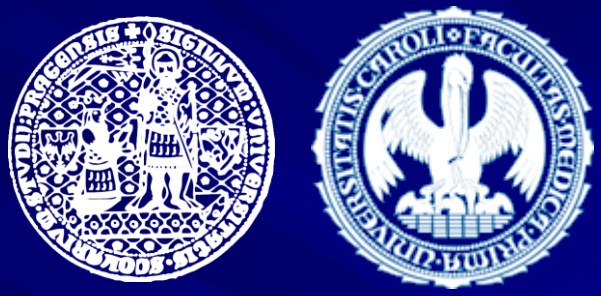
UNIVERSITAS CAROLINA PRAGENSIS

Charles University in Prague, First Faculty of Medicine



GRAM-NEGATIVE RODS

ENTEROBACTERIACEAE

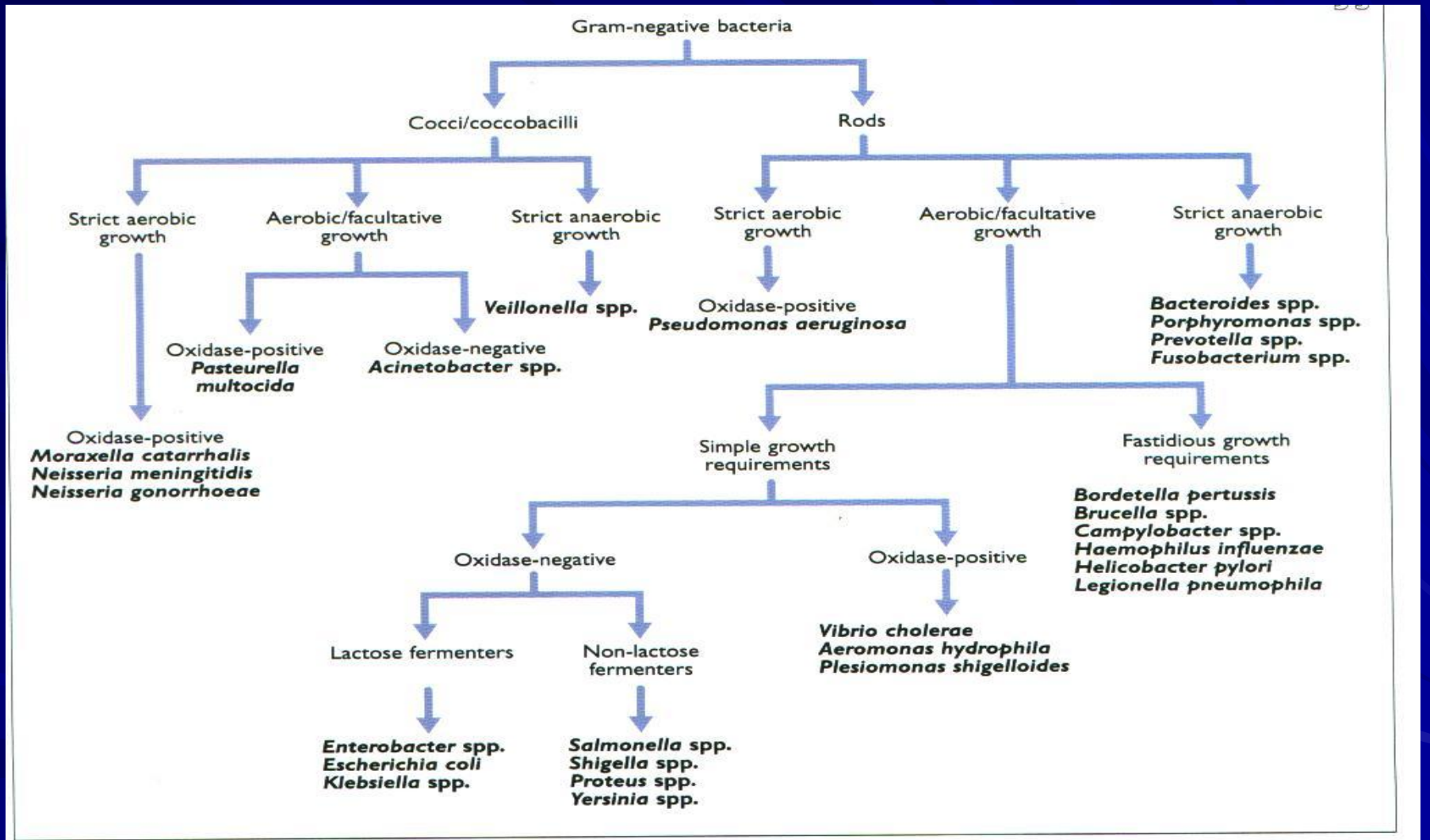
Department of Immunology and Microbiology and Department of Clinical Biochemistry and Laboratory Diagnostics

Author: MUDr. Emil PAVLÍK, CSc.

Subject: MICROBIOLOGY 1, MICROBIOLOGY 2

Date: 30.05.2013

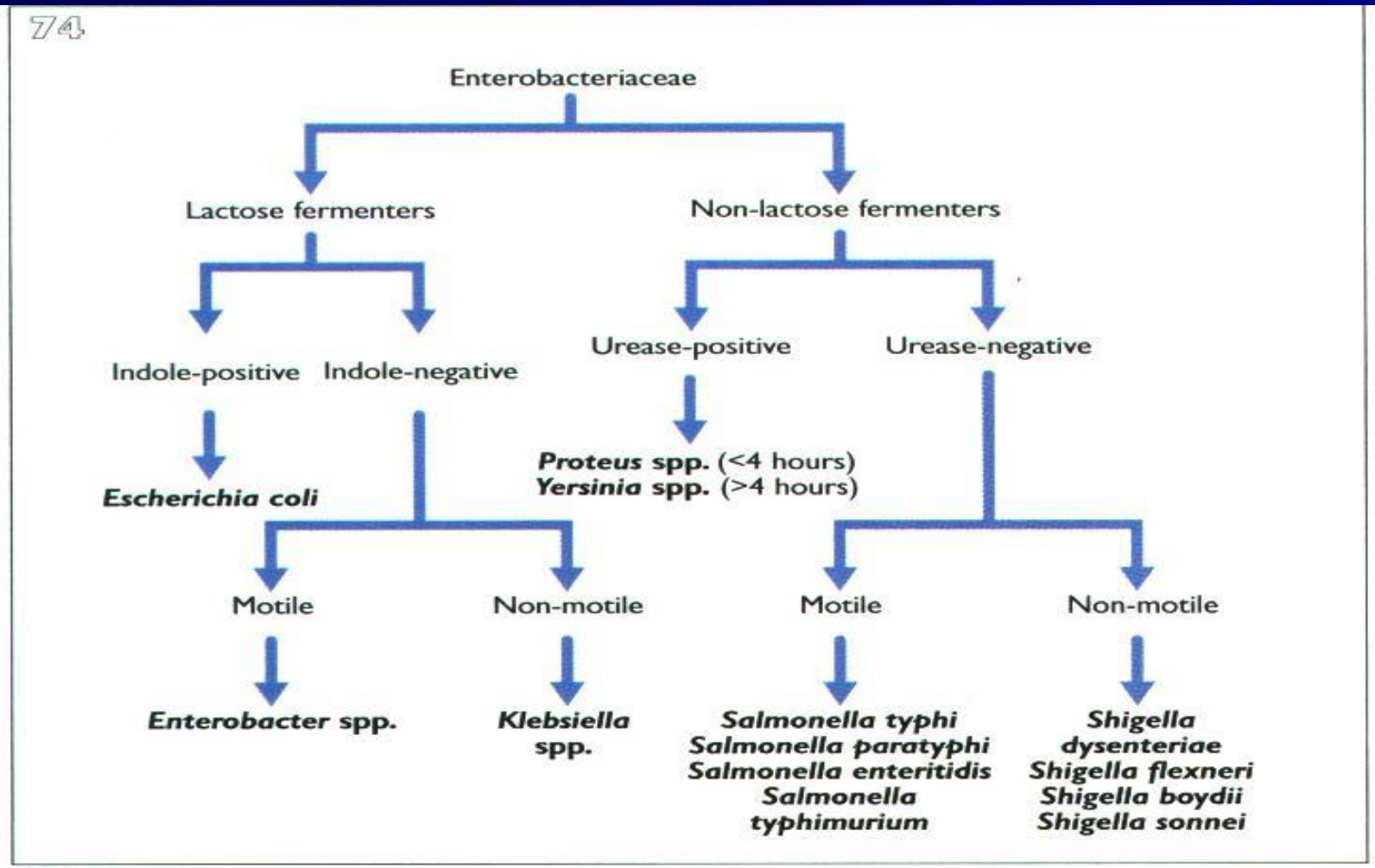
G- bacteria



53 Flow diagram showing the classification of gram-negative bacteria.

Murray P.R., Rosenthal K.S., Pfaller M.A.: MEDICAL MICROBIOLOGY 6th ED, Mosby/Elsevier 2009

G- rods



74 Flow diagram of the classification of members of the Enterobacteriaceae. Simple laboratory tests identify most bacteria to genus level.

Murray P.R., Rosenthal K.S., Pfaller M.A.: MEDICAL MICROBIOLOGY 6th ED, Mosby/Elsevier 2009

Family: ENTEROBACTERIACEAE

- Largest and most heterogenous collection of medically important G- bacilli
- 32 genera, over 130 species
- Classification based on:

  - biochemical properties

  - antigenic structure

  - nucleic acid hybridization and sequencing
- Less than 20 species responsible for over 95% of infections

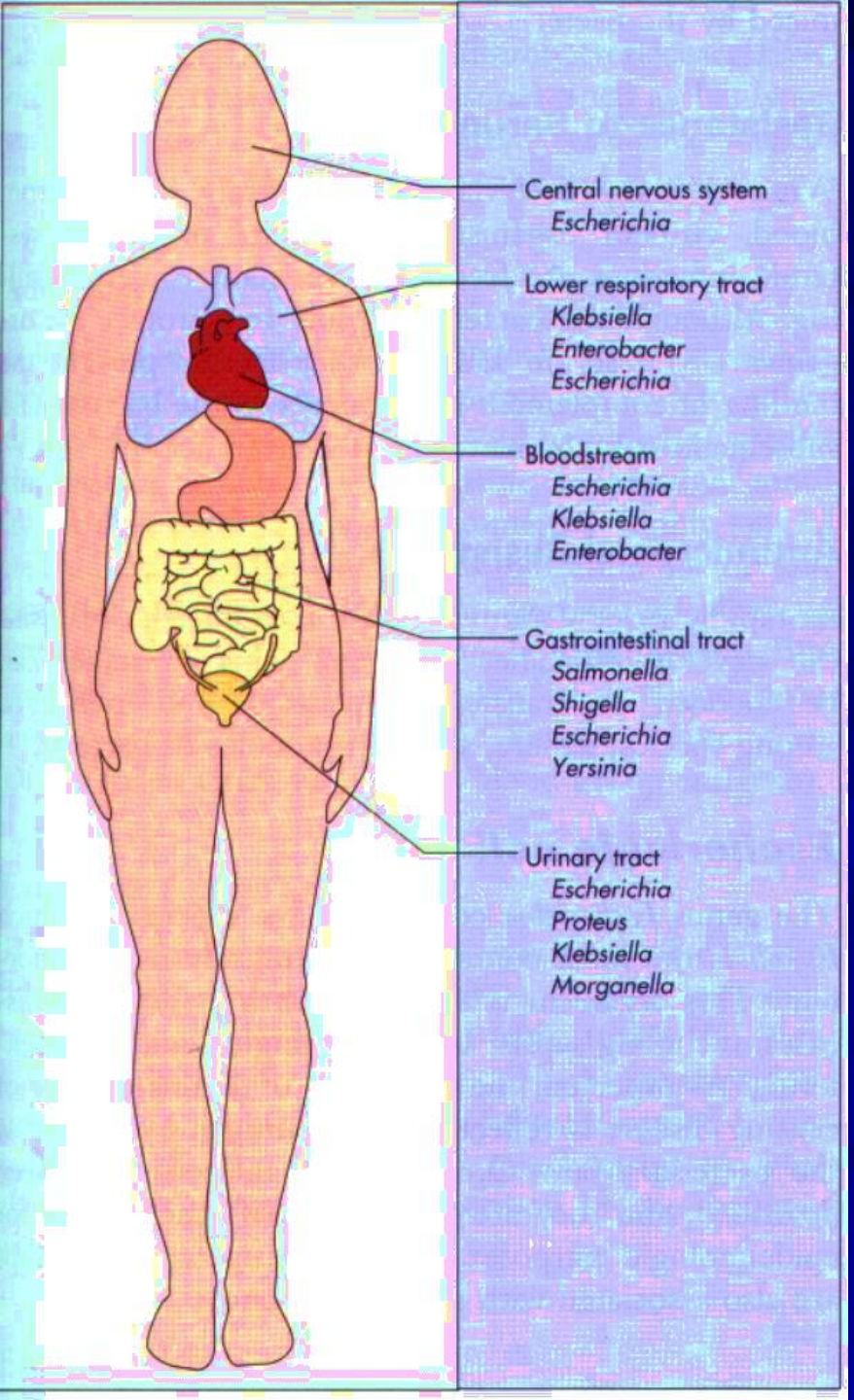
Enterobacteriaceae

- Ubiquitous organisms found worldwide in
  - soil
  - water
  -vegetation
- Some of them are part of normal intestinal flora of most animals
- Cause variety of human diseases:
  - up to 35% of all septicaemias
  - over 70% of urinary tract infections
  - diarrheas

- Some organisms are strict patogens: *Shigella, Salmonella typhi, Yersinia pestis* (always associated with disease)
- Members of normal intestinal flora able to cause opportunistic infections:

  Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae
- Normally commensal flora becoming pathogenic after acquiring virulence factor genes on plasmids, bacteriophages or pathogenicity islands:

  E.coli associated with gastroenteritis



COMMON MEDICALLY IMPORTANT ENTEROBACTERIACEAE:

Citrobacter fruendii, C. buseri, Enterobacter cloaceae, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca,Morganella morganii, Proteus vulgaris, Proteus mirabilis, Serratia marcescens, Shigella flexneri, Shigella sonnei, Salmonella typhi, Salmonella enterica,Yersinia pestis, Yersinia enterocolitica,

Y.pseudotuberculosis

Enterobacteriaceae infections

can originate from

- **animal reservoir:** most *Salmonella* and *Yersinia* species
- **human carrier:** *Salmonella typhi* and *Shigella* species
- through **endogenous spread** of organisms in a susceptible patient

Structure and Physiology

- Gram-negative bacilli
- Size: 0.3 – 1.0 x 1.0 – 6.0 μm
- Do not form spores (non-sporogenous)
- Motile (with peritrichous flagella) / non-motile
- Fast aerobic or anaerobic growth (facultative anaerobes) on variety of nonselective and selective media
- Ferment glucose, reduce nitrate, catalase+, oxidase- (absence of cytochromeoxidase)

Structure and Physiology – cont´d

- Lactose fermenting strains (Endo Agar): Escherichia, Klebsiella, Citrobacter, Serratia and Enterobacter
- Resistant to bile-salts: Salmonella, Shigella
- Some have prominent capsules (Klebsiella)
- Others surrounded by a diffusible slime layer
- Antigens:

somatic O polysaccharide + lipid A (endotoxin)

flagellar H proteins (heat-labile)

capsular K proteins or polysaccharides (heat-labile)

Antigenic structure

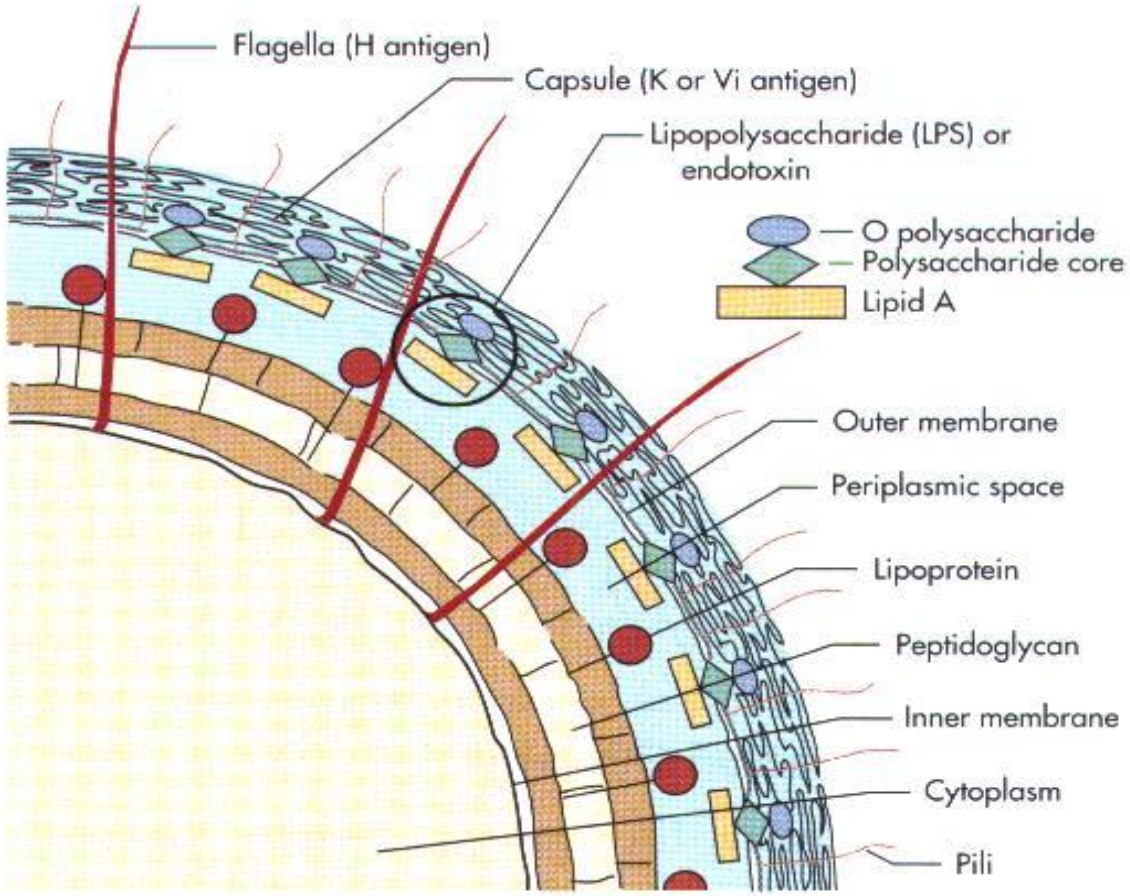


FIGURE 29–3. Antigenic structure of Enterobacteriaceae.

Pathogenesis and Immunity

- **FACTORS OF VIRULENCE:**
- **Endotoxin**
- **Capsule**
- **Antigenic Phase Variation**
- **Type III Secretion Systems**
- **Sequestration of Growth Factors**
- **Resistance to Serum Killing**
- **Antimicrobial resistance**

Endotoxin

Activity based on Lipid A released at cell lysis

- Activation of complement
- Release of cytokins
- Leukocytosis
- Thrombocytopenia
- Disseminated intravascular coagulation
- Fever
- Decreased peripherial circulation
- Shock
- Death

Capsule

- Protects bacteria from phagocytosis by hydrophilic capsular antigens which repel the hydrophobic phagocytic cell structure.
- These antigens interfere with the binding of antibodies to bacteria and are poor immunogens or complement activators.
- !!! Development of specific anti-capsullar antbodies

Antigenic Phase Variation

- Protects bacteria from antibody-mediated cell death
- = genetic control of expression of capsular and flagellar antigens
- Alternative expression of H and K antigens

Type III Secretion Systems

- Salmonella, Escherichia, Shigella, Yersinia have common effector system for delivering their virulence genes into targeted eukaryotic cells.
- Type III Secretion System consists of approx. 20 proteins that facilitate secretion of bacterial virulence into the host cell.
- In the absence of TIIISS the bacteria loose their virulence.

Sequestration of Growth Factors

- Nutritional scavengers of bacteria growing in vivo.
- Iron – bound in heme proteins (haemoglobin, myoglobin) or in iron-chelating proteins (transferrin, lactoferrin)

Bacteria counteract the binding by producing own competitive iron-chelating compounds (siderophore enterobactin)

Iron can also be released from host cells by hemolysins produced by bacteria.

Resistance to Serum Killing

- Virulent organisms capable for producing systemic infections are often resistant to serum killing:
- Bacterial capsule
- Factors preventing binding of complement components to the bacteria and
- subsequent complement-mediated clearence

Escherichia coli

- Normal flora of intestine
- Pathogenic effect depends on E. coli strain
- ETEC (enterotoxigenic)
- EPEC (enteropathogenic)
- EIEC (enteroinvasive)
- EHEC (enterohemorrhagic)

  HUS (hemolytic-uremic-syndrome)

UTI – have P pilli

Meningitis, pneumonia

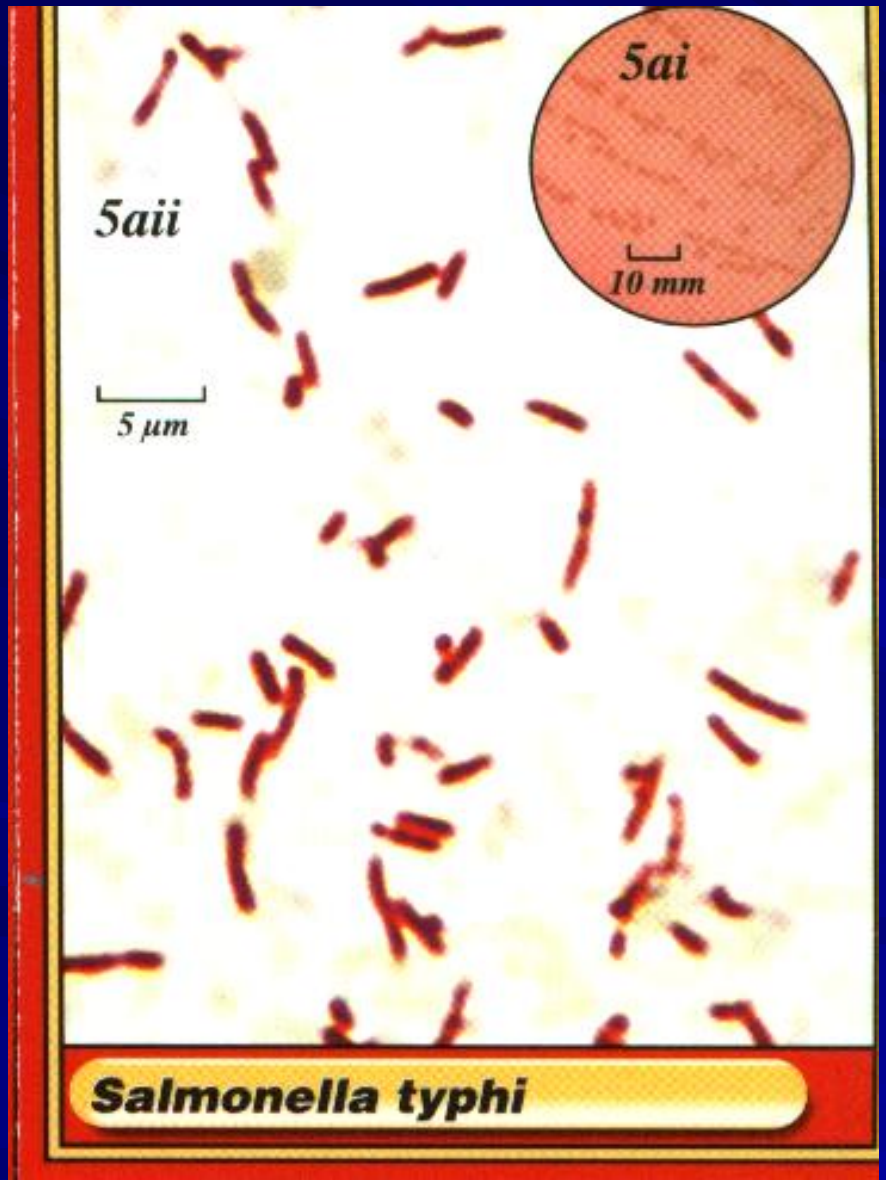
Escherichia coli

- **ETEC** – labile and/or stable toxins causes deregulation of intestinal cells and a volumi- nous watery diarrhea (traveller´s diarrhea)
- **EPEC** – binds to intestinal cells with bundle-forming pilli and causes cupping of intestinal epithelial cells, altered function, diarrhea.
- **EIEC** – Shigella-like: bind to and invade M cells – lateral spread to enterocytes. Cause bloody diarrhea.
- **EHEC** – bind to enterocytes by BFP, produce shigatoxin (causes bloody diarrhea) HUS – hemolytic uremic syndrom (hamburger disease)

Escherichia coli

- E. coli with K1 capsule – newborn meningitis
- Pneumonia: aspiration of GIT organisms
- Urinary tract infections
- Immunity : strain-specific. Protective antibodies against toxins, pilli, adhesins
- Epidemiology: contaminated food, carriers, endogenous infections – displacement from GIT
- Diagnostics: culture+microscopy, lactose +, biochemical properties, serotyping (O,H,K).

Salmonella



- S. typhi
- S. paratyphi
- S. typhimurium
- S. enterica

- Salmonella typhi

Diseases caused: typhoid fever (blood-born infection involving multiple organs, starting as obstipation

Carriers of salmonella

Salmonella typhi

- **Pathogenesis**: Salmonella typhi invades through M cells in the small intestine – transport through lymphatics --- bloodstream --- phagocy-tosis of organisms – grow in macrophages of the liver, spleen and other organs.

Typhoid fever – organisms released from lysed macrophages reseed the bloodstream

Carriers harbor bacteria in tissues (gall bladder) and pass microorganisms in the stools

Immunity: protective antibodies to O-antigen (LPS), vaccination

Salmonella typhi

- **Epidemiology:** human-human spread, water contaminated with feces (drinking water)
- **Diagnostics:** culture (blood, endo, DC-agar, Wilson-Blair agar, McConkey agar)

  G- bacilli with flagella

  Serotyping (O,H,Vi antigens)

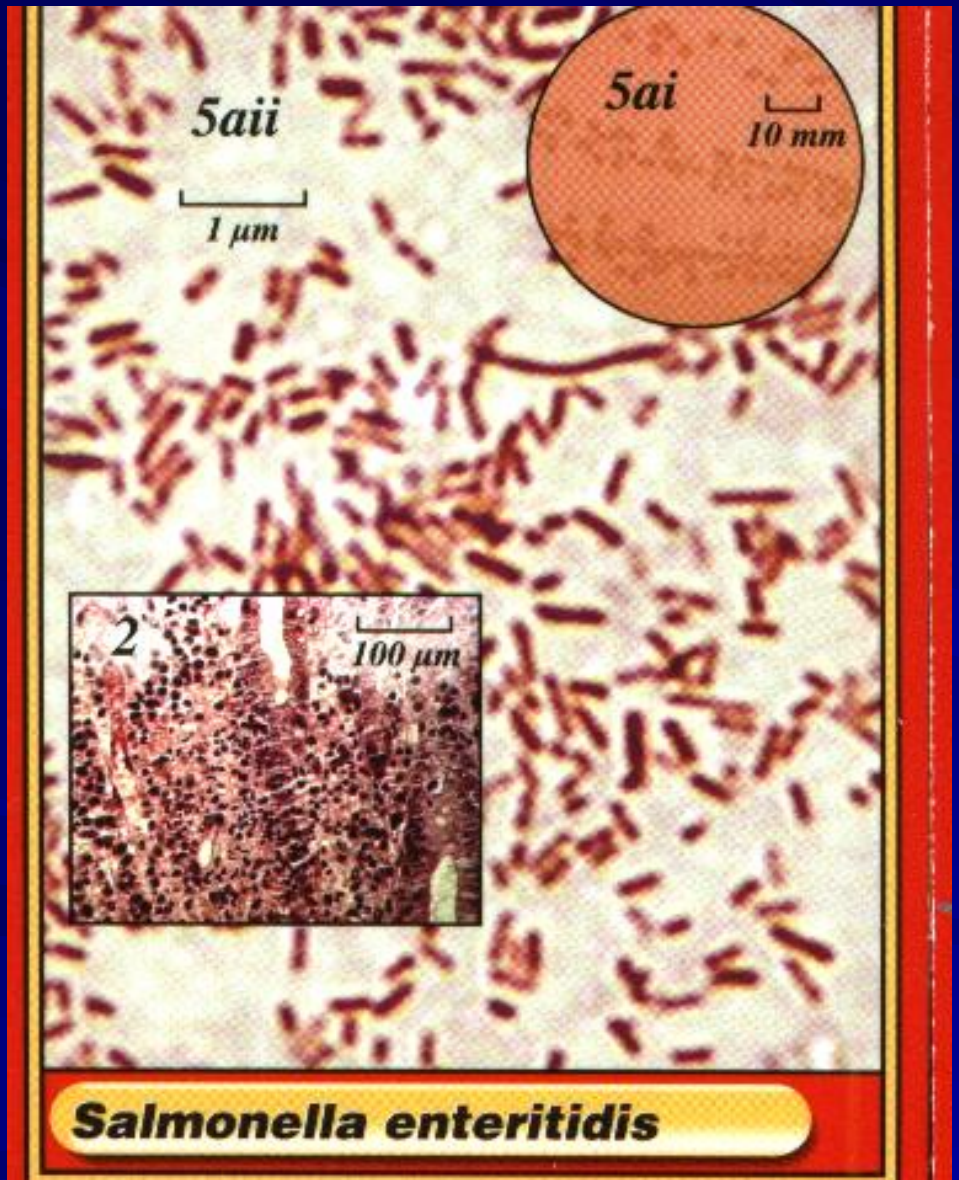
THERAPY:

chloramphenicol

PROTECTION:

live vaccine (oral)

Salmonella enterica



- causes gastroenteritis
- Organisms bind to entero-cytes by pilli in the small intestine and cause ruffles on the cell surface. Bacteria invade the cells, migrate through the cells into the lamina propria of small intestine causing an intense inflammation.
- This leads to malabsorption and diarrhea. Disease is usually self-limiting in healthy people

Salmonella enterica

- Immunity: antibody to LPS O-antigen can be protective, but protection is strain-specific
- Epidemiology: Common pathogenic strains are acquired by food contaminated with feaces from infected animals or humans. Most animal sources: eggs and poultry.
- More than 1500 different serotypes can cause diarrhea in humans
- Most frequent: Salmonella enterica serotype enteritidis

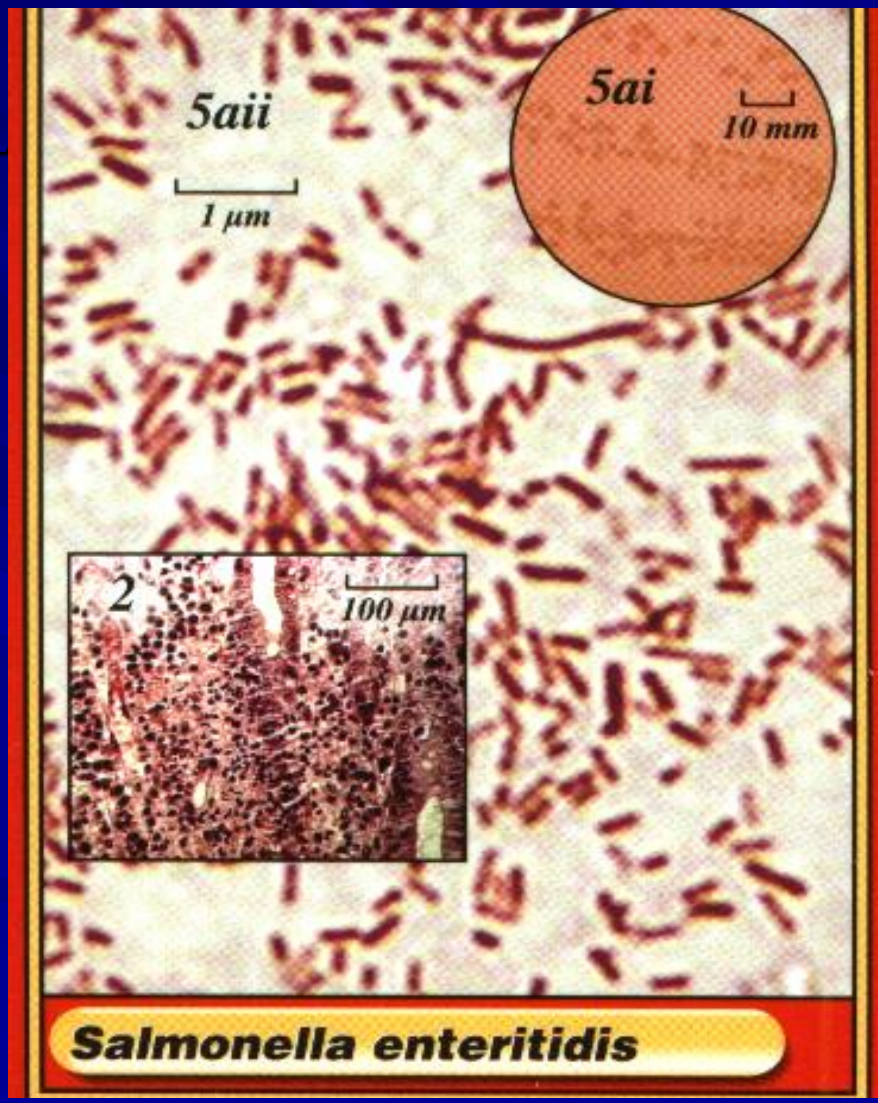
Salmonella enterica

- Diagnostics: stool samples plated solid medium (Blood, Endo, DC-agar McConkey)

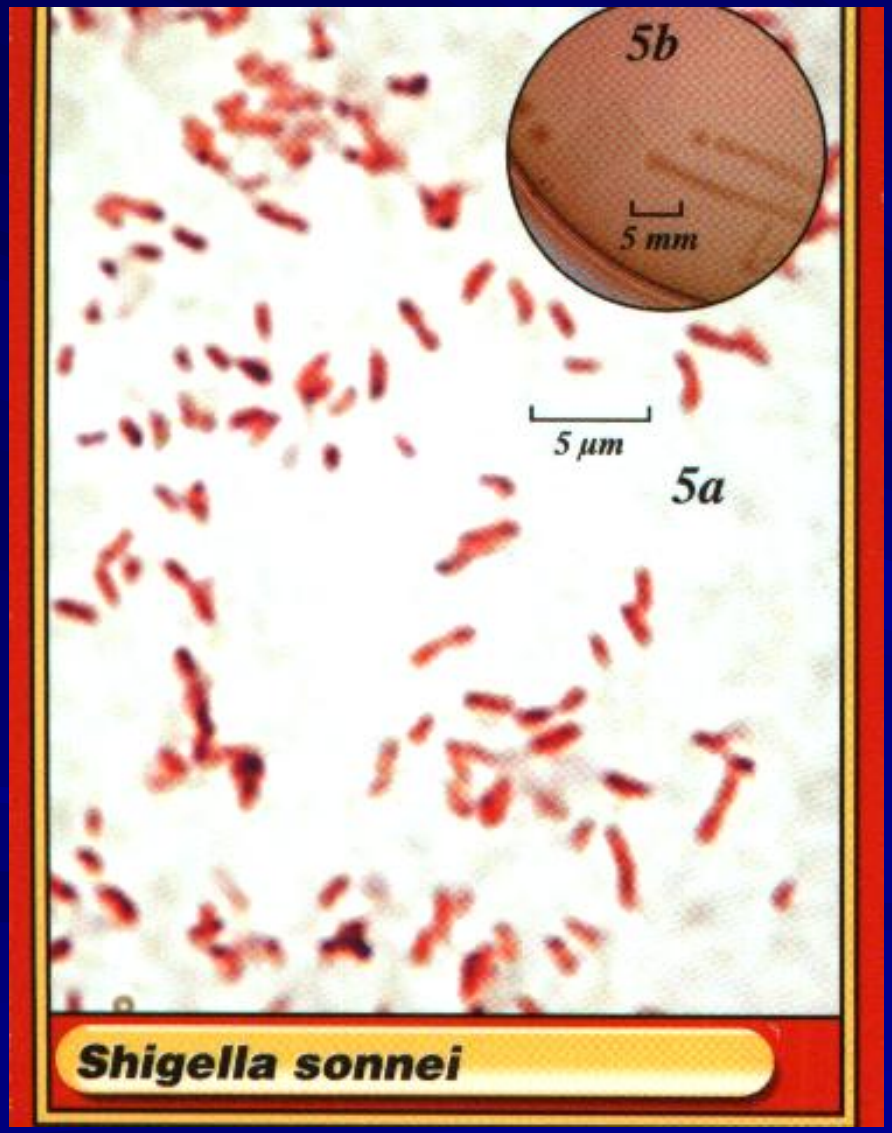
Microscopy: G- rods

Serotyping: O and H antigens

Biochemical characterisation (API, Enterotest)



Shigella



- S. dysenteriae
- S. flexneri
- S. sonnei

Causes dysentery : frequent, low-volume stools containing inflammatory cells and blood

30 or more portions a day

HIGHLY INFECTIVE!!!!

10 bacteria initiate disease

Shigella

- **Pathogenesis:** Descending infection from small intestine to large intestine (main site). Organisms bind to M cells and invade lamina propria, then invade neighboring enterocytes from the bottom. Bacteria grow and induce actin polymerization that pushes them laterally into neighboring cells, where continue to spread causing cell-death and inflammation
- **Immunity:** little innate protection. Convalescent antibodies to O-antigen (LPS)

Shigella

- **Epidemiology:** Highly infectious, fecal-oral spread. Human are the only reservoir
- **Diagnosis:** culture+microscopy

  G- rods without flagella, do not grow on WB, serotyping (O antigen)

NO VACCINE AVAILABLE

Yersinia

- Y. pestis :

  Plague – bubonic – potentially fatal

  - pneumonic – highly contagious, lethal

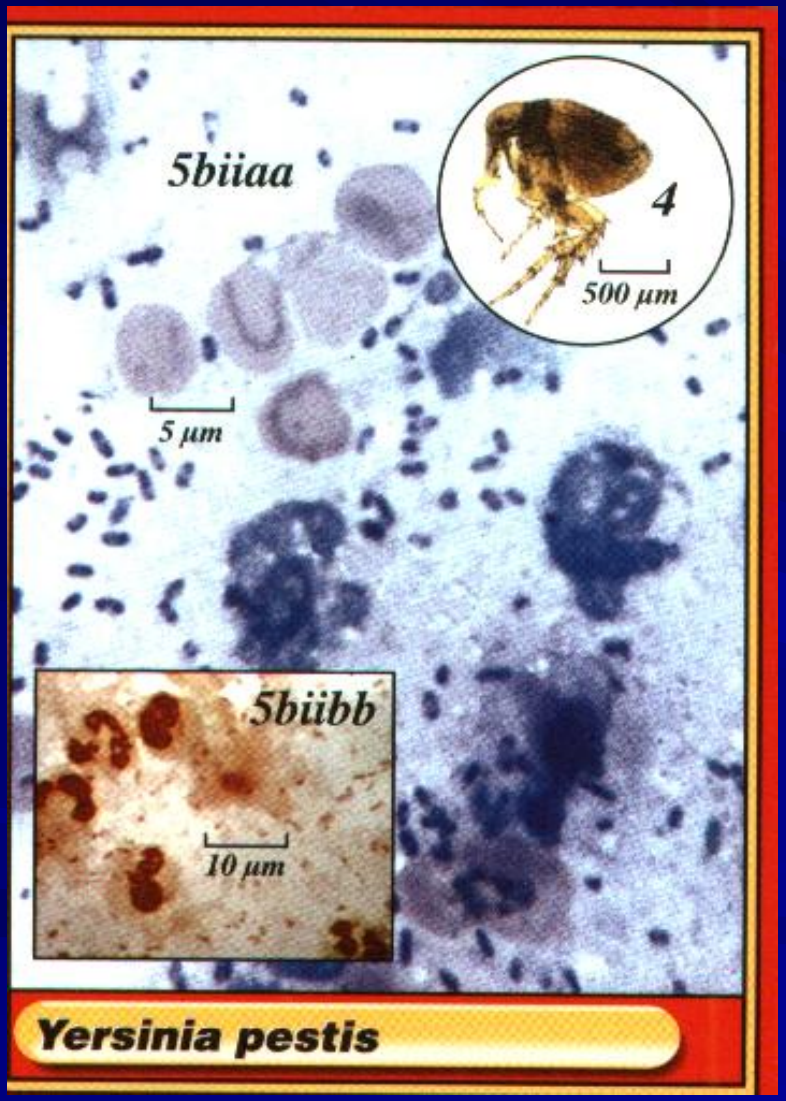
- Y. pseudotuberculosis:

  mesenteric lymphadenitis (pseudoappendicitis)

- Y. enterocolitica:

  gastroenteritis, mesenteric lymphadenitis

Yersinia pestis

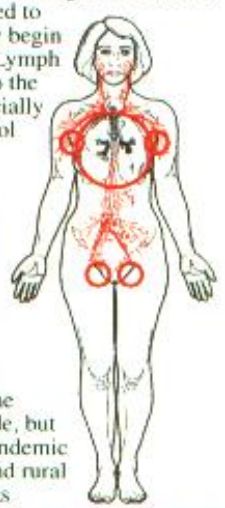


Yersinia pestis

54

1. **Diseases caused:** Plague: a) bubonic, potentially fatal infection of lymph nodes; b) pneumonic, lethal, highly contagious infection of lungs.

2. **Pathogenesis:** a) Infected flea transmits bacteria during a blood meal. Bacteria are readily phagocytosed and are carried to regional lymph nodes where intracellularly they begin to express antiphagocytic F1 capsular antigen. Lymph nodes swell (buboes) and organisms escape into the bloodstream to be carried to other organs, especially b) lung, where they can be transmitted by aerosol to other humans.



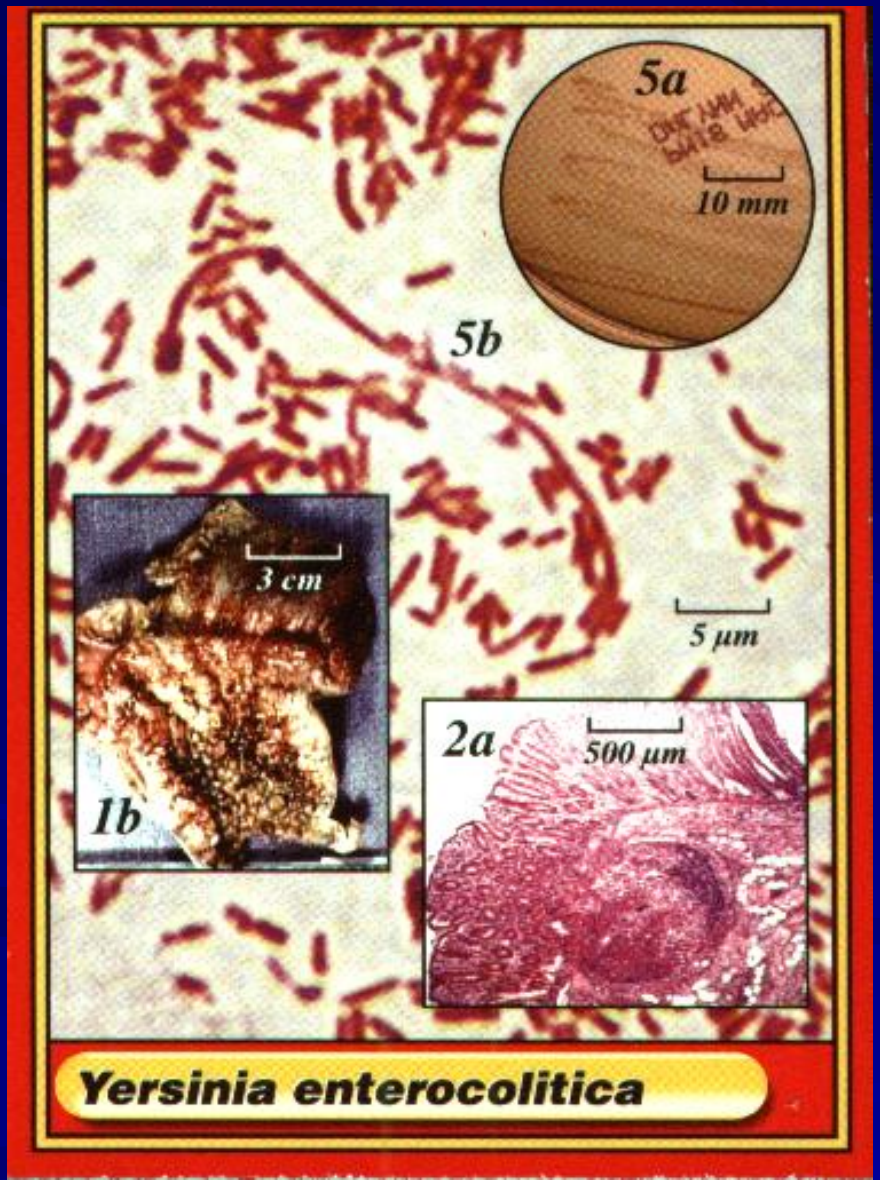
3. **Immunity:** Little natural immunity exists to plague, which is why it can be so deadly when acquired. Antibody to F1 and lcrV (part of the type III secretion system) is protective in convalescent sera and in experimental models by limiting spread of organisms and allowing efficient phagocytic killing.

4. **Epidemiology:** Plague killed a quarter of the population of Europe in the "Black Death" of the Middle Ages. Today *Y. pestis* is found worldwide, but outbreaks of plague occur in Asia and Africa. Endemic in rodent reservoirs in 2 settings: urban (rats) and rural or sylvatic (ground squirrels, prairie dogs). Fleas (e.g., *Xenopsylla cheopis*) transmit bacteria among rodents. Humans are accidental hosts when they contact infected rodents or their fleas.

5. **Diagnosis:** a) Clinical signs and history in areas of endemicity; *b)* bubo aspirate for i) isolation on BAP and *ii)* observation of bipolar-staining short rods by *aa)* Wright or *bb)* Gram stain, iii) DFA for bacteria; c) serum for antibody to F1 antigen.

6. **Control:** a) Eliminate rodent and flea reservoirs; b) avoid contact with infected animal (DEET can deter fleas); c) treat disease with streptomycin for 10 days; d) prophylactic (e.g., doxycycline) for travelers with unavoidable risk of exposure; d) killed, whole cell vaccine has been discontinued. New vaccines that protect against pneumonic plague are in development.

Yersinia enterocolitica

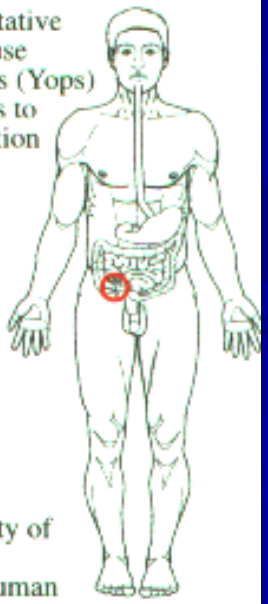


Yersinia enterocolitica

53

1. **Diseases caused:** Yersiniosis: a) gastroenteritis; *b)* mesenteric lymphadenitis (resected bowel shown).

2. **Pathogenesis:** *a) Y. enterocolitica* is a facultative intracellular pathogen. Ingested organisms use adhesins (Yad, Inv, Ail) and effector proteins (Yops) in concert with a type III secretion apparatus to invade M cells in the terminal ileum. Alteration of the mucosa due to cell damage and inflammatory response leads to diarrhea. b) Spread to mesenteric lymph nodes can occur, as can bacteremia.



3. **Immunity:** CMI is necessary for complete recovery. Experimental studies suggest that neutralization of adhesins and certain Yops may be protective. Reiter's syndrome, an immune-related arthritis, can occur after convalescence, especially in people with HLA-B27 histocompatibility cell types.

4. **Epidemiology:** Found worldwide in a variety of domesticated animals (e.g., pigs), but more common in northern Europe as a cause of human diarrhea than elsewhere. There are >50 serotypes, but O3, O8, and O9 account for majority of disease.

5. **Diagnosis:** Stool sample is *a)* cultured on standard (e.g., MacConkey agar, shown) or selective (CIN) agar, often with cold enrichment for *b)* isolation of gram-negative rods, motile at 25°C and nonmotile at 37°C. c) For Reiter's syndrome, detect IgA to Yops by immunoblot.

6. **Control:** a) Eliminate animal reservoirs in area of outbreaks; b) proper food handling; c) possible treatment of invasive disease with gentamicin or tetracycline.

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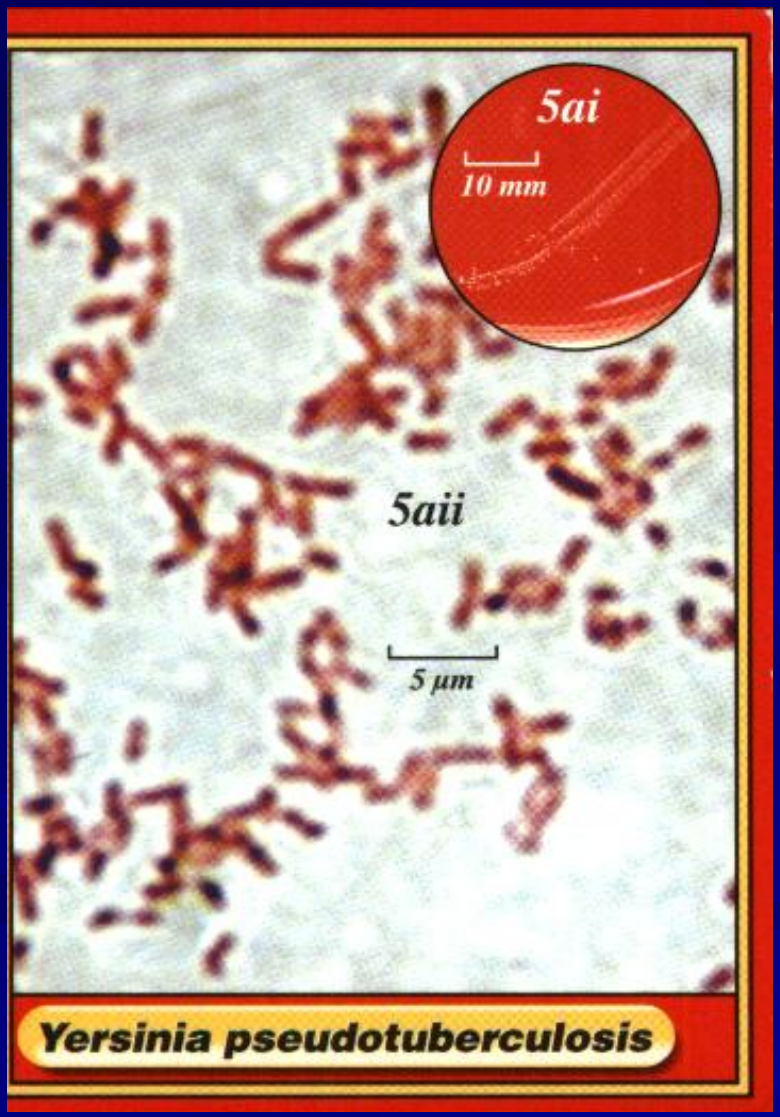
Yersinia pseudotuberculosis



Yersinia pseudotuberculosis

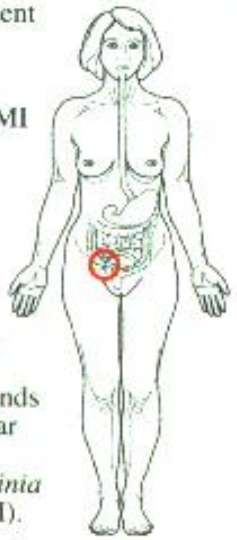
55

1. **Diseases caused:** Yersiniosis: mesenteric lymphadenitis ("pseudoappendicitis").

2. **Pathogenesis:** More invasive than *Y. enterocolitica*, with little production of diarrhea and more involvement of mesenteric lymph nodes.

3. **Immunity:** Convalescent serum contains antibodies to *Y. pseudotuberculosis*, but CMI is necessary for clearing intracellular organisms. Reiter's sydrome can occur in people with HLA-B27 histocompatibility antigen types.

4. **Epidemiology:** Six antigenic O types (I–VI) and 6 biotypes are known, but O type I accounts for 90% of human disease. Found in domestic animals and birds, but zoonotic infection in humans is rare and tends to occur in winter. A unique strain in the Far East can cause a scarlet fever-like disease because it bears a superantigen called *Yersinia pseudotuberculosis*-derived mitogen (YPM).



5. **Diagnosis:** *a)* Blood, stool, lymph node aspirate for *i)* culture on standard media (BAP shown) at 30–35°C ± cold enrichment, or on CIN selective medium, and *ii)* characterization of gram-negative rods (motile at 25°C and nonmotile at 37°C), serotype, biotype, presence of 70-kb virulence plasmid (by PCR or autoagglutination). b) Serum titer to formalin-killed bacteria ("OH antigens") of >1:160, or 4-fold rise between paired sera, is confirmatory. c) For Reiter's syndrome, detect IgA to Yops by immunoblot.

6. **Control:** a) Eliminate animal source of infection; b) treat human disease with aminoglycoside antibiotics in severe cases.

ASM PRESS

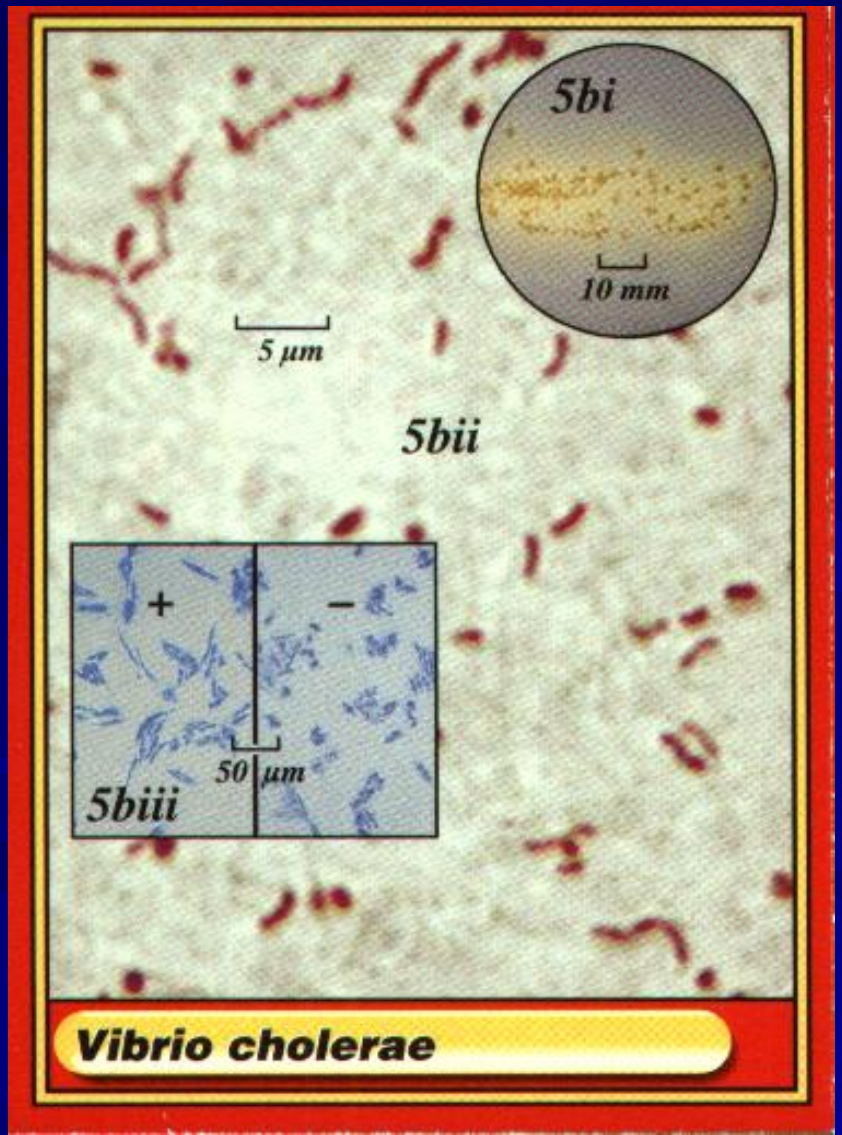
Family: Vibrionaceae
Genus: Vibrio

Species	Source of Infection	Clinical Disease
V. cholerae	Water, food	Gastroenteritis
V. parahaemolyticus	Shellfish, seawater	Gastroenteritis, wound infection, bacteremia
V. vulnificus	Shellfish, seawater	Bacteremia, wound infection, cellulitis
V. alginolyticus	Seawater	Wound infection, external otitis
V. hollisae	Shellfish	Gastroenteritis, wound infection, bacteremia
V. fluvialis	Seafood	Gastroenteritis, wound infection, bacteremia
V. damsela	Seawater	Wound infection
V. metschnikovii	Unknown	Bacteremia
V. mimicus	Fresh water	Gastroenteritis, wound infection, bacteremia
*V. furnissii**	Seawater	Gastroenteritis
*V. cincinnatiensis**	Unknown	Bacteremia, meningitis
*V. carchariae**	Seawater	Wound (shark bite)

* Isolates rarely associated with human infection.

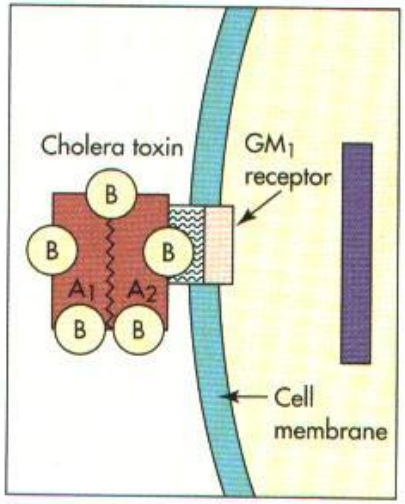
Family: *Vibrionaceae*

Vibrio cholerae

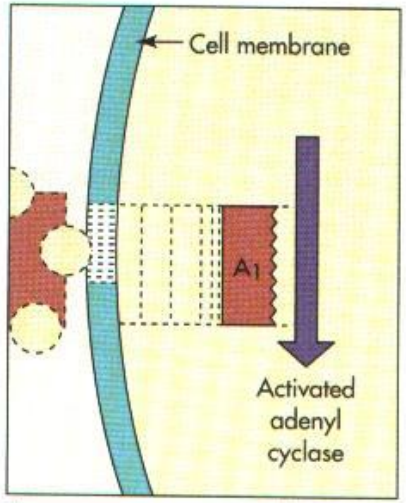


- Disease caused: CHOLERA (voluminous watery diarrhea, life-threat through dehydration
- Pathogenesis: ingestion of fecally contaminated water or food. Flagellar motility + mucinase – penetration to epithelium of small intestine. Toxin-corregulated pilli – attachment, toxin production causes deregulation of crypt-cells by ADP-ribosylating Gs protein of adenylate cyclase system.Efflux of water + ions into the lumen

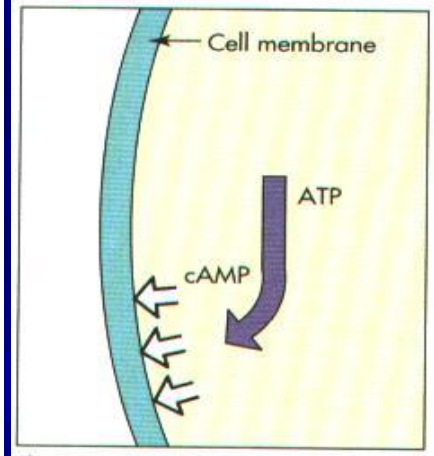
Vibrio cholerae



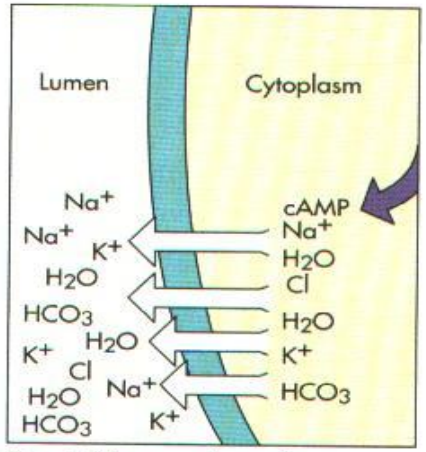
The complete toxin binding to the GM_1-ganglioside receptor on the cell membrane via the binding subunits (B).



The active portion (A_1) of the A subunit enters the cell and activates adenyl cyclase.



This activity results in accumulation of cyclic adenosine 3′, 5′–monophosphate (cAMP) along the cell membrane.



The cAMP causes the active secretion of sodium (Na^+), chloride (Cl^-), potassium (K^+), bicarbonate (HCO_3^-), and water (H_2O) out of the cell into the intestinal lumen.

Vibrio cholerae

- Immunity: Antibody to cholera toxin greatly reduces the severity. VACCINATION
- Epidemiology: Virulent organisms – O1 or O139 antigens. O1 serotypes AB (Inaba), AC (Ogama) ABC (Hikojima). 2 biovars: classical and El Tor.
- Organisms live in salt water attached to algae copepods or shells of crustaceans. If conditions become unfavorable – dormant and unculturable
- Contamination of water sources - epidemies

Vibrio cholerae, serotype O1 and O139 virulence factors

Virulence Factor	Biologic Effect
Cholera toxin	Hypersecretion of electrolytes and water
Coregulated pilus	Adherence to mucosal cells
Accessory colonization	Adhesin factor
Hemagglutination-protease (mucinase)	Induces intestinal inflammation and degradation of tight junctions
Siderophores	Iron sequestration
Neuraminidase	Increase toxin receptors

Family: *Campylobacteriaceae*

Spiral G- bacteria with Low C-G DNA ratio, inable to ferment or oxidize carbohydrates, with microaerophilic growth requirements, motile

- **Campylobacter** *C. jejuni, C. ilei*
- **Arcobacter**

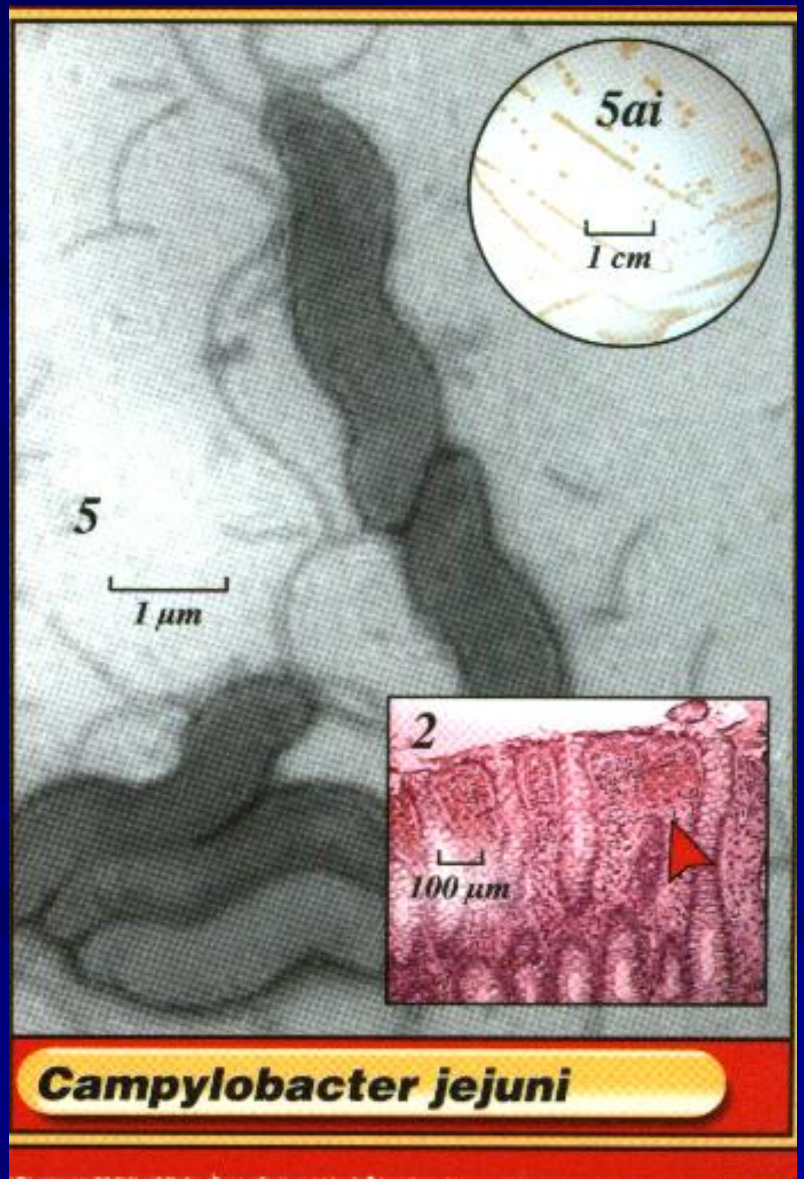
Family: unnamed

- **Walinella**
- **Helicobacter** *H. pylori*
- **Flexispira**

Genus: Campylobacter

Species	Reservoir Host	Human Disease	Frequency
C. jejuni	Poultry, pigs, bulls, dogs, cats, birds, minks, rabbits, insects	Gastroenteritis, septicemia, meningitis, spontaneous abortion, proctitis, Guillain-Barré syndrome	Common
C. jejuni subsp. *doylei*	Humans	Gastroenteritis, gastritis, septicemia	Uncommon
C. coli	Pigs, poultry, bulls, sheep, birds	Gastroenteritis, septicemia, gastroenteritis, spontaneous abortion, meningitis	Uncommon
C. upsaliensis	Dogs, cats	Gastroenteritis, septicemia, abscesses	Uncommon
C. fetus	Cattle, sheep	Septicemia, gastroenteritis, spontaneous abortion, meningitis	Uncommon
C. fetus subsp. *venerealis*	Cattle	Septicemia	Uncommon
C. byointestinalis	Pigs, cattle, hamsters, deer	Gastroenteritis	Rare
C. concisus	Humans	Periodontal disease, gastroenteritis	Rare
C. sputorum subsp. *sputorum*	Humans, cattle, pigs	Abscesses, gastroenteritis	Rare
C. curvus	Humans	Periodontal disease, gastroenteritis	Rare
C. rectus	Humans	Periodontal disease	Rare
C. showae	Humans	Periodontal disease	Rare
C. lari	Poultry, birds, dogs, cats, monkeys, horses, seals	Gastroenteritis, septicemia	Rare

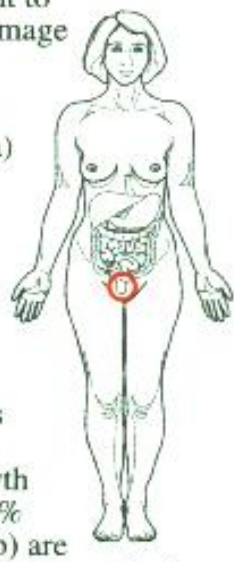
Campylobacter jejuni



Campylobacter jejuni

30

1. **Diseases caused:** Diarrhea.
2. **Pathogenesis:** Similar mechanism as non-Typhi *Salmonella*. *Campylobacter* is thought to invade cells of the small intestine, damage them, and disrupt fluid absorption.
3. **Immunity:** Antibody responses to O antigen (LPS) and H antigen (flagella) are thought to be protective.
4. **Epidemiology:** Very common food- and waterborne organism, particularly from poultry. Disease is more common in the summer and in children <5 yr. old.
5. **Diagnosis:** Gram-negative spiral rods with polar flagella *a)* can be cultured from stool by *i)* microaerophilic growth (5% oxygen, 10% carbon dioxide, 85% nitrogen) and ii) incubation at 42°C; b) are identified by darting motility on wet mount. c) Reference antibody to O and H antigens. d) Clinical signs of diarrhea.
6. **Control:** a) Proper hygiene (hand washing); b) elimination of reservoirs; c) antibiotics are used for most serious cases especially if patient is immunocompromised.



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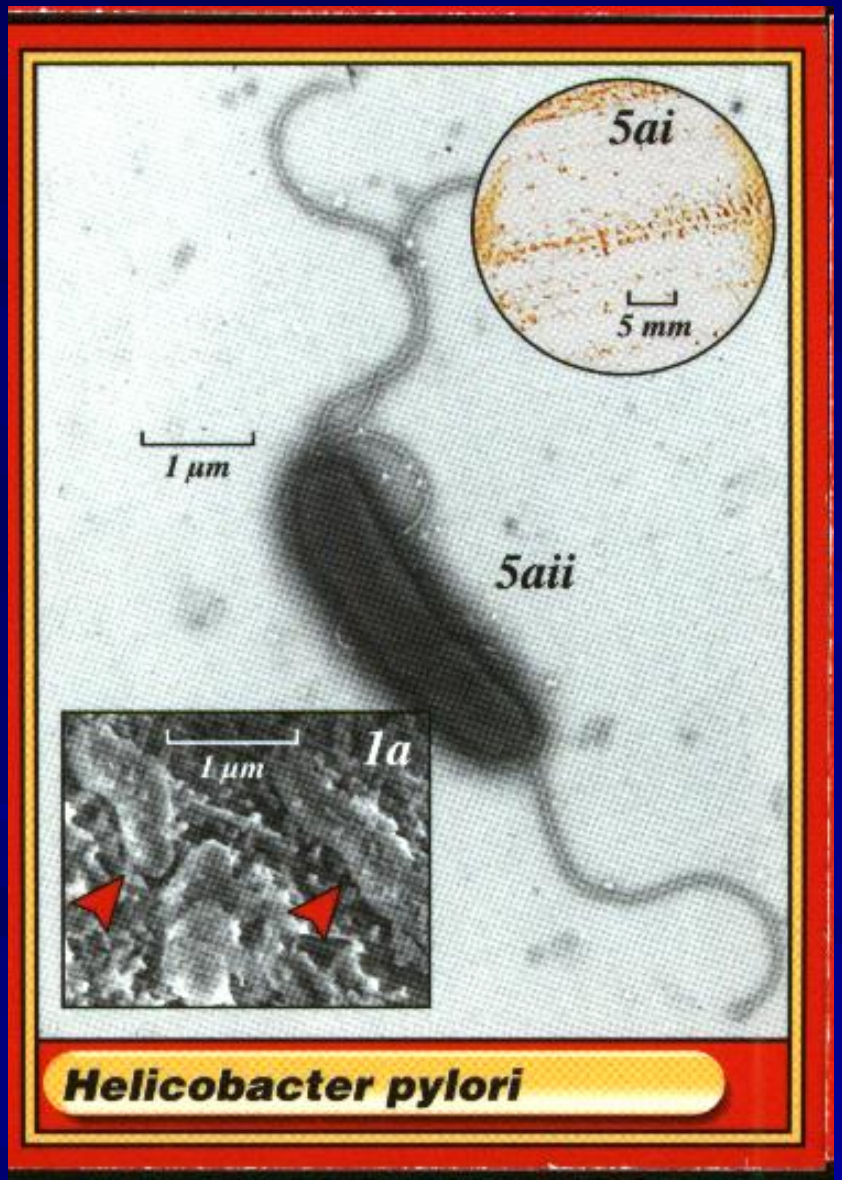
Helicobacter pylori



Helicobacter pylori

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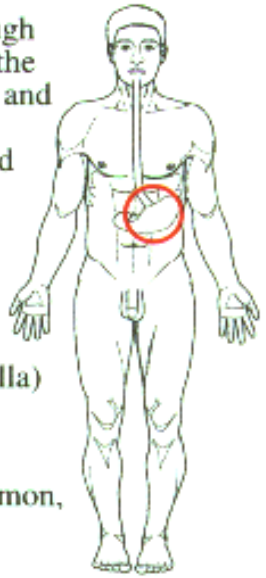
1. **Diseases caused:** *a)* Duodenal and stomach ulcers; b) associated with gastric adenocarcinoma and lymphoma.
2. **Pathogenesis:** Bacteria migrate through stomach mucus and between cells of the stomach lumen. They produce urease and ammonia which neutralize acid and damage cells, leading to cell death and ulcer formation. It is speculated that these organisms may also lead to stomach cancer but how this might occur is not known.



3. **Immunity:** Antibody responses to O antigen (LPS) and H antigen (flagella) are thought to be protective.
4. **Epidemiology:** Serology suggests exposure to the organism is very common, but why some people develop ulcers remains unknown.
5. **Diagnosis:** *a)* Stomach biopsy for *i)* growth on agar medium, *ii)* detection of gram-negative spiral rods with polar flagella; b) reference antibody to detect O and H antigens; c) detection of urease with a breath test for radiolabeled carbon dioxide.
6. **Control:** a) Antibiotics can successfully treat infected patients; b) organism appears to be ubiquitous, so elimination of exposure is not realistic.

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Helicobacter pylori

Virulence Factors	Function
Urease	Neutralizes gastric acids; stimulates monocytes and neutrophil chemotaxis; stimulates production of inflammatory cytokines
Heat shock protein (HspB)	Enhances expression of urease
Acid-inhibitory protein	Induces hypochlorhydria during acute infection by blocking acid secretion from parietal cells
Flagella	Allow penetration into gastric mucous layer and protection from acid environment
Adhesins	Mediate binding to host cells; examples of adhesins are hemagglutinins, sialic acid–binding adhesin, Lewis blood group adhesin
Mucinase	Disrupts gastric mucus
Phospholipases	Disrupt gastric mucus
Superoxide dismutase	Prevents phagocytic killing by neutralizing oxygen metabolites
Catalase	Prevents phagocytic killing by neutralizing peroxides
Vacuolating cytotoxin	Induces vacuolation in epithelial cells; stimulates neutrophil migration into mucosa
Poorly defined factors	*H. pylori:*
	Stimulates interleukin-8 secretion by gastric epithelial cells, which recruits and activates neutrophils
	Stimulates gastric mucosal cells to produce platelet-activating factor (PAF), which stimulates gastric acid secretion
	Induces nitric oxide synthase in gastric epithelial cells, which mediates tissue injury
	Induces death of gastric epithelial cells

Pseudomonas aeruginosa

- Straight or slightly curved G- bacilli, motile (polar flagella), 0.5 to 1.0 x 1.5 – 5.0 μm.
- Contain cytochromeoxidase
- Produce different pigments (pyocyanin – blue), fluorescein –yellow and pyorubin- red/blue).
- Main cause of nosocomial infections

Pseudomonas aeruginosa

Virulence Factors	Biologic Effects
Structural Components	
Capsule	Mucoid exopolysaccharide; adhesin; inhibits antibiotic (e.g., aminoglycoside) killing; suppresses neutrophil and lymphocyte activity
Pili	Adhesin
Lipopolysaccharide (LPS)	Endotoxin activity
Pyocyanin	Impairs ciliary function; stimulates inflammatory response; mediates tissue damage through production of toxic oxygen radicals (i.e., hydrogen peroxide, superoxide, hydroxyl radicals)
Toxins and Enzymes	
Exotoxin A	Inhibitor of protein synthesis; produces tissue damage (e.g., skin, cornea); immunosuppressive
Exotoxin S	Inhibits protein synthesis; immunosuppressive
Cytotoxin (leukocidin)	Cytotoxic for eukaryotic membranes (e.g., disrupts leukocyte function, produces pulmonary microvascular injury)
Elastase	Destruction of elastin-containing tissues (e.g., blood vessels, lung tissue, skin), collagen, immunoglobulins, and complement factors
Alkaline protease	Tissue destruction; inactivation of interferon and tumor necrosis factor-α
Phospholipase C	Heat-labile hemolysin; mediates tissue damage; stimulates inflammatory response
Rhamnolipid	Heat-stable hemolysin; disrupts lecithin-containing tissues; inhibits pulmonary ciliary activity
Antibiotic resistance	Complicates antimicrobial therapy

Acknowledgement

Schemes, Tables and Photos in this presentation were taken from following educational Sources:

- 1. *Murray P.R., Rosenthal K.S., Pfaller M.A.: MEDICAL MICROBIOLOGY 6th ED, Mosby/Elsevier 2009*
- 2. Microbe Cards, American Society for Microbiology 2005