Infectious diseases

	4/5th Semester Classes on Infectious Diseases, 8-9AM, Tuesdays (LT-1)
	Topics
1	Approach to Infectious Diseases and their prevention
2	Antibiotic stewardship practices
3	Community-Acquired Infections
4	Health Care–Associated Infections
5	Gram-Positive Bacteria (part-1)
6	Gram-Positive Bacteria (part-2)
7	Gram-Negative Bacteria (part-1)
8	Gram-Negative Bacteria (part-2)
9	Spirochetal Diseases
10	Diseases Caused by Atypical/Miscellaneous Bacterial Infections
11	**Revision-cum-exam on bacteria (Must to know type)**
12	Infections Due to DNA Viruses
13	Infections Due to RNA Viruses (part 1)
14	Infections Due to RNA Viruses (part 2)
15	HIV/AIDS – part 1
16	HIV/AIDS – part 2
17	Fungal Infections
18	Parasitic Infections (part 1)
19	Parasitic Infections (part 2)
20	**Revision-cum-exam on Virus, Fungal, and Parasite (Must to know type)**

1

ENTEROBACTERIACEAE
(E. coli, Klebsiella, Proteus, Enterobacter)

- In healthy humans, *E. coli* is the predominant species of gram-negative bacilli (GNB) in the **colonic flora**; *Klebsiella* and *Proteus* are less prevalent
- Multiple bacterial virulence factors are required for the **pathogenesis**

Bacterial Goal	Host Obstacle	Bacterial Solution
Extraintestinal attachment	Flow of urine, mucociliary blanket	Multiple adhesins (e.g., type 1, S, and F1C fimbriae; P pili)
Nutrient acquisition for growth	Nutrient sequestration (e.g., iron via intracellular storage and extracellular scavenging via lactoferrin and transferrin)	Cellular lysis (e.g., hemolysin), multiple mechanisms for competing for iron (e.g., siderophores) and other nutrients
Initial avoidance of host bactericidal activity	Complement, phagocytic cells, antimicrobial peptides	Capsular polysaccharide, lipopolysaccharide
Dissemination (within host and between hosts)	?	Irritant tissue damage resulting in increased excretion (e.g., toxins such as hemolysin)
Late avoidance of host bactericidal activity	Acquired immunity (e.g., specific antibodies), treatment with antibiotics	?Cell entry, acquisition of antimicrobial resistance

TABLE 186-2 INTESTINAL PATHOGENIC *E. COLI*

Pathotype	Epidemiology	Clinical Syndrome[a]	Defining Molecular Trait	Responsible Genetic Element[b]
STEC/EHEC/STEAEC	Food, water, person-to-person; all ages, industrialized countries	Hemorrhagic colitis, hemolytic-uremic syndrome	Shiga toxin	Lambda-like Stx1- or Stx2-encoding bacteriophage
ETEC	Food, water; young children in and travelers to developing countries	Traveler's diarrhea	Heat-stable and labile enterotoxins, colonization factors	Virulence plasmid(s)
EPEC	Person-to-person; young children and neonates in developing countries	Watery diarrhea, persistent diarrhea	Localized adherence, attaching and effacing lesion on intestinal epithelium	EPEC adherence factor plasmid pathogenicity island (locus for enterocyte effacement [LEE])
EIEC	Food, water; children in and travelers to developing countries	Dysentery	Invasion of colonic epithelial cells, intracellular multiplication, cell-to-cell spread	Multiple genes contained primarily in a large virulence plasmid
EAEC	?Food, water; children in and travelers to developing countries; all ages, industrialized countries	Traveler's diarrhea, acute diarrhea, persistent diarrhea	Aggregative/diffuse adherence, virulence factors regulated by AggR	Chromosomal or plasmid-associated adherence and toxin genes

- Certain strains of *E. coli* are capable of causing diarrheal disease
- **ExPEC** strains are the most common enteric GNB to cause community-acquired and health care–associated bacterial infections (**All age groups, all types of hosts, and nearly all organs and anatomic sites**)
- Humans are the **major reservoir** [except for STEC/EHEC]

- Transmission occurs predominantly **via contaminated food and water** for ETEC, STEC/EHEC/STEAEC, EIEC, and EAEC and by **person-to-person** spread for EPEC (and occasionally STEC/EHEC/STEAEC)
- **Except in the cases of EHEC and EAEC**, disease occurs primarily in developing countries
- Distinguish **noninflammatory (mainly by** ETEC, EPEC, and DAEC) **from inflammatory diarrhea** (suggested by grossly bloody or mucoid stool or a positive test for fecal leukocytes)
- Definitive diagnosis generally is not necessary except for STEC
- The mainstay of treatment for all diarrheal syndromes is replacement of water and electrolytes, especially for STEC/EHEC/STEAEC **infection where antibiotics may increase the incidence of HUS**
- If **diarrhea persists for >10 days** despite treatment, *Giardia* or *Cryptosporidium* should be sought

- Person-to-person spread is the predominant mode of acquisition of **Klebsiella**
- **cKP Causes** pneumonia, UTI, abdominal infection, intravascular device infection, surgical site infection, soft tissue infection, and subsequent bacteremia
- **hvKP (of Asian origin)** infection distinguished from traditional infections due to **cKP** by
  - (1) presentation as community-acquired pyogenic liver abscess
  - (2) occurrence in patients lacking a history of hepatobiliary disease, and
  - (3) a propensity for metastatic spread to distant sites
- Urine samples with unexplained alkalinity should be cultured for ***Proteus***, and identification of a *Proteus* species in urine should prompt consideration of an evaluation for urolithiasis
- ***Enterobacter/citrobacter/serratia/morganella/edwardsiella*** causes a spectrum of extraintestinal infections similar to other GNB

SALMONELLA

- *Two species: Salmonella enterica* and *Salmonella bongori*
- Serotyping is based on **the somatic O antigen** (lipopolysaccharide cellwall components), the surface **Vi antigen** (restricted to *S. typhi* and *S. paratyphi* C), and the flagellar **H antigen**
- The growth of **serotypes *Salmonella typhi* and *Salmonella paratyphi* is restricted to human host**s, remaining serotypes (nontyphoidal *Salmonella*, or **NTS**) can colonize the gastrointestinal tracts of a broad range of animals, reptiles, birds, and insects
- Ingestion in contaminated food or water with **the ingested dose as determinant** of incubation period and disease severity
- Conditions that **decrease either stomach acidity or intestinal integrity** increase susceptibility to infection
- Once **reach the small intestine**, they penetrate the mucus layer of the gut, traverse the intestinal layer through phagocytic microfold (M) cells that reside within Peyer's patches, phagocytosed by macrophages but in a protective manner, and then via the lymphatics **colonize reticuloendothelial tissues**
- In contrast to enteric fever, NTS gastroenteritis is characterized by massive **polymorphonuclear** leukocyte infiltration **into both the large- and small-bowel** mucosa

- Enteric (**typhoid**) fever is a systemic disease characterized by fever and abdominal pain and caused by dissemination of *S. typhi* or *S. paratyphi*
- Most commonly, food-borne or waterborne transmission results from fecal contamination; **Sexual transmission between male partner**s has been described; Health care workers occasionally acquire too
- **IP;** 10–14 days but ranges from 5 to 21 days
- **Risk factors** include
  1. contaminated water or ice,
  2. flooding,
  3. food and drinks purchased from street vendors,
  4. raw fruits and vegetables grown in fields fertilized with sewage,
  5. ill household contacts,
  6. lack of hand washing and toilet access, and
  7. evidence of prior *Helicobacter pylori* infection
- It is estimated that there is **one case of paratyphoid fever for every four cases** of typhoid fever

SYMPTOMS	SIGNS
Fever (>75%) **headache** (80%) anorexia (55%) chills (35–45%) **Abdominal pain** (30-40%) **cough** (30%) sweating (20–25%) myalgias (20%), nausea (18–24%), vomiting (18%), **diarrhea** (22–28%) Constipation (13–16%) malaise (10%) arthralgia (2–4%).	**coated tongue** (51–56%), **relative bradycardia** at the peak of high fever (<50%) **rose spots (30%),** splenomegaly (5–6%), abdominal tenderness (4–5%) hepatosplenomegaly (3–6%), epistaxis,

The **development of severe disease** (which occurs in ~10–15% of patients) depends on host factors, strain virulence and inoculum, and choice of antibiotic therapy

- Gastrointestinal bleeding (10–20%)
- Intestinal perforation (1–3%)
- Neurologic manifestations (2-40%)

- Up to 10% of untreated patients excrete *S. typhi* in the feces **for up to 3 months**, and 1–4% develop chronic asymptomatic carriage, shedding *S. typhi* in either urine or stool **for >1 year**
- The **definitive diagnosis** of enteric fever requires the isolation of *S. typhi* or *S. paratyphi* from blood, bone marrow, intestinal secretions,(**THESE 3 IN COMBINATION POSITIVE >90%**) other sterile sites, rose spots, and stool
- Serologic tests, including the classic Widal test for "febrile agglutinins," and rapid tests to detect antibodies to outermembrane proteins **have lower positive predictive** values than blood culture

Indication	Agent	Dosage (Route)	Duration, Days
Empirical Treatment			
	Ceftriaxone[a]	2 g/d (IV)	10–14
	Azithromycin[b]	1 g/d (PO)	5
Fully Susceptible			
Optimal treatment	Ciprofloxacin[c]	500 mg bid (PO) or 400 mg q12h (IV)	5–7
	Azithromycin	1 g/d (PO)	5
Alternative treatment	Amoxicillin	1 g tid (PO) or 2 g q6h (IV)	14
	Chloramphenicol	25 mg/kg tid (PO or IV)	14–21
	Trimethoprim-sulfamethoxazole	160/800 mg bid (PO)	7–14
Multidrug-Resistant			
Optimal treatment	Ceftriaxone[a]	2 g/d (IV)	10–14
	Azithromycin	1 g/d (PO)	5
Alternative treatment	Ciprofloxacin	500 mg bid (PO) or 400 mg q12h (IV)	5–14

Two typhoid vaccines:
(1) Ty21a, (given on days 1, 3, 5, and 7, with a booster every 5 years);
(2) Vi CPS, (given in a single dose, with a booster every 2 years)
cumulative efficacy was **48%** for Ty21a at 2.5–3.5 years and **55%** for Vi CPS at 3 years

SHIGELLA

- *Shigella* **cannot be distinguished from *Escherichia coli*** by DNA hybridization and remains a separate species only on hstorical and clinical grounds
- Unlike *E. coli*, is **nonmotile and does not produce gas from sugars**
- Human intestinal tract represents the major **reservoir**
- Bacteria are transmitted **most efficiently by the fecal-oral route** via hand carriage, rarely by flies and sexually
- Highest prevalences in the most **impoverished areas**
- Shigellosis typically evolves through **four phases**:
  1. Incubation (1–4 days),
  2. Watery diarrhea,
  3. Dysentery - **dysentery—a** clinical syndrome of fever, intestinal cramps, and frequent passage of small, bloody, mucopurulent stools
  4. Postinfectious phase – **Reactive arthritis**, **toxic megacolon, and HUS (in developing countries)**
- **Ciprofloxacin is recommended** as first-line treatment; others like ceftriaxone, azithromycin, pivmecillinam, and some fifth-generation quinolones

VIBRIO

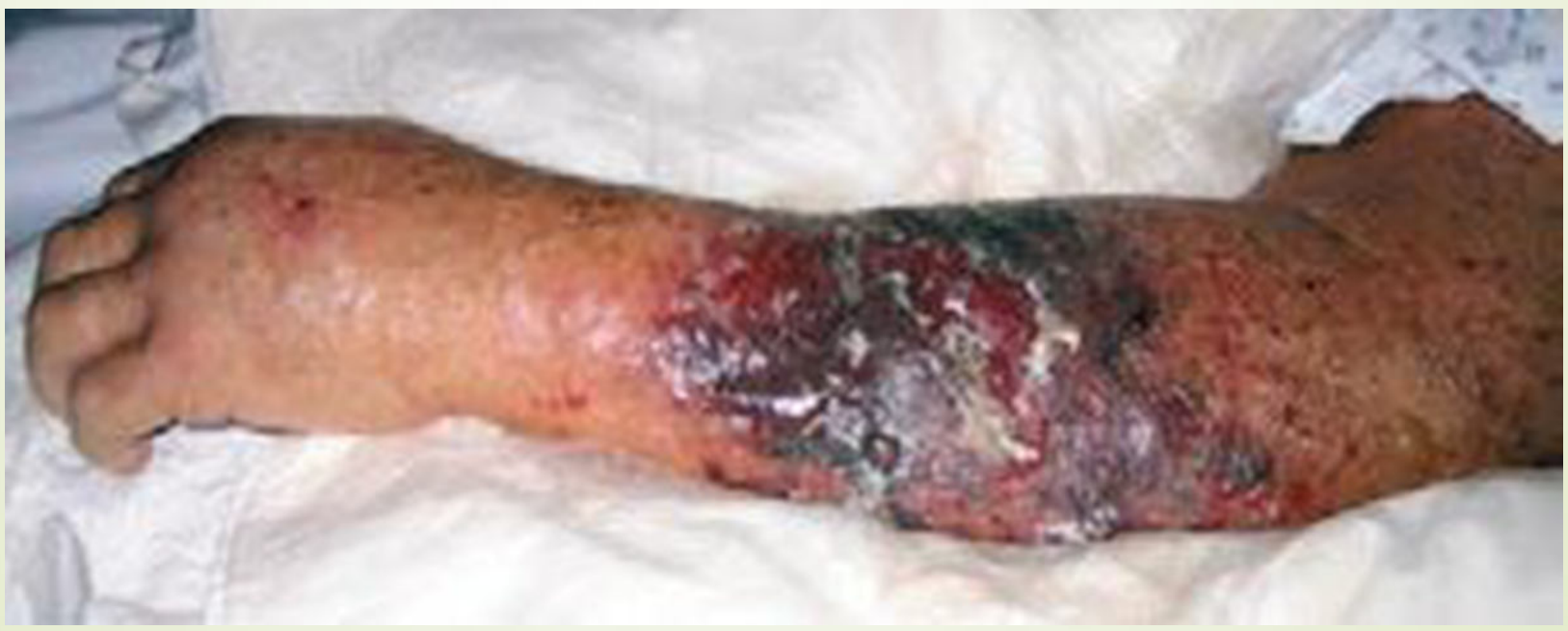
- ***Cholera*** now refers to disease caused by *V. cholerae* serogroup O1 or O139—i.e., the serogroups with epidemic potential
- Responsible for **seven** global pandemics and much suffering over the past two centuries
- In nature, vibrios most commonly reside in tidal rivers and bays under conditions of moderate **salinity**; They proliferate in the **summer months**
- Cholera is predominantly a pediatric disease in endemic areas, but it affects adults and children **equally when** newly introduced into a population
- **Cholera toxin, toxin-coregulated pilus**, and several other virulence factors are coordinately regulated by ToxR With **IP 24- to 48-h**

- Some individuals are asymptomatic or have only mild diarrhea; others present with the sudden onset of explosive and life-threatening diarrhea **(*cholera gravis*)**; "rice-water" stool WITH absent fever; **Complications** derive exclusively from the effects of volume and electrolyte depletion
- Clinical suspicion of cholera can be confirmed by the identification in stool
- **Treatment;** first and foremost requires fluid resuscitation **with macrolides (DOC**)

PSEUDOMONADS (an inability to ferment lactose)

- ***Pseudomonas, Burkholderia*, and *Stenotrophomonas***
- The pathogenicity is based on **opportunism** with the exceptions (melioidosis by *Burkholderia pseudomallei* and glanders by *B. mallei*)
- *P. aeruginosa* remains the most common contributing factor to respiratory failure in **Cystic Fibrosis**
- *B. cepacia* gained notoriety as the cause of a rapidly fatal syndrome of respiratory distress and septicemia (the "**cepacia syndrome**") in CF patients
- Cytotoxic chemotherapy, mechanical ventilation, and broad-spectrum antibiotic therapy probably paved the way for colonization and infection
- *P. aeruginosa* is found in most moist environments; infection Often occurs **concomitantly with host defense compromise**
- Of the common gram-negative bacteria, no other species produces **such a large number of putative virulence factors**
- Among gram-negative bacteria, *it* probably produces the **largest number of substances that are toxic** to cells and thus may injure tissues

- *P. aeruginosa* causes infections at almost all sites in the body but shows a rather **strong predilection for the lungs**
- **Bacteremia**; only point differentiating this entity from gram-negative sepsis of other causes may be **ecthyma gangrenosum**, which occur almost exclusively in markedly neutropenic patients and patients with AIDS
- **Combination therapy** became the standard of care, recently newer antipseudomonal drugs (colistin, tigecycline, cefepime) can be used as monotherapy



ACINETOBACTER

- *Acinetobacter baumannii* is particularly formidable because of its propensity to acquire antibiotic resistance determinants
- **Contrary to previous thought of nonmotile** characteristic it demonstrate motility under certain growth conditions
- **Widely distributed in nature**, *like* water, soil, on vegetables, a component of the skin flora, and sometimes a contaminant in blood samples
- Colonizes patients **exposed to heavily contaminated hospital environments or to the hands of health care workers**
- *It* **must be considered in the differential diagnosis** of hospital-acquired pneumonia, central line–associated bloodstream infection, posttraumatic wound infection in military personnel, and postneurosurgical meningitis
- It should be suspected **when plump coccobacilli** are seen in Gram's-stained samples
- **Only sulbabctam**, cotrimoxazole, carbapenams, amikacin, tigecycline, colistin are possible treatment

HELICOBACTER

- It colonizes the **stomach in ~50%** of the world's human population, essentially **for life** unless eradicated by antibiotic treatment
- Humans are the **only important reservoir**
- Lifelong colonization may offer some **protection** against complications of gastroesophageal reflux disease (GERD), including esophageal adenocarcinoma
- Treatment against the organism prevent/treat PUD and low-grade gastric MALT lymphoma, however, **no benefit in the treatment** of gastric adenocarcinoma
- **Nongastric (intestinal) *Helicobacter* species** can cause clinical features resembling those of *Campylobacter* infections
- **Prevalence varies with age:** *H. pylori* is usually acquired in childhood, The age association is due mostly to **a birth-cohort effect**
- Combination of factors lead to disease state: **bacterial strain differences, host susceptibility to disease, and environmental factors**

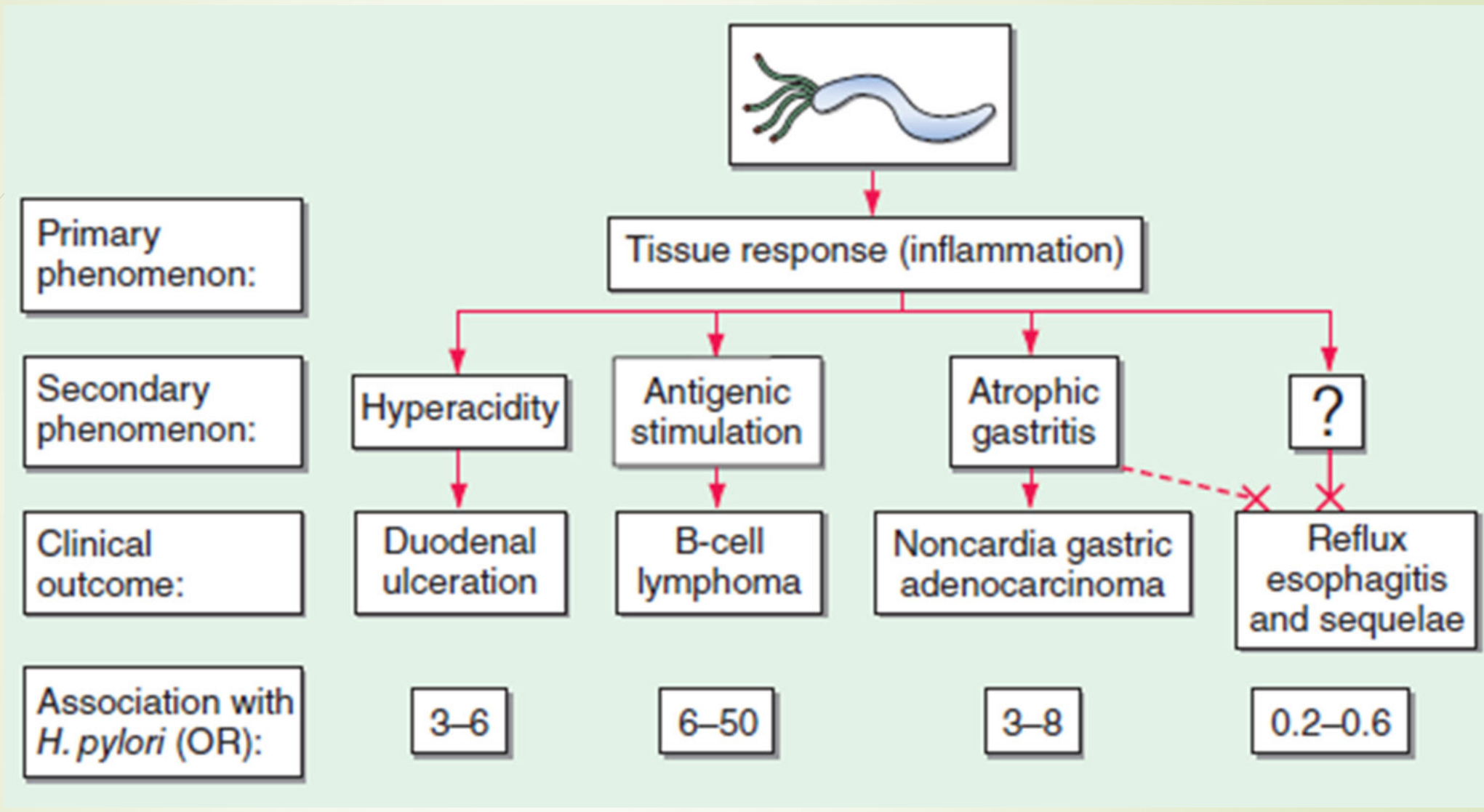
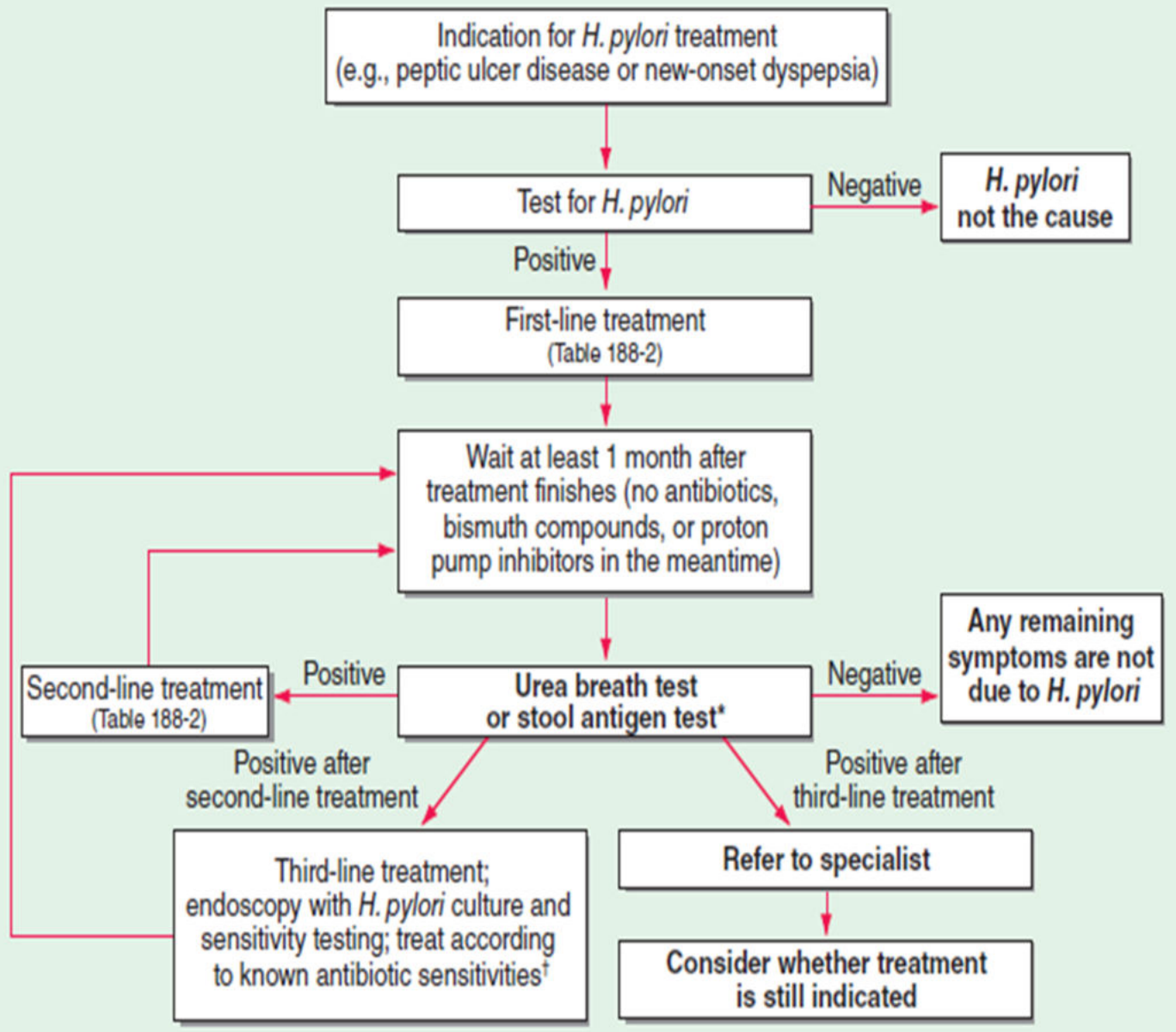


TABLE 188-1 TESTS COMMONLY USED TO DETECT *HELICOBACTER PYLORI*

Test	Advantages	Disadvantages
Tests Based on Endoscopic Biopsy		
Biopsy urease test	Quick, simple	Some commercial tests not fully sensitive before 24 h
Histology	May give additional histologic information	Sensitivity dependent on experience and use of special stains
Culture	Permits determination of antibiotic susceptibility	Sensitivity dependent on experience
Noninvasive Tests		
Serology	Inexpensive and convenient; not affected by recent antibiotics or proton pump inhibitors to the same extent as breath and stool tests	Cannot be used for early follow-up after treatment; some commercial kits inaccurate, and most less accurate than urea breath test
^{13}C urea breath test	Inexpensive and simpler than endoscopy; useful for follow-up after treatment	Requires fasting; not as convenient as blood or stool tests
Stool antigen test	Inexpensive and convenient; useful for follow-up after treatment; may be useful in children	Stool-based tests are disliked by people from some cultures



- Whether or not the ulcers are currently active, *H. pylori* **should be eradicated** in patients with documented ulcer disease to prevent Relapse
- Overall most treatment of **asymptomatic *H. pylori* carriage is given** without a firm evidence base
- **Test-and-treat** has emerged as a common clinical practice

TABLE 188-2 COMMONLY RECOMMENDED TREATMENT REGIMENS FOR *HELICOBACTER PYLORI*

Regimen[a] (Duration)	Drug 1	Drug 2	Drug 3	Drug 4
Regimen 1: OCM (7–14 days)[b]	Omeprazole (20 mg bid[c])	Clarithromycin (500 mg bid)	Metronidazole (500 mg bid)	—
Regimen 2: OCA (7–14 days)[b]	Omeprazole (20 mg bid[c])	Clarithromycin (500 mg bid)	Amoxicillin (1 g bid)	—
Regimen 3: OBTM (14 days)[d]	Omeprazole (20 mg bid[c])	Bismuth subsalicylate (2 tabs qid)	Tetracycline HCl (500 mg qid)	Metronidazole (500 mg tid)
Regimen 4[e]: sequential (5 days + 5 days)	Omeprazole (20 mg bid[c])	Amoxicillin (1 g bid)	—	—
	Omeprazole (20 mg bid[c])	Clarithromycin (500 mg bid)	Tinidazole (500 mg bid[g])	—
Regimen 5[f]: concomitant (14 days)	Omeprazole (20 mg bid[c])	Amoxicillin (1 g bid)	Clarithromycin (500 mg bid)	Tinidazole (500 mg bid[g])
Regimen 6[h]: OAL (10 days)	Omeprazole (20 mg bid[c])	Amoxicillin (1 g bid)	Levofloxacin (500 mg bid)	—

CAMPYLOBACTER

- ***Campylobacter, Arcobacter,* and *Helicobacter***
- It is **more common than that due to *Salmonella* and *Shigella* combined**
- Although acute diarrheal illnesses are most common, these organisms may cause infections in virtually **all parts of the body**, especially **in compromised hosts**, and these infections may have **late nonsuppurative sequelae (Reactive A, GBS)**
- The human pathogens fall into two major groups:
  - those that primarily cause diarrheal disease **(*C. jejuni mainly*)**
  - those that cause extraintestinal infection **(*C. fetus mainly*)**
- Transmitted to humans **in raw or undercooked food product**s or through direct contact with infected animals
- The symptoms of *Campylobacter* enteritis are not sufficiently unusual to distinguish this illness from **that due to *Salmonella, Shigella, Yersinia***, and **clostridium (inflammatory bacterial diarrhea)**
- Diagnosis of **inflammatory bowel disease should not be made** until *Campylobacter* infection has been ruled out
- **Indications for therapy** include high fever, bloody diarrhea, severe diarrhea, persistence for >1 week, and worsening of symptoms
- A **5- to 7-day course of erythromycin** (250 mg orally four times daily) is DOC

Thank you