Seminar 4

Bugs on the Move

Carleton Learning in Retirement
What’s Bugging You?
Daniel Burnside
Epidemiology
Epidemiology and Public Health

• Epidemiology is the study of the distribution and cause of disease in populations
• It serves as the foundation and logic of interventions needed in the interest of public health and preventive medicine
• How many people are affected, where, the outcome of the disease (recovery, death, disability, and so on)
Epidemiology a Better Definition

• Epidemiology is the study of the patterns, causes, and effects of health and in defined populations.
John Snow
The Founder of Modern Epidemiology
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The Founder of Modern Epidemiology

- Early pioneer of anesthetic use in medical procedures – gave Queen Victoria chloroform Queen Victoria in the 1850s

- Skeptic of the then-dominant miasma theory that stated that diseases such as cholera and the plague were caused by pollution – Germ theory was still a topic of debate

- In 1854 Snow surveyed the public and created a dot map that allowed him to trace the current cholera outbreak to a single water pump on Broad Street in London – they subsequently removed the handle
Descriptive Epidemiology

• Collecting and tabulating data concerning the disease
• Includes information on the affected individuals, the location, and period of disease occurrence
• Age, gender, occupation, health history, sexual behavior, eating habits, socioeconomic status
• Time course and chain of transmission
  • Index case
Analytical Epidemiology

• Attempts to demonstrate a cause-and-effect relationship
• Uses analysis of the data collected in descriptive epidemiology
• Retrospective
  • Data are analyzed after an epidemic
• Prospective
  • Data are collected during the epidemic
How Fast and Cheap DNA Sequencing Is Changing the Field of Epidemiology

- Genome sequencing provides better resolution (accuracy) that conventional genotyping
- Genomic epidemiology will help better tracking of outbreaks
- Traditional microbiology provides the tools to identify, characterize and track pathogens
- Laboratory surveillance will help with preliminary identification of isolates
- Identifying several similar isolates associated with cases of disease symptoms warrants sequencing
- Sequencing identifies similar elements between the samples
## Current Institutional Outbreak Status for November 22, 2018 at 3 PM

<table>
<thead>
<tr>
<th>Facility Name</th>
<th>Floor</th>
<th>Date Active</th>
<th>Date Over</th>
<th>Pathogen</th>
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<tbody>
<tr>
<td>Revera Lynwood Park Retirement Residence</td>
<td>Facility Wide</td>
<td>2018-11-21</td>
<td></td>
<td>Respiratory Infection Unspecified</td>
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<tr>
<td>St. Patrick’s Home</td>
<td>Donegal and Kerry</td>
<td>2018-11-09</td>
<td></td>
<td>Respiratory Infection Unspecified</td>
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<tr>
<td>The Ravines</td>
<td>Facility Wide</td>
<td>2018-11-20</td>
<td></td>
<td>Gastroenteritis Unspecified</td>
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</tbody>
</table>
Lab Techniques and Sequencing
1. Sputum liquefaction and inactivation with 2:1 sample reagent
2. Transfer of 2 ml material into test cartridge
3. Cartridge inserted into MTB-RIF test platform (end of hands-on work)
4. Sample automatically filtered and washed
5. Ultrasonic lysis of filter-captured organisms to release DNA
6. DNA molecules mixed with dry PCR reagents
7. Seminested real-time amplification and detection in integrated reaction tube
8. Printable test result

Time to result, 1 hour 45 minutes
Sample of Nucleic Acid Amplification Test

1. Obtain human sample for testing.

2. Lyse bacterial cells to access ribosomal RNA (rRNA).

3. Wash lysate over beads coated with DNA that will hybridize to rRNA of interest.

4. Pull down beads, isolating rRNA of interest.

5. Make double-stranded DNA (dsDNA) copy of rRNA.

6. Transcription mediated amplification of dsDNA into millions of RNA molecules.

Classification
16S Ribosomal Subunit Sequencing

- Bacterial ribosomes have a 30S subunit and a 50S subunit

One part of the 30S subunit is the 16S ribosomal RNA subunit

The sequence of this gene rarely mutates

It has a long conserved region and a very short (10-12BP region) that is unique different bacterial families
Routes of transmission

**Direct**
- Skin-skin
  - Herpes type 1
- Mucous-mucous
  - STI
- Across placenta
  - toxoplasmosis
- Through breast milk
  - HIV
- Sneezes-coughs
  - Influenza

**Indirect**
- Food-borne
  - Salmonella
- Water-borne
  - Hepatitis A
- Air-borne
  - Chickenpox

**Vector**
- A carrier of an infectious agent
- Ex. Malaria parasite carried by Mosquito
Disease Categories

• **Endemic disease**
  • Repeatedly present in a given population or geographical area
    • i.e. Malaria in Sub-Saharan Africa

• **Sporadic disease**
  • Breaks out only occasionally
    • i.e. Tetanus

• **Epidemic disease**
  • Occurs with greater frequency than usual in a population of a given area
    • i.e. SARS in China

• **Pandemic disease**
  • Is a worldwide epidemic
    • SARS spreading across the world
* Severe acute respiratory syndrome (SARS)
  * SARS coronavirus - zoonotic (transfers from animals to human)
  * Found in dogs, badgers, cats, and other species
  * In 2006, genetic link between human SARS and feline SARS found
  * Person-to-person transmission by respiratory droplets
  * Can be life threatening, especially in vulnerable populations
  * High fever, headache, body aches, dry cough, followed by pneumonia
  * Treatment includes antipyretics, supplemental oxygen, additional ventilator support
How was SARS contained?

* In May 2003, the WHO was following cases of a unique new respiratory disease

* They had been notified that a doctor from Singapore who had been treating patients was flying from New York to Frankfurt, authorities in Germany were alerted

* That day (a Saturday) - the Dr. Bruntland, the Director General was fully briefed on the findings and issued a worldwide notice simultaneously to health professionals and the media - a bold move

* This was the first major outbreak of the internet age. Cases and information were quickly shared. Virus was identified within a month

* All transmission chains were broken by July 5th, 4 months later
WATERBORNE DIGESTIVE INFECTIONS KILL

Ugunja market shut following cholera outbreak
By Magdalene Odua, Citizen Digital
Published on: 10th June 2016

Cholera killing dozens a month in Haiti

Rochester Hospitals Unite to Defeat a Common Foe: C. Difficile
Health-care providers are finding that when it comes to safety issues like infections, collaboration trumps competition

Suspected typhoid fever, dysentery kills 13 in Abuja
February 23, 2016 - Premium Times
Cholera

Digestive infection caused by *Vibrio cholera*

*V. Cholera* is a gram negative comma shaped organism with a flagellum as well as pilli

Most common natural environment is salt water

Secretes the **cholera toxin** that causes watery diarrhea

Toxin binds cells, is welcome in, processed by the cell, makes its own energy, targets the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)

Causes salt to be pumped into the intestine, water then follows, dehydration insues

Toxin co-regulated pili allow bacteria to bind one-another and form tight protected units
In 2010, an earthquake rocked Haiti and infrastructure was destroyed.

9 months after the earthquake, cholera was devastating the country.

There were two hypotheses to the origin of this cholera outbreak:

1. The climate hypothesis - cholera living in the water had evolved to be pathogenic.
2. The human transmission hypothesis - an infected individual(s) from another country brought the new pathogenic strain with them.

This 7th generation pathogenic strain had obtained the ctx toxin gene from a bacteriophage AND the TCP island which allowed for colonization of the intestine (island is a segment of DNA with genes for a similar purpose) AND the VSP island.

Genomic epidemiology supported the human transmission hypothesis and traced the outbreak to a group of soldiers from Nepal.
*Pertussis (whooping cough)*

* Highly contagious
* Caused by *Bordetella pertussis*—small, aerobic, gram-negative coccobacillus
* Slow incubation, begins with cold-like symptoms and leads to severe coughing spells 10-12 days, can last 4-8 weeks, can lead to vomiting
* Can cause permanent disability and death
* Person-to-person transmission by airborne droplets
* Vaccine available - but not widespread

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100 susceptible people
(e.g. not vaccinated against pertussis) + About 80 people will catch pertussis.

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139'786 reported cases
89'000 estimated deaths (2008)
86% estimated DTP3 coverage

Source: WHO (2014)
*Common cold:* viral infection of the upper-respiratory tract that primarily effects the nose and nasal cavity

*Most frequent human disease*
*Variety of viruses invade the nasopharynx (more than 200)*
*Rhinoviruses (Group IV +ssRNA) are the leading cause*
*Lasts 3 to 5 days in healthy patients*
*Highly contagious—spreads rapidly, often opportunistic*
*No specific treatment—rest, lots of fluids - COLD FX DOES NOT WORK*
*Over-the-counter medication to help relieve the *symptoms*
*Influenza (flu): an infectious viral disease caused by influenza viruses

* Caused by orthomyxoviruses - Group V neg ssRNA viruses. Three genera of Influenza virus are identified by antigenic differences in their nucleoprotein and matrix proteins;
  * Influenza virus A infects humans, other mammals, birds, and causes all flu pandemics
  * Influenza virus B infects humans and seals
  * Influenza virus C infects humans, pigs, and dogs

* Person-to-person infection, or by fomites (any object/material that can transmit infection)

* Causes complications; secondary infections, worsening of chronic conditions such as asthma or congestive heart failure
- Fever, headache, fatigue, dry cough, sore throat, rhinitis, myalgia
- Gastrointestinal symptoms (sometimes)—nausea, vomiting, diarrhea—more common in children than adults
Why Winter? From the Italian “influenza di freddo” meaning “influence of the cold. In the northern hemisphere, the peak of flu season typically runs from September - March, peaking in February.

* In 2007, Dr. Peter Palese recognized that guinea pigs could be infected with influenza - a great model organism
  * This showed that influenza is more infectious at cool dry temperatures but no explanation of WHY is given
* A later study (Elert, 2013) showed influenza virion survival at 43°F/low humidity was ~24 hrs, whereas at 90°F/high humidity it was around 1 hour
* HOWEVER, viruses in other climates (tropical) show different patterns
  * Adopted from Hannah Foster, Harvard