Seminar 5
Bad Bugs in the Body

Carleton University
Learning in Retirement Program
Daniel Burnside
A Quick Look Into Sexually Transmitted Infections

Prevalence, Treatment, and Recent Advances
Why are we so susceptible to STIs

• direct contact between bodily fluids

• urinary and reproductive tracts have large surfaces exposed to the external environment

• most areas are lined with mucous membranes

• we are stubborn by nature and often don’t protect ourselves

• STIs can lead to STDs
• Human Papilloma Virus: 4,300/100,000
• Chlamydia: 895/100,000
• Gonorrhea: 252/100,000
• Genital Herpes: 235/100,000
• Syphilis: 17/100,000
• HIV: 15/100,000
How Prevalent are STIs?

- Rates of most STIs have increased steadily in Canada since 1990s

- Approximately 1/3 people in the USA are living with an STI

- Largely due to trend of people becoming sexually active earlier and marrying later

- Also, the divorce rate has increased significantly

- Overall, a higher average number of sexual partners in a lifetime

Data from the Public Health Agency of Canada 2012 Retrospective Data
Multiple STIs are increasing in prevalence
Are online hookups behind Canada’s rising STI rates?

By Sheryl Ubelacker  The Canadian Press

In 2015, the latest year for which national figures are available, there were almost 116,500 cases of chlamydia, the most commonly reported STI in Canada, with females accounting for two-thirds of infections, says the Public Health Agency of Canada (PHAC). Between 2010 and 2015, chlamydia rates increased by almost 17 per cent.
How Prevalent are STIs
Young People Have the Highest Rates of STIs
Numbers from the U.S.

- The US experiences approximately 20 million new cases per year
- These numbers demonstrate identified cases only
- Over 24,000 women/year become infertile because of untreated STDs
Bacterial STIs

Neisseria gonorrhoeae

Courtesy advocatesaz.org
• **Gonorrhea**
  • Most *reported* STI in the United States
  • first described by Albert Neisser in 1879
  • Caused by *Neisseria gonorrhoeae*
    - Gram negative, diplococci - bean shaped
    - Peritrichous fimbriae
    - Move through jerky fashion, “grappling hook mechanism”
    - Release peptidoglycan fragments that act as toxins, kill cells
  
  • Transmitted primarily through vaginal, anal, oral sexual activity
  • Can be transmitted by asymptomatic individuals (females more likely to be asymptomatic but more like to see a doctor)

**FEMALE**
• Vaginal discharge
• Painful burning during urination
• Painful intercourse
• Bleeding between periods

**MALE**
• White, yellow, or green discharge from the penis
• Painful burning during urination
• Swelling of testicles
Chocolate media is a variety of blood agar, contains lysed red blood cells
- type of media for growing pathogenic organisms not cultured under
  standard lab conditions
- other factors also added

Thayer-Martin agar is a variety of chocolate agar that contains several
antibiotics (vancomycin, colistin, nystatin, and trimethoprim) that select for
Neisseria

Can grow on a variety of carbon sources to select further
• Gonorrhea cont’d

• Increases risk for other infections such as HIV and chlamydia

• Prolonged infections in males can lead to *epidymitis* (testicular inflammation) which can cause infertility

• Can pass to child during birth

• Can disseminate and cause skin lesions
Syphilis

- **Cause: *Treponema pallidum***
  - *Gram negative spirochette*
- **Only host is humans**

Incubation time: 10 to 90 days after initial infection – resembles other diseases (like chlamydia) in early stages

- **Primary syphilis**
  - Small red chancre, will disappear, may leave scars on skin
- **Secondary syphilis**
  - 2 to 10 weeks after primary stage – variety of symptoms; rashes on skin, throat, cervix elsewhere
  - Swollen lymph nodes, sore throat, fever

**Tertiary syphilis**
- Characterized by **gummas** in vital organ
  - Gumma – type of granuloma – accumulation of immune cells
Background: In the 1990s, rates of reported cases of infectious syphilis were relatively low and were similar among males and females. In 2001, rates began to increase, particularly among males.

Results: Rates of reported cases of infectious syphilis increased by 101.0% between 2003 and 2012, from 2.9 to 5.8 per 100,000. It increased among males by 128.3% and decreased among females by 40.9%.

Highest
Males 25-29
Females 20-24

Conclusion: In Canada rates of reported infectious syphilis cases in males have markedly increased over the last 10 years.
For an infection to be caused by an exogenous agent, the following criteria must be met:

* A sufficient number (dose) of infectious agents (airborne or contained in droplet nuclei) must be inhaled
* The infectious organism must remain alive and viable in air
* The organism must find susceptible tissue for attachment/growth
* Once in the respiratory tract, the organism must colonize on surfaces before it can cause disease - more possible in infected/inflamed tissue

The most common bacteria found in the normal flora of the upper respiratory tract are *Staphylococcus aureus* and *S. epidermidis*. 
Damage to the mucosal lining of the RT allows bacteria in the normal flora to become infectious.

The mucosal surface can be damaged by smoking, dryness, air pollution, laryngitis, allergies etc.

Often viral infections cause this damage, allowing bacterial species to develop secondary infections.

About 90% of acute respiratory and 50% of lower respiratory infections are primarily caused by viruses. The most common viral infections include the common cold and influenza.
Bacterial Infections
* **Streptococcus pneumoniae**
  * Gram-positive, **encapsulated** alpha-hemolytic
  * *Diplococcus (Pneumococcus)*
  * Can be found in resident flora
  * Common cause of mild respiratory illness
  * Main cause of community-acquired pneumonia and meningitis in children and the elderly
  * Pneumococcal conjugate vaccine is available

* Capsule avoids phagocytosis - susceptible to cell mediated immunity via alveolar macrophages if immunity is present
* Historically treated with antibiotics including penicillins, macrolides, cephalosporins, vancomycin, and trimethoprim-sulfamethoxazole.
Strep throat or streptococcal pharyngitis
* Caused by group A Streptococcus - specifically *Streptococcus pyogenes*
* Most common bacterial infection of the throat
* Can occur at any age, most common in children
* Affects the back of the throat, uvula and tonsils
* Red or white spots, inflammation

Scarlet fever
* Group A beta-hemolytic streptococci; S. pyogenes
* Begins with fever and sore throat; might also exhibit chills, vomiting, abdominal pain
* “Strawberry tongue” due to erythrogenic exotoxin that damages capillaries under the skin - causing the red rash
Manifestations: Pneumonia, bacteremia, meningitis...

Since 2007, resistant strains have become common. Resistance to penicillin and cephalosporins is through alteration of cell wall targets, penicillin-binding proteins (PBPs).

Can be overcome if the antibiotic concentration at the site of infection exceeds the MIC of the organism for 40%-50% of the dosing interval.
*Other Common Bacterial Infections*

*Tuberculosis (TB)*

*Caused by Mycobacterium tuberculosis, usually infects lungs*

*Airborne*

*Infected persons may not show symptoms but may have latent tuberculosis*

*8 million people worldwide / 2 million deaths annually*

*Initial symptoms—fever, night sweats, and loss of appetite*

*Some may go into remission; some become more chronic and debilitating*

*TB vaccines are available, recommended in countries where disease is endemic*

*Transmission largely prevented if infected persons are on strict antibiotic regimen*
Cystic Fibrosis

CF is caused by a mutation in the gene cystic fibrosis transmembrane conductance regulator (CFTR)

Causes thick, sticky mucus to build up in the lungs

Autosomal Recessive
Biofilms

* Collection of surface-associated microbes

* Enclosed by extracellular, mostly polysaccharide matrix

* Can include noncellular material
  * Mineral crystals
  * Corrosive particles
  * Blood
  * Other substances

• First colony adheres to surface and anchors permanently if not removed immediately

• Biofilms form a strong, protective structure that protects and sustains the colony against a variety of threats
*Cells function differently depending on:
  * the current biofilm architecture and/or
  * their location within the film

*pseudo-tissue structure*
What is *P. aeruginosa*?

- A Gram-negative rod that is implicated in human disease, such as Cystic Fibrosis (does not cause CF, just takes advantage of it)
- Therefore, it is an opportunistic pathogen
- Apart of the genus *Pseudomonas*
- Able to produce a biofilm and special metabolites that aid in defense (will go into more later)
Antibiotic Resistance in *P. aeruginosa*

- My specialty is resistance of *P. aeruginosa* to ciprofloxacin, a fluoroquinolone.
- This antibiotic will target DNA Gyrase, thus preventing transcription.
- However, *P. aeruginosa* has evolved resistance to ciprofloxacin.
- Now, whenever *P. aeruginosa* is treated with cip, well there is no treatment because the bacterium simply pumps out the antibiotic.
- There are a few other mechanisms of resistance, but due to time constraints...
Identification of Genes Involved in *Pseudomonas aeruginosa* Biofilm-Specific Resistance to Antibiotics

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Abstract

*Pseudomonas aeruginosa* is a key opportunistic pathogen characterized by its biofilm formation ability and high-level multiple antibiotic resistance. By screening a library of random transposon insertion mutants with an increased biofilm-specific antibiotic susceptibility, we previously identified 3 genes or operons of *P. aeruginosa* UCBPP-PA14 (*ndvB*, *PA1875–1877* and *tssC*) that do not affect biofilm formation but are involved in biofilm-specific antibiotic resistance. In this study, we demonstrate that *PA0756–0757* (encoding a putative two-component regulatory system), *PA2070* and *PA5033* (encoding hypothetical proteins of unknown function) display increased expression in biofilm cells and also have a role in biofilm-specific antibiotic resistance. Furthermore, deletion of each of *PA0756*, *PA2070* and *PA5033* resulted in a significant reduction of lethality in *Caenorhabditis elegans*, indicating a role for these genes in both biofilm-specific antibiotic resistance and persistence *in vivo*. Together, these data suggest that these genes are potential targets for antimicrobial agents.
Convergent evolution and adaptation of *Pseudomonas aeruginosa* within patients with cystic fibrosis

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Little is known about how within-host evolution compares between genotypically different strains of the same pathogenic species. We sequenced the whole genomes of 474 longitudinally collected clinical isolates of *Pseudomonas aeruginosa* sampled from 34 children and young individuals with cystic fibrosis. Our analysis of 36 *P. aeruginosa* lineages identified convergent molecular evolution in 52 genes. This list of genes suggests a role in host adaptation for remodeling of regulatory networks and central metabolism, acquisition of antibiotic resistance and loss of extracellular virulence factors. Furthermore, we find an ordered

Superbugs set to meet their match thanks to Mac research

Mac researchers find drug combo that might tackle antibiotic-resistant superbugs
• Article published in Nature Microbiology

• Overuse of polymyxins coupled with sharing of resistance plasmids has created gram-negative “superbugs”

• Colistin resistance arises from covalent modifications of lipid A - reduces affinity of polymyxins

• Researchers searched for an effective adjuvant

• Pentamidin showed synergy with other antibiotics that were previously used to treat Gram positive species

Pentamidin sensitizes Gram-negative pathogens to antibiotics and overcomes acquired colistin resistance

Infections that Cross the Blood-Brain Barrier

The Blood Brain Barrier

Normal Blood Vessels vs. Brain Blood Vessels

- Pore passage
- Lipid-soluble substances
- Water-lined pore
- Glial brain cells support the barrier
- Carrier-mediated transport
- Tight Junctions (no pores) create the barrier

Capillaries in cross section
Meningitis

- The blood-brain barrier only allows some specific molecules to enter the cerebrospinal fluid.

- The BBB prevents most microorganisms from ever infecting the brain/central nervous system.

- A limited number of immune cells circulate in the CSF.

- The brain and spinal cord are protected by three protective layers collectively called the meninges – inflammation of the meninges in response to infection/disease is called meningitis.

- Inflammation of the brain is referred to as encephalitis and inflammation of both the brain and meninges is meningoencephalitis.
Meningitis

• A viral infection of the CSF/meninges causes an increase in lymphocytes and monocytes as well as a slight increase in protein levels
  • **Aseptic meningitis**: the CSF remains clear

• A bacterial infection of the CSF/meninges causes a sharp increase in granulocytes and proteins which causes the CSF to become visibly turbid
  • **Septic meningitis**: the CSF becomes turbulent/cloudy
Bacterial Meningitis (Cont.)

• Initial symptoms
  • Nausea, vomiting, fever, headache, stiff neck

• Followed by other symptoms
  • Confusion, sleepiness, light sensitivity, possible progression to convulsion and coma

• Less common but more severe than viral meningitis, due to production of bacterial toxins

• Early diagnosis and treatment is essential to prevent permanent neurological damage
Meningococcal Meningitis

• Caused by *Neisseria meningitides*
• Gram-negative, aerobic diplococcus, polysaccharide capsule
• Depending on geographic location, 20% of the population are asymptomatic carriers—nose and throat
• Transmission: Person-to-person or respiratory droplets
• Sudden onset after 1-3 days of incubation
• Antibiotic therapy reduces mortality rate by 9% to 12%
• Polysaccharide vaccines are available against serotypes A, B, C, Y and W-135
Pneumococcal Meningitis

• Caused by *Streptococcus pneumoniae*
• Gram-positive, encapsulated, facultative anaerobic diplococcus
• Carried in throat of many healthy individuals
• Approximately 90 different serotypes

• REMEMBER – You had a presentation on West Nile Encephalitis – this will also be on exam
Athletes Foot – Tinea Pedis

- Skin infection caused by fungus
- Results in itching, redness, odour and drying in minor cases
- Can cause severe cracking, blistering, loss of toenails etc
- Provide opportunity for other pathogens to enter
- Caused by a variety of fungal species including Epidermophyton, Trichophyton, and Microsporum species
Athletes Foot – Tinea Pedis

- Produces a multibillion industry of over the counter and prescription drugs (20% of population will experience)
- Best treatment – keep your feet clean and dry
- Anti-fungal drug **miconazole** has been shown to slow the progression of MS in early studies (Nature, 2015)
  1. Chronic interdigital athlete's foot,
  2. Plantar (chronic scaly) athlete's foot (aka "moccasin foot")
  3. Acute ulcerative tinea pedis – macerated lesions + scales
  4. Vesiculobullous – mucocutaneous, blisters
Conjunctivitis

Conjunctivitis (pinkeye)
- *Haemophilus influenzae* is major cause
- *S. aureus, H. influenza, Chlamydia sp.*, *N. gonorrhea, S. pyogenes* also
- Various microbes
- Associated with unsanitary contact lenses
- Fast onset
- Some vaccines such as Hib vaccine are effective against conjunctivitis

Neonatal gonorrheal ophthalmia
- *Neisseria gonorrhoeae*
- Transmitted to a newborn’s eyes during passage through the birth canal
- Prevented by treatment of a newborn's eyes with antibiotics