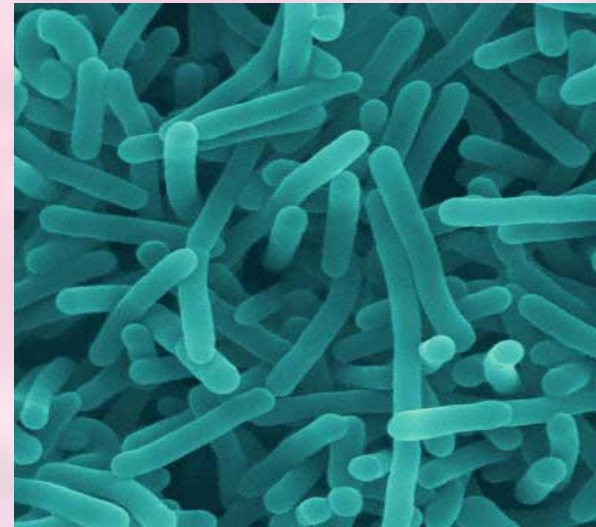
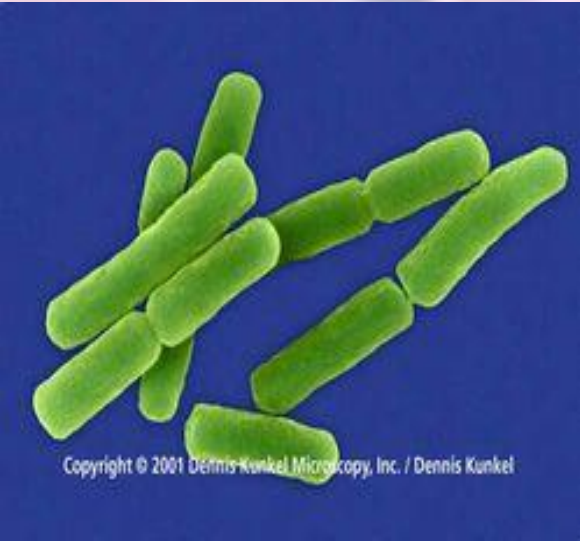
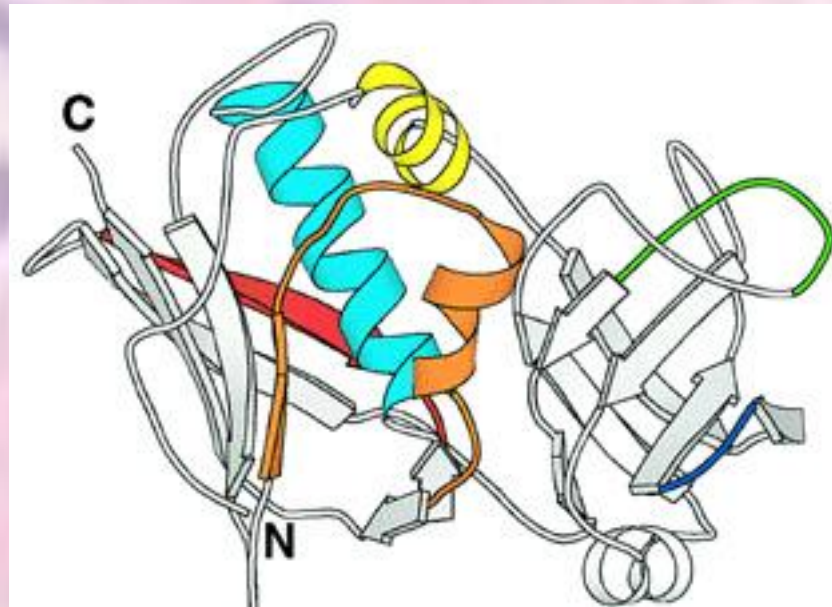


Gram Positive Bacilli



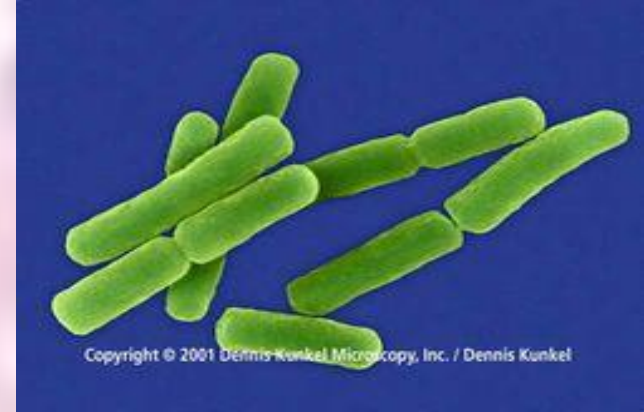
Spore Forming Rods

- *Bacillus* and *Clostridium*
- Release of potent exotoxins causes disease

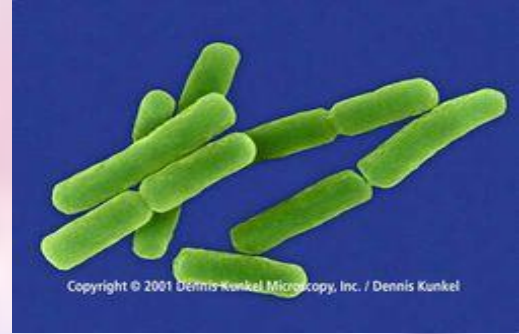


Bacillus anthracis

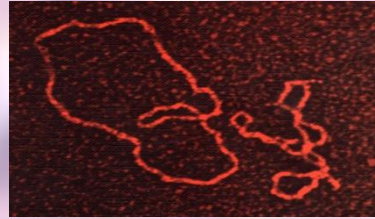
- Causative agent of anthrax
- UNIQUE protein capsule, antiphagocytic
- Aerobic growth conditions
- Spores are very stable, resistant to heat, drying, UV and disinfectants; spores germinate and toxins are made
- Humans exposed to spores usually through contact with animals or soil
- Used in bio-terrorism and warfare



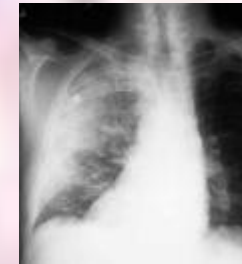
Bacillus anthracis exotoxin



- Encoded on pXO1 plasmid



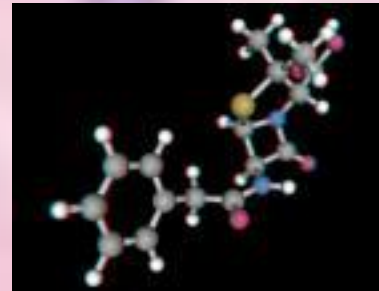
- Plasmid contains virulence factors which are transcribed optimally @ 37 C, increased CO₂ and serum proteins
- ?? Where are these conditions found ??



- Exotoxin composed of 3 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, doxycyclin, ciprofloxacin or levofloxacin
- Vaccine against PA protein is available



PENICILLIN

Remember:

- capsule protects AND is made of protein
- cutaneous and respiratory routes for spores
 - animal hides and/or soil

Bacillus cereus

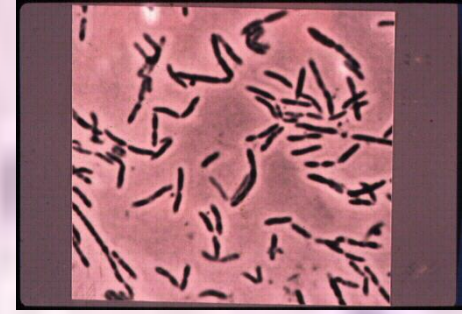


- Causes food poisoning when spores enter food product



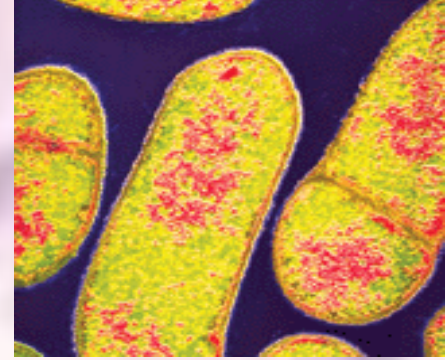
- Motile, non-encapsulated, resistant to penicillin
- ENTEROTOXIN is responsible for illness
- 2 types of enterotoxin
 - (i) Heat labile: nausea, abdominal pain, diarrhea. Lasts 12-24hrs
 - (ii) Heat stable: SEVERE nausea and vomiting, short incubation
- Antibiotic treatment useless....preformed toxins

Clostridium



- Anaerobic → differentiates this bacteria from other spore-forming bacilli
- Botulism, tetanus, gas gangrene and pseudomembranous colitis
- POWERFUL EXOTOXINS → RAPID DIAGNOSIS

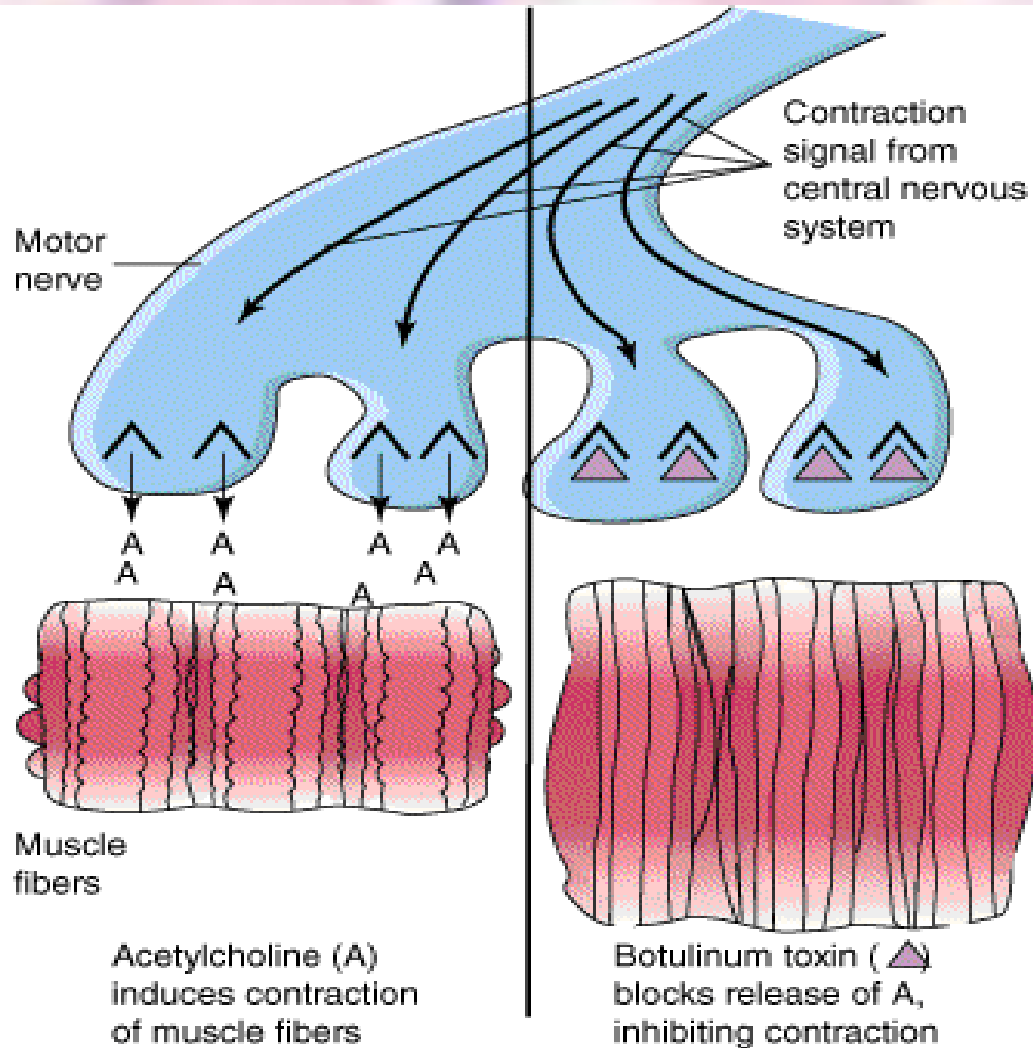
Clostridium botulinum



- 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



Infant Botulism

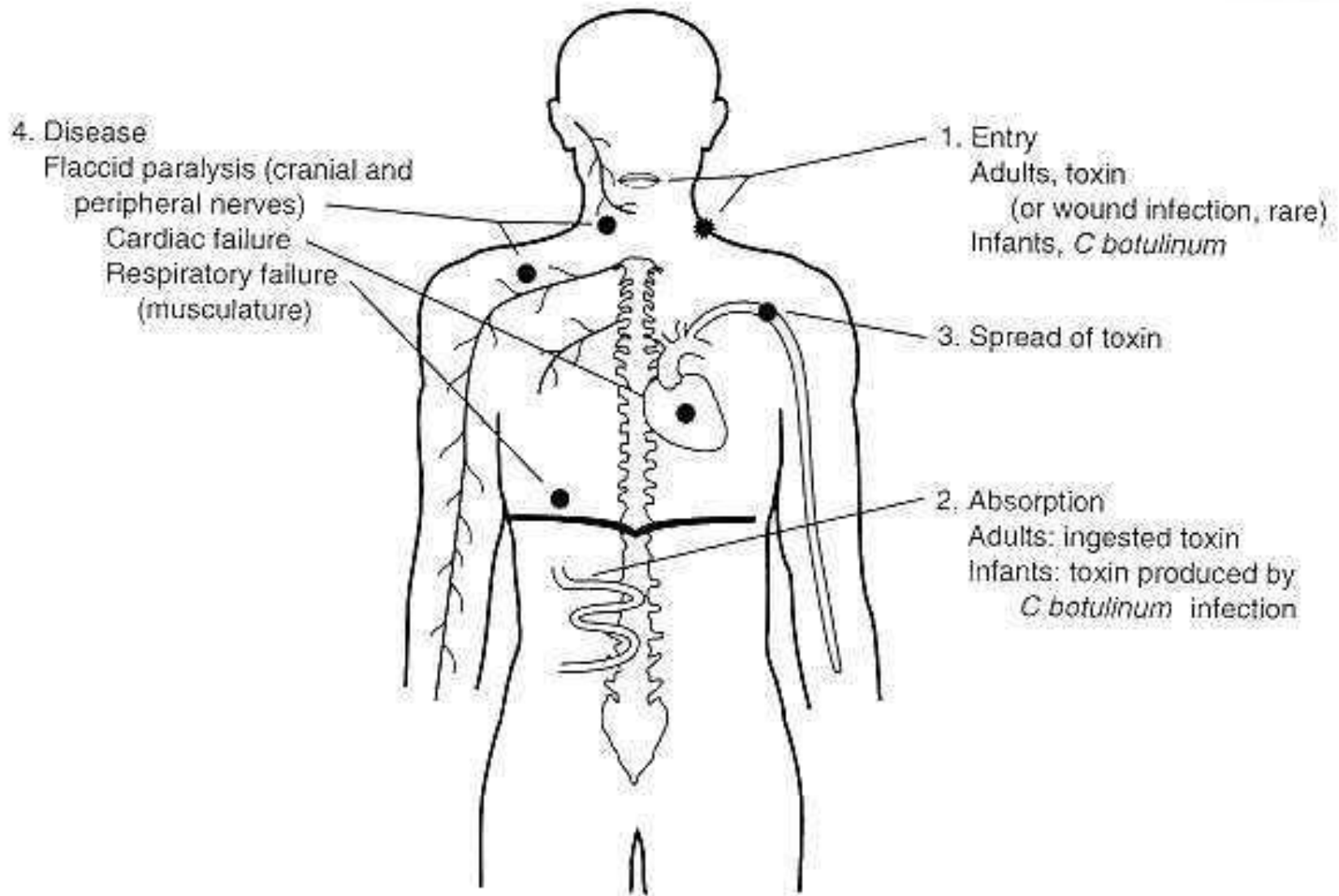
- Honey contamination with spores
 - Spores germinate and bacteria colonizes intestine
 - Neurotoxin release

2-3 days of constipation

Trouble swallowing, muscle weakness



Clinical Manifestations of *Clostridium botulinum*

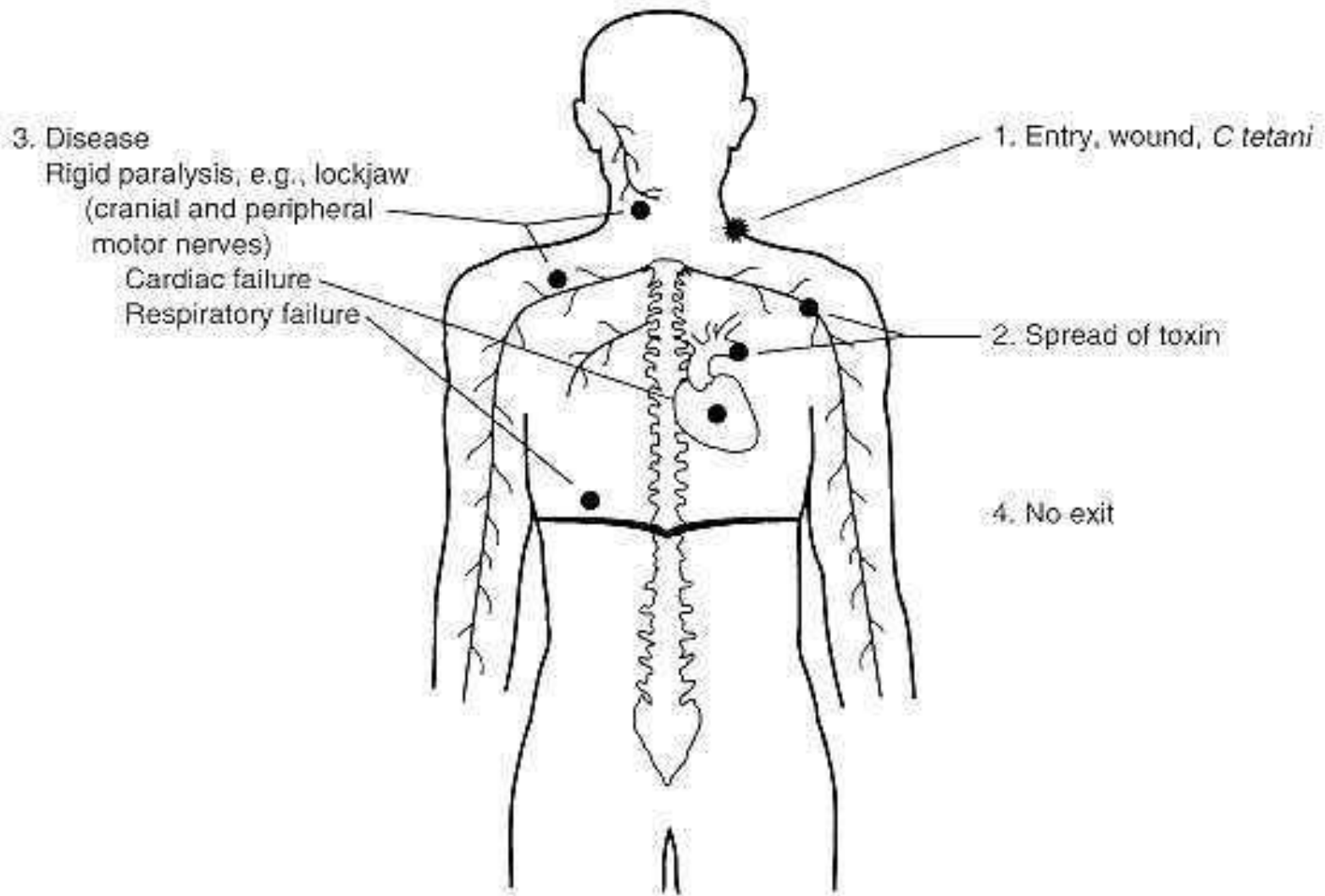


Clostridium tetani

- 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



Clinical Manifestations of *Clostridium tetani*



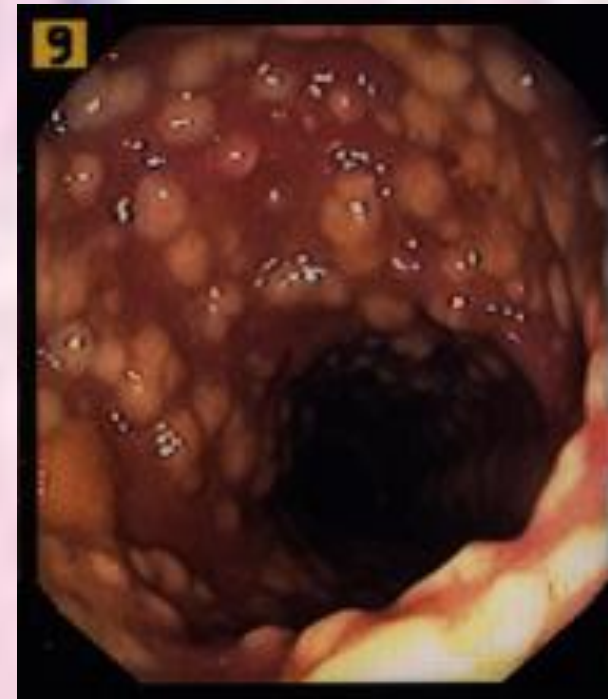
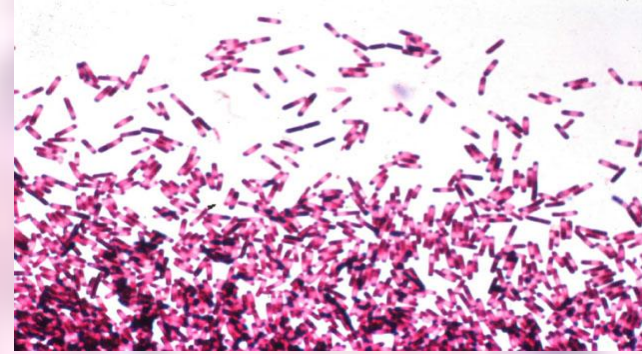
Clostridium perfringens



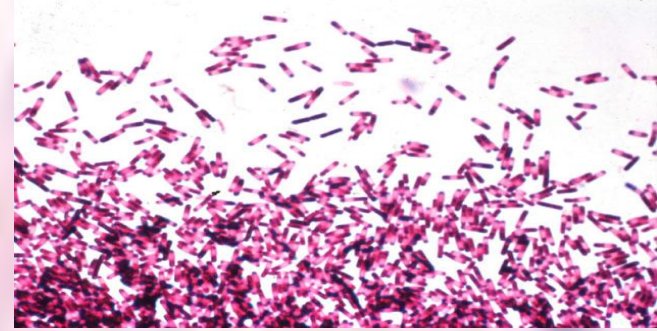
- Gas gangrene
- Seen in soldiers wounded in battle
- 2 classes of infection:
 - (i) Wound infection/cellulitis
 - necrotic skin exposed to bacteria, damage to local tissues; skin feels moist, spongy, with 'crackly' pockets
 - (ii) Clostridial myonecrosis
 - bacteria inoculated from trauma into muscles; 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

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

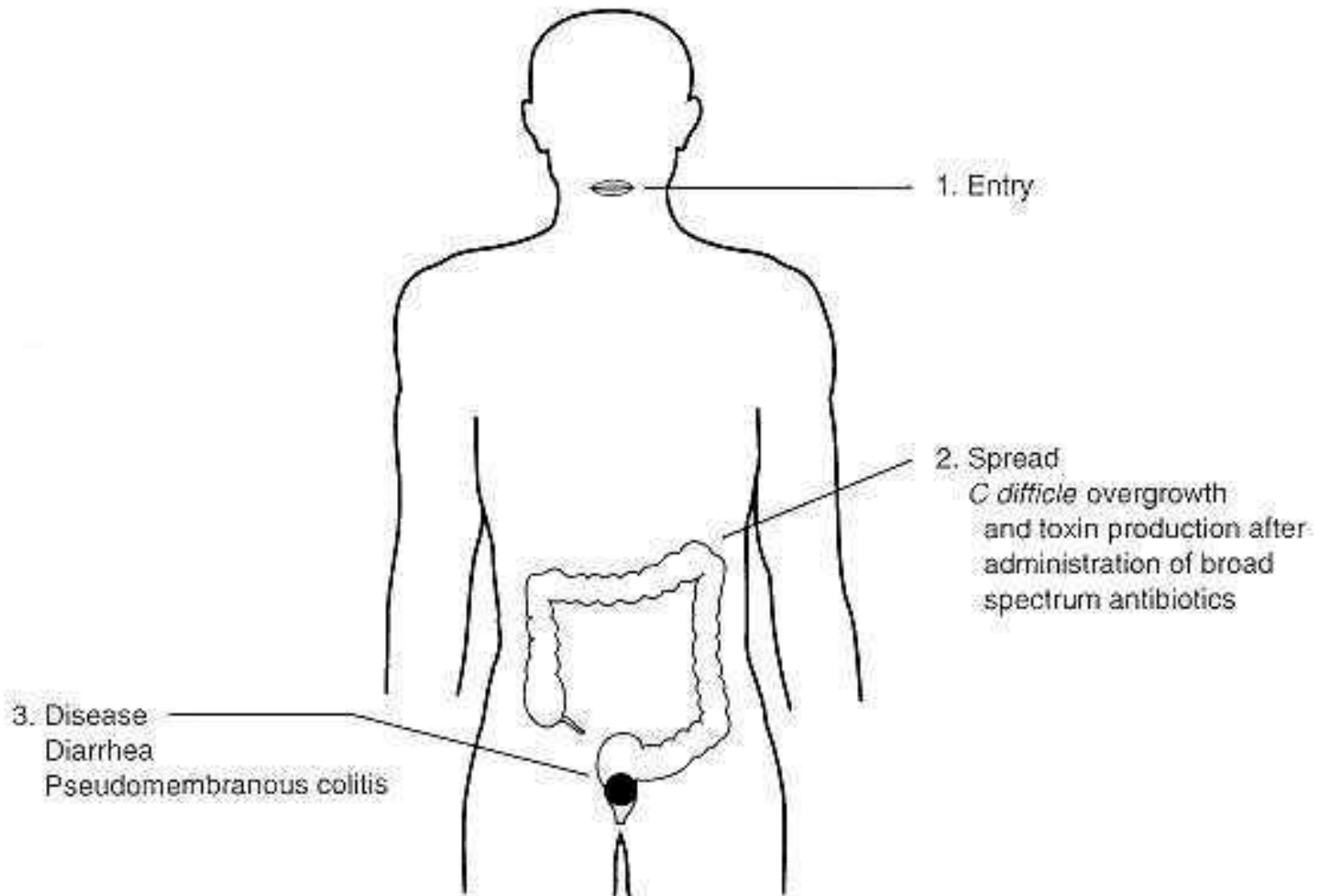


Clostridium difficile



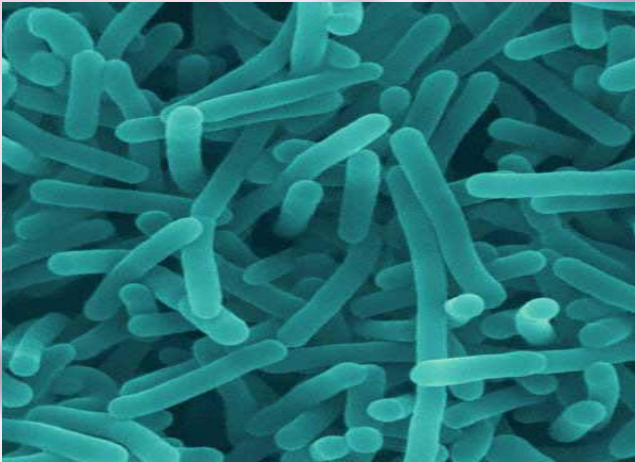
- Symptoms: severe diarrhea, abdominal cramping, fever
- Possible cause of diarrhea in patients on antibiotics
- Treatment
 - discontinue antibiotic treatment
 - Administer metronidazole or vancomycin
 - ?? What is different about these antibiotics ??

Clinical manifestations of *Clostridium difficile*



Non-Spore Forming Rods

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

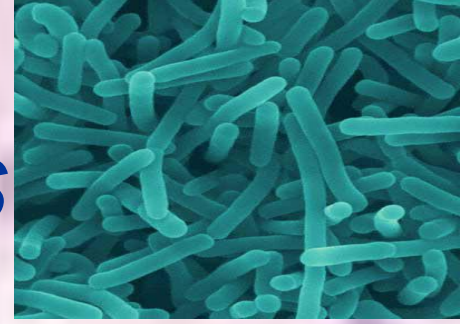


L. monocytogenes

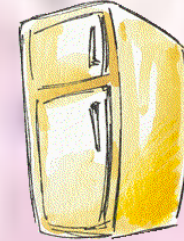


C. diphtheriae

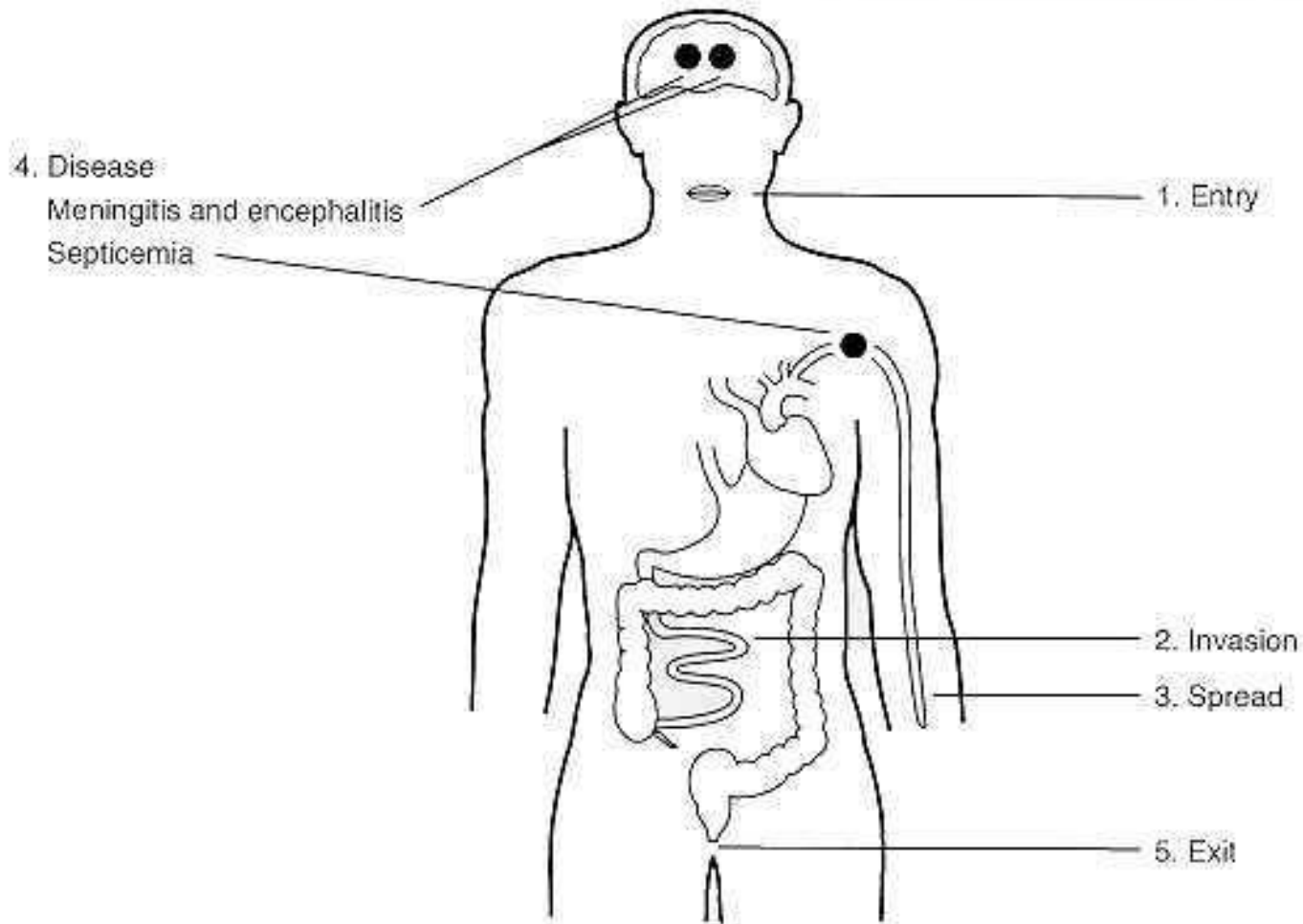
Listeria monocytogenes



- 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 feto-placental)
- Treatment: ampicillin or trimethoprim-sulfamethoxazole



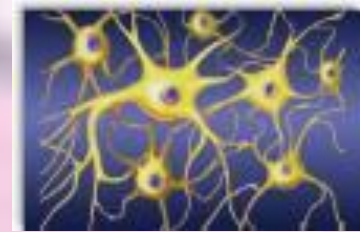
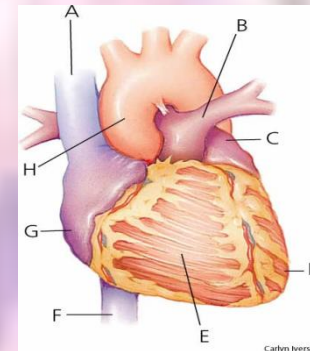
Clinical Manifestations of *Listeria monocytogenes*



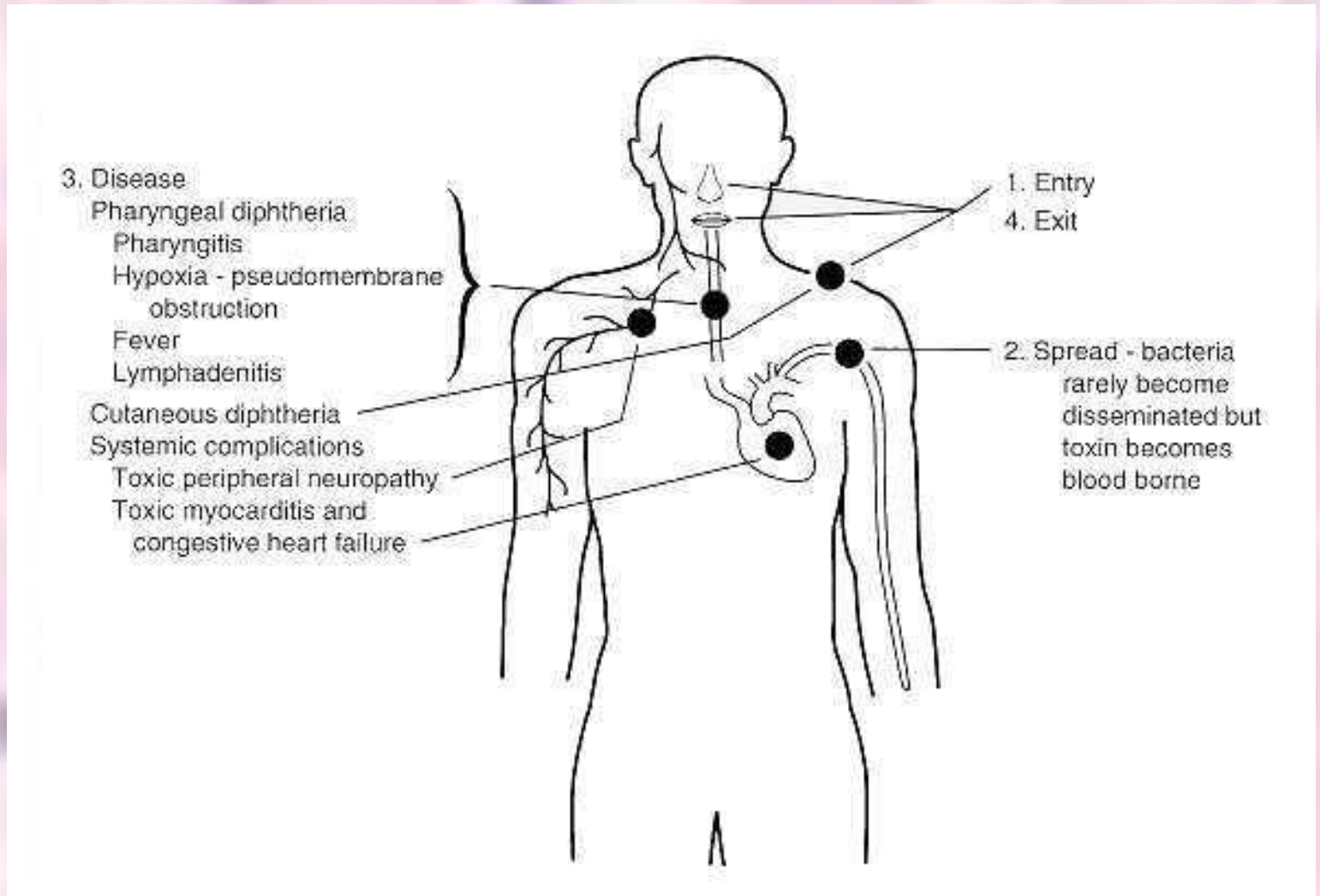
Corynebacterium diphtheriae



- Causative agent of diphtheria
 - 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)

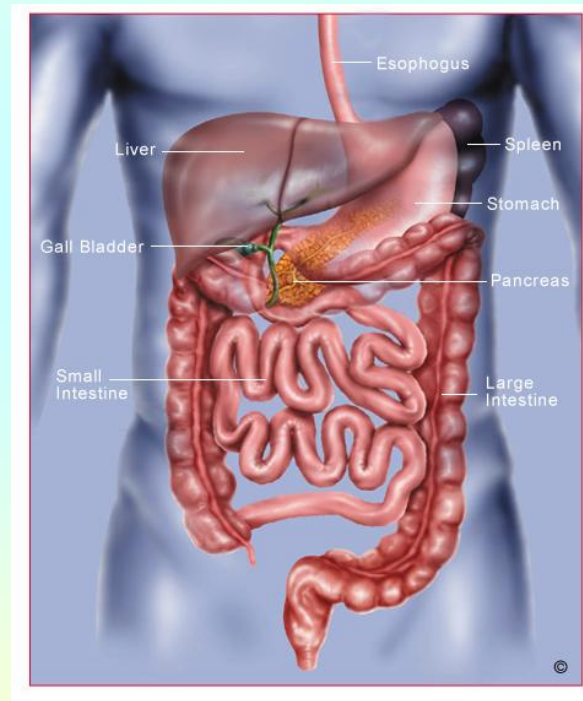


Clinical manifestations of *C. diphtheriae*



Gram Negative Bacilli

The Enterics



Enterics

- Found as part of normal intestinal flora BUT can also cause disease
- 4 Major Groups: Enterobacteriaceae (Salmonellae, Shigellae, *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 fermentors are dark purple/black
 - Inhibits Gram positive bacteria
 - MacConkey Media:
 - Lactose fermentors are pink-purple
 - Inhibits Gram positive bacteria



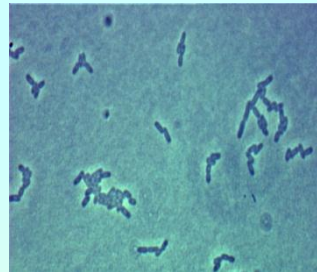
?? What type of media are these ??
SELECTIVE/DIFFERENTIAL

Biochemical Classifications cont'd



- H₂S production
- Hydrolysis of urea

- Liquefy gelatin

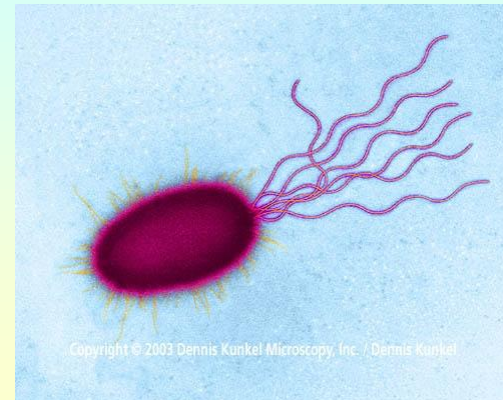


- Decarboxylation of amino acids



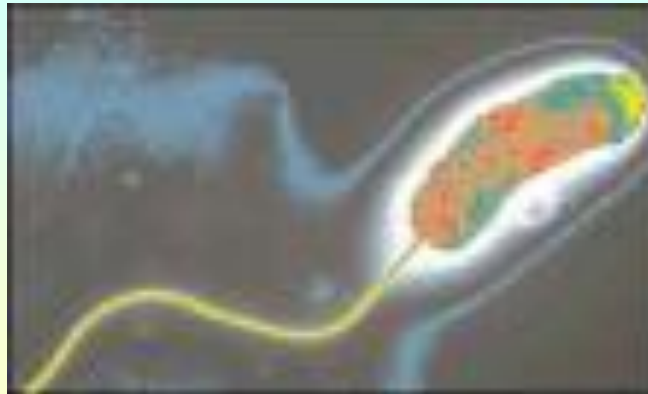
Classification Using Surface Antigens

- 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
- 1) 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
 - ETEC and *Vibrio cholera*

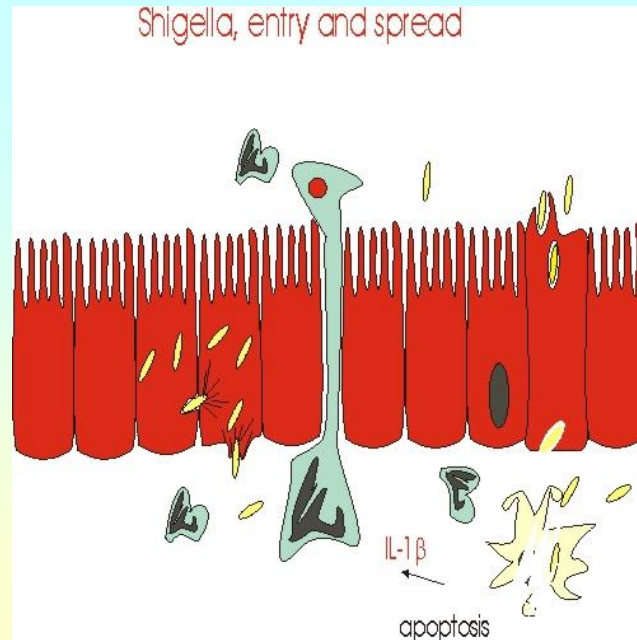


Vibrio cholera

Enteric Diseases cont'd

2) Diarrhea with intestinal cell invasion

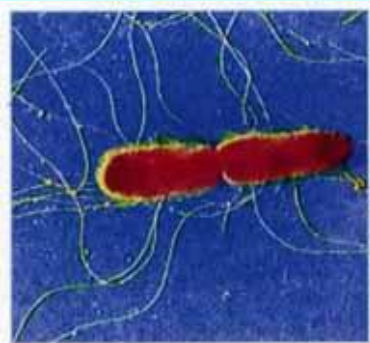
- Bacterial virulence factors allow binding and invasion of cells
- Toxin release destroys cells → bloody stools
- Fever response
- EIEC, *Shigella*, *Salmonella* enteritidis, VTEC



Enteric Diseases cont'd

3) Diarrhea with invasion of lymph nodes and bloodstream

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



S. Typhi



Y. enterocolitica



C. jejuni

Other Enteric Infections

- Urinary tract infects, 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

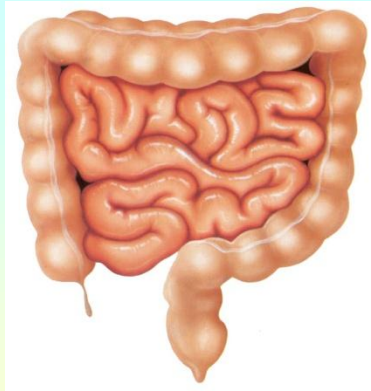


- Member of Enterobacteriaceae family
- Unable to ferment lactose
- All have animal reservoirs EXCEPT *S. enterica* serovar Typhi → Humans
- Two species: *S. enterica* and *S. bongori*
- Enterocolitis (tummy problems):
 - *S. enterica* serovar Enteritidis
 - *S. enterica* serovar Typhimurium
- Enteric fever:
 - *S. enterica* serovar Typhi
 - *S. enterica* serovar Paratyphi
- Types of infections in humans: enterocolitis, enteric fever, opportunistic infections, septicemia and osteomyelitis

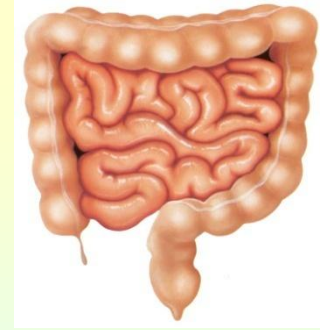
S. enterica serovar Enteritidis

→ 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



Enterocolitis



- **Symptoms**

- Nausea, vomiting, profuse diarrhoea, abdominal pain
- Fever, chills, headache, myalgia
- 2-3 years recovery
- Septicaemia → Rare



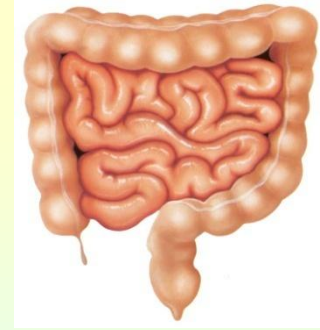
- Use stool culture for lab diagnosis



***Salmonella* on MacConkey**

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, 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



Enteric Fever

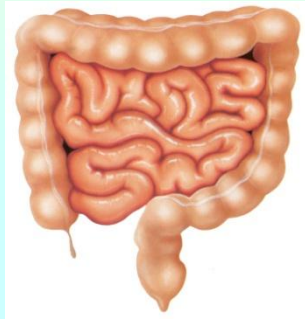


- Diagnosis: Isolation of bacteria from blood (1st week)
Stool and urine (2nd-3rd week)
- Infective dose is 10^6 organisms
- Sources are contaminated drinking water, shellfish, milk and milk products
- Clean handling of food, water treatment and safe sewage disposal are essential
- Vaccine available, but only effective against small bacterial load

Escherichia coli



- Most numerous aerobic bacteria of normal gut flora



- Lactose fermenting



***E. Coli* on
MacConkey agar**

- 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



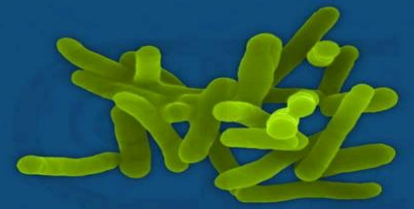
- Enteroinvasive *E. coli*
 - Symptoms similar to shigellosis

E. coli → Gastroenteritis

- Enteropathogenic *E. coli*
 - older name for some serotypes causing infant diarrhoea
- *E. coli* 0157: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 fermentors
- 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 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**





Vibrio cholerae



- Causes cholera: acute gastrointestinal illness
- Profuse watery diarrhoea, cramps and vomiting
- Enterotoxin binds cells in small intestine
 - Cells secrete chlorides, ↓ Na⁺ 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

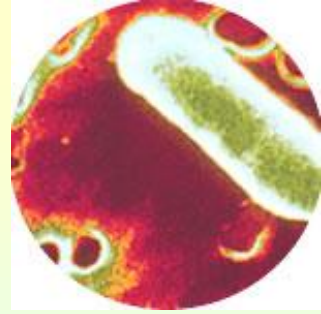


Pseudomonas cepacia

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



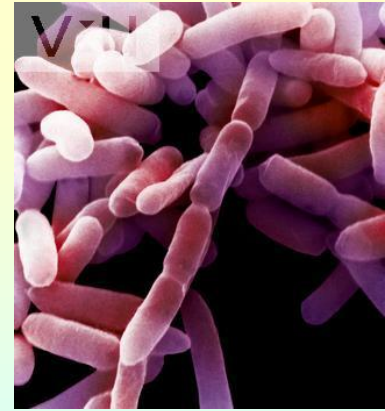
Haemophilus influenzae



- 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.



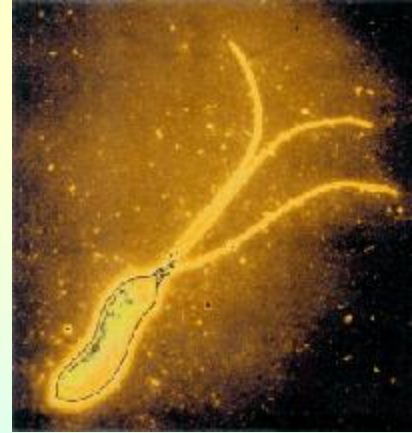
- Can cause nosocomial infections



- Wound infections, pneumonia, bacteremia
- *E. sakazakii* linked to infant illness from powdered infant formula



Helicobacter pylori

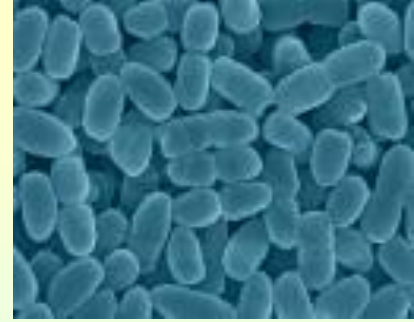


- Microaerophilic, spiral bacilli
- Most common cause of stomach ulcers
 - In the past, cause was thought to be stress and diet
 - 1982-Dr. Robin Warren and Dr. Barry Marshall discovered link between *H. pylori* and ulcers
 - Medical community slow to accept their theory (1994-National Institute of Health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



Duodenal Ulcer

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 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
- Exposure is by aerosol and there is **NO** person-to-person transmission