Lecture 1

micro = small
bio = life
logy = study (of) or science
Immunology = study of our protection from foreign macromolecules or invading organisms and our responses to them

Different classes of organisms

- Viruses / chlamydia (grow only in living cells)
- Mycoplasma (grow on non-living media)
- Bacteria (no separate nucleus; unicellular)
- Parasites
- Small (microscopic)
    - 1-2 microns (1 mm = 1000 microns)
    - Address them by their proper names !!! - (i.e., not “germs”, “bugs”)
    - Listeria monocytogenes
        - Species is the second name
        - The genus capitalized species undercase

What are organisms made of?

Viruses

- Nucleic acid, RNA or DNA never both
- Surrounded by protein shells
- Attach, inject nucleic acid, highjack synthetic processes inside cells to make more viruses, package, get out while going is good

Bacteria

- Rigid cell wall
- Genetic material meaning circular chromosomes
- No nucleus = both DNA and RNA
- Binary fission

Eukaryotes

- Unicellular and multicellular animals and plants
- Genetic material organized into nucleus

Are all bacterias bad?

- No, not all but biotechnology, functionals foods, etc are

Can we live without bacteria?

- No we cannot they help with digestion, breaking down food

Where should there be no bacteria?

- Heart
- Cardiovascular system
- Genitals in men, causes urinary infection
- But women can have bacteria to maintain temperature and pH

What do bacterias do for us?

- Protection from the bad bacteria

- Metabolism, immune stimulation

Mechanical Barriers
- **Skin,** saliva, mucous, tears, hair

Other helpers
- Antibodies
- Complement
- Immune cells= T-cells, macrophages
- Immune system= cell mediated;humoral

How do bacteria enter?
- Adherence
- Toxin production
- Opportunism
- Compromised host

Bacteraemia = bacteria in blood, a type of septicaemia
Anemia = involves blood
Colonize = activity do something to colonize and break through barriers
Contamination = no need to colonize because it is already prepared

Microbial disease
- Enter-live-multiply
- To enter they need to colonize in or on the body; clinical infection (disease) can result when damage occurs to host [contamination = deposition without multiplication]
- Clinical disease = easy to recognize
- Subclinical infection = hard to diagnose (no symptoms)

How do we measure how dangerous a bacteria/virus/parasite is?
- Pathogenicity = ability to produce disease
- Virulence = relative capacity to cause damage (i.e., the degree of pathogenicity)
- Opportunistic = do not normally cause disease but can do so when defense mechanism(s) breached or compromised (organism that usually does not cause problems unless not in the right spot)

Pathogenesis of infectious diseases
A pathogenic microorganism enters your body...two things happen:
- 1. Microorganism (invader) tries to multiply / invade and cause disease (2o event)
- 2. Host tries to prevent #1

Whether the invader wins or not is dependent on several factors
- Transmission:
  - 2 MAJOR WAYS —> inhalation, ingestion - break in protective barrier, direct deposit
  - Pathogenicity

- invasiveness (adherence, persistence, avoidance of immune system)
- toxigenicity (ability to make toxins) “help bacteria”

How does a pathogen adhere to us?

- A bacteria needs to adhere, evade and invade the host
- Tools used to achieve these huge objectives:
  - surface structures (pili, fimbriae)
  - Capsules
  - Enzymes

Toxigenicity

- Toxins are substances (usually proteins) secreted by bacteria with the hope to cause damage
- Two classes:
  - Exotoxins
    - excreted/secrete by living cells (exo=exit)
    - specific affinities
    - Thermolabile
    - Organism will make it release and go to another area of the body
    - Very potent - sensitive to heat
  - Endotoxins
    - Endo - inside
    - Produces from a live bacteria
    - liberated when cell wall disintegrates (bacteria dies inside) Does not have a specific affinity
    - causes fever, malaise, shock
    - thermostable
    - less potent than exotoxins - resistant to heat

Lecture 2

What is immunity?

- Immunity = protection against infectious disease
- How our body protects itself from forgein invaders (pathogens that live outside our organs - blood born, versus pathogens that make their way inside our cells)
- 2 types of immunity - arms of the immune system

2 types of immunity:

- Non-specific (innate) does not change, the first line of immunity
- Specific (adaptive, acquired) - unique response, to get rid of the pathogen or will be very specific to the pathogen living inside

Innate immunity

- Skin (largest organ)
- What characteristics of the skin make it an effective mechanical barrier?
  - ➔ It’s a physical barrier

➔ Low pH
➔ Selective secretion anti-micorable
➔ It's dry

Mucous membranes (mechanical)

➔ Cilia in respiratory tract
➔ Lysosomes, pH

- Iron-binding proteins
  ➔ Some bacteria require iron for growth
  ➔ Transferrin, lactoferrin
- Phagocytosis
  ➔ PMNs, monocytes, and macrophages.
- Complement:
  ➔ It's a set of circulatory proteins in the blood
  ➔ Variety of functions

Opsonization:

- One of the functions is to help make stuff more attractive to the immune system

Membrane attack complex:

- When the complement protein comes together, they make a hole in the bacterial cell wall, the bacteria then dies

Specific immunity: (is the pathogen outside, or inside (intercellular, intercellular):

- Humoral and cell-mediated (CMI)

What is the difference between innate immunity and adaptive immunity:

- Innate: protects against ANY invader, does not discriminate
- Adaptive: directed against

Where do immune cells come from?

- Immune cells - Lymphocytes (T-cells, B- cells and NK cells), neutrophils, and monocytes/macrophages - all types of white blood cells
- T cells are one of two primary types of lymphocytes—B cells being the second type—that determine the specificity of immune response to antigens (foreign sub- stances) in the body.
- B cells make antibodies to specific anti- gens
- T helper 2 cells bind to B cell and inform it to make antibodies, other extracellular parasites

Humoral immunity:

- Circulating antibodies in the blood

Antibody:

- made out of protein that binds specifically to a substance (it's antigen)
- Igs or immunoglobulins
- Produced by B-lymphocytes upon stimulation from antigen presenting T-cells
- B cells are activated (turned on) by TH2

- After that, the T cells will able to recognize toxins, capsules, some viral protein,

Antigen:
- "Non-self" - not part of the human body
- Things that can cause damage to me
- Could be protein, glycoprotein, lipoprotein, polysaccharide

What structures could be "antigen" to make antibodies against? Why?
- Unique to yourself (that's not found out or inside you)
- Last thing you want is the antibody to bind to your liver
- Non-self
- Specific antibodies made unique to that invading pathogen

Agglutination:
- Antibody binds to one bacteria at one time
- Signal to get rid of the clumps, let our immune system know it's not good

Immunoglobulins aka antibodies:
- Antibody: Ig produced in response to stimulation
- Distinguish "non-self" from "self"
- Two regions: variables constant region
- Variable region is response for binding the antigen
- Every antibody has the same structure in all humans

Classes of Igs
- 5 classes:
  - IgG, IgA, IgM, IgE, IgD

IgG:
- Host defense
- And cross the placenta and protect the newborn
- Good while you're developing

IgD:
- Role is unknown (we don't know 100%)
- Very low in concentration of blood
- Parasitic infections
- Looks similar to IgG

IgA:
- Host defense.
- Found in secretions
  -tears, saliva, milk (women breastfeed pass on to newborns)
- Dimer (meaning two antibodies are tied together)

IgM:

- Host defense
- Early immune response
- Pentamer (5 Y shaped antibodies are held together by constant region)
- First antibody produced

IgE:

- Involved with allergies (hypersensitive) body produces lots of IgE
- Defends against parasites
- Structure looks like IgG and IgD

1 Primary Response:

- Ab production triggered on first antigen introduction
- Antibody detectable after 5-10 days
- Antibody in serum is maximum at -21 days, then drops to low levels. because the paths gone has been taken care of

2 Secondary Response: Ag = antigen Ab = antibody

- Basics for immunizations along with 1 response
- Occurs when Ag (NOT AB) is introduced 2nd, 3rd, 4th
- Booster injections to maximize Ab levels. (to make sure the secondary immune responses kicks in soon)

Memory cells:

- Already been trained and told to become antibodies
- If they're needed again
- B-cells and T-helper cells become the memory cells?

Serological reaction:

- detects presence of antibodies in serum sample (blood sample)
- Antigen and antibody interact; agglutination
- Detects unknown microorganisms using known antisera

What happens if the bacteria comes inside the house? (pathogens)

- We need cell-mediated immunity (CMI)

How does your body know whether to activate hormonal or cell mediated immunity based on the antigen it sees?

- Antigen presenting cells
- it will prepare for presentation
- After presented will know whether helper cells are th 1 or the2
- take it and process it to the correct antigen cell
- eventually turn on t helper 2
- T helper 1 train them to be powerful against a specific response
  Pathogens taken in by macrophage (type of antigen) then present it t helper will recognize and pathogen is then activated

Cell-Mediated Immunity (CMI)

- T-cells NOT antibodies
  - ➔ Helper, suppressive, cytotoxic (killer)
- Exposure to antigen induces response from trained T-cells
- Essential for defense against intracellular organisms, parasites, tumors and other foregin cells (i.e., transplants, grafts
- Immune-suppressive medication for transplant

How does your immune system know how to process an antigen?
How does your body know whether to activate humoral or cell-mediated immunity based on the antigen it sees?

- Antigen presenting cell (APC)

*******General role of the antigen presenting cell (APC)

- Take in the entity and prepares antigen for presentation
- Presentation depends on how antigen is viewed
- intercellular vs extracellular
- take in an antigen and present it to a tH1 or tH2

Pathway of specific immune

1. invader Taken in by antigen presenting cells.
2. Either show the antigen to tH1 or tH2 which will stimulate the B cell.
3. if it shows it to tH1 (cell mediated)
4. if it shows to tH2, it will find a b cell and turn it on and make some antibodies (some memory cell will remain)

Disorders of immunity

Allergy and hypersensitivity:

- ➔ Immune system, over-reacts to specific antigens in the absence of true infection
- ➔ Can be fatal….ANAPHYLAXIS
- ➔ Want the immune system to be unique to unique antigen

Auto-immune disease:

- ➔ Immune system reacts to its own “self” antigens”
- ➔ “Auto-antibodies”
- ➔ Type I diabetes, MS, rheumatoid arthritis, lupus

Immunodeficiency states:

- ➔ Inability to produce antibodies and/or disfunctional CMI.
- ➔ Diseases, AIDS

Graft rejection:

- ➔ NORMAL immune reaction to “non-self”
- ➔ Control by immuno-suppressive medication

➔ Failed blood transfusion

Immunization:

- Passive immunization:
  - Administration of preformed antibody against a specific microbial agent
  - Used during birth
  - When you're traveling for a short period of time

- Active immunization:
  - Stimulates immune system by administration of antigen
  - Longer lasting (they become memory cells)

How to introduce vaccines:

- Live-attenuated vaccine:
  - Sub-clinical or mild illness mimicking the disease
  - Local (IgA) and humoral (IgG) immunity
  - Rapid immunity development
  - Serious illness in immuno-compromised individual
  - Beat up the pathogen until an no longer kill, then injected in people

- Killed vaccines, subunit vaccines and toxoids. Package into vaccine and assign,
  - Antigens without infectivity (it's destroyed)
  - Sometimes you require a booster

- Recombinant vaccines
  - Remove DNA
  - Hep B vaccine, you remove parts of it and place it into the person

- Adsorbed vaccines:
  - Vaccines mixed with inorganic salt, allow the antigen to be slow and longer-lasting.
  - Inorganic salt binds to the antigen and is not toxic to the human body.

- Conjugate vaccines:
  - Designed for poorly antigenic microorganisms
  - Conjugate antigen of interest to immunogenic, non-toxic protein

- Combined vaccines:
  - For ease of administration
  - If they don't interact, you can immunize against more than pathogens

- Combined Active-Passive immunization
  - Immediate protection after possible exposure to microbes
  - Inject on different sites, antigens that are per-formed and antigens will be bind

Three major mechanisms of resistance:

- Alteration in drug target (for example enzymes in the shape of the triangle, it does something useful for the bacteria, the bacteria is able to change the shape)
- Production of inactivating enzymes (modify structure of antibiotic)
- Decreased uptake of antibiotic (bacteria will sense that antibiotic is around and will prevent the antibiotic from coming in)

Antibiotic resistance:

- Resistance occurs when a susceptible microorganism is no longer inhibited by an antibiotic agent
- Many reasons. Two being intrinsic, acquired

The chromosome: role in antibiotic resistance:

- Mutations lead to change in site of antibiotic target

Post-antibiotic era: is it possible?

- With current overuse of antibiotics, we are forcing bacteria to change (evolve) in order to survive.

How is this achieved/helped by us:

- Daycare centers

Decreasing antimicrobial resistance?

- Use narrowest spectrum antimicrobial agents
- Withhold antibiotics
- Hospitals

Antibiotic therapy

- Effective chemotherapy depends on selective toxicity
    - good against pathogen, does not affect host

- Exploit pathogen processes not seen in humans
    - cell wall, metabolism, etc.

- Knowledge of likely microorganisms is crucial…
    - Site
    - Organism
    - allergy to host?

- Other considerations…
    - route of administration - orally, IV, creams

- Monitoring therapy
- Adverse effects
    - GI-tract, skin, haemopoietic system, renal system, liver

Acquired Resistance

- Three major mechanisms of resistance
    - Alteration in drug target
        - ex antibiotic against something , change something and then the antibiotic can't do anything to it anymore
- Production of inactivating enzymes
- Decreased uptake of antibiotic (bacteria will sense that antibiotic is around and will prevent the antibiotic from coming in)
- Alteration in drug target
- Production of inactivating enzymes
- Decreased antibiotic uptake

Lecture 3

Current hypotheses: Does vaccine cause autism

- The combination measles-mumps-rubella vaccine causes autism by damaging the intestinal lining, which allows the entrance of encephalopathic proteins.
- The administration of multiple vaccines overwhelms or weakens the immune system.
- Vaccinations will be linked to various diseases but no scientific study has been done of this which disregards this.

Diagnostic microbiology:

Isolation of pure culture specimen

- The Importance of healthcare to go about and study them.
- Isolate bacteria

Culture media

Why?
What?
Who?

Inoculation methods

- 3 methods

Streak method:

1. take a lope, have a circle, dip the lope in the fluid.
2. The lope gets flamed
3. Flame sterilizes the lope.
4. Once you sterilize, you let it cool, you let it streak where it's already streaked.
5. The process of streaking continues. (after you strike it, you dilute it)
6. You place it and the appearance of isolated colonies are visible.

Observations:

- Streak in order to say isolated colonies
- Reason you want an isolated colony is because it's a pure culture specimen.

- Most common

Pour plates:

1. Inoculate empty plate
2. Add melted nuteitnagar
3. Swir to mix
4. Colonies grow on and in solidified medium

- Bacteria grow inside agar
- Used for enumeration of bacteria
- Keep dilutating until you get a countable number, countable number starts from 50 and above.

Spread plates:

1. Inoculate plate containing solid medium
2. Spread inoculum over surface evenly
3. Colonies grow only on the surface of the medium.

Identification:

- Take the colony and dissolve it in buffer, and look at the individual colony
- Resolving power = ability to loom at two things that are closely located and able to tell it apart.

Colonial morphology:

- Clues to what the patient might have, once you have isolated colonies you can do all the tests.
  - ➔ Color, shape, size (clues of the pathogen)
- Good impression of what's growing = better treatment.

Identification (staining technique)

1. Make a smear
2. Heat fix it (turn on bunsen burner, pass over the bunsen burner)
   - ➔ By heat fixing, it allows the substances on the glass slides to STICK.
   - ➔ Last thing you want to do is wash the bacteria away.
3. Stain with desired dye

Simple stain:

- Single dye normally used.
- All organisms same colour
- Size, shape, number, arrangement,

Differential stain:

- Two different dyes, gives you a good clue about what's causing the problem to the patient.

The gram stain:

Bacteria are invisible

Gram +

- Flood slide with crystal violet (leave it for a bit)
- Add iodine (iodine binds the violet to the cell well)
- Wash with water
- Decolorize with 95% ethanol (8-10 seconds)
- After the ethanol, you remain purple
- Add safranin (pink colour)

Gram -

Cell well is the key

- Peptidoglycan layer
    - ➔ Peptidoglycan layer is thick in gram positive
    - ➔ Peptidoglycan
    - ➔ is thin in gram negative

Comparing gram positive and gram negative:

- In gram negative you have an outer cell wall.
- Gram positives do not have a cell wall.

Gram negative cell envelope:

Gram positive:

- You have the cell wall (similar to gram negative)
- No secondary cell wall (no outerlayer)
- Gram positives don't have endotoxins.

Characteristics of bacteria:

- Bacteria are very small
    - ➔ High surface area/volume ratio
        - ★ Higher metabolism
        - ★ Faster growth
        - ★ Replication rate (20 minutes)

With what do we grow bacteria?

- Different agars are used for different bacteria.

Definitions:

- Chemical defined
    - ➔ Exact composition known.
- Chemically undefined
    - ➔ One or more of the components you can't control
        - ★ Example is blood agar

Agar can either be selective, differential and s/d media

Selective media
- Whats in the agar will suppress gram positive.

Differential media:
- Ask.

selective/differential media

MacConkey - S/D media - IMPORTANT FOR EXAM
- Has stuff that allows

Urinalysis dipstick
- Bacteremia versus bacteriua versus septicemia?
  - ➔ Bacteremia = presence of bacteria in the blood.
  - ➔ Bacteruria = presence of bacteria in the urine.
  - ➔ Septicemia = blood poisoning

Antibiotic susceptibility test:
- Touch the colony.
- Swap up and down
- Turn the plate
- And swap at a 45 degree along
- Now that you're swapping, you can see the growth
- Before putting the plate in the incubator, you put on the disk (different antibiotic)
- If the antibiotic works, you see a zone (antibody killing bacteria)
- If there's no zone, antibiotic has no zone = no effect on the bacteria.

Phage typing: use of bacteriophages:
- Bacterial phage only affects bacteria (very specific)
- Bacterial phages could be given to patients

Hypotonic solution:
- Dip it into liquid media.

Isotonic solution:
- Solutes have the same concentration inside the bacteria
- Water comes in and out of osmosis and diffusion

Hypertonic solution:
- Solutes are more concentration on the outside rather than inside
- Water will be drawn out through diffusion and osmosis

What if you make a hypotonic:

- Water will be drawn, pathogens will swell up and blow up.

The power of antibodies:

- Direct vs indirect ELISA
- Allows you to detect the pathogen using antigen.

Direct ELISA test:
IMPORTANT : direct ELISA detect antigen (pathogen)

- Blood sample.
- Strep that has an antibody variable binds to the antigen.
- Pass the blood sample over antibodies.
- If he has HIV, the HIV will bind to the star.
- If he doesn't, there will be no bind.
- Add the same antibody and if there's HIV, it will bind.
- Secondary antibodies will bind, so you're HIV positive.
- If you're not HIV negative, secondary antibodies will NOT BIND.

Indirect ELISA:
IMPORTANT: indirect ELISA detect the host (human) immune response (i.e, did your patient produce antibodies)

- Put HIV virus on the surface
- Take blood.
- Continue notes*

Takes about 5-10 days for antibodies to be produced
If the symptoms are new, you won't be able to use indirect examples, so direct is good.

After we finish with indirect or direct test - EXAM hint

- Characteristics that are unique to the pathogen.
- For example, pathogens cause bloody diarrhea.
- In real life, lots of pathogens, chemicals, toxins, can cause similar symptoms.
- Challenge is how you go about teasing the symptoms and it's due to a certain paathogen and eliminate other ones.
- For example if someone had unprotected sex and the other person has HIV.
- Patient has HIV, you do various testing.

Listeria:

- Widespread
- Psychotropic (temperature)

➔ Listeria is able to divide, multiply and thrive

- High case-fatality rate

Why does listeriosis remain an issue?

- Able to escape.

Lecture 4

Gram positive Cocci:

Gram positive, stay in purple, not endotoxins present, don't have a second layer.

- Grow in size.
- Different types

Staphylococcus aureus:

- Toxins are quite the problem.
- It produces either cytotoxins (binds and destroys our cells)
- Hemolysins (binds and destroys our red blood cells)
- Enterotoxin (damages intestinal tracts)
- Exfoliative toxins (causes the skin to pill of)
- Last time of toxins, toxic shock syndrome (dna that encodes that, then you could get toxic
- Carrier in anterior nares, throat, hands
    - ➔ Most of the trains are penicillin resistant.

Staphylococcus aureus continued:

Most protective barrier = skin.

- Why is the skin important?
    - ➔ Aside from the fact that it's mechanimal barrier, we need to be careful in the ER and OR and wound precaution.

Staphylococcus epidermidis:

- Found on skin, part of the normal skin flora.
- Non pathogenic, unless something happens.
- Could be considered an opportunistic pathogen.

Streptococci:

- Circular and purple
- Beads on a string - arranged in pairs or forming chains
- Divided into groups (3 different types of group)
- Haemolytic (enzymes)
- Beta hemolytic destroys blood cells.
- Alpha partially destroys red blood cell, hemobolin gets oxidized and bacteria becomes brown.
-

Streptococcus pyogenes:

- Group A, beta- hemolytic (destroys red blood cells)
- Causes acute tonsillitis, rash, fever, septicaemia.
- Exotoxin, can affect white blood cells
- Causes scarlet fever rash

Where do we find hylauronside?

- In tissues

Continuous of streptococcus pyogenes:

- Group A is sensitive
- Can cause Necrotizing fasciitis (flesh eating diseases)
    - ➔ Bacteria doesn't eat, dissolving of tissue
- Toxin is picked up, and it's responsible
- Bacteria are able to hijack human plasminogen from blood and attach and spread.
- Bacteriophage that infects bacteria and gives it a piece of DNA that encodes for the enzyme allowing bacteria to escape entrapment by killing white blood cells.
- Bacteriophages
    - ➔ virus that can infect and destroy bacteria

Streptococcus agalactiae:

- Group B
- Found in vagina of healthy women

Streptococcus pneumoniae:

- Group C
- Causes pneumonia
- If it leaves the lung, it can cause problems in the central nervous system
- Prevention strategies
    - ➔ Elderly, alcoholics, crowded living)
- Make a capsule, circle around the bacteria (extra fur coat) prevents complement from binding.

Gram negative cocci:
Has endotoxins, has the second layer.
Two types.

N.Meningitidis:

- respiratory issue
- Gram negative diplococci
- Found in healthy individuals
- 13 different types of antigens
- Some people might be healthy carriers
- Only infects humans
    - ➔ Respiratory issue so people that live in crowded areas
- Infection can result in different stages.
- Can start as a skin rash, lead to septicaemia and waterhouse syndrome, and then can cause meningitis
- antibiotic s is penicillin
- Vaccination is recommended for children

N.gonorrhoeae:

- Sensitive to dry and changes in temperature
- Causative agent of STD gonorrhea
- Second highest reported STD after chlamydia
- In male acute infection of urethra
- Women 50% are asympotamic (don't know if we're carrying the pathogen, allowing us to spread it.)

- If you're passing through a birthing canal, it can cause eye infection and pick it up.
- Penicillin resistance
- No vaccine available

Group a strep:
Accurate tonsillitis, if you get it treated
If you don't get it treated, then what can happen is heart fever it's a result of your immune system making antibodies that will attack your heart

Why are elderly and alcoholic people put at a higher risk of strep pneumoniae infections:

- Due to it being respiratory, they have reduced immune systems, and alcoholics their life charge becomes shortened.

Lecture 5

Nucleic acid gets pushed to one side, and gets protected by a coat.

- A spore will sense what's in the environment which will cause the outside to break down and revert to vegative state

Spore Forming Rods (able to make endospore)

- Bacillus and clostridium
- Release of potent exotoxins causes disease
- Gram positive = only exotoxins, cannot make exotoxins because of no second cell wall.

Bacillus Anthracis

- Causative agent of anthrax
- Unique because it has a protein capsule
- Aerobic growth conditions
- Spores are very stable , resistant to heat, drying, uv and disinfectants, spores germinate and toxins are made
- Humans exposed to spores usually through contact with animal hive or soil
- Used in bio-terrorism and warfare

Bacillus anthracis produces an exotoxin

- Encoded on pXO1 plasmid
- Plasmid contains virulence factors which are transcribed optimally
- Produces an exotoxins
- DNA can code for certain things
- Contains two plasmid

Exotoxin contains 3 separate proteins:

- Edema factor
- Protective antigen
- Lethal factor

Separately proteins are not toxic but combined are lethal

- pXO2 plasmid encodes capsule genes
- Both plasmids required for virulence

- If the spores get into the lungs, the lungs are good environment that allows it to grow and divide

Prevention and treatment

- Rapid treatment is essential
- Antibiotics; penicillin, doxycycline, ciprofloxacin or levofloxacin
- Vaccine against PA protein available
    - Used for people in army

Bacillus cereus

- Spores enter a food product when you prepare it and somehow not cooking the food properly
    - Reheating food improperly, spores can germinate and bacteria can grow and divide in the food
- CAUSES Enterotoxin, responsible for illness
    - Illness
    - 2 types of enterotoxin:
        - Heat labile: nausea, abdominal pain, diarrhea
        - Heat stable: severe nausea, vomiting

Clostridium

- Anaerobic: differentiates this bacteria from other spore forming bacilli (does not like oxygen)
- Botulism, tetanus, gas gangrene and pseudomembranous colitis
- Powerful exotoxins: rapid diagnosis
- If the spores come into the body, they need to find an area where there is little to no oxygen present to germinate and release bacteria

Clostridium botulinum

- If it gets into it, it'll produce an exotoxin that acts on the central nervous system
- Fatal food poisoning from lethal neurotoxin
- Neurotoxin blocks ach release in autonomic system: flaccid muscle paralysis:
    - Afebrile, bilateral cranial nerve palsies, double vision, trouble swallowing, muscle weakness
    - Respiratory paralysis: death
    - Treatment: antitoxin and respiratory assistance
- Neurotoxin blocks Ach release in autonomic system
- Problem when muscles don’t contract, botulinum will kill you because you’re not able to move.
- How do we get it?
    - ➔ Home tanning
    - ➔ Abroginial communities are at risk (the way they process their foods)
- Get antibiotics to try and kill
- Antitoxins that bind to neurotoxin to try and pull it away, but the ability of the receptor is stronger than the antitoxins.
    - ➔ Learning how to function again will take years.
- smoked fish, improperly canned vegetables
- proper cooking destroys spores

- Don't buy dented cans from the store, franco said so
- People who have botox, neurotoxin A (type A) is what botox is what it consists of, paralyzes muscle to make you look smoother

Infant Botulism
- Honey contamination with spores
- Spores germinate and bacteria colonizes intestine
- Neurotoxin release
- 2-3 days of constipation
- Trouble swallowing, muscle weakness

Good uses for botulinum neurotoxin
- Botox = type A
- Botox was first approved in 1989 to treat muscle disorders
- Excessive sweating, treatment for chronic pain, jaw tension

Clostridium tetani
- Causes Tetanus
- Rusty nail contaminated with spores punctures skin; wound provides anaerobic environment
- Exotoxin: tetanospasmin
    - Sustained contraction of skeletal muscles
    - Severe muscle spasms (lock jaw); high mortality at this stage
- Booster (inactivated toxoid) given every 10 years
    - Need a secondary immune response because it is quick, which we get it very 10 years
    - Causes rigid paralysis and you could die of heart failure

How do you get tetanus:
- Get the spore inside, if you step on the rusted nail with no spore, you may get a wound but no tetanus

Clostridium perfringens
- Gas gangrene
- Seen in soldiers wounded in battle
- 2 classes of infection:
    - (i) Wound infection/cellulitis
        - -necrotic skin exposed to bacteria, damage to local tissues; skin feels moist, spongy, with ‘crackly’ pockets
    - (ii) Clostridial myonecrosis
        - bacteria inoculated from trauma into muscles; exotoxin secretion destroys adjacent muscles; as muscles degrade get black fluid excreted from skin
        - FATAL unless treated with oxygen, antibiotics (penicillin) and removal of damaged tissue
    - In other words
    - Skin starts to die, there's a production of crackly noise (bubble wraps with the toys)

- Bacteria gets into the muscle, if it's anaerobic it will grow and divide
- We treat it with oxygen, blast it with oxygen kills it
- Treat it with antibiotic and remove damage tissue

Clostridium difficile

- Causes antibiotic-associated pseudomembranous colitis
- Seen more commonly in hospitals than tetanus, anthrax or botulism
- Overuse of broad-spectrum antibiotics destroys normal intestinal flora
- Infects colon and releases exotoxins
    - Toxin A: diarrhea
    - Toxin B: cytotoxic to colon cells
- Symptoms: severe diarrhea, abdominal cramping, fever
- Possible cause of diarrhea in patients on antibiotics \
- Treatment
    - discontinue antibiotic treatment
        - Rethink what your diagnostic was
    - Administer metronidazole or vancomycin ??
        - What is different about these antibiotics ??

Non-Spore Forming Rods

- 2 medically important bacilli
    - Listeria monocytogenes and Corynebacterium diphtheriae

Listeria monocytogenes

- If you are immunocompromised you are at risk
- Found in foods such as soft cheese, milk, cold cuts
- It's a psychotropic - bacteria is able to grow and survive in regierator
- It causes variety problems
- It can cross the intestinal barrier, become blood borne, if you happen to be pregnant it can cause still-borne or cause the baby to die
- Causative agent of listeriosis; immunocompromised are at high risk
- Found in foods such as soft cheeses, unpasteurized milk, cold cuts, pâté
- PSYCHROPHILE: survives in refrigerator
- Variety of symptoms: General malaise, diarrhea, meningitis, septicaemia, still-birth/abortions
- Facultative intracellular aerobe Crosses 3 protective barriers (blood-brain, GI and fetoplacental)
- Treatment: ampicillin or trimethoprim-sulfamethoxazole (treated with oxygen)
- Through ingestion, don't chew your food properly because listeria survives that
- Foodborne pathogen
- Gastroenteritis
- Abortion: still birth
- Septicemia
- Meningitis: death

^causes these

Listeriosis:

- Cna get into the bloodstream, make its way to the liver, white blood cells defend, it becomes blood borne again, it can cross either the fetoplacental or blood brain.
- Clinically it's a food borne pathogen
- Can cause septicemia, still born abortion
- No actual toxin, the bacteria destroys tissue which leads to these bad issue

Gram positive but no spore forming:

Corynebacterium diphtheriae

- Causative agent of diphtheria
- Gram positive
- Colonization of pharynx and release of exotoxins into bloodstream
- Exotoxin damages heart and neural cells
- Treatment (3 steps):
    - (i) Antitoxin
    - (ii) Penicillin or erythromycin
    - (iii) DPT vaccine
- Can be lysogenized by a bacteriophage (virus that infects bacteria)
- Vaccinate against this because the bacteria will release exotoxins damaging the heart
- The bacteria colonizes the upper respiratory tract

^end of gram positive bacilli

Gram Negative Bacilli The Enterics

Enterics

- Found as part of normal intestinal flora BUT can also cause disease
- 4 Major Groups:
    - Enterobacteriaceae (Salmonellae, Shigella, E. coli)
    - Vibrionaceae (Vibrio, Campylobacter)
    - Pseudomonadaceae (Pseudomonas)
    - Bacteroidaceae
- Organisms are divided into groups based on biochemical and antigenic properties

Biochemical Classifications:

- Ability to ferment lactose
    - EMB Media:
        - Lactose fermenters are dark purple/black
        - Inhibits Gram positive bacteria

    - MacConkey Media:
        - Lactose fermenters are pink-purple
        - Inhibits Gram positive bacteria

Some examples of biochem classifications

- H2S production

- Hydrolysis of urea
- Liquefy gelatin
- Decarboxylation of amino acids

3 Types of Surface Antigens

- O-antigen: outermost layer of LPS
    - Changes between enterics
- K-antigens: covers the O-antigens
- H-antigens: flagellar sub-unit
    - Only in motile bacteria

Diseases Caused by Enterics

- Cause diarrhea with various complications and other infections
- The deeper you go in, the more damage is caused
- Gram negative bacteria that binds but don't cross can produce exotoxin which causes diarrhea (called enteroxin)
- If we find bacteria that are not only bind but are able to cross, in the process of crossing you cause damage such as bloody stool.
- Similar to above, it becomes blood borne

1) Diarrhea-with/without systemic invasion

- Bacteria bind intestinal cells but do not enter
- EXOTOXIN release causes diarrhea;
- ENTEROTOXIN causes fluid/electrolyte loss
- Watery diarrhea, NO FEVER
- Vibrio cholera

2) Diarrhea with intestinal cell invasion

- Bacterial virulence factors allow binding and invasion of cells
- Toxin release destroys cells bloody stools
- Fever response
- Shigella

3) Diarrhea with invasion of lymph nodes and bloodstream

- Abdominal pain with diarrhea containing white and red cells
- Fever, headache, increased white cell counts
- Salmonella Typhi, Yersinia enterocolitica, Campylobacter jejuni

Other Enteric Infections

- Urinary tract infection, pneumonia, bacteremia and sepsis
- Nosocomial infections by: E. coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter, Serratia, Pseudomonas aeruginosa
- Pseudomonas aeruginosa: opportunistic pathogen, often infects burn patients and can disseminate through body into CNS

Salmonellae

- Member of Enterobacteriaceae family
- Unable to ferment lactose

- All have animal reservoirs EXCEPT S. enterica serovar Typhi (humans are the only host!!)
- Types of infections in humans: enterocolitis, enteric fever, opportunistic infections, septicemia and osteomyelitis
- Creamish/brown because it is unable to ferment lactose

- Two species: S. enterica and S. bongori
- Enterocolitis (tummy problems):
    - S. enterica serovar Enteritidis
    - S. enterica serovar Typhimurium

- Enteric fever:
    - S. enterica serovar Typhi
    - S. enterica serovar Paratyphi
    -

S. enterica serovar Enteritidis: Enterocolitis

- Pathogenesis depends on:
    - Dose of ingested organism (min 105)
    - Immune status of host
    - Virulence of strain
- Incubation time: 6-48h; multiplication in small intestine

Enterocolitis

- Symptoms
    - Nausea, vomiting, profuse diarrhea, abdominal pain
    - Fever, chills, headache, myalgia
    - 2-3 days recovery
    - Septicaemia: Rare
- Use stool culture for lab diagnosis

S. enterica serovar Enteritidis: Enterocolitis

- Ingestion of contaminated food
- Poultry, eggs, meat and milk
- Person to person spread
- Most cases occur at home
- Under-reported and undiagnosed
- Antibiotics NOT RECOMMENDED WHY?
    -

Enteric Fever

- S. enterica serovar Typhi typhoid fever
- S. enterica serotypes Paratyphi A, Schottmuelleri, Hirschfeldii paratyphoid fever (milder)
- Enteric fever: generalized infection; bacterial multiplication in lymphoid tissue
- Necrosis of intestinal lymphoid tissue ulceration, hemorrhage, perforation
- Untreated: 10% mortality
- Convalescent carriers: excrete bacteria for 3 months

- Chronic carriers (1-2%): excrete bacteria for at least 6 months, sometimes life long
- Diagnosis: Isolation of bacteria from blood (1st week) Stool and urine (2nd-3rd week)
- Infective dose is 106 organisms
- Sources are contaminated drinking water, shellfish, milk and milk products
- Clean handling of food, water treatment and safe sewage disposal are essential
- Vaccine available, but only effective against small bacterial load

Escherichia coli

- Most numerous aerobic bacteria of normal gut flora
- Lactose fermenting
- Pathogenic to other parts of the body
- responsible for 85% of bacteriuria
- pink

E. coli to Gastroenteritis

- Enterotoxigenic E. coli
- Infant diarrhea (developing countries)
- Traveller's diarrhea
- Enterotoxins
- Enteroinvasive E. coli
- Symptoms similar to shigellosis
- Enteropathogenic E. coli
    - older name for some serotypes causing infant diarrhoea
- E. coli O157:H7
    - Hemorrhagic colitis
    - Hamburger disease
    - Proper handling of food, safe preparation and proper cooking practices are essential to prevent illness
- E. coli is also implicated in neonatal meningitis and nosocomial urinary and wound infections

Shigella

- Cause acute diarrhea with mucus, pus and blood
- Generally non-lactose fermenters
- Shigella sonnei to Europe and North America
- S. dysenteriae:
    - Tropics
    - EVERE illness: watery diarrhea, cramps, fever
    - Infection from SMALL numbers of organism
- Most commonly seen in children; poor sanitation and crowding
- Prevention by safe handling of food, treatment of water, safe disposal of sewage
- NO VACCINE
- Very small numbers of shigella can cause problems, found in kids because their immune system is not strong enough

Vibrio cholerae

- Causes cholera: acute gastrointestinal illness
- Profuse watery diarrhea, cramps and vomiting
- Enterotoxin binds cells in small intestine
    - Cells secrete chlorides, Na+ absorption
    - Water accumulates in gut to watery diarrhea
    - Can lead to severe dehydration and death if untreated
- Endemic in South East Asia and parts of Africa
    - Lack of clean drinking water!
- Mainly water-borne
- Massive (10-15 liters per day) loss

Campylobacter
- C. jejuni and C. coli
- Major cause of human enteritis
- Normal flora in birds and domestic animals
- Some strains invasive, others toxigenic
- Symptoms: fever, abdominal pain, bloody diarrhea
- Maybe one cause of traveler's diarrhea

Pseudomonas
- Opportunistic pathogen
- Found in many moist habitats and water
- Source of infection can be humidifiers etc.
- Treatment is difficult because all Pseudomonas sp. are resistant to many antibiotics!!!!

Pseudomonas aeruginosa
- Respiratory pathogen in cystic fibrosis patients
- Infections in lesions of burn patient

Pseudomonas cepacia
- Common contaminant of saline solutions and water
- Able to multiply in low nutrient environment
- Respiratory pathogen of cystic fibrosis patients

Haemophilus influenzae
- part of normal nasopharyngeal flora in many adults and children
- Causes invasive infections of young children
    - Meningitis, pneumonia, joint infections
    - Development of vaccine, now used routinely, decreased the number of cases in Canada
- Can cause increased bronchial inflammation in patients already having chronic bronchitis

Cronobacter spp
- Can cause nosocomial infections
- Wound infections, pneumonia, bacteremia
- C. sakazakii linked to infant illness from powdered infant formula

Helicobacter pylori

- Microaerophilic, spiral bacilli
- Most common cause of stomach ulcers
    - In the past, cause was thought to be stress and diet
    - 1982-Dr.Robin Warren and Dr. Barry Marshall discovered link between H. pylori and ulcers
    - Medical community slow to accept their theory (1994- National Institute of Health Conference concludes strong association between ulcers and H. pylori)
- Urease: protection from low pH
- Triple therapy treatment: antibiotics and H+ pump inhibitors

Bordetella pertussis

- Whooping cough *VIOLENT COUGH*
- 4 Virulence Factors
    - Pertussis toxin (A-B)
    - Extra cytoplasmic adenylate cyclase (weakens host defense)
    - Filamentous hemagglutinin (bronchial attachment and exotoxin release)
    - Tracheal cytotoxin (destroys ciliated cells poor clearance of mucus and bacteria)
- Prevention: vaccination with heat-killed organism

Legionella pneumophila

- Causes Legionnaires disease
- Opportunistic pathogen
- May cause severe pneumonia
- Grows in water and is found in shower heads, water tanks, air cooling/heating tanks
- Exposure is by aerosol and there is NO person-to-person transmission