The Struggle with Infectious Disease

Lecture 3
Cholera
Cholera in London

• 1854 Outbreak of Asiatic Cholera in major cities in England
  – Outbreak had started in 1831 but killed more than 12,000 in specific areas of the city
  – Southwark and Lambeth were particularly affected, smaller outbreak in Soho
  – In 3 days 127 people living around Broad Street died
  – Only those who could not afford to stayed
  – Death toll in this small area reach 500.
Cholera in London
Cholera in London
London, 1854

- Dr John Snow, 1854 London England
  - Physician who lived near the neighbourhood
  - Had published a pamphlet in 1849 suggesting that “Cholera Poison” reproduced in the human body and was transmitted through contamination of food and water
  - Opposed ridiculed and ignored by the establishment
  - Current theory was “miasma in the atmosphere”
London, 1854
London, 1854

[Map showing pump sites and deaths from cholera in London, 1854]
London, 1854

- By removing the handle from the pump deaths in that neighbourhood stopped

- Two suppliers of water to London
Spread of Disease

• From ancient times usual belief was that disease was either
  – “Act of God”
  – Spread through the air
    • Miasma Theory
Spread of Disease

• The earliest written record suggesting that invisible living things might cause illness came from the Roman writer Marcus Terentius Varro. In the first century A.D. he wrote:

— "Care should be taken where there are swamps in the neighborhood, because certain tiny creatures which cannot be seen by the eyes breed there. These float through the air and enter the body by the mouth and nose and cause serious disease."

—

Read more: http://www.scienceclarified.com/scitech/Bacteria-and-Viruses/Early-Discoveries.html#ixzz2CmjdPWcM
Spread of Disease

• Girolamo Fracastro (1564):
  – *epidemic diseases ‘were transmitted by seed-like entities that transmitted infection by direct or indirect contact or even over long distances’*

• *Spontaneous Generation Theory* was more popular at the time.
Spontaneous Generation

• Most clearly recorded by Aristotle
  – Representing preceding and then current views

• Small living organisms could arise from inanimate objects
  – Ticks could arise from dust
  – Maggots could arise from dead flesh

• Disproved in 1668 by Francesco Redi
Redi’s Experiment

• Three bottles with raw meat
  – One uncovered
  – One Covered with gauze
  – One corked
Gauze on Top
Maggots found on top of gauze, none survived

Open Top
Flies entered, maggots formed on meat

Sealed top
No maggots
Redi’s Experiment

- Redi also followed maggots and determined the metamorphosed into flies
- Results were not accepted
Spread of Disease

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Microorganisms

• Anton van Leeuwenhoek invented the microscope in 1668
• He described and estimated quantities of microorganisms in water
• Reported his work to Royal Society of London in 1676
Microorganisms

- Observations were initially ridiculed.
- 1680 he convinced the Royal Society to send a delegation to determine if others could replicate his observations
Miasma Theory

• His observations were not taken up and were replaced by the more “logical” miasma theory:
  – From the Greek for pollution; noxious, bad air
  – Emanating from rotting organic matter
  – Poisonous gas or mist
  – Due to environmental factors
  – Not passed from individual to individual
Robert Koch

- Developed the criteria for determining if a microorganism was a *causative agent*
- 1870’s, worked with anthrax derived from dead sheep.
  - Extracted the material
  - Cultured the material
  - Injected the cultured material into mice
  - The mice contracted anthrax
Robert Koch

• Koch studied 30 generations of mice before publishing his results

• He developed external culture media (agar)
  – Easier to work with than liquid culture

• His assistant was Julius Richard Petri
Implications of Theory

• Disease has a specific cause
• Disease can be transmitted from person to person
• It is possible to eliminate the cause of a disease
  – One does not have to move to avoid it
• It is possible to protect against acquiring a disease
Infectious Agents

- **Four primary types:**
  - **Virus**
    - Smallpox, influenza
  - **Bacteria**
    - Tuberculosis, cholera
  - **Parasite**
    - Plague, malaria
  - **Prion**
    - CJD, Kuru
Louis Pasteur

- Discovered, together with Koch much of foundations of microbiology
- Pasteur was largely responsible for popularization of the concept
- 1860-1864 described the pathology of *puerperal fever* and suggested boric acid to kill the micro-organisms
  - Had been applied in Vienna in 1846 by Ignaz Semmelweis
Louis Pasteur

- Developed vaccines (attenuated live bacterial) against chicken cholera and then rabies
- Awarded a patent for anthrax vaccine before he had actually demonstrated that it worked
  - Lab books indicate he had used another method to create original vaccine, but that method had already been published by Toussaint
Cholera

- Cholera is a bacterial infection caused by *Vibrio Cholerae*
- Fecal contaminated water or sometimes shellfish
- Results in diarrhea and vomiting of clear liquid
- Symptoms appear rapidly within 1 to 5 days
- Fluid loss in untreated patients can be 10 -20 litres per day, resulting in death
- Death rate between 25% and 40% when untreated
Cholera

• Bacteria has three distinct stages in response to local environment
  – Survival mode through the stomach (most are killed)
  – Flagellate stage (corkscrew) to propel the bacteria through the mucus to the wall of the small intestine
  – Toxin production stage results in secretion of H₂O, Na⁺, K⁺, Cl⁻, HCO₃⁻ and rapid dehydration
Cholea

- Severe cases can result in fluid loss of 5-7 lites in a 2 hour period
- Can result in death within hours
Cholera

• Treatment with rehydration (oral or IV)
• Basic antibiotics are generally effective (doxycycline)
• Antibiotic resistance is developing (Bangladesh)
• Estimated to affect 3-5 million people worldwide (2010) ~130,000 deaths
• Perhaps as many as 3 million per year in 1980
Cholera

- Prevalent (endemic) in Ganges delta since recorded history
- Spread along trade routes to Russia (1817 then Europe and North/South America
- Seven cholera pandemics in the past 200 years
  - First in Bengal, India 1817 – 1824
  - Last in Indonesia in 1961
- Interesting case of evolution in India/Pakistan
Cholera Vaccine

• The first Cholera vaccine was developed by Jaime Ferran (Spain) 1885.
  – Attenuated whole cell vaccine after methods of Pasteur
  – Results were downplayed by French Academia, but eventually accepted
• Replaced by oral vaccine. Both show ~65% efficacy
Cholera

• Disappeared from prominence in many countries due to water filtration and chlorination
• Endemic in many more countries
• May re-appear due to breakdown of infrastructure or occasional carelessness
Haiti

- January 2010 earthquake
- Cholera appeared late 2010
- Some cases were so severe individuals died within several hours of symptom onset
- “most likely source of outbreak: UN workers from Nepal (where cholera is widespread)
- Exact strain match (derivative form Indonesian pandemic)
Haiti

- 650,000 cases almost 8000 deaths
- UN program to irradiate Cholera from Haiti (which had been Cholera free)
- Costed at $2.2 billion

- Recent case in Cuba due to contaminated food
  - Aggressive response
  - Rapid containment (700 cases, 3 deaths)
Typhoid

- Typhoid is caused by the *salmonella typhi* bacteria
- Unique as the only known *salmonella* bacteria with only human host
- Spread through food contaminated by feces or urine
- Enters body through small intestine
- Mortality ~16% untreated 1% treated with antibiotics
Typhoid

• Typically lasts four weeks (untreated)
  – Fever rises throughout the first week
  – Plateaus at ~40° during the second week with delirium and irregular pulse, enlarged liver and spleen
  – Complication in third week include: intestinal hemorrhage or perforation, neuropsychiatric symptoms, dehydration and delirium with high fever
  – Fever subsides during fourth week
Interesting Facts

• Approximately 5% who contract the disease become asymptomatic carriers who continue to carry (and shed) the bacteria after recovery
  – Marry Mallon

• Cystic fibrosis may confer protection against typhoid due to changes in the small intestine (may also be true for Cholera)
Typhoid

• Once transmission mechanism was understood (late 1800’s)
• Quarantine was used to control spread (Mary Mallon was quarantined for 26 years 1907)
• First vaccine 1896 in US in 1909 entire army was vaccinated
Typhoid

• Water treatment has effectively eliminated the disease in developed countries

• Vaccines are not currently used in Canada

• Oral and injectable vaccines are available