

Gram Positive and Negative Bacilli

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Spore Forming Rods

- Bacillus and Clostridium
- Release of potent exotoxins causes disease

Bacillus Anthracis

- Causative agent of anthrax
- Unique protein capsule, antiphagocytic
- 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 animals or soil
- Used in bio-terrorism and warfare

Bacillus Anthracis Exotoxin

- Encoded on pXO1 plasmid
 - Plasmid contains virulence factors which are transcribed optimally at 37C, increased carbon dioxide and serum proteins
 - Where are these conditions found?
- Exotoxin composed of three separate proteins:
 - Edema factor (EF)
 - Protective antigen (PA)
 - Lethal factor (LF)
 - Separately proteins are not toxic, but combined are lethal
- pXO2 plasmid encodes capsule genes
- Both plasmids required for virulence
- Prevention and treatment
 - Rapid treatment is essential
 - Antibiotics: penicillin, doxycycline, ciprofloxacin or levofloxacin
 - Vaccine against PA protein is available

Bacillus cereus

- Causes food poisoning when spores enter food product

- Motile, non-encapsulated, resistant to penicillin
- Enterotoxin is responsible for illness
- Two types of enterotoxin
 - a. Heat labile: nausea, abdominal pain, diarrhea, lasts 12-24 hours
 - b. Heat stable: severe nausea and vomiting, short incubation
- Antibiotic treatment useless... preformed toxins

Clostridium

- Anaerobic >> differentiates this bacteria from other spore-forming bacilli
- Botulism, tetanus, gas gangrene and pseudomembranous colitis
- Powerful exotoxins >> rapid diagnosis

Clostridium Botulinum

- Rapidly 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
- Smoked fish, improperly canned vegetables
 - Proper cooking destroys spores
- Action of Botulinum Neurotoxin
 - Acetylcholine induces contraction of muscle fibers
 - Botulinum toxin blocks release of acetylcholine inhibiting contraction
- Infant Botulism
 - Honey contamination with spores
 - Spores germinate and bacteria colonizes intestine
 - Neurotoxin release >> 2-3 days of constipation >> trouble swallowing, muscle weakness

Clostridium Tetani

- 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

Clostridium Perfringens

- Gas gangrene
- Seen in soldiers wounded in battle
- Two classes of infection:
 - a. Wound infection/cellulitis
 - Necrotic skin exposed to bacteria, damage to local tissues; skin feels moist, spongy, with 'crackly' pockets
 - b. 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

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
 - Administer metronidazole or vancomycin
 - What is different about these antibiotics?

Non-Spore Forming Rods

- Two medically important bacilli
 - *Listeria monocytogenes* and *Corynebacterium diphtheriae*

Listeria Monocytogenes

- Causative agent of listeriosis; immunocompromised are at high risk
- Found in foods such as soft cheeses, unpasteurized milk, cold cuts, pate
- Psychrophile >> survives in refrigerator
- Variety of symptoms:

- General malaise, diarrhea, meningitis, septicemia, still-birth/abortions
- Facultative intracellular aerobe
- Crosses three protective barriers (blood-brain, GI and feto-placental)
- Treatment: ampicillin or trimethoprim-sulfamethoxazole

Corynebacterium diphtheriae

- Causative agent of diphtheria
 - Colonization of pharynx and release of exotoxins into bloodstream
- Exotoxin damages heart and neural cells
- Treatment (3 steps):
 - Antitoxin
 - Penicillin or erythromycin
 - DPT vaccine
- Can be lysogenized by a bacteriophage (virus that infects bacteria)

Gram Negative Bacilli - The Enterics

Enterics

- Found as part of normal intestinal flora but can also cause disease
- Four major groups:
 - enterobacteriaceae (salmonellae, shingellae, 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
- What type of media are there?
 - Selective/differential
- H₂S production

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

Classification Using Surface Antigens

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

Diseases Caused by Enterics

- Cause diarrhoea with various complications and other infections
 - Diarrhea -with/without systemic invasion
 - Bacteria bind intestinal cells but do not enter
 - Exotoxin release causes diarrhoea; enterotoxin causes fluid/electrolyte loss
 - Watery diarrhoea, no fever
 - Vibrio cholera
 - Diarrhea with intestinal cell invasion
 - Bacterial virulence factors allow binding and invasion of cells
 - Toxin release destroys cells >> bloody stools
 - Fever response
 - Shigella
 - Diarrhea with invasion of lymph nodes and bloodstream
 - Abdominal pain with diarrhoea containing white and red cells
 - Fever, headache, increased with cell counts
 - Salmonella Typhi, Yersinia Enterocolitica, Campylobacter Jejuni

Other Enteric Infections

- Urinary tract infections, 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

- Unable to ferment lactose
- All have animal reservoirs except *S. enterica* serovar Typhi (humans are only host)
- Types of infections in humans: enterocolitis, enteric fever, opportunistic infections, septicemia and osteomyelitis
- 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 10^5)
 - Immune status of host
 - Virulence of strain
- Incubation time: 6-48h; multiplication in small intestine
- 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?

Enterocolitis

- Symptoms
 - Nausea, vomiting, profuse diarrhoea, abdominal pain
 - Fever, chills, headache, myalgia
 - 2-3 days recovery
 - Septicaemia >> rare
- Use stool culture for lab diagnosis

Enteric Fever

- *S. enterica* serovar Typhi >> typhoid fever
- *S. enterica* serotypes Paratyphi A, Schottmuelleria Hirschfeldii >> paratyphoid fever (milder)

- Enteric fever: generalized infection; bacterial multiplication in lymphoid tissue
- Necrosis of intestinal lymphoid tissue >> ulceration, haemorrhage, 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 (first week) stool and urine (second to third week)
- Infective dose is 10^6 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

e. coli >> Gastroenteritis

- Enterotoxigenic E. coli
 - Infant diarrhoea (developing countries)
 - Traveller's diarrhoea
 - Enterotoxins
- Enteroinvasive E. coli
 - Symptoms similar to shigellosis
- Enteropathogenic E. coli
 - Older name for some serotypes causing infant diarrhoea
- E. coli O157:H7
 - Haemorrhagic 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

Shigellae

- Cause acute diarrhoea with mucus, pus and blood
- Generally non-lactose fermenters

- Generally non-invasive
- Dose of 10^5 infects 25% of people, 10^9 infects 95%
- *Shigella sonnei* >> Europe and North America
- *S. dysenteriae*:
 - Tropics
 - Severe illness: watery diarrhoea, cramps, fever
 - Infection from small numbers of organisms
- Most commonly seen in children; poor sanitation and crowding
- Prevention by safe handling of food, treatment of water, safe disposal of sewage
- No vaccine

Vibrio Cholerae

- Causes cholera: acute gastrointestinal illness
- Profuse watery diarrhoea, cramps and vomiting
- Enterotoxin binds cells in small intestine
 - Cells secrete chlorides, decreasing sodium absorption
 - Water accumulates in gut >> watery diarrhoea
 - 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 litres 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 diarrhoea
- Maybe one cause of traveller's diarrhoea

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 patients

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

Enterobacter spp.

- Can cause nosocomial infections
- Wound infections, pneumonia, bacteremia
- *E. 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
- Four virulence factors

- Pertussis toxin (A-B)
- Extra cytoplasmic adenylate cyclase (weakens host defense)
- Filamentous hemagglutinin (brochial attachment and exotoxin release)
- Tracheal cytotoxin (destroys ciliated cells >> poor clearance of mucous 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