

## Gastrointestinal Tract Infections

Gastrointestinal tract  
Protection  
Normal flora  
Diseases

## Gastro-Intestinal Tract

- Mouth
- Pharynx
- Esophagus

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- Stomach
- Small intestine
- Large intestine
- Rectum
- Anus



## Protection (Barriers)

- Intestinal surfaces - layer of mucus
- Muscular walls (peristalsis)
- Saliva
- Secretory IgA
- Stomach acid
- Bile
- Gut-associated lymphoid tissue (GALT)
- Commensal or normal flora
- Peptide Antibiotics - Defensins

## Normal Flora

Numerous species present

- Bacteria
- Fungi
- Protozoa
  
- Oral cavity
  - more than 550 species of bacteria
- Stomach and small intestine
  - Relatively sparsely populated
- Large intestine
  - more than  $10^{11}$  cells per gram of contents

## Normal Flora

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DOI: 10.1126/science.1124234

### Diversity of the Human Intestinal Microbial Flora

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The human endogenous intestinal microflora is an essential "organ" in providing nourishment, regulating epithelial development, and instructing innate immunity; yet, surprisingly, basic features remain poorly described. We examined 13,355 prokaryotic ribosomal RNA gene sequences from multiple colonic mucosal sites and feces of healthy subjects to improve our understanding of gut microbial diversity. A majority of the bacterial sequences corresponded to uncultivated species and novel microorganisms. We discovered significant intersubject variability and differences between stool and mucosa community composition. Characterization of this immensely diverse ecosystem is the first step in elucidating its role in health and disease.

>250 Novel bacterial  
species

## Diseases

- Tooth and gum infections
- Mumps
- Gastritis and ulcers
- Acute Infectious Diarrhea
- Acute diarrhea with vomiting
- Chronic diarrhea
- Helminthic intestinal infections
- Liver and intestinal disease
  - Hepatitis

## Tooth and gum infections

- Dental caries
- Periodontal diseases

## Dental caries

- Bacterial infection
- Most common infection
- Dissolution of solid tooth surface
  - Carbohydrates are fermented by bacteria and produce acids

Features of dental caries.

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✓ CHECKPOINT 22.1 Dental Caries	
Causative Organism(s)	<i>Streptococcus mutans</i> , <i>Streptococcus sobrinus</i> , others
Most Common Modes of Transmission	Direct contact
Virulence Factors	Adhesion, acid production
Culture/Diagnosis	–
Prevention	Oral hygiene, fluoride supplementation
Treatment	Removal of diseased tooth material

Checkpoint 22.1 Dental caries

## Periodontitis

- Communities of different bacterial species
- Periodontitis – late or more serious infection, following Gingivitis
- Plaque
- Calculus

## Necrotizing ulcerative gingivitis and periodontitis

- Synergistic effects caused by community of different bacterial species
- Severe condition
- At risk
  - poor hygiene
  - AIDS patients
  - Diabetes patients
  - Smoking patients

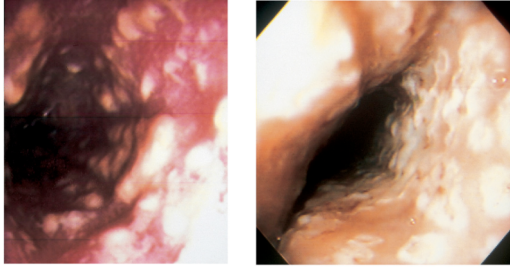
Features of periodontal diseases.

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✓ CHECKPOINT 22.2 Periodontal Diseases		
Disease	Periodontitis	Necrotizing Ulcerative Gingivitis and Periodontitis
Causative Organism(s)	Polymicrobial community including some or all of: <i>Simoneella foreshoii</i> , <i>Actinobacillus actinomycetemcomitans</i> , <i>Porphyromonas gingivalis</i> , others?	Polymicrobial community ( <i>Treponema ritzenii</i> , <i>Peptostreptococcus</i> species)
Most Common Modes of Transmission	–	–
Virulence Factors	Induction of inflammation, enzymatic destruction of tissues	Inflammation, invasiveness
Culture/Diagnosis	–	–
Prevention	Oral hygiene	Oral hygiene
Treatment	Removal of plaque and calculus, gum reconstruction, tetracycline	Debridement of damaged tissue, tetracycline or erythromycin

Checkpoint 22.2 Periodontal diseases

## Esophagitis



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Endoscopic appearance of **esophageal candidiasis** (left), showing typical **white plaques and nodules**, in a patient with multiple myeloma. **Herpes simplex esophagitis** (right), characterized by numerous small ulcerations, in an immunocompetent adult with fever and odynophagia.

## Etiology of Esophagitis

Common	Rare
<b>Infectious</b> Candidiasis Cytomegalovirus Herpes simplex virus HIV infection, acute	<i>Mycobacterium tuberculosis</i> <sup>4-8</sup> <i>Mycobacterium avium</i> complex <sup>9,10</sup> <i>Cryptococcus neoformans</i> <sup>11,12</sup> <i>Histoplasma capsulatum</i> <sup>13</sup> <i>Actinomyces</i> <sup>14,15</sup> <i>Saccharomyces cerevisiae</i> <sup>16</sup> <i>Cryptosporidium</i> <sup>17</sup> <i>Pneumocystis jirovecii</i> <sup>18</sup> Varicella-zoster virus <sup>19,21</sup> Epstein-Barr virus <sup>20</sup>
<b>Noninfectious</b> Gastroesophageal reflux Mucositis from cancer chemotherapy Mucositis from radiation therapy Aphthous ulcers	Ingestion of corrosives (e.g., lye) Local mucositis from tablets or capsules <sup>22</sup> (e.g., doxycycline, zidovudine, <sup>23</sup> ddC <sup>24</sup> )

ddC, didoxycytidine (zalcitabine); HIV, human immunodeficiency virus.

## Treatment of Esophagitis

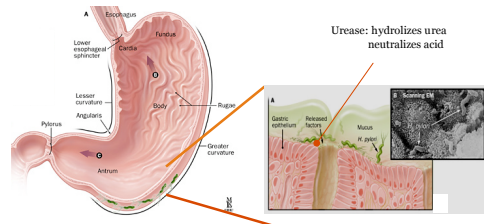
Cause	Usual Treatment (Adult Dose)	Alternative Drugs
<i>Candida</i>	Fluconazole, 100-200 mg/day PO or IV for 14-21 days; maintenance suppressive therapy may be necessary in AIDS (fluconazole, 100-200 mg/day PO)	Itraconazole, 100-200 mg bid oral suspension PO Amphotericin B, 0.2-0.4 mg/kg/day IV for 7 days Caspofungin, 50 mg/day IV after 70-mg loading dose Voriconazole, <sup>25</sup> 200 mg bid PO <sup>26</sup>
Herpes simplex	Acyclovir, 5 mg/kg IV q6h for 7-14 days or 400 mg 5 times daily PO for 14-21 days or valacyclovir, 1g PO bid for 14-21 days <sup>27</sup> ; maintenance suppressive therapy may be necessary in AIDS	Famciclovir, 500 mg bid PO for 14-21 days (not for acyclovir-resistant infection) Foscarnet, 90 mg/kg q12h IV for 7-14 days (used for acyclovir-resistant infection)
Cytomegalovirus	Ganciclovir, 5 mg/kg IV q12h for 14-21 days; maintenance suppressive therapy usually is necessary in AIDS (ganciclovir, 5 mg/kg/day IV 7 days/wk or 6 mg/kg/day IV 5 days/wk)	Foscarnet, 90 mg/kg q12h IV for 14-21 days; suppression with foscarnet, 90-120 mg/kg/d IV Valganciclovir, 900 mg bid PO for treatment, and 900 mg qd for maintenance/suppression <sup>28</sup>
Aphthous (in AIDS)	Prednisone, <sup>29</sup> 40 mg/day PO for 14 days, then taper	Thalidomide, <sup>30,31</sup> 200 mg/day PO <sup>32</sup>

<sup>28</sup>Not approved by the U.S. Food and Drug Administration for this indication. AIDS, acquired immunodeficiency syndrome.

## Gastritis and gastric ulcers

- Bacterial infections
- Pain & lesions (peptic ulcers) in the abdomen
- More common for blood type O individuals
- Bacteria neutralize stomach acid environment
- Immune response may damage epithelium
- Possibly zoonotic

## *Helicobacter pylori* : The gastric niche



Gastric cancer, peptic ulcer disease, duodenal ulcer, acute and chronic gastritis

## Acute infectious diarrhea

- Bacterial infections
  - Non-bacterial infections
- 
- Common, particular day care centers
  - Developing countries – serious health effects, fatal
  - In the U.S., 1/3 due to contaminated food

## Nausea, Vomiting, and Noninflammatory Diarrhea EPEC, EHEC, ETEC .....

Enteropathogenic (EP) & enterohemorrhagic (EH)  
*Escherichia coli* serotypes classically recognized in Infantile Diarrhea outbreaks \*

Serotypes of *Escherichia coli* that appear with increased frequency among enterotoxigenic (ET) isolates

Serotype	Difco Serogroup (References)	LT, E, coli	ST, E, coli
Class I (EAF-positive) EPEC		06:K23:H16	079:H11, 076:H12
055:K30:H5, H 367	A (18-20)	08:K40:H9, 08:K25:H9	0115:H40
011:K6:K9:H9, 012	A (15, 17, 19, 20)	LT, -ST, E, coli	0124:H7
012:K6:K9:H9	A (20)	01:K87	0146:H5
019:K6:H14	B (20)	025:H- (025:H1)	055:H-
025:K7:H7, 025:K10:H2	B (20)	025:K10:H2	0156:K10
025a:K7:H7, 025:H- (H-)	B (20)	025:K10:H-	0166, 0167
025b:K10:H2	B (20)	027:H7	063:H1
042	(6, 20, 21)	060:K62, 0139	
048	(20, 22)		
Class II (EAF-negative) EPEC			
044:K74	C (20)		
044:K74	H, 30, 23, 24		
086a:K40:H7	B (20)		
075:H7	(25-27)		
026:B6	A (20)		

\*See also Table 91.4.  
EAF, enterohemorrhagic factor probe for focal H<sub>2</sub>O<sub>2</sub> cell adherence plasmid pEAEC; EHEC, enterohemorrhagic *E. coli*; EPEC, enteropathogenic *E. coli*.

====> sero-typing

## HKO antigens

- H = flagellar antigen
- K = capsular antigen
- O = cell wall antigen

Example: *E. coli* O157:H7

## Etiology of Traveler's Diarrhea

Characteristic	Latin America (15 Studies)	Africa (3 Studies)	Asia (9 Studies)
Duration of stay (days)	21 (2-42) <sup>a</sup>	28 (28-35)	(28-42)
Attack rate (%)	52 (21-100)	54 (36-62)	(39-57)
Percentage with Enterotoxigenic <i>Escherichia coli</i>	46 (28-72)	36 (31-75)	(20-34)
<i>Shigella</i>	0 (0-30)	0 (0-15)	(4-7)
<i>Salmonella</i>	0 (0-0)	0 (0-0)	(1-15)
<i>Campylobacter jejuni</i>	—	—	(2-15)
<i>Vibrio parahaemolyticus</i>	—	—	(1-13)
Rotavirus	23 (0-36)	0 (0-0)	—

## Viral Pathogens Causing Gastroenteritis

Established pathogens*	Likely and emerging pathogens*
Adenoviruses (enteric types)	Coronaviruses
Astroviruses	Enteroviruses (various)
Caliciviruses	Picornaviruses, picotrinaviruses
Rotoviruses	Pestiviruses
Rotoviruses groups A-C	Toroviruses
Cytomegalovirus	

Rotavirus has a unique "spoked-wheel" appearance.

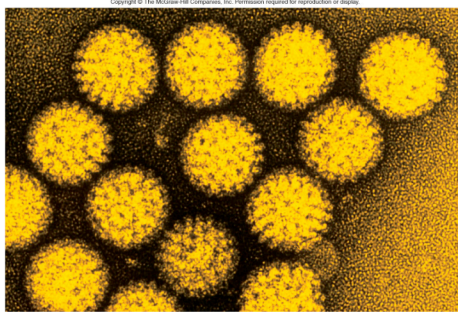


Fig. 22.18 Rotavirus in a sample of feces from a child with gastroenteritis

## Comparison of the Three Types of Enteric Infection

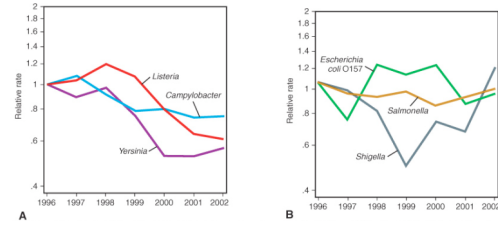
	Type I	Type II	Type III
Mechanism	Noninflammatory (enterotoxin or adherence/superficial invasion)	Inflammatory (invasion, cytotoxin)	Penetrating
Location	Proximal small bowel	Colon	Distal small bowel
Illness	Watery diarrhea	Dysentery	Enteric fever
Stool examination	No fecal leukocytes	Focal polymorphonuclear leukocytes	Focal mononuclear leukocytes
Examples	<i>Vibrio cholerae</i> <i>Escherichia coli</i> (ETEC, LT, ST) <i>Citrobacter perfringens</i> <i>Bacillus cereus</i> <i>Staphylococcus aureus</i> Aba? <sup>b</sup> <i>Giardia lamblia</i> Rotavirus Norwalk-like viruses <i>Cryptosporidium parvum</i> <i>E. coli</i> (EPEC, EAEC) Microsporidia <i>Cyclospora cayentensis</i>	<i>Shigella</i> <i>E. coli</i> (EHEC, EHEC) <i>Salmonella enteritidis</i> <i>Vibrio parahaemolyticus</i> <i>Chlamydia jejuni</i> <i>Campylobacter jejuni</i> <i>Entamoeba histolytica</i> <sup>c</sup>	<i>Salmonella typhi</i> <i>Yersinia enterocolitica</i> <i>Campylobacter jejuni</i>

\*Although an enteric dysentery involves tissue inflammation, the leukocytes are characteristically pyknotic or absent, having been destroyed by the virulent amoeba. Although not typically enterotoxic, these pathogens alter bowel physiology via adherence, superficial cell entry, cytotoxin induction, or toxins that inhibit cell function. EAEC, enteraggregative *E. coli*; EHEC, enterohemorrhagic *E. coli*; EHEC, enterohemorrhagic *E. coli*; EPEC, enteropathogenic *E. coli*; ETEC, enterotoxigenic *E. coli*; LT, heat-labile; ST, heat-stable.

## Possible Enteric Pathogens in Patients with Acquired Immunodeficiency Syndrome (AIDS)

Pathogen	Diarrhea (%) (n = 181)	No Diarrhea (%) (n = 28)
Cytomegalovirus	12-45	15
Cryptosporidium	14-30	0
Microsporidia	7.5-33	0
Entamoeba histolytica	0-15	0
Giardia lamblia	2-15	5
Salmonella spp.	0-15	0
Campylobacter spp.	2-11	8
Shigella spp.	5-10	0
Clostridium difficile toxin	6-7	0
Vibrio parahaemolyticus	4	0
Mycobacterium spp.	2-25	0
Isospora belli	2-6	0
Cyclospora	0-11	0
Blastocystis hominis	2-15	16
Candida albicans	6-53	24
Histresis simplex	5-18	40
Chlamydia trachomatis	11	13
Strongyloides	0-6	0
Intestinal spirochetes	11	11
One or more pathogens	55-86	39

## Foodborne Disease



Foodborne Diseases Active Surveillance Network, United States, 1996-2002. A, Relative rates (compared with 1996) of laboratory-diagnosed cases of *Campylobacter*, *Listeria*, and *Yersinia*, by year. B, Relative rates (compared with 1996) of laboratory-diagnosed cases of *Escherichia coli* O157, *Salmonella*, and *Shigella*, by year.

## Foodborne Disease

Annual Incidence of Diagnosed Infections Identified through Active Surveillance in the Foodborne Disease Active Surveillance Network—United States, 2002

Pathogen	Incidence per 100,000 Population
<i>Campylobacter</i>	13.17
<i>Escherichia coli</i> O157	1.73
<i>Listeria</i>	0.27
<i>Salmonella</i>	16.10
<i>Shigella</i>	10.34
<i>Vibrio</i>	0.44
<i>Yersinia</i>	0.44
<i>Cryptosporidium</i>	1.42
<i>Cyclospora</i>	0.11
Hemolytic uremic syndrome*	1.78

\*Incidence per 100,000 children aged less than 5 years.

## Foodborne Disease

Pathogenic Mechanisms in Bacterial Foodborne Disease

Preformed Toxin	Toxin Production in Vivo	Toxin Invasion	Toxin Production and/or Toxin Invasion
<i>Staphylococcus aureus</i> <i>Bacillus cereus</i> (short incubation) <i>Clostridium botulinum</i>	<i>Clostridium perfringens</i> <i>B. cereus</i> (long incubation) <i>C. botulinum</i> (infant botulism) <i>Enterococcus faecalis</i> / <i>coli</i> <i>Vibrio cholerae</i> O1 or O139 <i>V. cholerae</i> non-O1 Shiga toxin-producing <i>E. coli</i>	<i>Campylobacter jejuni</i> <i>Salmonella</i> <i>Shigella</i> <i>Enteric E. coli</i>	<i>Vibrio parahaemolyticus</i> <i>Yersinia enterocolitica</i>

## Foodborne Disease

Outbreak cases of Known Cause Reported to the CDC, 1973-2000

Etiologic Agent	Outbreaks		Outbreak-Associated Cases	
	Number	%	Number	%
<b>Bacterial</b>				
<i>Bacillus cereus</i>	121	2.0	2787	1.2
<i>Campylobacter</i>	140	2.3	3696	1.5
<i>Clostridium botulinum</i>	316	5.2	713	0.3
<i>Clostridium perfringens</i>	364	5.9	22,885	9.5
<i>Escherichia coli</i>	202	3.3	7992	3.2
<i>Listeria monocytogenes</i>	13	0.2	466	0.2
<i>Salmonella</i>	2147	35.1	102,574	42.7
<i>Shigella</i>	216	3.5	24,631	10.2
<i>Staphylococcus aureus</i>	517	8.4	22,000	9.2
<i>Streptococcus</i> , group A	16	0.3	2178	0.9
<i>Vibrio cholerae</i>	13	0.2	960	0.4
<i>Vibrio cholerae</i> , non-O1	3	0.0	113	0.0
<i>Vibrio parahaemolyticus</i>	51	0.8	1371	0.6
<i>Yersinia enterocolitica</i>	11	0.2	844	0.4
Other bacteria	27	0.4	1170	0.5
<b>Chemical</b>				
Ciguatera	376	6.1	1610	0.7
Heavy metals	58	0.9	826	0.3
Maduroon poisoning	78	1.2	239	0.1
Scombroid toxin	423	6.9	2369	1.0
Shellfish	37	0.6	283	0.1
Other chemical	161	2.6	1443	0.6
<b>Parasitic</b>				
<i>Giardia</i>	22	0.4	547	0.2
<i>Trichinella spiralis</i>	152	2.5	1113	0.5
Other parasites	29	0.5	2531	1.1
<b>Viral</b>				
Hepatitis A	219	3.6	7188	3.0
Novavirus	390	6.4	26,374	11.0
Other viruses	24	0.4	1985	0.8
Total	6123	100	246,428	100

CDC, Centers for Disease Control and Prevention.

## Foodborne Disease

Estimated Frequency of Hospitalizations and Deaths for Known Foodborne Pathogens, United States, 1997

Disease or Agent	Percent Hospitalized	Percent Died
<b>Bacterial</b>		
<i>Bacillus cereus</i>	0.6	0.00
Bovine botulism	80.0	7.99
<i>Brucella</i> spp.	55.0	5.00
<i>Campylobacter</i> spp.	10.2	0.10
<i>Clostridium perfringens</i>	0.3	0.05
<i>Escherichia coli</i> O157:H7	29.5	0.83
<i>E. coli</i> , non-O157 STEC	29.5	0.83
<i>E. coli</i> , enterohemorrhagic	0.5	0.01
<i>E. coli</i> , other enterohemorrhagic	0.5	0.01
<i>Listeria monocytogenes</i>	92.2	20.00
<i>Salmonella enteritidis</i> /Typhimurium	22.1	0.40
<i>Shigella</i> spp.	75.0	0.78
<i>Shigella</i> spp.	22.1	0.16
<i>Staphylococcus aureus</i> food poisoning	18.0	0.02
<i>Streptococcus</i> , foodborne	13.3	0.00
<i>Vibrio cholerae</i> , toxigenic	34.0	0.60
<i>Vibrio vulnificus</i>	91.0	39.60
Other vibrios	12.6	2.50
<i>Yersinia enterocolitica</i>	24.2	0.05
<b>Parasitic</b>		
<i>Cryptosporidium parvum</i>	15.0	0.50
<i>Cyclospora cayentensis</i>	2.0	0.05
<i>Giardia lamblia</i>	n/a	n/a
<i>Trichostrongylus axei</i>	n/a	n/a
<i>Trichinella spiralis</i>	8.1	0.30
<b>Viral</b>		
Nonwalk-like viruses	n/a	n/a
Rotavirus	n/a	n/a
Adenovirus	n/a	n/a
Hepatitis A virus	13.0	0.30

STEC, Shiga toxin-producing *E. coli*.  
Modified from Mead PS, Shanker L, Dietz V, et al. Food-related illness and death in the United States. *Emerg Infect Dis.* 1999;5:607-624.

## Types of water related diseases

Waterborne	Diseases transmitted by ingestion of contaminated drinking water. Examples: cholera, typhoid fever, cryptosporidiosis.
Water-carried	Diseases acquired by accidental ingestion of, or exposure to, contaminated recreational water. Examples: cryptosporidiosis, giardiasis, <i>Pseudomonas dermatitis</i> .
Water-washed	Diseases transmitted person-to-person as a result of poor sanitation due to inadequate quantities of water for washing hands, utensils, and so on. Examples: shigellosis, hepatitis A, cryptosporidiosis.
Water-based	Diseases caused by pathogens with an obligatory life-cycle phase occurring in the water. Examples: schistosomiasis, dracunculiasis.
Water-vectored	Diseases transmitted by insects that breed or bite in or near water. Examples: malaria, yellow fever, dengue, African trypanosomiasis.

Adapted from data published in Steiner TS, Theilman NM, Guerrant RL. Protozoal agents: What are the dangers for the public water supply? *Annu Rev Med.* 1997;48:329-340.

==> access to clean (drinking) water !!!!!

## Cryptosporidium infection

- Protozoan infection
- Zoonotic
- Oocysts
- Intracellular
- AIDS patients are at risk
- Associated with fresh water outbreaks

## Hepatitis (Inflammation of the liver)

- Viral infection
  - Hepatitis A
  - Hepatitis B
  - Hepatitis C
- Jaundice
- Noninfectious conditions may cause hepatitis

## Features of Hepatitis.

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CHECKPOINT 22.8 Hepatitis			
Causative Organism(s)	Hepatitis A or E virus	Hepatitis B virus	Hepatitis C virus
Most Common Modes of Transmission	Fecal-oral, vehicle	Parenteral (blood contact), direct contact (especially sexual), vertical	Parenteral (blood contact), vertical
Virulence Factors	–	Latency	Core protein suppresses immune function?
Culture/Diagnosis	IgM serology	Serology (ELISA, radioimmunoassay)	Serology
Prevention	Hepatitis A vaccine or combined HAV/HBV vaccine	HBV recombinant vaccine	–
Treatment	Immune globulin	Interferon, nucleoside analogs	(Pegylated) interferon with or without ribavirin
Long-Term Consequences	None	Chronic infection, liver cancer, death	Chronic infection and liver disease very common; cancer, death
Incubation Period	2-7 weeks	1-6 months	2-8 weeks

## Checkpoint 22.8 Hepatitis

## Infectious Diseases Affecting the Gastrointestinal Tract.

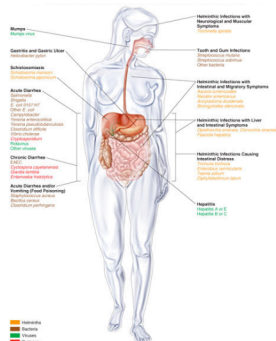


Fig. 22.p730

## Approach to diagnosis and management of infectious diarrhea.

