INTRA-ABDOMINAL INFECTIONS

I. INTESTINAL
BACTERIAL & PARASITIC – Grouped by virulence mechanism

I. SECRETORY (WATERY) DIARRHEA (NON-INFLAMMATORY)
(toxogenic bacterial, viral, or noninvasive parasitic)
Separation into non-inflammatory (secretory) vs. inflammatory intestinal infection is based in part on the presence of leukocytes in stool as an indication of inflammatory infection. Bacteria causing secretory diarrhea include members of the Enterobacteriaceae and Vibrionaceae.

A. BACTERIAL ENTEROTOXIGENIC DIARRHEA

*Vibrio cholerae* O1 & O139

1. Virulence factors:
   a. Motility - Single polar flagellum
   b. Adherence
      Long filamentous pili (Tcp pili = toxin C coregulated pili)
      Hemagglutinin - agglutinate erythrocytes; may contribute to adherence to mucosal cells.
   c. Accessory colonization factor (acf)
   d. Mucinase production
      A protease (hap = hemagglutinin-protease) can cause hemagglutination but more important for role in detaching organism from mucosal cell surface. Allows bacteria to free themselves from sloughing cells of mucosa and re-attach to newly formed cells.
   e. Choleratoxin (choleragen). An A-B type ADP-ribosylating toxin:
      A (enzymatic) subunit
      B (binding) five identical subunits
A-B Toxin Model

The 5:1 stoichiometry in the final form of the toxin is dictated by interactions between the B subunits and between the five subunit complex and the A subunit. Intact A subunit is not enzymatically active but must be nicked to produce fragments: A1 and A2. Excreted toxin attaches to the surface of a patient mucosal cell by binding to host cell GM1 gangliosides. Once cholera toxin is bound to GM1, the A1 subunit is released from the toxin and the A1 subunit enters the host cell. The A1 subunit ADP-ribosylates a membrane protein called Gs. This is one of the family of GTP-hydrolyzing proteins called G proteins that regulate many aspects of eucaryotic cell functions. Gs is the G protein that regulates the activity of host cell adenylate cyclase in a hormone-dependent manner and thus determines the level of cyclic AMP (cAMP) in patient cells. cAMP is a regulatory molecule in eucaryotic cells that has a variety of effects, the most important of which is to control activities of sodium and chloride transporters. The increased cAMP causes alterations that produce the ion imbalance that results in the water loss associated with cholera (hypersecretion of fluids and chloride ions and inhibition of sodium absorption).
2. Etiology/Pathogenesis:
   a. Large number of organisms ingested (need $10^8$ for disease)

   b. Attachment to the brush borders of epithelial cells in the small intestine - aided by flagella and pili

   c. Organism replicates to very high numbers; produce and excrete choleragen which binds to ganglioside receptors on patient epithelial cells.

   d. Massive watery diarrhea - no PMNs - mucosal surface with mucus - resemble rice in clear watery fluid = rice water stool.

   e. Patients rapidly become dehydrated and electrolyte loss

   f. Seventh pandemic (1961 to present) by Ogawa serotype.

3. Clinical identification of organism:
   a. Stool only specimen for diagnosis
      “Boil it, cook it, peel it, or forget
   b. Special medium: TCBS (Thiosulfate Citrate Bile Sucrose)
   c. Oxidase positive; curved Gram negative bacillus
   d. Serotype O1 virulent from less virulent other serotypes
      Epidemic cholerae caused by two biotypes of O1 V. cholerae:
      - Classic
      - El Tor
      Three serological subgroups of each biotype:
      - Ogawa = AB
      - Inaba = AC
      - Hikojima = ABC
   e. Treatment: fluid and electrolyte replacement

   Vibrio cholerae O139 Bengal
   b. Epidemic cholera-like illness and seems to have replaced O1 in endemic area
   c. Symptoms indistinguishable from cholerae caused by O1 strains.
   d. Rapid spread of V. cholerae O139 suggests that preexisting immunity to V. cholerae O1 offers little or no protection to O139.
**Escherichia coli** -

*E. coli* strains are a heterogeneous group of bacteria with a wide spectrum of interactions with humans. Strains vary from nonpathogenic or normal flora to true pathogens and include opportunistic organisms such as uropathogenic *E. coli*. *E. coli* causing diarrhea have been divided into various groups according to their virulence properties:

- ETEC = enterotoxigenic *E. coli*
- EIEC = enteroinvasive *E. coli*
- STEC = shiga-toxin *E. coli* (EHEC = enterohemorrhagic *E. coli*)
- EPEC = enteropathogenic *E. coli*
- EAEC = enteroadherent *E. coli*

### Classification of Pathogenic *Escherichia coli*

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Enterotoxigenic *E. coli* (ETEC)

1. Virulence factors:
   
   a. Adherence
      
      Colonization factor antigens I and II (CFA/I and CFA/II)
      
      CFA genes are usually located on plasmids
      
      CFA on pili and act as adhesions
      
      Receptors are glycoproteins on cell surface
      
      Other adhesions factors recently identified
      
      Bundle-forming - structure similar to that of the Tcp
      pili of *V. cholerae*. (also called “longus” because of
      length)
      
      ETEC strains adhere preferentially to differentiated cells with
      microvilli on their cell surface.
   
   b. Toxins
      
      Heat labile toxin (LT) - 100°C for 30 minutes
      
      LT- Shares a high degree (ca. 75%) of amino
      acid sequence identity with cholera toxin.
      
      LT has the same structure (five B subunits and
      one A subunit.
      
      Mechanism of action similar to cholera toxin:
      ADP- ribosylation of Gs, which raises host cell
      cAMP level
      
      B subunits of LT binds to same cell receptor as
      cholera toxin - Gm1. Unlike cholera toxin, LT-I
      is not excreted out of the bacterium but is
      localized in the periplasm.

      Heat stable toxin (ST) - not inactivated at 100°C for 30
      minutes. Not a single toxin but a family of small
      molecules. ST is methanol soluble. Acts by
      binding to a guanylate cyclase that is located in
      the apical membrane of the host cell. The
      binding results in an activation of the guanylate
      cyclase which causes an increase in cyclic GMP
      (cGMP). The cGMP is an important signaling
      molecule in eucaryotic cells and causes fluid
      and electrolyte loss.
2. **Etiology/Pathogenesis:**

   a. Genes for CFA, LT, and ST are often carried on the same plasmid.

   b. ETEC colonizes the small intestines by means of fimbrial or aflagellar adhesions (CFAs). Bacteria producing LT and/or ST lead to diarrhea.

   c. Contaminated food and beverages are the major vehicles of infection.

   d. Highest incidence in tropics and in young.

   e. Most common cause of “Travelers Diarrhea”

   f. Incubation period of 1 to 2 days. Starts as nausea, abdominal pain, and vomiting: followed by watery diarrhea (mild to severe)

3. **Identification of Organism:**

   a. No simple clinically diagnostic test available to distinguish ETEC from other *E. coli*. Research testing available include: cell culture toxicity, ELISA, and PCR.

**Enteropathogenic *E. coli* (EPEC)**

1. **Virulence factors:**

   a. **Step one.** Bacteria adhere to target epithelial cells in a distant manner (“**nonintimate**”). Binds via a “**bundle-forming-pilus**”

   b. **Step two.** Bacteria attach more closely, cell **actin** is polymerized immediately beneath the organism and alters the shape of the microvillus. This rearrangement is known as “**effacement**” of the plasma membrane.

   c. **Step three.** The “**intimate**” contact between the bacteria and epithelial cells is mediated by a number of new bacterial proteins (i.e., **intimin** and **39kDa**)

These three steps result in the characteristic pathology known as: **attaching and effacing lesion.** It is not understood how this causes diarrhea but is thought to involve cell membrane signaling and cell surface damage interfering with adsorption.
Bacterial Neurtoxin Group

Clostridium botulinum

1. Virulence factors:
   a. Botulinal toxin
      (1) A large protein, binds to peripheral neurons.
      (2) Bound toxin is internalized and inhibits release of acetylcholine (a neurotransmitter)
      (3) Eight different serotypes: A, B, Cα, Cβ, D, E, F, and G. Type A and B mostly in United States. Humans usually caused by toxins A, B, and E.
      (4) Toxin is an AB toxin. The B portion binds to ganglioside receptors on nerve cells.
      (5) The toxin affects peripheral nerve endings at the neuromuscular junction, blocking presynaptic release of acetylcholine, which prevents muscle contraction and causes flaccid paralysis.

2. Etiology/Pathogenesis
   Food botulism.
   a. C. botulinum is an anaerobic Gram positive, spore forming bacillus.
   b. Found animal feces, soil, and lake sediment.
   c. Contaminates food; spore germinates with bacterial growth and toxin production. Food must be anaerobic.
   d. Botulinum toxin inactivated by boiling for 10 to 15 minutes.
   e. Ingested botulinum toxin is absorbed from the stomach and enters the blood stream.
   f. Toxin binds to the peripheral nerve endings - blocks
neurotransmitter release. Nerve impulses cannot be transmitted and muscles connected to the nerves are not stimulated - results in flaccid paralysis.
g. Symptoms occur in 4 to 36 hours after ingestion of toxin

**Infant botulism** - infants without complete colonic microflora. *C. botulinum* colonize infant colon and grow to high number with toxin production. A rare cause of “Sudden Infant Death Syndrome”.

**Wound botulism** - Colonizes deep wounds (anaerobic). Botulinum toxin leaks into the blood.

3. **Identification of organism:**
   a. Usually a clinical identification without culture
   b. Organism can be grown in oxygen free laboratory environment
   a. Laboratory confirmation usually made by demonstrating toxin in food substance, gastric contents, or blood.

**Other organisms producing neurotoxins**

* Bacillus cereus* (*emetic toxin*)
* Staphylococcus aureus* (*enterotoxin b*) - acts on the central autonomic nervous system rather than destruction or fluid secretion in the intestine

**C. NON-INFLAMMATORY PARASITIC**

*Giardia lamblia*

1. **Virulence factors:**
   a. Flagellated enteric protozoan whose life cycle contains two stages: the trophozoite (free living stage) and cyst
   b. Infective stage is the cyst and there is an incubation period of 7 to 10 days (range 3 to 25 days).
   c. Ventral surface disk referred to as the sucking or adhesive Disk responsible for attachment to the upper small intestine Mucosal surface.
   d. Flagella are involved in motility and attachment
d. Symptoms: acute onset of diarrhea, abdominal Cramps, bloating, and flatulence.
f. Causes a watery or non-inflammatory diarrhea
2. Etiology/Pathogenesis:
   a. Infection occurs following oral ingestion of cysts since
trophozoites are destroyed by gastric acidity.
b. Acute diarrhea with some progressing to chronic diarrhea with
malabsorption. Syndrome may wax & wan over months. Weight
loss usual.

3. Identification of organism:
   a. Microscopic examination of stool, duodenal aspiration, or
duodenal biopsy for “Ova & Parasite”
Examination.
   Trophozoite is pear shaped and dorsoventrally flattened and has a
large ventral surface sucking disk, two nuclei, eight flagella, and a
pair of curved bodies in the center called “median bodies”.
Trophozoite is 9 - 21µ in length.
   Cyst is oval and 8 - 14 µ in length and contains four
nuclei, the median bodies
b. Antigen tests for G. lamblia antigen in stool.
c. String test. A gelatin capsule containing a nylon string, the free
end is secured at the mouth and the capsule is swallowed. It
dissolves in the stomach and the string continues through the
duodenum to the jejunum. After 4 to 6 hours or overnight
incubation while fasting, the string is removed, the bile stained
mucus is squeezed onto microscopic slide and the preparation
examined microscopically for trophozoites.
d. Eosinophilia is not found in giardiasis.

Other noninvasive parasitic agents of non-inflammatory diarrhea:

   Cryptosporidium parvum - small coccidian protozoan parasite
causes severe, watery, prolonged diarrhea, especially in
immunocompromised patients.
   Microsporidia (Microspora) - five genera
   Cyclospora cayetanensis - (cyanobacterium-like bodies)
   Isospora belli - clinically almost indistinguishable from
giardiasis, cryptosporidiosis, and microsporidiosis, presenting as
diarrhea without blood or leukocyte
Cryptosporidium spp.
oocyst containing 4 sporozoites
4 μm

Cyclospora
immature oocyst
8 to 10 μm

Microsporidians
II. INVASIVE AND TISSUE-DAMAGING DIARRHEA (INFLAMMATORY DIARRHEA)

A. BACTERIAL CYTOTOXIN CAUSED INFLAMMATION

*Clostridium difficile* - *C. difficile* is a spore forming, anaerobic, Gram Positive bacillus that is normal flora in about 3% of healthy adults. Under appropriate conditions, the organism can cause an acute inflammation of the colonic mucosa (a pseudo-membrane may be absent or extensive). The pseudomembranes and plaques consist of fibrin, mucus, necrotic epithelial cells, and leukocytes adherent to the underlying inflamed mucosa. aka “Antibiotic associated colitis”

1. Virulence factors:
   a. **Toxin-A** Enterotoxin. and causes an accumulation of fluid (not watery; more viscous and bloody). Damages mucosal cells.
      Chemotactic for PMNs and lyses them resulting in release of inflammatory mediators which cause fluid secretions, altered membrane permeability, and hemorrhagic necrosis of mucosa.

   b. **Toxin-B** Cytotoxin. No enterotoxin activity but kills cells. Potent cytotoxin which disrupts the microfilament system of cells and decreases cellular protein synthesis (action similar to diphtheria toxin).

   c. Adhesins. Not identified yet.

2. Etiology/Pathogenesis:
   a. Endogenous or from environment (nosocomial)

   b. Altered intestinal flora from antibiotics

   c. Colon on gross inspection varies: normal mucosa, erythema, edema, severe inflammation, or pseudomembranous lesions (composed of fibrin, mucus, inflammatory cells, and sloughed mucosal cells).

   d. Age related susceptibility to toxins. Newborns remain well despite high levels of toxins.
3. Identification of organism:
   a. Selective medium - CCFA (cycloserine, cefoxitin, fructose agar). Culturing organism not helpful.
   b. Toxin tests in stool clinically most useful:
      Toxin A (enterotoxin). EIA test on stool

Escherichia coli – Shiga-toxin E. coli (STEC) also referred to as Enterohemorrhagic E. coli (EHEC) or Verocytotoxin E. coli - Causes diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome (HUS).

1. Virulence factors:
   a. Adhesions - tight binding to mucosal cells
      Produce intimin (eaeA gene) - mediates tight binding of bacteria to the host cells.
   b. Toxins: Shiga-Like or VeroToxin is an AB type toxin. The A subunit enzymatically modifies 28S ribosomal RNA of the 60S-ribosomal subunit by removing an adenine base. This prevents elongation-factor-1-dependent binding of amino acyl tRNA to the ribosome. This blocks protein synthesis and eventually leads to cell death.
      The toxin causes capillary thrombosis and associated inflammation of the colonic mucosa which leads to hemorrhagic colitis.
      Shiga-Like Toxin - I or Vero-Toxin 1
      Shiga-Like Toxin - II or Verotoxin 2
      Bacteriophage encoded genes (Stx1 and Stx 2.
      Receptor mediated cytopathic effect (CPE) on endothelial cells of capillaries and small blood vessels of the kidneys, intestines, central nervous system and other organs.
2. Etiology/Pathogenesis:

a. The Shiga-like-toxin(AB toxin) producing strains colonize the intestinal tracts of cattle and other farm animals.

b. Small number of organisms can cause infection

c. Contaminated meat (particularly hamburger), milk, and apple cider have been implicated in out-breaks.

d. Incubation period of 3 - 4 days. Median duration of 3 to 8 days. Patient develops severe crampy abdominal pain and copious watery diarrhea which develops into grossly bloody diarrhea. No fecal leukocytes seen. Little or no fever.

e. Serotype O157:H7 causes 50 to 80% of infections.
   - Endemic in cattle - 4% positive.
   - Under-cooked ground beef is major source.

f. Hemolytic Uremic Syndrome (HUS) develops in 5 to 10% of patients, particularly in younger children.
   - Characterized by acute renal failure, thrombocytopenia, And hemolytic anemia. Shiga toxins cause injury to The endothelial cells lining the capillaries of the renal Glomeruli and other tissues.

3. Identification of organism:

b. Serotype O157:H7 does not ferment sorbitol and almost all other strains do. Use sorbitol MacConkey agar (MacConkey agar contains sorbitol in place of lactose). Problem since sorbitol positive strains may also produce the toxins

c. Serogroup with specific anti-O157:H7 serum.

c. Demonstrate cytotoxic activity with Vero Cells
d. DNA probe for detection of shiga-toxin genes.

Other Organisms Causing Cytotoxin Diarrhea:

- *Clostridium perfringens*
- *Vibrio parahemolyticus*
- *Staphylococcus aureus* –superantigen enterotoxins
- *Campylobacter jejuni*
B. BACTERIAL INVASIVE INFECTION

Shigella (bacillary dysentery - blood and mucus in stool)

1. Virulence factors:
   a. Human pathogen and do not infect animals
   b. Adherence.
      (1). Attachment provokes reorganization of host cell actin in the vicinity of the bound bacteria.
      (2). Actin rearrangement causes pseudopods to form on mucosal cell
      (3). Normally nonphagocytic mucosal cell ingests attached bacteria
      (4). Ingested Shigella escape the endocytic vesicle and multiple in the cytoplasm
      (5). Actin rearrangements occur in the vicinity of the Shigella and they move through the mucosal cell
      The Shigella invade adjacent cells and repeat infection and replication. Shallow ulcers develop
      (6). Growth of shigellae in the mucosal cell cytoplasm results in death of the host cell
      (7). Local inflammation occurs with abundant neutrophils, RBCs, and mucus in the stool.
   c. Invasion of the intestinal mucosa. Infection is superficial with very rare penetration beyond the mucosa. Invasiveness is associated with a mixture of soluble bacterial proteins.
   d. Toxin production: an exotoxin with enterotoxin activity and also some cytotoxin properties.
      Invasiveness is the primary virulence characteristic of Shigella strains, but toxin plays a role in the local destruction of the mucosa.

2. Etiology/Pathogenesis:
   a. Shigella are the most communicable of the bacterial diarrheas and as little as 200 viable organisms produce disease. There are four serogroups of Shigella:
      S. dysenteriae - Group A Shiga bacillus; largest producer of toxin
      . S. flexneri - Group B
      S. boydii - Group C
      S. sonnei - Group D 60 to 80% of United States cases
b. Disease:
   Organisms ingested and multiply in the small intestine to concentrations of $10^9$ viable *Shigella* per ml of luminal contents. Higher numbers occur lower in the intestine.
   Abdominal pain, cramping, and fever occur while the bacteria are localized in the small intestine. This occurs during the first 12 hours.
   After a few days, organism no longer detectable in upper intestine, fever decreases, but pain becomes more severe and localizes to lower quadrants.
   Dysentery develops (urgency, tenesmus, and bloody mucoid stool) with diffuse colonic localization.
   Large numbers of PMNs in mucoid stool.
   >200,000,000 cases worldwide per year
   650,000 deaths per year (mostly in children)

   e. Invasiveness demonstrated by positive Sereny test - keratoconjunctivitis following conjunctival inoculation of *Shigella*.

3. Identification of Organism:
   a. Lactose negative colonies on selective media (MacConkey or Hektoen agars) for enteric bacterial pathogens.
   b. Oxidase negative.
   c. Non-motile Gram negative bacillus
   d. Biochemical and physiological profile distinguishes *Shigella*.
   e. Serological identification of serogroup or species.

*Escherichia coli* – *enteroinvasive* (EIEC)

**Virulence Factors** –
   Behaves like *Shigella*
   No Shiga toxin
   Infects and spreads cell-to-cell like *Shigella*
Salmonella

1. Virulence Factors:
   a. Adherence. Organism binds to microvilli.
   b. Binding causes change on surface of mucosal cell - ruffle-like appearance (ruffling)
   c. Extensive actin rearrangement in the vicinity of the attached bacteria
   d. Bacteria are engulfed in a vesicle and surface of the cell returns to normal
   e. Salmonella remain inside vesicle (phagosome) and replicate. Survive killing by:
      (1). Resistance to reactive forms of oxygen: catalase superoxide dismutase
      (2). Resistance to defensins (toxic peptides that kill bacteria)
   f. LPS - induce inflammatory response and contribute to mucosal damage.
   g. Systemic infection - serum resistance aided by length of the O antigen of the LPS and production of an outer membrane protein which blocks killing by complement.
   h. Vi antigen in S. typhi. Capsular polysaccharide which contributes to extra virulence and invasion by this species.

2. Etiology/Pathogenesis
   a. Outer Membrane in Gram Negative Bacteria:
      (1). Inner side is phospholipids
      (2). Outer side of membrane contains Lipopolysaccharide (LPS).

   b. Genus is biochemically and antigenically complex. Serologically diverse group (over 2000 serotypes based on O and H antigens).
      (1). O antigens: branched polysaccharide portion of LPS that extends out from gram negative bacterial surface.
      (2). H antigen: protein structural antigen of bacterial flagella
c. Endotoxin - LPS of outer membrane. Lipid A is responsible for toxic aspect of Endotoxin. In outer membrane and released upon lysis.
Activates complement
Stimulates release of cytokines.

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Structure of LPS.

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d. Salmonella are widely distributed in animal kingdom. Some serotypes are only found in humans. Highest incidence in children
e. Large inoculum needed ($10^4$ - $10^8$)
f. Clinical Syndromes:

1. **Gastroenteritis**: ranging from mild to fulminant, which is often accompanied by nausea, vomiting, and a low grade fever; frequently have a zoonotic origin
   Most common form of *Salmonella* infection
   Incubation period is 6 to 48 hours. Last 2 to 3 days
   Ingest organisms ---+ stomach ---+ adhere to brush boarder of mucosal cells
   ---+ induce ruffling ---+ invade cells in vesicles ---+ replicate intracellularly in vesicles ---+ spreads to lamina properia layer ---+ multiply in lymphoid follicles
   ---+ leukocyte response ---+ stimulates prostaglandin mediated production of cyclic AMP ---+ fluid secretion.

Stools are loose, of moderate volume, without gross blood. Involve small and large intestine.
Organisms found in stool for several weeks.
(2). **Bacteremia** – accompanied by a high spiking fever that may be accompanied by gastrointestinal symptoms
   All serotypes can cause, some more frequently than others.
   Secondary infection can occur anywhere in the body
   Rare event that sometimes develop following gastroenteritis
   *S. cholerasuis* regularly causes a bacteremia because it penetrates intestinal mucosa.

(3). **Enteric Fever** – classically associated with *Salmonella* serotype typhi but may also involve other serotypes.
   In humans, adapted species is *S. typhi* which causes Typhoid Fever.

   Ingest organism ---> binds to intestinal M cells ---> bacteria replicate and kill M cell ---> spread to Peyer’s patches ---> invade macrophages and replicate within membrane-bound vacuoles ---> carried to reticuloendothelial system ---> spread to blood stream ---> to organs including gall bladder ---> re-enters intestinal tract

   Signs of sepsis develop after 10 - 14 days.
   Intestinal symptoms develop upon re-entry to intestinal tract

   Chronic carriers source is gall bladder (1 to 5 %)

3. **Identification of organism**
   a. Depends on Clinical Syndrome as to which specimen to test:

   (1). Gastroenteritis - stool cultured for lactose negative, oxidase negative isolate which yields biochemical and physiological reactions of *Salmonella*. Serological testing to determine serotype.
(2). Bacteremia - blood cultures. Two samples of 20 ml each. Collection separated by at least one hour.
Stool sample (as above)

(3). Typhoid Fever - Depends on stage of infection:
   Blood culture early
   Stool later in disease.

**Campylobacter**

1. **Virulence Factors:**
   a. Flagella - motility through mucus layer of small intestine. Multiplies in mucus layer
   b. Adhesions - attachment to intestinal epithelium
   c. Syndromes varies:
      (1). Watery diarrhea - enterotoxin contributes
      (2). Bloody diarrhea - cytotoxin destroys intestinal cells and results in bloody diarrhea.
      (3). Invasion of intestinal cells - enterocolitis
   d. Protein S - surface protein that functions as a capsule; blocks complement binding and causes serum resistance to phagocytosis.
   e. Lipopolysaccharide
   f. *Campylobacter* elicit an autoimmune-mediated attack against nerve tissue – “Guillain-Barre” syndrome

2. **Etiology/Pathogenesis:**
   a. Infective dose from 500 to 1,000,000.
   b. Incubation period 1 to 7 days.
   c. Variety of syndromes.
3. Clinical Identification of Organism:
   a. Gastroenteritis - stool; characteristic darting motility
   b. Culture - selective medium; 42°C incubation; microaerophilic; capnophilic
   c. Gram stain: curved Gram negative bacillus; oxidase positive

Other Bacterial Agents of Inflammatory Diarrhea:

*Vibrio parahemolyticus*
- Halophilic, contaminates seafood,
- Invade intestinal cells
- Produce heat stable cytotoxin
- Major problem in Japan

*Yersinia enterocolitica*
- Invasion of terminal ileum
- Necrosis of Peyer’s patches
- Inflammation of mesenteric lymph nodes
- Found in animals (pigs, etc)
- Grows at lower temperatures (blood units)

C. PARASITIC INVASIVE:

*Entamoeba histolytica* (amebic dysentery) - Amebiasis

1. Virulence factors:
   a. Cyst stage - infectious phase; environmental resistant
   b. Trophozoite stage - invasive in tissue
   c. Adherence to luminal surface of the bowel by the parasite’s galactose-inhibitable surface protein - galactose-specific adhesion
   d. Organism contains numerous proteolytic enzymes which are involved in dissolution of the extracellular matrix anchoring cells in tissue structure. Also produce cytolytic enzymes.

2. Etiology/Pathogenesis:
   a. Organisms are found worldwide
   b. Cyst ingested and cyst walls break down in the small intestine. Trophozoites form from the nuclei and cytoplasm of cyst
   c. Trophozoites colonize the colon; disease when invasion
d. Erosion of colonic mucosa begins in the base of the crypts and progresses to ulceration. The ulcers may extend into the submucosa and undermine the normal mucosa to produce flask shaped lesions.
e. Rarely, the trophozoites can enter venules of the colon wall and can be carried to extraintestinal sites with the liver the most frequent area and lead to amebic liver abscess. Difficult to demonstrate organism in extra-intestinal amoebiasis and serological test needed.

3. Clinical Identification of Organism:
a. Microscopic examination of stool or colonoscopic sample
b. Irregular shedding of organisms in stool; X3 samples
c. Identification based on characteristic ultra-structure of cyst and/or trophozoite. (Distinguish invasive *E. histolytica* from non-invasive *E. dispar* by antigenic differences).
**Helicobacter pylori**

*H. pylori* is the major etiological agent of chronic gastritis and peptic ulcers and a major risk factor for gastric cancer.

1. **Virulence Factors:**
   a. *vacA* – encodes for a cytotoxin that damages epithelial cells by inducing vacules.
   b. *cagA* – cytotoxin-associated gene not present in all strains; marker for a genomic pathogenicity island whose presence is associated with more severe clinical outcomes. The *cag* island contains genes encoding proteins that enhance virulence of the strain.
   c. Urease - converts urea to ammonia and carbon dioxide. Bacteria surrounded by layer of ammonia which protects it from acid. Bacteria become established in mucin layer.
   d. Adhesins - several have recently been identified.
   e. Inflammation - several agents believed to contribute and lead to:
      - PMNs
      - B and T cells
   f. Host cells destroyed by inflammation with destruction of mucosa and ulcer development.

2. **Etiology/ Pathogenicity**
   b. Stomach colonization - 50% of adults have antibody.
   c. Believed to cause 90% of duodenal ulcers and 70 to 80% of gastric ulcers.

3. **Clinical Identification of Organism**
   a. Enriched medium in 6 - 8 % oxygen at 37°C; 3 - 7 days incubation
   b. Gastric biopsy for culture or urease test (CLO test)
**E. Food-borne Bacteremia and Menigoencephalitis**

*Listeria monocytogenes*

An uncommon cause of illness in the general population. However, foodborne outbreaks have been increasingly reported over the last few years. Particular groups can be at increased risk to develop life-threatening bacteremia and meningo-encephalitis.

**ORGANISM:**

*L. monocytogenes* is a small, facultatively anaerobic, non-spore forming, catalase positive, oxidase negative, Gram positive bacillus. It is beta hemolytic on blood agar plates and has a characteristic tumbling motility at room temperature and non-motile at 37°C. The organism does not grow on MacConkey agar. There are six species of *Listeria* but only *monocytogenes* is pathogenic for humans.

**EPIDEMIOLOGY:**

*L. monocytogenes* is an important cause of zoonoses (acquired from animals). Widespread in nature and commonly found in soil, decaying vegetation, and fecal flora of many mammals. Many foods are contaminated such as raw vegetables, raw milk, fish, poultry, and meats, including fresh or processed chicken, and beef available at supermarkets or delicatessen counters. The highest infection rates are seen in infants younger than 1 month and adults older than 60 years. Pregnant women account for about 30% of all cases. Most cases not associated with perinatal infections occur in those with hematologic malignancy, AIDS, or organ transplantation, or those receiving corticosteroid therapy. Most foodborne outbreaks are associated with: milk, soft cheeses, and ready to eat meat products (hot dogs).

**PATHOGENESIS:**

Although transmission from mother to fetus has been reported, almost all human infection is from food.

Incubation periods ranging from 11 to 70 days have been reported (mean of 31 days). In the intestine, *L. monocytogenes* crosses the mucosal barrier and enters the blood stream from which hematogenous dissemination may occur to any site. It has particular predilection for the central nervous system (CNS) and the placenta.

**VIRULENCE FACTORS:**

- **Internalin** – bacterial surface protein induces phagocytosis
- **Listeriolysin O** – enables bacteria to escape from phagosome and avoid intracellular killing
- **Act A** protein enables organism to travel to host cell surface and spread from cell-to-cell and avoid antibodies, complement, and neutrophils.
1. **NEMATODES** (round worms)

<table>
<thead>
<tr>
<th>Parasite &amp; Disease</th>
<th>Location in Patient</th>
<th>Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ascaris lumbricoides</em>&lt;br&gt; (larval stage: passes through lungs)</td>
<td>small intestine</td>
<td>ingest eggs</td>
</tr>
<tr>
<td><em>Enterobius vermicularis</em>&lt;br&gt; (pinworm)</td>
<td>cecum, colon</td>
<td>fecal - oral</td>
</tr>
<tr>
<td><em>Ancylostoma duodenale</em>&lt;br&gt; (larval stage: pass through lungs)</td>
<td>small intestines</td>
<td>through skin</td>
</tr>
<tr>
<td><em>Necator americanus</em>&lt;br&gt; (hookworms)</td>
<td>small intestines</td>
<td>through skin</td>
</tr>
<tr>
<td><em>Strongyloides stercoralis</em>&lt;br&gt; (threadworm)</td>
<td>duodenum and jejunum</td>
<td>through skin</td>
</tr>
<tr>
<td><em>Trichuris trichiura</em>&lt;br&gt; (whipworm)</td>
<td>cecum, colon</td>
<td>ingest eggs</td>
</tr>
</tbody>
</table>

2. **TREMATODES** (flukes)

<table>
<thead>
<tr>
<th>Parasite &amp; Disease</th>
<th>Location in Patient</th>
<th>Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Clonorchis sinensis</em>&lt;br&gt; (Chinese liver fluke)</td>
<td>liver (bile ducts)</td>
<td>raw freshwater fish</td>
</tr>
<tr>
<td><em>Fasciola hepatica</em>&lt;br&gt; (sheep liver fluke)</td>
<td>liver (bile ducts)</td>
<td>aquatic vegetation</td>
</tr>
<tr>
<td><em>Fasciolopsis buski</em>&lt;br&gt; (giant intestinal fluke)</td>
<td>small intestine</td>
<td>aquatic vegetation</td>
</tr>
<tr>
<td><em>Schistosoma japonicum</em>&lt;br&gt;</td>
<td>venous vessels of intestine</td>
<td>cercariae through skin</td>
</tr>
<tr>
<td><em>Schistosoma mansoni</em>&lt;br&gt;</td>
<td>venous vessels of colon</td>
<td>cercariae through skin</td>
</tr>
</tbody>
</table>

3. **CESTODES** (tapeworms)

<table>
<thead>
<tr>
<th>Parasite &amp; Disease</th>
<th>Location in Patient</th>
<th>Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Taenia saginata</em>&lt;br&gt; (beef tapeworm)</td>
<td>small intestine</td>
<td>uncooked beef</td>
</tr>
<tr>
<td><em>Taenia solium</em>&lt;br&gt; (pork tapeworm)</td>
<td>small intestine</td>
<td>uncooked pork</td>
</tr>
<tr>
<td>Cysticercosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## FOOD-BORNE DISEASE

<table>
<thead>
<tr>
<th>Agents</th>
<th>Incubation period</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NAUSEA AND VOMITING</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>1 to 6 hours</td>
<td>pre-formed toxin</td>
</tr>
<tr>
<td><em>Bacillus cereus</em></td>
<td>1 to 6 hours</td>
<td>pre-formed toxin</td>
</tr>
<tr>
<td><strong>ABDOMINAL CRAMPS AND DIARRHEA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>8 to 16 hours</td>
<td>toxin form in vivo</td>
</tr>
<tr>
<td><em>Bacillus cereus</em></td>
<td>8 to 16 hours</td>
<td>toxin form in vivo</td>
</tr>
<tr>
<td><strong>FEVER, ABDOMINAL CRAMPS AND WATERY DIARRHEA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Salmonella</em></td>
<td>16 to 48 hours</td>
<td>tissue invasion</td>
</tr>
<tr>
<td><em>Shigella</em></td>
<td>16 to 48 hours</td>
<td>tissue invasion</td>
</tr>
<tr>
<td><em>Campylobacter jejuni</em></td>
<td>16 to 48 hours</td>
<td>tissue invasion</td>
</tr>
<tr>
<td><em>Vibrio parahemolytic</em></td>
<td>16 to 48 hours</td>
<td>tissue invasion</td>
</tr>
<tr>
<td><em>E. coli invasive</em></td>
<td>16 to 48 hours</td>
<td>tissue invasion</td>
</tr>
<tr>
<td><strong>ABDOMINAL CRAMPS AND WATERY DIARRHEA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>E. coli enterotoxogenic</em></td>
<td>16 to 72 hours</td>
<td>enterotoxin in vivo</td>
</tr>
<tr>
<td><em>Vibrio parahemolyticus</em></td>
<td>16 to 72 hours</td>
<td>enterotoxin in vivo</td>
</tr>
<tr>
<td><em>Vibrio cholera</em></td>
<td>16 to 72 hours</td>
<td>enterotoxin in vivo</td>
</tr>
<tr>
<td><strong>FEVER AND ABDOMINAL CRAMPS (mesenteric adenitis)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Yersinia enterocolitica</em></td>
<td>16 to 48 hours</td>
<td>tissue invasion</td>
</tr>
<tr>
<td><strong>BLOODY DIARRHEA WITHOUT FEVER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>E. coli enterohemorrhagic</em></td>
<td>72 to 120 hours</td>
<td>verotoxogenic</td>
</tr>
</tbody>
</table>