthrax was caused by *Bacillus anthracis*
The basics of Koch’s work

- (a) Demonstration of the suspected agent in every case of the disease.
- (b) Isolation and cultivation of the suspected agent in pure culture.
- (c) Inoculation of the pure culture into healthy normal animals, resulting in a typical form of the disease.
- (d) Demonstration and recovery of the same suspected agent from the experimentally inoculated animals.

Bacillus anthracis
Formally, these are the four postulates:

Within 20 years the agents of all major bacterial diseases were discovered.
Contagion ➔ Microbes ➔ Biogenesis

Fermentation ➔ Putrefaction

Specific bacteria ➔ Pure Cultures

Koch’s Postulates ➔ Germ Theory of Disease
Figure 19-8  Three forms of anthrax that might be contracted by exposure to infected animal products.
Cutaneous Anthrax lesions

Early skin lesion, on neck (hide porters)

Central area of necrosis (eschar) slow to heal

Wrist & hand lesions common in butchers

Patient worked in a paint-brush factory
Hemorrhagic monkey brain after experimental inhalation of anthrax spores