

Microbiology

“That within one linear centimeter of your lower colon there lives and works more bacteria (about 100 billion) than all humans who have ever been born. Yet many people continue to assert that it is we who are in charge of the world.”

—Neil deGrasse Tyson

“What lies behind us and what lies ahead of us are tiny matters compared to what lies within us.”

—Henry S. Haskins

“Wise and humane management of the patient is the best safeguard against infection.”

—Florence Nightingale

“I sing and play the guitar, and I’m a walking, talking bacterial infection.”

—Kurt Cobain

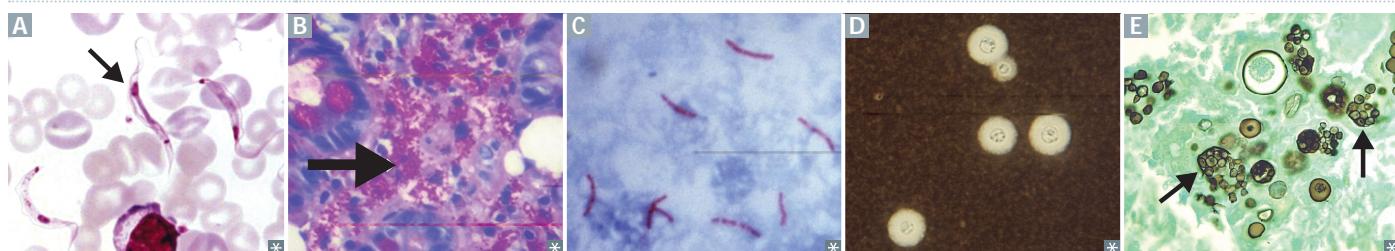
► Basic Bacteriology	122
► Clinical Bacteriology	132
► Mycology	149
► Parasitology	152
► Virology	159
► Systems	175
► Antimicrobials	184

Microbiology questions on the Step 1 exam often require two (or more) steps: Given a certain clinical presentation, you will first need to identify the most likely causative organism, and you will then need to provide an answer regarding some features of that organism or relevant antimicrobial agents. For example, a description of a child with fever and a petechial rash will be followed by a question that reads, “From what site does the responsible organism usually enter the blood?”

This section therefore presents organisms in two major ways: in individual microbial “profiles” and in the context of the systems they infect and the clinical presentations they produce. You should become familiar with both formats. When reviewing the systems approach, remind yourself of the features of each microbe by returning to the individual profiles. Also be sure to memorize the laboratory characteristics that allow you to identify microbes.

Stains

Gram stain	First-line lab test in bacterial identification. Bacteria with thick peptidoglycan layer retain crystal violet dye (gram \oplus); bacteria with thin peptidoglycan layer turn red or pink (gram \ominus) with counterstain. These bugs do not Gram stain well (These Little Microbes May Unfortunately Lack Real Color But Are Everywhere):	
	Treponema, Leptospira	Too thin to be visualized
	Mycobacteria	Cell wall has high lipid content
	Mycoplasma, Ureaplasma	No cell wall
	Legionella, Rickettsia, Chlamydia, Bartonella, Anaplasma, Ehrlichia	Primarily intracellular; also, <i>Chlamydia</i> lack classic peptidoglycan because of \downarrow muramic acid
Giemsa stain	<i>Chlamydia, Rickettsia, Trypanosomes A, Borrelia, Helicobacter pylori, Plasmodium</i>	Clumsy Rick Tripped on a Borrowed Helicopter Plastered in Gems
Periodic acid-Schi stain	Stains glycogen , mucopolysaccharides; used to diagnose Whipple disease (<i>Tropheryma whipplei</i> B)	PaSs the sugar
Ziehl-Neelsen stain (carbol fuchsin)	Acid-fast bacteria (eg, <i>Mycobacteria</i> C, <i>Nocardia</i> ; stains mycolic acid in cell wall); protozoa (eg, <i>Cryptosporidium</i> oocysts)	Auramine-rhodamine stain is more often used for screening (inexpensive, more sensitive)
India ink stain	<i>Cryptococcus neoformans</i> D; mucicarmine can also be used to stain thick polysaccharide capsule red	
Silver stain	<i>Helicobacter pylori, Legionella, Bartonella henselae</i> , and fungi (eg, <i>Coccidioides</i> E, <i>Pneumocystis jirovecii, Aspergillus fumigatus</i>)	HeLiCoPters Are silver
Fluorescent antibody stain	Used to identify many bacteria, viruses, <i>Pneumocystis jirovecii</i> , <i>Giardia</i> , and <i>Cryptosporidium</i>	Example is FTA-ABS for syphilis



Special culture requirements

BUG	MEDIA USED FOR ISOLATION	MEDIA CONTENTS/OTHER
<i>Hin uenzae</i>	Chocolate agar	Factors V (NAD^+) and X (hematin)
<i>N gonorrhoeae</i> , <i>N meningitidis</i>	Thayer-Martin agar	Selectively favors growth of <i>Neisseria</i> by inhibiting growth of gram \oplus organisms with vancomycin, gram \ominus organisms except <i>Neisseria</i> with trimethoprim and colistin, and fungi with nystatin
<i>B pertussis</i>	Bordet-Gengou agar (Bordet for <i>Bordetella</i>) Regan-Lowe medium	Very typically cultures <i>Neisseria</i> Potato extract Charcoal, blood, and antibiotic
<i>C diphtheriae</i>	Tellurite agar, Löffler medium	
<i>M tuberculosis</i>	Löwenstein-Jensen medium, Middlebrook medium, rapid automated broth cultures	
<i>M pneumoniae</i>	Eaton agar	Requires cholesterol
Lactose-fermenting enterics	MacConkey agar	Fermentation produces acid, causing colonies to turn pink
<i>E coli</i>	Eosin-methylene blue (EMB) agar	Colonies with green metallic sheen
<i>Brucella</i> , <i>Francisella</i> , <i>Legionella</i> , <i>Pasteurella</i>	Charcoal yeast extract agar buffered with cysteine and iron	The Ella siblings, Bruce, Francis, a legionnaire, and a pasteur (pastor), built the Sistine (cysteine) chapel out of charcoal and iron
Fungi	Sabouraud agar	“Sab’s a fun guy!”

Anaerobes

Examples include **Clostridium**, **B**

Catalase-positive organisms



Catalase degrades H₂O₂ into H₂O and bubbles of O₂ **A** before it can be converted to microbicidal products by the enzyme myeloperoxidase. People with chronic granulomatous disease (NADPH oxidase deficiency) have recurrent infections with certain catalase \oplus organisms.

Big Catalase \oplus organisms include *Bordetella pertussis*, *Helicobacter pylori*, *Burkholderia cepacia*, *Nocardia*, *Pseudomonas*, *Listeria*, *Aspergillus*, *Candida*, *E. coli*, *Serratia*, *Staphylococci*. **Cats Have BeeN to PLACESS.**

Pigment-producing bacteria

Actinomyces israelii—**yellow** “sulfur” **granules**, which are composed of filaments of bacteria

Israel has yellow sand

S. aureus—**golden** yellow pigment

Aureus (Latin) = **gold**

P. aeruginosa—blue-**green** pigment (pyocyanin and pyoverdin)

Aerugula is **green**

Serratia marcescens—**red** pigment

Think **red Sriracha** hot sauce

In vivo bio Im-producing bacteria

S. epidermidis

Catheter and prosthetic device infections

Viridans streptococci (*S. mutans*, *S. sanguinis*)

Dental plaques, infective endocarditis

P. aeruginosa

Respiratory tree colonization in patients with cystic fibrosis, ventilator-associated pneumonia
Contact lens–associated keratitis

Nontypeable (unencapsulated) *H. influenzae*

Otitis media

Spore-forming bacteria

Some gram \oplus bacteria can form spores when nutrients are limited. Spores lack metabolic activity and are highly resistant to heat and chemicals. Core contains dipicolinic acid (responsible for heat resistance). Must autoclave to kill spores (as is done to surgical equipment) by steaming at 121°C for 15 minutes. Hydrogen peroxide and iodine-based agents are also sporcidal.

Examples: *B anthracis* (anthrax), *B cereus* (food poisoning), *C botulinum* (botulism), *C difficile* (pseudomembranous colitis), *C perfringens* (gas gangrene), *C tetani* (tetanus).

Autoclave to kill **Bacillus** and **Clostridium (ABC)**.

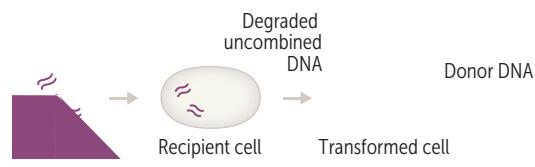
Bacterial virulence factors

Capsular polysaccharide	Highly charged, hydrophilic structure. Acts as barrier to phagocytosis and complement-mediated lysis. Major determinant of virulence.
Protein A	Binds Fc region of IgG. Prevents opsonization and phagocytosis. Expressed by <i>S aureus</i> .
IgA protease	Enzyme that cleaves IgA, allowing bacteria to adhere to and colonize mucous membranes. Secreted by <i>S pneumoniae</i> , <i>H influenzae</i> type b, and <i>Neisseria (SHiN)</i> .
M protein	Helps prevent phagocytosis. Expressed by group A streptococci. Sequence homology with human cardiac myosin (molecular mimicry); possibly underlies the autoimmune response seen in acute rheumatic fever.

Bacterial genetics

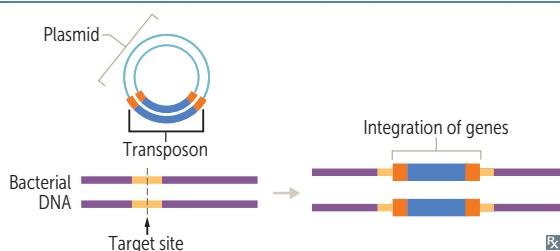
Transformation

Competent bacteria can bind and import short pieces of environmental naked bacterial chromosomal DNA (from bacterial cell lysis). The transfer and expression of newly transferred genes is called transformation. A feature of many bacteria, especially *S. pneumoniae*, *H. influenzae* type b, and *Neisseria (SHiN)*. Adding deoxyribonuclease degrades naked DNA, preventing transformation.

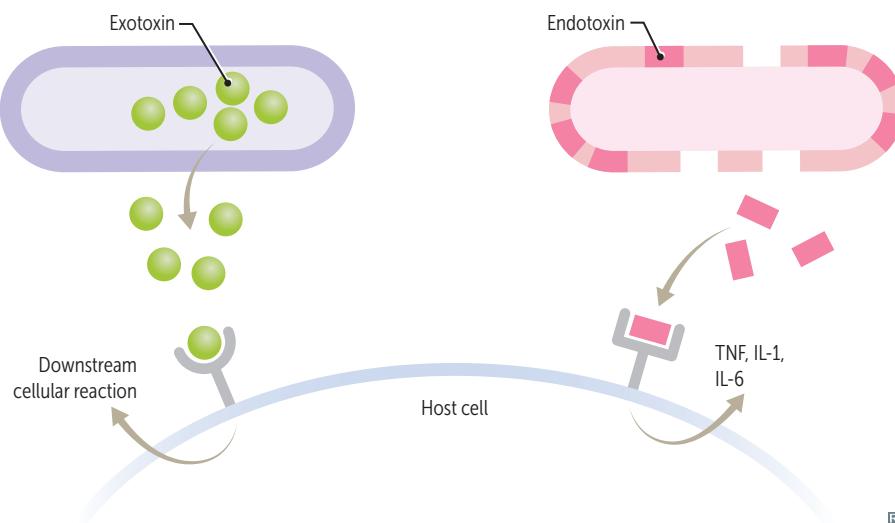


Bacterial genetics (continued)**Transposition**

A “jumping” process involving a transposon (specialized segment of DNA), which can copy and excise itself and then insert into the same DNA molecule or an unrelated DNA (eg, plasmid or chromosome). Critical in creating plasmids with multiple drug resistance and transfer across species lines (eg, Tn1546 with *vanA* from *Enterococcus* to *S aureus*).

**Main features of exotoxins and endotoxins**

	Exotoxins	Endotoxins
SOURCE	Certain species of gram \oplus and gram \ominus bacteria	Outer cell membrane of most gram \ominus bacteria
SECRETED FROM CELL	Yes	No
CHEMISTRY	Polypeptide	Lipid A component of LPS (structural part of bacteria; released when lysed)
LOCATION OF GENES	Plasmid or bacteriophage	Bacterial chromosome
TOXICITY	High (fatal dose on the order of 1 μg)	Low (fatal dose on the order of hundreds of micrograms)
CLINICAL EFFECTS	Various effects (see following pages)	Fever, shock (hypotension), DIC
MODE OF ACTION	Various modes (see following pages)	Induces TNF, IL-1, and IL-6
ANTIGENICITY	Induces high-titer antibodies called antitoxins	Poorly antigenic
VACCINES	Toxoids used as vaccines	No toxoids formed and no vaccine available
HEAT STABILITY	Destroyed rapidly at 60°C (except staphylococcal enterotoxin and <i>E coli</i> heat-stable toxin)	Stable at 100°C for 1 hr
TYPICAL DISEASES	Tetanus, botulism, diphtheria, cholera	Meningococcemia; sepsis by gram \ominus rods



Bacteria with exotoxins

BACTERIA	TOXIN	MECHANISM	MANIFESTATION
Inhibit protein synthesis			
<i>Corynebacterium diphtheriae</i>	Diphtheria toxin ^a	Inactivate elongation factor (EF-2) through ADP-ribosylation	Pharyngitis with pseudomembranes in throat and severe lymphadenopathy (bull neck), myocarditis
<i>Pseudomonas aeruginosa</i>	Exotoxin A ^a		Host cell death
<i>Shigella</i> spp	Shiga toxin ^a	Inactivate 60S ribosome by removing adenine from rRNA	Damages GI mucosa → dysentery
<i>Enterohemorrhagic E. coli</i>			Enhances cytokine release → hemolytic-uremic syndrome (HUS; prototypically in EHEC serotype O157:H7) Unlike <i>Shigella</i> , EHEC does not invade host cells
Increase fluid secretion			
<i>Enterotoxigenic E. coli</i>	Heat-labile toxin (LT) ^a	Overactivates adenylate cyclase (\uparrow cAMP) → \uparrow Cl ⁻ secretion in gut and H ₂ O efflux	Watery diarrhea: “ labil e in the Air (Adenylate cyclase), stable on the Ground (Guanylate cyclase)”
	Heat-stable toxin (ST)	Overactivates guanylate cyclase (\uparrow cGMP) → \downarrow resorption of NaCl and H ₂ O in gut	Bacteria that \uparrow cAMP include Cholera, Anthracis, Pertussis, <i>E. coli</i> ; “ Increase cAMP with CAPE
<i>Bacillus anthracis</i>	Anthrax toxin ^a	Mimics adenylate cyclase (\uparrow cAMP)	Likely responsible for characteristic edematous borders of black eschar in cutaneous anthrax
<i>Vibrio cholerae</i>	Cholera toxin ^a	Overactivates adenylate cyclase (\uparrow cAMP) by permanently activating G _s	Voluminous “rice-water” diarrhea
Inhibit phagocytic ability			
<i>Bordetella pertussis</i>	Pertussis toxin ^a	Activates adenylate cyclase (\uparrow cAMP) by inactivating inhibitory subunit (G _i)	Whooping cough —child coughs on expiration and “whoops” on inspiration; can cause “100-day cough” in adults; associated with posttussive emesis
Inhibit release of neurotransmitter			
<i>Clostridium tetani</i>	Tetanospasmin ^a	Both are proteases that cleave SNARE (soluble NSF attachment protein receptor), a set of proteins required for neurotransmitter release via vesicular fusion	Toxin prevents release of inhibitory (GABA and glycine) neurotransmitters from Renshaw cells in spinal cord → spastic paralysis, risus sardonicus, trismus (lockjaw), opisthotonus
<i>Clostridium botulinum</i>	Botulinum toxin ^a		Infant botulism—caused by ingestion of spores (eg, from soil, raw honey). Toxin produced in vivo Foodborne botulism—caused by ingestion of preformed toxin (eg, from canned foods)

^aAn AB toxin (also called two-component toxin [or three for anthrax]) with **B** enabling **Binding** and triggering uptake (endocytosis) of the **Active A** component. The A components are usually ADP ribosyltransferases; others have enzymatic activities as listed in chart.

Bacteria with exotoxins (continued)

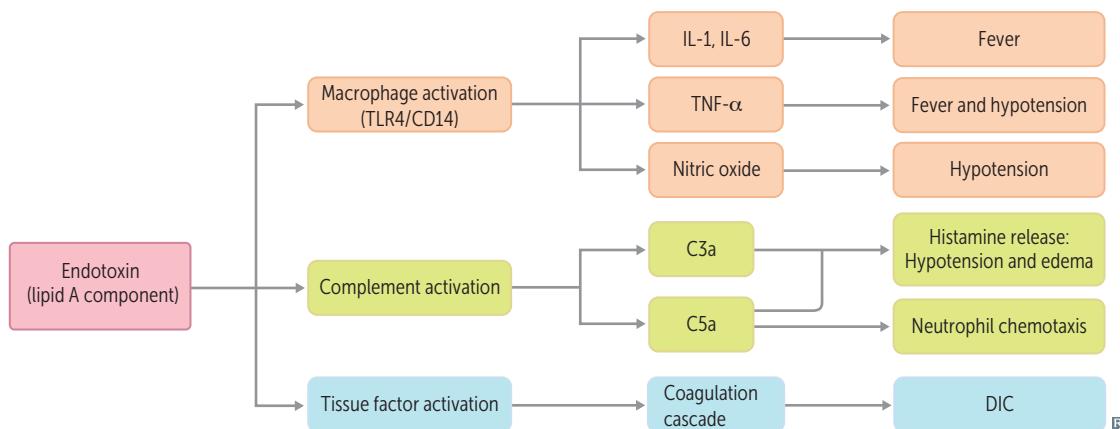
BACTERIA	TOXIN	MECHANISM	MANIFESTATION
Lyse cell membranes			
<i>Clostridium perfringens</i>	Alpha toxin	Phospholipase (lecithinase) that degrades tissue and cell membranes	Degradation of phospholipids → myonecrosis (“gas gangrene”) and hemolysis (“double zone” of hemolysis on blood agar)
<i>Streptococcus pyogenes</i>	Streptolysin O	Protein that degrades cell membrane	Lyses RBCs; contributes to β-hemolysis; host antibodies against toxin (ASO) used to diagnose rheumatic fever (do not confuse with immune complexes of poststreptococcal glomerulonephritis)
Superantigens causing shock			
<i>Staphylococcus aureus</i>	Toxic shock syndrome toxin (TSST-1)	Cross-links β region of TCR to MHC class II on APCs outside of the antigen binding site → overwhelming release of IL-1, IL-2, IFN-γ, and TNF-α → shock	Toxic shock syndrome: fever, rash, shock; other toxins cause scalded skin syndrome (exfoliative toxin) and food poisoning (heat-stable enterotoxin)
<i>Streptococcus pyogenes</i>	Erythrogenic exotoxin A		Toxic shock-like syndrome: fever, rash, shock; scarlet fever

Endotoxin

LPS found in outer membrane of gram \ominus bacteria (both cocci and rods). Composed of O-antigen + core polysaccharide + lipid A (the toxic component). *Neisseria* have lipooligosaccharide. Released upon cell lysis or by living cells by blebs detaching from outer surface membrane (vs exotoxin, which is actively secreted). Three main effects: macrophage activation (TLR4/CD14), complement activation, and tissue factor activation.

ENDOTOXINS:

Edema
Nitric oxide
DIC/Death
Outer membrane
TNF- α
O-antigen + core polysaccharide + lipid A
extremely heat stable
IL-1 and IL-6
Neutrophil chemotaxis
Shock



Hemolytic bacteria **α -hemolytic bacteria**

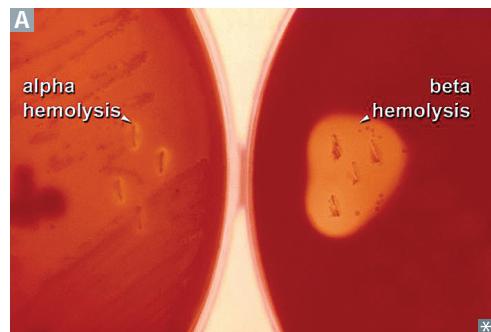
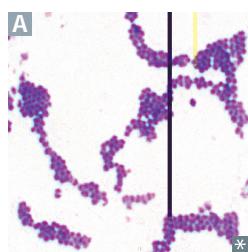
Partial oxidation of hemoglobin → greenish or brownish color without clearing around growth on blood agar **A**.

Include *Streptococcus pneumoniae* and viridans streptococci.

 β -hemolytic bacteria

Complete lysis of RBCs → pale/clear area surrounding colony on blood agar **A**.

Include *Staphylococcus aureus*, *Streptococcus pyogenes* (group A strep), *Streptococcus agalactiae* (group B strep), *Listeria monocytogenes*.

***Staphylococcus aureus***

Gram \oplus , β -hemolytic, catalase \oplus , coagulase \oplus cocci in clusters **A**. Protein A (virulence factor) binds Fc-IgG, inhibiting complement activation and phagocytosis. Commonly colonizes the nares, ears, axilla, and groin.

Causes:

- Inflammatory disease—skin infections, organ abscesses, pneumonia (often after influenza virus infection), infective endocarditis, septic arthritis, and osteomyelitis.
- Toxin-mediated disease—toxic shock syndrome (TSST-1), scalded skin syndrome (exfoliative toxin), rapid-onset food poisoning (enterotoxins).

MRSA (methicillin-resistant *S. aureus*)—important cause of serious healthcare-associated and community-acquired infections. Resistance due to altered penicillin-binding proteins (conferred by *mecA* gene). Some strains release Panton-Valentine leukocidin (PVL), which kills leukocytes and causes tissue necrosis.

TSST-1 is a superantigen that binds to MHC II and T-cell receptor, resulting in polyclonal T-cell activation and cytokine release.

Staphylococcal toxic shock syndrome (TSS)—fever, vomiting, diarrhea, rash, desquamation, shock, end-organ failure. TSS results in \uparrow AST, \uparrow ALT, \uparrow bilirubin. Associated with prolonged use of vaginal tampons or nasal packing.

Compare with *Streptococcus pyogenes* TSS (a toxic shock-like syndrome associated with painful skin infection).

S. aureus food poisoning due to ingestion of preformed toxin \rightarrow short incubation period (2–6 hr) followed by nonbloody diarrhea and emesis. Enterotoxin is heat stable \rightarrow not destroyed by cooking.

S. aureus makes coagulase and toxins. Forms fibrin clot around itself \rightarrow abscess.

Staphylococcus epidermidis

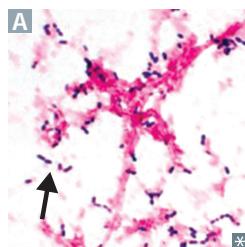
Gram \oplus , catalase \oplus , coagulase \ominus , urease \oplus cocci in clusters. Novobiocin sensitive. Does not ferment mannitol (vs *S. aureus*).

Normal microbiota of skin; contaminates blood cultures.

Infects prosthetic devices (eg, hip implant, heart valve) and IV catheters by producing adherent biofilms.

Staphylococcus saprophyticus

Gram \oplus , catalase \oplus , coagulase \ominus , urease \oplus cocci in clusters. Novobiocin resistant. Normal microbiota of female genital tract and perineum. Second most common cause of uncomplicated UTI in young females (most common is *E coli*).

Streptococcus pneumoniae

Gram \oplus , α -hemolytic, lancet-shaped diplococci **A**.

Encapsulated. IgA protease. Optochin sensitive and bile soluble.

Most commonly causes **MOPS**:

- **Meningitis**
- **Otitis media** (in children)
- **Pneumonia**
- **Sinusitis**

Pneumococcal pneumonia is associated with “rusty” sputum.

Patients with anatomic or functional hyposplenia or asplenia are predisposed to infection.

No virulence without capsule.

Pneumococcal vaccines are available in both conjugate (PCV13, PCV15, PCV20) and polysaccharide (PPSV23) formulations.

Viridans group streptococci

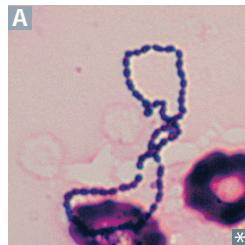
Gram \oplus , α -hemolytic cocci. Optochin resistant and bile insoluble. Normal microbiota of the oropharynx.

Streptococcus mutans and *S mitis* cause dental caries.

S sanguinis makes dextrans that bind to fibrin-platelet aggregates on damaged **heart** valves, causing infective endocarditis.

Viridans group strep live in the mouth, because they are not afraid **of-the-chin** (**op-to-chin** resistant).

Sanguinis = blood. Think, “there is lots of **blood** in the **heart**” (infective endocarditis).

Streptococcus pyogenes (group A streptococci)

Gram \oplus cocci in chains **A**. Group A strep cause:

- Pyogenic—pharyngitis, cellulitis, impetigo (“honey-crusted” lesions), erysipelas
- Toxigenic—scarlet fever, toxic shock-like syndrome, necrotizing fasciitis
- Immunologic—rheumatic fever, glomerulonephritis

Bacitracin sensitive, β -hemolytic, pyrrolidonyl arylamidase (PYR) \oplus . Hyaluronic acid capsule and M protein inhibit phagocytosis. Antibodies to M protein enhance host defenses. Structurally similar to host proteins (ie, myosin); can lead to autoimmunity (ie, carditis seen in acute rheumatic fever).

Diagnose strep pharyngitis via throat swab, which can be tested with an antigen detection assay (rapid, in-office results) or cultured on blood agar (results in 48 hours).

“**Ph**”yogenes **ph**aryngitis can result in rheumatic “**p**fever” and glomerulone**ph**ritis.

Strains causing impetigo can induce glomerulonephritis.

Key virulence factors include DNase, erythrogenic exotoxin, streptokinase, streptolysin O. ASO titer or anti-DNase B antibodies indicate recent *S pyogenes* infection.

Scarlet fever—blanching, sandpaperlike body rash, strawberry tongue, and circumoral pallor in the setting of group A streptococcal pharyngitis (erythrogenic toxin \oplus).

Streptococcus agalactiae (group B streptococci)

Gram \oplus cocci, bacitracin resistant, β -hemolytic, colonizes vagina; causes pneumonia, meningitis, and sepsis, mainly in **babies**. Polysaccharide capsule confers virulence. Produces CAMP factor, which enlarges the area of hemolysis formed by *S aureus*. (Note: CAMP stands for the authors of the test, not cyclic AMP.) Hippurate test \oplus . PYR \ominus . Screen pregnant patients at 35–37 weeks of gestation with rectal and vaginal swabs. Patients with \oplus culture receive intrapartum penicillin/ampicillin prophylaxis.

Streptococcus gallolyticus

Formerly *S bovis*. Gram \oplus cocci, colonizes the gut. Can cause bacteremia and infective endocarditis. Patients with *S gallolyticus* endocarditis have \uparrow incidence of colon cancer.

Bovis in the **blood** = **cancer** in the **colon**.

Enterococci

Gram \oplus cocci. Enterococci (*E faecalis* and *E faecium*) are normal colonic microbiota that are penicillin G resistant and cause UTI, biliary tract infections, and infective endocarditis (following GI/GU procedures). Catalase \ominus , PYR \oplus , typically nonhemolytic. VRE (vancomycin-resistant enterococci) are an important cause of healthcare-associated infection.

Enterococci are more resilient than streptococci, can grow in 6.5% NaCl and bile (lab test).

Enter = intestine, *faecalis* = feces, *strepto* = twisted (chains), *coccus* = berry.

Bacillus anthracis

Gram \oplus , spore-forming rod that produces anthrax toxin, exotoxins consisting of protective antigen, lethal factor (inhibits MAP kinase \rightarrow macrophage apoptosis), and edema factor (acts as adenylyl cyclase \rightarrow \uparrow intracellular cAMP, upsetting homeostasis \rightarrow edema, necrosis). Has a polypeptide capsule (poly D-glutamate). Colonies show a halo of projections, sometimes called “medusa head” appearance.

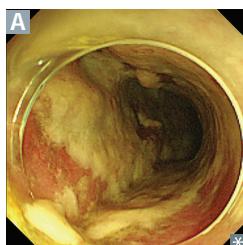
Cutaneous anthrax—painless papule surrounded by vesicles \rightarrow ulcer with black eschar **A** (painless, necrotic) \rightarrow uncommonly progresses to bacteremia and death.

Pulmonary anthrax—inhalation of spores, most commonly from contaminated animals or animal products, although also a potential bioweapon \rightarrow fulminant symptoms that rapidly progress to fever, pulmonary hemorrhage, mediastinitis (CXR may show widened mediastinum), and shock. Also called woolsorter’s disease. Prophylaxis with ciprofloxacin or doxycycline when exposed.

Both cutaneous and pulmonary anthrax may be complicated by hemorrhagic meningitis.

Bacillus cereus

Gram \oplus rod. Causes food poisoning. Spores survive cooking rice (reheated rice syndrome). Keeping rice warm results in germination of spores and enterotoxin formation. Emetic type causes nausea and vomiting within 1–5 hours. Caused by cereulide, a preformed toxin. Diarrheal type causes watery, nonbloody diarrhea and GI pain within 8–18 hours. Management: supportive care (antibiotics are ineffective against toxins).

Clostridioides difficile

Produces toxins A and B, which damage enterocytes. Both toxins lead to watery diarrhea \rightarrow pseudomembranous colitis **A**. Often 2^o to antibiotic use, especially clindamycin, ampicillin, cephalosporins, fluoroquinolones; associated with PPIs.

Fulminant infection: toxic megacolon, ileus, shock.

Difficile causes **diarrhea**.

Diagnosed by PCR or antigen detection of one or both toxins in stool.

Treatment: oral vancomycin or fidaxomicin.

For recurrent cases, consider repeating prior regimen or fecal microbiota transplant.

Clostridia

Gram \oplus , spore-forming, obligate anaerobic rods. Tetanus toxin and botulinum toxin are proteases that cleave SNARE proteins involved in neurotransmission.

Clostridium tetani

Pathogen is noninvasive and remains localized to wound site. Produces tetanospasmin, an exotoxin causing tetanus. **Tetanospasmin** spreads by retrograde axonal transport to CNS and blocks release of GABA and glycine from Renshaw cells in spinal cord.

Causes **spastic** paralysis, trismus (lockjaw), risus sardonicus (raised eyebrows and open grin), opisthotonus (spasms of spinal extensors).

Tetanus is **tetanic** paralysis.

Prevent with tetanus vaccine. Treat with antitoxin $+/-$ vaccine booster, antibiotics, diazepam (for muscle spasms), and wound debridement.

Clostridium botulinum

Produces a heat-labile toxin that inhibits ACh release at the neuromuscular junction, causing botulism. In babies, ingestion of spores (eg, in honey) leads to disease (**floppy** baby syndrome). In adults, disease is caused by ingestion of preformed toxin (eg, in canned food).

Symptoms of botulism (the **5 D's**): **diplopia**, **dysarthria**, **dysphagia**, **dyspnea**, **descending flaccid** paralysis. Does not present with sensory deficits.

Botulinum is from bad **bottles** of food, juice, and honey.

Treatment: human botulinum immunoglobulin. Local botulinum toxin A (Botox) injections used to treat focal dystonia, hyperhidrosis, muscle spasms, and cosmetic reduction of facial wrinkles.

Clostridium perfringens

Produces α -toxin (lecithinase, a phospholipase) that can cause myonecrosis (gas gangrene **A**; presents as soft tissue crepitus) and hemolysis. If heavily spore-contaminated food is cooked but left standing too long at $< 60^{\circ}\text{C}$, spores germinate \rightarrow vegetative bacteria \rightarrow heat-labile enterotoxin \rightarrow late-onset (10-12 hours) food poisoning symptoms, resolution in 24 hours.

Perfringens perforates a gangrenous leg.

Spontaneous gas gangrene (via hematogenous seeding; associated with colonic malignancy) is most commonly caused by ***Clostridium septicum***.

Corynebacterium diphtheriae

Gram \oplus rods occurring in angular arrangements; transmitted via respiratory droplets. Causes diphtheria via exotoxin encoded by β -prophage. Potent exotoxin inhibits protein synthesis via ADP-ribosylation of EF-2, leading to possible necrosis in pharynx, cardiac, and CNS tissue. Symptoms include pseudomembranous pharyngitis (grayish-white membrane **A**) with lymphadenopathy (“bull’s neck” appearance). Toxin dissemination may cause myocarditis, arrhythmias, neuropathies. Lab diagnosis based on gram \oplus rods with metachromatic (blue and red) granules and \oplus Elek test for toxin. Toxoid vaccine prevents diphtheria.

Coryne = club shaped (metachromatic granules on Löffler media).

Black colonies on cystine-tellurite agar.

ABCDEFG:

ADP-ribosylation

β -prophage

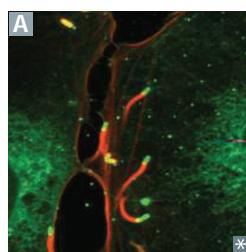
Corynebacterium

Diphtheriae

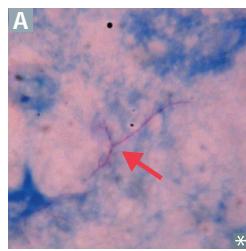
Elongation Factor 2

Granules

Treatment: diphtheria antitoxin $+/-$ erythromycin or penicillin.

Listeria monocytogenes

Gram \oplus , facultative intracellular rod; acquired by ingestion of unpasteurized dairy products and cold deli meats, transplacental transmission, by vaginal transmission during birth. Grows well at refrigeration temperatures (“cold enrichment”). Forms “rocket tails” (red in **A**) via actin polymerization that allow intracellular movement and cell-to-cell spread across cell membranes, thereby avoiding antibody. Listeriolysin generates pores in phagosomes, allowing its escape into cytoplasm. Characteristic tumbling motility in broth. Can cause amnionitis, septicemia, and spontaneous abortion in pregnant patients; granulomatosis infantiseptica; meningitis in immunocompromised patients, neonates, and older adults; mild, self-limited gastroenteritis in healthy individuals. Treatment: ampicillin.

Nocardia* vs *Actinomyces

Both are gram \oplus and form long, branching filaments resembling fungi.

Nocardia

Aerobe

Acid fast (weak) **A**

Found in soil

Causes pulmonary infections in immunocompromised (can mimic TB but with \ominus PPD); cutaneous infections after trauma in immunocompetent; can spread to CNS \rightarrow cerebral abscess

Treat with sulfonamides (TMP-SMX)

Treatment is a **SNAP**: Sulfonamides—*Nocardia*; *Actinomyces*—Penicillin

Actinomyces

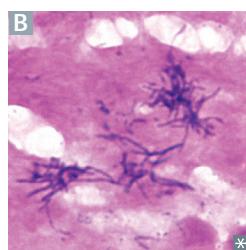
Anaerobe

Not acid fast **B**

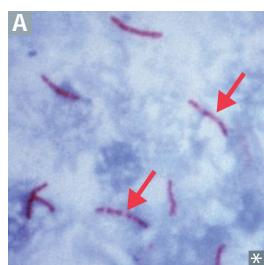
Normal oral, reproductive, and GI microbiota

Causes oral/facial abscesses that drain through sinus tracts; often associated with dental caries/extraction and other maxillofacial trauma; forms yellow “sulfur granules”; can also cause PID with IUDs

Treat with penicillin



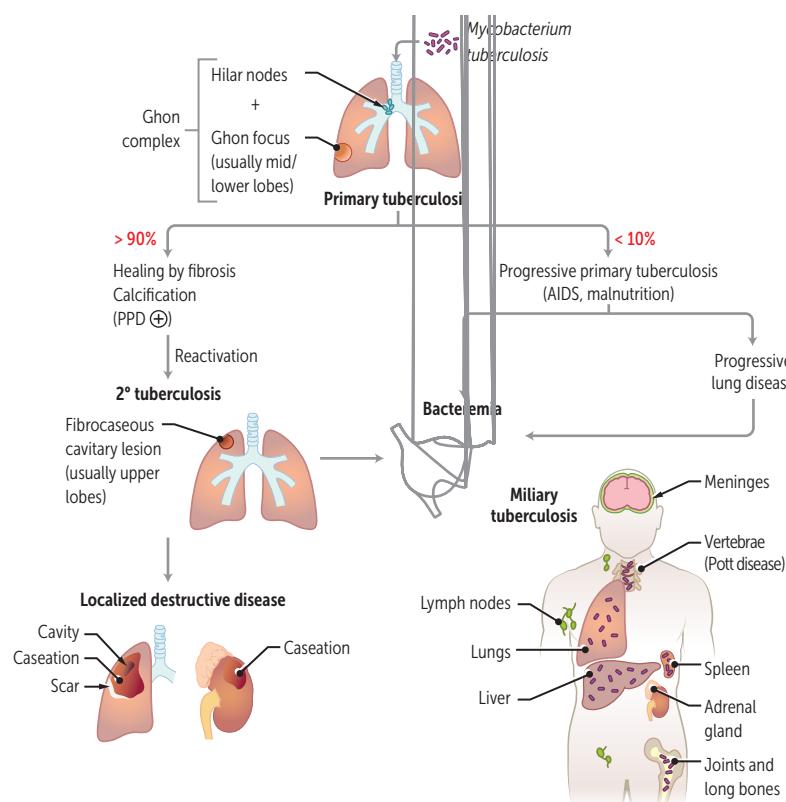
Mycobacteria



Acid-fast rods (pink rods, arrows in **A**).
Mycobacterium tuberculosis (TB, often resistant to multiple drugs).
M avium-intracellulare (causes disseminated, non-TB disease in AIDS; often resistant to multiple drugs).
M scrofulaceum (cervical lymphadenitis in children).
M marinum (hand infection in aquarium handlers).

TB symptoms include fever, night sweats, weight loss, cough (nonproductive or productive), hemoptysis. Cord factor creates a “serpentine cord” appearance in virulent *M tuberculosis* strains; activates macrophages (promoting granuloma formation) and induces release of TNF- α . Sulfatides (surface glycolipids) inhibit phagolysosomal fusion.

Tuberculosis



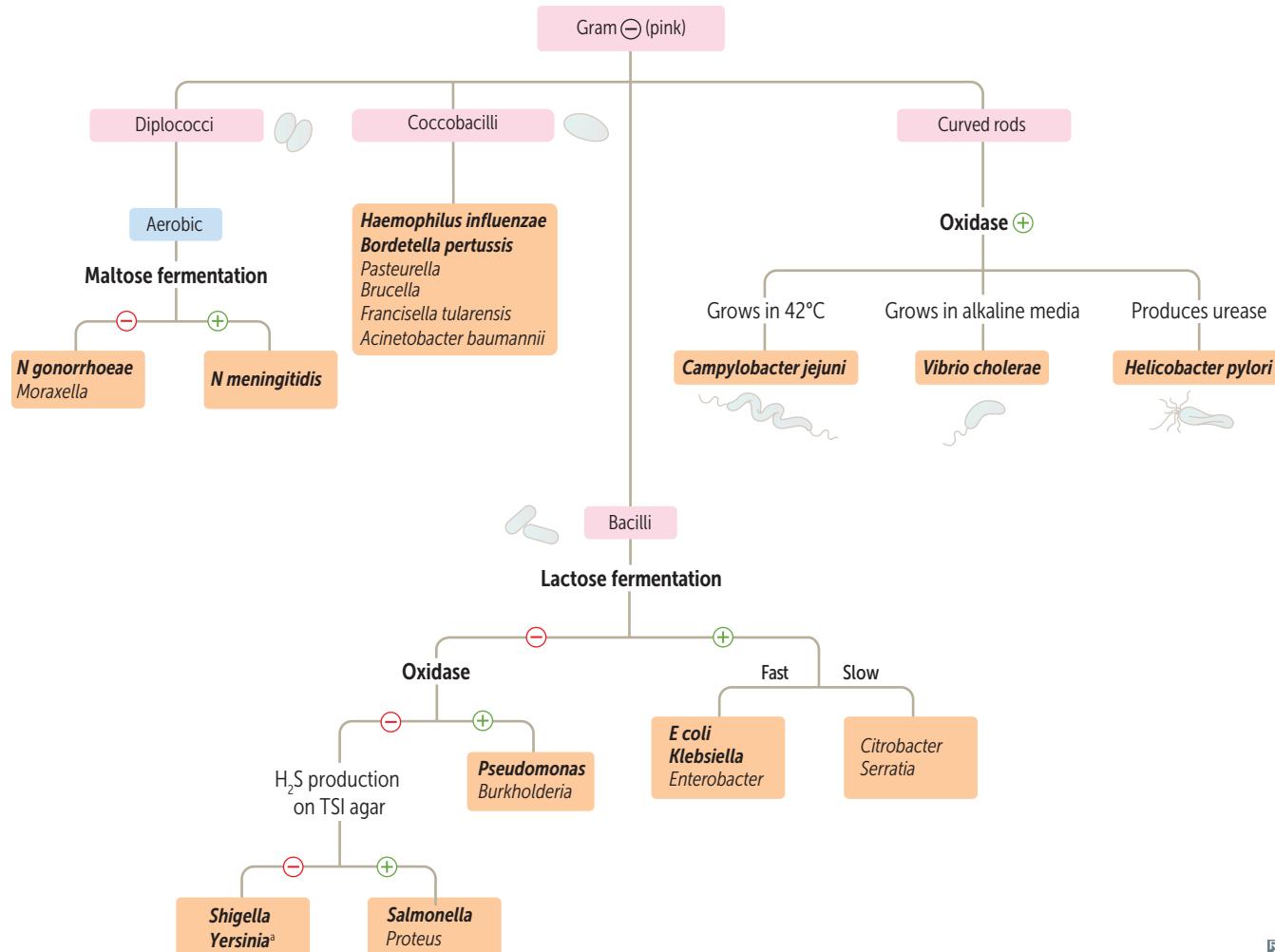
Leprosy

Also called Hansen disease. Caused by *Mycobacterium leprae*, an acid-fast bacillus that likes cool temperatures (infects skin and superficial nerves—“glove and stocking” loss of sensation) and cannot be grown in vitro. Diagnosed via skin biopsy or tissue PCR. Reservoir in United States: armadillos.

Leprosy has 2 forms (many cases fall temporarily between two extremes):

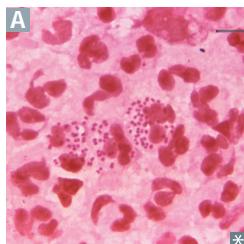
- **Lepromatous**—presents diffusely over the skin, with **leonine** (**lionlike**) facies **A**, and is communicable (high bacterial load); characterized by low cell-mediated immunity with a largely Th2 response. Lepromatous form can be **lethal**.
- **Tuberculoid**—limited to a few hypoesthetic, hairless skin plaques **B**; characterized by high cell-mediated immunity with a largely Th1-type response and low bacterial load.

Treatment: dapsone and rifampin for tuberculoid form; clofazimine is added for lepromatous form.

Gram-negative lab algorithm

Important **tests** are in **bold**. Important **pathogens** are in **bold italics**.

^aPleomorphic rod/coccobacillus

Neisseria

Gram \ominus diplococci. Metabolize glucose and produce IgA proteases. Contain lipooligosaccharides (LOS) with strong endotoxin activity.

N gonorrhoeae is often intracellular (within neutrophils) **A**.

Acid production: **meningococci**—maltose and glucose; **gonococci**—glucose.

Gonococci

No polysaccharide capsule

No maltose acid detection

No vaccine due to antigenic variation of pilus proteins

Sexually or perinatally transmitted

Meningococci

Polysaccharide capsule

Maltose acid detection

Vaccine (type B vaccine available for at-risk individuals)

Transmitted via respiratory and oral secretions. More common among individuals in close quarters (eg, army barracks, college dorms)

Causes gonorrhea, septic arthritis, neonatal conjunctivitis (2–5 days after birth), pelvic inflammatory disease (PID), and Fitz-Hugh-Curtis syndrome

Causes meningococcemia with petechial hemorrhages and gangrene of toes **B**, meningitis, Waterhouse-Friderichsen syndrome (acute hemorrhagic adrenal insufficiency)

Diagnosed with NAAT

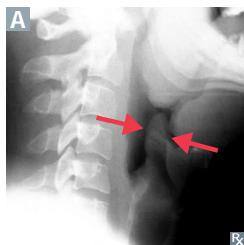
Diagnosed via culture-based tests or PCR

Condoms \downarrow sexual transmission, erythromycin eye ointment prevents neonatal blindness

Rifampin, ciprofloxacin, or ceftriaxone prophylaxis in close contacts

Treatment: single dose IM ceftriaxone; if chlamydial coinfection not excluded by molecular testing, add doxycycline

Treatment: ceftriaxone or penicillin G

Haemophilus in uenzeae

Small gram \ominus (coccobacillary) rod. Transmitted through respiratory droplets. Nontypeable (unencapsulated) strains are the most common cause of mucosal infections (otitis media, conjunctivitis, bronchitis) as well as invasive infections since the vaccine for capsular type b was introduced. Produces IgA protease. Culture on chocolate agar, which contains factors V (NAD^+) and X (hematin) for growth; can also be grown with *S aureus*, which provides factor V via RBC hemolysis.

Haemophilus causes **epiglottitis** (endoscopic appearance can be “cherry red” in children; “thumb sign” on lateral neck x-ray **A**), **meningitis**, **otitis media**, and **pneumonia**.

Vaccine contains type b capsular polysaccharide (polyribosylribitol phosphate) conjugated to diphtheria toxoid or other protein. Given between 2 and 18 months of age.

Does not cause the flu (influenza virus does).

Treatment: amoxicillin +/- clavulanate for mucosal infections; ceftriaxone for meningitis; rifampin prophylaxis for close contacts.

***Burkholderia cepacia* complex**

Aerobic, catalase \oplus , gram \ominus rod. Causes pneumonia in and can be transmitted between patients with cystic fibrosis. Often multidrug resistant. Infection is a relative contraindication to undergoing lung transplant due to its association with poor outcomes.

Bordetella pertussis

Gram \ominus , aerobic coccobacillus. Virulence factors include pertussis toxin (disables G_i), adenylate cyclase toxin (\uparrow cAMP), and tracheal cytotoxin. Three clinical stages:

- **Catarrhal**—low-grade fevers, **coryza**.
- **Paroxysmal**—paroxysms of intense cough followed by inspiratory “whoop” (“whooping cough”), posttussive vomiting.
- **Convalescent**—gradual recovery of chronic cough.

Prevented by Tdap, DTaP vaccines.

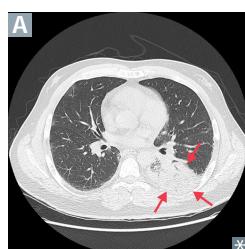
Produces lymphocytosis (unlike most acute bacterial infections).

Treatment: macrolides; if allergic use TMP-SMX.

Brucella

Gram \ominus , aerobic coccobacillus. Transmitted via ingestion of contaminated animal products (eg, unpasteurized milk). Survives in macrophages in the reticuloendothelial system. Can form non-caseating granulomas. Typically presents with undulant fever, night sweats, and arthralgia.

Treatment: doxycycline + rifampin or streptomycin.

Legionella pneumophila

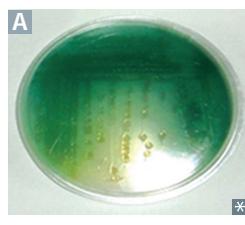
Gram \ominus rod. Gram stains poorly—use **silver** stain. Grow on **charcoal** yeast extract medium with **iron** and **cysteine**. Detected by presence of antigen in urine. Labs may show hyponatremia. Aerosol transmission from environmental water source habitat (eg, air conditioning systems, hot water tanks). Outbreaks associated with cruise ships, nursing homes. No person-to-person transmission.

Treatment: macrolide or quinolone.

Think of a French **legionnaire** (soldier) with his **silver** helmet, sitting around a campfire (**charcoal**) with his **iron** dagger—he is missing his **sister** (cysteine).

Legionnaires' disease—severe pneumonia (often unilateral and lobar **A**), fever, GI and CNS symptoms. Risk factors include older age, tobacco smoking, chronic lung disease.

Pontiac fever—mild flulike symptoms.

Pseudomonas aeruginosa

Aeruginosa—aerobic; motile, catalase \oplus , gram \ominus rod. Non-lactose fermenting. Oxidase \oplus .

Frequently found in water. Increased virulence in acidic environments. Has a grapelike odor.

PSEUDOMONAS is associated with:

Pneumonia, Sepsis, Ecthyma gangrenosum, UTIs, Diabetes, Osteomyelitis, Mucoid polysaccharide capsule, Otitis externa (swimmer's ear), Nosocomial (healthcare-associated) infections (eg, catheters, equipment), Addiction (injection drug use), Skin infections (eg, hot tub folliculitis, wound infection in burn victims).

Mucoid polysaccharide capsule may contribute to chronic pneumonia in patients with cystic fibrosis due to biofilm formation.

Produces **PEEP**: Phospholipase C (degrades cell membranes); **Endotoxin** (fever, shock); **Exotoxin A** (inactivates EF-2); **Pigments**: pyoverdine and pyocyanin (blue-green pigment **A**; also generates ROS).



Corneal ulcers/keratitis in contact lens wearers/ minor eye trauma.

Ecthyma gangrenosum—rapidly progressive, necrotic cutaneous lesion **B** caused by *Pseudomonas* bacteremia. Typically seen in immunocompromised patients.

Treatments:

- Antipseudomonal penicillins in combination with β -lactamase inhibitor (eg, piperacillin-tazobactam)
- 3rd- and 4th-generation cephalosporins (eg, ceftazidime, cefepime)
- Monobactams
- Fluoroquinolones
- Carbapenems

Despite antipseudomonal activity, aminoglycoside monotherapy is avoided due to poor performance in acidic environments.

Salmonella vs Shigella Both *Salmonella* and *Shigella* are gram \ominus rods, non-lactose fermenters, oxidase \ominus , and can invade the GI tract via M cells of Peyer patches.

	<i>Salmonella typhi</i> (ty-Vi)	<i>Salmonella</i> spp. except <i>S typhi</i>	<i>Shigella</i>
RESERVOIRS	Humans only	Humans and animals	Humans only
SPREAD	Hematogenous spread	Hematogenous spread	Cell to cell; no hematogenous spread
H ₂ S PRODUCTION	Yes	Yes	No
FLAGELLA	Yes (salmon swim)	Yes (salmon swim)	No
VIRULENCE FACTORS	Endotoxin; Vi capsule (pronounce “ty Vi ”)	Endotoxin	Endotoxin; Shiga toxin (enterotoxin)
INFECTIOUS DOSE (ID ₅₀)	High—large inoculum required; acid-labile (inactivated by gastric acids)	High	Low—very small inoculum required; acid stable (resistant to gastric acids)
EFFECT OF ANTIBIOTICS ON FECAL EXCRETION	Prolongs duration	Prolongs duration	Shortens duration (shortens <i>Shigella</i>)
IMMUNE RESPONSE	Primarily monocytes	PMNs in disseminated disease	Primarily PMN infiltration
GI MANIFESTATIONS	Constipation, followed by diarrhea	Diarrhea (possibly bloody)	Crampy abdominal pain → tenesmus, bloody mucoid stools (bacillary dysentery)
VACCINE	Oral vaccine contains live attenuated <i>S typhi</i> IM vaccine contains Vi capsular polysaccharide	No vaccine	No vaccine
UNIQUE PROPERTIES	Causes typhoid fever (salmon-colored truncal macular rash, abdominal pain, fever [pulse-temperature dissociation]; later GI ulceration and hemorrhage); treat with ceftriaxone or fluoroquinolone Carrier state with gallbladder colonization	Poultry, eggs, pets, and turtles are common sources Treatment is supportive; antibiotics are not indicated in immunocompetent individuals	4 F's: f ingers, f lies, f ood, f eces In order of decreasing severity (less toxin produced): <i>S dysenteriae</i> , <i>S flexneri</i> , <i>S boydii</i> , <i>S sonnei</i> Invasion of M cells is key to pathogenicity; infectious dose is low

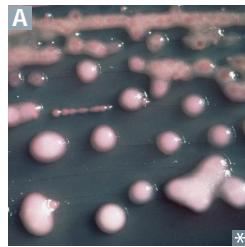
Yersinia enterocolitica Gram \ominus pleomorphic rod/coccobacillus with bipolar staining. Usually transmitted from pet feces (eg, cats, dogs), contaminated milk, or pork. Can cause acute bloody diarrhea, pseudoappendicitis (right lower abdominal pain due to mesenteric adenitis and/or terminal ileitis), reactive arthritis in adults.

Lactose-fermenting enteric bacteria Fermentation of **lactose** → pink colonies on Mac**Con**key agar. Examples include **Citrobacter**, **E coli**, **Enterobacter**, **Klebsiella**, **Serratia**. **McCowkey CEEKS** milk. EMB agar—lactose fermenters grow as purple/black colonies. *E coli* grows colonies with a green sheen.

Escherichia coli

Gram \ominus , indole \oplus rod. *E coli* virulence factors: fimbriae (ie, P pili)—cystitis and pyelonephritis; K capsule—pneumonia, neonatal meningitis; LPS endotoxin—septic shock.

STRAIN	TOXIN AND MECHANISM	PRESENTATION
Enteroinvasive <i>E coli</i>	Microbe invades intestinal mucosa and causes necrosis and inflammation.	EIEC is Invasive ; dysentery. Clinical manifestations similar to <i>Shigella</i> .
Enterotoxigenic <i>E coli</i>	Produces heat-labile and heat-stable enterotoxins. No inflammation or invasion.	ETEC ; Traveler's diarrhea (watery).
Enteropathogenic <i>E coli</i>	No toxin produced. Adheres to apical surface, flattens villi, prevents absorption.	Diarrhea, usually in children (think EPEC and Pediatrics).
Enterohemorrhagic <i>E coli</i>	O157:H7 is most common serotype in US. Often transmitted via undercooked meat, raw leafy vegetables. Shiga toxin causes hemolytic-uremic syndrome —triad of anemia, thrombocytopenia, and acute kidney injury due to microthrombi forming on damaged endothelium → mechanical hemolysis (with schistocytes on peripheral blood smear), platelet consumption, and ↓ renal blood flow.	Dysentery (toxin alone causes necrosis and inflammation). Does not ferment sorbitol (vs other <i>E coli</i>). EHEC associated with hemorrhage , hamburgers , hemolytic-uremic syndrome .

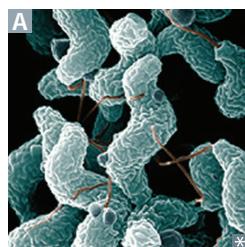
Klebsiella

Gram \ominus rod; intestinal microbiota that causes lobar pneumonia; more common in patients with heavy alcohol use or with impaired host defenses. Very mucoid colonies **A** caused by abundant polysaccharide capsules. Dark red “currant jelly” sputum (blood/mucus).

Also cause of healthcare-associated UTIs.
Associated with evolution of multidrug resistance (MDR).

ABCDE's of Klebsiella:

Aspiration pneumonia
Bscess in lungs and liver
Current jelly” sputum
Diabetes mellitus
EtOH overuse

Campylobacter jejuni

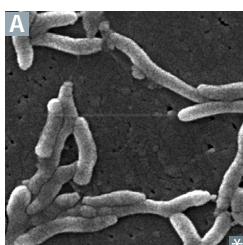
Gram \ominus , comma or S shaped (with polar flagella) **A**, oxidase \oplus , grows at **42°C** (“**Campylobacter** likes the **hot campfire**”).

Major cause of bloody diarrhea, especially in children. Fecal-oral transmission through person-to-person contact or via ingestion of undercooked contaminated poultry or meat, unpasteurized milk. Contact with infected animals (dogs, cats, pigs) is also a risk factor.
Common antecedent to Guillain-Barré syndrome and reactive arthritis.

Vibrio cholerae

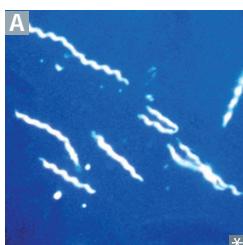
Gram \ominus , flagellated, comma shaped **A**, oxidase \oplus , grows in alkaline media. Endemic to developing countries. Produces profuse rice-water diarrhea via enterotoxin that permanently activates G_s, \uparrow cAMP. Sensitive to stomach acid (acid labile); requires large inoculum (high ID₅₀) unless host has \downarrow gastric acidity. Transmitted via ingestion of contaminated water or uncooked food (eg, raw shellfish). Treat promptly with oral rehydration solution.

Vibrio vulni cus—gram \ominus bacillus, usually found in marine environments. Causes severe wound infections or septicemia due to exposure to contaminated sea water. Presents as cellulitis that can progress to necrotizing fasciitis in high-risk patients, especially those with liver disease (eg, cirrhosis, hemochromatosis). Serious wound infection requires surgical debridement.

Helicobacter pylori

Curved, flagellated (motile), gram \ominus rod **A** that is **triple** \oplus : catalase \oplus , oxidase \oplus , and urease \oplus (can use urea breath test or fecal antigen test for diagnosis). Urease produces ammonia, creating an alkaline environment, which helps *H pylori* survive in acidic mucosa. Colonizes mainly antrum of stomach; causes gastritis and peptic ulcers (especially duodenal). Risk factor for peptic ulcer disease, gastric adenocarcinoma, and MALT lymphoma.

Most common initial treatment is **triple** therapy: **a**moxicillin (metronidazole if penicillin allergy) + **c**larithromycin + **p**roton pump inhibitor; **a**ntibiotics **cure** *Pylori*. Bismuth-based quadruple therapy if concerned about macrolide resistance.

Spirochetes

Spiral-shaped bacteria **A** with axial filaments.

Includes *Leptospira*, *Treponema*, and *Borrelia*. Only *Borrelia* can be visualized using aniline dyes (Wright or Giemsa stain) in light microscopy due to size. *Treponema* is visualized by dark-field microscopy or direct fluorescent antibody (DFA) microscopy.

Little Twirling **B**acteria.

Jarisch-Herxheimer reaction—flu-like symptoms (fever, chills, headache, myalgia) after antibiotics are started due to host response to sudden release of bacterial antigens. Usually occurs during treatment of spirochetal infections.

Lyme disease

Caused by *Borrelia burgdorferi*, which is transmitted by the *Ixodes* deer tick **A** (also vector for *Anaplasma* spp. and protozoa *Babesia*). Natural reservoir is the mouse; deer are essential to tick life cycle but do not harbor *Borrelia*.

Common in northeastern United States. Stage 1—early localized: erythema migrans (typical “bulls-eye” configuration **B** is pathognomonic but not always present), flu-like symptoms.

Stage 2—early disseminated: secondary lesions, carditis, AV block, facial nerve (Bell) palsy, migratory myalgias/transient arthritis.

Stage 3—late disseminated: encephalopathy, chronic arthritis, peripheral neuropathy.

A Key **Lyme** pie to the **FACE**:

Facial nerve palsy (typically bilateral)

Arthritis

Cardiac block

Erythema migrans

Treatment: doxycycline (1st line); amoxicillin (pregnant patients, children < 8 years old); ceftriaxone if IV therapy required



Leptospira interrogans Spirochete with hook-shaped ends found in water contaminated with animal urine.

Leptospirosis—flu-like symptoms, myalgias (classically of calves), jaundice, photophobia with conjunctival suffusion (erythema without exudate). Prevalent among surfers and in tropics (eg, Hawaii).

Weil disease (icterohemorrhagic leptospirosis)—severe form with jaundice and azotemia from liver and kidney dysfunction, fever, hemorrhage, and anemia.

Syphilis

Caused by spirochete *Treponema pallidum*. Treatment: penicillin G.

Primary syphilis

Localized disease presenting with **painless** chancre. Use fluorescent or dark-field microscopy to visualize treponemes in fluid from chancre **A**. VDRL \oplus in $\sim 80\%$.

Secondary syphilis

Disseminated disease with constitutional symptoms, maculopapular rash **B** (including palms **C** and soles), condylomata lata **D** (smooth, painless, wartlike white lesions on genitals), lymphadenopathy, patchy hair loss; also confirmable with dark-field microscopy.

Serologic testing: VDRL/RPR (nonspecific), confirm diagnosis with specific test (eg, FTA-ABS). Secondary syphilis = **systemic**. Latent syphilis (\oplus serology without symptoms) may follow.

Tertiary syphilis

Gummas **E** (chronic granulomas), aortitis (vasa vasorum destruction), neurosyphilis (tabes dorsalis, “general paresis”), Argyll Robertson pupil (constricts with accommodation but is not reactive to light).

Signs: broad-based ataxia, \oplus Romberg, Charcot joint, stroke without hypertension.

Congenital syphilis

Presents with facial abnormalities such as rhagades (linear scars at angle of mouth, black arrow in **F**), snuffles (nasal discharge, red arrow in **F**), saddle nose, notched (Hutchinson) teeth **G**, mulberry molars, and short maxilla; saber shins; CN VIII deafness.

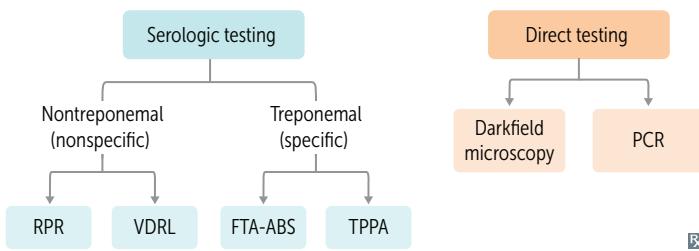
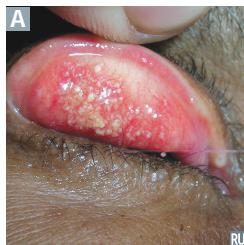
To prevent, treat patient early in pregnancy, as placental transmission typically occurs after first trimester.



Diagnosing syphilis

VDRL and RPR detects nonspecific antibody that reacts with beef cardiolipin. Quantitative, inexpensive, and widely available test for syphilis (sensitive but not specific). Nontreponemal tests (VDRL, RPR) revert to negative after treatment. Direct treponemal test results will remain positive.

False-Positive results on **VDRL** with:
Pregnancy
Viral infection (eg, EBV, hepatitis)
Drugs (eg, chlorpromazine, procainamide)
Rheumatic fever (rare)
Lupus (anticardiolipin antibody) and **L**eprsy

**Chlamydiae**

Chlamydiae cannot make their own ATP. They are obligate intracellular organisms that cause mucosal infections. 2 forms:

- **Elementary body** (small, dense) is “**enfectious**” and **enters** cell via **endocytosis**; transforms into **reticulate body**.
- **Reticulate body** **replicates** in cell by **fission**; **reorganizes** into elementary bodies.

Chlamydia trachomatis causes neonatal and follicular adult conjunctivitis **A**, nongonococcal urethritis, PID, and reactive arthritis.

Chlamydophila pneumoniae and *Chlamydophila psittaci* cause atypical pneumonia; transmitted by aerosol.

Chlamydial cell wall lacks classic peptidoglycan (due to reduced muramic acid), rendering β -lactam antibiotics ineffective.

Chlamys = cloak (intracellular).

C psittaci—has an avian reservoir (**parrots**), causes atypical **pneumonia**.

Lab diagnosis: PCR, NAAT. Cytoplasmic inclusions (reticulate bodies) seen on Giemsa or fluorescent antibody-stained smear.

Treatment: doxycycline, azithromycin (for pregnant patients). Add ceftriaxone for possible concomitant gonorrhea.

Chlamydia trachomatis* serotypes*Types A, B, and C**

Chronic infection, cause blindness due to follicular conjunctivitis in resource-limited areas.

ABC = **A**frica, **B**lindness, **C**hronic infection.

Types D–K

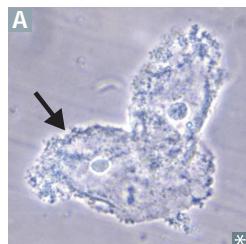
Urethritis/PID, ectopic pregnancy, neonatal pneumonia (staccato cough) with eosinophilia, neonatal conjunctivitis (1–2 weeks after birth).

D–K = everything else.

Neonatal disease can be acquired during vaginal birth if pregnant patient is infected.

Types L1, L2, and L3

Lymphogranuloma venereum—small, painless ulcers on genitals → swollen, painful inguinal lymph nodes that ulcerate (bubo). Treat with doxycycline.

Gardnerella vaginalis

A pleomorphic, gram-variable rod involved in bacterial vaginosis. Presents as a gray vaginal discharge with a fishy smell; nonpainful (vs vaginitis). Associated with sexual activity, but not sexually transmitted. Bacterial vaginosis is also characterized by overgrowth of certain anaerobic bacteria in vagina (due to ↓ lactobacilli). Clue cells (vaginal epithelial cells covered with *Gardnerella*) have stippled appearance along outer margin (arrow in A).

Amine whiff test—mixing discharge with 10% KOH enhances fishy odor.
Vaginal pH >4.5 during infection.
Treatment: metronidazole or clindamycin.

Zoonotic bacteria

Zoonosis—infectious disease transmitted between animals and humans.

SPECIES	DISEASE	TRANSMISSION AND SOURCE
<i>Anaplasma</i> spp	Anaplasmosis	<i>Ixodes</i> ticks (live on deer and mice)
<i>Bartonella</i> spp	Cat scratch disease, bacillary angiomatosis	Cat scratch
<i>Borrelia burgdorferi</i>	Lyme disease	<i>Ixodes</i> ticks (live on deer and mice)
<i>Borrelia recurrentis</i>	Relapsing fever	Louse (recurrent due to variable surface antigens)
<i>Brucella</i> spp	Brucellosis/undulant fever	Unpasteurized dairy; inhalation of or contact with infected animal tissue or fluids
<i>Campylobacter</i>	Bloody diarrhea	Feces from infected pets/animals; contaminated meats/foods/hands
<i>Chlamydophila psittaci</i>	Psittacosis	Parrots, other birds
<i>Coxiella burnetii</i>	Q fever	Aerosols of cattle/sheep amniotic fluid
<i>Ehrlichia chaffeensis</i>	Ehrlichiosis	<i>Amblyomma</i> (Lone Star tick)
<i>Francisella tularensis</i>	Tularemia	Ticks, rabbits, deer flies
<i>Leptospira</i> spp	Leptospirosis	Animal urine in water; recreational water use
<i>Mycobacterium leprae</i>	Leprosy	Humans with lepromatous leprosy; armadillo (rare)
<i>Pasteurella multocida</i>	Cellulitis, osteomyelitis	Animal bite, cats, dogs
<i>Rickettsia prowazekii</i>	Epidemic typhus	Human to human via human body louse
<i>Rickettsia rickettsii</i>	Rocky Mountain spotted fever	<i>Dermacentor</i> (dog tick)
<i>Rickettsia typhi</i>	Endemic typhus	Fleas
<i>Salmonella</i> spp (except <i>S typhi</i>)	Diarrhea (which may be bloody), vomiting, fever, abdominal cramps	Reptiles and poultry
<i>Yersinia pestis</i>	Plague	Fleas (rats and prairie dogs are reservoirs)

Rickettsial diseases and vector-borne illnesses

RASH COMMON

Rocky Mountain spotted fever

Treatment: doxycycline.

Rickettsia rickettsii, vector is tick. Despite its name, disease occurs primarily in the South Atlantic states, especially North Carolina. Rash typically starts at wrists **A** and ankles and then spreads to trunk, palms, and soles.

Classic triad—headache, fever, rash (vasculitis).

Palms and soles rash is seen in Coxsackievirus A infection (hand, foot, and mouth disease), Rocky Mountain spotted fever, and 2° Syphilis (you drive CARS using your palms and soles).

Rickettsii on the wrists, typhus on the trunk.

Typhus

Endemic (fleas)—*R typhi*. Epidemic (human body louse)—*R prowazekii*. Rash starts centrally and spreads out, sparing palms and soles.

RASH RARE

Ehrlichiosis

Ehrlichia, vector is tick. Monocytes with morulae **B** (mulberrylike inclusions) in cytoplasm.

MEGA:

Monocytes = Ehrlichiosis

Granulocytes = Anaplasmosis

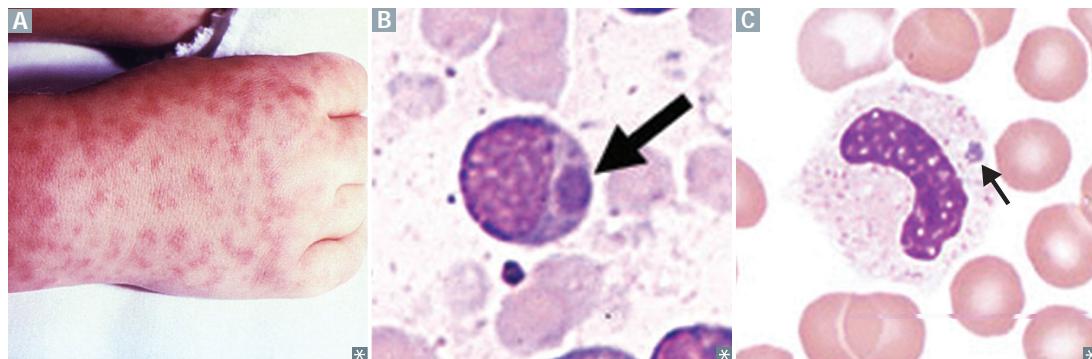
Anaplasmosis

Anaplasma, vector is tick. Granulocytes with morulae **C** in cytoplasm.

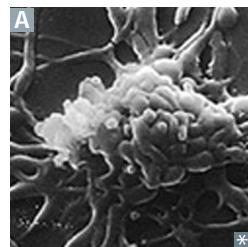
Q fever

Coxiella burnetii, no arthropod vector. Bacterium inhaled as aerosols from cattle/sheep amniotic fluid. Presents with headache, cough, flulike symptoms, pneumonia, possibly in combination with hepatitis. Common cause of culture ⊖ endocarditis.

Q fever is caused by a **Quite Complicated bug** because it has no rash or vector and its causative organism can survive outside in its endospore form. Not in the *Rickettsia* genus, but closely related.



Mycoplasma pneumoniae



Classic cause of atypical “walking pneumonia” (insidious onset, headache, nonproductive cough, patchy or diffuse interstitial infiltrate, macular rash).

Occurs frequently in those <30 years old; outbreaks in military recruits, prisons, colleges. Treatment: macrolides, doxycycline, or fluoroquinolone (penicillin ineffective since *Mycoplasma* has no cell wall).

Not seen on Gram stain. Pleomorphic **A**.

Bacterial membrane contains sterols for stability. Grown on Eaton agar.

CXR appears more severe than patient presentation. High titer of **cold** agglutinins (IgM), which can agglutinate RBCs. *Mycoplasma* gets **cold** without a **coat** (no cell wall).

Can cause atypical variant of Stevens-Johnson syndrome, typically in children and adolescents.

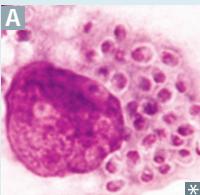
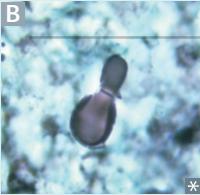
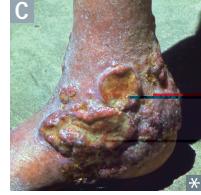
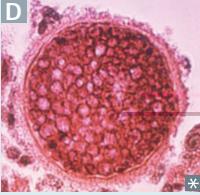
► MICROBIOLOGY—MYCOLOGY

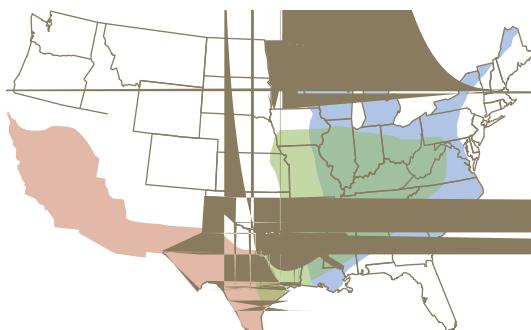
Systemic mycoses

All of the following can cause pneumonia and can disseminate.

All are caused by dimorphic fungi: **cold** (20°C) = **mold**; **heat** (37°C) = **yeast**. Only exception is *Coccidioides*, which is a spherule (not yeast) in tissue.

Systemic mycoses can form granulomas (like TB); cannot be transmitted person-to-person (unlike TB). Treatment: fluconazole or itraconazole for **local** infection; amphotericin B for **systemic** infection.

DISEASE	ENDEMIC LOCATION	PATHOLOGIC FEATURES	UNIQUE SIGNS/SYMPOMTS	NOTES
Histoplasmosis 	Mississippi and Ohio River Valleys	Macrophage filled with <i>Histoplasma</i> (smaller than RBC) A	Palatal/tongue ulcers, splenomegaly, pancytopenia, erythema nodosum	Histo hides (within macrophages) Associated with bird or bat droppings (eg, caves) Diagnosis via urine/serum antigen
Blastomycosis 	Eastern and Central US, Great Lakes	Broad -based budding of <i>Blastomyces</i> (same size as RBC) B	Inflammatory lung disease Disseminates to bone/skin (verrucous lesions C , may mimic SCC).	Blasto buds broadly 
Coccidioidomycosis 	Southwestern US, California	Spherule filled with endospores of <i>Coccidioides</i> (much larger than RBC) D	Disseminates to bone/skin Erythema nodosum (desert bumps) or multiforme Arthralgias (desert rheumatism) Can cause meningitis	Associated with dust exposure in endemic areas (eg, archeological excavations, earthquakes)
Paracoccidioidomycosis 	Latin America	Budding yeast of <i>Paracoccidioides</i> with “ captain’s wheel ” formation (much larger than RBC) E	Similar to blastomycosis, males > females	Paracoccido parasails with the captain’s wheel all the way to Latin America



Opportunistic fungal infections

Candida albicans

alba = white. Dimorphic; forms pseudohyphae and budding yeasts at 20°C **A**, germ tubes at 37°C **B**.

Systemic or superficial fungal infection. Causes oral **C** and esophageal thrush in immunocompromised (neonates, steroids, diabetes, AIDS), vulvovaginitis (diabetes, use of antibiotics), diaper rash, infective endocarditis (people who inject drugs), disseminated candidiasis (especially in neutropenic patients), chronic mucocutaneous candidiasis.

Treatment: oral fluconazole/topical azoles for vaginal; nystatin, azoles, or, rarely, echinocandins for oral; fluconazole, echinocandins, or amphotericin B for esophageal or systemic disease.

Aspergillus fumigatus

Acute angle (45°) **D** branching of septate hyphae.

Causes invasive aspergillosis in immunocompromised patients, especially those with neutrophil dysfunction (eg, chronic granulomatous disease) because *Aspergillus* is catalase \oplus .

Can cause aspergillomas **E** in pre-existing lung cavities, especially after TB infection.

Some species of *Aspergillus* produce aflatoxins (induce TP53 mutations leading to hepatocellular carcinoma).

Treatment: voriconazole or echinocandins (2nd-line).

Allergic bronchopulmonary aspergillosis (ABPA)—hypersensitivity response to *Aspergillus* growing in lung mucus. Associated with asthma and cystic fibrosis; may cause bronchiectasis and eosinophilia.

Cryptococcus neoformans

5–10 μm with narrow budding. Heavily encapsulated yeast. Not dimorphic. \oplus PAS staining.

Found in soil, pigeon droppings. Acquired through inhalation with hematogenous dissemination to meninges. Highlighted with India ink (clear halo **F**) and mucicarmine (red inner capsule **G**). Latex agglutination test detects polysaccharide capsular antigen and is more sensitive and specific. Causes cryptococcosis, which can manifest with meningitis, pneumonia, and/or encephalitis (“soap bubble” lesions in brain), primarily in immunocompromised.

Treatment: amphotericin B + flucytosine followed by fluconazole for cryptococcal meningitis.

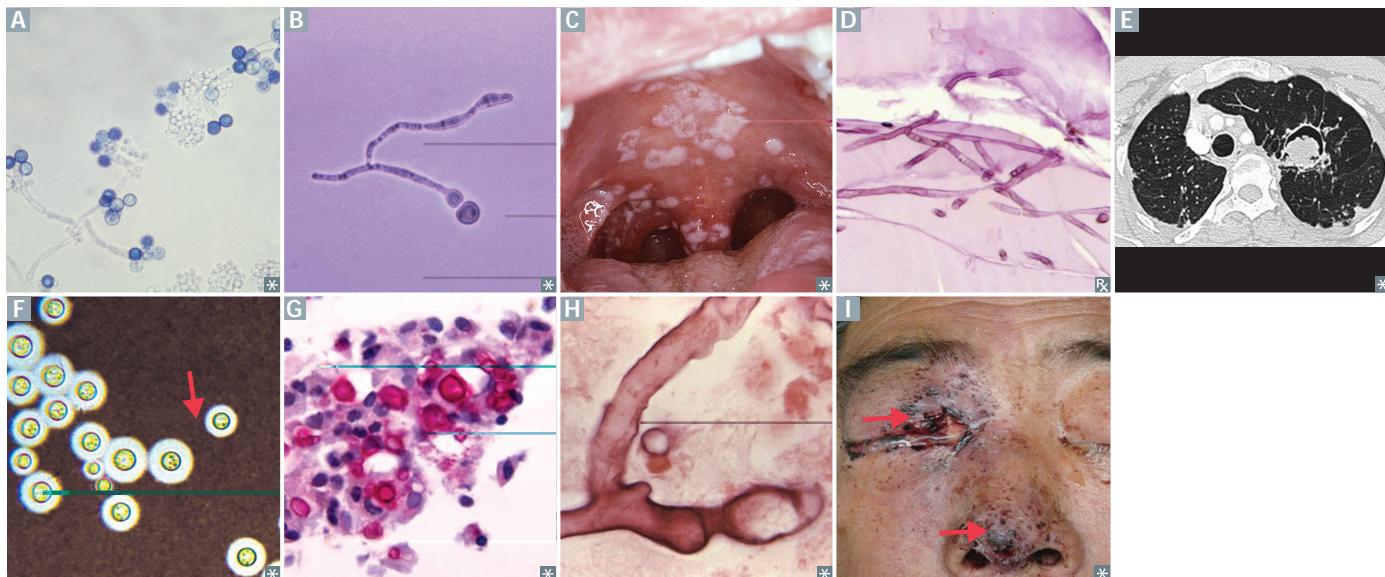
Mucor and Rhizopus spp

Irregular, broad, nonseptate hyphae branching at wide angles **H**.

Causes mucormycosis, mostly in patients with DKA and/or neutropenia (eg, leukemia). Inhalation of spores \rightarrow fungi proliferate in blood vessel walls, penetrate cribriform plate, and enter brain.

Rhinocerebral, frontal lobe abscess; cavernous sinus thrombosis. Headache, facial pain, black necrotic eschar on face **I**; may have cranial nerve involvement.

Treatment: surgical debridement, amphotericin B or isavuconazole.



Pneumocystis jirovecii

Causes *Pneumocystis* pneumonia (PCP), a diffuse interstitial pneumonia **A**. Yeastlike fungus (originally classified as protozoan). Most infections are asymptomatic. Immunosuppression (eg, AIDS) predisposes to disease. Diffuse, bilateral ground-glass opacities on chest imaging, with pneumatoceles **B**. Diagnosed by bronchoalveolar lavage or lung biopsy. Disc-shaped yeast seen on methenamine silver stain of lung tissue **C** or with fluorescent antibody. Treatment/prophylaxis: TMP-SMX, pentamidine, dapsone (prophylaxis as single agent, or treatment in combination with TMP), atovaquone. Start prophylaxis when CD4+ cell count drops to < 200 cells/mm³ in people living with HIV.

***Sporothrix schenckii***

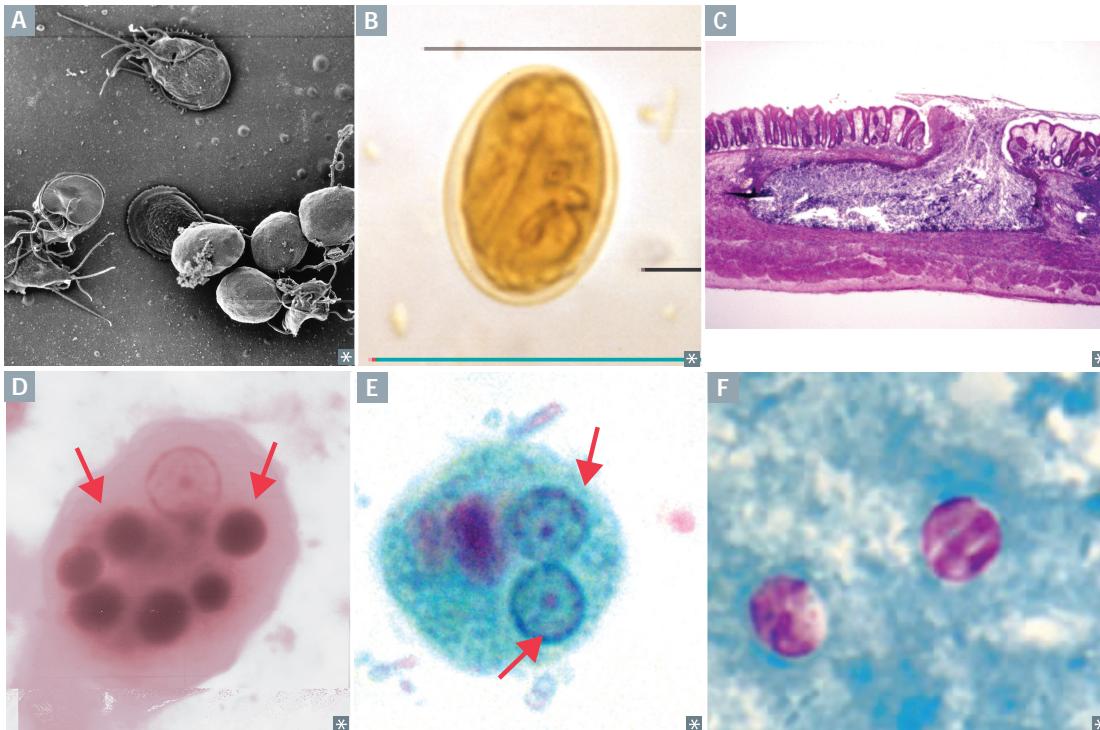
Causes sporotrichosis. Dimorphic fungus. Exists as a **cigar**-shaped yeast at 37 °C in the human body and as hyphae with spores in soil (conidia). Lives on vegetation. When spores are traumatically introduced into the skin, typically by a thorn ("**rose gardener**'s disease"), causes local pustule or ulcer with nodules along draining lymphatics (ascending lymphangitis **A**). Disseminated disease possible in immunocompromised host.

Treatment: itraconazole or **potassium iodide** (only for cutaneous/lymphocutaneous). Think of a **rose gardener** who smokes a **cigar** and **pot**.

► MICROBIOLOGY—PARASITOLOGY

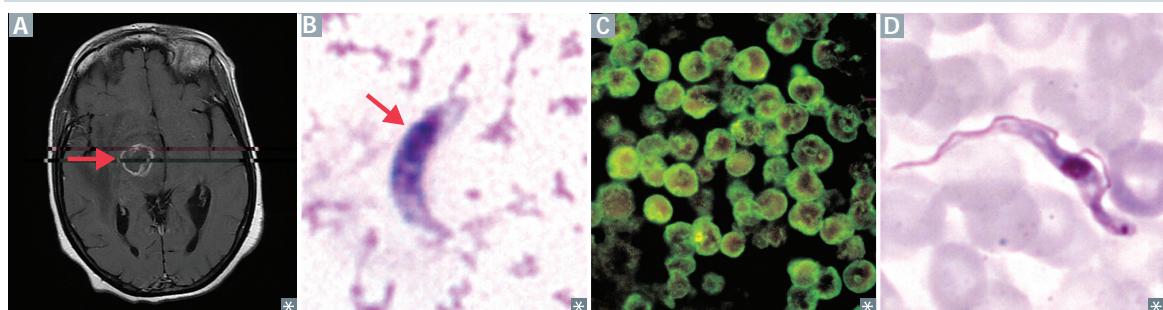
Protozoa—gastrointestinal infections

ORGANISM	DISEASE	TRANSMISSION	DIAGNOSIS	TREATMENT
<i>Giardia lamblia</i>	Giardiasis —bloating, flatulence, foul-smelling, nonbloody, fatty diarrhea (often seen in campers/hikers)—think fat -rich Ghirardelli chocolates for fatty stools of Giardia	Cysts in water	Multinucleated trophozoites A or cysts B in stool, antigen detection, PCR	Tinidazole, nitazoxanide, or metronidazole
<i>Entamoeba histolytica</i>	Amebiasis —bloody diarrhea (dysentery), liver abscess (“anchovy paste” exudate), RUQ pain; histology of colon biopsy shows flask-shaped ulcers C	Cysts in water	Serology, antigen testing, PCR, and/or trophozoites (with engulfed RBCs D in the cytoplasm) or cysts with up to 4 nuclei in stool E ; Entamoeba Eats Erythrocytes	Metronidazole; paromomycin for asymptomatic cyst passers
<i>Cryptosporidium</i>	Severe diarrhea in AIDS Mild disease (watery diarrhea) in immunocompetent hosts	Oocysts in water	Oocysts on acid-fast stain F , antigen detection, PCR	Prevention (by filtering city water supplies); nitazoxanide in immunocompromised hosts



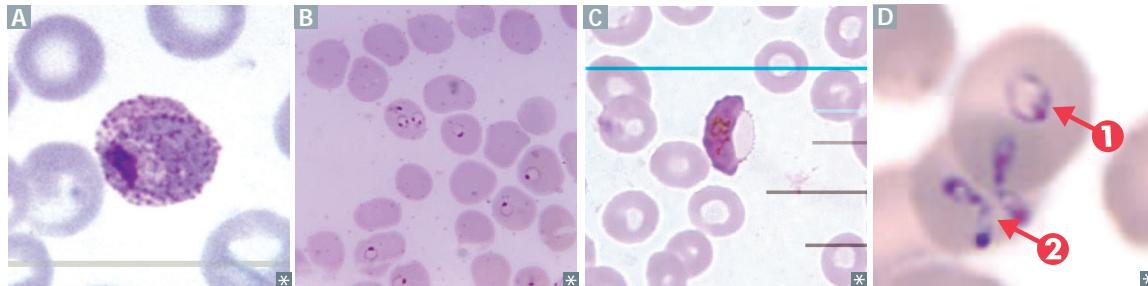
Protozoa—CNS infections

ORGANISM	DISEASE	TRANSMISSION	DIAGNOSIS	TREATMENT
<i>Toxoplasma gondii</i>	Immunocompetent: mononucleosis-like symptoms, ⊖ heterophile antibody test Reactivation in AIDS → brain abscesses usually seen as multiple ring-enhancing lesions on MRI A Congenital toxoplasmosis: classic triad of chorioretinitis, hydrocephalus, and intracranial calcifications	Cysts in meat (most common); oocysts in cat feces; crosses placenta (pregnant patients should avoid cats)	Serology, biopsy (tachyzoite) B ; PCR of amniotic fluid for possible intrauterine disease	Sulfadiazine + pyrimethamine Prophylaxis with TMP-SMX when CD4+ cell count < 100 cells/mm ³
<i>Naegleria fowleri</i>	Rapidly fatal meningoencephalitis	Swimming in warm freshwater; enters CNS through olfactory nerve via cribriform plate	Amoebas in CSF C	Amphotericin B has been effective for a few survivors
<i>Trypanosoma brucei</i>	African sleeping sickness— enlarged lymph nodes, recurring fever (due to antigenic variation), somnolence, coma	Tsetse fly, a painful bite	Trypomastigote in blood smear D	Suramin for blood- borne disease or melarsoprol for CNS penetration ("I sure am mellow when I'm sleeping ")



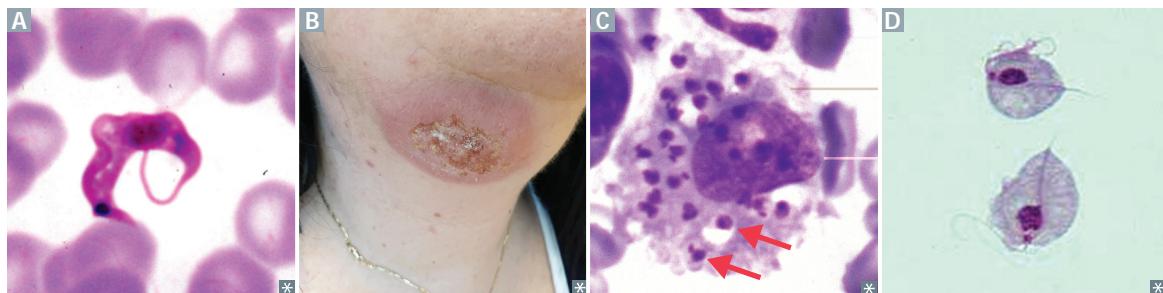
Protozoa—hematologic infections

ORGANISM	DISEASE	TRANSMISSION	DIAGNOSIS	TREATMENT
<i>Plasmodium</i>	Malaria —cyclic fevers, headache, anemia, splenomegaly; hypoglycemia in severe disease	<i>Anopheles</i> mosquito		If sensitive, chloroquine; if resistant, mefloquine, doxycycline or atovaquone/proguanil If life threatening, use intravenous quinine or artesunate (test for G6PD deficiency)
<i>P malariae</i>	72-hr fever cycle (quartan)		Blood smear with trophozoite ring within RBC	
<i>P vivax/ovale</i>	48-hr fever cycle (tertian); dormant form (hypnozoite) in liver		Blood smear with trophozoites and Schüffner stippling (small red granules) within RBC cytoplasm A	Add primaquine to target hypnozoites
<i>P falciparum</i>	Severe, irregular fever pattern; parasitized RBCs may occlude capillaries in brain (cerebral malaria), kidneys, lungs		Blood smear with trophozoite ring (headphone shaped) within RBC B ; crescent-shaped gametocytes C	
<i>Babesia</i>	Babesiosis —fever and hemolytic anemia; predominantly in northeastern and north central United States; asplenia ↑ risk of severe disease due to inability to clear infected RBCs	<i>Ixodes</i> tick (also vector for <i>Borrelia burgdorferi</i> and <i>Anaplasma</i> spp)	Blood smear: ring form D1 , “Maltese cross” D2 ; PCR	Atovaquone + azithromycin



Protozoa—others

ORGANISM	DISEASE	TRANSMISSION	DIAGNOSIS	TREATMENT
Visceral infections				
<i>Trypanosoma cruzi</i>	Chagas disease—dilated cardiomyopathy with apical atrophy, megacolon, megaesophagus; (<i>T cruzi</i> causes big problems); predominantly in South America Unilateral periorbital swelling (Romaña sign) characteristic of acute stage	Triatome insect (kissing bug) bites and defecates around the mouth or eyes → fecal transmission into bite site or mucosa	Trypomastigote in blood smear A	Benznidazole or nifurtimox
<i>Leishmania</i> spp	Visceral leishmaniasis (kala-azar) —spiking fevers, hepatosplenomegaly, pancytopenia Cutaneous leishmaniasis —skin ulcers B	Sandfly	Macrophages containing amastigotes C	Amphotericin B, sodium stibogluconate
Sexually transmitted infections				
<i>Trichomonas vaginalis</i>	Vaginitis —foul-smelling, greenish discharge; itching and burning; do not confuse with <i>Gardnerella vaginalis</i> , a gram-variable bacterium associated with bacterial vaginosis	Sexual (cannot exist outside human because it cannot form cysts)	Trophozoites (motile) D on wet mount; punctate cervical hemorrhages (“strawberry cervix”)	Metronidazole for patient and partner(s) (prophylaxis; check for STI)

**Nematode routes of infection**

Ingested—*Enterobius*, *Ascaris*, *Toxocara*, *Trichinella*, *Trichuris*

Cutaneous—*Strongyloides*, *Ancylostoma*, *Necator*

Bites—*Loa loa*, *Onchocerca volvulus*, *Wuchereria bancrofti*

You'll get sick if you **EATTT** these!

These get into your feet from the **SAND**

Lay **LOW** to avoid getting bitten

Nematodes (roundworms)

ORGANISM	DISEASE	TRANSMISSION	TREATMENT
Intestinal			
<i>Enterobius vermicularis</i> (pinworm)	Causes anal pruritus, worse at night (eggs A visualized via tape test).	Fecal-oral.	Bendazoles, pyrantel pamoate.
<i>Ascaris lumbricoides</i> (giant roundworm)	May cause obstruction at ileocecal valve, biliary obstruction, intestinal perforation, migrates from nose/mouth. Migration of larvae to alveoli → Löeffler syndrome (pulmonary eosinophilia).	Fecal-oral; knobby-coated, oval eggs seen in feces under microscope B .	Bendazoles.
<i>Strongyloides stercoralis</i> (threadworm)	GI (eg, duodenitis), pulmonary (eg, dry cough, hemoptysis), and cutaneous (eg, pruritus) symptoms. Hyperinfection syndrome can be caused by accelerated autoinfection in the immunocompromised.	Larvae in soil penetrate skin; rhabditiform larvae seen in feces under microscope.	Ivermectin or bendazoles.
<i>Ancylostoma spp.</i> , <i>Necator americanus</i> (hookworms)	Cause microcytic anemia by sucking blood from intestinal wall. Cutaneous larva migrans —pruritic, serpiginous rash C .	Larvae penetrate skin from walking barefoot on contaminated beach/soil.	Bendazoles or pyrantel pamoate.
<i>Trichinella spiralis</i>	Larvae enter bloodstream, encyst in striated muscle D → myositis. Trichinosis —fever, vomiting, nausea, periorbital edema, myalgia.	Undercooked meat (especially pork); fecal-oral (less likely).	Bendazoles.
<i>Trichuris trichiura</i> (whipworm)	Often asymptomatic; loose stools, anemia, rectal prolapse in children.	Fecal-oral.	Bendazoles.
Tissue			
<i>Toxocara canis</i>	Visceral larva migrans —migration into blood → inflammation of liver, eyes (visual impairment), CNS (seizures, coma), heart (myocarditis). Patients often asymptomatic.	Fecal-oral.	Bendazoles.
<i>Onchocerca volvulus</i>	Black skin nodules, river blindness (“ black sight”).	Female black fly.	Ivermectin (iver mectin for river blindness).
<i>Loa loa</i>	Swelling in skin, worm in conjunctiva.	Deer fly, horse fly, mango fly.	Diethylcarbamazine.
<i>Wuchereria bancrofti</i> , <i>Brugia malayi</i>	Lymphatic filariasis (elephantiasis) —worms invade lymph nodes → inflammation → lymphedema E ; symptom onset after 9 mo–1 yr.	Female mosquito.	Diethylcarbamazine.



Cestodes (tapeworms)

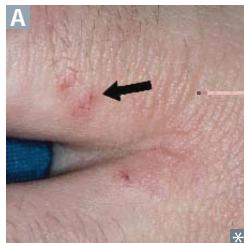
ORGANISM	DISEASE	TRANSMISSION	TREATMENT
<i>Taenia solium</i> A	Intestinal tapeworm	Ingestion of larvae encysted in undercooked pork	Praziquantel
	Cysticercosis, neurocysticercosis (cystic CNS lesions, seizures) B	Ingestion of eggs in food contaminated with human feces	Praziquantel; albendazole for neurocysticercosis
<i>Diphyllobothrium latum</i>	Vitamin B ₁₂ deficiency (tapeworm competes for B ₁₂ in intestine) → megaloblastic anemia	Ingestion of larvae in raw freshwater fish	Praziquantel, niclosamide
<i>Echinococcus granulosus</i> C	Hydatid cysts D (“eggshell calcification”) most commonly in liver E and lungs; cyst rupture can cause anaphylaxis	Ingestion of eggs in food contaminated with dog feces Sheep are an intermediate host	Albendazole; surgery for complicated cysts

**Trematodes (flukes)**

ORGANISM	DISEASE	TRANSMISSION	TREATMENT
<i>Schistosoma</i>	Liver and spleen enlargement (A shows <i>S mansoni</i> egg with lateral spine), fibrosis, inflammation, portal hypertension; <i>S mansoni</i> and <i>S japonicum</i> can both also cause intestinal schistosomiasis, presenting with diarrhea, abdominal pain, iron deficiency anemia Chronic infection with <i>S haematobium</i> (egg with terminal spine B) can lead to squamous cell carcinoma of the bladder (painless hematuria) and pulmonary hypertension	Snails are intermediate host; cercariae penetrate skin of humans in contact with contaminated fresh water (eg, swimming or bathing)	Praziquantel
<i>Clonorchis sinensis</i>	Biliary tract inflammation → pigmented gallstones Associated with cholangiocarcinoma	Undercooked fish	Praziquantel

Ectoparasites

Sarcoptes scabiei

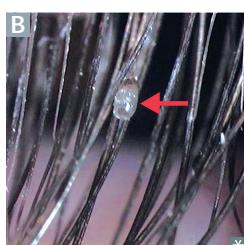


Mites burrow into stratum corneum and cause **scabies**—pruritus (worse at night) and serpiginous burrows (lines) often between fingers and toes **A**.

Common in children, crowded populations (jails, nursing homes); transmission through skin-to-skin contact (most common) or via fomites.

Treatment: permethrin cream, oral ivermectin, washing/drying all clothing/bedding, treat close contacts.

Pediculus humanus and *Phthirus pubis*



Blood-sucking lice that cause intense pruritus with associated excoriations, commonly on scalp and neck (head lice), waistband and axilla (body lice), or pubic and perianal regions (pubic lice).

Body lice can transmit *Rickettsia prowazekii* (epidemic typhus), *Borrelia recurrentis* (relapsing fever), *Bartonella quintana* (trench fever).

Treatment: pyrethroids, malathion, or ivermectin lotion, and nit **B** combing. Children with head lice can be treated at home without interrupting school attendance.

Cimex lectularius and *Cimex hemipterus*

Bed bugs. Blood-feeding insects that infest dwellings. Painless bites result in a range of skin reactions, typically pruritic, erythematous papules with central hemorrhagic punctum. A clustered or linear pattern of bites seen upon awakening is suggestive. Diagnosis is confirmed by direct identification of bed bugs in patient's dwelling.

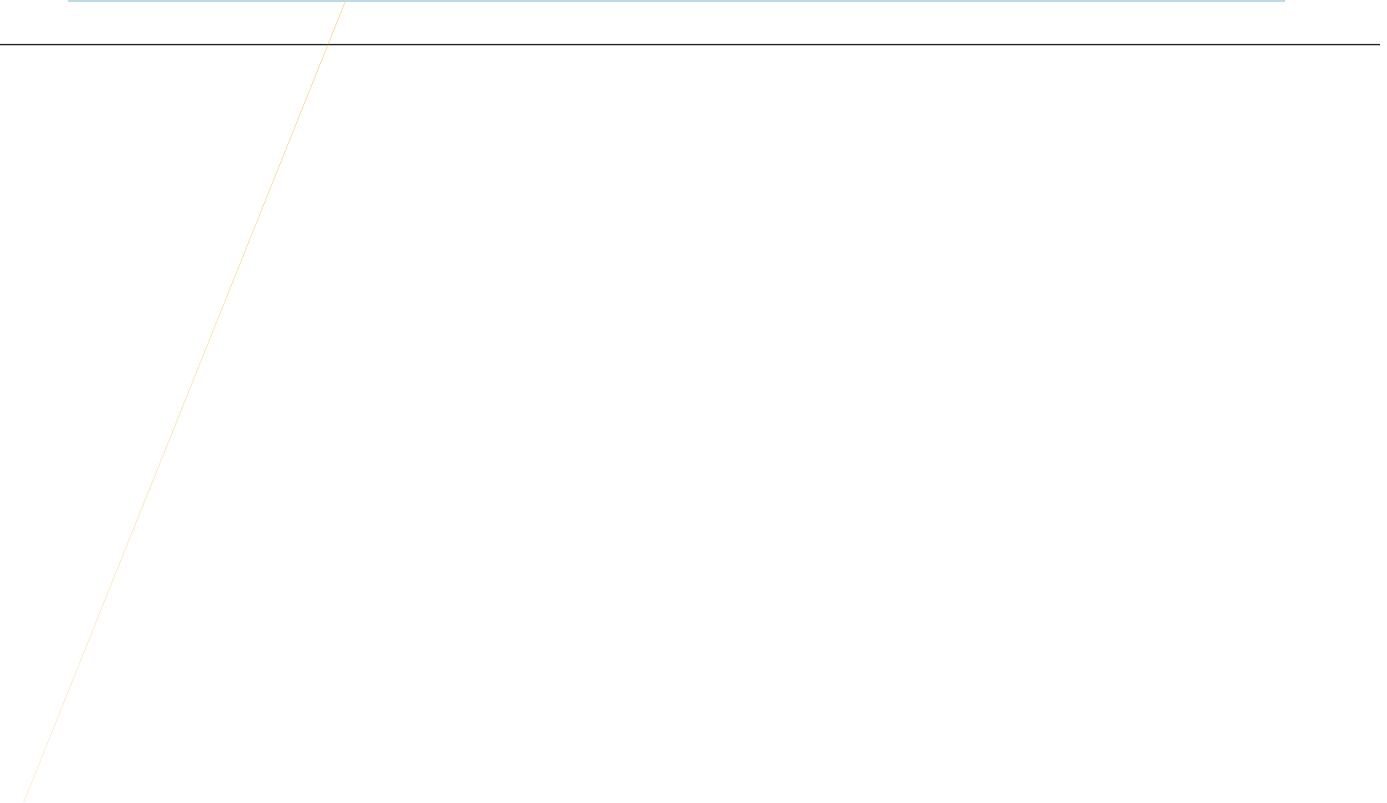
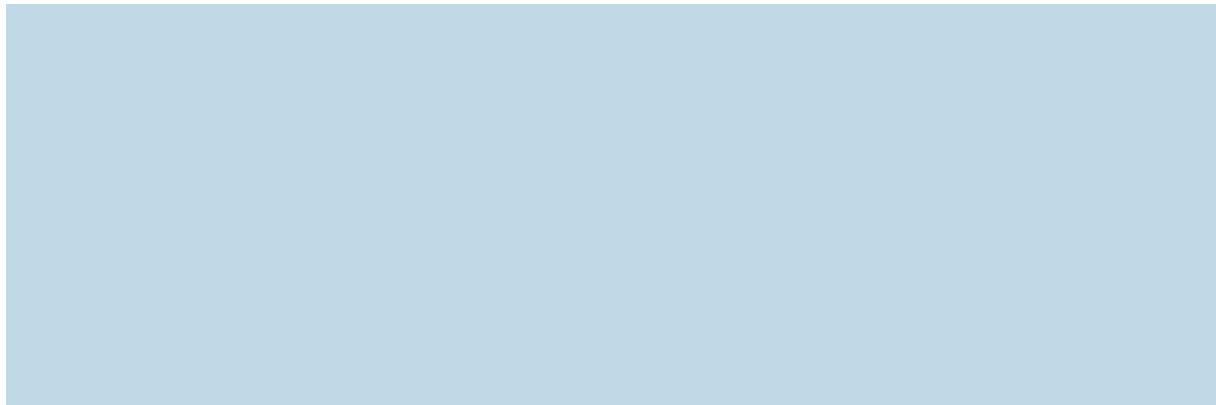
Bed bugs can spread among rooms; cohabitants may exhibit similar symptoms. Infestations can also spread via travelers from infested hotels and the use of unwashed, used bedding.

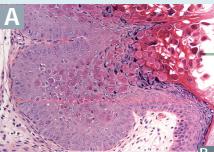
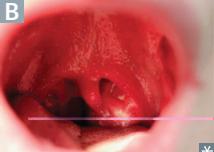
Treatment: bites self resolve within 1 week. Eradication of the infestation is critical.

Parasite hints

ASSOCIATIONS	ORGANISM
Biliary tract disease, cholangiocarcinoma	<i>Clonorchis sinensis</i>
Brain cysts, seizures	<i>Taenia solium</i> (neurocysticercosis)
Hematuria, squamous cell bladder cancer	<i>Schistosoma haematobium</i>
Liver (hydatid) cysts, exposure to infected dogs	<i>Echinococcus granulosus</i>
Iron deficiency anemia	<i>Ancylostoma, Necator</i>
Myalgias, periorbital edema	<i>Trichinella spiralis</i>
Nocturnal perianal pruritus	<i>Enterobius</i>
Portal hypertension	<i>Schistosoma mansoni, Schistosoma japonicum</i>
Vitamin B ₁₂ deficiency	<i>Diphyllobothrium latum</i>

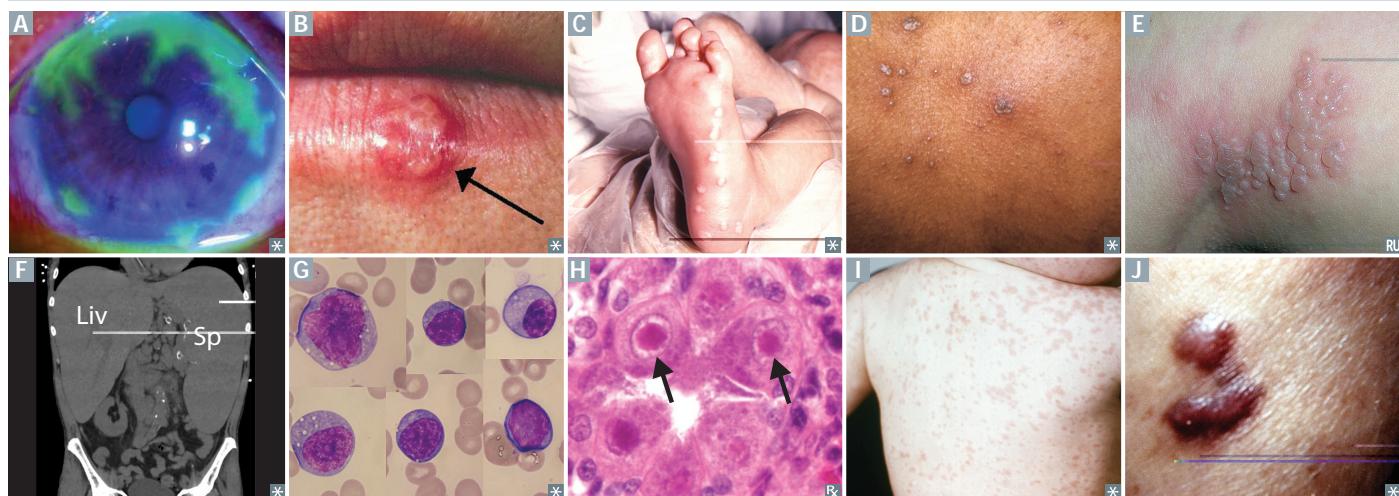
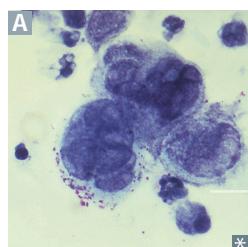
► MICROBIOLOGY—VIROLOGY

Viral structure—general features

DNA viruses			
VIRAL FAMILY	ENVELOPE	DNA STRUCTURE	MEDICAL IMPORTANCE
Herpesviruses	Yes	DS and linear	See Herpesviruses entry
Poxvirus 	Yes	DS and linear (largest DNA virus)	Smallpox eradicated world wide by use of the live-attenuated vaccine Cowpox (“milkmaid blisters”) Molluscum contagiosum —flesh-colored papule with central umbilication; keratinocytes contain molluscum bodies A
Hepadnavirus	Yes	Partially DS and circular	HBV: ■ Acute or chronic hepatitis ■ Not a retrovirus but has reverse transcriptase
Adenovirus 	No	DS and linear	Febrile pharyngitis B —sore throat Acute hemorrhagic cystitis Pneumonia Conjunctivitis—“pink eye” Gastroenteritis Myocarditis
Papillomavirus	No	DS and circular	HPV—warts, cancer (cervical, anal, penile, or oropharyngeal); serotypes 1, 2, 6, 11 associated with warts; serotypes 16, 18 associated with cancer
Polyomavirus	No	DS and circular	JC virus—progressive multifocal leukoencephalopathy (PML) in immunocompromised patients (eg, HIV) BK virus—transplant patients, commonly targets kidney JC : Junky Cerebrum; BK : Bad Kidney
Parvovirus	No	SS and linear (smallest DNA virus; <i>parvus</i> = small)	B19 virus—aplastic crises in sickle cell disease, “slapped cheek” rash in children (erythema infectiosum, or fifth disease); infects RBC precursors and endothelial cells → RBC destruction → hydrops fetalis and death in fetus, pure RBC aplasia and rheumatoid arthritis-like symptoms in adults

Herpesviruses Enveloped, DS, and linear viruses. Recent data suggest both HSV-1 and HSV-2 can affect both genital and extragenital areas.

VIRUS	ROUTE OF TRANSMISSION	CLINICAL SIGNIFICANCE	NOTES
Herpes simplex virus-1	Respiratory secretions, saliva	Gingivostomatitis, keratoconjunctivitis A , herpes labialis (cold sores) B , herpetic whitlow on finger, temporal lobe encephalitis, esophagitis, erythema multiforme. Responsible for a growing percentage of herpes genitalis.	Most commonly latent in trigeminal ganglia Most common cause of sporadic encephalitis, can present as altered mental status, seizures, and/or aphasia
Herpes simplex virus-2	Sexual contact, perinatal	Herpes genitalis, neonatal herpes C	Most commonly latent in sacral ganglia Viral meningitis more common with HSV-2 than with HSV-1
Varicella-zoster virus (HHV-3)	Respiratory secretions, contact with fluid from vesicles	Varicella-zoster (chickenpox D , shingles E), encephalitis, pneumonia Most common complication of shingles is post-herpetic neuralgia	Latent in dorsal root or trigeminal ganglia; CN V ₁ branch involvement can cause herpes zoster ophthalmicus
Epstein-Barr virus (HHV-4)	Respiratory secretions, saliva; also called “kissing disease,” (common in teens, young adults)	Mononucleosis —fever, hepatosplenomegaly F , pharyngitis, and lymphadenopathy (especially posterior cervical nodes); avoid contact sports until resolution due to risk of splenic rupture Associated with lymphomas (eg, endemic Burkitt lymphoma), nasopharyngeal carcinoma (especially Asian adults), lymphoproliferative disease in transplant patients	Infects B cells through CD21, “Must be 21 to drink Beer in a BarrAtypical lymphocytes on peripheral blood smear G—not infected B cells but reactive cytotoxic T cells ⊕ Monospot test—heterophile antibodies detected by agglutination of sheep or horse RBCs Use of amoxicillin (eg, for presumed strep pharyngitis) can cause maculopapular rash
Cytomegalovirus (HHV-5)	Congenital, transfusion, sexual contact, saliva, urine, transplant	Mononucleosis (⊖ Monospot) in immunocompetent patients; infection in immunocompromised, especially pneumonia in transplant patients; esophagitis; AIDS retinitis (“ sight omegalovirus”): hemorrhage, cotton-wool exudates, vision loss Congenital CMV	Infected cells have characteristic “owl eye” intranuclear inclusions H Latent in mononuclear cells
Human herpesviruses 6 and 7	Saliva	Roseola infantum (exanthem subitum): high fevers for several days that can cause seizures, followed by diffuse macular rash (starts on trunk then spreads to extremities) I ; usually seen in children < 2 years old	Roseola : fever first, Rosy (rash) later Self-limited illness HHV-7—less common cause of roseola
Human herpesvirus 8	Sexual contact	Kaposi sarcoma (neoplasm of endothelial cells). Seen in HIV/AIDS and transplant patients. Dark/violaceous plaques or nodules J representing vascular proliferations	Can also affect GI tract and lungs

Herpesviruses (continued)**HSV identification**

PCR of skin lesions is test of choice.

CSF PCR for herpes encephalitis.

Tzanck test (outdated)—a smear of an opened skin vesicle to detect multinucleated giant cells **A** commonly seen in HSV-1, HSV-2, and VZV infection.

Intranuclear eosinophilic Cowdry A inclusions also seen with HSV-1, HSV-2, VZV.

Receptors used by viruses

VIRUS	RECEPTOR(S)
CMV	Integrins (heparan sulfate)
EBV	CD21
HIV	CD4, CXCR4, CCR5
Parvovirus B19	P antigen on RBCs
Rabies	Nicotinic AChR
Rhinovirus	ICAM-1 (I CAMe to see the rhino)
SARS-CoV-2	ACE2

RNA viruses				
VIRAL FAMILY	ENVELOPE	RNA STRUCTURE	CAPSID SYMMETRY	MEDICAL IMPORTANCE
Reoviruses	No	DS linear Multisegmented	Icosahedral (double)	Rotavirus—important cause of diarrhea in young children; may be fatal.
Picornaviruses	No	SS \oplus linear	Icosahedral	Poliovirus—polio-Salk/Sabin vaccines—IPV/OPV Echoviruses—aseptic meningitis Rhinovirus—“common cold” Coxsackievirus—aseptic meningitis; herpangina (mouth blisters, fever); hand, foot, and mouth disease; myocarditis; pericarditis HAV—acute viral hepatitis
Hepevirus	No	SS \oplus linear	Icosahedral	HEV
Caliciviruses	No	SS \oplus linear	Icosahedral	Norovirus—viral gastroenteritis
Flaviviruses	Yes	SS \oplus linear	Icosahedral	HCV Yellow fever ^a Dengue ^a West Nile virus ^a —meningoencephalitis, acute asymmetric flaccid paralysis Zika virus ^a
Togaviruses	Yes	SS \oplus linear	Icosahedral	Toga CREW—Chikungunya virus ^a (co-infection with dengue virus can occur), Rubella (formerly a togavirus), Eastern and Western equine encephalitis ^a
Matonavirus	Yes	SS \oplus linear	Icosahedral	Rubella
Retroviruses	Yes	SS \oplus linear	Icosahedral (HTLV), conical (HIV)	Have reverse transcriptase HTLV—T-cell leukemia HIV—AIDS
Coronaviruses	Yes	SS \oplus linear	Helical	“Common cold,” SARS, COVID-19, MERS
Orthomyxoviruses	Yes	SS \ominus linear Multisegmented	Helical	Influenza virus
Paramyxoviruses	Yes	SS \ominus linear	Helical	PaRaMyxovirus: Parainfluenza—croup RSV—bronchiolitis in babies Measles, Mumps
Rhabdoviruses	Yes	SS \ominus linear	Helical	Rabies
Filoviruses	Yes	SS \ominus linear	Helical	Ebola/Marburg hemorrhagic fever—often fatal.
Arenaviruses	Yes	SS \oplus and \ominus circular Multisegmented	Helical	LCMV—lymphocytic choriomeningitis virus Lassa fever encephalitis—spread by rodents
Bunyaviruses	Yes	SS \ominus circular Multisegmented	Helical	California encephalitis ^a Sandfly/Rift Valley fevers ^a Crimean-Congo hemorrhagic fever ^a Hantavirus—hemorrhagic fever, pneumonia
Delta virus	Yes	SS \ominus circular	Uncertain	HDV is “Defective”; requires presence of HBV to replicate

SS, single-stranded; DS, double-stranded; \oplus , positive sense; \ominus , negative sense; ^a = arbovirus, arthropod borne (mosquitoes, ticks).

Picornavirus

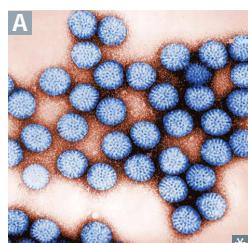
Includes **Poliovirus**, **Echovirus**, **Rhinovirus**, **Coxsackievirus**, and **HAV**. RNA is translated into 1 large polypeptide that is cleaved by virus-encoded proteases into functional viral proteins. Poliovirus, echovirus, and coxsackievirus are enteroviruses and can cause aseptic (viral) meningitis.

Pico**RNA**virus = small **RNA** virus.
PERCH on a “peak” (pico).

Rhinovirus

A picornavirus. Nonenveloped RNA virus. Cause of common cold; > 100 serologic types. Acid labile—destroyed by stomach acid; therefore, does not infect the GI tract (unlike the other picornaviruses).

Rhino has a runny **nose**.

Rotavirus

Segmented dsRNA virus (a reovirus) **A**.

Most important global cause of infantile gastroenteritis. Major cause of acute diarrhea in the United States during winter, especially in day care centers, kindergartens. Villous destruction with atrophy leads to ↓ absorption of Na^+ and loss of K^+ .

Rotavirus = **right out the anus**.

CDC recommends routine vaccination of all infants except those with a history of intussusception (rare adverse effect of rotavirus vaccination) or SCID.

Influenza viruses

Orthomyxoviruses. Enveloped, \ominus ssRNA viruses with segmented genome. Contain hemagglutinin (binds sialic acid and promotes viral entry) and neuraminidase (promotes progeny virion release) antigens. Patients at risk for fatal bacterial superinfection, most commonly *S. aureus*, *S. pneumoniae*, and *H. influenzae*. Treatment: supportive +/- neuraminidase inhibitor (eg, oseltamivir, zanamivir).

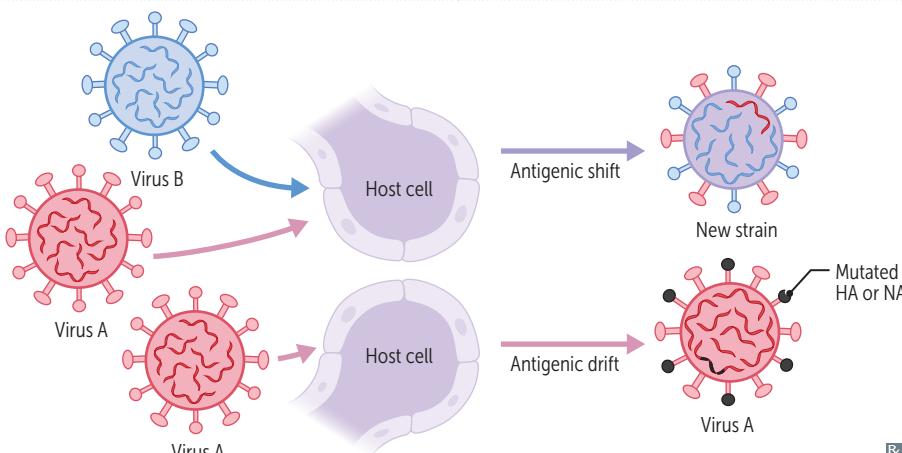
Hemagglutinin: lets the virus **in**
Neuraminidase: sends the virus **away**
 Reformulated vaccine ("the flu shot") contains viral strains most likely to appear during the flu season, due to the virus' rapid genetic change. Killed viral vaccine is most frequently used. Live attenuated vaccine contains temperature-sensitive mutant that replicates in the nose but not in the lung; administered intranasally.
Sudden shift is more deadly than gradual **drift**.

Genetic/antigenic shift

Infection of 1 cell by 2 different segmented viruses (eg, swine influenza and human influenza viruses) → RNA segment reassortment → dramatically different virus (genetic shift) → major global outbreaks (pandemics).

Genetic/antigenic drift

Random mutation in hemagglutinin (HA) or neuraminidase (NA) genes → minor changes in HA or NA protein (drift) occur frequently → local seasonal outbreaks (epidemics).

**Rubella virus**

A morbillivirus. Causes rubella, formerly called German (3-day) measles. Fever, postauricular and other lymphadenopathy, arthralgias, and fine, maculopapular rash that starts on face and spreads centrifugally to involve trunk and extremities **A**.

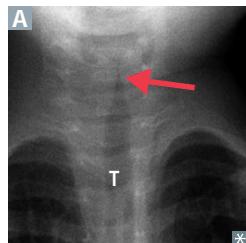
Causes mild disease in children but serious congenital disease (a TORCH infection). Congenital rubella findings include classic triad of sensorineural deafness, cataracts, and patent ductus arteriosus. "Blueberry muffin" appearance may be seen due to dermal extramedullary hematopoiesis.

Paramyxoviruses

Paramyxoviruses cause disease in children. They include those that cause parainfluenza (croup), mumps, measles, RSV, and human metapneumovirus. All subtypes can cause respiratory tract infection (bronchiolitis, pneumonia) in infants. All contain surface F (fusion) protein, which causes respiratory epithelial cells to fuse and form multinucleated cells. Palivizumab (monoclonal antibody against F protein) prevents pneumonia caused by RSV infection in premature infants.

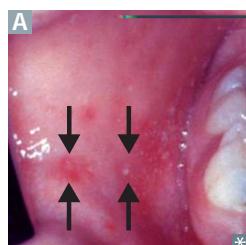
Palivizumab for paramyxovirus (RSV) prophylaxis in preemies.

Acute laryngotracheobronchitis



Also called croup. Caused by parainfluenza viruses. Virus membrane contains hemagglutinin (binds sialic acid and promotes viral entry) and neuraminidase (promotes progeny virion release) antigens. Results in a “seal-like” barking cough and inspiratory stridor. Narrowing of upper trachea and subglottis leads to characteristic steeple sign on x-ray **A**.

Measles (rubeola) virus



Usual presentation involves prodromal fever with cough, coryza, and conjunctivitis, then eventually Koplik spots (bright red spots with blue-white center on buccal mucosa **A**), followed 1–2 days later by a maculopapular rash that starts at the head/neck and spreads downward.

Lymphadenitis with Warthin-Finkeldey giant cells (fused lymphocytes) in a background of paracortical hyperplasia. Possible sequelae:

- Subacute sclerosing panencephalitis (SSPE): personality changes, dementia, autonomic dysfunction, death (occurs years later)
- Encephalitis (1:1000): symptoms appear within few days of rash
- Giant cell pneumonia (rare except in immunosuppressed)

4 C's of measles:

- Cough
- Coryza
- Conjunctivitis
- “C”oplik spots

Vitamin A supplementation can reduce morbidity and mortality from measles, particularly in malnourished children. Pneumonia is the most common cause of measles-associated death in children.

Mumps virus



Uncommon due to effectiveness of MMR vaccine.

Symptoms: Parotitis **A**, Orchitis (inflammation of testes), aseptic Meningitis, and Pancreatitis. Can cause sterility (especially after puberty).

Mumps makes your parotid glands and testes as big as **POM-Poms**.

Arboviruses transmitted by *Aedes* mosquitoes

	Chikungunya virus	Dengue virus
VIRUS TYPE	Alphavirus/togavirus	Flavivirus
SYMPTOMS	High fever, maculopapular rash, headache, lymphadenopathy, and inflammatory polyarthritides Arthralgias are more commonly reported (vs dengue); joint swelling is highly specific for Chikungunya. Thrombocytopenia, leukopenia, and hemorrhagic manifestations are less common.	Dengue fever: fever, rash, headache, myalgias, arthralgias, retro-orbital pain, neutropenia. Dengue hemorrhagic fever: dengue fever + bleeding and plasma leakage due to severe thrombocytopenia and RBC perturbations. Most common if infected with a different serotype after initial infection due to antibody-dependent enhancement of disease. May progress to dengue shock syndrome: plasma leakage → circulatory collapse.
DIAGNOSIS	RT-PCR, serology	
TREATMENT	Supportive. Steroids or DMARDs for chronic arthritis.	Supportive. Intravascular volume repletion or blood transfusion if severe shock.
PREVENTION	Minimize mosquito exposure. No vaccine currently available.	Live, recombinant vaccine available. Derived from the yellow fever virus backbone with insertion of genes for the envelope and pre-membrane proteins of dengue virus.

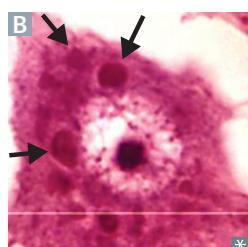
Yellow fever virus

A flavivirus (also an arbovirus) transmitted by *Aedes* mosquito bites. Virus has monkey or human reservoir. *Flavi* = yellow, jaundice.
Symptoms: high fever, black vomitus, jaundice, hemorrhage, backache. May see Councilman bodies (eosinophilic apoptotic globules) on liver biopsy.
Live, attenuated vaccine recommended for travelers to endemic countries.

Zika virus

A flavivirus most commonly transmitted by *Aedes* mosquito bites.
Causes conjunctivitis, low-grade pyrexia, and itchy rash in 20% of cases. Outbreaks more common in tropical and subtropical climates. May be complicated by Guillain-Barré syndrome. Supportive care, no definitive treatment.
Diagnose with RT-PCR or serology.
Sexual and vertical transmission occurs.
In pregnancy, can lead to miscarriage or congenital Zika syndrome: brain imaging shows ventriculomegaly, subcortical calcifications. Clinical features in the affected newborn include

- Microcephaly
- Ocular anomalies
- Motor abnormalities (spasticity, seizures)

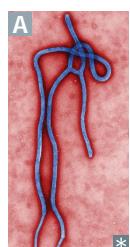
Rabies virus

Bullet-shaped virus **A**. Negri bodies (cytoplasmic inclusions **B**) commonly found in Purkinje cells of cerebellum and in hippocampal neurons. Rabies has long incubation period (weeks to months) before symptom onset. Postexposure prophylaxis is wound cleaning plus immunization with killed vaccine and rabies immunoglobulin. Example of passive-active immunity.

Travels to the CNS by migrating in a retrograde fashion (via dynein motors) up nerve axons after binding to ACh receptors.

Progression of disease: fever, malaise
→ agitation, photophobia, hydrophobia, hypersalivation → paralysis, coma → death.

Infection more commonly from bat, raccoon, and skunk bites than from dog bites in the United States; aerosol transmission (eg, bat caves) also possible.

Ebola virus

A filovirus **A**. Following an incubation period of up to 21 days, presents with abrupt onset of flulike symptoms, diarrhea/vomiting, high fever, myalgia. Can progress to DIC, diffuse hemorrhage, shock.

Diagnosed with RT-PCR within 48 hr of symptom onset. High mortality rate.

Transmission requires direct contact with bodily fluids, fomites (including dead bodies), infected bats or primates (apes/monkeys); high incidence of healthcare-associated infection.

Supportive care, no definitive treatment.

Vaccination of contacts, strict isolation of infected individuals, and barrier practices for healthcare workers are key to preventing transmission.

Hepatitis viruses

Signs and symptoms of all hepatitis viruses: episodes of fever, jaundice, ↑ ALT and AST. Naked viruses (HAV and HEV) lack an envelope and are not destroyed by the gut: the **vowels** hit your **bowels**.

HBV DNA polymerase has DNA- and RNA-dependent activities. Upon entry into nucleus, the polymerase completes the partial dsDNA. Host RNA polymerase transcribes mRNA from viral DNA to make viral proteins. The DNA polymerase then reverse transcribes viral RNA to DNA, which is the genome of the progeny virus.

HCV lacks 3'-5' exonuclease activity → no proofreading ability → antigenic variation of HCV envelope proteins. Host antibody production lags behind production of new mutant strains of HCV.

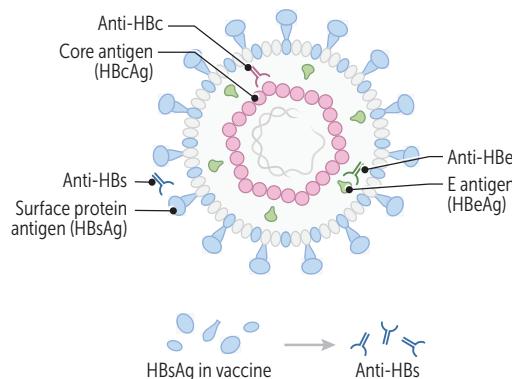
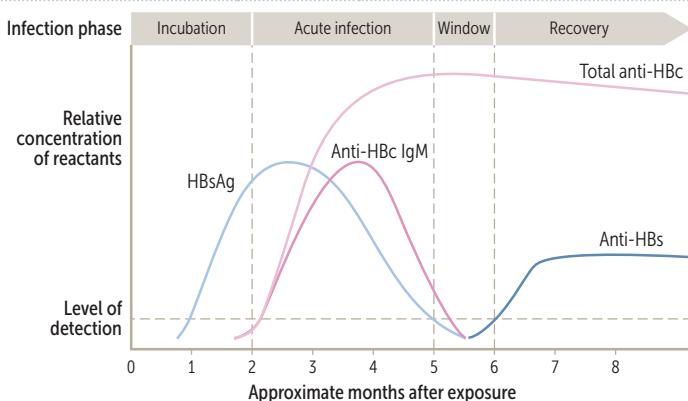
Virus	HAV	HBV	HCV	HDV	HEV
FAMILY	RNA picornavirus	DNA hepadnavirus	RNA flavivirus	RNA deltavirus	RNA hepevirus
TRANSMISSION	Fecal-oral (shellfish, travelers, day care)	Parenteral (Blood), sexual (Bedroom), perinatal (Birth)	Primarily blood (injection drug use, posttransfusion)	Parenteral, sexual, perinatal	Fecal-oral, especially waterborne
INCUBATION	Short (weeks)	Long (months)	Long	Superinfection (HDV after HBV) = short Coinfection (HDV with HBV) = long	Short
CLINICAL COURSE	Acute and self limiting (adults), Asymptomatic (children)	Initially like serum sickness (fever, arthralgias, rash); may progress to carcinoma	May progress to Cirrhosis or Carcinoma	Similar to HBV	Fulminant hepatitis in Expectant (pregnant) patients
PROGNOSIS	Good	Adults → mostly full resolution; neonates → worse prognosis	Majority develop stable, Chronic hepatitis C	Superinfection → worse prognosis	High mortality in pregnant patients
HCC RISK	No	Yes	Yes	Yes	No
LIVER BIOPSY	Hepatocyte swelling, monocyte infiltration, Councilman bodies	Granular eosinophilic “ground glass” appearance due to accumulation of surface antigen within infected hepatocytes; cytotoxic T cells mediate damage	Lymphoid aggregates with focal areas of macrovesicular steatosis	Similar to HBV	Patchy necrosis
NOTES	Absent (no) carrier state	Carrier state common	Carrier state very common	Defective virus, Depends on HBV HBsAg coat for entry into hepatocytes	Enteric, Epidemic (eg, in parts of Asia, Africa, Middle East), no carrier state

Extrahepatic manifestations of hepatitis B and C

	Hepatitis B	Hepatitis C
HEMATOLOGIC	Aplastic anemia	Essential mixed cryoglobulinemia, ↑ risk B-cell NHL, ITP, autoimmune hemolytic anemia
RENAL	Membranous GN > membranoproliferative GN	Membranoproliferative GN > membranous GN
VASCULAR	Polyarteritis nodosa	Leukocytoclastic vasculitis
DERMATOLOGIC		Sporadic porphyria cutanea tarda, lichen planus
ENDOCRINE		↑ risk of diabetes mellitus, autoimmune hypothyroidism

Hepatitis serologic markers

Anti-HAV (IgM)	IgM antibody to HAV; best test to detect acute hepatitis A.
Anti-HAV (IgG)	IgG antibody indicates prior HAV infection and/or prior vaccination; protects against reinfection.
HBsAg	Antigen found on surface of HBV; indicates hepatitis B infection.
Anti-HBs	Antibody to HBsAg; indicates immunity to hepatitis B due to vaccination or recovery from infection.
HBcAg	Antigen associated with core of HBV.
Anti-HBc	Antibody to HBcAg; IgM = acute/recent infection; IgG = prior exposure or chronic infection. IgM anti-HBc may be the sole + marker of infection during window period.
HBeAg	Secreted by infected hepatocyte into circulation. Not part of mature HBV virion. Indicates active viral replication and therefore high transmissibility and poorer prognosis.
Anti-HBe	Antibody to HBeAg; indicates low transmissibility.



	HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe
Incubation	+				
Acute infection	+		+ (IgM)	+	
Window			+ (IgM)		+
Recovery		+	+ (IgG)		+
Chronic infection (high infectivity)	+		+ (IgG)	+	
Chronic infection (low infectivity)	+		+ (IgG)		+
Immunized		+			

Rx

Common diseases of HIV-positive adults ↓ CD4+ cell count → reactivation of past infections (eg, TB, HSV, shingles), dissemination of bacterial infections and fungal infections (eg, coccidioidomycosis), and non-Hodgkin lymphomas.

PATHOGEN	PRESENTATION	FINDINGS
CD4+ cell count < 500/mm³		
<i>Candida albicans</i>	Oral thrush	Scrapable white plaque, pseudohyphae on microscopy
EBV	Oral hairy leukoplakia	Unscrapable white plaque on lateral tongue
HHV-8	Kaposi sarcoma, localized cutaneous disease	Perivascular spindle cells invading and forming vascular tumors on histology
HPV	Squamous cell carcinoma at site(s) of sexual contact (most commonly anus, cervix, oropharynx)	
Mycobacterium tuberculosis	Increased risk of reactivation of latent TB infection	
CD4+ cell count < 200/mm³		
<i>Histoplasma capsulatum</i>	Fever, weight loss, fatigue, cough, dyspnea, nausea, vomiting, diarrhea	Oval yeast cells within macrophages
HIV	Dementia, HIV-associated nephropathy	Cerebral atrophy on neuroimaging
JC virus (reactivation)	Progressive multifocal leukoencephalopathy	Nonenhancing areas of demyelination on MRI
HHV-8	Kaposi sarcoma, disseminated disease (pulmonary, GI, lymphatic)	
<i>Pneumocystis jirovecii</i>	<i>Pneumocystis</i> pneumonia	"Ground-glass" opacities on chest imaging
CD4+ cell count < 100/mm³		
<i>Bartonella</i> spp	Bacillary angiomatosis	Multiple red to purple papules or nodules Biopsy with neutrophilic inflammation
<i>Candida albicans</i>	Esophagitis	White plaques on endoscopy; yeast and pseudohyphae on biopsy
CMV	Colitis, Retinitis, Esophagitis, Encephalitis, Pneumonitis (CREEP)	Linear ulcers on endoscopy, cotton-wool spots on fundoscopy Biopsy reveals cells with intranuclear (owl eye) inclusion bodies
<i>Cryptococcus neoformans</i>	Meningitis	Encapsulated yeast on India ink stain or capsular antigen +
<i>Cryptosporidium</i> spp	Chronic, watery diarrhea	Acid-fast oocysts in stool
EBV	B-cell lymphoma (eg, non-Hodgkin lymphoma, CNS lymphoma)	CNS lymphoma—ring enhancing, may be solitary (vs <i>Toxoplasma</i>)
<i>Mycobacterium avium-intracellulare</i> , <i>Mycobacterium avium complex</i>	Nonspecific systemic symptoms (fever, night sweats, weight loss) or focal lymphadenitis	Most common if CD4+ cell count < 50/mm ³
<i>Toxoplasma gondii</i>	Brain abscesses	Multiple ring-enhancing lesions on MRI

Prions

Prion diseases are caused by the conversion of a normal (predominantly α -helical) protein termed prion protein (PrP^{C}) to a β -pleated form (PrP^{Sc}), which is transmissible via CNS-related tissue (iatrogenic CJD) or food contaminated by BSE-infected animal products (variant CJD). PrP^{Sc} resists protease degradation and facilitates the conversion of still more PrP^{C} to PrP^{Sc} . Resistant to standard sterilizing procedures, including standard autoclaving. Accumulation of PrP^{Sc} results in spongiform encephalopathy and dementia, ataxia, startle myoclonus, and death.

Creutzfeldt-Jakob disease—rapidly progressive dementia, typically sporadic (some familial forms).

Bovine spongiform encephalopathy—also called “mad cow disease.”

Kuru—acquired prion disease noted in tribal populations practicing human cannibalism.

► MICROBIOLOGY—SYSTEMS

Normal microbiota: dominant

Neonates delivered by C-section have microbiota enriched in skin commensals.

LOCATION	MICROORGANISM
Skin	<i>S epidermidis</i>
Nose	<i>S epidermidis</i> ; colonized by <i>S aureus</i>
Oropharynx	Viridans group streptococci
Dental plaque	<i>S mutans</i>
Colon	<i>B fragilis</i> > <i>E coli</i>
Vagina	<i>Lactobacillus</i> ; colonized by <i>E coli</i> and group B strep

Bugs causing food-borne illness

S aureus and *B cereus* food poisoning starts quickly and ends quickly.

MICROORGANISM	SOURCE OF INFECTION
<i>B cereus</i>	Reheated rice. “Food poisoning from reheated rice? Be serious!” (<i>B cereus</i>)
<i>C botulinum</i>	Improperly canned foods (toxins), raw honey (spores)
<i>C perfringens</i>	Reheated meat
<i>E coli</i> O157:H7	Undercooked meat
<i>L monocytogenes</i>	Deli meats, soft cheeses
<i>Salmonella</i>	Poultry, meat, and eggs
<i>S aureus</i>	Meats, mayonnaise, custard; preformed toxin
<i>V parahaemolyticus</i> and <i>V vulnificus</i> ^a	Raw/undercooked seafood

^a*V vulnificus* predominantly causes wound infections from contact with contaminated water or shellfish.

Bugs causing diarrhea**Bloody diarrhea**

<i>Campylobacter</i>	Comma- or S-shaped organisms; growth at 42°C
<i>E histolytica</i>	Protozoan; amebic dysentery; liver abscess
Enterohemorrhagic <i>E coli</i>	O157:H7; can cause HUS; makes Shiga toxin
Enteroinvasive <i>E coli</i>	Invades colonic mucosa
Salmonella (non-typhoidal)	Lactose \ominus ; flagellar motility; has animal reservoir, especially poultry and eggs
Shigella	Lactose \ominus ; very low ID ₅₀ ; produces Shiga toxin; human reservoir only; bacillary dysentery
Y enterocolitica	Day care outbreaks; pseudoappendicitis

Watery diarrhea

<i>C difficile</i>	Pseudomembranous colitis; associated with antibiotics and PPIs; occasionally bloody diarrhea
<i>C perfringens</i>	Also causes gas gangrene
Enterotoxigenic <i>E coli</i>	Travelers' diarrhea; produces heat-labile (LT) and heat-stable (ST) toxins
Protozoa	<i>Giardia, Cryptosporidium</i>
V cholerae	Comma-shaped organisms; rice-water diarrhea; often from infected seafood
Viruses	Norovirus (most common cause in developed countries), rotavirus (\downarrow incidence in developed countries due to vaccination), enteric adenovirus

Common causes of pneumonia

NEONATES (< 4 WK)	CHILDREN (4 WK–18 YR)	ADULTS (18–40 YR)	ADULTS (40–65 YR)	ADULTS (65 YR +)
Group B streptococci	Viruses (RSV)	<i>Mycoplasma</i>	<i>S pneumoniae</i>	<i>S pneumoniae</i>
<i>E coli</i>	<i>Mycoplasma</i>	<i>C pneumoniae</i>	<i>H influenzae</i>	Influenza virus
	<i>C trachomatis</i> (infants–3 yr)	<i>S pneumoniae</i>	Anaerobes	Anaerobes
	<i>C pneumoniae</i> (school-aged children)	Viruses (eg, influenza)	Viruses	<i>H influenzae</i>
	<i>S pneumoniae</i>		<i>Mycoplasma</i>	Gram \ominus rods
	Runts May Cough			
	Chunky Sputum			

Special groups

Alcohol overuse	Klebsiella, anaerobes usually due to aspiration (eg, <i>Peptostreptococcus, Fusobacterium, Prevotella, Bacteroides</i>)
Injection drug use	<i>S pneumoniae, S aureus</i>
Aspiration	Anaerobes
Atypical	<i>Mycoplasma, Chlamydophila, Legionella</i> , viruses (RSV, CMV, influenza, adenovirus)
Cystic fibrosis	<i>Pseudomonas, S aureus, S pneumoniae, Burkholderia cepacia</i>
Immunocompromised	<i>S aureus</i> , enteric gram \ominus rods, fungi, viruses, <i>P jirovecii</i> (with HIV)
Healthcare-associated	<i>S aureus, Pseudomonas</i> , other enteric gram \ominus rods
Postviral	<i>S pneumoniae, S aureus, H influenzae</i>
COPD	<i>S pneumoniae, H influenzae, M catarrhalis, Pseudomonas</i>

Common causes of meningitis

NEWBORN (0–6 MO)	CHILDREN (6 MO–6 YR)	6–60 YR	60 YR +
Group B <i>Streptococcus</i>	<i>S pneumoniae</i>	<i>S pneumoniae</i>	<i>S pneumoniae</i>
<i>E coli</i>	<i>N meningitidis</i>	<i>N meningitidis</i>	<i>N meningitidis</i>
<i>Listeria</i>	<i>H influenzae</i> type b	Enteroviruses	<i>H influenzae</i> type b
	Group B <i>Streptococcus</i>	HSV	Group B <i>Streptococcus</i>
	Enteroviruses		<i>Listeria</i>

Give ceftriaxone and vancomycin empirically (add ampicillin if *Listeria* is suspected).

Viral causes of meningitis: enteroviruses (especially coxsackievirus), HSV-2 (HSV-1 = encephalitis), HIV, West Nile virus (also causes encephalitis), VZV.

In HIV: *Cryptococcus* spp.

Note: Incidence of Group B streptococcal meningitis in neonates has ↓ greatly due to screening and antibiotic prophylaxis in pregnancy. Incidence of *H influenzae* meningitis has ↓ greatly due to conjugate *H influenzae* vaccinations. Today, cases are usually seen in unimmunized children.

Cerebrospinal fluid findings in meningitis

	OPENING PRESSURE	CELL TYPE	PROTEIN	GLUCOSE
Bacterial	↑	↑ PMNs	↑	↓
Fungal/TB	↑	↑ lymphocytes	↑	↓
Viral	Normal/↑	↑ lymphocytes	Normal/↑	Normal

Infections causing brain abscess

Most commonly viridans streptococci and *Staphylococcus aureus*. If dental infection or extraction precedes abscess, oral anaerobes commonly involved.

Multiple abscesses are usually from bacteremia; single lesions from contiguous sites: otitis media and mastoiditis → temporal lobe and cerebellum; sinusitis or dental infection → frontal lobe. *Toxoplasma* reactivation in AIDS.

Osteomyelitis

RISK FACTOR	ASSOCIATED INFECTION
Assume if no other information is available	<i>S aureus</i> (most common overall)
Sexually active	<i>Neisseria gonorrhoeae</i> (rare), septic arthritis more common
Sickle cell disease	<i>Salmonella</i> and <i>S aureus</i>
Prosthetic joint replacement	<i>S aureus</i> and <i>S epidermidis</i>
Vertebral involvement	<i>S aureus</i> , <i>M tuberculosis</i> (Pott disease)
Cat and dog bites	<i>Pasteurella multocida</i>
Injection drug use	<i>S aureus</i> ; also <i>Pseudomonas</i> , <i>Candida</i>

Elevated ESR and CRP sensitive but not specific.

Radiographs are insensitive early but can be useful in chronic osteomyelitis (A, left). MRI is best for detecting acute infection and detailing anatomic involvement (A, right). Biopsy or aspiration with culture necessary to identify organism.

Red rashes of childhood

AGENT	ASSOCIATED SYNDROME/DISEASE	CLINICAL PRESENTATION
Coxsackievirus type A	Hand-foot-mouth disease	Oval-shaped vesicles on palms and soles A ; vesicles and ulcers in oral mucosa (herpangina)
Human herpesvirus 6	Roseola (exanthem subitum)	Asymptomatic rose-colored macules appear on body after several days of high fever; can present with febrile seizures; usually affects infants
Measles virus	Measles (rubeola)	Confluent rash beginning at head and moving down B ; preceded by cough, coryza, conjunctivitis, and blue-white (Koplik) spots on buccal mucosa
Parvovirus B19	Erythema infectiosum (fifth disease)	“Slapped cheek” rash on face C
Rubella virus	Rubella	Pink macules and papules begin at head and move down, remain discrete → fine desquamating truncal rash; postauricular lymphadenopathy
<i>Streptococcus pyogenes</i>	Scarlet fever	Sore throat, Circumoral pallor , group A strep, Rash (sandpaperlike D , from neck to trunk and extremities), Lymphadenopathy , Erythrogenic toxin , strawberry Tongue (SCARLET)
Varicella-zoster virus	Chickenpox	Vesicular rash begins on trunk E , spreads to face and extremities with lesions of different stages



Urinary tract infections

Cystitis presents with dysuria, frequency, urgency, suprapubic pain, and WBCs (but not WBC casts) in urine. Primarily caused by ascension of microbes from urethra to bladder. Ascension to kidney results in pyelonephritis, which presents with fever, chills, flank pain, costovertebral angle tenderness, hematuria, and WBC casts.

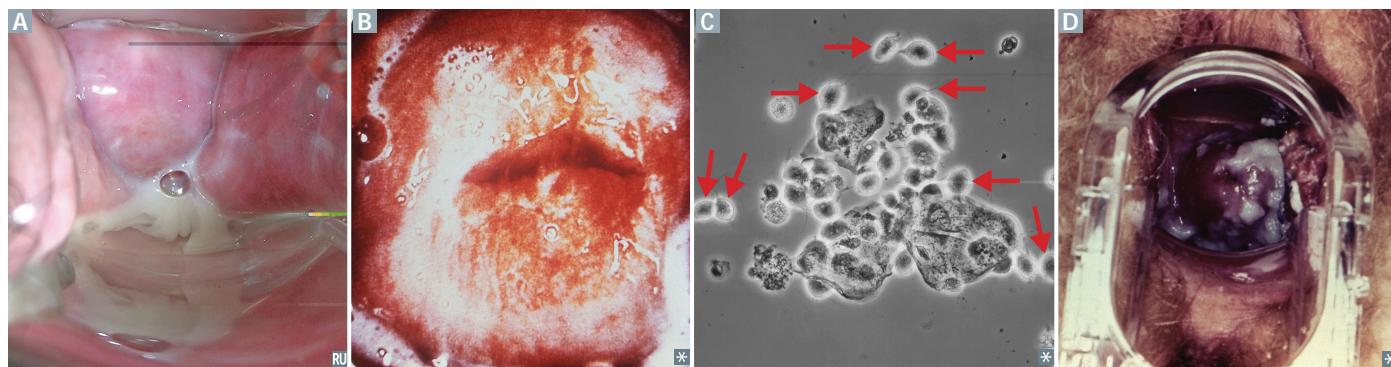
Ten times more common in females (shorter urethras colonized by fecal microbiota).

Risk factors: obstruction (eg, kidney stones, enlarged prostate), kidney surgery, catheterization, congenital GU malformation (eg, vesicoureteral reflux), diabetes, pregnancy.

SPECIES	FEATURES	COMMENTS
<i>Escherichia coli</i>	Leading cause of UTI. Colonies show strong pink lactose-fermentation on MacConkey agar.	Diagnostic markers: ⊕ Leukocyte esterase = evidence of WBC activity. ⊕ Nitrite test = reduction of urinary nitrates by gram ⊥ bacterial species (eg, <i>E. coli</i>).
<i>Staphylococcus saprophyticus</i>	2nd leading cause of UTI, particularly in young, sexually active females.	
<i>Klebsiella pneumoniae</i>	3rd leading cause of UTI. Large mucoid capsule and viscous colonies.	
<i>Serratia marcescens</i>	Some strains produce a red pigment; often healthcare-associated and drug resistant.	
<i>Enterococcus</i>	Often healthcare-associated and drug resistant.	
<i>Proteus mirabilis</i>	Motility causes “swarming” on agar; associated with struvite stones. Produces urease.	
<i>Pseudomonas aeruginosa</i>	Blue-green pigment and fruity odor; usually healthcare-associated and drug resistant.	

Common vaginal infections

	Bacterial vaginosis	<i>Trichomonas vaginalis</i>	<i>Candida vulvovaginitis</i>
SIGNS AND SYMPTOMS	No inflammation Thin, white discharge A with fishy odor	Inflammation B (“strawberry cervix”) Frothy, yellow-green, foul-smelling discharge	Inflammation Thick, white, “cottage cheese” discharge D
LAB FINDINGS	Clue cells pH > 4.5 ⊕ KOH whiff test	Motile pear-shaped trichomonads C pH > 4.5	Pseudohyphae pH normal (4.0–4.5)
TREATMENT	Metronidazole or clindamycin	Metronidazole Treat sexual partner(s)	Azoles



Sexually transmitted infections

DISEASE	CLINICAL FEATURES	PATHOGEN
AIDS	Opportunistic infections, Kaposi sarcoma, lymphoma	HIV
Chancroid	Painful genital ulcer(s) with exudate, inguinal adenopathy A	<i>Haemophilus ducreyi</i> (it's so painful, you “do cry”)
Chlamydia	Urethritis, cervicitis, epididymitis, conjunctivitis, reactive arthritis, PID	<i>Chlamydia trachomatis</i> (D–K)
Condylomata acuminata	Genital warts B , koilocytes	HPV-6 and -11
Herpes genitalis	Painful penile, vulvar, or cervical vesicles and ulcers C with bilateral tender inguinal lymphadenopathy; can cause systemic symptoms such as fever, headache, myalgia	HSV-2, less commonly HSV-1
Gonorrhea	Urethritis, cervicitis, PID, prostatitis, epididymitis, arthritis, creamy purulent discharge	<i>Neisseria gonorrhoeae</i>
Granuloma inguinale (Donovanosis)	Painless, beefy red ulcer that bleeds readily on contact D Uncommon in US	<i>Klebsiella (Calymmatobacterium) granulomatis</i> ; cytoplasmic Donovan bodies (bipolar staining) seen on microscopy
Hepatitis B	Jaundice	HBV
Lymphogranuloma venereum	Infection of lymphatics; painless genital ulcers, painful lymphadenopathy (ie, buboes E)	<i>C trachomatis</i> (L1–L3)
Primary syphilis	Painless chancre F , regional lymphadenopathy	<i>Treponema pallidum</i>
Secondary syphilis	Fever, diffuse lymphadenopathy, skin rashes, condylomata lata	
Tertiary syphilis	Gummas, tabes dorsalis, general paresis, aortitis, Argyll Robertson pupil	
Trichomoniasis	Vaginitis, strawberry cervix, motile in wet prep	<i>Trichomonas vaginalis</i>



TORCH infections

Microbes that may pass from mother to fetus. Transmission is transplacental in most cases, or via vaginal delivery (especially HSV-2). Nonspecific signs common to many **ToRCHHeS** infections include hepatosplenomegaly, jaundice, thrombocytopenia, and growth restriction. Other important infectious agents include *Streptococcus agalactiae* (group B streptococci), *E. coli*, and *Listeria monocytogenes*—all causes of meningitis in neonates. Parvovirus B19 causes hydrops fetalis.

AGENT	MATERNAL ACQUISITION	MATERNAL MANIFESTATIONS	NEONATAL MANIFESTATIONS
<i>Toxoplasma gondii</i>	Cat feces or ingestion of undercooked meat	Usually asymptomatic; lymphadenopathy (rarely)	Classic triad: chorioretinitis, hydrocephalus, and intracranial calcifications, +/− “blueberry muffin” rash A
Rubella	Respiratory droplets	Rash, lymphadenopathy, polyarthritis, polyarthralgia	Classic triad: abnormalities of eye (cataracts B) and ear (deafness) and congenital heart disease (PDA); +/− “blueberry muffin” rash. I (eye) ♥ rub y (rubella) earrings
Cytomegalovirus	Sexual contact, organ transplants	Usually asymptomatic; mononucleosis-like illness	Hearing loss, seizures, petechial rash, “blueberry muffin” rash, chorioretinitis, periventricular calcifications C CMV = Chorioretinitis, Microcephaly, periVentricular calcifications
HIV	Sexual contact, needlestick	Variable presentation depending on CD4+ cell count	Recurrent infections, chronic diarrhea
Herpes simplex virus-2	Skin or mucous membrane contact	Usually asymptomatic; herpetic (vesicular) lesions	Meningoencephalitis, herpetic (vesicular) lesions
Syphilis	Sexual contact	Chancres (1°) and disseminated rash (2°) are the two stages likely to result in fetal infection	Often results in stillbirth, hydrops fetalis; if child survives, presents with facial abnormalities (eg, notched teeth, saddle nose, short maxilla), saber shins, CN VIII deafness



Pelvic inflammatory disease



Ascending infection causing inflammation of the female gynecologic tract. PID may include salpingitis, endometritis, hydrosalpinx, and tubo-ovarian abscess.

Signs include cervical motion tenderness, adnexal tenderness, purulent cervical discharge **A**.

Top bugs—*Chlamydia trachomatis* (subacute, often undiagnosed), *Neisseria gonorrhoeae* (acute).

C trachomatis—most common bacterial STI in the United States.

Salpingitis is a risk factor for ectopic pregnancy, infertility, chronic pelvic pain, and adhesions. Can lead to perihepatitis (**Fitz-Hugh-Curtis syndrome**)—infection and inflammation of liver capsule and “violin string” adhesions of peritoneum to liver **B**.

Healthcare-associated infections

E coli (UTI) and *S aureus* (wound infection) are the two most common causes.

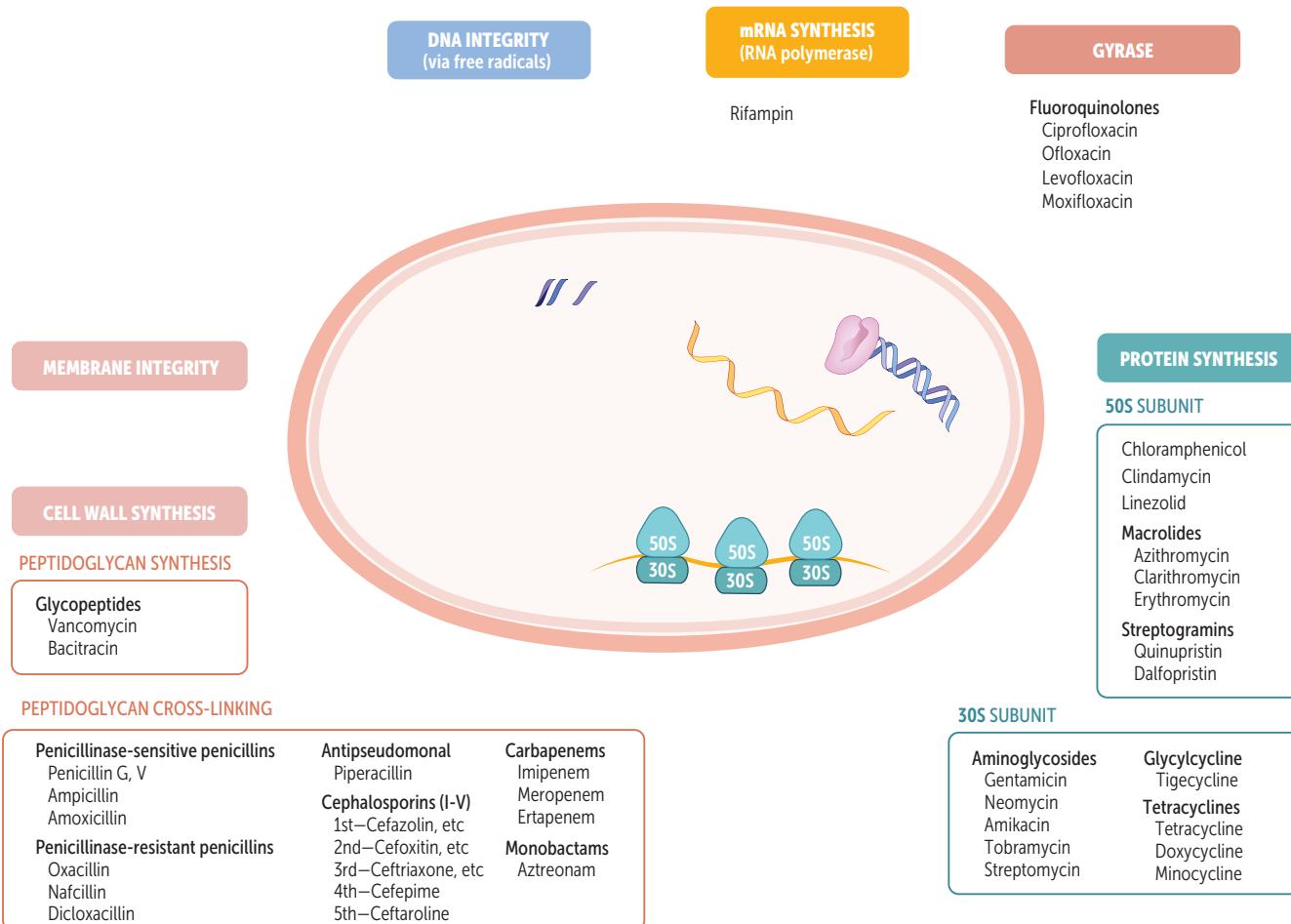
RISK FACTOR	PATHOGEN	UNIQUE SIGNS/SYMPTOMS
Antibiotic use	<i>Clostridioides difficile</i>	Watery diarrhea, leukocytosis
Aspiration (2° to altered mental status, old age)	Polymicrobial, gram ⊖ bacteria, often anaerobes	Right lower lobe infiltrate or right upper/middle lobe (patient recumbent); purulent malodorous sputum
Decubitus ulcers, surgical wounds, drains	<i>S aureus</i> (including MRSA), gram ⊖ anaerobes (<i>Bacteroides</i> , <i>Prevotella</i> , <i>Fusobacterium</i>)	Erythema, tenderness, induration, drainage from surgical wound sites
Intravascular catheters	<i>S aureus</i> (including MRSA), <i>S epidermidis</i> (long term)	Erythema, induration, tenderness, drainage from access sites
Mechanical ventilation, endotracheal intubation	Late onset: <i>P aeruginosa</i> , <i>Klebsiella</i> , <i>Acinetobacter</i> , <i>S aureus</i>	New infiltrate on CXR, ↑ sputum production; sweet odor (<i>Pseudomonas</i>)
Renal dialysis unit, needlestick	HBV, HCV	
Urinary catheterization	<i>Proteus</i> spp, <i>E coli</i> , <i>Klebsiella</i> (PEcK)	Dysuria, leukocytosis, flank pain or costovertebral angle tenderness
Water aerosols	<i>Legionella</i>	Signs of pneumonia, GI symptoms (diarrhea, nausea, vomiting), neurologic abnormalities

Bugs affecting unvaccinated children

CLINICAL PRESENTATION	FINDINGS/LABS	PATHOGEN
Dermatologic		
Rash	Beginning at head and moving down with postauricular, posterior cervical, and suboccipital lymphadenopathy Beginning at head and moving down; preceded by cough, coryza, conjunctivitis, and Koplik spots	Rubella virus Measles virus
Neurologic		
Meningitis	Microbe colonizes nasopharynx Can also lead to myalgia and paralysis	<i>H influenzae</i> type b Poliovirus
Tetanus	Muscle spasms and spastic paralysis (eg, lockjaw, opisthotonus)	<i>Clostridium tetani</i>
Respiratory		
Epiglottitis	Fever with dysphagia, drooling, inspiratory stridor, and difficulty breathing due to edema	<i>H influenzae</i> type b (also capable of causing epiglottitis in fully immunized children)
Pertussis	Low-grade fevers, coryza → whooping cough, posttussive vomiting → gradual recovery	<i>Bordetella pertussis</i>
Pharyngitis	Grayish pseudomembranes (may obstruct airways)	<i>Corynebacterium diphtheriae</i>

► MICROBIOLOGY—ANTIMICROBIALS

Antimicrobial therapy



Penicillinase-sensitive penicillins Amoxicillin, ampicillin; aminopenicillins.

MECHANISM	Same as penicillin. Wider spectrum; penicillinase sensitive. Also combine with clavulanic acid to protect against destruction by β -lactamase.	Aminopenicillins are amped-up penicillin. Amoxicillin has greater oral bioavailability than ampicillin.
CLINICAL USE	Extended-spectrum penicillin— <i>H influenzae</i> , <i>H pylori</i> , <i>E coli</i> , Enterococci, <i>Listeria monocytogenes</i> , <i>Proteus mirabilis</i> , <i>Salmonella</i> , <i>Shigella</i> .	Coverage: ampicillin/amoxicillin HHELPSS kill enterococci.
ADVERSE EFFECTS	Hypersensitivity reactions, rash, pseudomembranous colitis.	
MECHANISM OF RESISTANCE	Penicillinase (a type of β -lactamase) cleaves β -lactam ring.	

Penicillinase-resistant penicillins Dicloxacillin, nafcillin, oxacillin.

MECHANISM	Same as penicillin. Narrow spectrum; penicillinase resistant because bulky R group blocks access of β -lactamase to β -lactam ring.	
CLINICAL USE	<i>S aureus</i> (except MRSA).	“Use naf (nafcillin) for staph .”
ADVERSE EFFECTS	Hypersensitivity reactions, interstitial nephritis.	
MECHANISM OF RESISTANCE	MRSA has altered penicillin-binding protein target site.	

Piperacillin Antipseudomonal penicillin.

MECHANISM	Same as penicillin. Extended spectrum. Penicillinase sensitive; use with β -lactamase inhibitors.
CLINICAL USE	<i>Pseudomonas</i> spp., gram \ominus rods, anaerobes.
ADVERSE EFFECTS	Hypersensitivity reactions.

Cephalosporins

MECHANISM	β -lactam drugs that inhibit cell wall synthesis but are less susceptible to penicillinases. Bactericidal.	Organisms typically not covered by 1st–4th generation cephalosporins are LAME : <i>Listeria</i> , A typicals (<i>Chlamydia</i> , <i>Mycoplasma</i>), MRSA , and E nterococci.
CLINICAL USE	<p>1st generation (cefazolin, cephalexin)—gram \oplus cocci, <i>Proteus mirabilis</i>, <i>E. coli</i>, <i>Klebsiella pneumoniae</i>. Cefazolin used prior to surgery to prevent <i>S. aureus</i> wound infections.</p> <p>2nd generation (cefaclor, cefoxitin, cefuroxime, cefotetan)—gram \oplus cocci, <i>H. influenzae</i>, <i>Enterobacter aerogenes</i>, <i>Neisseria</i> spp., <i>Serratia marcescens</i>, <i>Proteus mirabilis</i>, <i>E. coli</i>, <i>Klebsiella pneumoniae</i>.</p> <p>3rd generation (ceftriaxone, cefpodoxime, ceftazidime, cefixime)—serious gram \ominus infections resistant to other β-lactams.</p> <p>4th generation (cefpipime)—gram \ominus organisms, with \uparrow activity against <i>Pseudomonas</i> and gram \oplus organisms.</p> <p>5th generation (ceftaroline)—broad gram \oplus and gram \ominus organism coverage; unlike 1st–4th generation cephalosporins, ceftaroline covers MRSA, and <i>Enterococcus faecalis</i>—does not cover <i>Pseudomonas</i>.</p>	<p>1st generation—\oplus PEcK.</p> <p>2nd graders wear fake fox fur to tea parties.</p> <p>2nd generation—\oplus HENS PEcK.</p> <p>Can cross blood-brain barrier.</p> <p>Ceftriaxone—meningitis, gonorrhea, disseminated Lyme disease.</p> <p>Ceftazidime for pseudomonaz.</p>
ADVERSE EFFECTS	Hypersensitivity reactions, autoimmune hemolytic anemia, disulfiram-like reaction, vitamin K deficiency. Low rate of cross-reactivity even in penicillin-allergic patients. \uparrow nephrotoxicity of aminoglycosides.	
MECHANISM OF RESISTANCE	Inactivated by cephalosporinases (a type of β -lactamase). Structural change in penicillin-binding proteins (transpeptidases).	

β-lactamase inhibitors	Include Clavulanic acid , Avibactam , Sulbactam , Tazobactam . Often added to penicillin antibiotics to protect the antibiotic from destruction by β -lactamase.	CAST (eg, amoxicillin-clavulanate, ceftazidime-avibactam, ampicillin-sulbactam, piperacillin-tazobactam).
------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------

Carbapenems

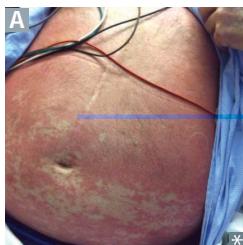
MECHANISM	Imipenem, meropenem, ertapenem.
CLINICAL USE	Gram \oplus cocci, gram \ominus rods, and anaerobes. Wide spectrum and significant adverse effects limit use to life-threatening infections or after other drugs have failed. Meropenem has a \downarrow risk of seizures and is stable to dehydropeptidase I.
ADVERSE EFFECTS	GI distress, rash, and CNS toxicity (seizures) at high plasma levels.
MECHANISM OF RESISTANCE	Inactivated by carbapenemases produced by, eg, <i>K pneumoniae</i> , <i>E coli</i> , <i>E aerogenes</i> .

Aztreonam

MECHANISM	Less susceptible to β -lactamases. Prevents peptidoglycan cross-linking by binding to penicillin-binding protein 3. Synergistic with aminoglycosides. No cross-allergenicity with penicillins.
CLINICAL USE	Gram \ominus rods only—no activity against gram \oplus rods or anaerobes. For penicillin-allergic patients and those with renal insufficiency who cannot tolerate aminoglycosides.
ADVERSE EFFECTS	Usually nontoxic; occasional GI upset.

Vancomycin

MECHANISM	Inhibits cell wall peptidoglycan formation by binding D-Ala-D-Ala portion of cell wall precursors. Bactericidal against most bacteria (bacteriostatic against <i>C difficile</i>). Not susceptible to β -lactamases.
CLINICAL USE	Gram \oplus bugs only—for serious, multidrug-resistant organisms, including MRSA, <i>S epidermidis</i> , sensitive <i>Enterococcus</i> species, and <i>Clostridium difficile</i> (oral route).
ADVERSE EFFECTS	Well tolerated in general but not trouble free: nephrotoxicity, ototoxicity, thrombophlebitis, diffuse flushing (vancomycin infusion reaction A —idiopathic reaction largely preventable by pretreatment with antihistamines and slower infusion rate), DRESS syndrome.
MECHANISM OF RESISTANCE	Occurs in bacteria (eg, <i>Enterococcus</i>) via amino acid modification of D-Ala-D-Ala to D-Ala-D-Lac . “If you Lack a D-Ala (dollar), you can’t ride the van (vancomycin).”



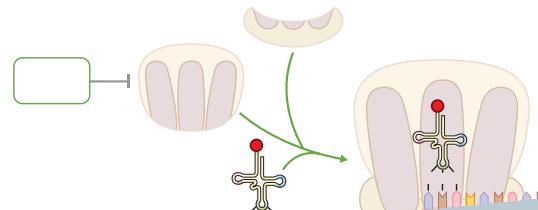
specifically target smaller bacterial ribosome (70S, made of 30S and 50S subunits), leaving human (80S) unaffected.

except aminoglycosides (bactericidal) and linezolid (variable).

"Buy at 30, ccel (sell) at 50."

ors

C
aztreonam
Cefotaxime
Ceftriaxone
Cefuroxime
Ciprofloxacin
Clindamycin
Erythromycin
(macrolides)
Linezolid



toxicity

neuromuscular

2

(especial

ephrotoxicit v
N

Bacterial

Tetracyclines

Tetracycline, doxycycline, minocycline.

MECHANISM	Bacteriostatic; bind to 30S and prevent attachment of aminoacyl-tRNA. Limited CNS penetration. Doxycycline is fecally eliminated and can be used in patients with renal failure. Do not take tetracyclines with milk (Ca^{2+}), antacids (eg, Ca^{2+} or Mg^{2+}), or iron-containing preparations because divalent cations inhibit drugs' absorption in the gut.
CLINICAL USE	<i>Borrelia burgdorferi</i> , <i>M pneumoniae</i> . Drugs' ability to accumulate intracellularly makes them very effective against <i>Rickettsia</i> and <i>Chlamydia</i> . Also used to treat acne. Doxycycline effective against community-acquired MRSA.
ADVERSE EFFECTS	GI distress, discoloration of teeth and inhibition of bone growth in children, photosensitivity. “ Teratocyclines ” are teratogenic ; generally avoided in pregnancy and in children (except doxycycline).
MECHANISM OF RESISTANCE	↓ uptake or ↑ efflux out of bacterial cells by plasmid-encoded transport pumps.

Tigecycline

Tetracycline derivative. Binds to 30S, inhibiting protein synthesis. Generally bacteriostatic.

MECHANISM	Tetracycline derivative. Binds to 30S, inhibiting protein synthesis. Generally bacteriostatic.
CLINICAL USE	Broad-spectrum anaerobic, gram \ominus , and gram \oplus coverage. Multidrug-resistant organisms (eg, MRSA, VRE).
ADVERSE EFFECTS	Nausea, vomiting.

Chloramphenicol

Blocks peptidyltransferase at 50S ribosomal subunit. Bacteriostatic.

MECHANISM	Blocks peptidyltransferase at 50S ribosomal subunit. Bacteriostatic.
CLINICAL USE	Meningitis (<i>Haemophilus influenzae</i> , <i>Neisseria meningitidis</i> , <i>Streptococcus pneumoniae</i>) and rickettsial diseases (eg, Rocky Mountain spotted fever [<i>Rickettsia rickettsii</i>]).
ADVERSE EFFECTS	Limited use due to toxicity but often still used in developing countries because of low cost.
MECHANISM OF RESISTANCE	Anemia (dose dependent), aplastic anemia (dose independent), gray baby syndrome (in premature infants because they lack liver UDP-glucuronosyltransferase).

Clindamycin

Blocks peptide transfer (translocation) at 50S ribosomal subunit. Bacteriostatic.

MECHANISM	Blocks peptide transfer (translocation) at 50S ribosomal subunit. Bacteriostatic.
CLINICAL USE	Anaerobic infections (eg, <i>Bacteroides</i> spp., <i>Clostridium perfringens</i>) in aspiration pneumonia, lung abscesses, and oral infections. Also effective against invasive group A streptococcal infection. Treats anaerobic infections above the diaphragm vs metronidazole (anaerobic infections below diaphragm).
ADVERSE EFFECTS	Pseudomembranous colitis (<i>C difficile</i> overgrowth), fever, diarrhea.

Linezolid

MECHANISM	Inhibits protein synthesis by binding to the 23S rRNA of the 50S ribosomal subunit and preventing formation of the initiation complex.
CLINICAL USE	Gram \oplus species including MRSA and VRE.
ADVERSE EFFECTS	Myelosuppression (especially thrombocytopenia), peripheral neuropathy, serotonin syndrome (due to partial MAO inhibition).
MECHANISM OF RESISTANCE	Point mutation of ribosomal RNA.

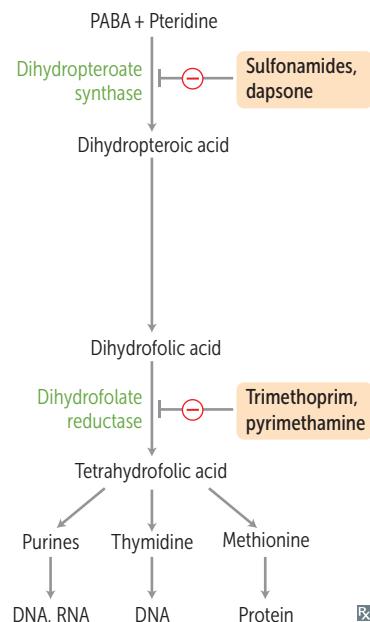
Macrolides

	Azithromycin, clarithromycin, erythromycin.
MECHANISM	Inhibit protein synthesis by blocking translocation (“ macrolides ”); bind to the 50S ribosomal subunit. Bacteriostatic.
CLINICAL USE	Atypical pneumonias (<i>Mycoplasma</i> , <i>Chlamydia</i> , <i>Legionella</i>), STIs (<i>Chlamydia</i>), gram \oplus cocci (streptococcal infections in patients allergic to penicillin), and <i>B pertussis</i> .
ADVERSE EFFECTS	MACRO: Gastrointestinal Motility issues, Arrhythmia caused by prolonged QT interval, acute Cholestatic hepatitis, Rash, eosinophilia. Increases serum concentration of theophylline, oral anticoagulants. Clarithromycin and erythromycin inhibit cytochrome P-450.
MECHANISM OF RESISTANCE	Methylation of 23S rRNA-binding site prevents binding of drug.

Polymyxins

	Colistin (polymyxin E), polymyxin B.
MECHANISM	Cation polypeptides that bind to phospholipids on cell membrane of gram \ominus bacteria. Disrupt cell membrane integrity \rightarrow leakage of cellular components \rightarrow cell death.
CLINICAL USE	Salvage therapy for multidrug-resistant gram \ominus bacteria (eg, <i>P aeruginosa</i> , <i>E coli</i> , <i>K pneumoniae</i>). Polymyxin B is a component of a triple antibiotic ointment used for superficial skin infections.
ADVERSE EFFECTS	Nephrotoxicity, neurotoxicity (eg, slurred speech, weakness, paresthesias), respiratory failure.

Sulfonamides	Sulfamethoxazole (SMX), sulfisoxazole, sulfadiazine.
MECHANISM	Inhibit dihydropteroate synthase, thus inhibiting folate synthesis. Bacteriostatic (bactericidal when combined with trimethoprim).
CLINICAL USE	Gram \oplus , gram \ominus , <i>Nocardia</i> . TMP-SMX for simple UTI.
ADVERSE EFFECTS	Hypersensitivity reactions, hemolysis if G6PD deficient, nephrotoxicity (tubulointerstitial nephritis), photosensitivity, Stevens-Johnson syndrome, kernicterus in infants, displace other drugs from albumin (eg, warfarin).
MECHANISM OF RESISTANCE	Altered enzyme (bacterial dihydropteroate synthase), \downarrow uptake, or \uparrow PABA synthesis.
Dapsone	
MECHANISM	Similar to sulfonamides, but structurally distinct agent.
CLINICAL USE	Leprosy (lepromatous and tuberculoid), <i>Pneumocystis jirovecii</i> prophylaxis, or treatment when used in combination with TMP.
ADVERSE EFFECTS	Hemolysis if G6PD deficient, methemoglobinemia, agranulocytosis.
Trimethoprim	
MECHANISM	Inhibits bacterial dihydrofolate reductase. Bacteriostatic.
CLINICAL USE	Used in combination with sulfonamides (trimethoprim-sulfamethoxazole [TMP-SMX]), causing sequential block of folate synthesis. Combination used for UTIs, <i>Shigella</i> , <i>Salmonella</i> , <i>Pneumocystis jirovecii</i> pneumonia treatment and prophylaxis, toxoplasmosis prophylaxis.
ADVERSE EFFECTS	Hyperkalemia (at high doses; similar mechanism as potassium-sparing diuretics), megaloblastic anemia, leukopenia, granulocytopenia, which may be avoided with coadministration of leucovorin (folinic acid). TMP Treats Marrow Poorly.



Fluoroquinolones

MECHANISM	Ciprofloxacin, ofloxacin; respiratory fluoroquinolones: levofloxacin, moxifloxacin.	
CLINICAL USE	Gram \ominus rods of urinary and GI tracts (including <i>Pseudomonas</i>), some gram \oplus organisms, otitis externa.	
ADVERSE EFFECTS	GI upset, superinfections, skin rashes, headache, dizziness. Less commonly, can cause leg cramps and myalgias. Contraindicated during pregnancy or breastfeeding and in children < 18 years old due to possible damage to cartilage. Some may prolong QT interval.	May cause tendonitis or tendon rupture in people > 60 years old and in patients taking prednisone. Ciprofloxacin inhibits cytochrome P-450. Fluoroquinolones hurt attachments to your bones .
MECHANISM OF RESISTANCE	Chromosome-encoded mutation in DNA gyrase, plasmid-mediated resistance, efflux pumps.	

Daptomycin

MECHANISM	Lipopeptide that disrupts cell membranes of gram \oplus cocci by creating transmembrane channels.	
CLINICAL USE	<i>S aureus</i> skin infections (especially MRSA), bacteremia, infective endocarditis, VRE.	Not used for pneumonia (avidly binds to and is inactivated by surfactant). “Dapto- myo-skin ” is used for skin infections but can cause myopathy .
ADVERSE EFFECTS	Myopathy, rhabdomyolysis.	

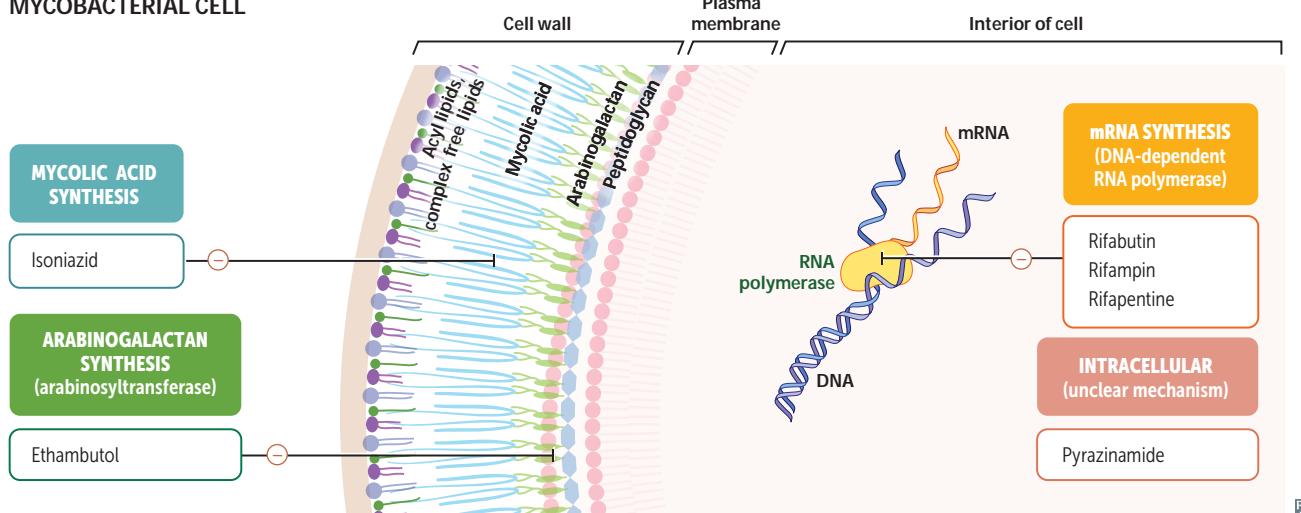
Metronidazole

MECHANISM	Forms toxic free radical metabolites in the bacterial cell that damage DNA. Bactericidal, antiprotozoal.	
CLINICAL USE	Treats <i>Giardia</i> , <i>Entamoeba</i> , <i>Trichomonas</i> , <i>Gardnerella vaginalis</i> , Anaerobes (<i>Bacteroides</i> , <i>C difficile</i>). Can be used in place of amoxicillin in <i>H pylori</i> “triple therapy” in case of penicillin allergy.	GET GAP on the Metro with metronidazole! Treats anaerobic infection below the diaphragm vs clindamycin (anaerobic infections above diaphragm).
ADVERSE EFFECTS	Disulfiram-like reaction (severe flushing, tachycardia, hypotension) with alcohol; headache, metallic taste.	

Antituberculous drugs

DRUG	MECHANISM	ADVERSE EFFECTS	NOTES
Rifamycins Rifampin, rifabutin, rifapentine	Inhibit DNA-dependent RNA polymerase → ↓ mRNA synthesis Rifamycin resistance arises due to mutations in gene encoding RNA polymerase	Minor hepatotoxicity, drug interactions (CYP450 induction), red-orange discoloration of body fluids (nonhazardous adverse effect)	Rifabutin favored over rifampin in patients with HIV infection due to less CYP450 induction Monotherapy rapidly leads to resistance
Isoniazid	Inhibits mycolic acid synthesis → ↓ cell wall synthesis Bacterial catalase-peroxidase (encoded by <i>katG</i>) is needed to convert INH to active form INH resistance arises due to mutations in <i>katG</i>	Vitamin B ₆ deficiency (peripheral neuropathy, sideroblastic anemia), hepatotoxicity, drug interactions (CYP450 inhibition), drug-induced lupus INH overdose can lead to seizures (often refractory to benzodiazepines)	Administer with pyridoxine (vitamin B ₆) INH Injures N eurons and H epatocytes (↑ risk of hepatotoxicity with ↑ age and alcohol overuse) Different INH half-lives in fast vs slow acetylators
Pyrazinamide	Mechanism uncertain	Hepatotoxicity, hyperuricemia	Works best at acidic pH (eg, in host phagolysosomes)
Ethambutol	Inhibits arabinosyltransferase → ↓ arabinogalactan synthesis → ↓ cell wall synthesis	Optic neuropathy (red-green color blindness or ↓ visual acuity, typically reversible)	Pronounce “ e ythambutol”

MYCOBACTERIAL CELL



Antimycobacterial therapy

BACTERIUM	PROPHYLAXIS	TREATMENT
<i>M tuberculosis</i>	Rifamycin-based regimen for 3–4 months	Rifampin, Isoniazid, Pyrazinamide, Ethambutol (RIPE for treatment)
<i>M avium-intracellulare</i>	Azithromycin, rifabutin	Azithromycin or clarithromycin + ethambutol Can add rifabutin or ciprofloxacin
<i>M leprae</i>	N/A	Long-term treatment with dapsone and rifampin for tuberculoid form Add clofazimine for lepromatous form

Antimicrobial prophylaxis

CLINICAL SCENARIO	MEDICATION
Exposure to meningococcal infection	Ceftriaxone, ciprofloxacin, or rifampin
High risk for infective endocarditis and undergoing surgical or dental procedures	Amoxicillin
History of recurrent UTIs	TMP-SMX
Malaria prophylaxis for travelers	Atovaquone-proguanil, mefloquine, doxycycline, primaquine, or chloroquine (for areas with sensitive species)
Pregnant patients carrying group B strep	Intrapartum penicillin G or ampicillin
Prevention of gonococcal conjunctivitis in newborn	Erythromycin ointment on eyes
Prevention of postsurgical infection due to <i>S aureus</i>	Cefazolin; vancomycin if \oplus for MRSA
Prophylaxis of strep pharyngitis in child with prior rheumatic fever	Benzathine penicillin G or oral penicillin V

Prophylaxis in HIV infection/AIDS

CELL COUNT	PROPHYLAXIS	INFECTION
CD4+ < 200 cells/mm ³	TMP-SMX	<i>Pneumocystis</i> pneumonia
CD4+ < 100 cells/mm ³	TMP-SMX	<i>Pneumocystis</i> pneumonia and toxoplasmosis

Antifungal therapy

Azoles

MECHANISM	Inhibit fungal sterol (ergosterol) synthesis by inhibiting the cytochrome P-450 enzyme that converts lanosterol to ergosterol.
CLINICAL USE	Local and less serious systemic mycoses. Fluconazole for chronic suppression of cryptococcal meningitis in people living with HIV and candidal infections of all types. Itraconazole may be used for <i>Blastomyces</i> , <i>Coccidioides</i> , <i>Histoplasma</i> , <i>Sporothrix schenckii</i> . Clotrimazole and miconazole for topical fungal infections. Voriconazole for <i>Aspergillus</i> and some <i>Candida</i> . Isavuconazole for serious <i>Aspergillus</i> and <i>Mucor</i> infections.
ADVERSE EFFECTS	Testosterone synthesis inhibition (gynecomastia, especially with ketoconazole), liver dysfunction (inhibits cytochrome P-450), QT interval prolongation.

Terbinafine

MECHANISM	Inhibits the fungal enzyme squalene epoxidase.
CLINICAL USE	Dermatophytoses (especially onychomycosis—fungal infection of finger or toe nails).
ADVERSE EFFECTS	GI upset, headaches, hepatotoxicity, taste disturbance.

Echinocandins

MECHANISM	Anidulafungin, caspofungin, micafungin.
CLINICAL USE	Inhibit cell wall synthesis by inhibiting synthesis of β-glucan.
ADVERSE EFFECTS	Invasive aspergillosis, <i>Candida</i> .
ADVERSE EFFECTS	GI upset, flushing (by histamine release).

Griseofulvin

MECHANISM	Interferes with microtubule function; disrupts mitosis. Deposits in keratin-containing tissues (eg, nails).
CLINICAL USE	Oral treatment of superficial infections; inhibits growth of dermatophytes (tinea, ringworm).
ADVERSE EFFECTS	Teratogenic, carcinogenic, confusion, headaches, disulfiram-like reaction, ↑ cytochrome P-450 and warfarin metabolism.

Antiprotozoal therapy

Pyrimethamine-sulfadiazine (toxoplasmosis), suramin and melarsoprol (*Trypanosoma brucei*), nifurtimox (*T cruzi*), sodium stibogluconate (leishmaniasis).

Anti-mite/louse therapy

Permethrin, malathion (acetylcholinesterase inhibitor), topical or oral ivermectin. Used to treat scabies (*Sarcoptes scabiei*) and lice (*Pediculus* and *Pthirus*).

Chloroquine

MECHANISM	Blocks detoxification of heme into hemozoin. Heme accumulates and is toxic to plasmodia.
CLINICAL USE	Treatment of plasmodial species other than <i>P falciparum</i> (due to drug resistance from membrane pump that ↓ intracellular concentration of drug).
ADVERSE EFFECTS	Retinopathy (dependent on cumulative dose); pruritus (especially in dark-skinned individuals).

Remdesivir

MECHANISM	Prodrug of an ATP analog. The active metabolite inhibits viral RNA-dependent RNA polymerase and evades proofreading by viral exoribonuclease (ExoN) → ↓ viral RNA production.
CLINICAL USE	Recently approved for treatment of COVID-19 requiring hospitalization.

Acyclovir, famciclovir, valacyclovir

MECHANISM	Guanosine analogs. Monophosphorylated by HSV/VZV thymidine kinase and not phosphorylated in uninfected cells → few adverse effects. Triphosphate formed by cellular enzymes. Preferentially inhibit viral DNA polymerase by chain termination.
CLINICAL USE	No activity against CMV because CMV lacks the thymidine kinase necessary to activate guanosine analogs. Used for HSV-induced mucocutaneous and genital lesions as well as for encephalitis. Prophylaxis in patients who are immunocompromised. Also used as prophylaxis for immunocompetent patients with severe or recurrent infection. No effect on latent forms of HSV and VZV. Valacyclovir, a prodrug of acyclovir, has better oral bioavailability. For herpes zoster, use famciclovir.
ADVERSE EFFECTS	Obstructive crystalline nephropathy and acute kidney injury if not adequately hydrated.
MECHANISM OF RESISTANCE	Mutated viral thymidine kinase.

Ganciclovir

MECHANISM	Guanosine analog. 5'-monophosphate formed by a CMV viral kinase. Triphosphate formed by cellular kinases. Preferentially inhibits viral DNA polymerase.
CLINICAL USE	CMV, especially in patients who are immunocompromised. Valganciclovir, a prodrug of ganciclovir, has better oral bioavailability.
ADVERSE EFFECTS	Myelosuppression (leukopenia, neutropenia, thrombocytopenia), renal toxicity. More toxic to host enzymes than acyclovir.
MECHANISM OF RESISTANCE	Mutated viral kinase.

Foscarnet

MECHANISM	Viral DNA/RNA polymerase inhibitor and HIV reverse transcriptase inhibitor. Binds to pyrophosphate-binding site of enzyme. Does not require any kinase activation.	Foscarnet = pyro foscarnet analog.
CLINICAL USE	CMV retinitis in immunocompromised patients when ganciclovir fails; acyclovir-resistant HSV.	
ADVERSE EFFECTS	Nephrotoxicity, multiple electrolyte abnormalities can lead to seizures.	
MECHANISM OF RESISTANCE	Mutated DNA polymerase.	

Cidofovir

MECHANISM	Preferentially inhibits viral DNA polymerase. Does not require phosphorylation by viral kinase.
CLINICAL USE	CMV retinitis in immunocompromised patients. Long half-life.
ADVERSE EFFECTS	Nephrotoxicity (coadminister cidofovir with probenecid and IV saline to ↓ toxicity).

HIV therapy

Antiretroviral therapy (ART): often initiated at the time of HIV diagnosis. Strongest indication for use with patients presenting with AIDS-defining illness, low CD4+ cell counts (< 500 cells/mm³), or high viral load. Regimen consists of 3 drugs to prevent resistance: 2 NRTIs and preferably an integrase inhibitor. Most ARTs are active against both HIV-1 and HIV-2 (exceptions: NNRTIs and enfuvirtide not effective against HIV-2). Tenofovir + emtricitabine can be administered as pre-exposure prophylaxis.

DRUG	MECHANISM	ADVERSE EFFECTS
NRTIs		
Abacavir (ABC)	Competitively inhibit nucleotide binding to reverse transcriptase and terminate the DNA chain (lack a 3' OH group).	Myelosuppression (can be reversed with granulocyte colony-stimulating factor [G-CSF] and erythropoietin), nephrotoxicity.
Emtricitabine (FTC)	Tenofovir is a nucleotide; the others are nucleosides. All need to be phosphorylated to be active.	Abacavir contraindicated if patient has HLA-B*5701 mutation due to ↑ risk of hypersensitivity.
Lamivudine (3TC)	ZDV can be used for general prophylaxis and during pregnancy to ↓ risk of fetal transmission.	
Tenofovir (TDF)		
Zidovudine (ZDV, formerly AZT)	Have you dined (vudine) with my nuclear (nucleosides) family?	
NNRTIs		
Doravirine	Bind to reverse transcriptase at site different from NRTIs. Do not require phosphorylation to be active or compete with nucleotides.	Rash and hepatotoxicity are common to all NNRTIs. Vivid dreams and CNS symptoms are common with efavirenz.
Efavirenz		
Rilpivirine		
Integrase strand transfer inhibitors		
Bictegravir	Also called integrase inhibitors. Inhibit HIV genome integration into host cell chromosome by reversibly inhibiting HIV integrase.	↑ creatine kinase, weight gain.
Dolutegravir		
Protease inhibitors		
Atazanavir	Prevents maturation of new virions. Maturation depends on HIV-1 protease (<i>pol</i> gene), which cleaves the polypeptide products of HIV mRNA into their functional parts. Thus, protease inhibitors prevent maturation of new viruses.	Hyperglycemia, GI intolerance (nausea, diarrhea).
Darunavir		Rifampin (potent CYP/UGT inducer) ↓ protease inhibitor concentrations; use rifabutin instead.
Lopinavir		Ritonavir (cytochrome P-450 inhibitor) is only used as a boosting agent.
Ritonavir	All protease inhibitors require boosting with either ritonavir or cobicistat. Navir (never) tease a protease.	
Entry inhibitors		
Enfuvirtide	Binds gp41, inhibiting viral entry. Enfuvirtide inhibits fusion.	Skin reaction at injection sites.
Maraviroc	Binds CCR-5 on surface of T cells/monocytes, inhibiting interaction with gp120. Maraviroc inhibits docking.	

Hepatitis C therapy Chronic HCV infection treated with multidrug therapy that targets specific steps within HCV replication cycle (HCV-encoded proteins). Examples of drugs are provided.

DRUG	MECHANISM	TOXICITY
NS5A inhibitors		
Elbasvir	Inhibits NS5A, a viral phosphoprotein that plays a key role in RNA replication	Headache, diarrhea
Ledipasvir		
Pibrentasvir	Exact mechanism unknown	
Velpatasvir		
NS5B inhibitors		
Sofosbuvir	Inhibits NS5B, an RNA-dependent RNA polymerase acting as a chain terminator Prevents viral RNA replication	Fatigue, headache
NS3/4A inhibitors		
Glecaprevir	Inhibits NS3/4A, a viral protease, preventing viral replication	Headache, fatigue
Grazoprevir		
Alternative drugs		
Ribavirin	Inhibits synthesis of guanine nucleotides by competitively inhibiting IMP dehydrogenase	Hemolytic anemia, severe teratogen

Disinfection and sterilization Goals include the reduction of pathogenic organism counts to safe levels (disinfection) and the inactivation of all microbes including spores (sterilization).

Autoclave ^a	Pressurized steam at > 120°C. May not reliably inactivate prions.
Alcohols	Denature proteins and disrupt cell membranes.
Chlorhexidine	Disrupts cell membranes and coagulates intracellular components.
Chlorine ^a	Oxidizes and denatures proteins.
Ethylene oxide ^a	Alkylating agent.
Hydrogen peroxide ^a	Free radical oxidation.
Iodine and iodophors	Halogenation of DNA, RNA, and proteins. May be sporicidal.
Quaternary amines	Impair permeability of cell membranes.

^aSporicidal.

Antimicrobials to avoid in pregnancy

ANTIMICROBIAL	ADVERSE EFFECT
Sulfonamides	Kernicterus
Aminoglycosides	Ototoxicity
Fluoroquinolones	Cartilage damage
Clarithromycin	Embryotoxic
Tetracyclines	Discolored teeth, inhibition of bone growth
Ribavirin	Teratogenic
Griseofulvin	Teratogenic
Chloramphenicol	Gray baby syndrome

Safe children take really good care.