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

NEISSERIA

HAEMOPHILUS

LEGIONELLA

BORDETELLA

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

SALMONELLA

SHIGELLA

VIBRIO

PSEUDOMONADS

ACINETOBACTER

HELICOBACTER

CAMPYLOBACTER

BRUCELLA

FRANCISELLA

YERSINIA

BARTONELLA

NEISSERIA (*N. meningitis & N. gonorrhoeae; IP-2-7days)*

- *N. meningitis;* diplococcus that **colonizes in the nasopharynx** of healthy adolescents and adults, use glucose and maltose to produce acid
- *N. gonorrhoeae;* grow on selective media and **to use glucose but not** maltose, sucrose, or lactose
- Meningococci invasive disease are usually **encapsulated with polysaccharide**, and the antigenic nature of the capsule determines an organism's serogroup
- Under capsule, an outer phospholipid membrane containing lipopolysaccharide **(LPS, endotoxin) and multiple outer-membrane proteins (serotype)**
- Gonococcus contains, on average, **three genome copies per coccal unit**; this polyploidy permits a high level of antigenic variation and the survival of the organism in its host and resistant to antibiotics
- Outer-Membrane Proteins (**PILLI, OPA, PORIN**, etc) and **lipooligosaccharide** (LOS): gonococcal structures that interact with epithelial cells, host factors seem to be important in mediating entry of gonococci into nonphagocytic cells (e.g. complement deficiency)

- There are several patterns of disease: **epidemic, outbreak, hyperendemic, and sporadic or endemic**
- Clusters of cases occur where there is an opportunity for increased transmission—i.e., in **(semi-)closed communities**
- **Smoking, crowding, and respiratory viral infection** increase the risk of carriage/disease
- **Endothelial injury** is central to many clinical features of meningococcemia, including increased vascular permeability, pathologic changes in vascular tone, loss of thromboresistance, intravascular coagulation, and myocardial dysfunction
- Most common clinical syndromes are **meningitis and meningococcal septicemia**
- **MENINGITIS:** While 30–50% of patients present with a meningitis syndrome alone OR up to 40% with some features of septicemia
- **SEPTICEMIA**: alone accounts for up to 20% of cases
- **CHRONIC MENINGOCOCCEMIA**, presents as repeated episodes of petechial rash associated with fever, joint pain/arthritis, and splenomegaly that may progress to acute meningococcal septicemia if untreated
- **POSTMENINGOCOCCAL REACTIVE DISEASE,** an immune complex disease develops ~4–10 days after the onset of meningococcal disease

TABLE 180-2 COMMON CAUSES OF PETECHIAL OR PURPURIC RASHES

Enteroviruses
Influenza and other respiratory viruses
Measles virus
Epstein-Barr virus
Cytomegalovirus
Parvovirus
Deficiency of protein C or S (including postvaricella protein S deficiency)
Platelet disorders (e.g., idiopathic thrombocytopenic purpura, drug effects, bone marrow infiltration)
Henoch-Schönlein purpura, connective tissue disorders, trauma (including nonaccidental injuries in children)
Pneumococcal, streptococcal, staphylococcal, or gram-negative bacterial sepsis

Usually initially blanching in nature and **indistinguishable from viral rashe**s, HOWEVER, petechial or frankly purpuric **over the hours after onset**, THEN purpura fulminans

(fewer than **<10%** of children of all rashes) – (occurs in **two-thirds** of Meningococcal cases)

- Clinical grounds and lab confirmation (blood cultures are positive in up to 75% of cases, (PCR) analysis of whole-blood samples, lumbar puncture
- Third-generation cephalosporin, treated **for 7 days**
- 10% DEATH, **most common complication** 10% of cases) is scarring after necrosis of purpuric skin lesions
- **Factors associated with a poorer prognosis** are shock; young age (infancy), old age, and adolescence; coma; purpura fulminans; disseminated intravascular coagulation; thrombocytopenia; leukopenia; absence of meningitis; metabolic acidosis; low plasma concentrations of antithrombin and proteins S and C; high blood levels of PAI-1; and **a low** erythrocyte sedimentation rate or C-reactive protein level
- **PREVENTION;**

1. Immunization- Polysaccharide Vaccines/Conjugate Vaccines/Vaccines Based on Subcapsular Antigens
   - A monovalent serogroup A vaccine, **manufactured in India**, was licensed in 2010 and rolled out to countries in the sub-Saharan African meningitis belt
- Chemoprophylaxis- Rifampin/Ceftriaxone as a single IM or IV/Ciprofloxacin/ofloxacin

GONORRHEA

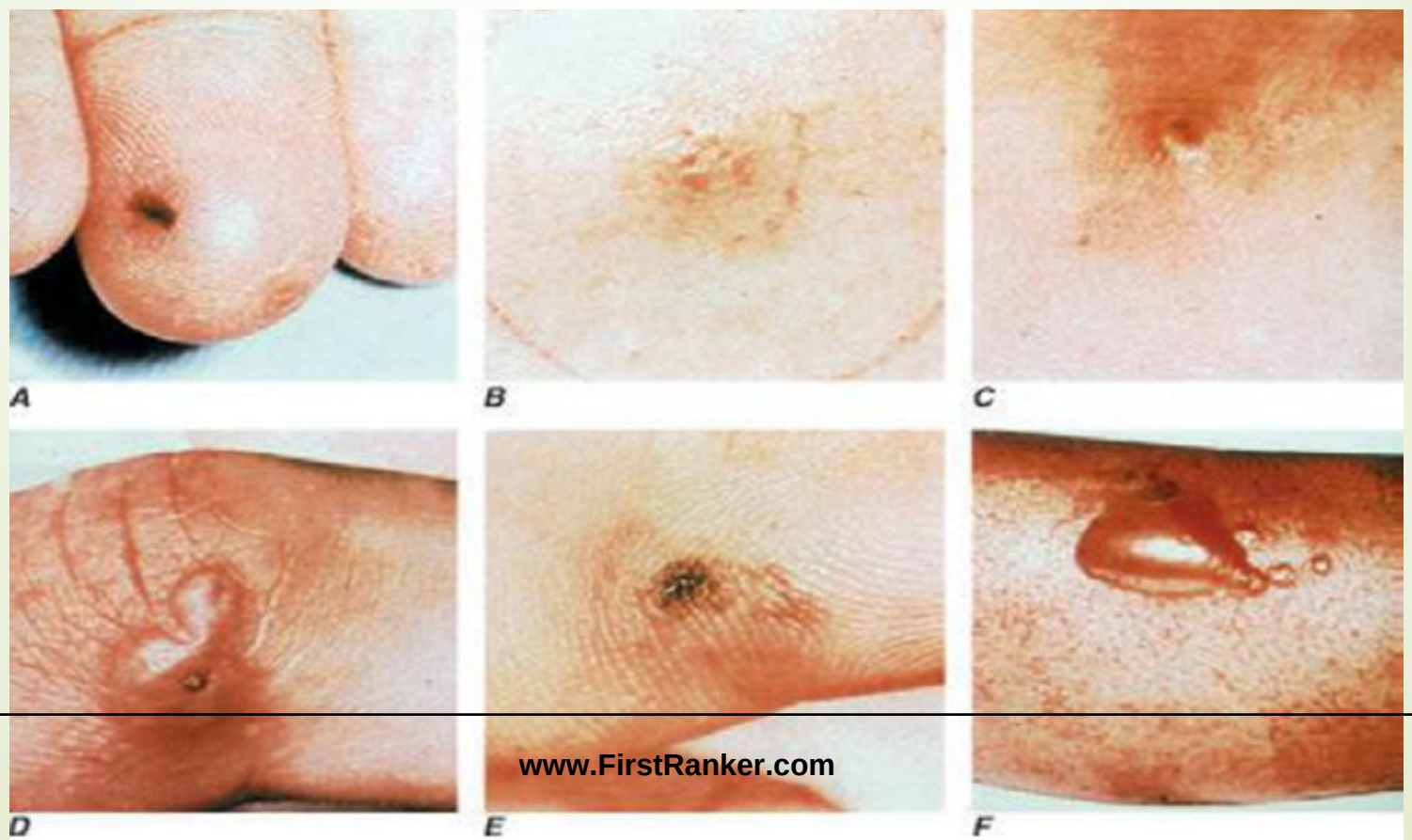
- Gonorrhea is a sexually transmitted infection (STI) of epithelium and commonly manifests as cervicitis, urethritis, proctitis, and conjunctivitis

Gonococcal Infections in Men	Gonococcal Infections in Women
Acute urethritis	*Cervicitis* (more **acute and intense** than those of chlamydial cervicitis)
Epididymitis/prostitis	Urethritis
Balanitis or further deep complications including abscesses	*Vaginitis* (occur in **anestrogenic** Women)

- Anorectal Gonorrhea
- Pharyngeal Gonorrhea
- Ocular Gonorrhea
- Gonorrhea in Pregnant Women, Neonates, and Children

Gonococcal Arthritis (DGI)

- **Menstruation** is a risk factor for dissemination, and two-thirds cases are in women
- **Bacteremic stage** and a joint-localized stage with **suppurative arthritis**
- **D/D;** reactive arthritis AND septic arthritis



- Rapid diagnosis - **Gram's staining** of urethral exudates
- Nucleic acid probe tests are being substituted for culture, **BUT NOT LEGALLY**
- Single IM dose of the third-generation cephalosporin, mainstay of therapy

OR azithromycine (1g single dose)

- Because **co-infection with *C. trachomatis*** occurs frequently, initial treatment regimens must also incorporate an agent
- DGI require **higher dosages and longer durations** of therapy
- All persons who experience **more than one episode of DGI should be evaluated** for complement deficiency
- **Condoms**, if properly used, effective protection against the transmission and acquisition of gonorrhea
- Patients should be instructed to abstain from sexual intercourse until therapy is completed and until they and their sex partners no longer have symptom

HAEMOPHILUS

- Grows both **aerobically** (requires two factors: hemin (X factor) and nicotinamide adenine dinucleotide (V factor) and **anaerobically as coccobacilli**
- Among a-f serotypes, **Type b and nontypable strains** are the most relevant strains clinically
- Spread by **airborne droplets or by direct contact** with secretions or fomites
- Colonization with nontypable is a dynamic process and are primarily **mucosal pathogens (EARS, BRONCHUS)**
- Hib strains cause systemic disease by invasion and **hematogenous** spread from the respiratory tract
- **DISEASES BY Hib;** *Meningitis, Epiglottitis (later age child), Cellulitis, Pneumonia*
- Nontypable *H. influenzae* is **the most common bacterial cause of exacerbations of COPD, Other diseases:** otitis media, puerperal sepsis, sinusitis, etc
- Recovery of the organism in **culture** is most reliable diagnostic method
- Initial therapy for meningitis due to Hib should consist of a cephalosporin
- **Hib conjugate vaccine** to all child and **chemoprophylaxis** with rifampin

- A **probable diagnosis of Chancroid** can be made when the following criteria are met:

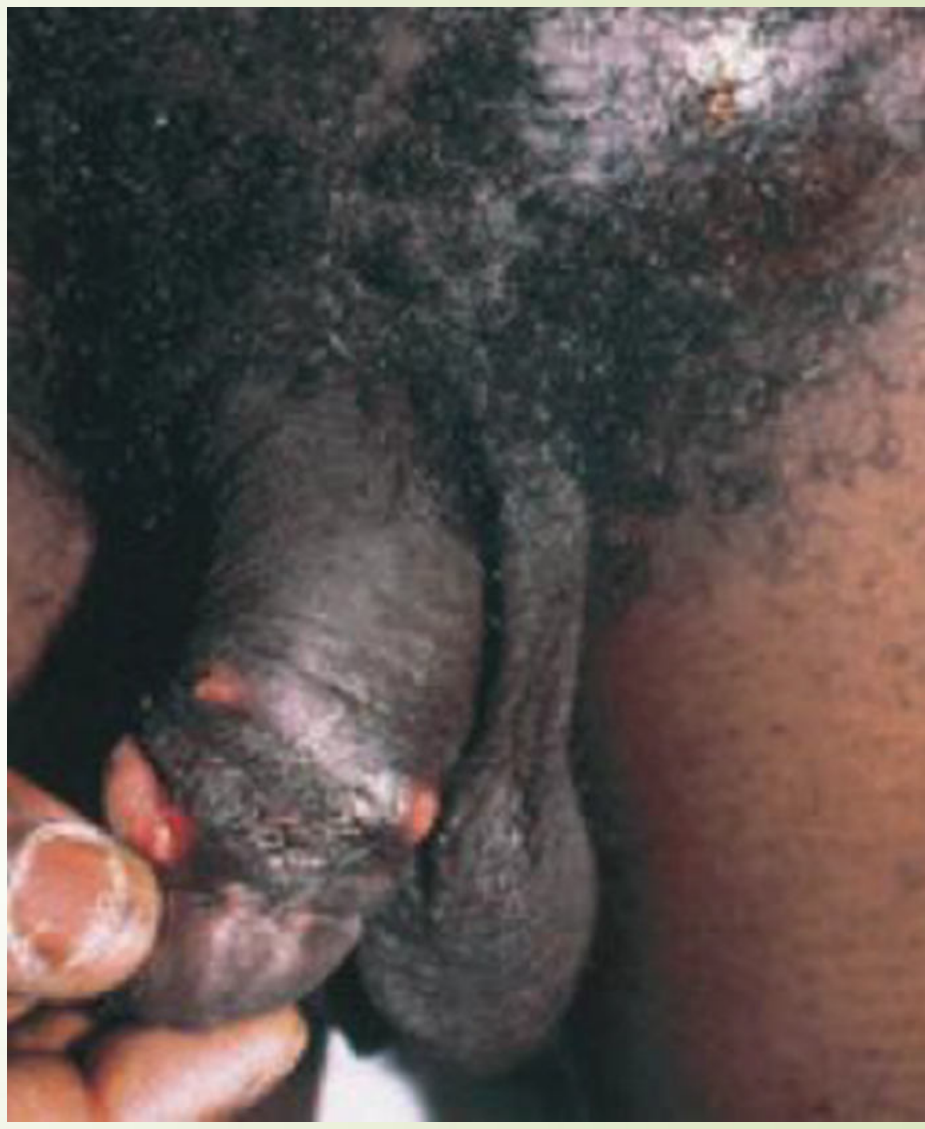
(1) one or more painful genital ulcers;

(2) no evidence of *Treponema pallidum* infection;

(3) a typical clinical presentation for chancroid;

(4) a negative test for herpes simplex virus in the ulcer exudate

- Sexually transmitted disease characterized by **genital ulceration and inguinal adenitis**
- Associated **with HIV infection**
- **Treated with** single dose of azithromycin or ceftriaxone



HACEK organisms

- Group of fastidious, slow-growing, gram negative bacteria whose growth **requires an atmosphere of carbon dioxide**
- Species belonging to this group include several *Haemophilus* species, *Aggregatibacter* (formerly *Actinobacillus*) species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*
- HACEK bacteria **normally reside in the oral cavity**
- The clinical course of HACEK **endocarditis** tends to be subacute, particularly with *Aggregatibacter* or *Cardiobacterium*, However, *K. kingae* endocarditis may have a more aggressive presentation

LEGIONELLA (IC pathogen)

- ***Legionellosis*** refers to the two clinical syndromes caused by bacteria of the genus *Legionella*
  - *Pontiac fever (IP- 24-48h)* is an acute epidemic, febrile, self-limited illness that has been **serologically** linked to *Legionella* species, whereas
  - *Legionnaires' disease (IP- 2-10d)* is the designation for pneumonia caused by these species
- Species *L. pneumophila* causes 80–90% of human infections
- Natural habitats for *L. pneumophila* are **aquatic bodies**
- Factors **known to enhance colonization** include warm temperatures (25°–42°C) and the presence of scale and sediment; The presence of **symbiotic microorganism**s, including algae, ameba, ciliated protozoa, and other water-dwelling bacteria, promotes the growth of *Legionella*
- Multiple **modes of transmission** including **aspiration**, aerosolization, and direct instillation into the lungs during respiratory tract manipulations
- **Incidence depends** on the degree of contamination of the aquatic reservoir, the immune status of the persons exposed to water from that reservoir, the intensity of exposure, and the availability of specialized laboratory tests

TABLE 184-1 CLINICAL CLUES SUGGESTIVE OF LEGIONNAIRES' DISEASE

Diarrhea
High fever (>40°C; >104°F)
Numerous neutrophils but no organisms revealed by Gram's staining of respiratory secretions
Hyponatremia (serum sodium level <131 mg/dL)
Failure to respond to β-lactam drugs (penicillins or cephalosporins) and aminoglycoside antibiotics
Occurrence of illness in an environment in which the potable water supply is known to be contaminated with *Legionella*
Onset of symptoms within 10 days after discharge from the hospital (hospital-acquired legionellosis manifesting after discharge or transfer)

Differential diagnosis of atypical pneumonia should be considered

- *Legionella* cultures - **best**
- *Legionella* urinary antigen test – **highly specific (**for *L. pneumophila* serogroup 1)
- Direct fluorescent antibody (DFA) staining
- Antibody testing

- **Macrolides (especially azithromycin) and the respiratory quinolones** are now the antibiotics of choice for 10-14 days
- For critically ill patients, the authors use **combination regimens** of azithromycin, a quinolone, and/or rifampin
- **Routine environmental culture of hospital water supplies (**from cold-water taps, hotwater taps, the hot-water recirculating line, and water-storage tanks) for *Legionella* is recommended as an approach to the prevention of hospital-acquired Legionnaires' disease
- **Copper-silver ionization** is a reliable method for eradication

BORDETELLA (IC pathogen)

- **Pertussis** ("whooping cough"/ "the 100-day cough")is an acute infection of the respiratory tract caused by *Bordetella pertussis*
- **Cyclical outbreaks every 3–5 years,** can affect people of all ages, However, Severe morbidity and high mortality rates, are **restricted almost entirely to infants**
- *B. pertussis* infects only humans, *B. parapertussis* causes a milder illness; and rarely by *B. holmesii*, and *B. bronchiseptica*
- Most important virulence factor is ***pertussis toxin***, others are *filamentous hemagglutinin*, *pertactin*, *Fimbriae,* tracheal cytotoxin, adenylate cyclase toxin, dermonecrotic toxin, and LOS
- Pathogenesis is unknown after attachment of the organism to the ciliated epithelial cells of the **nasopharynx**
- **IP-** 7–10 DAYS

- Prolonged coughing illness with clinical manifestations that **vary by age**
- ***Catarrhal phase, 1-2WKS,*** *(*indistinguishable from the common Cold)evolves into the ***paroxysmal phase, 2-4WKS,*** (the cough becomes more frequent and spasmodic with repetitive bursts of 5–10 coughs, often within a single expiration, episode may be terminated by an audible **whoop**, which occurs upon rapid inspiration against a closed glottis at the end of a paroxysm), Later **into *convalescent phase***, **4-12WKS,** (gradual resolution of coughing episodes)
- **Vomiting with cough is the best predictor** of pertussis as the cause of prolonged cough in adults
- Pneumothorax, severe weight loss, inguinal hernia, rib fracture, carotid artery aneurysm, and cough syncope – **COMPLICATIONS**
- **Laboratory confirmation (**Culture of nasopharyngeal secretions) should be attempted in all cases, nowadays being replaced by PCR
- **Lymphocytosis** (an absolute lymphocyte count of >1–10,000/cc) is common
- **Pertussis should be suspected** when any patient has
  - a cough that does not improve within 14 days,
  - a paroxysmal cough of any duration,
  - a cough followed by vomiting (adolescents and adults), or
  - any respiratory symptoms after contact with a laboratory-confirmed case of pertussis
- **Purpose of antibiotic therapy** for pertussis is to eradicate the infecting bacteria from the nasopharynx; therapy does not substantially alter the clinical course unless given early in the catarrhal phase; *Macrolide antibiotics are the drugs of choice*

BRUCELLA (*undulant fever, IC organism)*)

- Brucellosis is a bacterial zoonosis transmitted directly or indirectly to humans from infected animals, predominantly domesticated ruminants and swine
- ***B. melitensis, B. abortus, B. suis, B. canis, B. neotomae, B. ceti,* and *B. pinnipedialis***
- Brucellosis may be acquired by ingestion, inhalation, or mucosal or percutaneous exposure
- **IP-** 1 week to several months
- Pathogenesis is unknown; The organism is a **"stealth" pathogen** who avoids triggering innate immune responses and that permit survival within monocytic cells
- Brucellosis almost invariably causes fever; **differs from other fevers**,
  - (1) Left untreated, the fever of brucellosis shows an **undulating pattern** that persists for weeks before the commencement of an afebrile period that may be followed by relapse
  - (2) The fever of brucellosis is associated with musculoskeletal symptoms and signs in about one-half of all patients

TABLE 194e-1 RADIOLOGY OF THE SPINE: DIFFERENTIATION OF BRUCELLOSIS FROM TUBERCULOSIS

	Brucellosis	Tuberculosis
Site	Lumbar and others	Dorsolumbar
Vertebrae	Multiple or contiguous	Contiguous
Diskitis	Late	Early
Body	Intact until late	Morphology lost early
Canal compression	Rare	Common
Epiphysitis	Anterosuperior (Pom's sign)	General: upper and lower disk regions, central, sub-periosteal
Osteophyte	Anterolateral (parrot beak)	Unusual
Deformity	Wedging uncommon	Anterior wedge, gibbus
Recovery	Sclerosis, whole-body	Variable
Paravertebral abscess	Small, well-localized	Common and discrete loss, transverse process
Psoas abscess	Rare	More likely

- **Often fits one of three patterns:**
  - febrile illness that resembles typhoid but is less severe;
  - fever and acute monoarthritis, typically of the hip or knee, in a young child;
  - long-lasting fever, misery, and low-back or hip pain in an older man
- **Diagnosis** must be based on a history of potential exposure, a presentation consistent with the disease, and supporting laboratory findings (Culture, PCR, serology)
- **Gold standard for the treatment** of brucellosis in adults is IM streptomycin (0.75–1 g daily for 14–**21** days) together with doxycycline(100 mg twice daily for **6** weeks)
- **Chemoprophylaxis**; the administration of rifampin plus doxycycline for 3 weeks after a low-risk exposure (e.g., an unspecified laboratory accident) and for 6 weeks after a major exposure to aerosol or injected material
- **Relapse occurs in up to 30%** of poorly compliant patients

FRANCISELLA

- **Tularemia** is a zoonosis caused by *Francisella tularensis*
- Humans of **any age, sex, or race** are universally susceptible to this systemic infection
- It is primarily a disease of wild animals and **persists** in contaminated environments, ectoparasites, and animal carriers
- Human infection is **incidental** and usually results from interaction with biting or blood-sucking insects, contact with wild or domestic animals, ingestion of contaminated water or food, or inhalation of infective aerosols
- Characterized by an **ulcerative lesion at the site of inoculation**, with regional lymphadenopathy and lymphadenitis
- Systemic manifestations, including pneumonia, typhoidal tularemia, meningitis, and fever without localizing findings may occur
- The diagnosis of tularemia is most frequently **confirmed by agglutination testing**
- Only **aminoglycosides, tetracyclines, chloramphenicol, and rifampin** are currently approved (7–10 days)

TABLE 195-2 CLINICAL SYNDROMES OF TULAREMIA

Syndrome	Rate of Occurrence, %	
	Children	Adults
Ulceroglandular	45	51
Glandular	25	12
Pulmonary (pneumonia)	14	18
Oropharyngeal	4	—
Oculoglandular	2	—
Typhoidal	2	12
Unclassified	6	11

YERSINIA

- Plague is a systemic zoonosis caused by *Yersinia pestis*
- It predominantly affects small rodents and is **usually transmitted** to humans by an arthropod vector (the flea), Less often, contact with animal tissues or respiratory droplets
- Patients can present with the **bubonic, septicemic, or pneumonic** form of the disease
- Although there is concern among the general **public about epidemic spread** of plague by the respiratory route, this is not the usual route of plague transmission
- Initial presumptive diagnosis followed by reference laboratory confirmation
- 10-day course of antimicrobial therapy is recommended
- Postexposure antimicrobial prophylaxis lasting 7 days is recommended following household, hospital, or other close contact with persons with untreated pneumonic plague. (***Close contact* is defined as contact with a patient at <2** m.)
- ***Yersiniosis*** is a zoonotic infection with an enteropathogenic *Yersinia* species, usually *Yersinia enterocolitica* or *Y. pseudotuberculosis*

TABLE 196-1 WORLD HEALTH ORGANIZATION CASE DEFINITIONS OF PLAGUE

Suspected case	Compatible clinical presentation ***and*** Consistent epidemiologic features, such as exposure to infected animals or humans and/or evidence of fleabites and/or residence in or travel to a known endemic focus within the previous 10 days
Presumptive case	Meeting the definition of a suspected case ***plus*** **Putative new or reemerging focus:** ≥2 of the following tests positive • Microscopy: gram-negative coccobacilli in material from bubo, blood, or sputum; bipolar appearance on Wayson or Wright-Giemsa staining • F1 antigen detected in bubo aspirate, blood, or sputum • A single anti-F1 serology without evidence of previous *Y. pestis* infection or immunization • Polymerase chain reaction (PCR) detection of *Y. pestis* in bubo aspirate, blood, or sputum **Known endemic focus:** ≥1 of the following tests positive • Microscopic evidence of gram-negative or bipolar (Wayson, Wright-Giemsa) coccobacilli from bubo, blood, or sputum sample • A single anti-F1 serology without evidence of previous plague infection or immunization • F1 antigen detected in bubo aspirate, blood, or sputum
Confirmed case	Meeting the definition of a suspected case ***plus*** • Identification of an isolate from a clinical sample as *Y. pestis* (colonial morphology and 2 of the 4 following tests positive: phage lysis of cultures at 20–25°C and 37°C; F1 antigen detection; PCR; *Y. pestis* biochemical profile) ***or*** • A fourfold rise in anti-F1 antibody titer in paired serum samples ***or*** • In endemic areas when no other [illegible] can be performed, a positive rapid diagnostic test with immunochromatography to detect F1 antigen

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TABLE 196-2 GUIDELINES FOR THE TREATMENT OF PLAGUE

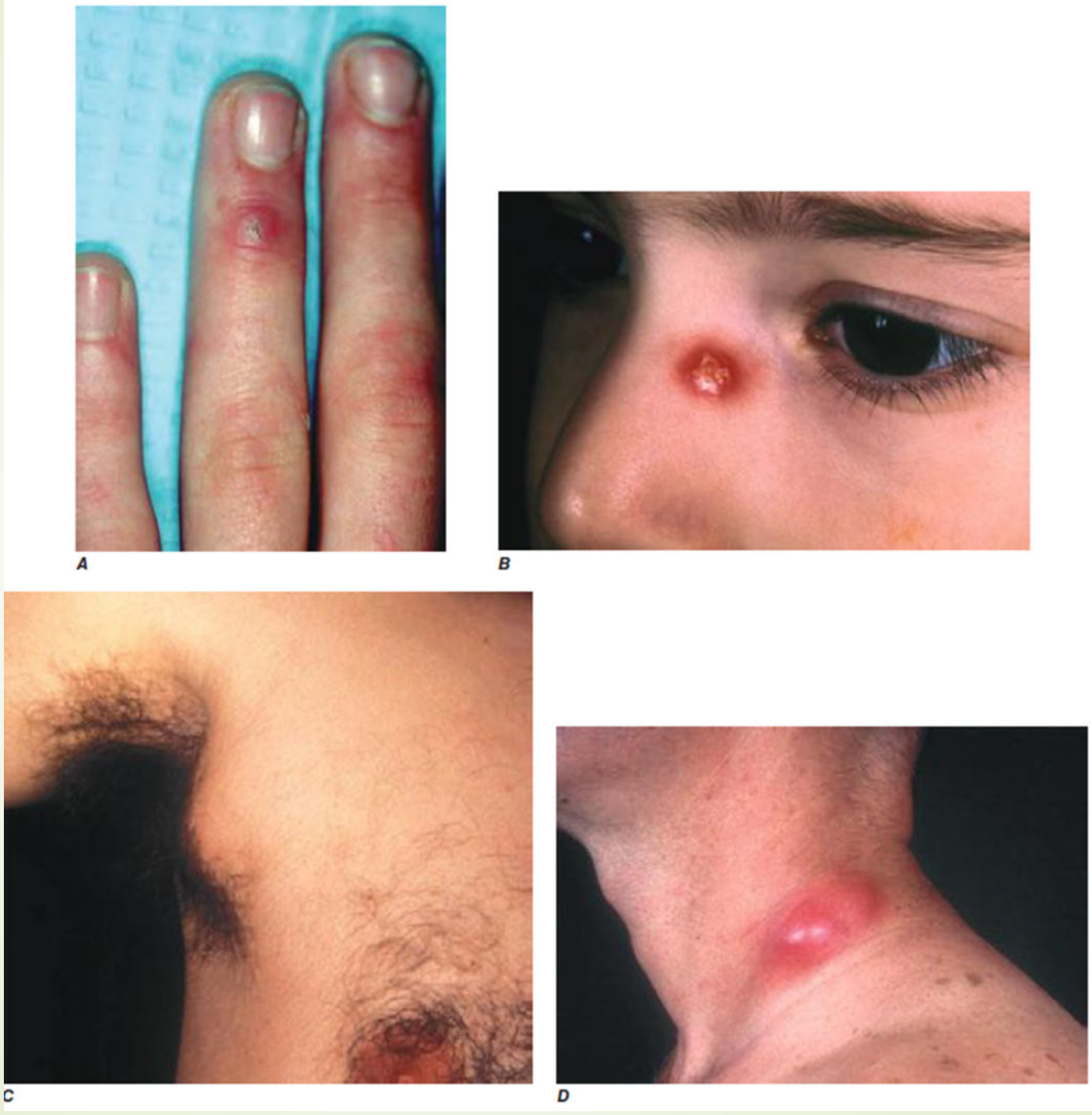
Drug	Daily Dose	Interval, h	Route
Gentamicin			
Adult	5 mg/kg[a]	24	IM/IV
	3–5 mg/kg	8 (2 mg/kg loading dose followed by 1.7 mg/kg tid, reduced)	IM/IV
Child	5 mg/kg[a]	24	IM/IV
	7.5 mg/kg	8 (2.5 mg/kg tid)	IM/IV
Streptomycin			
Adult	2 g	12	IM
Child	30 mg/kg	12	IM
Levofloxacin			
Adult and child >50 kg	500 mg	24	PO/IV
Child <50 kg and ≥6 months	8 mg/kg (not to exceed 250 mg/dose)	12	PO/IV
Doxycycline			
Adult	200 mg	12 or 24	PO/IV
Child >8 y	4.4. mg/kg	12 or 24	PO/IV
Tetracycline			
Adult	2 g	6	PO/IV
Child >8 y	25–50 mg/kg	6	PO/IV
Chloramphenicol			
Adult	50 mg/kg	6	PO/IV
Child >1 y	50 mg/kg	6	PO/IV

TABLE 196-3 GUIDELINES FOR PLAGUE PROPHYLAXIS

Drug	Daily Dose	Interval, h	Route
Doxycycline			
Adult	200 mg	12 or 24	PO
Child ≥8 y	If ≥45 kg, give adult dosage; if <45 kg, give 2.2 mg/kg PO bid (maximum, 200 mg)	12	PO
Tetracycline			
Adult	1–2 g	6 or 12	PO
Child ≥8 y	25–50 mg/kg	6 or 12	PO
Levofloxacin			
Adult and child >50 kg	500 mg	24	PO
Child <50 kg and ≥6 months	8 mg/kg (not to exceed 250 mg/dose)	12	PO
Ciprofloxacin			
Adult	1 g	12	PO
Child	40 mg/kg	12	PO
Trimethoprim-Sulfamethoxazole			
Adult	320 mg	12	PO
Child	40 mg/kg	12	PO

BARTONELLA

- Clinical presentation generally depends on both theinfecting *Bartonella* species and the immune status of the infected individual
- Usually a self-limited illness, **cat-scratch disease (CSD)** has two general clinical presentations;
  - *Typical* CSD, the more common, is characterized by subacute regional lymphadenopathy;
  - *atypical* CSD is the collective designation for numerous extranodal manifestations involving various organs.
- ***B. henselae* is the principal etiologic agent** of CSD
- A history of cat contact, a primary inoculation lesion, and regional lymphadenopathy are **highly suggestive** of CSD
- **Azithromycin** may be given, but limited role
- Suppurative nodes should be drained by large-bore needle aspiration and not by incision and drainage in order to avoid chronic draining tracts



Thank you