Microbiology

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Enterobacteriaceae Classification

- **Introduction**
  - Over 50 genera and hundreds of species/subspecies, ubiquitous in soil, water, vegetation, and part of normal intestinal flora in most animals, including humans.
  - Can be part of normal intestinal flora, associated with disease, opportunistic infections, or become pathogenic when acquiring virulence genes.
  - Non-spore-forming, gram-negative rods (0.3–1.0 × 1.0–6.0 μm), facultative anaerobes with a common antigen (enterobacterial common antigen).

- **Pathogenesis & Immunity**
  - *Endotoxin* activity depends on *lipid A* component of LPS released during cell lysis.
  - Hydrophilic *capsular* antigens repel phagocytes, but anticapsular antibodies reduce capsule role.
  - *Antigenic Phase Variation* (somatic O, capsular K, and flagellar H antigens alternate).
  - *Type III Secretion Systems*.
  - Counteract iron sequestration via *siderophores* or iron-chelating compounds (e.g., enterobactin, aerobactin).
  - Resistance to serum killing and antimicrobial resistance.

- **MacConkey's Agar**
  - Contains *bile salts* (inhibit Gram-positive bacteria), *crystal violet dye*, and *neutral red dye* (turns pink for lactose fermenters).
  - Lactose fermenting colonies appear pink, non-fermenters are colorless.
  - Classification based on biochemical properties, antigenic structure, and molecular/genomic analysis.

- **Antibiotic Resistance**
  - Resistance in Enterobacteriaceae, especially to β-lactam antibiotics, due to mobilized genes encoding drug-modifying enzymes.
  - Multi-drug resistance (*MDR*) is a significant global problem, often worsened by empiric antibiotic use without susceptibility testing.
  - Shift from natural resistance mechanisms (*membrane impermeability*, drug efflux) to *mobile gene pools* transmitting resistance.

- **Pathogens Discussed are :**
  - **Escherichia coli**
  - **Salmonella**
  - **Shigella**
  - **Yersinia**
  - **Klebsiella**
  - **Proteus**

- **Escherichia coli**
  - Most studied and common member of Enterobacteriaceae, both a commensal and pathogen.
  - Causes diarrheal diseases and is a frequent cause of bloodstream infections and urinary tract infections (UTIs).
  - **Strains:**
    - ✓ *Commensal*: Typically harmless, can cause disease with a large inoculum or compromised host.

- ✓ *Diarrhoeagenic*: Varied clinical presentations based on virulence traits.
- ✓ Extraintestinal pathogenic E. coli **(***ExPEC***)**: Colonizes the gut but can invade extraintestinal sites to cause disease.

➢ ***Enterotoxigenic E. coli (ETEC)***

- ✓ Common cause of bacterial diarrhea in developing countries and traveler's diarrhea.
- ✓ Transmitted via contaminated food or water, person-to-person spread does not occur.
- ✓ **Symptoms**: Watery, non-bloody diarrhea, abdominal cramps; can be fatal in undernourished individuals.
- ✓ **Toxins**:
  - Heat-stable toxin (increases cGMP → hypersecretion of fluids, decreased absorption).
  - Heat-labile toxin (increases cAMP → enhanced chloride secretion, decreased sodium/chloride absorption).

➢ ***Shiga Toxin–Producing E. coli (STEC)***

- ✓ Often from undercooked meat, unpasteurized milk/juice, raw vegetables/fruits. . Ingestion of fewer than 100 bacteria can produce disease, and person-to-person spread occurs
- ✓ Mild diarrhea to hemorrhagic colitis with severe pain and bloody diarrhea; Severe disease is more commonly associated with STEC O157:H7.
- ✓ *Complication*: Hemolytic uremic syndrome (HUS) in 5-10% of children under 10 years, leading to renal failure.

➢ **Extraintestinal Infections**

- ✓ Urinary Tract Infection *(UTI):* Most common cause of UTIs, especially in women (80% of cases). UTI originates from the colon.
- ✓ *Neonatal Meningitis*: E. coli causes many CNS infections in infants under 1 month.
- ✓ *Septicemia*: Commonly caused by E. coli infections in urinary/GI tracts, with high mortality in immunocompromised patients.

- **Salmonella**

➢ Colonizes animals, especially poultry. Types like *Salmonella Typhi* and *Salmonella Paratyphi* are adapted to humans.

➢ **Invasion**: After ingestion and passage through the stomach, salmonellae attach to the mucosa of the small intestine and invade into the M (microfold) cells located in Peyer patches, as well as into enterocytes. The bacteria remain in endocytic vacuoles, where they replicate. The bacteria can also be transported across the cytoplasm and released into the blood or lymphatic circulation. The inflammatory response confines the infection to the GI tract, mediates the release of prostaglandins, and stimulates cAMP and active fluid secretion.

➢ **Virulence**: Dependent on pathogenicity islands encoding toxins, attachment proteins, immune evasion mechanisms.

➢ **Epidemiology and Diseases**

- ✓ *Sources of Infection*: Poultry, eggs, dairy, contaminated surfaces , large inoculum (e.g., 106 to 108 bacteria) is required for symptomatic disease
  - The infectious dose for Salmonella Typhi infections is low, so person-to-person spread is common, occur when food or water contaminated by infected food handlers is ingested.
- ✓ *Gastroenteritis*: Common, with nausea, vomiting, nonbloody diarrhea, resolving in 2-7 days.
- ✓ *Septicemia*: Caused by all Salmonella species, with a bacteremic phase more common in *Salmonella Typhi* and *Salmonella Paratyphi*.
- ✓ *Typhoid Fever*: Caused by *Salmonella Typhi*, characterized by gradually increasing fever, headache, malaise, and anorexia.
- ✓ *Paratyphoid fever*, is produced by other Salmonella (e.g paratyphi).[milder]

- **Shigella**
  - **Species**: *S. dysenteriae*, *S. flexneri*, *S. boydii*, *S. sonnei* (genetically part of *E. coli*).
  - **Mechanism**: Invades and replicates in colon cells, with toxin-mediated damage to intestinal epithelium and possible renal failure (HUS).
    - ✓ Shigella passes the epithelial cell (EC) barrier by *transcytosis through M cells* and encounters resident macrophages. The bacteria *evade degradation in macrophages by inducing an apoptosis-like cell death*, which is accompanied by proinflammatory signaling. Free bacteria invade the EC from the basolateral side, move into the cytoplasm by actin polymerization, and spread to adjacent cells. Proinflammatory signaling by macrophages and EC further activates the innate immune response and attracts PMN. The influx of PMN *disintegrates the EC lining,* which initially exacerbates the infection and tissue destruction by facilitating the invasion of more bacteria. Ultimately, PMN phagocytose and kill Shigella, thus contributing to the resolution of the infection.
  - **Toxin**: Shiga toxin disrupts protein synthesis by cleaving 28S rRNA.
  - **Spread**: Person-to-person via the fecal-oral route, highly contagious with a low infectious dose (100-200 bacteria).
  - **Epidemiology & Diseases**
    - ✓ *Reservoir*: Humans only.
    - ✓ *Common Strains*: *S. sonnei* in the U.S., *S. flexneri* in developing countries.
    - ✓ *Symptoms*: Abdominal cramps, diarrhea, fever, bloody stools (appears 1-3 days post-ingestion).
    - ✓ *Treatment*: Typically self-limiting, but antibiotics reduce secondary spread.

- **Klebsiella**
  - Found in the human nose, mouth, and gastrointestinal tract.
  - Common Species: *K. pneumoniae*, causes pneumonia, wound infections, and UTIs.
  - Hospital-Acquired Infections: Spreads via contaminated surfaces, especially in hospitals.

- **Proteus**
  - Species: *P. mirabilis*, causes urinary tract infections.
  - Mechanism: Produces urease, leading to increased urine pH, kidney stones (struvite/apatite crystals), respectively, and results in the formation of renal (kidney) stones. The increased alkalinity of the urine is also toxic to the uroepithelium.

- **Yersinia**
  - Pathogen: *Y. pestis* causes bubonic plague.
  - Transmission: Zoonotic, spread by flea bites (urban plague from rats, sylvatic plague from animals like squirrels).
  - Symptoms: Fever, painful lymph node swelling (bubo), bacteremia, and high mortality if untreated.
  - Spread: Person-to-person via aerosol in pneumonic plague.

- **Antibiotic Resistance**
  - *Carbapenem-resistant Enterobacteriaceae (CRE):* Resistant to carbapenem antibiotics (last-resort treatment).
  - *Mechanism*: Produce carbapenemases that disable antibiotics.
  - *Risk Factors*: Healthcare exposure, prior antibiotic use. CRE poses a major public health threat, with a high mortality rate (up to 50% in bloodstream infections).

Questions

1. Which of the following media is selective and differential for Enterobacteriaceae?
    - •A. Blood agar
    - •B. MacConkey agar
    - •C. Chocolate agar
    - •D. Sabouraud agar

2. Which of the following is NOT a characteristic feature of Enterobacteriaceae?
    - •A. Gram-negative rods
    - •B. Ferment glucose
    - •C. Oxidase-positive
    - •D. Facultative anaerobes

3. What component of the Enterobacteriaceae cell wall is responsible for triggering a strong immune response?
    - •A. Lipid A of lipopolysaccharide (LPS)
    - •B. Peptidoglycan layer
    - •C. Outer membrane proteins
    - •D. Teichoic acids

4. What is the primary mode of transmission for non-typhoidal Salmonella species?
    - •A. Contaminated water
    - •B. Respiratory droplets
    - •C. Contaminated food, particularly poultry and eggs
    - •D. Insect vectors

5. Case Scenario: A 6-year-old child in a daycare center develops bloody diarrhea and fever. Stool culture identifies a non-motile, Gram-negative bacillus. What is the most likely pathogen?
    - •A. Escherichia coli
    - •B. Salmonella Enteritidis
    - •C. Shigella flexneri
    - •D. Klebsiella pneumonia

6. Which toxin produced by enterohemorrhagic Escherichia coli (EHEC) is responsible for hemolytic uremic syndrome (HUS)?
    - •A. Heat-labile toxin (LT)
    - •B. Heat-stable toxin (ST)
    - •C. Shiga-like toxin
    - •D. Endotoxin

7. Which Yersinia species is associated with the bubonic plague?
    - •A. Yersinia enterocolitica
    - •B. Yersinia pseudotuberculosis
    - •C. Yersinia pestis
    - •D. Yersinia kristensenii

8. Which condition is commonly associated with Klebsiella pneumoniae infections?
    - •A. Urinary tract infections in young children

•B. Lobar pneumonia with "currant jelly" sputum
•C. Skin abscesses
•D. Diarrheal disease in travelers

9. Case Scenario: A patient with recurrent urinary tract infections has urine cultures showing a swarming Gramnegative rod that is urease-positive. What is the most likely organism?
•A. Escherichia coli
•B. Proteus mirabilis
•C. Klebsiella pneumoniae
•D. Salmonella Typhi

10. A 25-year-old female presents with a urinary tract infection. The causative organism is found to be lactose-fermenting and indole-positive. What is the most likely organism?
•A. Escherichia coli
•B. Klebsiella pneumoniae
•C. Proteus mirabilis
•D. Salmonella Typhi

11. A second-year medical student experiences watery diarrhea and mild abdominal cramps during his 2-week travel to Egypt. With his little medical knowledge, he makes several assumptions, which of those assumption is false?

a) This is probably a case of traveler's diarrhea that should resolve within a few days.
b) Enterotoxigenic E. coli (ETEC) is a probable causative agent.
c) He would not have become sick if he washed his hands properly.
d) Liquids are important to prevent dehydration and loss of electrolytes.
e) If it is traveler's diarrhea, he probably contracted the pathogen in a meal he ate 2 days ago.

Answers

1. Which of the following media is selective and differential for Enterobacteriaceae?
   - B. MacConkey agar
2. Which of the following is NOT a characteristic feature of Enterobacteriaceae?
   - C. Oxidase-positive
3. What component of the Enterobacteriaceae cell wall is responsible for triggering a strong immune response?
   - A. Lipid A of lipopolysaccharide (LPS)
4. What is the primary mode of transmission for non-typhoidal Salmonella species?
   - C. Contaminated food, particularly poultry and eggs
5. Case Scenario: A 6-year-old child in a daycare center develops bloody diarrhea and fever. Stool culture identifies a non-motile, Gram-negative bacillus. What is the most likely pathogen?
   - C. Shigella flexneri
6. Which toxin produced by enterohemorrhagic Escherichia coli (EHEC) is responsible for hemolytic uremic syndrome (HUS)?
   - C. Shiga-like toxin
7. Which Yersinia species is associated with the bubonic plague?
   - C. Yersinia pestis
8. Which condition is commonly associated with Klebsiella pneumoniae infections?
   - B. Lobar pneumonia with "currant jelly" sputum
9. Case Scenario: A patient with recurrent urinary tract infections has urine cultures showing a swarming Gram-negative rod that is urease-positive. What is the most likely organism?
   - B. Proteus mirabilis

10. A 25-year-old female presents with a urinary tract infection. The causative organism is found to be lactose-fermenting and indole-positive. What is the most likely organism?
    - A. Escherichia coli
11. The false assumption is:
    c) He would not have become sick if he washed his hands properly.

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