# Chapter 20 - Pathogenic Gram-Negative Cocci and Bacilli

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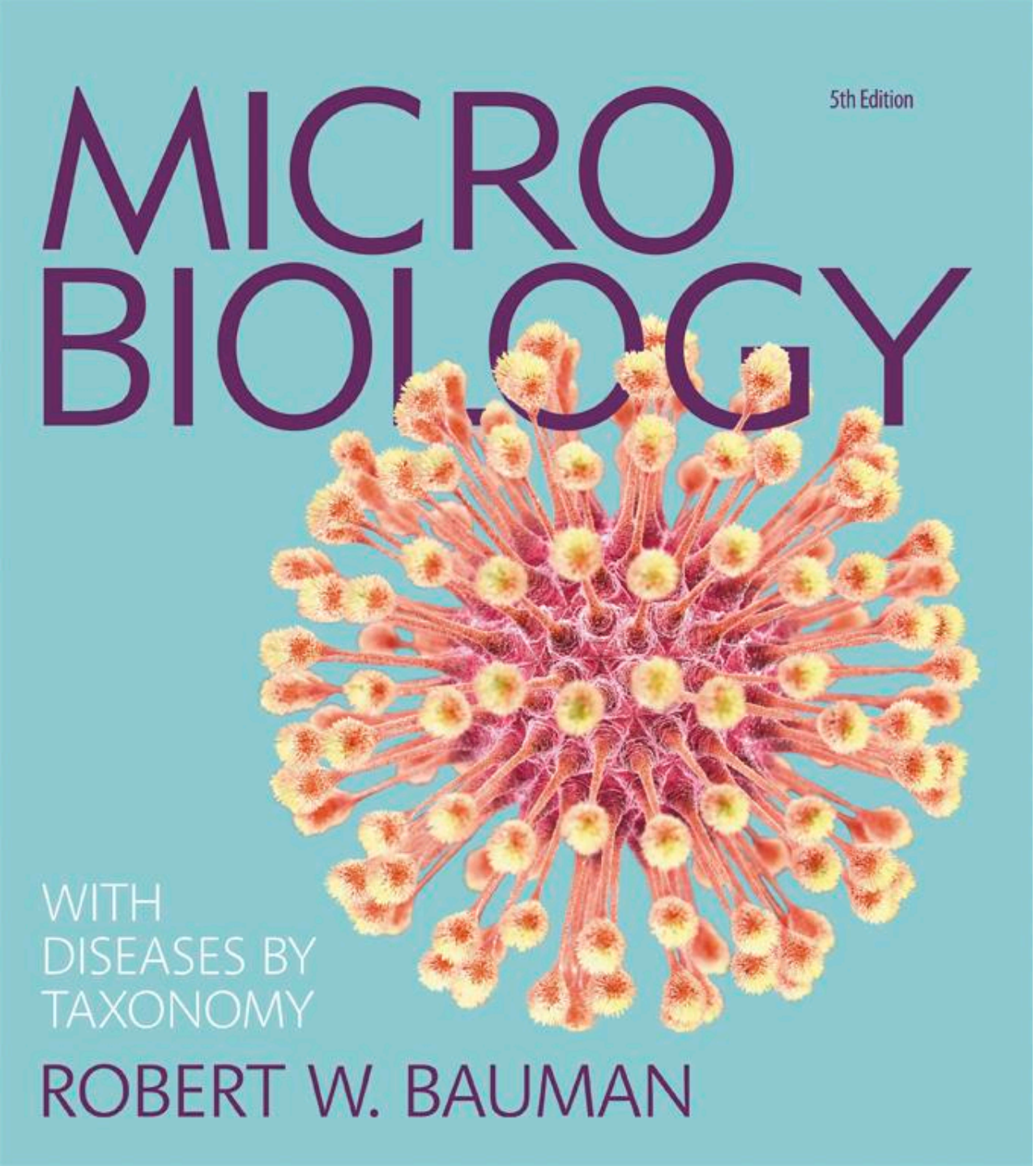
OCTOBER 24, 2017

# Reminder

- Email the final version of your presentation (PDF format)
- Test 2: November 2 – November 4, 2017
  - Reattempt: November 5 – November 7, 2017
  - Materials discussed **including** and up to Oct 31 will be included in the second test
    - Excludes the materials tested in the first test

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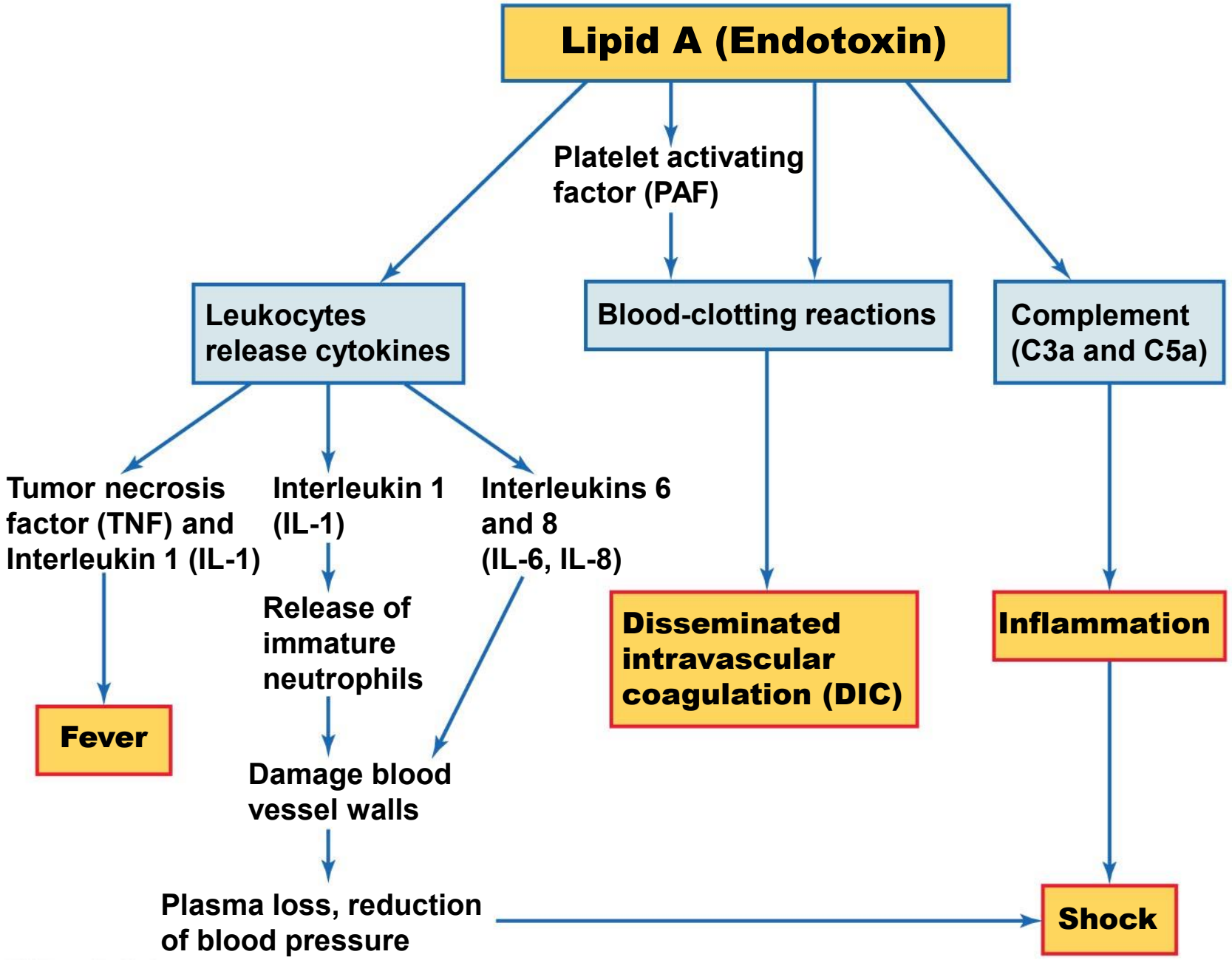
CHAPTER 20

# Pathogenic Gram-Negative Cocci and Bacilli

# Gram-Negative Bacteria

- Constitute largest group of human bacterial pathogens
  - Due in part to lipid A in the bacterial cell wall
    - Triggers fever, vasodilation, inflammation, shock, and disseminated intravascular coagulation (DIC)
- Most Gram-negative bacteria that breach skin or mucous membranes, grow at 37° C, and evade the immune system can cause disease in humans

Figure 20.1 Potential effects of lipid A (endotoxin).



# Pathogenic Gram-Negative Cocci: *Neisseria*

- **Structure and Physiology of *Neisseria***
  - Only genus of Gram-negative cocci that regularly causes disease in humans
  - Aerobic, nonmotile, arranged as diplococci
  - Oxidase positive
    - Distinguishes from many other Gram-negative pathogens
  - Pathogenic strains have fimbriae, a polysaccharide capsule, and a cell wall containing lipid A
  - Two species are pathogenic to humans:
    - *N. gonorrhoeae*
    - *N. meningitidis*

# Pathogenic Gram-Negative Cocci: *Neisseria*

- **The Gonococcus: *Neisseria gonorrhoeae***
  - Pathogenesis, Epidemiology, and Disease
    - Causes **gonorrhea**
      - Only occurs in humans
      - Sexually transmitted disease
        - Increased risk of infection with increasing sexual encounters
      - Most cases in the United States occur in adolescents
        - Cases have declined over the past decades
      - More common in females than in males

# Pathogenic Gram-Negative Cocci: *Neisseria*

- **The Gonococcus: *Neisseria gonorrhoeae***
  - Pathogenesis, Epidemiology, and Disease
    - Gonococci adhere to the genital, urinary, and digestive tract
    - Gonococci can evade the immune system
      - Secrete protease that cleaves secretory immunoglobulin A (IgA)
      - Survive within neutrophils

# Pathogenic Gram-Negative Cocci: *Neisseria*

- **The Gonococcus: *Neisseria gonorrhoeae***
  - Pathogenesis, Epidemiology, and Disease
    - Gonorrhea in men
      - Inflammation causes painful urination and pus-filled discharge
    - Gonorrhea in women
      - Often asymptomatic
      - Can trigger pelvic inflammatory disease **(PID)**
    - Infections can occur outside the reproductive tract
      - Cause proctitis, pharyngitis, and gingivitis
    - Infection of the cornea (*Ophthalmia neonatorum*) or respiratory tract of newborns can occur during childbirth

# Pathogenic Gram-Negative Cocci: *Neisseria*

- **The Gonococcus: *Neisseria gonorrhoeae***
  - Diagnosis, Treatment, and Prevention
    - Diagnosis
      - Asymptomatic cases identified with genetic probes
      - Gram-negative diplococci in pus from inflamed penis
    - Treatment
      - Complicated due to resistant strains
      - Broad-spectrum intramuscular cephalosporins
      - **Partner screening and treatment is necessary**
    - Prevention
      - Sexual abstinence, monogamy, and proper condom use
      - Eye infections in newborns prevented with antimicrobials

# Pathogenic Gram-Negative Cocci: *Neisseria*

- **The Meningococcus: *Neisseria meningitidis***
  - Pathogenicity, Epidemiology, and Disease
    - Most common cause of meningitis in individuals under 20 years of age
    - Can be normal microbiota of the upper respiratory tract
    - Bacteria transmitted by respiratory droplets among people living in close contact
    - **Meningitis can cause death within 6 hours of symptoms**
    - Meningococcal septicemia can also be life threatening

**Figure 20.4 Petechiae in meningococcal septicemia.**

(a)

(b)

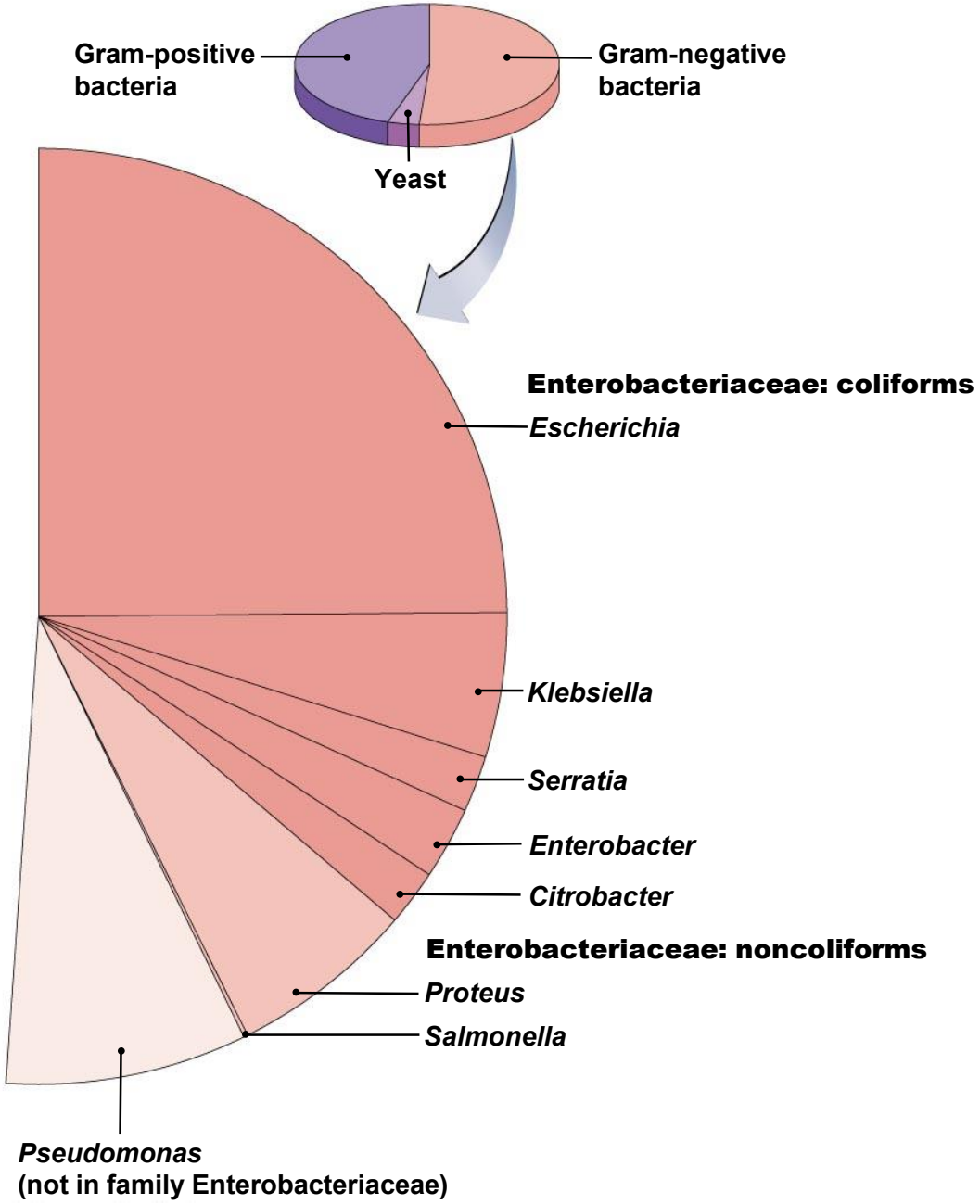
# Pathogenic Gram-Negative Cocci: *Neisseria*

- **The Meningococcus: *Neisseria meningitidis***
  - Diagnosis, Treatment, and Prevention
    - Diagnosis
      - Rapid diagnosis critical
      - Gram-negative diplococci in phagocytes of the CNS
    - Treatment
      - Immediate administration of intravenous penicillin
    - Prevention
      - Family members, classmates, and other contacts are treated with antibiotics prophylactically to prevent the disease.
      - Asymptomatic carriers make eradication unlikely
      - Vaccine against some meningococcal strains is available

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- Two families contain most human pathogens:
  - Enterobacteriaceae (oxidase negative)
  - Pasteurellaceae (oxidase positive)
- Oxidase test distinguishes between these families
- Includes important healthcare-associated pathogens

**Figure 20.6 Relative causes of healthcare-associated infections in the United States.**



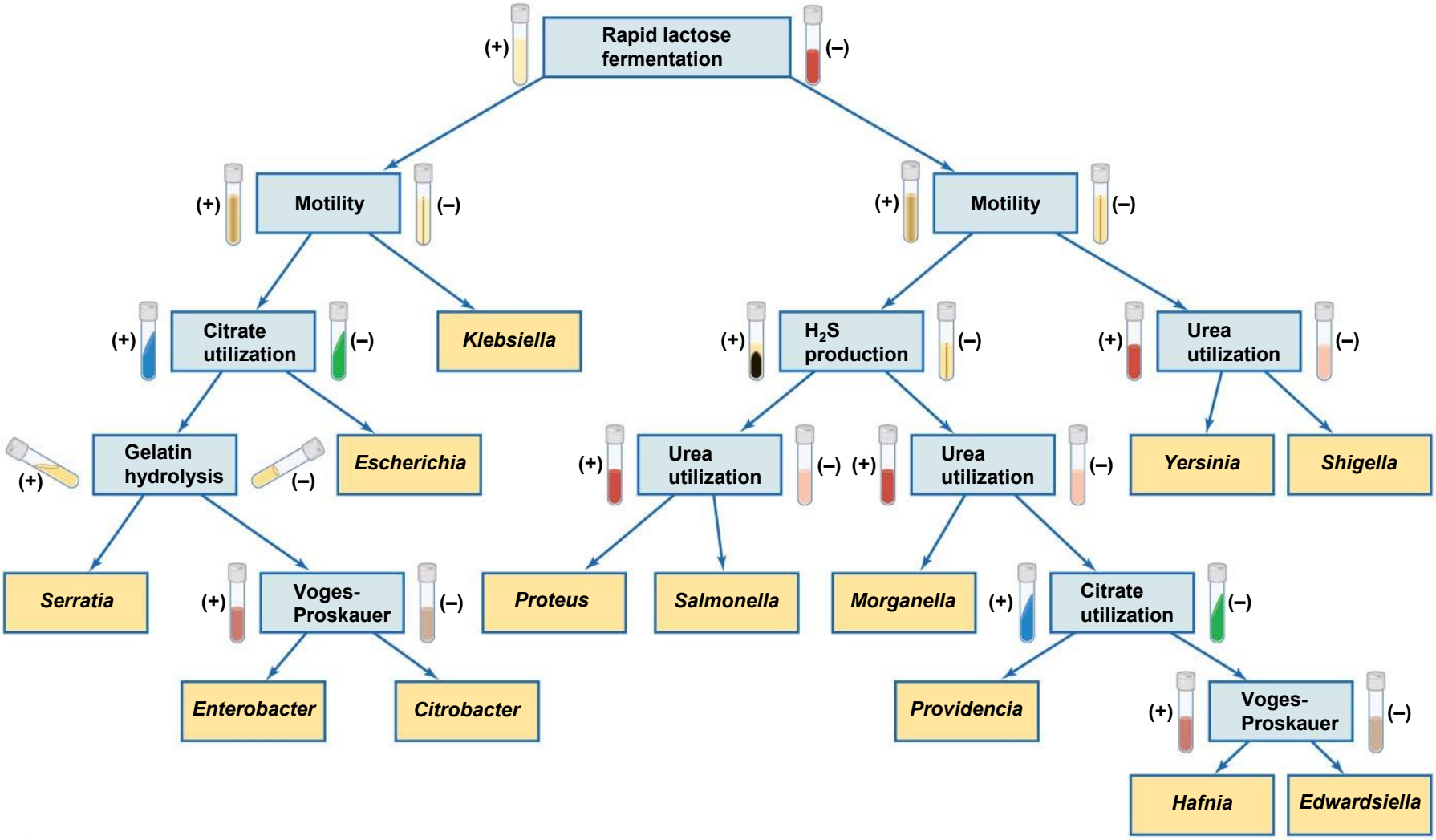
# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Enterobacteriaceae: An Overview**
  - Also called as **enteric bacteria**
  - Intestinal microbiota of most animals and humans
  - Ubiquitous in water, soil, and decaying vegetation
  - Enteric bacteria are the most common Gram-negative pathogens of humans

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Enterobacteriaceae: An Overview**
  - Structure and Physiology
    - Motile bacilli and coccobacilli
    - All reduce nitrate to nitrite and ferment glucose
    - Grow best in aerobic environments
    - Species distinguished based on biochemical properties, motility, and colony characteristics

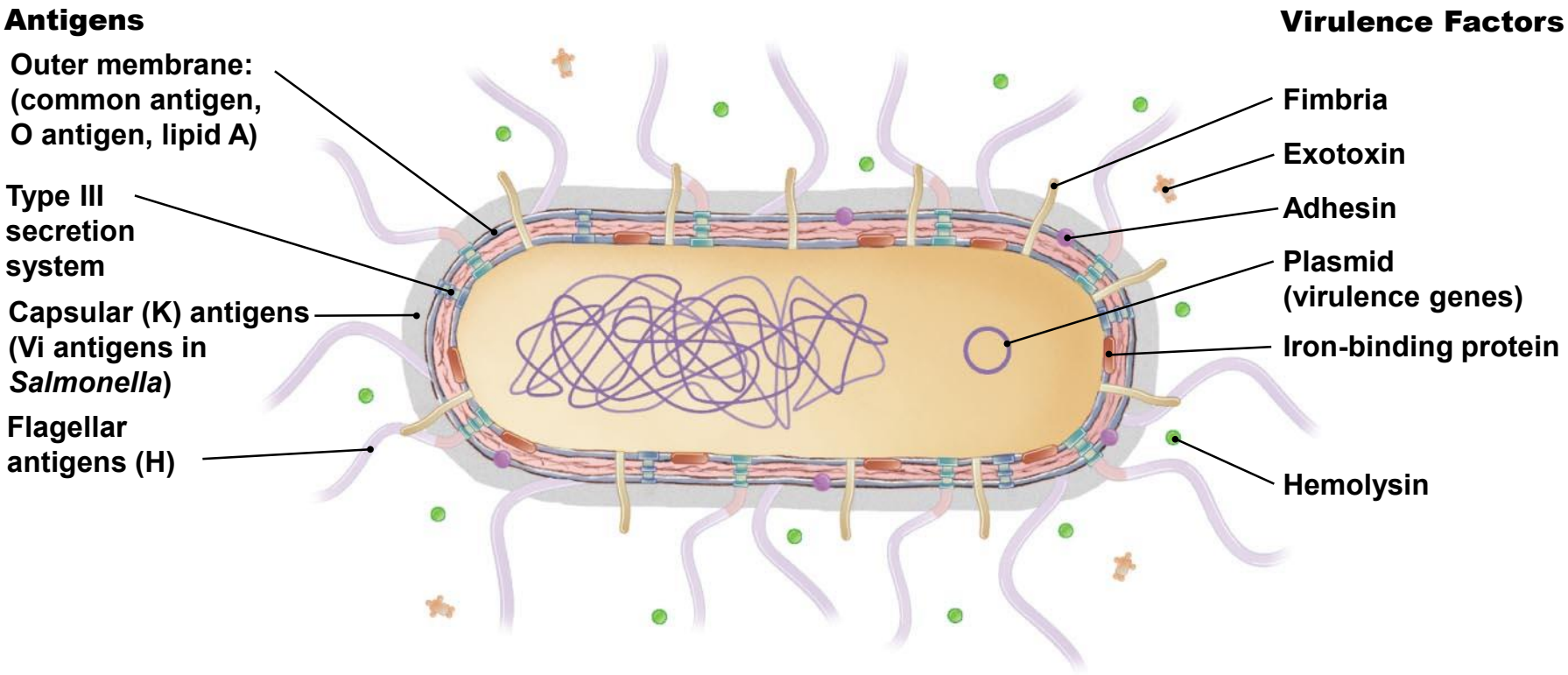
**Figure 20.8 A dichotomous key for distinguishing among enteric bacteria.**



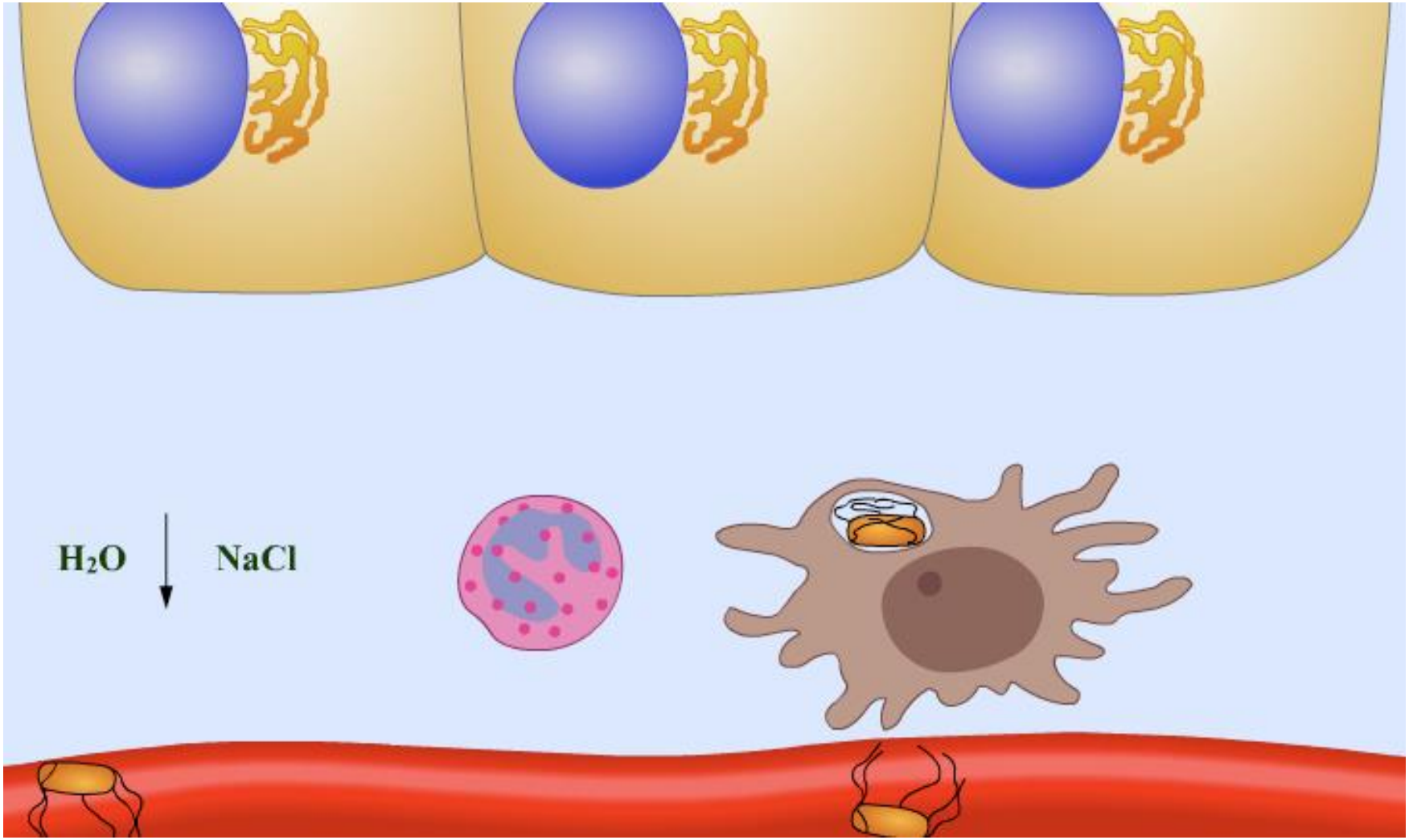
# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Enterobacteriaceae: An Overview**
  - Pathogenesis
    - Variety of antigenic components
      - Membrane components
      - Protein and polysaccharide capsular antigens
      - Used to distinguish among strains and species
    - Numerous virulence factors
      - Some common to all genera and others are unique to certain strains

Figure 20.9 Antigens and virulence factors of typical enteric bacteria.



# Virulence Factors: Enteric Pathogens




PLAY **Virulence Factors: Enteric Pathogens**

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Enterobacteriaceae: An Overview**
  - Diagnosis, Treatment, and Prevention
    - Diagnosis
      - Enteric bacteria in urine, blood, and cerebrospinal fluid
      - Biochemical tests rapidly identify enteric bacteria
    - Treatment
      - Diarrhea is typically self-limited
      - Internal infections treated with antimicrobials
    - Prevention
      - Good personal hygiene and proper sewage control

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Enterobacteriaceae: An Overview**
  - Pathogenic Enterobacteriaceae classified into three groups:
    - Coliforms
      - Rapidly ferment lactose
      - Normal microbiota but may be opportunistic pathogens
    - Noncoliform opportunists
      - Do not ferment lactose
    - True pathogens

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Coliform Opportunistic Enterobacteriaceae**
  - Coliforms
    - Aerobic or facultatively anaerobic, Gram-negative, rod-shaped bacteria that ferment lactose to form gas in lactose broth
  - Commonly found in soil, on plants, and on decaying vegetation
  - Colonize the intestinal tracts of animals and humans
  - Coliforms in water indicate impure water and poor sewage treatment

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Coliform Opportunistic Enterobacteriaceae**
  - *Escherichia coli*
    - Most common and important of the coliforms
    - *E. coli* antigens used to identify particular strains
    - Virulent strains have virulence plasmids
      - Have genes for fimbriae, adhesins, and exotoxins
    - Causes several diseases
    - Gastroenteritis is most common disease
      - Produces diarrhea, cramps, nausea, and vomiting
      - Often mediated by enterotoxins
      - Major cause of pediatric diarrhea in developing countries

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Coliform Opportunistic Enterobacteriaceae**
  - *Escherichia coli*
    - Common cause of healthcare-associated urinary tract infections
      - Occur more often in women than men
    - ***E. coli* O157:H7**
      - Most prevalent pathogenic *E. coli* in developed countries
      - Causes diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome
      - Associated with consumption of undercooked ground beef or contaminated milk or fruit juice
      - Produces type III secretion system and Shiga-like toxin

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Coliform Opportunistic Enterobacteriaceae**
  - ***Klebsiella***
    - In digestive and respiratory systems of humans and animals
    - Capsule protects the bacteria from phagocytosis
    - Can cause opportunistic infections
    - ***K. pneumoniae***
      - Most commonly isolated pathogenic species
      - Causes pneumonia
      - May be involved in bacteremia, meningitis, wound infections, UTIs

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Coliform Opportunistic Enterobacteriaceae**
  - ***Serratia***
    - Produce a red pigment when grown at room temperature
    - Can grow on catheters, in saline solutions, and on other hospital supplies
    - Can cause life-threatening opportunistic infections in immunocompromised patients
    - Frequently resistant to antimicrobial drugs

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Coliform Opportunistic Enterobacteriaceae**
  - ***Enterobacter, Hafnia,* and *Citrobacter***
    - Found in soil, water, decaying vegetation, and sewage
    - Reside in the digestive tracts of animals and humans
    - *Enterobacter* can contaminate dairy products
    - All can be opportunistic pathogens
      - Cause healthcare-associated infections in immunocompromised patients
    - Difficult to treat due to resistance to antimicrobial drugs

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Noncoliform Opportunistic Enterobacteriaceae**
  - ***Proteus***
    - Facultative anaerobe
    - *Proteus mirabilis*
      - Most commonly associated with human disease
      - Associated with urinary tract infections in patients with long-term urinary catheters
      - Infection-induced kidney stones can develop
      - Resistant to many antimicrobial drugs

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Noncoliform Opportunistic Enterobacteriaceae**
  - ***Morganella, Providencia,* and *Edwardsiella***
    - Healthcare-associated infections in immunocompromised patients
    - Primarily involved in urinary tract infections
    - *Providencia* may cause kidney stones

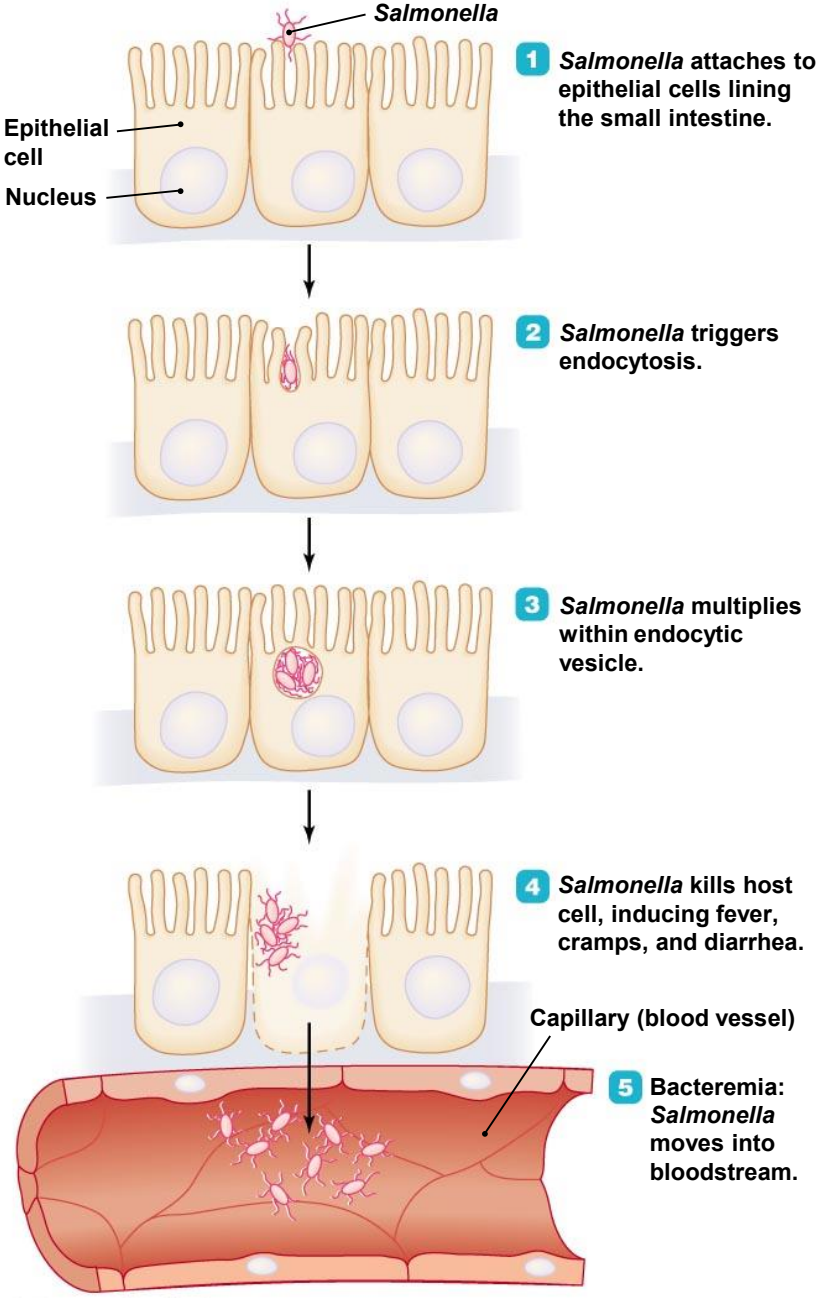
# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - **Include *Salmonella, Shigella,* and *Yersinia***
  - Almost always pathogenic due to numerous virulence factors
  - Produce type III secretion systems
    - Introduce proteins into host cells
      - Inhibit phagocytosis
      - Rearrange the cytoskeletons of eukaryotic cells
      - Induce apoptosis

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - ***Salmonella***
    - Motile, peritrichous bacilli
    - Live in the intestines of birds, reptiles, and mammals
    - Most human infections due to consuming food contaminated with animal feces
    - Poultry and eggs are also common sources of *Salmonella*
    - Infections with fewer than 1 million cells of most strains are usually asymptomatic in people with healthy immune systems
    - Can cause **salmonellosis** and **typhoid fever**
      - Salmonellosis: Non-bloody diarrhea, nausea, vomiting

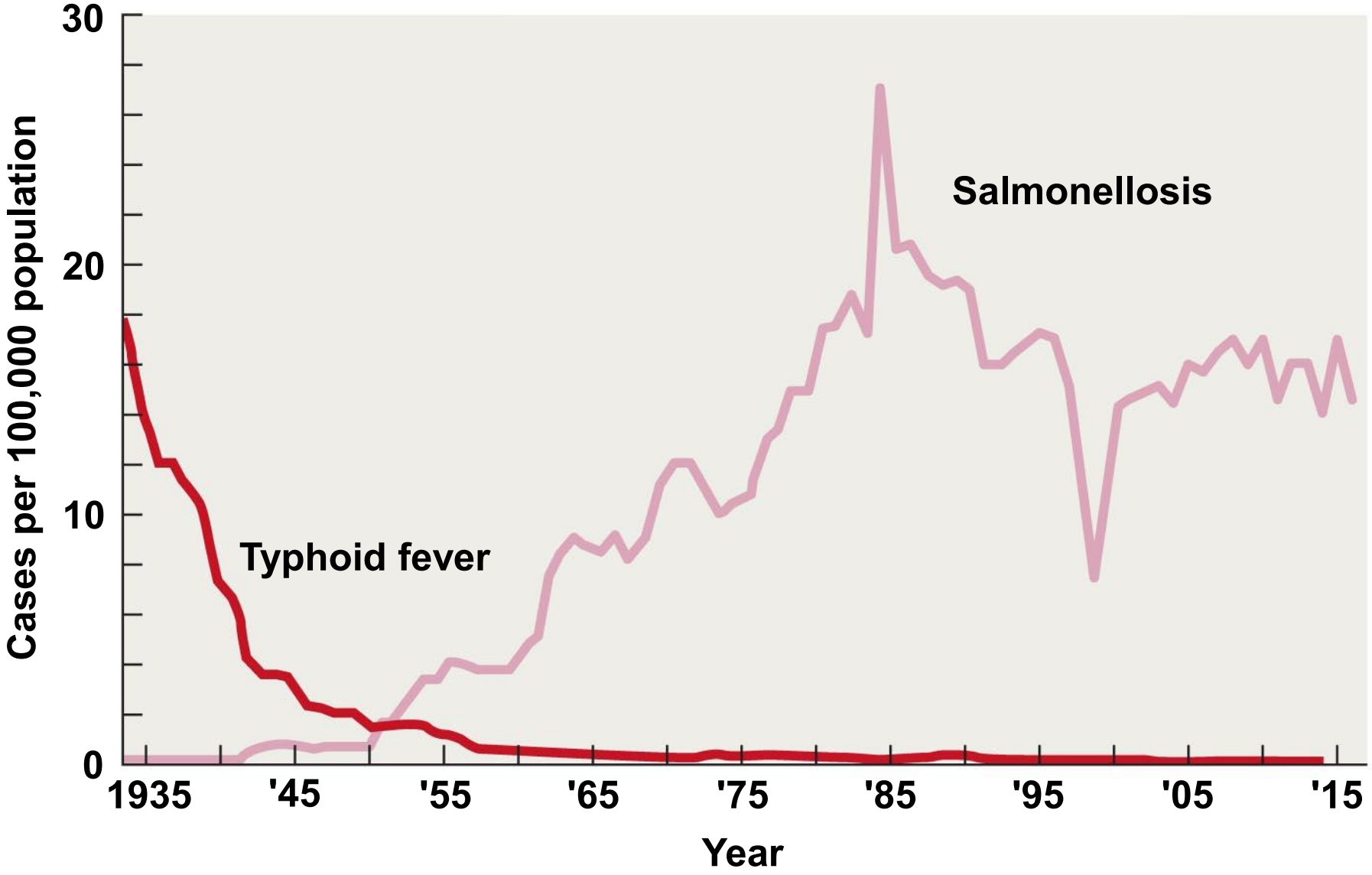
Figure 20.14 The events in salmonellosis.



# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Salmonella*
    - Typhoid fever
      - Caused by *Salmonella enterica* serotype Typhi
        - Humans are the only host
        - Carriers are often asymptomatic
      - Bacteria ingested in contaminated food or water
      - Bacteria pass through intestines into the bloodstream
        - Phagocytic cells ingest the bacteria and carry them to various organs, including liver and gall bladder
        - Causes gastroenteritis, bacteremia, and peritonitis

Figure 20.15 The incidences of diseases caused by *Salmonella* in the United States.



# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Salmonella*
    - Salmonellosis treated with fluid and electrolyte replacement
    - Typhoid fever treated with antimicrobial drugs
    - Gallbladder may be removed from carriers to prevent infection of others
    - Vaccines provide temporary protection to travelers

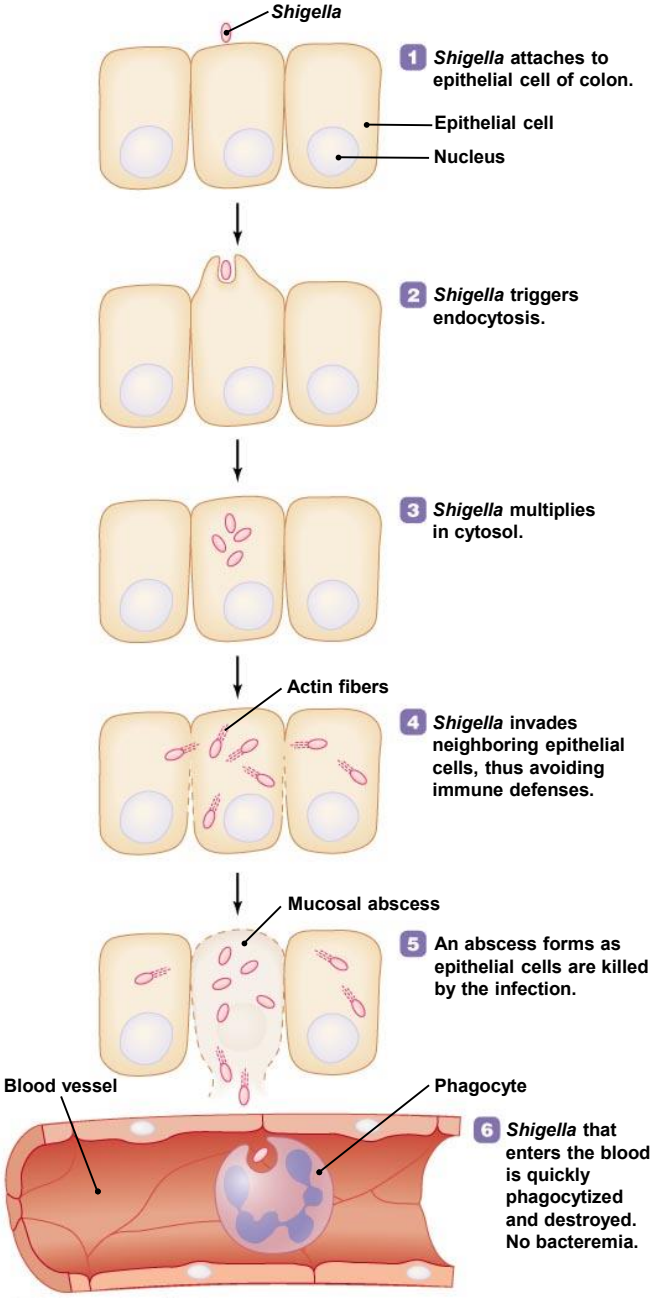
# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - ***Shigella***
    - Oxidase-negative, nonmotile pathogens
    - Primarily a parasite of the digestive tract of humans
    - Produce diarrhea-inducing enterotoxin
    - Four well-defined species
      - *S. dysenteriae*
      - *S. flexneri*
      - *S. boydii*
      - *S. sonnei*

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Shigella*
    - Shigellosis (bloody, pus containing stools)
      - Severe form of dysentery (diarrhea with blood)
      - *S. sonnei* is predominant cause in industrialized nations
      - *S. flexneri* predominates in developing countries
      - Associated with poor hygiene and sewage treatment
      - People ingest bacteria present on their own contaminated hands or in contaminated food
      - Person-to-person spread is possible

## Figure 20.16 The events in shigellosis.



# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Shigella*
    - Shiga toxin
      - Secreted by *S. dysenteriae*
      - Stops protein synthesis in host cells
      - Produces more severe disease (mortality rate as high as 20%)
    - Shigellosis is typically self-limiting
      - Treated with fluid and electrolyte replacement
    - Work on an attenuated vaccine against *S. flexneri* is ongoing

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - ***Yersinia***
    - Normal pathogen of animals
    - Three important species
      - All contain virulence plasmids
        - Adhesins
          - Allow attachment to human cells
        - Type III secretion systems
          - Injection of proteins that causes apotosis of macrophage and neutrophils

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Yersinia*
    - *Y. enterocolitica*
      - Acquired by consumption of contaminated food or water
      - Causes inflammation of the intestinal tract
    - *Y. pseudotuberculosis*
      - Causes less severe inflammation of the intestines
    - *Y. pestis*
      - Highly virulent, nonenteric pathogen
      - Causes bubonic and pneumonic plague

**Figure 20.17 The natural history and transmission of *Yersinia pestis.***

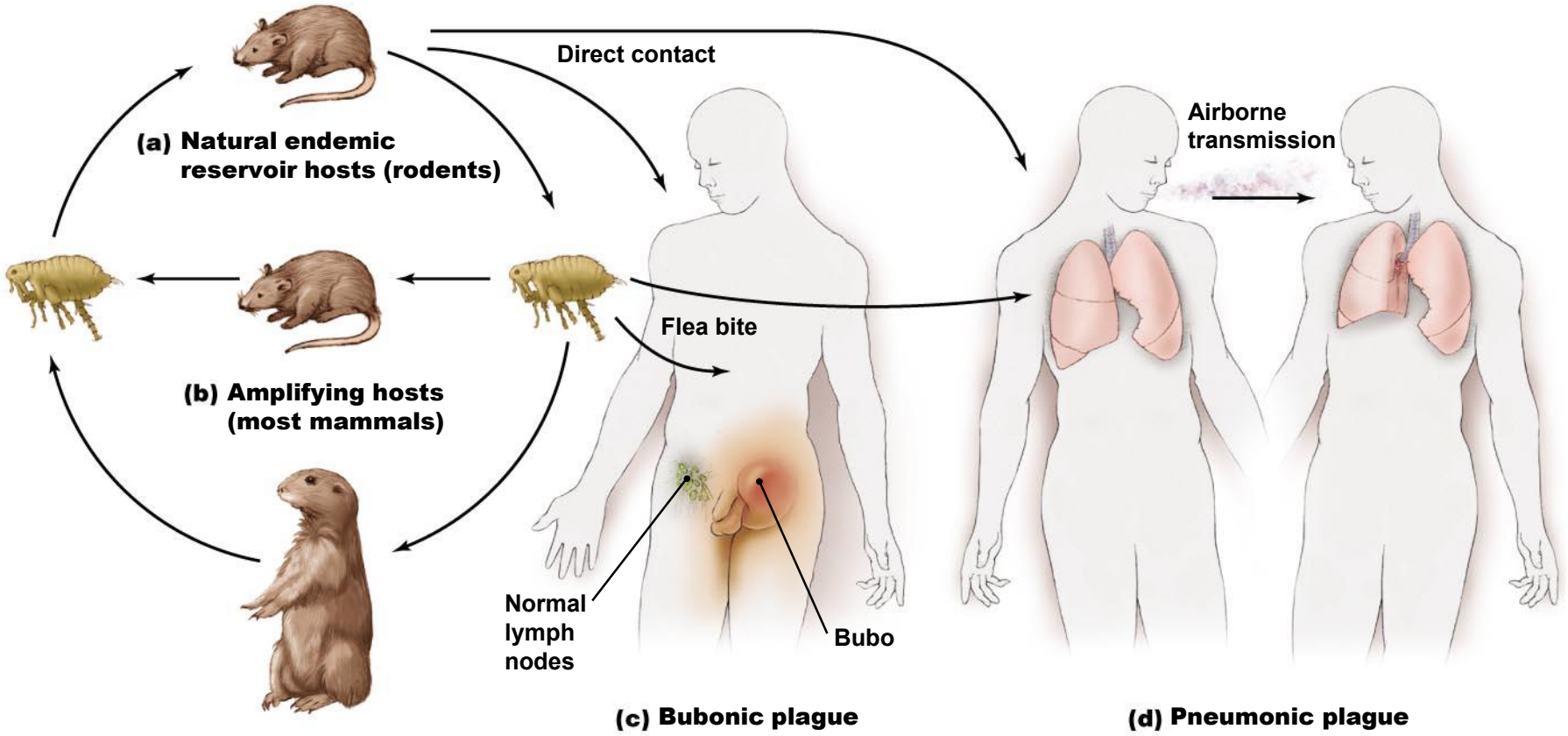


**Figure 20.18 Bubo in an eight-year-old patient.**

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Yersinia*
    - *Bubonic plague*
      - High fever and swollen, painful lymph nodes called ***buboes*** - develop within a week following a bite from an infected flea
      - Untreated infection progresses to bacteremia (the "Black Death"), DIC, hemorrhaging, and necrosis
      - Fatal in 50% of cases. Even with treatment, up to 15% of patients die

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Yersinia*
    - *Pneumonic plague*
      - Enters the lungs from the bloodstream, causing respiratory distress that is fatal if untreated in nearly all cases
      - **Can spread from person to person**

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - ***Y. pestis:* *Potential Bioweapon***
    - Aerosol attack - pneumonic form of plague
    - *Onset of disease since exposure: 1 – 6 days*
      - People could travel over a large area before becoming contagious and possibly infecting others
      - Controlling the disease would then be more difficult
    - A bioweapon carrying *Y. pestis* is possible because the bacterium occurs in nature and could be isolated and grown in quantity in a laboratory

Source: https://emergency.cdc.gov/agent/plague/faq.asp

The New York Times

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# Thousands Flee Indian City In Deadly Plague Outbreak

By JOHN F. BURNS,
Published: September 24, 1994



**NEW DELHI, Sept. 23—** As many as 200,000 people have fled the city of Surat in western India after an outbreak of pneumonic plague that medical experts described as one of the most serious reported in the world in recent decades, officials here said today.

Less than 48 hours after the first confirmed death from the disease, officials in the industrial city said that 24 people had died and 137 others were being treated in hospitals. But unofficial reports, including accounts from doctors working in Surat, said that at least 100 people had died, and that the toll was expected to rise as house-to-house searches turned up scores of new patients.

Residents of Surat, a city of 1.6 million in Gujarat state, reported scenes of confusion and panic reminiscent of the plague outbreaks that devastated India before the advent of effective antibiotic treatment and insecticides in the 1960's.

The bubonic form of plague, which leads to the swelling of lymph nodes, is spread by fleas. Pneumonic plague, a fatal pneumonia, can result from the spread of plague from the lymph nodes to the lungs or can be transmitted by droplets in the air.

Witnesses in Surat described huge crowds at the city's main railroad and bus stations and on roads leading out of the city. Judging from ticket sales, officials said as many as 200,000 people may have left over the last two days.

Medical officials said that there appeared to be two possible causes of the plague outbreak. One was that the disease had been carried to Surat by the large population of migrant workers from the Latur area of Maharashtra state, 250 miles east of Bombay, where an earthquake killed about 10,000 people a year ago.

In August, officials reported an outbreak of bubonic plague in 25 villages around the town of Mamla, on the fringes of the Latur earthquake zone.

Reports from Mamla have said that officials there believed the disease took hold when villagers fearing a new earthquake moved out of their houses but left stores of grain and other foods that attracted rats, leading to a rapid increase in the rat population.

Another theory was that the earthquake caused large numbers of forest-dwelling rats infected with the plague bacillus to migrate to nearby villages. Reports today said that a total of 81 villagers have been diagnosed as suffering from bubonic plague but that none had died.

An alternative theory offered by officials in Surat was that the outbreak there was caused by unusually heavy monsoon rains that caused widespread flooding in the poorest sections of the city along the Tapti River, worsening poor sanitary conditions caused by mounds of uncollected garbage. The floods were said to have drowned large numbers of cows and oxen, as well as dogs and cats. Many were left to putrify on mud flats after the floods receded, attracting rats.

Source: http://www.nytimes.com/1994/09/24/world/thousands-flee-indian-city-in-deadly-plague-outbreak.html

# Blessed by the plague

The grand makeover of Surat in Gujarat, that filthy city hit by the plague scare in 1994,



Uday Mahurkar

July 4, 2005 | UPDATED 16:34 IST



Is this the city that led to an exodus of frightened inhabitants due to the plague scare in 1994 and evoked hysterical media coverage the world over?

Is this that same old filthy city along the Tapti river that forced foreign tourists to stay away from India in droves and massively hurt the country's tourist trade for a few years? Well, 11 years on, it is hard to believe that was once the reality.

But now it is one of the cleanest cities in India and its makeover, as if blessed by the plague, is awe-inspiring.

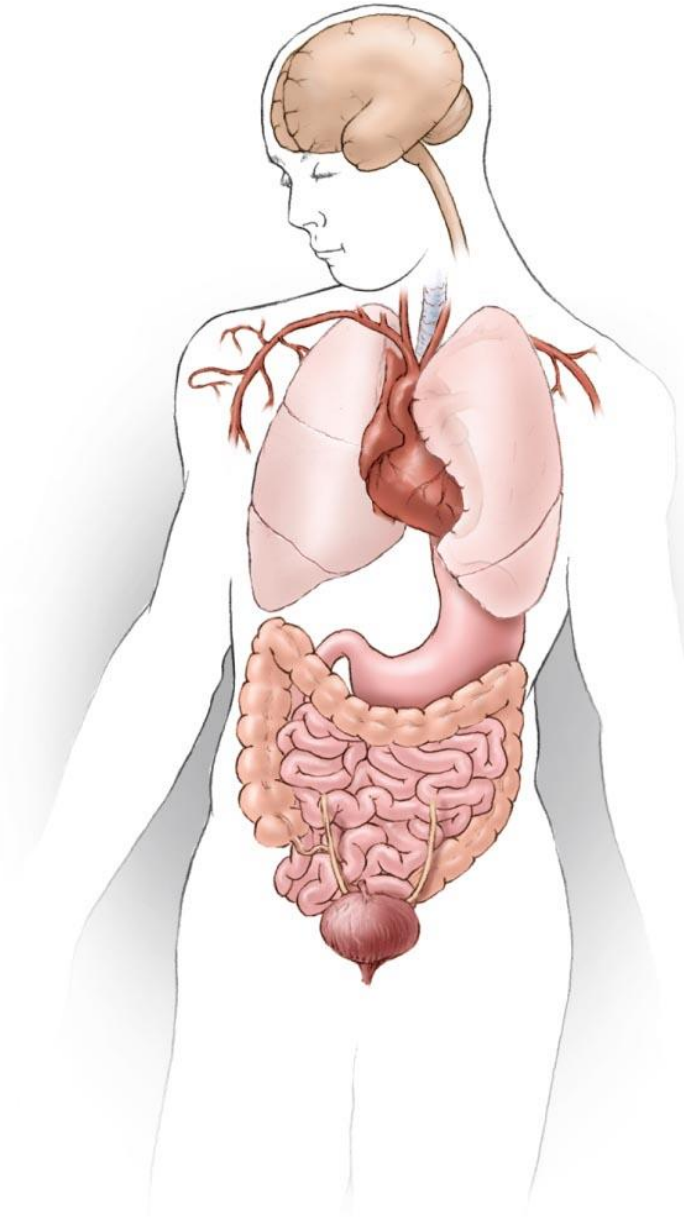
Surat, known as India's diamond capital because of its vast diamond polishing business, continues to tread the blazing path it chose for itself after the plague alarm. Today, the city's roads, flyovers, traffic islands and overall cleanliness leave one spellbound.

The Surat Municipal Corporation (SMC) has one of the best water-treatment plants in the country, while its solid waste-disposal system is arguably the best in the country, meticulously conforming to the Supreme Court guidelines. Compared with 15 gardens in 1995, Surat now has 62 gardens.

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **Truly Pathogenic Enterobacteriaceae**
  - *Yersinia*
    - *Y. pestis*
      - Diagnosis and treatment must be rapid
        - Fast progression and deadliness of the plague
        - Characteristic symptoms are usually diagnostic
        - Many antibacterial drugs are effective

**Figure 20.19 Sites of infection by some common members of the Enterobacteriaceae.**



**Central nervous system**
***Escherichia***

**Lower respiratory tract**
***Klebsiella***
***Enterobacter***
***Escherichia***
***Yersinia***

**Bloodstream**
***Escherichia***
***Klebsiella***
***Enterobacter***

**Gastrointestinal tract**
***Salmonella***
***Shigella***
***Escherichia***
***Yersinia***

**Urinary tract**
***Escherichia***
***Proteus***
***Klebsiella***
***Morganella***

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Pasteurellaceae**
  - Most are small, nonmotile, facultative anaerobes
  - Require heme or cytochromes for growth
  - Two genera contain most human pathogens of this family:
    - *Pasteurella*
    - *Haemophilus*

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Pasteurellaceae**
  - ***Pasteurella***
    - Normal microbiota in oral and nasopharyngeal cavities of animals
    - Humans infected via animal bites or inhalation of aerosols
    - Most cases produce localized inflammation
    - Widespread infection and bacteremia can occur in immunosuppressed individuals
    - Diagnosis is by identification of bacteria in patient specimens
    - Antibacterial drugs are effective treatment

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Pasteurellaceae**
  - ***Haemophilus***
    - Small, pleomorphic bacilli
    - Require heme and $NAD^+$ for growth
    - Colonize mucous membranes of humans and some animals
    - Some species cause opportunistic infections
    - *Haemophilus influenzae* is the most significant pathogen in this genus
    - *H. ducreyi* causes sexually transmitted disease

# Pathogenic, Gram-Negative, Facultatively Anaerobic Bacilli

- **The Pasteurellaceae**
  - *Haemophilus*
    - *Haemophilus influenzae*
      - Most strains have capsule that resists phagocytosis
      - *H. influenzae* type b(Hib) is most significant strain
        - Common cause of meningitis prior to vaccination
        - Hib vaccine has eliminated most disease by *H. influenzae* in the United States
      - Other *H. influenzae* strains cause a variety of diseases
        - Conjunctivitis, sinusitis, dental abscesses, meningitis