Gastroenterology

(Med I, Block 6, GI)
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Objectives

1. Understand how the incorporation of the dorsal yolk sac during embryo folding results in the formation of the early GI tract
2. List the derivatives of each of the foregut, midgut, and hindgut and their major blood supply
3. Describe the process of stomach rotation and development of the lesser sac
4. Describe how herniation, rotation, reduction, and fixation each act to produce the final position of the gut
5. Understand development of GI tract innervation
6. Describe the partitioning of the cloaca and formation of the anal canal
7. Understand the basic principles involved in the histogenesis of the intestine, liver, and pancreas
8. Describe the specific malformations of GI tract that result in omphalocele, intestinal stenosis, Meckel diverticulum, annular pancreas, biliary atresia, tracheoesophageal fistula, anorectal agenesis, pyloric stenosis, Hirschsprung's disease

References:
The Developing Human: Clinically Oriented Embryology (6th Ed.); Moore & Persaud, Chapter 12, pp 271-302

Overview:
The development of the GI system begins during the second and third weeks during head, tail, and lateral body folding. Folding results in the delineation (pinching off) of the GI tract from the yolk sac. The foregut is initially sealed by the oropharyngeal membrane and the hindgut is closed by the cloacal plate (proctodeal membrane). Beginning in week four, inductive interactions between the epithelium of the developing GI tract tube and the surrounding mesenchyme form the digestive/endocrine glands including the liver and pancreas. The spleen develops independently from proliferating mesenchyme cells. Beginning in the fifth week, the tubular portion of the gut grows very rapidly resulting in mechanical stresses that cause a series of folds and twists to produce the final orientation of the stomach and intestine. This rapid growth also causes the developing bowel to herniate into the body stalk (umbilical cord) until the abdominal cavity is sufficiently large to contain the bowel (by the tenth week.) With reduction of the herniated bowel, the mesentery of some of organs and portions of bowel are forced against the posterior abdominal wall resulting in retroperitoneal locations. Blood and nerve supplies to the organs develop by local angiogenesis and the migration of neural crest cells, respectively. The complexity of the formation of the GI system results in significant potential for malformations including agenesis, atresia, and duplication.
Development of the GI Tract II
University of Manitoba
Faculty of Medicine
Med II / GI 03 (L)
Dr. M. G. Torchia
2008 - 2009

Objectives

Continuation of GI #02

1. pyloric stenosis, omphalocele, incomplete rotation and volvulus of the midgut
2. intestinal stenosis and atresia, and Mechel’s
3. imperforate anus and anorectal agenesis with fistula
4. see accompanying clinical problems and notes)
Development of the GI Tract

Dr. Mark G. Torchia
Department of Surgery

**Figures Reference: The Developing Human, 7th ed., Moore and Persaud.**

Applications of Embryology

- “Anatomical and functional relationships”
- “Congenital abnormalities”
- “Development of new therapies aimed at inducing embryonic developmental capacities”

Illustrative case

- A 48y previously very healthy man
- Non-radiating, waxing and waning epigastric abdominal pain of 12h duration, with associated nausea and anorexia
- Normal abdominal sounds; normal exam
- Pain continued at home in evening
- Found dead in bedroom next morning

Illustrative case – Appendicitis?

The classic history of pain beginning in the periumbilical region and migrating to the right lower quadrant occurs in only 50 percent of patients.

Objectives

- Define the importance of the incorporation of the dorsal yolk sac
- Describe derivatives of the foregut, hindgut, and midgut and their major blood supply
- Explain the development of the lesser sac during stomach rotation
- Describe how herniation, rotation, reduction, and fixation produce the final position of the gut

Objectives

- List the origin of GI tract innervation
- Describe the partitioning of the cloaca and formation of the anal canal
- Review histogenesis of the liver and pancreas
- Describe specific malformations of GI tract
Recurring Themes

- Inductive interactions between gut epithelium and the surrounding mesenchyme
- Cell proliferation followed by apoptosis
- Symmetry followed by asymmetry
- Tissue/organ growth leads to movement

Primordial Gut (Fig. 5-1)

- Formed by the envelopment of the dorsal yolk sac into the embryo during folding (head, tail, lateral)
- Endoderm forms endothelium

Embryo Folding - Membranes

- Proximal oropharyngeal membrane and distal cloacal membrane
- Communicates with yolk sac

Division of Embryonic Gut

- Foregut - oral cavity, esophagus, stomach, prox. duodenum, liver, biliary app, pancreas (celiac trunk)
- Midgut - distal duodenum, small intestine, cecum, appendix, ascending and right transverse colon (superior mesenteric artery)
- Hindgut - left transverse colon, descending colon, rectum, superior anal canal (inferior mesenteric artery)

Foregut - Esophagus

- Proximal 33% striated muscle
  - pharyngeal arch mesenchyme
- Distal 66% smooth muscle
  - splanchnic mesenchyme

- Vascular supply shared (inf thyroid, bronchial, aortic branches, phrenic, L gastric)
- Trachea forms as an outpouch of esophagus
**Foregut – Stomach (Fig. 12-2)**
- tubular form enlarges dorsally
  - greater curvature
- suspended - ventral and dorsal mesentery
  - dorsal = greater omentum with lesser sac

**Developing Stomach (Fig. 12.2)**
- 90 degree clockwise rotations
- semi-transverse position with greater curvature on L side (nausea/vomiting)

**Developing Duodenum (Fig 12.2)**
- tube rotates with stomach and grows to form a C-shape

**Developing Gut (Fig. 12-6)**
- endothelial hyperplasia (obliteration) followed by apoptosis and vacuolation
  - lumen by end of week 8

**Foregut – Liver & Biliary Apparatus**
- hepatic diverticulum grows into ventral mesentery
  - cranial portion - liver
  - caudal portion – gallbladder, cystic duct, bile duct
- hepatic cells
  - endoderm
    - endothelial cells of venous sinusoids
  - mesenchyme (ventral)
    - hematopoietic (6 wk)
    - Kupffer cells (macrophages - reticuloendothelial cells)

**Foregut - Pancreas**
- two pancreatic buds (ventral and dorsal mesentery)
  - dorsal portion is larger
  - ventral portion rotates with duodenum to fuse with dorsal portion
  - ventral portion brings duct with it to form main pancreatic duct
  - parenchyma from endoderm
Nodal Cilia

Cilia on nodal cells sweep counterclockwise

(Kartegener’s syndrome
Primary Ciliary Dyskinesia - situs inversus)

Division of Embryonic Gut

- Foregut - oral cavity, esophagus, stomach, prox. duodenum, liver, biliary, pancreas (celiac trunk)
- **Midgut** - distal duodenum, small intestine, cecum, appendix, ascending and right transverse colon (superior mesenteric artery)
- Hindgut - left transverse colon, descending colon, rectum, superior anal canal (inf. mesenteric a.)

Midgut

- Elongates to form a long U-shaped midgut loop
  - yolk stalk attached between cranial/caudal limbs
- Abdominal cavity volume small (liver/kidneys)
  - midgut herniates into umbilical cord (wk 6)
- Midgut rotates CCW 90° then 180°
  - axis of superior mesenteric artery
- Cranial loop grows much faster (small intestine)

Midgut Loop Rotation (Fig 12-13)

- Reduction of herniated bowel (wk 10)
  - Small bowel returns first; cecum last
  - Presses mesentery of ascending colon, (descending colon (H) and duodenum (F) against posterior abdominal wall (retroperitoneal)
- Appendix position depends on growth of ascending colon (retrocecal, pelvic, etc.)
**Hindgut**

- Cloaca separated into urinary/rectal divisions by caudal growth of urorectal septum (complete 7 wk)
- Anal membrane ruptures wk 9 (amniotic sac)
- Anal canal – pectinate line
  - superior 66% hindgut (inferior mesenteric artery + autonomic nerves)
  - inferior 33% - surface ectoderm (internal pudendal artery + inferior rectal nerve - sensory)

**Congenital Defects**

**Tracheoesophageal Fistula/Atresia**
(Fig. 11-5)

1:2500, male >> female, coughing, choking, regurg, aspiration

**Pyloric Stenosis (Hypertrophy)**
(Fig. 12-4)

1:150 Male, 1:750 female, projectile vomiting

**Annular Pancreas**

Vomiting, poor nutrition, duodenal obstruction, chronic pancreatitis, few symptoms

**Omphalocele – non-closure umbilicus**
(Fig 12-7)

1:6000, herniated bowel, peritoneum+amnion
Meckel’s Diverticulum (Fig. 12-21)

3:100, male >> female, remnant yolk sac, ectopic tissue <90 cm from ileocecal junction

Hirschsprung Disease

Abdominal distension, absent bowel movements, poor nutrition, surgery, mild cases

What you should know:
- Incorporation of the dorsal yolk sac
- Derivatives of the foregut, midgut, and hindgut and major blood supply
- Stomach rotation and development of the lesser sac
- Herniation, rotation, reduction, and fixation produce the final position of the gut

What you should know:
- Origin of GI tract innervation
- Partitioning of the cloaca and formation of the anal canal
- Histogenesis of the liver and pancreas
- Specific malformations of GI tract

MCQ evaluation

1) The rectum and urogenital sinus are formed during the division of the cloaca by the:
   a) developing urinary bladder
   b) remnant of the yolk sac
   c) cloacal membrane
   d) urorectal septum
   e) Meckel’s diverticulum

Thank you
2) Non-reduction of the physiological midgut hernia results in formation of:
   - a) a Meckel’s diverticulum
   - b) an inguinal hernia
   - c) an omphalocele
   - d) a subhepatic cecum
   - e) a megacolon

3) In the embryo, the duodenum is formed from:
   - a) foregut
   - b) midgut
   - c) hindgut
   - d) foregut and midgut
   - e) midgut and cranial portions of the hindgut

4) Formation of the primordial gut during the fourth week results from:
   - 1) caudal budding of oropharyngeal membrane
   - 2) incorporation of the yolk sac into the embryo
   - 3) cranial budding from GI mesenchyme
   - 4) involution of the splanchnic mesoderm
   - 5) none of the above
Objectives:

1. Describe the elements of the epidemiological triangle and their attributes as they relate to enteric infections.
2. Describe the features of the normal alimentary tract that form a barrier to infection.
3. Describe the pathogenesis and clinical findings associated with non-inflammatory diarrhea, inflammatory diarrhea and diarrhea due to penetrating organisms.
4. Describe the difference between enteroinvasion, enteroadhesion and mucosal damage as mechanisms of diarrhea and food poisoning.
5. Describe the different types of food poisoning in terms of etiology and mechanism.
6. Discuss the pathogenesis, diagnosis and treatment of pseudomembranous colitis.

Outline:

1. Definition and Classification of Diarrhea
2. Host Factors that Form a Barrier to Infection: Personal hygiene, barriers of gastrointestinal tract (gastric acid, intestinal motility, normal bowel flora, immunoglobulin secretion)
3. Etiology: Infectious (bacterial, viral, protozoal, parasitic)
4. Factors Associated with Increased Morbidity and Mortality: Malnutrition immunosuppression, lack of rehydration, overwhelming infection, invasive pathogen
5. Pathogenic Mechanisms of Diarrhea: Mucosal adherence, toxin production (neurotoxin, enterotoxin, cytotoxin), mucosal invasion
6. Clinical Features: Watery diarrhea, dysenteric syndrome, enteric fever, enteric fever-like syndrome
7. What is food poisoning and how is it caused
8. Pseudomembranous Colitis
9. Diagnostic Evaluation
10. Prevention
11. Management

Suggested Reading:

2. Medical Microbiology and Immunology, Levinson and Jawetz 4th Edition
6. Your favorite text book about Medical Microbiology and Infectious Diseases

1. Definition and Classification of Diarrhea:

As in all other pathologic conditions, an interaction between the host, the microorganism and the environment exists in infectious diarrhea.
Acute diarrhea is a self-limiting condition resulting from an alteration in bowel habit with an increase in frequency and decrease in consistency of stool. More specifically, it is associated with an increased stool weight (> 200 g/day – normal, 50-150 g/day).

The adult digestive tract generally receives approximately 10 liters of fluid per day. 80% of the fluid is absorbed in the small intestine while the remaining 20% is reabsorbed in the colon. Diarrhea results whenever there is an imbalance between secretion and absorption of fluids and electrolytes. The mucosa of the small intestine is made up of absorptive, villous surfaces where nutrients, electrolytes and fluids are absorbed and crypt cells where electrolytes and fluids are secreted. When the surface villi are destroyed or absorption is inhibited, then that result is electrolyte and fluid secretion into the bowel movement. Intestinal water absorption and secretion are passive and follow an osmotic gradient created by the active transport of sodium.

Table 1: Classification of Diarrhea
Diarrhea is summarized according to its type and mechanism

**Secretory:** Caused by an increased secretion or decreased absorption of sodium and chloride leaving them in the bowel lumen. This, in turn, increases the volume of water in the intestinal lumen. It is characterized by large volume, watery diarrhea without blood or pus and there is little response to fasting. It may be mediated by bacterial toxins (*Vibrio cholera*) Figure 1, bile salt enteropathy and fatty acid-induced diarrhea. Solute gap absent.

**Osmotic:** Increased non-absorbable molecules in the bowel lumen leading to a decrease in the absorption of solute from the bowel. This results in watery stool without blood or pus but improves with fasting. An increased solute gap is present. Examples included lactose intolerance, carbohydrate malabsorption and magnesium laxatives.

**Inflammatory:** This is caused by destruction of the bowel mucosa leading to impaired absorption and associated with an outpouring of blood and mucous. The frequently associated symptoms include small, frequent stools with blood and pus. There is associated fever. Examples include enteroinvasive pathogens such as *Entamoeba histolytica* (amebiasis) and *Shigella dysenteriae* (shigellosis).

**Decreased Absorptive Surface:** Here there is decreased reabsorption of electrolytes as a consequence of a shortened, absorptive surface also known as “short gut” syndrome. This may be due to a bowel resection, or enteric fistula, whereby solutes and other material bypass the absorptive area. The characteristics are variable and the diarrhea may improve with fasting.

**Motility Disorders:** This is a complex condition caused by either increased motility with decreased time for absorption of electrolytes and nutrients. This may be due to hyperthyroidism or irritable bowel syndrome. Decreased bowel motility with bacterial overgrowth may be observed in conditions such as scleroderma and diabetes. This results in a malabsorption syndrome.

**Figure 1: Diarrhea due to secretory mechanism mediated by toxin**
Figure 1 demonstrates the mechanism of toxigenic diarrhea. The outpouring of water and electrolytes is due to the action of toxin stimulating adenyl cyclase receptors, with activation of cyclic adenosine monophosphate.

**Figure 2: Diarrhea Due to Viral or Bacterial Enteroinvasion**
Figure 2 demonstrates viral or bacterial enteroinvasion. Here there is loss of mature absorptive surfaces resulting in immature secretory surfaces.

2. Host Factors:

After exposure to a pathogen, the manifestation and severity of diarrheal disease depend upon the status of the host, specifically, personal hygiene, barriers of the gastrointestinal tract (gastric acid, intestinal motility, normal bowel microflora and immunoglobulin secretion). Extremes of age play a role in the susceptibility to enteric infections. Rotavirus, enteropathogenic E coli frequently cause infectious diarrhea in children but are uncommon in older adults. Infectious agents lead to more significant complications in those at the extremes of age.

Acquisition of nearly all forms of diarrheal disease depend upon the ingestion of specific microorganisms. Most intestinal pathogens originate from other mammalian species although reptiles are colonized with Salmonella spp. The most frequent mode of transmission is fecal-oral. Poor personal hygiene and proper sanitation are important factors in the fecal-oral route of disease transmission. The gastrointestinal tract of the healthy host is capable of reducing the virulence of the majority of ingested pathogens. Virtually all ingested bacteria are destroyed within 30 minutes in a normal gastric pH, whereas more than one hour is required for pathogen destruction in achlorhydric individuals or individuals who ingest acid neutralizing agents or gastric acid reducing agents. The natural motility of the gastrointestinal tract promotes the proper distribution and flow of resident bowel flora, this also facilitates the rapid passage of pathogens to the gastrointestinal tract and aids in fluid reabsorption. Drugs that slow peristalsis such as opiates and anticholinergics may delay the transit and excretion of pathogens and may lead to significant complications. The immune system of the host is important as intestinal secretions of antigens and specific immunoglobulin have bactericidal, neutralizing or opsonic effect on pathogens. Hereditary or acquired alterations in intestinal secretion of immunoglobulins will put the host at increased risk. Hypogammaglobulinemia may be associated with an increased incidence of diarrheal illnesses.

Although host factors are important, microorganisms are also important, specifically the infectious dose in humans of Shigella spp is low, 10-100 bacteria compared to Salmonella spp which requires thousands of microorganisms to cause disease in humans.

3. Etiology

It is important to note that although diarrhea may be caused by infectious agents such as bacteria, viruses, protozoa and parasites, other etiology such as toxic ingestion’s, laxatives, osmotically acting agents, neuroendocrine abnormalities, neoplasms, inflammatory bowel disease, ischemia and gastrointestinal hemorrhage, may lead to acute diarrhea. It is critical to maintain an open mind in approaching the patient with both acute and chronic diarrhea.

4. Factors Associated with Increased Morbidity and Mortality (Table 2):

Table 2:

The major factors that translate to a higher death rate associated with diarrhea include host, therapeutic and microbial factors, which can be further broken down into:

- Malnutrition
- Complications of diarrhea, including dehydration, pneumonia, sepsis and hemolytic uremic syndrome
- Infection by an agent more likely to cause dehydration such as Vibrio cholera and rotavirus (infants)
- Infection by invasive pathogens such as Shigella spp and failure to receive adequate rehydration or antimicrobial therapy for illnesses requiring active intervention.

Oral rehydration programs in developing countries have reduced morbidity and overall mortality rates from diarrheal illness. This supportive measure, however, has not eliminated diarrhea as a significant cause of death in children.
5. Pathogenic Mechanisms of Diarrhea (Table 3):

### Table 3: Pathogenic Mechanisms

**Mucosal Adherence:** Here the microorganisms attach to and colonize the intestinal mucosa. Examples include enteropathogenic *E coli* (EPEC). This may lead to alterations in ion permeability of the membrane (increased secretion or reduced absorption) resulting in a secretory diarrhea.

**Toxin Production:** A variety of different microorganisms can produce different toxins leading to diarrhea.

- **Neurotoxins:** These are proteins which may activate the autonomic nervous system. The most frequently encountered is *Staphylococcal enterotoxin*, this leads to food poisoning associated with violent nausea, vomiting and diarrhea with rapid convalescence. The incubation period is 1-8 hours. The characteristic history is that of large groups of individuals attending communal gatherings such as church picnics or wedding receptions. Foods may be contaminated by *S. aureus* from a food worker with a paronychia or other localized *S. aureus* infection. *Bacillus cereus* can produce 2 distinct forms of food poisoning mediated by toxins. The emetic type is associated with rice dishes. The classic history is that of someone consuming rice in a Chinese restaurant followed by an acute onset of vomiting 1-6 hours after ingestion. The diarrheal form is associated with the consumption of meat and sauce dishes and having an incubation of 1-24 hours. *Clostridium botulinum* may lead to an acute toxin mediated food poisoning. Table 7 summarizes some of the causes and characteristics of food poisoning. More about food poisoning later…

- **Enterotoxin:** A number of different bacteria produce toxins ([Figure 1](#)) which lead to an outpouring of water and electrolytes from the bowel mucosa into the intestinal lumen resulting in a secretory diarrhea.

- **Cytotoxins:** Cytotoxins are defined by their ability to produce damage to the mucosa resulting in an inflammatory colitis usually by the inhibition of protein synthesis. The key example is Shiga toxin which is produced by *S. dysenteriae*. This toxin is very similar to that of *E coli* O 157: H7. *Clostridium difficile* produces two toxins, Toxin A, an enterotoxin, and Toxin B a cytotoxin, they work synergistically to produce significant morbidity and in some cases mortality.

- **Mucosal Invasiveness:** Bacteria such as *Shigella spp.*, *Campylobacter spp*, *Yersinia spp*, possess the ability to penetrate into the intestinal mucosa and destroy the epithelial cells causing a dysentery-like syndrome.

### 6. Clinical Features (Table 4):

The pathophysiology mechanisms that produce infectious diarrhea are as follows:

- Increased active intestinal secretion of electrolytes causing fluxes of water and ions, mediated by bacterial enterotoxins (watery diarrhea, [Figure 1](#))

- Malabsorption of nutrients and electrolytes secondary to damage to the brush-border in either the small or large intestine

- Increased intestinal osmolality secondary to saccharidase deficiency when the brush-border is damaged, with resultant lactose intolerance ([Figure 2](#))

- Altered intestinal motility

### Table 4: Clinical-Pathologic Features and Causes

**Watery Diarrhea:** This is a non-inflammatory process (absence of fecal leukocytes). This is characterized by large volume stool and increased number of stools because the colonic reservoir is intact. This condition may be characterized by nausea and vomiting but other constitutional symptoms such as cramping, and abdominal pain, arthralgias, myalgias, chills and fever rarely occur. This diarrhea is mediated by bacterial enterotoxins that alter fluid and electrolyte transport. The prototype of an enterotoxigenic diarrhea is that caused by *V. cholera*. After an incubation period of several hours to 5 days, the illness may begin with sudden onset of
profuse, watery diarrhea or anorexia and abdominal discomfort followed by diarrhea. The stool has the
characteristic “rice water” appearance because of the mucous content and may have a mild fishy odor.
Tenesmus is absent and vomiting may occur several hours after the onset of diarrhea. Signs and symptoms of
cholera result from the severity of dehydration caused by the food and electrolyte losses from the intravascular
and extravascular spaces into the gut lumen. A small proportion of individuals may proceed very quickly to a
severe hypovolemic shock. Fever is absent. Muscle cramps may occur as a consequence of electrolyte
imbalance. Other microorganisms which may cause a watery diarrhea include rotavirus (most common in
children a Norwalk agent. Giardia lamblia is a protozoan which causes “beaver fever” and causes diarrhea by
altering fluid reabsorption in the proximal small bowel.

Dysenteric Syndrome:
• Acute dysentry: This inflammatory or invasive process involves the colon and occasionally the distal
small intestine. Numerous leukocytes in the feces indicate the diffuse colonic inflammation or
invasion of the colonic mucosa. Frequent enteroinvasive pathogens include Shigella spp, enteroinvasive E. coli, Salmonella spp, Yersinia enterocolitica, C jejuni, V parahaemolyticus. Individuals inflicted with acute dysenteric syndromes may become very ill and develop complications such as hemolytic uremic syndrome encountered with E. coli O 157: H7 (Hamburger Disease).
• Pseudomembranous colitis: Pseudomembranous colitis is a condition associated with the
administration of antimicrobial agents. Although any antibiotic may lead to this condition, the most
frequently associated clindamycin, amoxicillin and the beta lactams. The onset of this antibiotic
associated diarrhea may be seen anytime after the starting of antibiotics. It may occur during
antibiotic therapy or long after it has been discontinued. The clinical manifestations vary from mild
watery or mucoid green diarrhea to a dysenteric syndrome with bloody diarrhea, high fever, marked
abdominal tenderness and the presence of fecal leukocytes. The proposed pathogenesis of
pseudomembranous colitis include an alteration of the normal bowel flora as a consequence of the
administration of a antimicrobial agent allowing the overgrowth of Clostridium difficile. This
microorganism produces two toxins (Toxin A -enterotoxin, Toxin B -cytotoxin) resulting in colonic
membrane damage. Sigmoidoscopy typically revealed the presence of small, raised
pseudomembranous nodules or plaque. Complications include severe diarrhea, hypovolemic shock,
toxic megacolon, peritonitis, cecal perforation, hemorrhage and sepsis. It is a frequent cause of
diarrhea in hospitalized patients who have received antibiotics.

Enteric Fever: Enteric Fever is an acute systemic illness characterized by fever, headache and abdominal
discomfort. This syndrome is characteristically produced by Salmonella typhi and is referred to as Typhoid
Fever, however, other Salmonella spp. may cause similar but less severe clinical syndromes. S. typhi is a
water and food borne microorganism for which humans are the only natural host. The salmonellae are ingested
orally and must traverse the acid barrier as well as various pancreatic enzymes, bile, and intestinal secretions
and secretory IgA, which are effective antimicrobial factors. The post-gastrectomy state, hypochlorhydria,
altered intestinal motility and prior antibiotic therapy are conditions predisposing to salmonellosis. Other
individuals at risk of salmonella infection include those with Sickle Cell Disease, chronic liver disease,
immunodeficiency and AIDS.

The incubation period S. typhi causing Typhoid Fever is 5-21 days depending upon the inoculum and immune
status of the host. The microorganisms make their way to the small bowel where they ultimately replicate in
the Peyer’s patches. The microorganisms enter the circulation through the lymphatic route and replicate in the
reticuloendothelial cells in the lymph nodes, liver, bone marrow and spleen. The onset of symptoms is gradual
and characterized by non-specific symptoms such as fever, headache and abdominal pain. Diarrhea occurs in
approximately 50% of individuals. Physical findings include abdominal tenderness, hepatosplenomegaly,
 evanescent maculopapular rash in the upper abdomen and lower thorax (Rose spots), bradycardia and mental
confusion. Complications of enteric fever may be related recurrent bacteremia with dissemination of the
microorganisms. These complications include pneumonia, endocarditis, osteomyelitis, arthritis or meningitis and local complications such as erosion of blood vessels in the Peyer’s patches which may result in gastrointestinal hemorrhage and perforation of the ilium.

*Yersinia enterocolitica* and *Campylobacter jejuni* may cause an enteric fever-like syndrome indistinguishable from that of Typhoid Fever.

**Traveler’s Diarrhea (Tables 5 and 6):** Traveler’s Diarrhea is defined as the passage of 3 or more unformed stools per day in a resident from an industrialized country traveling in or returning from a developing nation. The onset of Traveler’s Diarrhea usually occurs within the first 2 weeks after arrival in a foreign country, most often within the first week of travel. The illness may occur after returning to one’s home. Table 6 demonstrates the most common etiologies according to location. **Enterotoxigenic *E. coli* is the most commonly isolated organism of Traveler’s Diarrhea.** Traveler’s Diarrhea is almost always a self-limiting illness rarely lasting more than 5 days even when untreated. The diarrhea is accompanied by abdominal pain and cramping and a minority of patients develop a fever. Traveler’s diarrhea may be avoided by simple measures (Table 5) such as avoiding local uncooked delicacies, only consuming fruits with a peel, avoiding raw vegetable which have been rinsed with tap water, consuming bottled water and beverages. Antibiotics may be of benefit only when diarrhea begins.

**Table 5: Etiologies of Traveler’s Diarrhea**

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<th>Etiologies of Traveler’s Diarrhea</th>
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**Table 6: Preventing Traveler’s Diarrhea**

7. **Food poisoning:**

Food poisoning can be classified according to the predominant symptoms produced: nausea and vomiting; non-inflammatory diarrhea; inflammatory diarrhea; neurologic symptoms; systemic or miscellaneous syndromes. The incubation period after the ingestion of the offending foodstuff may provide clues as to the potential etiology, as shown in table 7. It is important to remember that food poisoning may be caused by both infectious and non-infectious etiologies. Food poisoning caused by some bacteria may be associated with only gastrointestinal symptoms while others may have neurologic symptoms as a major component.

- How does *Clostridium botulinum* cause botulism?
- How does *C. tetani* cause tetanus
- Why is *Staphylococcus aureus* food poisoning so severe?
- What types of food poisoning would you get if you ate at the following:
  - Japanese/sushi restaurant
  - Chinese restaurant
  - Organic bakery and honey shop
  - Your well meaning relatives who can preserves
  - Mary Malone’s diner

**Table 7: Food Poisoning**

8. **Pseudomembranous Colitis:**

Some of the details about pseudomembranous colitis (PMC) were previously outlined in the section above entitled, “Dysenteric Syndromes”. PMC refers to colitis characterized by the formation of a pseudomembrane. The pseudomembrane is composed of fibrin, mucin, sloughed mucosal epithelial cells, and acute inflammatory cells. On endoscopy, PMC displays multiple, elevated yellowish white plaques. PMC is the most severe mucosal change associated with antibiotic associated diarrhea and is virtually always caused by *C. difficile*. When PMC is associated with antibiotic use, it is almost 100% guaranteed that *C. difficile* is the culprit
pathogen. *C. difficile* produces two toxins, noted above, which differ in their activity and potency in terms of tissue toxicity. They work synergistically to cause tissue injury. Different laboratory investigations are necessary to detect the different toxins.

9. **Diagnostic Evaluations (Table 8):**

- **Fecal leukocyte test:** The presence of leukocytes in fecal material suggests an inflammatory process, whether it is caused by an enteroinvasive pathogen, or an uninvasive colitis such as Crohn’s Disease.
- **Stool Culture:** Stool Culture is indicated for non-hospitalized patients or those who are hospitalized with diarrhea. It is important to specify in the Microbiology Requisition, the exact nature of the patient’s symptoms and whether blood is present. This will help guide the diagnostic evaluation in the laboratory.
- **Toxin Analysis:** In those individuals who have a history of prior antibiotic ingestion and diarrhea, *C. difficile* may be the causative organism. It is important to specify that this is a consideration and, therefore, toxin analysis will be undertaken.
- **Parasite Evaluation:** Once again, it is important to specify to the Microbiology Laboratory what symptoms are present and whether the history of travel or consumption of tainted water exists. The evaluation of stool specimen for parasites and/or their ova can be time consuming. It is important to specify which microorganisms are being contemplated as different techniques may be necessary.
- **Direct Visualization:** Either a proctosigmoidoscopy or colonoscopy may be necessary when all other investigations have not been fruitful. Direct visualization will demonstrate the plaques of pseudomembranous colitis or ulcerations compatible with amebiasis. Direct visualization is helpful to help differentiate between infectious and non-infectious etiologies of diarrhea which has been long-standing.
- **Upper endoscopy:** The history of dysphagia and diarrhea particularly in those who are immunocompromised may be an indication for an evaluation of the upper gastrointestinal tract.

10. **Prevention:**

Any measure that can be undertaken to prevent the acquisition of diarrheal disease must be emphasized. Simple measures such as:

1. Handwashing after the handling of infectious or potentially infectious material (diapers, soiled garments, bedpans) will help minimize the chances of disease transmission.
2. While traveling, only consume cooked foods, avoid drinking unprocessed water, consume bottled water and beverages, only consume fruits with a peel, avoid raw vegetables which have been rinsed with tap water. Avoid drinking from lakes and streams. **Table 6** summarizes the key details of traveling safely.

11. **Management:**

**Table 9: Treatment**

*Table 9* summarizes specific treatments according to pathogens for adults and children. It is important to note that this is merely a guide to the treatment of different bacteria and parasites. Should you be faced with an individual with a specific pathogen causing diarrhea, it is important to check a current reference source for the most up to date information.

There are 4 basic principles in the management of individuals who have acute diarrhea.

1. Fluid and electrolyte replacement: This is the cornerstone of therapy for acute diarrhea. It may be life saving for infants and the elderly. In most cases, oral rehydration therapy is satisfactory, however, in some with profound dehydration and decreased level of consciousness, parenteral rehydration may be indicated.
2. Dietary modification: After an episode of an acute infectious diarrhea which affects the small bowel, the only foods to be avoided are milk products, since transient secondary lactase deficiency is common in diarrheal states. The use of formula diets or elemental diets are rarely indicated because digestive functions are not impaired. For infants, breast milk or lactose-free formula may be administered. A bland diet consisting of boiled starches and cereals such as potatoes, noodles, rice, wheat and oats may be of benefit for older children and adults. When stools are formed, the diet may return to normal.
3. Symptomatic Therapy: Antiperistaltic agents are seldom indicated as they inhibit gastrointestinal motility and may lead to an ileus and some situations may have grave repercussions. It should be avoided in cases of known C. difficile disease.

_Clostridium difficile_ may be managed as follows:
- First episode: Metronidazole 500 mg po tid for 10 days
- Second episode: Metronidazole 500 po tid for 10 days.
- Third episode: Vancomycin 125 mg po qid and rifampin 600 po bid for 7 days.
Objectives-

1. develop an approach to diagnosis and management of gastroenteritis in a child utilizing the information from GI-42 and the reference tests
2. list the characteristics that can be used to distinguish the many different bacterial food poisoning syndromes
3. appreciate the existence of non-bacterial causes of food-borne illness
4. develop a plan for investigating cases and outbreaks of food poisoning
5. be familiar with procedures required to prevent food-borne illness

References:

Objectives

1. Be aware of the congenital disorders involving the gastrointestinal tract
2. Be aware of the clinical manifestations of these disorders
3. Be aware of aberrations in normal embryologic development and how they lead to the congenital disorders described
4. Be aware of some clinical investigative methods used to diagnose these disorders
5. Be aware of surgical or medial therapy to correct these disorders
Objectives

1. Be aware of common symptoms of clinical problems of the gastro-intestinal problems of children
2. Be aware of common reasons for these symptoms
3. Be aware of the basic approaches to diagnostic investigation of these problems
4. Be aware of the basic approaches to surgical or medical management of these problems
CONGENITAL DISORDERS OF THE GASTROINTESTINAL TRACT

- Mechanical Obstruction
  - Failure of lumen to develop (atresia, stenosis)
  - Failure of lumen to recanalize (duodenal atresia)
  - Occlusion of lumen with meconium (cystic fibrosis)
  - Incomplete rotation of bowel during development

- Functional Obstruction
  - Dismotility due to abnormal innervation

Case 1

- Newborn
- Mother had polyhydramnios
- Baby has had difficulty swallowing from birth
- Baby chokes on own secretions

Case 1

- What are some possible explanations for this problem?

- What investigations would you consider?

- Differential Diagnosis
  - Meconium aspiration
  - Cardiac anomaly
  - Esophageal atresia with or without fistula
  - Other
    - Pneumonia
    - Sepsis
Esophageal Atresia
Tracheoesophageal Fistula

- Failure of separation of esophagus and trachea
- 1:3000-1:4500 births
- Rarely familial
- 5 types
- Signs and symptoms
  - Depend on type
  - Respiratory distress
  - Inability to feed
  - Choking during feeding
  - Other anomalies

Types

Investigations
lateral chest x-ray

Investigations
lateral chest x-ray with water soluble contrast

Case 2

- Newborn infant with bilious emesis since birth
- Maternal polyhydramnios
- Infant has abdominal distension

What are the possible explanations for this problem?

What investigations would you perform?

Differential Diagnosis
- Bowel atresia or stenosis
  - Pyloric, duodenal, small bowel
  - Meconium ileus or plug
  - Malrotation with volvulus
  - Abnormal intrinsic bowel innervation
    - e.g. Hirschsprung
Look for the Bubbles

- Single Bubble
- Double Bubble
- Multiple Bubbles

Single Bubble
suggests gastric outlet obstruction

Double Bubble
suggests duodenal obstruction

Many Bubbles
suggests more distal obstruction

- Jejunal or ileal atresia
- Meconium ileus

Meconium Ileus
resected bowel

Thick meconium
Intestinal Malrotation / Volvulus

Malrotation
barium enema

Volvulus
congested ischemic small bowel

Case 3
respiratory distress from birth

Case 3
abdomen and chest exposed at autopsy

Case 3
chest wall removed
Case 3

- Diaphragmatic hernia
  - Usually left side through Foramen of Bochdalek
  - Survival dependent on lung development
  - Associated with other anomalies
  - Herniation may occur later in life if defect is small

Case 4

- Newborn infant
- Fails to pass meconium during 1st 24 hrs
- Abdomen distended
- Emesis

What are some possible explanations for this problem?

Case 4

- Differential Diagnosis
  - Anal stenosis/Imperforate anus
  - Rectal atresia
  - Hirschsprung's disease
Case 4

- **Hirschsprung’s disease**
  - Due to defective development of intramural nerve plexus
  - Usually affects distal colon but extent variable
  - Clinical features:
    - History
      - Delayed meconium passage
    - Rectal exam
      - Snug anal canal
      - Empty rectum

Case 4

- **Hirschsprung’s disease**
  - Investigations
    - Abdominal x-ray
      - Colon full of stool, rectum empty
    - Barium enema
      - Dilated colon, transition zone
    - Anorectal manometry
      - Hypertonic anal sphincter
      - Failure internal sphincter to relax with rectal distension
    - Rectal biopsy-definition test
      - Absent intramural ganglion cells
      - Abnormal nerve plexuses

Case 5

- Male infant
- Projectile emesis shortly after feeding
- Onset 6 weeks of age
- Emesis not bile-stained
- Losing weight, borderline hydration
Case 5

• What is the most likely diagnosis?
• What physical findings would be most helpful to confirm the diagnosis?
• What investigations would you consider?
• How would you treat this child?

Case 5

• Hypertrophic pyloric stenosis
  – Etiology unknown
  – 1:500 births
  – Occasionally familial
  – Often affects 1st born male infants
  – Emesis causes dehydration, metabolic hypochloremic alkalosis and failure to thrive
  – Visible gastric waves following feeds
  – Palpable pyloric “tumor”

Case 5

Pyloric Stenosis

• Investigations
  – Abdominal x-ray
    • Single bubble, wavy gastric gas pattern
  – Abdominal ultrasound
    • Hypertrophied pylorus
  – Barium study
    • Narrow pyloric canal (string sign)
    • Antral beak sign
    • Gastric waves

Case 5

• Pyloric Stenosis
  • Ultrasound

Case 5

• Pyloric Stenosis
  • Barium study

Case 5

• Pyloric Stenosis
  • Endoscopy
**Pyloric Stenosis**

*Pyloromyotomy*

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**ACQUIRED DISORDERS OF THE GASTROINTESTINAL TRACT**

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**Case 1**

- Previously healthy 1 yr old
- 48 hrs emesis, diarrhea, fever
- Sib with similar problem 1 wk earlier

What is most likely cause of this child's illness?

What concerns would you have about this child?

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**Rotavirus**

- Most common cause of gastroenteritis in children esp fall and winter
- Severity variable
- Stools watery, bloodless
- Most children infected by age 2 yrs

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**Giardia lamblia**

- Variable presentation-acute diarrhea, chronic, insidious
- Common in some endemic areas, locations where children in close proximity

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Giardia lamblia

Special problems of diarrhea in children

- Relatively greater fluid requirements
- Larger proportion of body weight due to extracellular fluid
- Immature renal compensatory mechanisms
- Immunologic immaturity-increased risk of infections
- Lower nutritional reserves
- Social factors-dependence on others for health care

Physiologic consequences of diarrhea

- Dehydration
- Increased serum osmolality
- Acidosis
- Electrolyte imbalance

Types of dehydration

- Isotonic (serum Na 135-149 mmol/L)-most common
- Hypotonic (serum Na <135 mmol/L)
- Hypertonic (serum Na>149 mmol/L)-most risky, must treat carefully

Case 2

- 1 year old child
- Well until 6 months
- Bulky, foul smelling stools
- Abdominal distension
- Irritability
- Falling off growth curve
**Case 2**

What is the most likely diagnosis?

**Celiac disease**

- Variable manifestations
- May be asymptomatic
- Detected by endomysial and transglutaminase antibodies
- Usually HLA DQ2 or DQ8 positive
- Confirmed by intestinal biopsy
- Treated by lifelong gluten-free diet

**Case 3**

- Previously well infant
- Sudden onset presumed abdominal pain
- Draws up knees
- Emesis
- Lethargy
- Bloody stool

**Case 3**

What are some of the causes of intestinal bleeding in children?

What is the most likely diagnosis in this child?

What investigations would you do?
Causes of intestinal bleeding

- **Upper (hematemesis)**
  - Gastroesophageal reflux (sign of esophagitis)
  - Varices (portal hypertension-hepatic, prehepatic)
  - Peptic ulcer (usually with pain)

- **Lower (hematochezia)**
  - Bacterial infections
  - Necrotizing enterocolitis
  - Polyps
  - Intussusception
  - Meckel's diverticulum
  - Inflammatory bowel disease

Intussusception

- Most common at 6-24 months of age
- Idiopathic
- May follow viral infection
- Acute pain, emesis, +/- bloody stool (currant jelly)
- Lethargy
- Risk of ischemia, perforation if treatment delayed

Intussusception

*abdominal x-ray, barium enema*

Case 4

- Ten year old presents to the ER
- 24 hour history of abdominal pain

What additional information would be helpful?
What are potential causes of abdominal pain in this child?
What investigations would be helpful?
What is the most likely diagnosis?
What complications can occur?
Case 4

helpful clinical information

• History
  — Onset and character of pain
  — Location and migration of pain
  — Aggravating and relieving factors
  — Associated symptoms

• Physical examination
  — Inspection
  — Auscultation
  — Palpation
    • Tenderness
    • Guarding
    • Referred and rebound tenderness
  — Percussion

Causes of abdominal pain

• Appendicitis
• Intussusception
• Crohn’s disease
• Cholelithiasis/cholecystitis
• Pancreatitis
• Peptic ulcer
• Functional-most common
• Extraintestinal-pneumonia, diabetes, abd. wall

Investigations for abdominal pain

• CBC, ESR
• Pancreatic enzymes
• Liver function studies
• Urinalysis/culture
• Imaging
  — Abdominal x-ray
  — Barium studies
  — Ultrasound
  — CT
• Endoscopy

Complications of appendicitis

• Perforation
• Peritonitis
• Leakage from appendiceal stump

Case 4

Appendicitis

• Very common
• 12-14 yrs of age most common
• Hx and px most important
• May need observation to clarify diagnosis
• Perforation more likely in younger children or more prolonged course
• Antibiotic therapy may be necessary
• Early surgical treatment best

Case 5

• 2 month old infant
• Jaundice since birth
• Clay colored stools, dark urine
• Hepatosplenomegaly
Case 5
hepatosplenomegaly

Do you think this child’s jaundice is “physiologic”?
What are the possible causes for this child’s jaundice?
What investigations would you perform?

Causes of cholestasis in infants

• Extrahepatic biliary atresia
• Choledochal cyst
• Intrahepatic biliary dysgenesis
• Neonatal hepatitis
  – Infection
  – Metabolic
  – Familial
  – Idiopathic
• Iatrogenic (TPN)

Investigation of cholestatic liver disease

• Liver function studies
  – Confirms cholestasis
  – Assesses impact on liver function
• Infection screen
  – STORCH, Hepatitis A, B, C
• Metabolic studies

Investigation of cholestatic liver disease (cont’d)

• Diagnostic imaging
  – Abdominal ultrasound
  – Biliary scan
• Needle biopsy liver
• Laparotomy
  – Biopsy
  – Cholangiogram
  – Repair atresia

THE END