Chapter 20
The Gram-Negative Bacilli of Medical Importance
## TABLE 20.1

### Gram Negative Pathogens

- **Gram-negative rods**
  - **Aerobes**
    - *Bordetella*
    - *Brucella*
    - *Francisella*
    - *Pseudomonas*
    - *Alcaligenes*
  - **Facultative anaerobes**
  - **Obligate anaerobes**
    - *Bacteroides*
- **Lactose fermenting**
  - *Citrobacter*
  - *Enterobacter*
  - *Escherichia*
  - *Klebsiella*
- **Non-lactose fermenting**
  - **Oxidase-negative**
    - *Edwardsiella*
    - *Hafnia*
    - *Morganella*
    - *Proteus*
    - *Providencia*
  - **Oxidase-positive**
    - *Salmonella*
    - *Serratia*
    - *Shigella*
    - *Yersinia*
  - *Haemophilus*
  - *Pasteurella*
Aerobic Gram-Negative Bacilli

- *Pseudomonas* – an opportunistic pathogen
- *Brucella* & *Francisella* – zoonotic pathogens
- *Bordetella* & *Legionella* – mainly human pathogens
- *Alcaligenes* – opportunistic pathogen
**Pseudomonas**

- small gram-negative rods with a single polar flagellum, produce oxidase & catalase
- highly versatile metabolism
Pseudomonas aeruginosa
*Pseudomonas aeruginosa*

- common inhabitant of soil & water
- intestinal resident in 10% normal people
- resistant to soaps, dyes, quaternary ammonium disinfectants, drugs, drying
- frequent contaminant of ventilators, IV solutions, anesthesia equipment
- opportunistic pathogen
Pseudomonas aeruginosa

- common cause of nosocomial infections in hosts with burns, neoplastic disease, cystic fibrosis
- complications include pneumonia, UTI, abscesses, otitis, & corneal disease
- endocarditis, meningitis, bronchopneumonia
- grapelike odor
- greenish-blue pigment (pyocyanin)
- multidrug resistant
- cephalosporins, aminoglycosides, carbenicillin, polymixin, quinolones, &
Pseudomonas aeruginosa
Pseudomonas aeruginosa
Bordetella pertussis

- minute, encapsulated coccobacillus
- causes pertussis or whooping cough, a communicable childhood affliction
- acute respiratory syndrome
- often severe, life-threatening complications in babies
- reservoir – apparently healthy carriers
- transmission by direct contact or inhalation of aerosols
Bordetella pertussis

- virulence factors
  - receptors that recognize & bind to ciliated respiratory epithelial cells
  - toxins that destroy & dislodge ciliated cells
- loss of ciliary mechanism leads to buildup of mucus & blockage of the airways
- vaccine – DTaP- acellular vaccine contains toxoid & other Ags
Pertussis

Reported Cases per 100,000 Population

Year


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Enterobacteriaceae Family

- enterics
- large family of gram-negative bacteria
- many members inhabit soil, water, & decaying matter & common occupants of large bowel of humans & animals
- all members are small, non-sporing rods
- facultative anaerobes, grow best in air
- cause diarrhea through enterotoxins
- divided into coliforms (lactose fermenters) and non-coliforms (non lactose fermenters)
Rapid lactose fermentation on triple-sugar iron (TSI)

+ Lactose  Lactose –
+ Glucose  Glucose –

Motility

+ Indole –
+ Voges-Proskauer (VP) –
– Klebsiella
– Erwinia Citrobacter
– VP+ Enterobacter VP− Citrobacter

H₂S

+ Indole –
+ Citrate –
+ Escherichia Moellerella
– Providencia Morganella
– Hafnia Edwardsiella

Phenylalanine (PA)

+ H₂S –
+ Citrate –
– Proteus
– Citrate
– ONPG gelatinase

ONPG

+ Motility –
+ Urease –
– Yersinia Shigella
– Serratia Salmonella

See table 20.2 for a brief discussion of each differential test.
**FIGURE 20.10**
Isolation media for enterics, showing differentiating reactions.
(a) Levine's eosin methylene blue (EMB) agar. (b) Hektoen enteric agar.
(See table 20.2.)
Antigens & virulence factors

- H – flagellar Ag
- K – capsule &/or fimbrial Ag
- O – somatic or cell wall Ag – all have
  - endotoxin
  - exotoxins
Capsule (K antigen, or $V_i$ in *Salmonella*)

Somatic (O antigen, or cell wall antigen)

Flagellar (H antigen)
**Escherichia coli**: the most prevalent enteric bacillus

- most common aerobic & non-fastidious bacterium in gut
- enterotoxigenic *E. coli* causes severe diarrhea due to heat-labile toxin & heat-stable toxin – stimulate secretion & fluid loss; also has fimbriae
- enteroinvasive *E. coli* causes inflammatory disease of the large intestine
- enteropathogenic *E. coli* linked to wasting from infantile diarrhea; O157:H7 strain causes hemorrhagic syndrome & kidney damage
Escherichia coli

- pathogenic strains frequent agents of infantile diarrhea – greatest cause of mortality among babies
- causes ~70% of traveler’s diarrhea
- causes 50-80% UTI

- indicator of fecal contamination in water
Other coliforms

- *Klebsiella pneumoniae*—normal inhabitant of respiratory tract, has large capsule, cause of nosocomial pneumonia, meningitis, bacteremia, wound infections & UTIs
- *Enterobacter*—UTIs, surgical wounds
- *Serratia marcescens*—produces a red pigment; causes pneumonia, burn & wound infections, septicemia & meningitis
- *Citrobacter*—opportunistic UTIs & bacteremia
Noncoliform lactose-negative enterics

- *Proteus*
- *Salmonella & Shigella*
Salmonella

- motile; ferments glucose
- resistant to chemicals – bile & dyes
- *S. typhi* – typhoid fever – ingested bacilli adhere to small intestine, cause invasive diarrhea that leads to septicemia
  - 2 new vaccines
- *S. cholerae-suis* - pigs
- *S. enteritidis* – 1,700 serotypes- salmonellosis – zoonotic
  - gastroenteritis 2-5 days
Outbreak caused by contaminated pasteurized milk, IL
Shigella

- shigellosis – incapacitating dysentery
- *S. dysenteriae*, *S. sonnei*, *S. flexneri* & *S. boydii*
- produce H$_2$S or urease
- invades villus of large intestine, can perforate intestine or invade blood
- enters Peyer’s patches instigates inflammatory response; endotoxin & exotoxins
- treatment – fluid replacement & ciprofloxacin & sulfa-trimethoprim
Yersinia pestis

- nonenteric
- tiny, gram-negative rod, unusual bipolar staining & capsules
- virulence factors – capsular & envelope proteins protect against phagocytosis & foster intracellular growth
  - coagulase, endotoxin, murine toxin
Yersinia pestis

White blood cell

Y. pestis
Yersinia pestis

- humans develop plague through contact with wild animals (sylvatic plague) or domestic or semidomestic animals (urban plague) or infected humans
- found in 200 species of mammals – rodents without causing disease
- flea vectors – bacteria replicates in gut, coagulase causes blood clotting that blocks the esophagus; flea becomes ravenous
Yersinia pestis

The diagram illustrates the life cycle of Yersinia pestis, which includes:

- **Endemic reservoir hosts**: Mice, ground squirrels, and chipmunks.
- **Amplifying hosts**: Humans, who can serve as accidental hosts.
- **Fleas**: Vectors that transmit the bacteria between hosts.

The cycle can lead to different forms of plague:

- **Bubonic plague**: Caused by the bacteria entering the bloodstream through a infected flea bite.
- **Pneumonic plague**: Caused by inhaling the bacteria from infected lung tissue of a dead or dying host.

The image also highlights the importance of ecological balance and human intervention in controlling the spread of the disease.
Pathology of plague

• 3-50 bacilli
• bubonic – bacillus multiplies in flea bite, enters lymph, causes necrosis & swelling called a bubo in groin or axilla
• septicemic – progression to massive bacterial growth; virulence factors cause intravascular coagulation subcutaneous hemorrhage & purpura – black plague
• pneumonic – infection localized to lungs, highly contagious; fatal without treatment
• treatment: streptomycin, tetracycline or chloramphenicol
• Killed or attenuated vaccine
bubos
Foundations in Microbiology
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Talaro

Chapter 21
Miscellaneous Bacterial Agents of Disease
Gram negative human pathogens

- *Treponema*
- *Leptospira*
- *Borrelia*
Treponema

• thin, regular, coiled cells
• live in the oral cavity, intestinal tract, & perigenital regions of humans & animals
• pathogens are strict parasites
Treponema pallidum

- human is the natural host
- extremely fastidious & sensitive, cannot survive long outside of the host
- causes syphilis
- infectious dose is 57 organisms
- Primary syphilis
- Secondary syphilis
- Tertiary syphilis
- Congenital syphilis – nasal discharge, skin eruptions, bone deformation, nervous system abnormalities
- treatment: penicillin G
<table>
<thead>
<tr>
<th>Stage</th>
<th>Average Duration</th>
<th>Clinical Setting</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation</td>
<td>3 weeks</td>
<td>No lesion; treponemes adhere and penetrate the epithelium; after multiplying, they disseminate</td>
<td>Asymptomatic phase</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Primary</td>
<td>2–6 weeks</td>
<td>Initial appearance of chancre at inoculation site; intense treponemal activity in body; chancre later disappears</td>
<td>Dark-field microscopy; VDRL, FTA-ABS, MHA-TP testing</td>
<td>Benzathine penicillin G, 2 × 10⁶ units; aqueous benzyl or procaine penicillin G, 4.8 × 10⁶ units</td>
</tr>
<tr>
<td>Primary latency</td>
<td>2–8 weeks</td>
<td>Healed chancre; little scarring; treponemes in blood; few if any symptoms</td>
<td>Serological tests (+)</td>
<td>As above</td>
</tr>
<tr>
<td>Secondary</td>
<td>2–6 weeks after chancre leaves</td>
<td>Skin, mucous membrane lesions; hair loss; patient highly infectious; fever, lymphadenopathy; symptoms can persist for months</td>
<td>Dark-field testing of lesions; serological tests</td>
<td>Double doses of penicillins listed above</td>
</tr>
<tr>
<td>Latency</td>
<td>6 months to 8 or more years</td>
<td>Treponemes quiescent unless relapse occurs; lesions can reappear</td>
<td>Seropositive blood test</td>
<td>As above</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Variable, up to 20 years</td>
<td>Neural, cardiovascular symptoms; gummas develop in organs; seropositivity</td>
<td>Treponeme may be demonstrated by DNA analysis of tissue</td>
<td>As above</td>
</tr>
</tbody>
</table>
Vibrio cholerae
Pathogenesis of cholera

(a) The specific action of cholera toxin (CT) upon the intestinal epithelial cells heightens the activity of an enzyme called adenyl cyclase (AC).

(b) This enzyme stimulates abnormally high levels of cAMP (cyclic adenosine monophosphate), a chemical messenger that normally mediates the action of hormones on cells, but in higher concentrations promotes removal of anions (chloride and carbonate) by the cell membrane.

(c) Under the constant action of cAMP, the cells begin to secrete large quantities of chloride (Cl⁻) and bicarbonate (CO₃²⁻) ions into the intestinal lumen. Electrolyte loss is followed by water loss from epithelial cells, which is what causes the major symptoms.
Campylobacter jejuni

- important cause of bacterial gastroenteritis
- transmitted by beverages & food
- reach mucosa at the last segment of small intestine near colon; adhere, burrow through mucus and multiply
- symptoms of headache, fever, abdominal pain, bloody or watery diarrhea
- heat-labile enterotoxin CJT
Campylobacter jejuni
Helicobacter pylori

• curved cells discovered in 1979 in stomach biopsied specimens
• causes 90% of stomach & duodenal ulcers
• people with type O blood have a 1.5-2X higher rate of ulcers
• produces large amounts of urease
Chlamydia

- obligate intracellular parasites
- small gram-negative cell wall
- alternate between 2 stages
  - elementary body – small metabolically inactive, extracellular, infectious form
  - reticulate body – grows within host cell vacuoles
Chlamydia
**Chlamydia trachomatis**

- human reservoir
- 2 strains
- trachoma – attacks the mucous membranes of the eyes, genitourinary tract & lungs
  - ocular trachoma – severe infection, deforms eyelid & cornea, may cause blindness
  - inclusion conjunctivitis – occurs as babies pass through birth canal; prevented by prophylaxis
  - **STD** – urethritis, cervicitis, salpingitis (PID), infertility, scarring
- lymphogranuloma venereum – disfiguring disease of the external genitalia & pelvic lymphatics
Chlamydia trachomatis
Chlamydia trachomatis
Chlamydia trachomatis

(a)

(b)

Inclusion body

Nucleus