

Infectology Database

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Tropical Diseases

Dengue Fever

Pathogen: Virus - Dengue virus (DENV 1-4) (RNA, Flaviviridae)

Epidemiology:

- Incidence: 390 million infections/year worldwide
- Seasonality: Rainy season
- Transmission: Aedes aegypti/albopictus mosquito bite
- Risk Groups: Tropical travelers, People living in endemic areas

Pathomechanism:

Steps:

- Mosquito bite
- Virus replication in dendritic cells/monocytes
- Viremia
- Antibody-dependent enhancement (ADE) in secondary infection (more severe course)
- Cytokine storm, capillary leakage

Virulence Factors:

- NS1 protein
- ADE

Clinical Features:

- Incubation: 4-10 days
- Onset: Sudden

Symptoms:

- **Fever:** High, sudden (>99% in symptomatic cases)
- **Breakbone fever:** Severe muscle and joint pain (>90%)
- **Headache/Retroorbital pain:** Pain behind the eyes (>90%)
- **Rash:** Maculopapular (50-80%), appears after fever
- **Nausea/Vomiting:** Can be a common warning sign

Physical Exam:

- Fever
- Rash ("white islands in a red sea")

- Tourniquet test positive (capillary fragility)
- Hepatomegaly
- Warning signs: abdominal pain, persistent vomiting, fluid accumulation

Complications:

- Dengue hemorrhagic fever (DHF)
- Dengue shock syndrome (DSS)
- Severe bleeding

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukopenia, thrombocytopenia	Characteristic
Hematocrit	Elevated	Hemoconcentration (leakage)

Microbiology:

- **NS1 antigen:** Positive (*Early phase (1-5 days)*)
- **PCR:** RNA (*Early phase*)
- **IgM/IgG:** Positive (*Late phase (>5 days)*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Fluids, antipyretics (Paracetamol). NSAIDs CONTRAINDICATED (bleeding risk)!

Targeted:

No specific antiviral agent.

Supportive:

- Fluid replacement (critical!)
- Blood products (in severe bleeding)

Prevention:

- Mosquito repellent
- Vaccine (Qdenga)

Zika Virus

Pathogen: Virus - Zika virus (ZIKV) (RNA, Flaviviridae)

Epidemiology:

- Incidence: Epidemic
- Seasonality: Mosquito season

- Transmission: Aedes mosquito, sexual, vertical
- Risk Groups: Pregnant women (fetal damage!), Travelers

Pathomechanism:

Steps:

- Entry via mosquito bite/sexual route
- Replication
- Viremia
- Neurotropism (adult: GBS, fetus: microcephaly)

Virulence Factors:

- Neurotropism

Clinical Features:

- Incubation: 3-14 days
- Onset: Mild

Symptoms:

- **Asymptomatic:** 80% of cases are asymptomatic
- **Rash:** Maculopapular, itchy (>90% in symptomatic cases)
- **Fever:** Low (65%), often absent
- **Arthralgia:** Small joints (65%), with edema
- **Conjunctivitis:** Non-purulent (55%)

Physical Exam:

- Rash
- Conjunctivitis
- Fever

Complications:

- Guillain-Barré syndrome
- Congenital Zika syndrome (microcephaly)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Mild leukopenia/thrombocytopenia	-

Microbiology:

- **PCR:** RNA (blood, urine) (*Diagnostic (excreted longer in urine)*)
- **IgM:** Positive (*Cross-reaction with Dengue possible!*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Rest, fluids

Targeted:

None.

Supportive:

- Symptomatic treatment

Prevention:

- Mosquito protection
- Safe sex (can be excreted in semen for months)
- Pregnant women should avoid endemic areas

Chikungunya

Pathogen: Virus - Chikungunya virus (CHIKV) (RNA, Togaviridae)

Epidemiology:

- Incidence: Epidemic
- Seasonality: Mosquito season
- Transmission: Aedes mosquito
- Risk Groups: Travelers

Pathomechanism:**Steps:**

- Mosquito bite
- Replication in fibroblasts
- Joint tropism
- Chronic inflammation

Virulence Factors:

- -

Clinical Features:

- Incubation: 3-7 days
- Onset: Sudden

Symptoms:

- **Fever and joint pain:** Sudden high fever and severe, symmetrical polyarthralgia (>95%)
- **Rash:** Maculopapular rash (50-75%)
- **Other symptoms:** Headache, myalgia, nausea

Physical Exam:

- Symmetrical polyarthritis/tenosynovitis (hand, wrist, ankle)
- Fever
- Maculopapular rash

Complications:

- Chronic, persistent arthritis (30-60%, mainly in elderly)

- Rarely: myocarditis, encephalitis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Lymphopenia	-

Microbiology:

- **PCR:** RNA (*Acute phase (< 1 week)*)
- **IgM/IgG:** Positive (*Later*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	NSAIDs can be given (if Dengue excluded!)

Targeted:

None.

Supportive:

- Pain relief (NSAIDs, steroids in chronic cases)
- Physiotherapy

Prevention:

- Mosquito protection
- Vaccine (Ixchiq - FDA approved)

Gastrointestinal Infections

Clostridioides difficile Infection

Pathogen: Bacterium - Clostridioides difficile (Gram-positive)

Epidemiology:

- Incidence: Most common cause of nosocomial diarrhea, 500,000 cases/year in the USA
- Seasonality: None
- Transmission: Fecal-oral (spores), nosocomial transmission, hand hygiene!
- Risk Groups: Elderly >65 years, Hospitalized patients, Antibiotic exposure, PPI use, Inflammatory bowel disease, Immunosuppressed

Pathomechanism:

Steps:

- Antibiotic → gut flora disruption
- C. difficile spore germination, colonization

- Toxin A (TcdA): enterotoxin – fluid secretion, inflammation
- Toxin B (TcdB): cytotoxin → epithelial damage
- Binary toxin (CDT): in hypervirulent strains (027/078)
- Pseudomembrane formation in the colon

Virulence Factors:

- Toxin A (TcdA)
- Toxin B (TcdB)
- Binary toxin (CDT)
- Spore formation
- Adherence factors

Clinical Features:

- Incubation: 2-10 days after AB, up to 8 weeks later
- Onset: Acute

Symptoms:

- **Watery diarrhea:** 3-15x/day, greenish, foul-smelling
- **Abdominal pain/cramps:** Diffuse, crampy
- **Fever:** Moderate-high
- **Nausea:** Variable
- **Anorexia:** Loss of appetite

Physical Exam:

- Diffuse abdominal tenderness
- Distension
- Fever, tachycardia
- Signs of dehydration
- Severe: signs of ileus, toxic megacolon

Complications:

- Fulminant colitis
- Toxic megacolon
- Bowel perforation
- Sepsis
- Hypovolemic shock
- Death
- Recurrence (20-30%)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (up to >30 G/L)	Marker of severity
Creatinine	Elevated	Severe CDI criterion (>1.5x baseline)

Albumin	Decreased (<2.5 g/dL)	Malnutrition, severity
Lactate	Elevated	Fulminant colitis

Imaging:

- **Abdominal X-ray:** Megacolon (>6cm) (*Toxic megacolon*)
- **Abdominal CT:** Colonic wall thickening, accordion sign, ascites (*Severity assessment*)

Microbiology:

- **Stool toxin (GDH + toxin A/B EIA):** Positive (*Two-step algorithm*)
- **Stool PCR (NAAT):** tcdB gene (*Most sensitive, but also detects colonization*)
- **Culture:** C. difficile isolation (*Typing, epidemiology*)
- **Sigmoidoscopy:** Pseudomembranes (*Not routine, diagnostic*)

Differential Diagnosis:

- **Other AB-associated diarrhea:** Toxin negative, milder
- **Inflammatory bowel disease flare:** History, endoscopy
- **Ischemic colitis:** Risk factors, CT angiography
- **Other infectious enterocolitis:** Stool culture, epidemiology

Therapy:**Outpatient:**

Drug	Dose	Note
Fidaxomicin	2x200mg PO	First choice (less recurrence)
Vancomycin	4x125mg PO	Alternative

Inpatient:

Drug	Dose	Note
Vancomycin	4x125mg PO	If fidaxomicin is not available
Fidaxomicin	2x200mg PO	Preferred

Icu:

Drug	Dose	Note
Vancomycin	4x500mg PO + rectal	Fulminant: higher dose
+ Metronidazole	3x500mg IV	In case of ileus (IV penetration)
Surgery	Colectomy	Toxic megacolon, perforation

Targeted:

Non-severe: Vancomycin or Fidaxomicin; Severe: Vancomycin; Fulminant: Vancomycin+Metronidazole±surgery

Supportive:

- Stop AB (if possible)
- Fluid replacement

- Electrolyte correction
- NO antimotility agents!
- Contact isolation

Prevention:

- Antibiotic stewardship
- Hand washing (alcohol does not kill spores!)
- Contact isolation
- Bezlotoxumab (recurrence prevention)
- FMT in recurrent cases

Salmonellosis (Non-typhoidal)

Pathogen: Bacterium - *Salmonella enterica* (e.g., *Enteritidis*, *Typhimurium*) (Gram-negative)

Epidemiology:

- Incidence: Common food poisoning (more common in summer)
- Seasonality: Summer-autumn
- Transmission: Fecal-oral: contaminated food (eggs, poultry, meat), contact with reptiles
- Risk Groups: Infants, Elderly, Achlorhydria (PPI), Immunosuppressed

Pathomechanism:

Steps:

- Ingestion (high bacterial load required, except in achlorhydria)
- Invasion through M-cells in the small intestine (Peyer's patches)
- Neutrophil infiltration, inflammation, fluid secretion

Virulence Factors:

- Type III secretion system (T3SS)
- Enterotoxin

Clinical Features:

- Incubation: 6-72 hours (average 12-36 hours)
- Onset: Sudden

Symptoms:

- **Diarrhea:** Watery, rarely bloody, foul-smelling
- **Fever:** Common (38-39°C)
- **Abdominal cramps:** Diffuse or periumbilical
- **Nausea, vomiting:** Often precedes diarrhea

Physical Exam:

- Fever
- Abdominal tenderness
- Signs of dehydration

Complications:

- Bacteremia (5%, mainly elderly/immunosuppressed)
- Septic arthritis
- Osteomyelitis (sickle cell anemia)
- Endovascular infection (aneurysm)

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
Inflammatory markers	CRP elevated	Bacterial origin

Microbiology:

- **Stool culture:** *Salmonella* sp. (*Diagnostic*)

Therapy:**Outpatient:**

Drug	Dose	Note
Supportive	-	Healthy adults do NOT need antibiotics (causes prolonged carriage!)

Inpatient:

Drug	Dose	Note
Ceftriaxone	1-2g IV	In severe/invasive cases
Ciprofloxacin	2x500mg PO	Alternative (if susceptible)

Targeted:

Only in risk groups (infant, elderly, immunosuppressed) or severe cases: Fluoroquinolone or Ceftriaxone.

Supportive:

- Fluid replacement (ORS)
- Probiotics

Prevention:

- Food hygiene
- Thorough cooking of eggs/meat

Shigellosis (Dysentery)

Pathogen: Bacterium - *Shigella* (*dysenteriae*, *flexneri*, *sonnei*) (Gram-negative)

Epidemiology:

- Incidence: Common worldwide, endemic in developing countries

- Transmission: Fecal-oral (person-to-person), very low infectious dose (10-100 bacteria)!
- Risk Groups: Children (daycare, kindergarten), Travelers, MSM

Pathomechanism:

Steps:

- Invasion of colonic epithelium
- Intercellular spread (actin polymerization)
- Shiga toxin (*S. dysenteriae*): protein synthesis inhibition, HUS
- Mucosal ulceration, inflammation

Virulence Factors:

- Shiga toxin (Stx)
- Invasion plasmid antigens

Clinical Features:

- Incubation: 1-3 days
- Onset: Sudden

Symptoms:

- **Dysentery:** Bloody, mucoid, purulent stool
- **Tenesmus:** Painful urge to defecate without passage
- **High fever:** Common, toxic state
- **Abdominal cramps:** Left lower quadrant dominance

Complications:

- Hemolytic uremic syndrome (HUS - *S. dysenteriae*)
- Toxic megacolon
- Rectal prolapse
- Reactive arthritis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis, left shift	Invasive infection

Microbiology:

- **Stool culture:** *Shigella* sp. (*Diagnostic*)

Therapy:

Outpatient:

Drug	Dose	Note
Azithromycin	1x500mg PO	First choice
Ciprofloxacin	2x500mg PO	Alternative (resistance increasing)

Targeted:

Antibiotics recommended to shorten illness and reduce infectivity. Azithromycin, Ceftriaxone, Ciprofloxacin.

Supportive:

- Fluid replacement
- Antimotility agents (Loperamide) are FORBIDDEN!

Prevention:

- Strict hand hygiene
- Patient isolation

Campylobacteriosis

Pathogen: Bacterium - *Campylobacter jejuni* (Gram-negative)

Epidemiology:

- Incidence: Most common bacterial gastroenteritis in the developed world
- Seasonality: Summer
- Transmission: Contaminated poultry (undercooked), raw milk, water
- Risk Groups: Infants, Young adults, Elderly

Pathomechanism:

Steps:

- Ingestion (low infectious dose)
- Colonization of jejunum/ileum/colon
- Invasion of epithelial cells
- Toxin production (cytotoxic distending toxin)
- Inflammatory response, bloody diarrhea

Virulence Factors:

- Flagellum (motility)
- Adhesins
- Cytotoxic distending toxin (CDT)

Clinical Features:

- Incubation: 2-5 days
- Onset: Sudden

Symptoms:

- **Diarrhea:** Watery, often bloody
- **Abdominal pain:** Severe, crampy (pseudoappendicitis)
- **Fever:** Can be a prodromal symptom

Physical Exam:

- Diffuse abdominal tenderness
- Fever

- Signs of dehydration

Complications:

- Guillain-Barré syndrome (GBS) - 1/1000 cases
- Reactive arthritis
- Erythema nodosum

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis	Inflammation
Stool	Leukocytes, RBCs	Invasive
CRP	Elevated	Bacterial origin

Microbiology:

- **Stool culture:** Campylobacter (special medium, 42°C) (*Diagnostic*)

Therapy:

Outpatient:

Drug	Dose	Note
Azithromycin	1x500mg PO	First choice in severe cases

Targeted:

Mild cases only fluid replacement. Severe cases: macrolides (Azithromycin). Fluoroquinolone resistance is high!

Supportive:

- Fluid replacement

Prevention:

- Proper cooking of poultry
- Avoid cross-contamination in the kitchen

E. coli enteritis (ETEC, EHEC)

Pathogen: Bacterium - Escherichia coli (pathogenic strains) (Gram-negative)

Epidemiology:

- Incidence: ETEC: traveler's diarrhea; EHEC: foodborne outbreaks
- Seasonality: Summer
- Transmission: Fecal-oral, contaminated water/food (beef, vegetables)
- Risk Groups: Travelers (ETEC), Children, elderly (EHEC)

Pathomechanism:

Steps:

- ETEC: Enterotoxins (LT/ST) → fluid secretion (cholera-like)
- EHEC (STEC): Shiga-toxin production → intestinal wall damage, systemic absorption → renal endothelial damage (HUS)

Virulence Factors:

- Enterotoxins
- Shiga-toxin (Stx1, Stx2)
- Adhesins

Clinical Features:

- Incubation: ETEC: 1-3 days; EHEC: 3-4 days
- Onset: Sudden

Symptoms:

- **ETEC: Watery diarrhea:** No fever, "Traveler's diarrhea"
- **EHEC: Bloody diarrhea:** Fever absent or low, severe abdominal cramps

Physical Exam:

- Dehydration
- Abdominal tenderness (EHEC: severe)
- Absence of fever (EHEC)

Complications:

- Hemolytic uremic syndrome (HUS) - 5-10% after EHEC infection (mainly children)
- TTP (adults)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Thrombocytopenia, anemia	Suspicion of HUS!
Renal function	Creatinine elevation	HUS

Microbiology:

- **Stool culture:** Sorbitol-MacConkey (E. coli O157:H7) (*EHEC screening*)
- **Shiga-toxin detection:** PCR or EIA (*Rapid diagnosis*)

Therapy:

Outpatient:

Drug	Dose	Note
ETEC: Rifaximin	2x200mg PO	Traveler's diarrhea
EHEC: ANTIBIOTICS CONTRAINDICATED!	-	Increases risk of HUS (toxin release)!

Targeted:

ETEC: Ciprofloxacin or Azithromycin (in severe cases). EHEC: ONLY supportive!

Supportive:

- Fluid replacement
- In HUS: dialysis, transfusion

Prevention:

- Food hygiene
- Thorough cooking of beef
- Travelers: bottled water

Yersiniosis

Pathogen: Bacterium - *Yersinia enterocolitica* (Gram-negative)

Epidemiology:

- Incidence: More common in temperate climates, in winter
- Seasonality: Winter
- Transmission: Raw pork, milk, contaminated water. Psychrophilic (grows in refrigerator!)
- Risk Groups: Children, Iron overload patients (hemochromatosis)

Pathomechanism:

Steps:

- Invasion through M-cells (ileum)
- Colonization of Peyer's patches
- Spread to mesenteric lymph nodes
- Formation of microabscesses
- Reactive immune response (arthritis)

Virulence Factors:

- *Yersinia* outer proteins (Yops)
- T3SS
- Invasin

Clinical Features:

- Incubation: 4-7 days
- Onset: Gradual

Symptoms:

- **Enterocolitis:** Fever, diarrhea (can be bloody)
- **Pseudoappendicitis:** Right lower quadrant pain (mesenteric lymphadenitis)
- **Pharyngitis:** Occurs in adults

Physical Exam:

- Right lower quadrant tenderness
- Fever
- Erythema nodosum (late)

Complications:

- Reactive arthritis (HLA-B27)
- Erythema nodosum
- Sepsis (in iron overload patients)

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
Inflammatory markers	Elevated	Bacterial

Imaging:

- **Abdominal US:** Mesenteric lymphadenopathy, terminal ileitis (*Exclusion of appendicitis*)

Microbiology:

- **Stool culture:** CIN agar (cold enrichment) (*Must be requested from the lab*)

Therapy:**Outpatient:**

Drug	Dose	Note
Supportive	-	Usually self-limiting

Inpatient:

Drug	Dose	Note
Ciprofloxacin	2x500mg PO	In severe cases
Doxycycline	2x100mg PO	Alternative

Targeted:

Fluoroquinolones, Doxycycline, TMP-SMX. Sepsis: Ceftriaxone.

Prevention:

- Avoid raw pork
- Pasteurization of milk

Giardiasis

Pathogen: Protozoan - Giardia duodenalis (lamblia) (-)

Epidemiology:

- Incidence: Widespread worldwide, most common parasitic intestinal infection
- Seasonality: Summer-autumn
- Transmission: Fecal-oral (cysts), water (chlorine-resistant!), food
- Risk Groups: Children, Campers (stream water), IgA deficient individuals

Pathomechanism:**Steps:**

- Cyst ingestion
- Excystation in the duodenum
- Trophozoite attachment to villi (sucking disc)
- Malabsorption, disaccharidase deficiency

Clinical Features:

- Incubation: 1-3 weeks
- Onset: Gradual

Symptoms:

- **Diarrhea:** Foul-smelling, greasy (steatorrhea), non-bloody
- **Bloating, gas:** Severe meteorism, sulfurous burps
- **Weight loss:** Due to malabsorption
- **Lactose intolerance:** Secondary, may persist after infection

Physical Exam:

- Meteorism
- Diffuse abdominal tenderness
- No fever

Complications:

- Chronic diarrhea
- Malabsorption (vitamin deficiency)
- Failure to thrive (children)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Normal, NO eosinophilia	Non-invasive parasite

Microbiology:

- **Stool parasite exam:** Cysts or trophozoites (*3 samples needed (intermittent shedding)*)
- **Stool antigen (EIA):** Positive (*More sensitive than microscopy*)

Therapy:

Outpatient:

Drug	Dose	Note
Metronidazole	3x250mg PO	First choice
Tinidazole	2g PO	More convenient

Targeted:

Nitroimidazoles (Metronidazole, Tinidazole). In pregnancy: Paromomycin.

Prevention:

- Boil/filter water (chlorine is not enough!)

- Hand washing

Amoebiasis

Pathogen: Protozoan - Entamoeba histolytica (-)

Epidemiology:

- Incidence: Endemic in tropical/subtropical areas
- Seasonality: None
- Transmission: Fecal-oral (cysts)
- Risk Groups: Travelers, Immigrants, Institutionalized individuals, MSM

Pathomechanism:

Steps:

- Cyst ingestion
- Trophozoite invasion of colonic mucosa
- Tissue lysis (histolytic enzymes)
- Ulcer formation (flask-shaped)
- Hematogenous spread (liver)

Clinical Features:

- Incubation: 2-4 weeks
- Onset: Gradual

Symptoms:

- **Amoebic dysentery:** Bloody, mucoid diarrhea, abdominal pain
- **Amoebic liver abscess:** Right upper quadrant pain, fever, weight loss (even without diarrheal!)

Physical Exam:

- Abdominal tenderness (cecum/colon)
- Hepatomegaly, liver percussion tenderness (abscess)

Complications:

- Bowel perforation
- Toxic megacolon
- Abscess rupture (pleura, peritoneum, pericardium)
- Brain abscess

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (in abscess)	Inflammation
Liver enzymes	ALP elevated	Abscess

Imaging:

- **Abdominal US/CT:** Solitary liver abscess (right lobe) (*Liver abscess diagnosis*)

Microbiology:

- **Stool parasite exam:** Trophozoites (with RBCs in cytoplasm!) (*Must be distinguished from E. dispar*)
- **Stool antigen/PCR:** E. histolytica specific (*Gold standard*)
- **Serology:** Positive (*Useful in invasive disease (liver abscess)*)

Therapy:**Outpatient:**

Drug	Dose	Note
Metronidazole	3x750mg PO	Tissue agent (invasive)
+ Paromomycin	3x500mg PO	Luminal agent (against cyst shedding) - MANDATORY addition!

Targeted:

Metronidazole (tissue) + Paromomycin/Diloxanide (luminal). Liver abscess: Metronidazole + drainage if needed.

Prevention:

- Water and food hygiene

Cryptosporidiosis

Pathogen: Protozoan - Cryptosporidium hominis/parvum (Acid-fast stain)

Epidemiology:

- Incidence: Common waterborne outbreaks (swimming pools)
- Seasonality: Summer-autumn
- Transmission: Fecal-oral, water (chlorine-resistant oocysts!)
- Risk Groups: AIDS patients (defining opportunist), Children, Veterinarians

Pathomechanism:Steps:

- Oocyst ingestion
- Sporozoite release
- Attachment to apical surface of epithelial cells (intracellular, but extracytoplasmic)
- Villus atrophy, crypt hyperplasia
- Malabsorption, secretory diarrhea

Virulence Factors:

- Adhesins
- Proteases

Clinical Features:

- Incubation: 7-10 days
- Onset: Sudden

Symptoms:

- **Watery diarrhea:** Profuse, can be cholera-like
- **Abdominal cramps, nausea:** General symptoms
- **Persistent diarrhea:** Can last for weeks/months in immunosuppressed, life-threatening

Physical Exam:

- Signs of dehydration
- Cachexia (in chronic cases)

Complications:

- Severe dehydration
- Malnutrition
- Biliary tract involvement (AIDS)

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CD4 count	<100/ μ L	Risk of severe course (HIV)

Microbiology:

- **Stool stain:** Acid-fast oocysts (modified Z-N) (*On special request*)
- **Stool antigen/PCR:** Positive (*More sensitive*)

Therapy:**Outpatient:**

Drug	Dose	Note
Nitazoxanide	2x500mg PO	For immunocompetent
ART (Antiretroviral therapy)	-	Restoring the immune system is key in HIV patients!

Targeted:

Immunocompetent: Nitazoxanide. Immunosuppressed: ART optimization, supportive, Nitazoxanide (less effective).

Supportive:

- Fluid replacement
- Antimotility agents (with caution)

Prevention:

- Water filtration (<1 micron), avoid swimming pools during diarrhea

Viral Gastroenteritis

Pathogen: Virus - Rotavirus, Norovirus, Adenovirus, Astrovirus (RNA/DNA)

Epidemiology:

- Incidence: Norovirus: most common epidemic GE (all ages); Rotavirus: infants (before vaccine)
- Seasonality: Winter (Rota, Noro)
- Transmission: Fecal-oral, aerosol (vomiting - Noro), fomites
- Risk Groups: Infants (Rota), Elderly (Noro), Closed communities (ships, barracks)

Pathomechanism:

Steps:

- Virus replication in small intestine villus epithelium
- Villus atrophy, reduced absorption surface
- Disaccharidase deficiency (lactose intolerance)
- Osmotic diarrhea
- NSP4 enterotoxin (Rotavirus)

Virulence Factors:

- Capsid stability
- NSP4 (Rota)

Clinical Features:

- Incubation: 12-48 hours (Noro), 1-3 days (Rota)
- Onset: Sudden

Symptoms:

- **Vomiting:** Dominant in Norovirus ("winter vomiting disease")
- **Watery diarrhea:** Non-bloody
- **Fever:** Mild or absent
- **Myalgia, headache:** Viral symptoms

Physical Exam:

- Signs of dehydration (dry tongue, decreased turgor)
- Diffuse abdominal tenderness

Complications:

- Severe dehydration (infants, elderly)
- Electrolyte imbalances

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Electrolytes	Imbalances	Dehydration
CBC	Normal	Not bacterial

Microbiology:

- **Stool antigen (Rota/Adeno):** Positive (*Rapid test in children*)
- **PCR:** Norovirus (*For epidemiological purposes*)

Therapy:**Outpatient:**

Drug	Dose	Note
None	-	Antibiotics are ineffective!

Targeted:

No specific antiviral agent.

Supportive:

- Oral rehydration (ORS) - crucial!
- Antiemetics (Ondansetron)
- Probiotics (Lactobacillus GG, S. boulardii)

Prevention:

- Rotavirus vaccine (infants)
- Hand washing (alcohol gel less effective against Norovirus!)
- Isolation

Cholera

Pathogen: Bacterium - Vibrio cholerae (O1, O139) (Gram-negative)

Epidemiology:

- Incidence: Endemic (Asia, Africa, Haiti), epidemic
- Seasonality: Rainy season
- Transmission: Fecal-oral (contaminated water/food)
- Risk Groups: People in extreme poverty, Victims of natural disasters, Travelers (rare)

Pathomechanism:**Steps:**

- Ingestion (high bacterial load, acid-sensitive)
- Small intestine colonization (TCP pilus)
- Cholera toxin (CTX) production
- Adenylate cyclase activation (cAMP increase)
- Massive Cl- and water secretion (CFTR)
- Secretory diarrhea (rice-water stool)

Virulence Factors:

- Cholera toxin (AB5 toxin)
- Toxin-coregulated pilus (TCP)

Clinical Features:

- Incubation: A few hours - 5 days
- Onset: Sudden

Symptoms:

- **Rice-water stool:** Painless, large volume (up to 1L/hour!)
- **Vomiting:** Common, even without nausea
- **Muscle cramps:** Due to electrolyte loss (K+, Ca2+, Mg2+)

Physical Exam:

- Severe dehydration (hypovolemic shock)
- Dry mucous membranes, decreased turgor
- Washerwoman's hands (wrinkled skin)
- Hypotension, tachycardia
- Fever is usually ABSENT

Complications:

- Hypovolemic shock
- Acute renal failure (ATN)
- Severe hypokalemia
- Metabolic acidosis
- Death (50% if untreated!)

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Hemoconcentration	Dehydration
Electrolytes	Hypokalemia, acidosis	Loss
Renal function	Prerenal failure	Volume depletion

Microbiology:

- **Stool culture:** TCBS agar (yellow colonies) (*Gold standard*)
- **Rapid test (RDT):** Crystal VC (*In outbreaks*)
- **Dark-field microscopy:** Shooting star motility (*Rapid*)

Therapy:**Outpatient:**

Drug	Dose	Note
Doxycycline	300mg PO	For adults
Azithromycin	1g PO	Pregnant women, children

Targeted:

Fluid replacement is most important! Antibiotics are only adjunctive (shorten the illness).

Supportive:

- ORS (Oral Rehydration Solution) - WHO formula
- IV Ringer's lactate (severe dehydration)

Prevention:

- Clean water, hygiene
- Oral cholera vaccine (Dukoral, Shanchol)

Traveler's Diarrhea

Pathogen: Syndrome - ETEC (most common), Campylobacter, Salmonella, Shigella, Viruses (Variable)

Epidemiology:

- Incidence: 20-60% of travelers (to developing countries)
- Seasonality: None
- Transmission: Fecal-oral (food, water)
- Risk Groups: Young adults, Immunosuppressed, PPI users

Pathomechanism:

Steps:

- Pathogen ingestion
- Enterotoxin production (ETEC) or invasion (Campy/Shigella)
- Inflammation/secretion

Virulence Factors:

- Variable

Clinical Features:

- Incubation: During travel or after return
- Onset: Acute

Symptoms:

- **Diarrhea:** Usually watery, 3-5 times/day
- **Abdominal cramps:** Common
- **Nausea/vomiting:** Occurs
- **Fever:** Suggests invasive pathogen (Campy/Shigella)

Physical Exam:

- Mild abdominal tenderness
- Signs of dehydration

Complications:

- Dehydration
- Post-infectious IBS
- Reactive arthritis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
-	-	Usually not necessary

Microbiology:

- **Stool culture/PCR:** Multiplex panel (*Only in persistent/severe cases or immunosuppressed*)

Therapy:Outpatient:

Drug	Dose	Note
Azithromycin	1000mg PO once or 500mg for 3 days	Southeast Asia (Campy resistance) or dysentery
Rifaximin	2x200mg PO	In non-invasive (afebrile) cases
Ciprofloxacin	2x500mg PO	Other regions (but resistance is increasing)

Targeted:

-

Supportive:

- Fluid replacement
- Loperamide (only if no fever/bloody stool!)

Prevention:

- "Boil it, cook it, peel it or forget it"
- Hand washing
- Rifaximin prophylaxis (only in high-risk cases)

Dysentery Syndrome

Pathogen: Syndrome - Shigella, EIEC, EHEC, Campylobacter, Entamoeba, Salmonella (Variable)

Epidemiology:

- Incidence: Variable
- Transmission: Fecal-oral
- Risk Groups: Children, Elderly, Immunocompromised

Pathomechanism:Steps:

- Colonic mucosa invasion
- Inflammation, ulceration
- Microabscesses

- Bleeding, mucus production

Virulence Factors:

- Invasins
- Cytotoxins

Clinical Features:

- Incubation: Variable
- Onset: Acute

Symptoms:

- **Bloody-mucoid diarrhea:** Small volume, frequent
- **Tenesmus:** Painful urge to defecate
- **Fever:** Common (except sometimes EHEC/Amoeba)
- **Abdominal pain:** Crampy, lower abdomen

Physical Exam:

- Lower abdominal tenderness
- Fever
- Toxic state

Complications:

- HUS (EHEC/Shigella)
- Toxic megacolon
- Perforation
- Sepsis
- Rectal prolapse

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis	Inflammation

Microbiology:

- **Stool culture:** Pathogen search (*Mandatory!*)
- **Parasite exam:** E. histolytica (*If culture is negative*)
- **Shiga toxin:** Positive (*EHEC/Shigella*)

Therapy:

Outpatient:

Drug	Dose	Note
Azithromycin	1x500mg PO	First choice
Ciprofloxacin	2x500mg PO	Alternative (resistance?)

Targeted:

Based on culture. Antibiotics contraindicated in EHEC! Amoeba: Metronidazole.

Supportive:

- Fluid replacement
- Antimotility agents (Loperamide) are CONTRAINDICATED!

Prevention:

- Hygiene
- Isolation



Viral Hepatitis

Hepatitis A

Pathogen: Virus - Hepatitis A virus (HAV) (ssRNA, Picornaviridae)

Epidemiology:

- Incidence: High in endemic areas, sporadic/epidemic in developed countries
- Seasonality: None
- Transmission: Fecal-oral (contaminated water, food), sexual (oral-anal)
- Risk Groups: Travelers, MSM, Intravenous drug users, Homeless

Pathomechanism:

Steps:

- Oral entry and absorption from the gut
- Infection of hepatocytes (HAVCR-1 receptor)
- Replication in the cytoplasm
- Virus excretion into bile and stool
- Immune-mediated hepatocyte damage (CD8+ T-cells and NK cells)
- Non-cytopathic virus

Virulence Factors:

- Capsid stability (acid-resistant)
- Membrane envelope in blood (eHAV) - immune evasion

Clinical Features:

- Incubation: 15-50 days (average 28 days)
- Onset: Sudden

Symptoms:

- **Fever:** Initial symptom
- **Icterus:** Jaundice (70% of adults, <10% of children)
- **Dark urine:** Bilirubinuria
- **Nausea, vomiting:** Common prodrome
- **Right upper quadrant pain:** Liver capsule stretching

Physical Exam:

- Icterus (sclera, skin)
- Hepatomegaly, tender liver
- Splenomegaly (rare)
- Exanthema (rare)

Complications:

- Fulminant hepatitis (<1%, more common in elderly)
- Cholestatic hepatitis (prolonged)
- Relapse (3-20%)
- NO chronic carriage

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Liver enzymes	ALT/AST > 1000 U/L	Acute hepatocellular necrosis
Bilirubin	Elevated (direct and indirect)	Icterus
ALP/GGT	Moderately elevated	Higher in cholestasis

Imaging:

- **Abdominal US:** Hepatomegaly, gallbladder wall thickening (*Non-specific*)

Microbiology:

- **Anti-HAV IgM:** Positive (*Diagnosis of acute infection (remains + for 3-6 months)*)
- **Anti-HAV IgG:** Positive (*Immunity (vaccination or recovery)*)
- **HAV RNA (PCR):** Positive (*Viremia (rarely needed)*)

Differential Diagnosis:

- **Other viral hepatitis:** Serology (HBV, HCV, HEV)
- **Toxic hepatitis:** Drug/alcohol history
- **Biliary obstruction:** US (dilated bile ducts), ALP dominance

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Rest, adequate calories, no alcohol

Inpatient:

Drug	Dose	Note
Supportive	-	In case of severe vomiting, dehydration, or coagulopathy

Icu:

Drug	Dose	Note

Liver transplant	Listing	In case of fulminant liver failure
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Targeted:

No specific antiviral agent.

Supportive:

- Fluid replacement
- Antiemetics
- Avoid alcohol and hepatotoxic drugs

Prevention:

- Vaccination (inactivated, 2 doses)
- Hygiene (hand washing)
- Post-exposure prophylaxis (vaccine or IG within 2 weeks)

Hepatitis B

Pathogen: Virus - Hepatitis B virus (HBV) (dsDNA (RT), Hepadnaviridae)

Epidemiology:

- Incidence: 290 million chronic carriers worldwide
- Seasonality: None
- Transmission: Parenteral (blood), sexual, perinatal
- Risk Groups: IV drug users, Sexual partners, Healthcare workers, Dialysis patients, Perinatal (mother-to-child)

Pathomechanism:**Steps:**

- Entry into hepatocytes (NTCP receptor)
- cccDNA formation in the nucleus (basis of persistence)
- Transcription/Translation
- Immune-mediated cell death (virus is not cytopathic)
- Integration into host cell genome (HCC risk)

Virulence Factors:

- HBsAg (decoy)
- HBeAg (immunotolerance)
- X protein (transactivator)

Clinical Features:

- Incubation: 45-160 days (average 90 days)
- Onset: Slow

Symptoms:

- **Fatigue:** Common
- **Joint pain:** Immune complex mediated (prodrome)

- **Icterus:** In acute phase (30-50%)
- **Asymptomatic:** Most chronic carriers

Physical Exam:

- Hepatomegaly
- Splenomegaly
- Spider naevi, palmar erythema (chronic/cirrhosis)
- Ascites, caput medusae (decompensated cirrhosis)

Complications:

- Chronic hepatitis (90% in infants, <5% in adults)
- Cirrhosis
- Hepatocellular carcinoma (HCC)
- Polyarteritis nodosa
- Glomerulonephritis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
ALT/AST	Elevated	Activity of inflammation

Microbiology:

- **HBsAg:** Positive (*Presence of infection (acute or chronic)*)
- **Anti-HBs:** Positive (*Immunity (vaccination or recovery)*)
- **Anti-HBc IgM:** Positive (*Acute infection (important in window period!)*)
- **Anti-HBc IgG:** Positive (*Past or chronic infection*)
- **HBeAg:** Positive (*High replication and infectivity*)
- **HBV DNA:** Positive (*Level of viral replication (therapy monitoring)*)

Differential Diagnosis:

- **Hepatitis D:** More severe in superinfection, Anti-HDV
- **Autoimmune hepatitis:** Autoantibodies (ASMA, ANA), elevated IgG

Therapy:

Guidelines: EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection

Outpatient:

Drug	Dose	Note
Entecavir	0.5 mg PO 1x/day	Nucleoside analogue. 1 mg in case of lamivudine resistance.
Tenofovir disoproxil (TDF)	300 mg PO 1x/day	Nucleotide analogue. Renal function and bone density monitoring required.
Tenofovir alafenamide (TAF)	25 mg PO 1x/day	Preferred if risk of bone/kidney disease.

Inpatient:

Drug	Dose	Note
Tenofovir (TDF/TAF) or Entecavir	Standard	Start immediately in severe acute hepatitis or acute liver failure.

Targeted:

Chronic HBV: Lifelong NA (Entecavir, TDF, TAF) to suppress viral replication. Finite treatment: Peg-IFN alpha (48 weeks) in selected patients.

Supportive:

- HCC screening (US every 6 months)
- Vaccination against HAV
- Screening of family members

Prevention:

- Vaccination (recombinant HBsAg, 0-1-6 months)
- Screening in pregnancy
- HBIG + vaccine for newborns (\leq 12 hours; continue vaccination series)

Hepatitis C

Pathogen: Virus - Hepatitis C virus (HCV) (ssRNA, Flaviviridae)

Epidemiology:

- Incidence: 71 million chronic patients worldwide
- Seasonality: None
- Transmission: Parenteral (blood), sexual (rare, higher in MSM), perinatal
- Risk Groups: IV drug users, Transfusion (before 1992), Tattoo/piercing, Healthcare workers (needlestick)

Pathomechanism:**Steps:**

- Entry into hepatocytes
- RNA replication in the cytoplasm (no nucleus phase - curable!)
- High mutation rate (quasispecies) - immune evasion
- Chronic inflammation \rightarrow fibrosis \rightarrow cirrhosis

Virulence Factors:

- NS3/4A protease
- NS5A/B polymerase
- Lipid metabolism modulation

Clinical Features:

- Incubation: 14-180 days
- Onset: Slow/Asymptomatic

Symptoms:

- **Asymptomatic:** Most cases (both acute and chronic)
- **Fatigue:** Non-specific
- **Icterus:** Rare in acute phase (20%)

Physical Exam:

- Often negative
- Signs of cirrhosis in late stage

Complications:

- Chronic hepatitis (70-80%)
- Cirrhosis (20-30% in 20 years)
- HCC
- Extrahepatic: Cryoglobulinemia, Porphyria cutanea tarda, Lichen planus, Diabetes

Diagnostics:Laboratory:

Test	Finding	Interpretation
ALT	Fluctuatingly elevated	Chronic inflammation

Microbiology:

- **Anti-HCV:** Positive (*Exposure (not necessarily active infection)*)
- **HCV RNA:** Positive (*Active infection (confirmation needed!)*)
- **Genotyping:** 1-6 (*Choice of therapy (though pangenotypic drugs dominate)*)

Differential Diagnosis:

- **Alcoholic liver disease:** History, AST>ALT
- **NASH/NAFLD:** Metabolic syndrome, US, biopsy

Therapy:

Guidelines: EASL Recommendations on Treatment of Hepatitis C 2020

Outpatient:

Drug	Dose	Note
Glecaprevir / Pibrentasvir (Maviret)	3 tabs (300/120mg) PO 1x	Pangenotypic. 8 weeks in both non-cirrhotic and compensated cirrhotic patients.
Sofosbuvir / Velpatasvir (Epclusa)	1 tab (400/100mg) PO 1x	Pangenotypic. Can be given in decompensated cirrhosis (with RBV).

Targeted:

Pangenotypic DAA treatment for all patients (Simplified treatment). Genotyping not necessarily required to start treatment (except in cirrhosis/previous treatment failure).

Supportive:

- Check drug interactions (www.hep-druginteractions.org)
- No alcohol

Prevention:

- No vaccine
- Screening of blood products
- Harm reduction (needle exchange)
- Safe sex

Hepatitis D

Pathogen: Virus - Hepatitis D virus (HDV) (ssRNA (defective))

Epidemiology:

- Incidence: 5% of HBV infected (approx. 15-20 million)
- Transmission: Parenteral, sexual (like HBV). Only infects in the presence of HBV!

Pathomechanism:**Steps:**

- HBV HBsAg required for entry and packaging
- Coinfection: HBV+HDV at the same time (usually resolves)
- Superinfection: chronic HBV + new HDV (severe, becomes chronic)
- Direct cytopathic effect possible

Virulence Factors:

- Delta antigen (HDAg)

Clinical Features:**Symptoms:**

- **Severe hepatitis:** More severe than HBV alone

Complications:

- Fulminant hepatitis
- Rapid progression to cirrhosis (most aggressive viral hepatitis)

Diagnostics:**Microbiology:**

- **Anti-HDV:** Positive (*Screening in all HBV patients*)
- **HDV RNA:** Positive (*Active replication*)

Therapy:

Guidelines: EASL Clinical Practice Guidelines on hepatitis delta virus 2023

Outpatient:

Drug	Dose	Note
Bulevirtide	2 mg SC daily	Entry inhibitor. Monotherapy or in combination with Peg-IFN. (Conditional approval)

Peg-IFN alfa	180 mcg SC weekly	Alternative, but low sustained response rate.
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Targeted:

Bulevirtide (long-term maintenance) or Peg-IFN (48 weeks). Nucleoside analogues (against HBV) should be continued but do not directly affect HDV.

Prevention:

- HBV vaccination also protects against HDV (as it needs HBsAg)

Hepatitis E

Pathogen: Virus - Hepatitis E virus (HEV) (ssRNA, Hepeviridae)

Epidemiology:

- Incidence: Developing countries (water), Developed (pork/wild boar)
- Seasonality: Rainy season (tropics)
- Transmission: Fecal-oral (water - Genotype 1,2), Zoonosis (raw pork/game meat - Genotype 3,4)
- Risk Groups: Pregnant women (severe course), Immunosuppressed (chronic), Liver patients, Pig farmers

Pathomechanism:**Steps:**

- Oral entry
- Absorption from gut, entry to liver
- Hepatocyte replication
- Biliary excretion
- Immune-mediated cytotoxicity

Virulence Factors:

- ORF3 protein (release)
- Capsid protein

Clinical Features:

- Incubation: 15-60 days (average 40)
- Onset: Sudden

Symptoms:

- **Acute hepatitis:** Similar to HAV
- **Acute hepatitis:** Similar to HAV, jaundice, fever
- **Abdominal pain:** Right upper quadrant

Physical Exam:

- Icterus
- Hepatomegaly

Complications:

- Fulminant hepatitis in pregnant women (20% mortality! - G1,2)
- Chronic hepatitis in immunosuppressed (G3)
- Neurological symptoms (Guillain-Barré, Neuralgic amyotrophy)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Liver enzymes	ALT/AST elevated	Hepatitis

Imaging:

- **Abdominal US:** Hepatomegaly (*Non-specific*)

Microbiology:

- **Anti-HEV IgM:** Positive (*Acute infection*)
- **HEV RNA:** Positive (*Confirmation, chronic case*)

Differential Diagnosis:

- **Hepatitis A:** Serology
- **Drug toxicity:** History

Therapy:

Guidelines: EASL Clinical Practice Guidelines on hepatitis E virus infection

Outpatient:

Drug	Dose	Note
Supportive	-	In immunocompetent acute infection (self-limiting).

Inpatient:

Drug	Dose	Note
Ribavirin	600-800 mg PO	Chronic HEV (immunosuppressed) or severe acute cases.

Targeted:

Chronic HEV (immunosuppressed): 1. Reduce immunosuppression (if possible). 2. Ribavirin for 12 weeks. If unsuccessful: Ribavirin for 24 weeks or Peg-IFN.

Supportive:

- Fluid replacement
- Close monitoring in pregnant women (risk of fulminant course!)

Prevention:

- Food safety (thorough cooking of pork/game meat)

Hepatitis G (GBV-C)

Pathogen: Virus - GB virus C (HGV) (ssRNA, Flaviviridae)

Epidemiology:

- Incidence: 1-4% of blood donors
- Seasonality: None
- Transmission: Blood, sexual, vertical
- Risk Groups: IV drug users, Hemodialysis patients, Multiple transfusions

Pathomechanism:

Steps:

- Lymphotropic virus
- Replication in lymphocytes
- Not hepatotropic (controversial)
- Interference with HIV replication

Virulence Factors:

- Unknown

Clinical Features:

- Incubation: Unknown
- Onset: Asymptomatic

Symptoms:

- **Asymptomatic:** Does not cause acute or chronic hepatitis

Physical Exam:

- Negative

Complications:

- In HIV coinfection slows AIDS progression (favorable effect)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Liver function	Normal	Does not cause hepatitis

Imaging:

- **None:** - (-)

Microbiology:

- **PCR:** RNA (*Research purpose, not used in clinical routine*)

Therapy:

Targeted:

Does not require treatment.

Prevention:

- Screening of blood products (not routine)

Torque teno virus (TTV)

Pathogen: Virus - Torque teno virus (ssDNA, Anelloviridae)

Epidemiology:

- Incidence: Ubiquitous (>90% of population are carriers)
- Seasonality: None
- Transmission: Blood, saliva, stool, breast milk
- Risk Groups: General population

Pathomechanism:

Steps:

- Persistent viremia
- Replication in many tissues
- Unproven pathogenicity

Virulence Factors:

- -

Clinical Features:

- Incubation: -
- Onset: Asymptomatic

Symptoms:

- **Asymptomatic:** Can be considered a commensal virus

Physical Exam:

- Negative

Complications:

- Pathogenicity not proven
- Can be an indicator of the degree of immunosuppression

Diagnostics:

Laboratory:

Test	Finding	Interpretation
-	-	-

Imaging:

- -: - (-)

Microbiology:

- **PCR:** DNA (*Research*)

Therapy:

Targeted:

None

Prevention:

- -

SEN virus

Pathogen: Virus - SEN virus (ssDNA, Anelloviridae)

Epidemiology:

- Incidence: Unknown
- Seasonality: None
- Transmission: Transfusion, via blood
- Risk Groups: Transfusion recipients

Pathomechanism:**Steps:**

- Spread via blood
- Can replicate in hepatocytes
- Can cause mild hepatitis (controversial)

Virulence Factors:

- -

Clinical Features:

- Incubation: -
- Onset: Slow

Symptoms:

- **Mild hepatitis?**: Associated with post-transfusion hepatitis, but causality not proven

Physical Exam:

- -

Complications:

- No significant liver damage proven

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
ALT	Mild elevation possible	?

Imaging:

- -: - (-)

Microbiology:

- **PCR:** DNA (*Research*)

Therapy:**Targeted:**

None

Prevention:

- -

Urinary Tract Infections

Uncomplicated Cystitis

Pathogen: Bacterium - Escherichia coli (75-95%) (Gram-negative)

Epidemiology:

- Incidence: 50% of women at least once in their lifetime
- Seasonality: None
- Transmission: Ascending infection (perineal flora)
- Risk Groups: Sexually active women, Postmenopause, Pregnancy, Diabetes, Catheter use

Pathomechanism:**Steps:**

- Perineal colonization by gut bacteria
- Ascension through the urethra to the bladder
- Adherence to bladder urothelium (P-fimbriae)
- Bacterial multiplication and inflammation
- Bladder mucosal irritation (dysuria, urgency)

Virulence Factors:

- P-fimbriae (adherence)
- Hemolysin
- Aerobactin (iron uptake)

Clinical Features:

- Incubation: Variable
- Onset: Sudden

Symptoms:

- **Dysuria:** Burning, stinging urination (>90% present)
- **Frequency:** Frequent, small-volume urination (>90%)
- **Urgency:** Sudden, compelling urge to urinate
- **Suprapubic pain:** Lower abdominal discomfort or tenderness (70-80%)
- **Hematuria:** Macroscopic bloody urine (approx. 30%), often at the end of urination

Physical Exam:

- Suprapubic tenderness

- Fever is usually ABSENT (if present, suspect pyelonephritis!)
- Flank is not tender
- Absence of vaginal discharge (increases probability of cystitis)

Complications:

- Ascending pyelonephritis
- Recurrent cystitis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Urine dipstick	Leukocyte esterase+, Nitrite+	High positive predictive value
Urine sediment	Pyuria (>10 WBC/field)	Common, but not specific

Imaging:

- **None:** Not necessary (*Except for atypical symptoms or persistence*)

Microbiology:

- **Urine culture:** $\geq 10^3$ CFU/ml (*Recommended only in complicated, recurrent, or atypical cases (EAU 2025)*)

Differential Diagnosis:

- **Vaginitis:** Discharge, itching, external dysuria
- **Urethritis (STD):** New partner, gradual onset, pyuria with sterile culture
- **Interstitial cystitis:** Chronic, negative culture

Therapy:

Outpatient:

Drug	Dose	Note
Fosfomycin trometamol	3g PO	First choice (EAU 2025)
Nitrofurantoin	2x100mg PO	First choice (EAU 2025)
Pivmecillinam	3x400mg PO	First choice (EAU 2025)

Inpatient:

Drug	Dose	Note
Does not require hospital treatment	-	Except complications

Icu:

Drug	Dose	Note
-	-	-

Targeted:

Based on culture. Fluoroquinolones (Ciprofloxacin, Levofloxacin) are NOT recommended empirically for uncomplicated cystitis!

Supportive:

- Ample fluid intake
- Frequent urination
- NSAID for pain relief

Prevention:

- Behavioral: Ample fluid intake, postcoital voiding
- Non-antibiotic (EAU 2025): Topical estrogen (postmenopause), OM-89 immunostimulation, D-mannose, Bladder instillation
- Antibiotic prophylaxis (last resort): Nitrofurantoin 50-100mg at night or Fosfomycin 3g every 10 days

Uncomplicated Pyelonephritis

Pathogen: Bacterium - Escherichia coli (80%) (Gram-negative)

Epidemiology:

- Incidence: Common complication of untreated cystitis
- Seasonality: None
- Transmission: Ascending infection (95%), rarely hematogenous
- Risk Groups: Women, Pregnancy, Obstruction (stone, prostate), Renal developmental anomaly, Diabetes

Pathomechanism:

Steps:

- Ascension of bacteria up the ureter to the renal pelvis
- Invasion of renal parenchyma
- Inflammatory reaction, edema, microabscesses
- Impairment of tubular function

Virulence Factors:

- P-fimbriae
- Endotoxin
- Capsule

Clinical Features:

- Incubation: Days after cystitis
- Onset: Sudden

Symptoms:

- **Fever and chills:** Fever >38°C (90-95%), often with chills
- **Flank pain:** Dull, continuous flank pain (90-95%), unilateral or bilateral
- **Gastrointestinal symptoms:** Nausea, vomiting, loss of appetite (common)

- **Lower urinary tract symptoms:** Dysuria, frequency (may be absent in 30-50% of cases!)

Physical Exam:

- Costovertebral angle tenderness (Giordano's sign)
- Fever, tachycardia
- Abdominal tenderness (less common)

Complications:

- Renal abscess
- Perinephric abscess
- Urosepsis
- Papillary necrosis
- Chronic renal failure (recurrent)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis, left shift	Systemic inflammation
CRP/PCT	Significantly elevated	Bacterial infection
Urinalysis	Leukocyturia, bacteriuria, white blood cell casts	Upper urinary tract origin
Renal function	Creatinine may be elevated	Acute kidney injury

Imaging:

- **Abdominal/pelvic CT:** Renal enlargement, perinephric fluid, wedge-shaped hypodensity (*Gold standard to rule out complications (EAU 2025)*)
- **Renal US:** Obstruction, abscess (*Radiation-free alternative*)

Microbiology:

- **Urine culture:** $\geq 10^4$ CFU/ml (*Always take! (EAU 2025)*)
- **Blood culture:** Positive (*Recommended on hospital admission*)

Differential Diagnosis:

- **Kidney stone:** Colicky pain, no fever (if no infection), hematuria dominates
- **Acute abdominal conditions:** Appendicitis, cholecystitis (abdominal status, US)
- **Pelvic inflammatory disease (PID):** Gynecological exam, discharge

Therapy:

Outpatient:

Drug	Dose	Note
Cefuroxime axetil	2x500mg PO	no activity against Enterococcus
Levofloxacin	1x750mg PO	Only an alternative if E. coli resistance <10% (EAU 2025)
Ceftibuten/Cefixime	PO	If quinolone cannot be given (less effective)

Inpatient:

Drug	Dose	Note
Ceftriaxone	1x1-2g IV	First choice
Ciprofloxacin	2x400mg IV	Alternative if E. coli resistance <10% (EAU 2025)
Gentamicin + Ampicillin	IV	In severe cases

Icu:

Drug	Dose	Note
Piperacillin/tazobactam	4x4.5g IV	Urosepsis, obstruction
Meropenem	3x1g IV	Suspicion of ESBL

Targeted:

Based on antibiogram. ESBL is common!

Supportive:

- Fluid replacement
- Antipyretics
- Resolution of obstruction (catheter, stent)

Prevention:

- Proper treatment of cystitis
- Correction of anatomical abnormalities

Complicated Urinary Tract Infection

Pathogen: Bacterium - E. coli, Enterococcus, Pseudomonas, Klebsiella, Proteus (Mixed)

Epidemiology:

- Incidence: Common in hospital settings and urological patients
- Seasonality: None
- Transmission: Ascending, catheter-associated, hematogenous
- Risk Groups: Catheter users, Men, Pregnant women, Anatomical/functional abnormality, Renal failure, Immunosuppression

Pathomechanism:**Steps:**

- Presence of a predisposing factor (e.g., obstruction, catheter)
- Biofilm formation (on catheter, stone)
- Selection of resistant pathogens
- Tissue invasion and persistence

Virulence Factors:

- Biofilm
- Multidrug resistance
- Urease (Proteus)

Clinical Features:

- Incubation: Variable
- Onset: Variable (can be oligosymptomatic)

Symptoms:

- **Mixed symptoms:** Combination of dysuria, frequency, fever, flank pain
- **Systemic signs:** Fever, chills, altered mental status (especially in the elderly)
- **Oligosymptomatic:** In catheterized patients or spinal cord injury patients, symptoms may be absent or atypical
- **Urine changes:** Cloudy, foul-smelling urine (not diagnostic on its own!)

Physical Exam:

- Can be unremarkable
- Suprapubic or flank tenderness
- Presence of a catheter
- Fever or hypothermia (urosepsis)
- Confusion (elderly)

Complications:

- Urosepsis
- Renal abscess
- Renal failure
- Recurrence
- Catheter obstruction

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Urine culture	Women: $\geq 10^5$ CFU/ml, Men: $\geq 10^4$ CFU/ml	Diagnostic thresholds (EAU 2025)
Catheter urine	$\geq 10^4$ CFU/ml	Significant bacteriuria
Renal function	Check creatinine	Obstruction/damage

Imaging:

- **CT urography:** Anatomical/functional abnormality (*MANDATORY to clarify predisposing factor*)

Microbiology:

- **Culture + Susceptibility:** Essential (*Basis for targeted therapy*)

Therapy:

Outpatient:

Drug	Dose	Note
Cefuroxime axetil	2x500mg PO	no activity against Enterococcus
Ciprofloxacin	2x500-750mg PO	Only if no fluoroquinolone treatment in the last 6 months and E. coli resistance >10% (EAU 2025)
Levofloxacin	1x750mg PO	Alternative if E. coli resistance <10% (EAU 2025)
Ceftibuten/Cefixime	PO	If quinolone cannot be given

Inpatient:

Drug	Dose	Note
Ceftriaxone	1x1-2g IV	In severe cases
Piperacillin/tazobactam	3x4.5g IV	Suspicion of Pseudomonas/previous AB treatment
Carbapenem (Meropenem)	3x1g IV	ESBL risk or septic shock
Amikacin/Gentamicin	IV	Synergism

Icu:

Drug	Dose	Note
Broad spectrum (Carbapenem + Amikacin)	IV	Urosepsis

Targeted:

Correction based on culture. Resolution of obstruction (catheter change, stent, nephrostomy) is essential!

Supportive:

- Fluid replacement
- Antipyretics

Prevention:

- Catheter care (closed system, prompt removal)
- Elimination of obstruction
- Avoidance of treating asymptomatic bacteriuria

Bacterial Prostatitis

Pathogen: Bacterium - E. coli, Klebsiella, Proteus, Enterococcus, Pseudomonas (Mixed)

Epidemiology:

- Incidence: 50% of men experience symptoms in their lifetime

- Seasonality: None
- Transmission: Ascending (reflux), hematogenous, lymphogenic, direct (biopsy)
- Risk Groups: Young/middle-aged men, Catheterization, Urological procedure (biopsy), HIV, Diabetes

Pathomechanism:

Steps:

- Intraprostatic urine reflux
- Ascending infection from the urethra
- Direct inoculation (e.g., transrectal biopsy)
- Biofilm formation (maintaining chronic infection)

Virulence Factors:

- Biofilm
- Anatomical location (poor AB penetration)

Clinical Features:

- Incubation: Variable
- Onset: Acute (ABP) or Chronic (CBP)

Symptoms:

- **Acute: Systemic symptoms:** Sudden fever, chills, myalgia, malaise
- **Pain:** Perineal, rectal, prostatic, radiating to testes/penis
- **LUTS (Lower Urinary Tract Symptoms):** Dysuria, frequency, urgency
- **Obstruction:** Urinary retention (due to swollen prostate)
- **Chronic symptoms:** Pelvic pain for >3 months, recurrent UTI

Physical Exam:

- Digital rectal exam (DRE):
- Acute: Swollen, warm, EXTREMELY tender prostate (Massage FORBIDDEN - risk of bacteremia!)
- Chronic: May be normal or slightly tender, not swollen

Complications:

- Prostate abscess
- Urosepsis
- Chronicity
- Epididymitis
- Urinary retention
- Sexual dysfunction

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Urinalysis	Pyuria, bacteriuria	Positive

CBC/CRP	Elevated (Acute)	Systemic inflammation
PSA	Elevated	Due to inflammation (not for cancer diagnosis in acute phase!)

Imaging:

- **Transrectal US (TRUS):** Abscess (hypoechoic area) (*Only if no improvement on treatment or suspicion of abscess*)

Microbiology:

- **Acute: Urine culture:** Midstream urine (*Prostate massage FORBIDDEN!*)
- **Chronic: Meares-Stamey test:** 4-glass test or 2-glass test (pre/post massage) (*Gold standard (EAU 2025)*)

Differential Diagnosis:

- **Cystitis:** No fever, no prostate tenderness
- **BPH:** No signs of infection, slow progression
- **Chronic pelvic pain syndrome (CPPS):** Negative culture, chronic pain
- **Prostate cancer:** PSA, DRE (nodular), biopsy

Therapy:**Outpatient:**

Drug	Dose	Note
Levofloxacin	1x500-750mg PO	EAU 2025: First choice (good penetration)
Ciprofloxacin	2x500mg PO	EAU 2025: First choice
Cotrimoxazole	2x960mg PO	Alternative

Inpatient:

Drug	Dose	Note
Ceftriaxone	1-2g IV	In severe acute cases (then switch to PO)
Piperacillin/tazobactam	3x4.5g IV	Urosepsis/suspicion of Pseudomonas
Gentamicin	5-7mg/kg IV	As an adjunct (synergism)

Icu:

Drug	Dose	Note
Meropenem	3x1g IV	Septic shock/ESBL

Targeted:

Fluoroquinolones (first choice in chronic). Macrolides (suspicion of Chlamydia). Fosfomycin (MDR - controversial penetration).

Supportive:

- NSAID for pain relief
- Alpha-blocker (Tamsulosin) to relieve symptoms
- Suprapubic catheter (in retention, urethral should be avoided in acute inflammation!)

Prevention:

- Early treatment of UTIs
- Prostate biopsy prophylaxis: Targeted (based on rectal swab) or Fosfomycin/Ceftriaxone (Fluoroquinolones should be avoided!)

Asymptomatic Bacteriuria

Pathogen: Bacterium - E. coli, Enterococcus, GBS, etc. (Variable)

Epidemiology:

- Incidence: Common (women 3-5%, elderly 10-50%, catheterized 100%)
- Seasonality: None
- Transmission: Endogenous colonization
- Risk Groups: Elderly, Diabetes, Catheter use, Pregnancy

Pathomechanism:**Steps:**

- Urinary tract colonization without virulence factors
- Commensal-like relationship with the host
- No tissue invasion or inflammatory response

Virulence Factors:

- Reduced virulence

Clinical Features:

- Incubation: -
- Onset: Asymptomatic

Symptoms:

- **Asymptomatic:** No dysuria, fever, or lower abdominal pain

Physical Exam:

- Negative
- Cloudy/foul-smelling urine alone is not diagnostic and does not require treatment!

Complications:

- Unnecessary antibiotic treatment → resistance
- Pyelonephritis (risk only in pregnancy/procedure)

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
Urine culture	$\geq 10^5$ CFU/ml (same strain)	Women: 2 consecutive samples, Men: 1 sample (EAU 2025)

Catheterized sample	$\geq 10^5$ CFU/ml	One sample is sufficient
Urine sediment	Pyuria is often present	Does NOT indicate treatment without symptoms!

Microbiology:

- **Culture:** Positive (*Only if screening is indicated (e.g., pregnancy, urological procedure)*)

Differential Diagnosis:

- **Cystitis:** Presence of symptoms (dysuria, urgency)
- **Contamination:** Low colony count, mixed flora

Therapy:**Outpatient:**

Drug	Dose	Note
NO treatment	-	General rule (not even in elderly, diabetics, catheterized patients!)

Inpatient:

Drug	Dose	Note
NO treatment	-	Except indications

Targeted:

Only if indicated (Pregnancy, Urological procedure with mucosal injury). In pregnancy: Fosfomycin, Nitrofurantoin, Cephalosporin.

Supportive:

- Education (urine smell/color does not warrant AB)

Prevention:

- Avoid unnecessary screening and treatment
- Catheter care

💡 Emerging Pathogens

Mpox (Monkeypox)

Pathogen: Virus - Mpox virus (MPXV) (dsDNA, Poxviridae)

Epidemiology:

- Incidence: Global outbreak (2022-), endemic in Africa
- Seasonality: None
- Transmission: Close skin-to-skin contact, respiratory droplets, fomites, zoonosis (rodents)
- Risk Groups: MSM population, Healthcare workers, Household contacts

Pathomechanism:Steps:

- Entry through broken skin/mucosa
- Replication at entry site and regional lymph nodes
- Viremia
- Development of skin and mucosal lesions

Virulence Factors:

- Immunomodulatory proteins

Clinical Features:

- Incubation: 5-21 days
- Onset: Sudden

Symptoms:

- **Rash:** Macule → Papule → Vesicle → Pustule → Scab (painful!)
- **Lymphadenopathy:** Characteristic (distinguishes from smallpox/chickenpox)
- **Fever:** Prodromal symptom
- **Proctitis:** Rectal pain (in sexual transmission)

Physical Exam:

- Centrifugal distribution of rash (palms/soles too)
- Swollen, painful lymph nodes
- Genital/perianal lesions

Complications:

- Bacterial superinfection
- Pneumonia
- Sepsis
- Encephalitis
- Corneal scarring (blindness)

Diagnostics:Laboratory:

Test	Finding	Interpretation
CBC	Non-specific	-

Microbiology:

- **PCR:** MPXV DNA (*Gold standard (sample from base/roof of lesion)*)
- **Electron microscopy:** Poxvirus morphology (*Rarely available*)

Therapy:**Outpatient:**

Drug	Dose	Note
Supportive	-	Pain relief, wound care, isolation

Targeted:

In severe cases: Tecovirimat (antiviral).

Supportive:

- Pain relief
- Fluid replacement

Prevention:

- Vaccination (JYNNEOS - 3rd generation smallpox vaccine)
- Isolation
- Contact tracing

Nipah Virus

Pathogen: Virus - Nipah virus (NiV) (RNA, Paramyxoviridae (Henipavirus))

Epidemiology:

- Incidence: Sporadic outbreaks (South Asia, Southeast Asia)
- Seasonality: Winter-spring (Bangladesh)
- Transmission: Bat (flying fox) urine/saliva (date palm sap), pigs, person-to-person
- Risk Groups: Pig farmers, Date palm sap collectors/consumers

Pathomechanism:**Steps:**

- Entry (oral/respiratory)
- Viremia
- Infection of endothelial cells (Ephrin-B2 receptor)
- Vasculitis, thrombosis, ischemia
- CNS and lung involvement

Virulence Factors:

- Fusion proteins
- Immune antagonists

Clinical Features:

- Incubation: 4-14 days
- Onset: Sudden

Symptoms:

- **Fever:** High
- **Headache:** Severe
- **Respiratory symptoms:** Cough, atypical pneumonia
- **Encephalitis:** Dizziness, altered mental status, coma (within 24-48 hours)

Physical Exam:

- Fever

- Nuchal rigidity
- Altered mental status
- Myoclonus
- Areflexia/Hyporeflexia

Complications:

- Severe encephalitis
- ARDS
- Relapse (months/years later)
- Death

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Thrombocytopenia, leukopenia	-

Imaging:

- **Brain MRI:** Multiple small infarcts, hyperintensity (*Encephalitis*)

Microbiology:

- **RT-PCR:** RNA (throat, urine, CSF) (*Acute phase*)
- **ELISA (IgM/IgG):** Positive (*Later*)

Therapy:

Outpatient:

Drug	Dose	Note
None	-	Immediate hospital/ICU admission

Targeted:

No proven antiviral. Monoclonal antibody (m102.4) in experimental phase.

Supportive:

- Intensive care
- Ventilation
- Seizure control

Prevention:

- Avoid contact with bats
- Avoid raw date palm sap
- Isolation/culling of sick pigs
- Hospital infection control



Central Nervous System Infections

Bacterial Meningitis (Empiric)

Pathogen: Bacterium - N. meningitidis, S. pneumoniae, L. monocytogenes (Mixed)

Epidemiology:

- Incidence: 2-5/100,000 per year in developed countries
- Seasonality: Meningococcus: winter-spring
- Transmission: Droplet (meningococcus), endogenous (pneumococcus), vertical (GBS, Listeria)
- Risk Groups: Newborns (<1 month), Children, Adults >65 years, Splenectomized, Complement deficiency, Cochlear implant

Pathomechanism:

Steps:

- Nasopharyngeal colonization
- Bacteremia (crossing the blood-brain barrier)
- Invasion of the subarachnoid space
- Inflammatory response (TNF- α , IL-1 β)
- Increased blood-brain barrier permeability → cerebral edema
- Increased intracranial pressure, cerebral ischemia

Virulence Factors:

- Polysaccharide capsule
- IgA protease
- Lipooligosaccharide (LOS)
- Pili/fimbriae

Clinical Features:

- Incubation: 2-10 days (meningococcus), shorter (pneumococcus)
- Onset: Acute, hours-days

Symptoms:

- **Classic triad:** Fever, headache, nuchal rigidity, altered mental status (triad not always present!)
- **Early "Red Flag" signs (NICE):** Leg/muscle pain, cold extremities, mottled skin (early signs of sepsis!)
- **Rash:** Non-blanching petechiae/purpura (suspect Meningococcus)
- **Headache:** Severe, generalized (>85%)
- **Fever:** >38°C (95%)
- **Nuchal rigidity:** Stiff neck (>80%)
- **Altered mental status:** GCS <14 (>80%)

Physical Exam:

- Meningeal signs: Kernig (+), Brudzinski (+), nuchal rigidity
- Fever (often >39°C)
- Altered mental status (decreased GCS)

- Focal neurological signs (cranial nerve palsy, paresis)
- Petechiae/purpura (meningococcemia)
- Papilledema (late sign)

Complications:

- Septic shock
- DIC
- ARDS
- Cerebral edema/herniation
- Subdural empyema
- Hearing loss
- Cognitive deficit

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (15-30 G/L), left shift	Bacterial infection
CRP/PCT	Significantly elevated (PCT >2)	Bacterial sepsis
Blood PCR	Meningococcus/Pneumococcus DNA	NICE recommendation: take in all suspected cases!
Coagulation panel	Signs of DIC (\downarrow fibrinogen, \uparrow D-dimer)	Meningococcus

Imaging:

- **Head CT:** Exclude contraindications (*Before LP if: GCS<9, seizures, focal signs, papilledema*)
- **MRI:** More sensitive, complications (*Empyema, infarction*)

Microbiology:

- **CSF analysis (NICE):** Cell count $>1000/\mu\text{L}$ (PMN), Protein $>1 \text{ g/L}$, Glucose $< 50\%$ of blood glucose (*Typical for bacterial meningitis!*)
- **CSF Lactate:** Elevated (*Helps differentiate from viral*)
- **CSF Gram stain:** 60-90% positive (*Quick orientation*)
- **CSF/blood culture:** Pathogen isolation (*Resistance testing*)
- **CSF PCR (multiplex):** DNA detection (*Fast, sensitive, pre-treated patient*)
- **CSF latex agglutination:** Antigen detection (*Fast, less sensitive*)

Differential Diagnosis:

- **Viral meningitis:** Milder, CSF: lymphocytes, normal glucose
- **Tuberculous meningitis:** Subacute, low glucose, basilar meningitis
- **Encephalitis:** Altered mental status dominates, focal signs, milder CSF changes
- **Subarachnoid hemorrhage:** Thunderclap headache, bloody/xanthochromic CSF
- **Carcinomatous meningitis:** Malignancy, cytology

Therapy:

Guidelines: NICE NG240 (2024): Meningitis (bacterial) and meningococcal disease

Outpatient:

Drug	Dose	Note
Benzylpenicillin or Ceftriaxone	IM/IV	Only if transport to hospital is significantly delayed (NICE)

Inpatient:

Drug	Dose	Note
Ceftriaxone	2g IV every 12 hours (or 4g every 24 hours)	First choice (NICE). Alternative: Cefotaxime.
+ Amoxicillin	2g IV every 4 hours	If Listeria risk (>60 years, immunosuppression, pregnancy).
Dexamethasone	10mg IV every 6 hours	BEFORE or WITH the first antibiotic dose. Do not give if septic shock without meningitis.

Icu:

Drug	Dose	Note
Supportive	-	Airway management, fluid resuscitation, vasopressors

Targeted:

Meningococcus: 7 days; Pneumococcus: 14 days; Listeria: 21 days; H. influenzae: 10 days; GBS: 14-21 days.

Supportive:

- Fluid/electrolyte balance
- ICP monitoring
- Seizure prophylaxis
- Isolation (meningococcus, can be discontinued after 24h of AB)

Prevention:

- MenACWY, MenB vaccines
- PCV13/PPSV23
- Hib vaccine
- Chemoprophylaxis for contacts: Rifampicin or Ciprofloxacin

Viral Encephalitis

Pathogen: Virus - HSV-1, VZV, enteroviruses, arboviruses (DNA/RNA viruses)

Epidemiology:

- Incidence: 0.5-7/100,000 per year

- Seasonality: Enterovirus: summer-autumn; HSV: all year
- Transmission: HSV: reactivation; Enterovirus: fecal-oral; Arbovirus: vector (mosquito, tick)
- Risk Groups: Newborns (HSV-2), Immunosuppressed, Elderly (VZV reactivation), Travelers to endemic areas (arbovirus)

Pathomechanism:

Steps:

- Primary infection or reactivation (HSV)
- Neurotropism: virus enters nervous tissue
- HSV: temporal lobe predilection (olfactory or trigeminal route)
- Direct neuronal damage + immune response
- Necrotizing encephalitis (HSV) vs. perivascular inflammation
- Cerebral edema, hemorrhage, necrosis

Virulence Factors:

- HSV: glycoprotein B, C, D (entry)
- VZV: latency in neurons
- Enterovirus: VP1 capsid protein

Clinical Features:

- Incubation: HSV reactivation: variable; Enterovirus: 3-7 days; Arbovirus: 4-14 days
- Onset: Acute-subacute

Symptoms:

- **Altered mental status:** Hallmark of encephalitis (100%): confusion, lethargy, coma
- **Fever:** Present in >90%
- **Headache:** Common accompanying symptom
- **Seizures:** Common (especially HSV, autoimmune)
- **Focal neurological signs:** Hemiparesis, cranial nerve palsy, ataxia
- **Behavioral changes:** Psychosis, hallucinations (HSV, limbic)

Physical Exam:

- Altered mental status (decreased GCS)
- Focal neurological signs (hemiparesis, cranial nerve palsy)
- Seizures
- Meningeal signs (moderate)
- Papilledema (late)

Complications:

- Permanent neurological damage
- Epilepsy
- Motor/cognitive deficit
- Death (untreated HSV 70%)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Variable, can be normal	Non-specific
CRP	Moderately elevated	Lower than in bacterial
Liver/kidney function	Baseline	Acyclovir toxicity

Imaging:

- **Brain MRI:** HSV: temporal + frontal T2/FLAIR hyperintensity, asymmetric (*Most sensitive! Perform early*)
- **Brain CT:** May be negative in early stages (*Exclude contraindications before LP*)

Microbiology:

- **CSF PCR:** HSV-1/2, VZV, enterovirus DNA/RNA (*Gold standard, early negativity possible!*)
- **CSF analysis:** Lymphocytic pleocytosis (10-500), normal/slightly↑ protein, normal glucose (*Viral pattern*)
- **CSF RBC:** Xanthochromia, elevated (*Hemorrhagic necrosis (HSV)*)
- **Serology:** Acute-convalescent titer rise (*Retrospective*)

Differential Diagnosis:

- **Bacterial meningitis:** Faster course, CSF: PMN, ↓glucose
- **Autoimmune encephalitis:** Anti-NMDA-R, limbic encephalitis, tumor search
- **Brain abscess:** CT/MRI: ring enhancement, septic focus
- **Toxic-metabolic encephalopathy:** Underlying disease, lab abnormalities
- **Status epilepticus:** EEG, history

Therapy:**Outpatient:**

Drug	Dose	Note
NO outpatient treatment!	Immediate hospital admission	HSV encephalitis is fatal without treatment!

Inpatient:

Drug	Dose	Note
Acyclovir	3x10mg/kg IV	Start IMMEDIATELY on suspicion of HSV!

Icu:

Drug	Dose	Note
Acyclovir	3x10mg/kg IV	Immunosuppressed, severe
Anticonvulsant	Levetiracetam or other	Prophylaxis/therapy

Targeted:

HSV/VZV: Acyclovir; CMV: Ganciclovir+Foscarnet; Enterovirus: supportive

Supportive:

- ICP control
- Seizure control
- Fluid balance
- Rehabilitation

Prevention:

- VZV vaccine
- Mosquito bite protection (arbovirus)
- Neonatal HSV: C-section if active genital herpes

Skin and Soft Tissue Infections

Necrotizing Fasciitis

Pathogen: Bacterium - Polymicrobial or Strep. pyogenes/S. aureus (Mixed)

Epidemiology:

- Incidence: Rare (0.4/100,000), but increasing incidence
- Seasonality: None
- Transmission: Endogenous (skin breach) or direct inoculation
- Risk Groups: Diabetes mellitus, Peripheral vascular disease, Immunosuppression, Chronic alcoholism, IV drug users, Post-trauma/surgery

Pathomechanism:

Steps:

- Bacteria enter subcutaneous tissues (trauma, wound, varicella)
- Rapid spread along fascial planes
- Bacterial toxins → thrombosis in microvasculature
- Tissue ischemia and necrosis
- Toxin-mediated shock (streptococcus)
- Skin initially intact as superficial blood supply is compromised later

Virulence Factors:

- Strep: M protein, Streptolysins, SpeA/B/C superantigens
- Staph: PVL, α -toxin
- Anaerobes: collagenases, proteases

Clinical Features:

- Incubation: Hours-days (after trauma)
- Onset: Hyperacute, rapidly progressing

Symptoms:

- **Intense pain:** DISPROPORTIONATE to physical findings (75-100%), early sign
- **Swelling/Edema:** Tense, spreading edema (75-100%)

- **Skin changes:** Erythema (70-100%), later livid discoloration, bullae, necrosis (late signs!)
- **Fever:** Common, but may be absent
- **Crepitus:** Gas formation (13-30% - not always present!)
- **Toxic state:** Hypotension, tachycardia, altered mental status

Physical Exam:

- Pain is disproportionately SEVERE to what is seen (early sign!)
- Tense edema, rapid spread
- Skin: erythema → livid → bullae → necrosis
- Anesthesia in the area (nerve damage)
- Crepitus on palpation (gas)
- Systemic signs: tachycardia, hypotension, confusion

Complications:

- Septic shock
- Multi-organ failure
- Limb loss
- Death (20-40% even with treatment)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
LRINEC score	>6: high probability	CRP, white blood cell, hemoglobin, sodium, creatinine, glucose
CBC	Leukocytosis or leukopenia	Sepsis
CRP/PCT	Extremely elevated	Severe bacterial infection
Lactate	Elevated	Tissue hypoperfusion
CK	Elevated	Muscle involvement

Imaging:

- **Contrast CT:** Fascial thickening, gas in soft tissues, fluid collection (*Fast, assesses extent*)
- **MRI:** More sensitive for fascial involvement (*If time permits and patient is stable*)

Microbiology:

- **Blood culture:** Positive in 20-40% (*Pathogen identification*)
- **Surgical tissue sample:** Culture + Gram (*Gold standard*)
- **Finger test:** Fascia can be dissected, "dishwater" pus (*Intraoperative diagnosis*)

Differential Diagnosis:

- **Cellulitis:** Less toxic, no disproportionate pain, slower progression
- **Deep Vein Thrombosis (DVT):** No fever, no significant erythema, confirmed by Doppler US
- **Gas gangrene (Clostridium):** Muscle necrosis dominates, faster, bronze skin

- **Pyomyositis:** Muscle abscess, MRI

Therapy:**Outpatient:**

Drug	Dose	Note
NO outpatient treatment!	IMMEDIATE SURGERY!	Surgical emergency!

Inpatient:

Drug	Dose	Note
Piperacillin/tazobactam	4x4.5g IV	Broad spectrum
+ Vancomycin	2x15-20mg/kg IV	MRSA coverage
+ Clindamycin	3x900mg IV	Toxin production inhibition!

Icu:

Drug	Dose	Note
Meropenem	3x1g IV	Alternative
+ Vancomycin + Clindamycin		Triple therapy
IVIG	1-2g/kg	In streptococcal toxic shock syndrome

Targeted:

Based on culture results. For Group A Strep (GAS): Penicillin G + Clindamycin. For MRSA: Vancomycin or Linezolid. For polymicrobial infections: continue broad-spectrum coverage guided by sensitivities.

Supportive:

- IMMEDIATE aggressive surgical debridement
- ICU admission
- Vasopressors
- Multiple revisions (every 24-48 hours)
- HBO therapy (adjunctive)

Prevention:

- Wound hygiene
- Diabetes control
- Early cellulitis treatment

Erysipelas

Pathogen: Bacterium - Streptococcus pyogenes (Group A Streptococcus) (Gram-positive)

Epidemiology:

- Incidence: Common skin infection, 10-100/100,000 per year
- Seasonality: Mostly winter-spring
- Transmission: Endogenous (skin breach) or contact
- Risk Groups: Elderly, Infants, Diabetes mellitus, Chronic venous insufficiency, Lymphedema, Skin lesions

Pathomechanism:

Steps:

- Bacteria enter the skin (injury, eczema, wound)
- Spread through the lymphatic system
- Local inflammatory response
- Toxin production (streptolysins, pyrogenic toxins)
- Systemic symptoms (fever, toxemia)

Virulence Factors:

- M protein
- Streptolysins (O, S)
- Hyaluronidase
- Streptokinase

Clinical Features:

- Incubation: 2-5 days
- Onset: Acute

Symptoms:

- **Prodrome:** Fever, chills often precede skin symptoms (by 4-48 hours)
- **Skin symptoms:** Sharp-edged, raised, bright red plaque ("flame-like")
- **Location:** Lower limb (70-80%), Face (5-20%)
- **Pain:** Burning, tense character
- **Lymph node:** Regional lymphadenitis is common

Physical Exam:

- Red, warm, swollen area
- Sharp, raised borders (characteristic)
- Bullae or pustules may be present
- Lymphadenitis (regional lymph nodes swollen)
- Systemic signs: tachycardia, hypotension

Complications:

- Progression to cellulitis
- Septic shock
- Glomerulonephritis
- Recurrence is common

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis	Inflammation
CRP	Elevated	Acute phase
Blood culture	Rarely positive	In systemic infection

Imaging:

- **Not routinely needed:** - (*Diagnosis is clinical. Ultrasound can rule out deeper abscess.*)

Microbiology:

- **Blood culture:** Rarely positive (<5%) (*Should be taken in severe/systemic cases*)

Differential Diagnosis:

- **Cellulitis:** Deeper, less sharp borders, no raised plaque
- **Herpes zoster:** Vesicles, along a dermatome
- **Erythema migrans (Lyme):** Centrifugal spread, history
- **Contact dermatitis:** No fever, pruritus

Therapy:**Outpatient:**

Drug	Dose	Note
Penicillin V	4x500mg PO	First choice
Amoxicillin	3x500mg PO	Alternative

Inpatient:

Drug	Dose	Note
Penicillin G	4x4-6 million IU IV	In severe cases
Ceftriaxone	1x2g IV	In case of penicillin allergy

Icu:

Drug	Dose	Note
Broad spectrum	IV	In complicated cases

Targeted:

Streptococcus pyogenes: Penicillin. Allergy: Erythromycin/Clindamycin

Supportive:

- Rest
- Elevated limb
- Analgesics
- Antipyretics

Prevention:

- Prevention of skin injuries

- Hygiene
- Prophylaxis for recurrence (Penicillin monthly)

Cellulitis

Pathogen: Bacterium - Streptococcus pyogenes or Staphylococcus aureus (most common) (Gram-positive)

Epidemiology:

- Incidence: Common, 200/100,000 per year
- Seasonality: Mostly summer
- Transmission: Endogenous (skin breach) or exogenous inoculation
- Risk Groups: Diabetes mellitus, Peripheral vascular disease, Obesity, Immunosuppression, Skin injuries, Lymphedema

Pathomechanism:

Steps:

- Bacteria enter the dermis and subcutaneous tissues
- Local inflammation (neutrophils, edema)
- Spread in subcutaneous planes
- Lymphatic obstruction → increased edema
- Systemic response (fever, leukocytosis)

Virulence Factors:

- Streptococcus: M protein, toxins
- Staphylococcus: PVL, coagulase

Clinical Features:

- Incubation: 1-3 days
- Onset: Acute

Symptoms:

- **Skin symptoms:** Diffuse, non-sharp-edged erythema, warmth, swelling
- **Pain:** Tenderness, tension
- **Systemic symptoms:** Fever, chills, malaise (common)
- **Lymphangitis:** Red streaks along lymphatic vessels
- **Location:** Most commonly lower limb (unilateral)

Physical Exam:

- Red, warm, swollen skin
- Diffuse, non-sharp borders
- Tenderness
- Lymphangitis (red streaks)
- Systemic: tachycardia, fever

Complications:

- Abscess
- Necrotizing fasciitis
- Septic shock
- Osteomyelitis
- Lymphedema

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis	Inflammation
CRP	Elevated	Acute phase
Blood culture	Rarely positive	In severe cases

Imaging:

- **Ultrasound:** Fluid collection, abscess (*If suspected*)
- **CT/MRI:** Deeper spread (*In complicated cases*)

Microbiology:

- **Blood culture:** Rarely positive (<5-10%) (*Recommended in severe cases, immunosuppression, or systemic toxicity*)

Differential Diagnosis:

- **Erysipelas:** Superficial, sharp borders, raised plaque
- **Abscess:** Fluctuant swelling, puncture
- **DVT:** No erythema, Doppler US
- **Gout:** Monoarthritis, hyperuricemia

Therapy:

Outpatient:

Drug	Dose	Note
Amoxicillin/Clavulanate	3x875/125mg PO	First choice
Cephalexin	4x500mg PO	Alternative

Inpatient:

Drug	Dose	Note
Ceftriaxone	1x2g IV	In severe cases
+ Vancomycin	2x15-20mg/kg IV	If MRSA is suspected

Icu:

Drug	Dose	Note
Piperacillin/Tazobactam	3x4.5g IV	Broad spectrum

Targeted:

Streptococcus: Penicillin; Staphylococcus: Flucloxacillin; MRSA: Vancomycin

Supportive:

- Rest
- Elevated limb
- Analgesics
- Topical antibiotics are not effective

Prevention:

- Prevention of skin injuries
- Hygiene
- Diabetes control

Bone and Joint Infections

Osteomyelitis

Pathogen: Bacterium - Staphylococcus aureus (most common) (Gram-positive)

Epidemiology:

- Incidence: Hematogenous in children, post-traumatic/diabetic foot in adults
- Seasonality: None
- Transmission: Hematogenous spread, direct spread (wound), inoculation (trauma)
- Risk Groups: Diabetes mellitus, Peripheral vascular disease, Trauma/surgery, IV drug users, Hemodialysis

Pathomechanism:**Steps:**

- Bacteria adhere to bone tissue/implant
- Biofilm formation (basis of chronic infection)
- Inflammatory exudate increases intraosseous pressure
- Vessel compression → bone necrosis (sequestrum)
- New bone formation around the necrosis (involucrum)

Virulence Factors:

- Biofilm formation
- Adhesins (MSCRAMM)
- Toxins

Clinical Features:

- Incubation: Days (acute) or weeks-months (chronic)
- Onset: Variable

Symptoms:

- **Local pain:** Deep, throbbing pain (>90%), worsens with weight-bearing
- **Fever:** Common in acute hematogenous form (50-70%), rare in chronic
- **Swelling/Erythema:** Soft tissue swelling and redness over the affected area
- **Sinus tract:** Purulent discharge to the skin surface (sign of chronic osteomyelitis)

Physical Exam:

- Local tenderness over the bone
- Warmth, swelling, erythema
- Limited movement of the affected limb
- Probe-to-bone test: Bone can be palpated with a probe at the base of an ulcer (high specificity)

Complications:

- Chronic osteomyelitis
- Pathological fracture
- Septic arthritis
- Systemic sepsis
- Need for amputation

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (acute)	Inflammation
CRP/ESR	Elevated	Good for monitoring
Blood culture	Positive (50%)	In hematogenous origin

Imaging:

- **X-ray:** Negative in early phase! Later periosteal reaction, lytic lesions (*Late sign*)
- **MRI:** Bone marrow edema, abscess (*Gold standard (most sensitive)*)
- **Bone scintigraphy:** Increased uptake (*If MRI cannot be performed*)

Microbiology:

- **Bone biopsy culture:** Pathogen identification (*Gold standard diagnosis*)
- **Sinus tract discharge:** Often contaminated (*Not reliable*)

Differential Diagnosis:

- **Charcot foot:** No fever/inflammatory labs, neuropathy dominates
- **Ewing sarcoma:** X-ray (onion skin), biopsy
- **Cellulitis:** Only soft tissue involved, MRI differentiates

Therapy:

Outpatient:

Drug	Dose	Note

None	-	Usually requires hospital treatment/investigation
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Inpatient:

Drug	Dose	Note
Vancomycin	15-20mg/kg IV	MRSA coverage
+ Ceftriaxone/Cefepime	IV	Gram-negative coverage

Icu:

Drug	Dose	Note
Broad spectrum	IV	In case of sepsis

Targeted:

Based on bone biopsy! S. aureus: Flucloxacillin/Cefazolin; MRSA: Vancomycin/Daptomycin.

Duration: 4-6 weeks (often IV)

Supportive:

- Surgical debridement (removal of necrotic bone) - CRITICAL!
- Immobilization
- Analgesics

Prevention:

- Immediate care of open fractures
- Surgical sterility
- Diabetic foot care

Septic Arthritis

Pathogen: Bacterium - Staphylococcus aureus, N. gonorrhoeae (Mixed)

Epidemiology:

- Incidence: 2-10/100,000 per year
- Seasonality: None
- Transmission: Hematogenous (most common), direct inoculation, per continuitatem
- Risk Groups: Rheumatoid arthritis, Joint prosthesis, Elderly (>80 years), Diabetes, IV drug users, Sexually active young people (Gonococcus)

Pathomechanism:**Steps:**

- Bacteria enter the joint space
- Colonization of the synovial membrane
- Acute inflammatory response (neutrophil influx)
- Release of proteolytic enzymes

- Rapid destruction of cartilage and bone (within days!)

Virulence Factors:

- Adhesins
- Toxins
- Cartilage-damaging enzymes

Clinical Features:

- Incubation: Rapid (hours-days)
- Onset: Sudden

Symptoms:

- **Acute monoarthritis:** Pain and swelling of a single joint (80-90%)
- **Pain:** Intense, even at rest, extreme on movement
- **Fever:** Common (60-80%), but may be absent (elderly, immunosuppressed)
- **Immobility:** Inability to use the affected joint

Physical Exam:

- Swollen, warm, red joint
- Extreme tenderness
- Painful passive and active movement
- Joint effusion
- Gonococcus: migratory polyarthritis, tenosynovitis, dermatitis (pustules)

Complications:

- Joint destruction (arthrosis)
- Ankylosis
- Sepsis
- Osteomyelitis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis	Systemic reaction
CRP/ESR	Significantly elevated	Inflammation

Imaging:

- **X-ray:** Initially negative/soft tissue swelling, later joint space narrowing (*Baseline*)
- **Ultrasound:** Joint fluid (*Guiding puncture*)

Microbiology:

- **Joint aspiration (Arthrocentesis):** Purulent, >50,000 WBC/ μ L, >90% PMN (*DIAGNOSTIC!*)
- **Synovial fluid culture:** Positive (*Gold standard*)
- **Blood culture:** Positive (50%) (*Always take*)
- **PCR:** Gonococcus/Lyme (*If culture is negative*)

Differential Diagnosis:

- **Gout:** Crystals in aspirate (negative birefringence)
- **Pseudogout (CPPD):** Positively birefringent crystals
- **Reactive arthritis:** Sterile inflammation, history (GI/GU infection)
- **Lyme arthritis:** Less painful, serology

Therapy:**Outpatient:**

Drug	Dose	Note
None	-	Emergency hospital admission!

Inpatient:

Drug	Dose	Note
Vancomycin	15-20mg/kg IV	Gram+ (MRSA) coverage
+ Ceftriaxone	1x2g IV	Gram- (Gonococcus) coverage

Icu:

Drug	Dose	Note
Broad spectrum	IV	In case of sepsis

Targeted:

S. aureus: Cefazolin/Oxacillin; MRSA: Vancomycin; Gonococcus: Ceftriaxone. Duration: 2-4 weeks (IV then PO)

Supportive:

- Joint drainage (daily needle aspiration OR arthroscopy) - MANDATORY!
- Analgesics
- Early mobilization after inflammation subsides

Prevention:

- Sterility in prosthesis surgeries
- Prevention of gonorrhea

Spondylodiscitis

Pathogen: Bacterium - Staphylococcus aureus (most common), Streptococcus spp., Gram-negatives (Mixed)

Epidemiology:

- Incidence: Rare, 2-7/100,000 per year
- Seasonality: None
- Transmission: Hematogenous (most common), direct (surgery, trauma), per continuitatem

- Risk Groups: Elderly (>50 years), Diabetes mellitus, Immunosuppression, IV drug users, Post-spine surgery, Urogenital infections

Pathomechanism:

Steps:

- Bacterial spread into the bloodstream (e.g., UTI, endocarditis)
- Adhesion in spinal vessels (end arteries)
- Colonization of intervertebral disc and vertebrae
- Inflammatory response → edema, necrosis
- Biofilm formation → chronic infection

Virulence Factors:

- Adhesins (MSCRAMM)
- Biofilm formation
- Toxins

Clinical Features:

- Incubation: Days-weeks
- Onset: Slow, insidious

Symptoms:

- **Back pain:** Leading symptom (>90%), gradually worsening, present even at rest
- **Fever:** Present in only ~50% of cases, often low-grade
- **Neurological symptoms:** Radicular pain, weakness, paresis (30-50%)
- **General symptoms:** Fatigue, weight loss, night sweats

Physical Exam:

- Local tenderness or percussion pain over the affected vertebra
- Paravertebral muscle spasm
- Limited spinal mobility
- Neurological deficit (paresis, loss of reflexes, sensory disturbance)

Complications:

- Epidural abscess
- Paravertebral abscess
- Septic shock
- Spinal deformity
- Chronic pain

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis or normal	Inflammation
CRP/ESR	Significantly elevated	Excellent for monitoring
Blood culture	Positive (50-70%)	Pathogen identification

Imaging:

- **X-ray:** Late sign: vertebral destruction, disc height reduction (*Not sensitive in early stage*)
- **MRI:** Bone marrow edema, disc inflammation, abscess (*Gold standard (sensitivity >90%)*)
- **CT:** Bone destruction, abscess (*If MRI is not feasible*)

Microbiology:

- **CT-guided biopsy:** Culture + histology (*Gold standard diagnosis*)
- **Blood culture:** Positive (*Often sufficient*)

Differential Diagnosis:

- **Degenerative spine disease:** No fever/CRP elevation, different MRI
- **Spinal tumor/metastasis:** History, biopsy
- **Ankylosing spondylitis:** Younger age, HLA-B27 positive
- **Tuberculous spondylitis:** Chronic, multiple vertebrae, tuberculin test

Therapy:**Outpatient:**

Drug	Dose	Note
None	-	Hospitalization required

Inpatient:

Drug	Dose	Note
Vancomycin	15-20mg/kg IV	MRSA coverage
+ Ceftriaxone/Cefepime	IV	Gram-negative coverage

Icu:

Drug	Dose	Note
Broad spectrum	IV	In case of sepsis/abscess

Targeted:

Based on biopsy! S. aureus: Flucloxacillin/Cefazolin; MRSA: Vancomycin; Gram-negative: Ceftriaxone. Duration: 6-12 weeks (IV then PO)

Supportive:

- Surgical debridement (for abscess) - often necessary!
- Spinal stabilization
- Analgesics
- Physiotherapy

Prevention:

- UTI/endo prophylaxis
- Surgical sterility
- Diabetes control

⚡ Sepsis and Systemic Infections

Sepsis

Pathogen: Syndrome - Bacteria (G+/G-), Fungi, Virus (Variable)

Epidemiology:

- Incidence: Worldwide 49 million cases/year, 11 million deaths (20% of all deaths)
- Seasonality: None (more common in winter due to respiratory origin)
- Transmission: Not contagious (the causative infection might be)
- Risk Groups: Elderly (>65 years), Infants (<1 year), Immunosuppressed, Chronic patients, Patients with invasive devices

Pathomechanism:

Steps:

- Recognition of infection (PAMPs) by innate immune system (TLR)
- Pro-inflammatory cytokine storm (TNF- α , IL-1, IL-6)
- Endothelial activation and damage (vascular permeability↑)
- Activation of coagulation cascade (DIC) + inhibition of fibrinolysis
- Microcirculatory dysfunction, tissue hypoxia, mitochondrial dysfunction
- Multiple organ dysfunction syndrome (MODS)

Virulence Factors:

- Endotoxin (LPS)
- Superantigens
- Exotoxins
- Capsule

Clinical Features:

- Incubation: Depends on underlying disease
- Onset: Can progress within hours

Symptoms:

- **Fever or Hypothermia:** >38°C or <36°C (10-20% of patients are hypothermic)
- **Altered mental status:** GCS <15, agitation, lethargy (common early sign in elderly)
- **Hypotension:** Systolic BP <100 mmHg or MAP <65 mmHg
- **Tachypnea:** >22/min (often the first sign)
- **Oliguria:** <0.5 ml/kg/hour (decreased renal perfusion)
- **Skin symptoms:** Mottling, cold extremities (signs of shock)

Physical Exam:

- Fever or hypothermia
- Tachycardia (>90/min)
- Tachypnea (>20/min)
- Prolonged capillary refill time (>3 sec)

- Mottled skin (mottling score)
- Confusion

Complications:

- Septic shock (vasopressor requirement + lactate >2)
- ARDS
- DIC
- Acute kidney injury
- Liver failure
- Death

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Lactate	>2 mmol/L	Tissue hypoxia/shock (Severe!)
Blood culture	Positive (30-50%)	Take BEFORE AB administration (2 sets)
PCT	Significantly elevated	Bacterial origin probable
CBC	Leukocytosis or leukopenia	Inflammation

Imaging:

- **CT/X-ray/US:** Source search (*Crucial for source control*)

Microbiology:

- **Blood culture:** Pathogen identification (*Basis for targeted therapy*)
- **Other cultures:** Urine, sputum, wound, CSF (*Source dependent*)

Differential Diagnosis:

- **Cardiogenic shock:** Echo (decreased EF), elevated CVP/JVP
- **Hypovolemic shock:** History (bleeding, fluid loss), dry mucous membranes
- **Anaphylaxis:** Allergen exposure, urticaria, stridor
- **Adrenal insufficiency:** Hyponatremia, hyperkalemia, cortisol level

Therapy:

Guidelines: Surviving Sepsis Campaign 2021

Initial management:

Drug	Dose	Note
Antibiotics	Broad spectrum IV	After taking blood cultures. Source-dependent choice (e.g., Pip/Tazo, Meropenem).
Fluid resuscitation	30 ml/kg crystalloid	If hypotension or lactate ≥ 4 mmol/L.

Icu:

Drug	Dose	Note

Norepinephrine	Maintain MAP >65 mmHg	First choice vasopressor.
Vasopressin	max 0.03 U/min	Can be added to norepinephrine to reduce dose or if dose is high.
Hydrocortisone	200mg/day (e.g., 50mg q6h)	If vasopressor requirement persists (refractory shock).

Targeted:

De-escalation based on antibiogram (PCT can help decision). Source control (abscess drainage, necrotic tissue removal) is essential.

Supportive:

- Lactate clearance monitoring
- Ventilation (ARDS protocol)
- Renal replacement therapy (CRRT)
- Blood glucose control
- Thrombosis prophylaxis
- Stress ulcer prophylaxis

Prevention:

- Hospital hygiene
- Vaccinations (Pneumococcus, Influenza)
- Early removal of catheters
- Proper wound care

Toxic Shock Syndrome (TSS)

Pathogen: Bacterium - *Staphylococcus aureus*, *Streptococcus pyogenes* (Gram-positive)

Epidemiology:

- Incidence: Rare (Staph: 0.5/100,000, Strep: 3/100,000)
- Seasonality: None
- Transmission: Not directly transmitted (toxin mediated)
- Risk Groups: Menstruating women (tampon - rarer now), Surgical patients, Burn victims, Skin infections

Pathomechanism:**Steps:**

- Local infection (vagina, wound) or colonization
- Exotoxin production (TSST-1, Enterotoxins, SpeA/C)
- Superantigen effect: Non-specific activation of T-cells (up to 20%)
- Massive cytokine release (Cytokine storm)
- Capillary leak, vasodilation, shock
- Multiple organ failure

Virulence Factors:

- TSST-1 (Staph)
- Streptococcal Pyrogenic Exotoxins (Spe)
- M-protein (Strep)

Clinical Features:

- Incubation: Rapid (hours-days)
- Onset: Sudden

Symptoms:

- **High fever:** >38.9°C (sudden onset)
- **Hypotension:** Systolic BP <90 mmHg (adult), orthostatic dizziness
- **Diffuse erythroderma:** Sunburn-like rash (Staph: >90%, Strep: rarer)
- **Multisystem symptoms:** GI (vomiting/diarrhea), Muscle pain (CK elevation), Mucosal hyperemia
- **Desquamation:** 1-2 weeks after onset (palms/soles)

Physical Exam:

- Diffuse red rash (erythroderma)
- Hypotension, tachycardia
- Mucosal hyperemia (conjunctiva, oropharynx, vagina)
- Strawberry tongue (mainly Strep TSS)
- Altered mental status (55%)
- Signs of local soft tissue infection (Strep TSS: necrotizing fasciitis, myositis)

Complications:

- Shock
- ARDS
- DIC
- Renal failure
- Limb necrosis (Strep)
- Death

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Leukocytosis, thrombocytopenia	Systemic inflammation
Kidney/Liver	Creatinine↑, Transaminases↑	Organ failure
CK	Elevated	Rhabdomyolysis
Blood culture	Staph: often negative (toxin!), Strep: often positive	Etiology

Imaging:

- **CT/MRI:** Search for deep tissue infection (*Strep TSS (necrotizing fasciitis)*)

Microbiology:

- **Culture:** Wound, vagina, throat, blood (*Pathogen identification*)
- **Toxin detection:** TSST-1 (*Reference lab*)

Differential Diagnosis:

- **Sepsis (other):** No characteristic rash/desquamation
- **Meningococcemia:** Petechiae/purpura, meningitis signs
- **Drug reaction (DRESS):** New drug, slower, eosinophilia
- **Scarlet fever:** Milder, no shock

Therapy:

Outpatient:

Drug	Dose	Note
None	-	Immediate ICU admission!

Inpatient:

Drug	Dose	Note
Clindamycin	900mg IV q8h	Inhibition of toxin production! (Crucial)
+ Vancomycin/Linezolid	IV	MRSA coverage
+ Pip/Tazo or Meropenem	IV	If polymicrobial suspicion

Icu:

Drug	Dose	Note
IVIG	1-2g/kg	Toxin neutralization (Strep TSS)
Vasopressors	Norepinephrine	Shock management

Targeted:

Staph (MSSA): Flucloxacillin + Clindamycin; Strep: Penicillin G + Clindamycin. Source control (tampon removal, surgical exploration)!

Supportive:

- Massive fluid resuscitation
- Ventilation
- Dialysis
- Wound care

Prevention:

- Tampon hygiene (frequent change)
- Wound disinfection

Invasive Candidiasis

Pathogen: Fungus - *Candida albicans* (and non-albicans species) (Yeast)

Epidemiology:

- Incidence: 4th most common cause of nosocomial bloodstream infections
- Seasonality: None
- Transmission: Endogenous (from GI tract), exogenous (hands, devices)
- Risk Groups: ICU patients, Central venous catheter (CVC), Broad-spectrum AB, TPN, Abdominal surgery

Pathomechanism:

Steps:

- Mucosal barrier damage (AB, chemo)
- Translocation into bloodstream
- Biofilm formation (catheter)
- Hematogenous spread (eye, heart, liver, spleen)

Virulence Factors:

- Biofilm
- Adhesins
- Enzymes (protease, phospholipase)

Clinical Features:

- Incubation: Variable
- Onset: Slow or acute

Symptoms:

- **Persistent fever:** Fever unresponsive to antibiotics (common)
- **Sepsis/Septic shock:** Hypotension, tachycardia, altered mental status
- **Endophthalmitis:** Visual disturbance, eye pain (10-20% in candidemia)
- **Skin symptoms:** Erythematous papules/pustules (5-10%)
- **Hepatosplenitis candidiasis:** Fever, abdominal pain after neutropenia

Physical Exam:

- Fever, hemodynamic instability (signs of sepsis/shock)
- Fundoscopy (mandatory!): White, cotton-wool spots (Roth spot), chorioretinitis
- Skin symptoms: Erythematous papules or pustules
- New heart murmur (suspicion of endocarditis)
- Muscle tenderness (myositis)

Complications:

- Septic shock
- Endophthalmitis (blindness)
- Endocarditis
- Osteomyelitis
- Death

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Blood culture	Positive (only 50-70% sensitive!)	Gold standard
Beta-D-glucan	Elevated (>80 pg/mL)	Pan-fungal marker (except Mucor/Crypto)

Imaging:

- **Abdominal US/CT:** Microabscesses (liver, spleen) (*Chronic disseminated*)
- **Ophthalmology:** Chorioretinitis (*Mandatory in all fungemic patients!*)

Microbiology:

- **Culture:** Candida sp. (*Species identification and resistance (fluconazole!)*)
- **T2Candida:** DNA detection from blood (*Fast, sensitive*)

Differential Diagnosis:

- **Bacterial sepsis:** Blood culture, PCT (though can be elevated in fungal too)
- **Aspergillosis:** Lung dominance, Galactomannan
- **Catheter infection (bact):** Culture

Therapy:**Outpatient:**

Drug	Dose	Note
None	-	Hospital treatment

Inpatient:

Drug	Dose	Note
Fluconazole	800mg loading, then 400mg	Only stable patient, no prior azole exposure

Icu:

Drug	Dose	Note
Echinocandin (Caspofungin)	70mg -> 50mg	First choice in unstable/severe patient

Targeted:

C. albicans: Fluconazole (if sensitive); C. glabrata/krusei: Echinocandin. Ophthalmology: systemic + intravitreal.

Supportive:

- CVC removal (strongly recommended!)
- Ophthalmology consultation

Prevention:

- Hand washing
- Catheter care
- Prophylaxis (transplant patients)

Invasive Aspergillosis

Pathogen: Fungus - Aspergillus fumigatus (Mold)

Epidemiology:

- Incidence: 5-10% of neutropenic patients
- Seasonality: None (construction dust risk)
- Transmission: Inhalation of conidia (from air)
- Risk Groups: Prolonged neutropenia, Allogeneic stem cell transplant, Solid organ transplant, High dose steroids

Pathomechanism:

Steps:

- Inhalation of conidia into alveoli
- Macrophage failure (immunosuppression)
- Germination into hyphae
- Angioinvasion (breaking into vessels)
- Thrombosis, infarction, tissue necrosis
- Hematogenous spread (brain, skin)

Virulence Factors:

- Angioinvasion
- Gliotoxin
- Melanin

Clinical Features:

- Incubation: Days-weeks (during immunosuppression)
- Onset: Subacute/Acute

Symptoms:

- **Fever:** Fever unresponsive to antibiotics (most common sign in neutropenia)
- **Cough:** Dry or productive cough
- **Pleuritic chest pain:** Sharp, stabbing pain (sign of angioinvasion)
- **Hemoptysis:** Bloody sputum (late, severe sign)
- **Sinusitis symptoms:** Facial pain, black nasal discharge (rhinosinusitis form)

Physical Exam:

- Fever, tachypnea
- Lung auscultation may be sparse, or pleural friction rub
- Nose/sinus exam: Black, necrotic eschar on turbinate (invasive sinusitis)
- Focal neurological signs (brain dissemination)
- Skin symptoms (necrotic ulcers in disseminated case)

Complications:

- Massive pulmonary hemorrhage
- Brain abscess

- Disseminated aspergillosis
- Death

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Galactomannan (GM)	Index >0.5	Serum or BAL (specific for Aspergillus)
Beta-D-glucan	Positive	Non-specific

Imaging:

- **Chest CT:** Halo sign (early), Air-crescent sign (late), nodules (*Gold standard imaging*)

Microbiology:

- **BAL culture:** Aspergillus sp. (*Proven case*)
- **Microscopy:** Septate hyphae, 45° branching (*Biopsy/BAL*)

Differential Diagnosis:

- **Mucormycosis:** No septa, 90° branching, Voriconazole ineffective!
- **Bacterial pneumonia:** Imaging (halo), GM negative
- **Pulmonary embolism:** Angio CT, D-dimer

Therapy:

Outpatient:

Drug	Dose	Note
None	-	Hospital treatment

Inpatient:

Drug	Dose	Note
Voriconazole	6mg/kg -> 4mg/kg IV/PO	GOLD STANDARD (level monitoring!)

Icu:

Drug	Dose	Note
Isavuconazole	200mg IV/PO	Fewer side effects
Liposomal Amphotericin B	3-5mg/kg IV	Alternative

Targeted:

Voriconazole or Isavuconazole. Salvage: L-AmB, Caspofungin (combination controversial).

Supportive:

- Reduction of immunosuppression (if possible)
- G-CSF (neutropenia recovery)
- Surgical resection (massive hemoptysis)

Prevention:

- Posaconazole prophylaxis (neutropenia)
- HEPA filtered rooms
- Mask wearing

Childhood Infections

Measles (Morbilli)

Pathogen: Virus - Measles morbillivirus (ssRNA, Paramyxoviridae)

Epidemiology:

- Incidence: Epidemic in unvaccinated populations
- Seasonality: Winter-Spring
- Transmission: Droplet infection (highly contagious! $R_0=12-18$)
- Risk Groups: Unvaccinated, Immunosuppressed

Pathomechanism:

Steps:

- Respiratory entry
- Viremia
- Infection of endothelial/epithelial/immune cells
- Immunosuppression (for months)

Virulence Factors:

- Hemagglutinin
- Fusion protein

Clinical Features:

- Incubation: 10-14 days
- Onset: Prodrome (fever, 3C)

Symptoms:

- **Prodrome (3C):** Fever ($>40^{\circ}\text{C}$), Cough, Coryza, Conjunctivitis - almost 100%
- **Koplik spots:** Pathognomonic salt grain-like spots on the buccal mucosa (60-70% before rash)
- **Rash:** Maculopapular, starts behind ears → face → trunk (3rd day) → limbs (confluent)

Physical Exam:

- Koplik spots
- Exanthema
- Fever
- Conjunctivitis

Complications:

- Otitis media

- Pneumonia (giant cell)
- Encephalitis
- SSPE (years later)

Diagnostics:Laboratory:

Test	Finding	Interpretation
CBC	Leukopenia	-

Microbiology:

- **IgM serology:** Positive (after rash) (*Diagnostic*)
- **PCR:** RNA (throat, urine) (*Early phase*)

Therapy:**Outpatient:**

Drug	Dose	Note
Supportive	-	Antipyretics, fluids

Targeted:

Vitamin A administration reduces morbidity/mortality (WHO recommendation).

Prevention:

- MMR vaccine (15 months, 11 years)

Mumps (Epidemic Parotitis)

Pathogen: Virus - Mumps orthorubulavirus (ssRNA, Paramyxoviridae)

Epidemiology:

- Incidence: In unvaccinated
- Seasonality: Winter-Spring
- Transmission: Droplet infection, saliva
- Risk Groups: Unvaccinated

Pathomechanism:Steps:

- Respiratory entry
- Viremia
- Infection of glandular tissues (parotid, testes, pancreas) and CNS

Virulence Factors:

- -

Clinical Features:

- Incubation: 16-18 days

- Onset: Acute

Symptoms:

- **Parotitis:** Parotid swelling (95% of symptomatic cases), initially unilateral, then bilateral (90%)
- **Fever:** Moderate, prodromal
- **Orchitis:** Testicular inflammation (20-30% of postpubertal boys), painful

Physical Exam:

- Parotid swelling (earlobe lifted)
- Testicular swelling/pain

Complications:

- Meningitis (aseptic)
- Orchitis (sterility rare)
- Pancreatitis
- Deafness

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Amylase	Elevated (salivary/pancreatic origin)	-

Microbiology:

- **IgM serology:** Positive (*Diagnostic*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Pain relief, compresses

Targeted:

None.

Prevention:

- MMR vaccine

Rubella (German Measles)

Pathogen: Virus - Rubella virus (ssRNA, Matonaviridae)

Epidemiology:

- Incidence: Rare (due to vaccination)
- Seasonality: Spring
- Transmission: Droplet infection

- Risk Groups: Unvaccinated, Pregnant women (fetus!)

Pathomechanism:

Steps:

- Respiratory entry
- Viremia
- Skin/lymph node involvement
- Transplacental transmission (teratogenic!)

Virulence Factors:

- -

Clinical Features:

- Incubation: 14-21 days
- Onset: Mild

Symptoms:

- **Rash:** Fine, pale pink (50-80%), spreads from face downwards, disappears in 3 days
- **Lymphadenopathy:** Occipital, retroauricular, posterior cervical (nearly 100%)
- **Arthralgia/Arthritis:** Common in adult women (up to 70%)

Physical Exam:

- Lymph node swelling (nape)
- Rash

Complications:

- Congenital Rubella Syndrome (CRS): heart defects, cataracts, deafness
- Arthritis
- Encephalitis (rare)

Diagnostics:

Microbiology:

- **IgM serology:** Positive (*Diagnostic*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	-

Targeted:

None.

Prevention:

- MMR vaccine
- Screening of pregnant women

Scarlet Fever (Scarlatina)

Pathogen: Bacterium - Streptococcus pyogenes (GAS) (Gram-positive)

Epidemiology:

- Incidence: Common in childhood
- Seasonality: Winter-Spring
- Transmission: Droplet infection
- Risk Groups: 5-15 years old

Pathomechanism:

Steps:

- Pharyngitis
- Erythrogenic toxin production (superantigen)
- Skin reaction

Virulence Factors:

- Erythrogenic toxin (SpeA, B, C)

Clinical Features:

- Incubation: 2-5 days
- Onset: Sudden

Symptoms:

- **Sore throat:** Severe pharyngitis (>90%)
- **Fever:** High, sudden onset
- **Rash:** Diffuse red, "sandpaper" feel, blanches on pressure (Pastia lines in folds)
- **Tongue:** White strawberry tongue (days 1-2) → Red raspberry tongue (days 4-5)

Physical Exam:

- Pharyngeal hyperemia
- Raspberry tongue
- Filatov's sign (circumoral pallor)
- Pastia lines (in folds)
- Desquamation (later)

Complications:

- Rheumatic fever
- Glomerulonephritis
- Peritonsillar abscess

Diagnostics:

Microbiology:

- **Throat swab culture:** Strep. pyogenes (*Gold standard*)
- **Rapid test (Strep A):** Positive (*Rapid*)

Therapy:

Outpatient:

Drug	Dose	Note
Penicillin V	PO	First choice
Amoxicillin	PO	Alternative
Macrolide (e.g., Azithromycin)	PO	In case of Penicillin allergy

Targeted:

Penicillin.

Prevention:

- Hygiene
- No vaccine

Infectious Mononucleosis (Kissing Disease)

Pathogen: Virus - Epstein-Barr virus (EBV) (dsDNA, Herpesviridae (HHV-4))

Epidemiology:

- Incidence: Adolescents/young adults (90% infected by adulthood)
- Seasonality: None
- Transmission: Saliva (kissing), droplet infection
- Risk Groups: Young people

Pathomechanism:**Steps:**

- Infection of oropharyngeal epithelium
- Infection of B-lymphocytes (immortalization)
- Cytotoxic T-cell response (atypical lymphocytes)
- Latency in B-cells

Virulence Factors:

- LMP, EBNA proteins

Clinical Features:

- Incubation: 4-6 weeks
- Onset: Gradual

Symptoms:

- **Sore throat:** Severe, often pseudomembranous (>80%)
- **Fever:** Prolonged (can last 10-14 days), >90%
- **Lymphadenopathy:** Generalized, symmetrical, mainly posterior cervical (>90%)
- **Fatigue:** Pronounced, can last for weeks to months

Physical Exam:

- Generalized lymphadenopathy (cervical dominance)
- Hepatosplenomegaly
- Tonsillar exudate
- Ampicillin rash (if AB was given)

Complications:

- Splenic rupture (rare but dangerous)
- Airway obstruction (tonsils)
- Hepatitis
- Burkitt lymphoma (late, endemic)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Lymphocytosis, atypical mononuclear cells (>10%)	Characteristic
Liver enzymes	Mild elevation	Common

Microbiology:

- **Monospot test:** Heterophile antibody positive (*Rapid (often negative in children!)*)
- **EBV serology:** VCA IgM+, EBNA- (acute) (*Confirmation*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Rest, fluids

Targeted:

None. Steroids only in case of airway obstruction.

Supportive:

- Physical rest (no sports for 3-4 weeks due to risk of splenic rupture!)

Prevention:

- Hygiene

Exanthema Subitum (Roseola infantum / Sixth Disease)

Pathogen: Virus - Human Herpesvirus 6 (HHV-6) (dsDNA, Herpesviridae)

Epidemiology:

- Incidence: Infants/toddlers (6 months - 2 years) almost all infected
- Seasonality: Year-round
- Transmission: Saliva (from asymptomatic carrier adults)
- Risk Groups: Infants

Pathomechanism:Steps:

- Mucosal infection
- Viremia
- T-cell tropism
- Latency

Virulence Factors:

- -

Clinical Features:

- Incubation: 5-15 days
- Onset: Sudden

Symptoms:

- **High fever:** 39-40°C, for 3-5 days (100%), with good general condition
- **Rash:** Appears AFTER fever subsides (important difference!), pink maculopapular
- **Nagayama spots:** Ulcers/papules at the base of the uvula

Physical Exam:

- Fever
- Nagayama spots (at base of uvula)
- Cervical/occipital lymphadenopathy
- Rash (later)

Complications:

- Febrile seizure (common cause!)
- Encephalitis (rare)

Diagnostics:Laboratory:

Test	Finding	Interpretation
CBC	Leukopenia	-

Microbiology:

- **Clinical picture:** Rash after fever (*Diagnostic*)

Therapy:**Outpatient:**

Drug	Dose	Note
Supportive	-	Antipyretics

Targeted:

None.

Prevention:

- -

Chickenpox (Varicella)

Pathogen: Virus - Varicella-zoster virus (VZV) (dsDNA, Herpesviridae (HHV-3))

Epidemiology:

- Incidence: Very common in childhood (unvaccinated)
- Seasonality: Winter-Spring
- Transmission: Droplet infection, vesicle fluid (airborne!)
- Risk Groups: Unvaccinated children, Immunosuppressed, Pregnant women, Adults (more severe)

Pathomechanism:

Steps:

- Respiratory entry
- Viremia
- Skin and mucosal infection
- Latency in sensory ganglia

Virulence Factors:

- -

Clinical Features:

- Incubation: 10-21 days
- Onset: Sudden

Symptoms:

- **Rash:** Polymorphic (macule-papule-vesicle-crust simultaneously), itchy (100%)
- **Fever:** Moderate (in children), higher in adults
- **Enanthema:** Oral mucosal vesicles, painful

Physical Exam:

- Polymorphic rash (also on scalp!)
- Fever
- Lymphadenopathy

Complications:

- Bacterial superinfection (impetiginization)
- Cerebellitis (ataxia)
- Pneumonia (adults)
- Encephalitis
- Reye syndrome (aspirin!)

Diagnostics:

Microbiology:

- **Clinical picture:** Characteristic (*Diagnostic*)
- **PCR:** VZV DNA (*In uncertain cases*)

Therapy:**Outpatient:**

Drug	Dose	Note
Supportive	-	Cooling lotions NOT recommended (superinfection), rather powder or nothing. Itch relief.

Targeted:

Acyclovir (for risk groups, adults, immunosuppressed).

Prevention:

- Varicella vaccine (mandatory)

Shingles (Herpes Zoster)

Pathogen: Virus - Varicella-zoster virus (VZV) reactivation (dsDNA)

Epidemiology:

- Incidence: Mainly elderly, but also in immunosuppressed children
- Seasonality: None
- Transmission: Vesicle fluid is infectious (can cause varicella in seronegative individuals)
- Risk Groups: Immunosuppressed, Previous varicella

Pathomechanism:**Steps:**

- Reactivation of latent virus in ganglion
- Axonal transport to skin
- Dermatomal rash

Virulence Factors:

- -

Clinical Features:

- Incubation: -
- Onset: Starts with pain

Symptoms:

- **Pain:** Prodromal (70-80%), burning, shooting in the dermatome
- **Rash:** Grouped vesicles on red base, unilateral, dermatomal

Physical Exam:

- Dermatomal distribution of vesicles (does not cross midline)

Complications:

- Postherpetic neuralgia (PHN)
- Zoster ophthalmicus (eye)
- Ramsay Hunt syndrome (ear/facial nerve)

Diagnostics:

Microbiology:

- **Clinical picture:** Characteristic (*Diagnostic*)

Therapy:

Outpatient:

Drug	Dose	Note
Acyclovir	5x800mg PO	Started within 72 hours
Valacyclovir	3x1000mg PO	Better bioavailability

Targeted:

Antiviral agent + Pain relief.

Prevention:

- Zoster vaccine (for elderly)

Herpes Simplex Infections (Gingivostomatitis)

Pathogen: Virus - Herpes Simplex Virus 1 (HSV-1) (dsDNA, Herpesviridae)

Epidemiology:

- Incidence: Common in early childhood (1-3 years)
- Seasonality: None
- Transmission: Saliva, direct contact
- Risk Groups: Toddlers

Pathomechanism:

Steps:

- Mucosal infection
- Vesicles, ulcers
- Latency in ganglia

Virulence Factors:

- -

Clinical Features:

- Incubation: 2-12 days
- Onset: Sudden

Symptoms:

- **Gingivostomatitis:** Fever, painful gingivitis, ulcers (most common primary form in children)

- **Herpes labialis:** Recurrence (cold sore), prodromal tingling
- **Eczema herpeticum:** Superinfection of atopic dermatitis (severe!)

Physical Exam:

- Swollen, bleeding gums
- Ulcers on tongue/palate
- Cervical lymphadenopathy
- Fever

Complications:

- Dehydration (refusal to drink due to pain)
- Eczema herpeticum
- Herpetic whitlow
- Encephalitis

Diagnostics:

Microbiology:

- **Clinical picture:** Characteristic (*Diagnostic*)
- **PCR:** HSV DNA (*In severe/atypical cases*)

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Pain relief, fluids, painting
Acyclovir	PO/IV	In severe cases or immunosuppression

Targeted:

Acyclovir.

Prevention:

- Avoid contact with active lesions

Pertussis (Whooping Cough)

Pathogen: Bacterium - *Bordetella pertussis* (Gram-negative)

Epidemiology:

- Incidence: Epidemic in unvaccinated children
- Seasonality: Winter-Spring
- Transmission: Droplet infection (highly contagious! $R_0=12-17$)
- Risk Groups: Infants (<6 months), Unvaccinated children, Adults (milder)

Pathomechanism:

Steps:

- Respiratory entry

- Adhesion to cilia (filamentous hemagglutinin)
- Toxin production (pertussis toxin → lymphocytosis, coughing fits)
- Destruction of cilia → impaired mucociliary clearance

Virulence Factors:

- Pertussis toxin (PT)
- Filamentous hemagglutinin (FHA)
- Adenylate cyclase toxin (ACT)

Clinical Features:

- Incubation: 7-10 days
- Onset: Catarrhal phase (1-2 weeks)

Symptoms:

- **Catarrhal phase:** Mild fever, coryza, cough (1-2 weeks) - most contagious phase
- **Paroxysmal phase:** Severe coughing fits (100%), whoop (inspiratory gasp 60-70%), vomiting (50%)
- **Convalescent phase:** Cough decreases, but can last for weeks ("100-day cough")

Physical Exam:

- Coughing fits (whoop characteristic in children)
- Apnea (infants)
- Lymphocytosis (>20,000/ μ L)
- Petechiae (due to straining)

Complications:

- Pneumonia (bacterial/viral)
- Encephalopathy
- Apnea/death (infants)
- Atelectasis
- Hernia (due to coughing)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Lymphocytosis (>20,000/ μ L)	Characteristic
CRP	Normal or slightly elevated	Non-inflammatory

Microbiology:

- **Nasopharyngeal aspirate culture:** *Bordetella pertussis* (*Gold standard (in early phase)*)
- **PCR:** DNA detection (*Rapid, sensitive*)
- **Serology:** IgG/IgA elevation (*Late diagnosis*)

Therapy:

Outpatient:

Drug	Dose	Note

Azithromycin	10mg/kg/day PO	First choice
Clarithromycin	15mg/kg/day PO	Alternative

Targeted:

Macrolide antibiotic (erythromycin, azithromycin).

Supportive:

- Supportive (oxygen, rehydration)
- Isolation (5 days after antibiotic)
- Cough suppressants NO (mucus retention!)

Prevention:

- DTP vaccine (mandatory, 3+1 doses)
- Adult booster

Sexually Transmitted Infections

Syphilis

Pathogen: Spirochete - *Treponema pallidum* (Gram-negative (stains poorly))

Epidemiology:

- Incidence: Increasing incidence worldwide, high in MSM population
- Seasonality: None
- Transmission: Direct contact with mucous membranes/skin, vertical (congenital)
- Risk Groups: MSM (men who have sex with men), HIV positive individuals, Sex workers, Multiple sexual partners, Drug users

Pathomechanism:**Steps:**

- *T. pallidum* enters through mucous membranes/skin
- Local multiplication → primary lesion (chancre)
- Hematogenous spread (primary viremia)
- Secondary syphilis: disseminated disease
- Latent phase: immune response keeps it under control
- Tertiary: chronic granulomatous inflammation (gumma) or vascular/neurological involvement

Virulence Factors:

- Fibronectin-binding proteins
- Hyaluronidase
- Antigenic variation
- Outer membrane proteins

Clinical Features:

- Incubation: Primary: 9-90 days (average 21 days)
- Onset: Phase-dependent

Symptoms:

- **Primary: Chancre:** Painless, hard-edged ulcer (single in 60-80%)
- **Secondary: Rash:** Generalized, non-pruritic (75-100%), involvement of palms/soles (60-80%)
- **Secondary: Lymphadenopathy:** Generalized, painless (50-85%)
- **Secondary: Condyloma lata:** Flat, weeping papules (10-20%)
- **Tertiary: Gumma:** Granulomatous lesions (15% in untreated cases)
- **Neurosyphilis:** In any stage! (Symptomatic: 5-10%)

Physical Exam:

- Primary: painless genital/extragenital ulcer + inguinal lymphadenopathy
- Secondary: generalized non-pruritic rash (palms/soles!), mucous patches, alopecia
- Latent: asymptomatic
- Tertiary: gumma (skin, bone), cardiovascular or nervous system involvement

Complications:

- Neurosyphilis
- Cardiovascular syphilis (aortitis)
- Gumma
- Congenital syphilis
- Increased risk of HIV coinfection

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
Non-treponemal test (RPR/VDRL)	Reactive (titer)	Screening, monitoring activity, treatment efficacy
Treponemal-specific test (TPHA/FTA-ABS)	Reactive	Confirmation, remains positive for life
Reverse algorithm	EIA/CIA → RPR → TPHA	Automated screening

Imaging:

- **Brain MRI:** Neurosyphilis: meningeal enhancement, infarcts (*In case of neurological symptoms*)
- **Echo/Chest CT:** Aortic dilatation (*Cardiovascular syphilis*)

Microbiology:

- **Dark-field microscopy:** Live spirochetes from primary lesions (*Early diagnosis, but rarely available*)
- **PCR:** T. pallidum DNA (*Sensitive, but not routine*)

- **CSF analysis:** VDRL positive, pleocytosis, protein↑ (*Neurosypphilis diagnosis*)

Differential Diagnosis:

- **Genital herpes:** Painful, grouped vesicles
- **Chancroid (H. ducreyi):** Painful ulcers, suppurative lymph nodes
- **Lymphogranuloma venereum:** Painful bubo, Chlamydia trachomatis L1-3
- **Drug rash:** Drug history, palm/sole involvement is rare
- **Pityriasis rosea:** Herald patch, Christmas tree pattern

Therapy:

Outpatient:

Drug	Dose	Note
Benzylpenicillin G (Bicillin LA)	2.4 million IU IM	Early syphilis (primary, secondary, early latent <1 year)
Penicillin allergy: Doxycycline	2x100mg PO	Alternative (compliance!)

Inpatient:

Drug	Dose	Note
Benzylpenicillin G	2.4 million IU IM	Late latent (>1 year) or unknown duration

Icu:

Drug	Dose	Note
Aqueous Penicillin G	3-4 million IU IV every 4 hours	Neurosypphilis!

Targeted:

Penicillin is always the first choice, no resistance

Supportive:

- Jarisch-Herxheimer reaction warning
- HIV testing
- Partner notification and treatment
- Serological follow-up (3, 6, 12, 24 months)

Prevention:

- Condom use
- Partner notification
- Regular screening in risk groups
- Screening of pregnant women

HIV Infection and AIDS

Pathogen: Virus - Human Immunodeficiency Virus (HIV-1, HIV-2) (RNA retrovirus)

Epidemiology:

- Incidence: ~38 million people living with HIV worldwide
- Seasonality: None
- Transmission: Sexual, parenteral (blood), vertical (mother-to-child)
- Risk Groups: MSM, IV drug users, Sex workers, Transfusion recipients (developing countries), Partners

Pathomechanism:

Steps:

- Virus binding to CD4 receptor and co-receptors (CCR5/CXCR4)
- Reverse transcription (RNA → DNA)
- Integration into the host cell genome (provirus)
- Progressive destruction of CD4+ T-cells
- Immune system depletion → Opportunistic infections (AIDS)

Virulence Factors:

- gp120/gp41 (entry)
- Reverse transcriptase (high mutation rate)
- Nef, Tat, Rev (regulators)

Clinical Features:

- Incubation: 2-4 weeks (acute retroviral syndrome)
- Onset: Acute (ARS) or latent

Symptoms:

- **Acute (ARS): Fever:** Most common symptom (>80-90%)
- **Acute (ARS): Fatigue:** Pronounced (>70-90%)
- **Acute (ARS): Rash:** Maculopapular (40-80%)
- **Acute (ARS): Pharyngitis:** Sore throat (50-70%)
- **Latent phase:** Asymptomatic or PGL (for years)
- **AIDS:** Opportunistic infections (CD4 <200)

Physical Exam:

- Generalized lymphadenopathy (PGL)
- Oral candidiasis (thrush)
- Seborrhea of the scalp
- Kaposi's sarcoma (purple skin lesions)

Complications:

- *Pneumocystis jirovecii* pneumonia (PCP)
- Toxoplasma encephalitis
- Cryptococcus meningitis
- CMV retinitis
- Kaposi's sarcoma
- Lymphoma

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CD4 count	Decreasing (<200/ μ L = AIDS)	Immune status
CBC	Lymphopenia, thrombocytopenia	Cytopenia

Microbiology:

- **Screening test (4th generation ELISA):** Ag/Ab positive (*Short window period (2-3 weeks)*)
- **Confirmatory test (Western Blot / Immunoblot):** Positive (*Diagnosis*)
- **HIV RNA PCR (Viral Load):** Copies/mL (*Therapy monitoring and acute infection*)

Differential Diagnosis:

- **Mononucleosis (EBV):** Heterophile antibody, atypical lymphocytes
- **Influenza:** Seasonality, faster course
- **Secondary syphilis:** Serology, palm/sole rash

Therapy:

Guidelines: EACS Guidelines Version 12.0 (2023)

Outpatient:

Drug	Dose	Note
Bictegravir / TAF / Emtricitabine	1 tab (50/25/200mg) PO 1x	Preferred first-line (STR). Does not require HLA testing.
Dolutegravir + TDF/TAF + FTC/3TC	Combination	Preferred first-line.
Dolutegravir / Lamivudine	1 tab (50/300mg) PO 1x	Dual therapy (if VL <500,000, no HBV, CD4 >200).

Targeted:

Immediate ART start (Rapid initiation) is recommended. Goal: undetectable viral load (<50 cp/mL).

Supportive:

- Opportunistic prophylaxis (PCP: TMP/SMX if CD4<200; Toxoplasma: TMP/SMX if CD4<100 and IgG+)
- Vaccinations (Pneumococcus, Influenza, HBV, HAV, HPV, Meningococcus, VZV - live vaccine contraindicated if CD4<200)

Prevention:

- PrEP (TDF/FTC or TAF/FTC)
- PEP (ART for 28 days, started <48 hours)
- U=U (Undetectable = Untransmittable)



Parasitic Infections

Malaria

Pathogen: Protozoan - Plasmodium falciparum, vivax, ovale, malariae (-)

Epidemiology:

- Incidence: >200 million cases/year worldwide, >400,000 deaths
- Seasonality: Rainy season (mosquitoes)
- Transmission: Anopheles mosquito bite
- Risk Groups: Travelers to endemic areas, Children (<5 years), Pregnant women, Immunosuppressed

Pathomechanism:

Steps:

- Mosquito bite → sporozoites into blood
- Liver phase (exoerythrocytic): schizont formation
- Blood phase (erythrocytic): RBC invasion, multiplication, rupture
- Cyclic fever attacks (RBC rupture)
- Cytoadherence (*P. falciparum*): microcirculation blockage (brain, kidney)

Virulence Factors:

- PfEMP1 (adhesion)
- Antigenic variation
- Hemozoin pigment

Clinical Features:

- Incubation: 7-30 days (species-dependent)
- Onset: Sudden

Symptoms:

- **Fever attack:** Chills → Fever → Sweating (cyclic)
- **Headache:** Intense
- **Nausea, vomiting:** Common
- **Severe anemia:** RBC destruction
- **Cerebral malaria:** Coma, seizures (*P. falciparum*)

Physical Exam:

- Fever, tachycardia
- Splenomegaly (common)
- Hepatomegaly
- Pallor (anemia)
- Jaundice (hemolysis)

Complications:

- Cerebral malaria

- Severe anemia
- ARDS
- Renal failure (blackwater fever)
- Hypoglycemia
- Shock

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Anemia, thrombocytopenia	Hemolysis/sequestration
LDH, Bilirubin	Elevated	Hemolysis
Blood glucose	May be low	Severe malaria

Imaging:

- **Head CT:** Cerebral edema (*Exclusion of cerebral malaria*)

Microbiology:

- **Thick/Thin blood smear:** Plasmodium forms (*GOLD STANDARD (Giemsa)*)
- **Rapid Diagnostic Test (RDT):** HRP-2 or pLDH antigen (*Fast, but less sensitive at low parasitemia*)
- **PCR:** DNA (*At low parasitemia*)

Differential Diagnosis:

- **Influenza:** No travel history, lack of periodicity
- **Dengue fever:** Retro-orbital pain, rash, bone-breaking pain
- **Typhoid fever:** Bradycardia, rose spots, GI symptoms dominate
- **Meningitis:** Nuchal rigidity, CSF findings

Therapy:

Guidelines: WHO Guidelines for malaria (2023)

Outpatient:

Drug	Dose	Note
Artemether-Lumefantrine	PO (weight-based)	First-line ACT for uncomplicated P. falciparum.
Dihydroartemisinin-Piperaquine	PO	Alternative ACT.
Artesunate-Pyronaridine	PO	Alternative ACT.
Chloroquine	PO	Only for P. vivax/ovale/malariae if from a chloroquine-sensitive area.

Inpatient:

Drug	Dose	Note

Artesunate	2.4 mg/kg IV/IM	First choice for severe malaria (adult/child/pregnant). Follow with a full course of ACT!
Artemether	3.2 mg/kg IM	Alternative if artesunate is not available.
Quinine	20 mg/kg loading, then 10 mg/kg q8h	Third-line, ECG monitoring required!

Targeted:

P. vivax/ovale radical cure: Primaquine (0.25-0.5 mg/kg for 14 days) or Tafenoquine (single dose) against hypnozoites. G6PD deficiency screening is mandatory!

Supportive:

- Fluid resuscitation (cautiously, risk of pulmonary edema!)
- Blood glucose monitoring (hypoglycemia is common)
- Antipyretics (paracetamol)
- Transfusion (severe anemia)
- Dialysis (renal failure)

Prevention:

- Chemoprophylaxis (Atovaquone-Proguanil, Doxycycline, Mefloquine)
- Mosquito net (LLIN)
- Vaccine (RTS,S/AS01 and R21/Matrix-M for children in endemic areas)

Toxoplasmosis

Pathogen: Protozoan - *Toxoplasma gondii* (-)

Epidemiology:

- Incidence: 30-50% of the world's population is seropositive (latent)
- Seasonality: None
- Transmission: Feco-oral (cat feces), raw meat (cyst), vertical
- Risk Groups: Immunosuppressed (HIV/AIDS, transplant), Pregnant women (fetus!), Cat owners

Pathomechanism:**Steps:**

- Ingestion of oocyst/tissue cyst
- Intestinal wall penetration → tachyzoites (rapid multiplication)
- Hematogenous spread (acute phase)
- Immune response → bradyzoites (slow) → tissue cyst formation (muscle, brain, eye)
- Latency (lifelong)
- Reactivation (immunosuppression): cyst rupture → encephalitis

Virulence Factors:

- Intracellular survival
- Cyst formation
- Immunomodulation

Clinical Features:

- Incubation: 5-23 days
- Onset: Slow/asymptomatic

Symptoms:

- **Asymptomatic:** 80-90% of immunocompetent individuals
- **Mononucleosis-like:** Fever, lymphadenopathy, fatigue
- **Cerebral (AIDS):** Headache, confusion, seizures, hemiparesis
- **Chorioretinitis:** Blurred vision, eye pain
- **Congenital:** Hydrocephalus, calcification, chorioretinitis (Sabin's tetrad)

Physical Exam:

- Cervical lymphadenopathy (painless)
- Fever (rare)
- Focal neurological signs (cerebral toxo)
- Fundoscopy: yellowish-white lesions

Complications:

- Toxoplasma encephalitis (TE)
- Blindness
- Pneumonitis
- Myocarditis
- Fetal death/damage

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Lymphocytosis	Non-specific
CD4 count	<100/ μ L	Risk of reactivation (HIV)

Imaging:

- **Brain MRI:** Multiple ring-enhancing lesions (basal ganglia) (*Cerebral toxo (AIDS)*)
- **Head CT:** Calcification (congenital) (*Newborn*)

Microbiology:

- **Serology (IgM/IgG):** IgM (acute), IgG (past/latent) (*Avidity test (pregnancy)*)
- **PCR:** DNA (CSF, amniotic fluid, blood) (*Proof of active infection*)
- **Histology:** Tachyzoites (*Biopsy (rare)*)

Differential Diagnosis:

- **Mononucleosis (EBV/CMV):** Serology, sore throat dominates
- **CNS Lymphoma:** MRI (solitary, periventricular), EBV PCR, Thallium SPECT

- **Cat-scratch disease:** Unilateral lymph node, inoculation site
- **Other encephalitis:** CSF findings, imaging

Therapy:**Outpatient:**

Drug	Dose	Note
None	-	Asymptomatic immunocompetent individuals do not require treatment

Inpatient:

Drug	Dose	Note
Pyrimethamine + Sulfadiazine	PO	Standard treatment (+Folinic acid!)
Trimethoprim/Sulfamethoxazole	PO/IV	Alternative

Icu:

Drug	Dose	Note
Steroid	Dexamethasone	In case of mass effect (cerebral edema)

Targeted:

Pregnancy: Spiramycin (1st trimester) or Pyrimethamine/Sulfadiazine (later). HIV prophylaxis: TMP/SMX.

Supportive:

- Folinic acid supplementation (Leucovorin) for bone marrow protection
- Anticonvulsants

Prevention:

- Thorough cooking of meat
- Avoid cat litter (pregnant women)
- Hand washing
- Prophylaxis if CD4<100 (TMP/SMX)

Ascariasis (Roundworm)

Pathogen: Helminth - Ascaris lumbricoides (-)

Epidemiology:

- Incidence: Most common helminth infection worldwide (>800 million)
- Seasonality: None
- Transmission: Feco-oral (soil/vegetables contaminated with eggs)
- Risk Groups: Children, People in poor hygienic conditions

Pathomechanism:**Steps:**

- Egg ingestion
- Larva hatches in the small intestine
- Migrates to the lungs via the venous system (Löffler's syndrome)
- Coughed up and swallowed
- Adult worm in the small intestine (nutrient deprivation, obstruction)

Virulence Factors:

- Protease inhibitors
- Migration ability

Clinical Features:

- Incubation: 4-8 weeks
- Onset: Slow

Symptoms:

- **Lung phase:** Cough, dyspnea, Löffler's syndrome
- **Intestinal phase:** Abdominal pain, bloating, nausea
- **Obstruction:** Ileus (worm bolus), biliary obstruction

Physical Exam:

- Often negative
- Abdominal tenderness
- Worm passage in stool/vomitus

Complications:

- Mechanical ileus
- Biliary ascariasis
- Pancreatitis
- Malnutrition (children)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Eosinophilia (during lung phase)	Parasitic infection

Imaging:

- **Chest X-ray:** Migratory infiltrates (Löffler) (*Lung phase*)
- **Abdominal US:** Worms in biliary tract/intestine ("railway track" sign) (*Complication*)

Microbiology:

- **Stool for ova and parasites:** Characteristic mammillated eggs (*Diagnostic*)

Differential Diagnosis:

- **Other helminth infections:** Stool examination
- **Asthma/Pneumonia:** Eosinophilia, migratory infiltrates
- **Gallstones:** US image

Therapy:

Outpatient:

Drug	Dose	Note
Mebendazole	2x100mg PO	First choice
Albendazole	400mg PO	Alternative

Targeted:

Benzimidazoles (Mebendazole, Albendazole). In pregnancy: Pyrantel pamoate.

Supportive:

- Surgical/endoscopic removal in case of obstruction

Prevention:

- Washing vegetables
- Hand washing
- Sewage treatment

Taeniasis (Tapeworm)

Pathogen: Helminth - *Taenia saginata* (beef), *Taenia solium* (pork) (-)

Epidemiology:

- Incidence: Widespread worldwide
- Transmission: Raw/undercooked meat (larva/cysticercus). *T. solium* eggs person-to-person
-> Cysticercosis!
- Risk Groups: Consumers of raw meat

Pathomechanism:**Steps:**

- Ingestion of cysticercus from meat -> adult worm in intestine (Taeniasis)
- Ingestion of *T. solium* EGG (feco-oral) -> larva hatches -> tissue migration -> Cysticercosis (brain, muscle, eye)

Virulence Factors:

- Scolex (hooks/suckers)

Clinical Features:

- Incubation: 8-14 weeks
- Onset: Asymptomatic/Mild

Symptoms:

- **Intestinal:** Mild abdominal discomfort, passage of proglottids (segments)
- **Neurocysticercosis (*T. solium*):** Epilepsy, headache, increased ICP

Physical Exam:

- Negative (intestinal worm)
- Neurological symptoms (cysticercosis)

Complications:

- Neurocysticercosis (leading cause of epilepsy in developing countries)
- Ocular cysticercosis

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Eosinophilia (rare in intestinal form)	-

Imaging:

- **Brain CT/MRI:** Cysts, calcifications (*Neurocysticercosis*)

Microbiology:

- **Stool:** Proglottids or eggs (*Diagnostic (species identification by proglottid)*)

Therapy:**Outpatient:**

Drug	Dose	Note
Praziquantel	5-10 mg/kg PO	For intestinal worm
Niclosamide	2g PO	Alternative

Targeted:

Neurocysticercosis: Albendazole + Praziquantel + Steroids (to reduce inflammation).

Prevention:

- Thorough cooking of meat
- Meat inspection
- Hand washing (against *T. solium* autoinfection)

Echinococcosis (Hydatid Disease)

Pathogen: Helminth - *Echinococcus granulosus* (cystic), *E. multilocularis* (alveolar) (-)

Epidemiology:

- Incidence: Endemic (Mediterranean, E-Europe, Asia)
- Transmission: Feco-oral: ingestion of eggs from dog/fox feces
- Risk Groups: Dog owners, shepherds, Consumers of wild berries (fox - *E. multilocularis*)

Pathomechanism:**Steps:**

- Egg ingestion -> oncosphere in the intestine
- Portal circulation -> Liver (most common) -> Lungs -> Other
- Hydatid cyst formation (slow growth)
- Cyst rupture -> anaphylaxis and dissemination

Virulence Factors:

- Laminated layer (immune protection)
- Protoscolices

Clinical Features:

- Incubation: Years (slow growth)
- Onset: Slow

Symptoms:

- **Liver cyst:** Right upper quadrant pain, hepatomegaly
- **Lung cyst:** Cough, chest pain, hemoptysis
- **Rupture:** Anaphylactic shock, fever, urticaria

Physical Exam:

- Hepatomegaly
- Palpable mass

Complications:

- Cyst rupture (anaphylaxis)
- Biliary obstruction
- Bacterial superinfection

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Eosinophilia (25%)	Not always present

Imaging:

- **US/CT:** Cyst, daughter cysts ("rosette"), calcification (*Diagnostic (WHO classification)*)

Microbiology:

- **Serology (ELISA, IHA):** Positive (*Confirmation (not always positive)*)

Therapy:**Outpatient:**

Drug	Dose	Note
Albendazole	2x400mg PO	Before/after surgery or in inoperable cases

Targeted:

PAIR technique (Puncture, Aspiration, Injection, Re-aspiration) or Surgical removal (careful of rupture!). E. multilocularis: radical surgery + lifelong Albendazole.

Prevention:

- Deworming of dogs
- Hand washing
- Washing of wild fruits

Enterobiasis (Pinworm)

Pathogen: Helminth - Enterobius vermicularis (-)

Epidemiology:

- Incidence: Most common helminth infection in temperate zones (also in developed countries)
- Transmission: Feco-oral, autoinfection (scratching -> mouth), inhalation (dust)
- Risk Groups: Small children, Communities (daycare, school), Family members

Pathomechanism:

Steps:

- Egg ingestion
- Larva in the small intestine
- Adult worm in the cecum
- Female migrates to the perianal region at night to lay eggs -> itching

Virulence Factors:

- -

Clinical Features:

- Incubation: 2-6 weeks
- Onset: Gradual

Symptoms:

- **Perianal itching:** Mainly at night (pruritus ani)
- **Sleep disturbance:** Due to itching
- **Vulvovaginitis:** In young girls (aberrant migration)

Physical Exam:

- Perianal excoriation (scratch marks)
- Worms may be visible (rare)

Complications:

- Bacterial superinfection (scratching)
- Salpingitis (rare)

Diagnostics:

Microbiology:

- **Scotch-tape test:** Eggs in the morning sample (*Gold standard (stool exam often negative!)*)

Therapy:

Outpatient:

Drug	Dose	Note
Mebendazole	100mg PO	Treat the whole family!

Albendazole	400mg PO	
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Targeted:

Repeat dose needed after 2 weeks (to prevent autoinfection).

Prevention:

- Nail trimming
- Washing pajamas/bedding in hot water
- Hand washing

Trichinellosis

Pathogen: Helminth - *Trichinella spiralis* (-)

Epidemiology:

- Incidence: Sporadic outbreaks (pig slaughter)
- Transmission: Consumption of meat containing larvae (improper cooking)
- Risk Groups: Consumers of raw/smoked pork, wild boar

Pathomechanism:**Steps:**

- Ingestion of encysted larva
- Adult worm in intestine -> new larvae (Enteral phase)
- Larvae into bloodstream -> migration to striated muscles
- Encystment in muscle (Parenteral phase)

Virulence Factors:

- Nurse cell formation in muscle

Clinical Features:

- Incubation: Enteral: 1-2 days; Parenteral: 1-4 weeks
- Onset: Sudden

Symptoms:

- **Enteral phase:** Diarrhea, nausea, abdominal pain
- **Fever:** High, prolonged
- **Myalgia:** Severe muscle pain, weakness
- **Periorbital edema:** Characteristic facial swelling
- **Splinter hemorrhages:** Under the nails

Physical Exam:

- Periorbital edema
- Muscle tenderness
- Fever
- Conjunctivitis

Complications:

- Myocarditis (cause of death!)
- Encephalitis
- Pneumonia

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Eosinophilia (up to 50%)	Very characteristic
CK, LDH	Elevated	Muscle damage

Microbiology:

- **Serology (ELISA):** Positive (from week 3) (*Diagnostic*)
- **Muscle biopsy:** Larvae (*Rarely needed*)

Differential Diagnosis:

- **Influenza:** Lack of eosinophilia
- **Leptospirosis:** Kidney/liver involvement, no eosinophilia
- **Myositis:** Autoantibodies

Therapy:

Outpatient:

Drug	Dose	Note
Mebendazole	3x200-400mg PO	More effective in early phase
Albendazole	2x400mg PO	

Inpatient:

Drug	Dose	Note
Steroid (Prednisolone)	40-60mg PO	In case of severe inflammation/allergic reaction (Herxheimer-like)

Targeted:

Anthelmintic + Steroid.

Prevention:

- Meat inspection (trichinelloscopy)
- Thorough cooking of meat (>71°C)
- Freezing (-15°C for 3 weeks - not always sufficient for wild boar!)

Toxocariasis (Visceral/Ocular Larva Migrans)

Pathogen: Helminth - *Toxocara canis* (dog), *Toxocara cati* (cat) (-)

Epidemiology:

- Incidence: Widespread zoonosis worldwide
- Seasonality: None
- Transmission: Feco-oral: ingestion of soil contaminated with eggs (not direct animal contact!)
- Risk Groups: Small children (sandbox, geophagia), Dog owners

Pathomechanism:

Steps:

- Egg ingestion
- Larva hatches in the small intestine
- Penetrates intestinal wall and enters circulation
- Tissue migration (liver, lung, brain, eye)
- Does NOT develop into adult worm in humans (paratenic host)
- Granulomatous inflammation around the larva

Virulence Factors:

- Tissue migration
- Excretory-secretory antigens (TES)

Clinical Features:

- Incubation: Weeks-months
- Onset: Slow

Symptoms:

- **Visceral Larva Migrans (VLM):** Fever, cough, abdominal pain, hepatomegaly
- **Ocular Larva Migrans (OLM):** Unilateral vision loss, strabismus, leukocoria
- **Covert toxocariasis:** Abdominal pain, headache, cough

Physical Exam:

- Hepatomegaly
- Fever
- Pulmonary rales (wheezing)
- Fundoscopy: retinal granuloma, chorioretinitis

Complications:

- Blindness (OLM)
- Myocarditis
- Epilepsy (cerebral granuloma)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Extreme eosinophilia (in VLM, may be absent in OLM!)	Parasitic infection
IgE	Elevated	Allergic/parasitic response

Imaging:

- **Abdominal US:** Hepatomegaly, hypoechoic lesions (*VLM*)
- **Ophthalmology:** Retinal granuloma (*OLM*)

Microbiology:

- **Serology (ELISA):** Positive (TES antigen) (*Diagnostic (Western blot for confirmation)*)
- **Stool examination:** NEGATIVE (*No adult worms in humans, no egg shedding!*)

Differential Diagnosis:

- **Retinoblastoma:** Distinction from OLM is critical (leukocoria)!
- **Ascariasis:** Eggs in stool, lung phase is shorter
- **Allergic asthma:** Serology, hepatomegaly

Therapy:

Outpatient:

Drug	Dose	Note
Albendazole	2x400mg PO	Take with fatty food
Mebendazole	2x100-200mg PO	Less absorbed

Targeted:

Albendazole + Steroids (to reduce inflammation, especially in OLM and severe VLM).

Supportive:

- Ophthalmic surgery (vitrectomy) if needed

Prevention:

- Deworming of dogs/cats
- Hand washing
- Covering sandboxes

Zoonoses

Leptospirosis

Pathogen: Spirochete - *Leptospira interrogans* (Gram-negative)

Epidemiology:

- Incidence: Tropical/subtropical: 10-100/100,000; Temperate: 0.1-1/100,000
- Seasonality: Summer-autumn, rainy season
- Transmission: Exposure to contaminated water/soil → skin/mucosa. Spread by urine of rodents/animals
- Risk Groups: Agricultural workers, Veterinarians, Slaughterhouse workers, Sewer workers, Water sports/extreme sports competitors, Soldiers (jungle environment)

Pathomechanism:

Steps:

- Leptospira enters through damaged skin/mucosa
- Rapid hematogenous spread to all organs
- Endothelial damage → increased vascular permeability
- Liver, kidney, lung involvement
- Weil's disease: severe form - liver and kidney failure, hemorrhages
- Immune-mediated inflammation (T-cell activation)

Virulence Factors:

- Outer membrane proteins (LipL32)
- Flagellum (motility)
- Hemolysins
- Lipopolysaccharide
- Adhesins

Clinical Features:

- Incubation: 2-30 days (average 7-12 days)
- Onset: Biphasic course

Symptoms:

- **Sudden fever:** Present in >95% (39-40°C), with chills
- **Headache:** >95%, severe, frontal/retrobulbar
- **Myalgia:** >80%, mainly calf and lumbar region (characteristic!)
- **Conjunctival suffusion:** 30-40%, but very specific (without jaundice)
- **Jaundice:** 5-10% (Weil's disease)
- **Hemorrhagic manifestations:** 30-40% in severe form (pulmonary hemorrhage, petechiae)

Physical Exam:

- High fever, tachycardia
- Conjunctival suffusion (conjunctival injection)
- Lymphadenopathy
- Hepatomegaly (Weil)
- Calf tenderness
- Jaundice (severe)
- Meningeal signs (25%)

Complications:

- Weil's disease (jaundice, renal failure)
- ARDS
- Myocarditis
- Rhabdomyolysis
- Uveitis (late)
- Aseptic meningitis
- Death (5-15% in severe cases)

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Leukocytosis, thrombocytopenia	Non-specific
Kidney	Creatinine↑, proteinuria, hematuria	Weil's disease
Liver	Bilirubin↑↑ (direct), mild transaminase↑	Cholestatic pattern
CK	Elevated	Myositis
CRP/ESR	Markedly elevated	Inflammation

Imaging:

- **Chest X-ray:** Diffuse infiltrate, alveolar hemorrhage (*Pulmonary hemorrhage*)
- **Abdominal US:** Hepatomegaly, ascites (*Severity assessment*)

Microbiology:

- **Microscopic Agglutination Test (MAT):** ≥1:400 titer or 4x↑ (*Gold standard, but late (7-10 days)*)
- **ELISA IgM:** Positive (*Faster, acute phase*)
- **Blood/urine culture:** Leptospira isolation (EMJH medium) (*Early (<7 days blood, >7 days urine), slow (weeks)*)
- **PCR:** Leptospira DNA (*Rapid, sensitive in early phase*)

Differential Diagnosis:

- **Dengue fever:** Thrombocytopenia more prominent, tourniquet test+, no calf pain
- **Malaria:** undefined
- **Hantavirus:** Rodent exposure, proteinuria more severe, thrombocytopenia
- **Rickettsiosis:** Rash characteristic, eschar, tick exposure
- **Viral hepatitis:** Transaminases much higher, serology

Therapy:**Outpatient:**

Drug	Dose	Note
Doxycycline	2x100mg PO	First choice in mild cases
Amoxicillin	3x500mg PO	Alternative (pregnant, child)

Inpatient:

Drug	Dose	Note
Penicillin G	6x1.5 million IU IV	Severe/Weil's disease
Ceftriaxone	1x1-2g IV	Alternative

Icu:

Drug	Dose	Note
Penicillin G	6x1.5 million IU IV	Severe Weil's disease
Dialysis	If renal failure	Supportive
Ventilation	Pulmonary hemorrhage	ARDS

Targeted:

Mild: Doxycycline; Severe: Penicillin G or Ceftriaxone

Supportive:

- Fluid replacement
- Dialysis (renal failure)
- Ventilation (ARDS)
- Transfusion (hemorrhage)

Prevention:

- Doxycycline chemoprophylaxis (200mg/week extreme sports)
- Protective clothing in high-risk work
- Rodent control
- Animal vaccination (dog)
- Water source sanitation

Hantavirus Infection

Pathogen: Virus - Hantavirus (multiple serotypes) (Negative-sense RNA virus, Bunyaviridae)

Epidemiology:

- Incidence: Europe: HFRS 10,000+ cases/year; USA: HPS <50 cases/year
- Seasonality: Spring-autumn (rodent population peak)
- Transmission: Aerosol (rodent feces/urine/saliva). NOT person-to-person!
- Risk Groups: Agricultural workers, Foresters, Soldiers, Campers/hikers, Rodent contact work, Cleaning poorly ventilated buildings

Pathomechanism:**Steps:**

- Hantavirus inhalation (rodent excreta dust)
- Virus infects endothelial cells (not cytopathic)
- Immune-mediated vascular permeability increase
- HFRS: kidney involvement (capillary leak syndrome)
- HPS: pulmonary capillary leak → pulmonary edema, cardiogenic shock
- Thrombocytopenia and coagulation disorders

Virulence Factors:

- Nucleocapsid protein (immune response)

- Glycoprotein Gn/Gc (cell entry)
- Endothelial tropism
- Immunomodulation

Clinical Features:

- Incubation: 1-8 weeks (average 2-4 weeks)
- Onset: Sudden

Symptoms:

- **Fever:** 100%, sudden onset (39-41°C)
- **Myalgia:** 85-100% (back, thighs)
- **Headache:** >90%
- **Abdominal pain:** 30-50% (more common in HFRS)
- **Vision problems:** 20-30% (HFRS - transient myopia)
- **HPS symptoms:** Cough, dyspnea (>90% at end of prodrome)
- **HFRS symptoms:** Oliguria/anuria, flank pain

Physical Exam:

- High fever
- Facial flush
- Conjunctival injection
- Petechiae (palate, axilla)
- Proteinuria, hematuria
- Hypotension (HPS)
- Pulmonary edema signs (HPS)

Complications:

- Acute renal failure (HFRS)
- Cardiogenic pulmonary edema (HPS)
- Shock
- Intracranial hemorrhage
- Pituitary hemorrhage
- Death (HFRS 1-15%, HPS 30-50%)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Thrombocytopenia (<100 G/L), leukocytosis, atypical lymphocytes	Characteristic triad!
Kidney	Creatinine↑↑, BUN↑↑, proteinuria+++, hematuria	HFRS
Hemoconcentration	Hematocrit↑	Capillary leak (HPS)
Coagulation	DIC signs possible	Severe case

Liver enzymes	Mild AST/ALT↑	Common
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Imaging:

- **Chest X-ray:** Bilateral interstitial infiltrates, pleural effusion (*HPS*)
- **Abdominal US:** Renal enlargement, echogenicity↑, ascites (*HFRS*)

Microbiology:

- **ELISA IgM/IgG:** Hantavirus specific antibodies (*Gold standard, early positive (3-7 days)*)
- **RT-PCR:** Viral RNA (blood, urine) (*Early phase, serotyping*)
- **Immunohistochemistry:** Tissue viral antigen (*Research, autopsy*)

Differential Diagnosis:

- **Leptospirosis:** Calf pain, conjunctival suffusion, water exposure
- **Rickettsiosis:** Rash, eschar, tick exposure
- **Acute glomerulonephritis:** Edema, hypertension, Streptococcus history
- **Septic shock:** High PCT, positive culture
- **Influenza severe pneumonia:** Seasonality, no thrombocytopenia/proteinuria

Therapy:**Outpatient:**

Drug	Dose	Note
NO specific antiviral	Supportive care	Home observation in mild cases

Inpatient:

Drug	Dose	Note
Ribavirin	33mg/kg IV loading, then 16mg/kg q6h	Effective in HFRS, early phase (<5 days)
Fluid replacement	Cautious! Due to capillary leak	Monitoring

Icu:

Drug	Dose	Note
Dialysis	Renal failure	HFRS
Invasive ventilation + ECMO	HPS	Cardiogenic shock
Inotropic support	Dobutamine, norepinephrine	HPS shock phase

Targeted:

Ribavirin in HFRS early phase; efficacy not proven in HPS

Supportive:

- Cautious fluid therapy (capillary leak!)
- Dialysis (renal failure)
- Ventilation/ECMO (HPS)

- Inotropic support
- Transfusion (thrombocytopenia)

Prevention:

- Rodent control
- Protective mask in dusty places
- Ventilation of buildings before cleaning
- Gloves
- NO vaccine (experimental)

Lyme Disease (Borreliosis)

Pathogen: Spirochete - *Borrelia burgdorferi sensu lato* (Gram-negative)

Epidemiology:

- Incidence: USA: 476,000 cases/year; Europe: 232,000 cases/year
- Seasonality: April-October (tick activity)
- Transmission: Ixodes tick bite (>24-36 hours attached)
- Risk Groups: Visitors to forested areas, Hikers, campers, Foresters, hunters, Gardeners, Children (summer play)

Pathomechanism:

Steps:

- Tick bite → *Borrelia* inoculation
- Local spread in skin → erythema migrans
- Hematogenous dissemination (days-weeks)
- Early disseminated: heart, nervous system, joints
- Late: chronic arthritis, neuroborreliosis
- Spirochete antigens may persist (immune response continues)

Virulence Factors:

- Outer surface proteins (OspA, OspC)
- VlsE (antigenic variation)
- Complement resistance
- Extracellular matrix adherence

Clinical Features:

- Incubation: 3-30 days (average 7 days)
- Onset: Staged

Symptoms:

- **Erythema migrans (EM):** Appears in 70-80% (bullseye or homogeneous)
- **General symptoms:** Fever, fatigue, headache (common in early phase)
- **Neuroborreliosis:** 10-15% (in untreated): Facial palsy, meningitis, radiculopathy
- **Lyme Carditis:** 1-5% (in untreated): AV block

- **Lyme Arthritis:** 60% (in untreated, USA): Knee joint swelling
- **Borrelia lymphocytoma:** Rare (<1%), earlobe/nipple (Europe)

Physical Exam:

- Early localized: EM (diameter 5-70cm, often central clearance)
- Multiple EM (disseminated)
- Lymphocytoma (earlobe, breast)
- Facial palsy (uni/bilateral)
- Meningeal signs
- Monoarthritis/oligoarthritis (knee)
- Skin atrophy (ACA)

Complications:

- Chronic Lyme arthritis
- Post-Lyme syndrome
- Encephalomyelitis
- Keratitis
- Chronic fatigue

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Two-tier serology: ELISA → Western blot	IgM (2-4 weeks), IgG (4-6 weeks)	Gold standard, but can be negative in early EM!
CSF	Lymphocytic pleocytosis, ↑protein, intrathecal Ab production	Neuroborreliosis
Joint fluid	Inflammatory (WBC >10,000), PCR+	Lyme arthritis

Imaging:

- **MRI brain:** White matter lesions (neuroborreliosis) (*Rare, differential diagnosis*)
- **ECG:** AV block (1-3 degree) (*Lyme carditis*)

Microbiology:

- **Serology (ELISA + Western blot):** IgM/IgG positive (*Two-tier algorithm! False positives common*)
- **PCR (joint fluid, CSF):** Borrelia DNA (*Low sensitivity*)
- **Culture:** Not routine (takes weeks) (*Only in special cases*)

Differential Diagnosis:

- **Tinea corporis (ringworm):** Does not expand, scaly, KOH microscopy
- **Southern tick-associated rash illness (STARI):** Lone Star tick, serology negative
- **Reactive arthritis:** GI/GU infection, HLA-B27
- **Rheumatoid arthritis:** RF/anti-CCP positive, symmetrical
- **MS:** MRI pattern, oligoclonal bands

Therapy:**Outpatient:**

Drug	Dose	Note
Doxycycline	2x100mg PO	First choice adult/child >8y
Amoxicillin	3x500mg PO	Pregnant, child <8y
Cefuroxime axetil	2x500mg PO	Alternative

Inpatient:

Drug	Dose	Note
Ceftriaxone	1x2g IV	Neuroborreliosis, Lyme carditis (AV block >1°)
Penicillin G	4x5 million IU IV	Alternative neuroborreliosis

Icu:

Drug	Dose	Note
Ceftriaxone	1x2g IV	Severe neuroborreliosis
Pacemaker (temporary)	Complete AV block	Carditis

Targeted:

Early: Doxycycline; Neuroborreliosis/Carditis: Ceftriaxone IV

Supportive:

- Jarisch-Herxheimer reaction possible
- NSAIDs (arthritis)
- Temporary pacemaker (complete block)

Prevention:

- Protective clothing in woods
- Repellents (DEET)
- Tick removal <24 hours
- Single dose doxycycline (200mg) <72 hours after bite (in endemic area)
- No effective vaccine

Tularemia (Rabbit Fever)

Pathogen: Bacterium - *Francisella tularensis* (Gram-negative)

Epidemiology:

- Incidence: USA: 100-200 cases/year; Europe: sporadic
- Seasonality: Summer (tick), winter (hunting)
- Transmission: Tick/fly bite, infected animal contact (rabbit, rodent), inhalation, water/food

- Risk Groups: Hunters, Leather workers, Agricultural workers, Lab workers, Foresters, Veterinarians

Pathomechanism:

Steps:

- Francisella enters through skin/mucosa/inhalation
- Phagocytosis by macrophages/dendritic cells
- Intracellular replication (escape from phagosome)
- Regional lymph nodes → necrotizing granuloma
- Lymphadenitis, typhoidal spread
- High infectivity (<10 organisms sufficient)

Virulence Factors:

- Capsule
- Phagosome escape (igIA-D locus)
- LPS (toxic)
- Siderophores
- Intracellular survival

Clinical Features:

- Incubation: 3-5 days (1-14 days)
- Onset: Sudden

Symptoms:

- **Fever:** >90%, sudden onset
- **Ulceroglandular:** 75-85%: Painful ulcer + regional lymph node
- **Glandular:** 5-10%: Only lymph node swelling (without ulcer)
- **Typhoidal:** 5-15%: Systemic febrile illness, without localization
- **Pneumonia:** 30-80% of typhoidal cases (or primary inhalation)
- **Oculoglandular:** 1-2%: Conjunctivitis + lymph node

Physical Exam:

- Ulceroglandular (75%): skin ulcer (black eschar) + tender lymph node
- Glandular: lymph node NO ulcer
- Oculoglandular: conjunctivitis, nodular lesions, lymph node
- Oropharyngeal: tonsillitis, cervical lymph node
- Typhoidal: fever, hepatosplenomegaly, NO localization
- Pulmonary: pneumonia signs

Complications:

- Abscess formation (lymph node)
- Sepsis
- ARDS
- Meningitis
- Pericarditis
- Osteomyelitis

- Death (untreated 5-15%, treated <2%)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Normal or leukopenia	Non-specific
CRP/ESR	Elevated	Inflammation
Liver enzymes	AST/ALT mild elevation	Typhoidal

Imaging:

- **Chest X-ray:** Infiltrate, hilar lymphadenopathy, pleural effusion (*Pulmonary/typhoidal*)
- **CT neck/chest:** Necrotizing lymphadenitis (*Abscess detection*)

Microbiology:

- **Serology (agglutination):** Titer $\geq 1:160$ or $4x\uparrow$ (*Retrospective diagnosis (2-3 weeks)*)
- **PCR:** F. tularensis DNA (ulcer, lymph node) (*Rapid, sensitive*)
- **Culture:** Special medium (BSL-3!), DANGEROUS! (*Avoid (lab infection risk)*)
- **Immunohistochemistry:** Antigen detection in tissue (*In case of biopsy*)

Differential Diagnosis:

- **Lyme disease:** EM rash, serology, less toxic
- **Cat-scratch disease:** Cat contact, Bartonella serology
- **Pyogenic lymphadenitis (Staph/Strep):** Faster, responds to antibiotics, culture
- **Mycobacteriosis (atypical):** Slower, AFB, culture
- **Plague:** Bubo even more painful, geography, Yersinia

Therapy:

Outpatient:

Drug	Dose	Note
Doxycycline	2x100mg PO	Mild form first choice
Ciprofloxacin	2x500mg PO	Alternative

Inpatient:

Drug	Dose	Note
Streptomycin	2x7.5-10mg/kg IM	Gold standard in severe cases
Gentamicin	1x5mg/kg IV	Streptomycin not available
Doxycycline	2x100mg IV	In combination

Icu:

Drug	Dose	Note
Gentamicin + Doxycycline	Combination	Typhoidal/pulmonary severe

Ciprofloxacin	2x400mg IV	Better penetration in meningitis
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Targeted:

Aminoglycoside (Streptomycin, Gentamicin) first choice; Doxycycline/Ciprofloxacin alternative

Supportive:

- Surgical drainage (fluctuating lymph node)
- Fluid replacement
- Isolation NOT required (no person-to-person spread)
- Antipyretics

Prevention:

- Protective gloves when handling animals
- Repellents (tick)
- Proper cooking of meat
- Vaccine (only military/lab personnel, USA)
- Antibiotic prophylaxis after high-risk exposure (doxycycline 14 days)

Cat-Scratch Disease

Pathogen: Bacterium - *Bartonella henselae* (Gram-negative)

Epidemiology:

- Incidence: USA: ~12,000 cases/year (estimate), underdiagnosed
- Seasonality: Autumn-winter (kittens)
- Transmission: Cat scratch/bite (95%), rarely dog, flea
- Risk Groups: Children <10 years, Cat contact, Flea exposure, Immunosuppressed (HIV), Veterinarians, shelter workers

Pathomechanism:**Steps:**

- *Bartonella* inoculation with cat saliva (scratch/bite)
- Local inoculation papule/pustule
- Regional lymph node invasion
- Granulomatous lymphadenitis (with stellate necrosis)
- Rare dissemination (immunosuppressed): bacillary angiomatosis, endocarditis
- Immune response usually eradicates (weeks-months)

Virulence Factors:

- Flagellum
- Pili
- Adhesins
- BadA autotransporter

- Intracellular survival (erythrocytes, endothelium)

Clinical Features:

- Incubation: 3-10 days (papule), 1-3 weeks (lymphadenitis)
- Onset: Subacute

Symptoms:

- **Lymphadenopathy:** 85-90%: Regional, painful lymph node swelling
- **Inoculation lesion:** 25-60%: Papule/pustule at scratch site
- **Fever:** 30-50%, usually mild
- **Systemic symptoms:** Fatigue, malaise (50%)
- **Parinaud syndrome:** 2-8%: Conjunctivitis + preauricular node
- **Neuroretinitis:** 1-2%: Unilateral vision loss

Physical Exam:

- Papule/pustule at scratch site (heals, scars)
- Unilateral regional lymphadenomegaly (axillary, epitrochlear, cervical)
- Lymph node: tender, 1-5cm, warm
- Fluctuant (10-15%) → suppurative
- Parinaud syndrome: conjunctivitis, preauricular lymph node
- Hepatosplenomegaly (disseminated)

Complications:

- Lymph node abscess formation
- Encephalitis/encephalopathy
- Osteomyelitis
- Endocarditis (rare)
- Bacillary angiomatosis (HIV+)
- Neuroretinitis
- Peliosis hepatis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Normal or mild leukocytosis	Non-specific
CRP/ESR	Mild-moderate elevation	Inflammation
Liver/spleen enzymes	Elevated (disseminated)	Hepatosplenic involvement

Imaging:

- **US (lymph node):** Enlarged, hypoechoic, fluctuant (abscess) (*Need for drainage*)
- **CT/MRI:** Spleen/liver lesions (bacillary angiomatosis) (*Disseminated disease*)

Microbiology:

- **Bartonella serology (IgG/IgM):** IgG $\geq 1:256$ (acute), $\geq 1:512$ (endocarditis) (*Gold standard, 2-6 weeks positive*)

- **PCR (lymph node biopsy):** Bartonella DNA (*Sensitive, rapid*)
- **Warthin-Starry silver stain:** Bacilli in tissue sample (*Histology*)
- **Blood culture (special):** Slow growth (6-8 weeks), difficult (*Endocarditis*)

Differential Diagnosis:

- **Pyogenic lymphadenitis (Staph/Strep):** Faster onset, rapid response to antibiotics
- **Toxoplasmosis:** Bilateral cervical lymph node, serology
- **Mycobacteriosis (atypical):** AFB positive, slower, culture
- **Tularemia:** Wild animal exposure, ulcer more severe, serology
- **Lymphoma:** Progressive, biopsy
- **Mononucleosis:** Sore throat, splenomegaly, monospot/EBV serology

Therapy:

Outpatient:

Drug	Dose	Note
Azithromycin	1x500mg D1, then 250mg/day	First choice, reduces lymph node size
Doxycycline	2x100mg PO	Alternative in adults
OBSERVATION	Self-limiting disease	Antibiotics not necessarily needed in mild cases

Inpatient:

Drug	Dose	Note
Azithromycin	1x500mg IV	If PO not tolerated
Doxycycline + Rifampicin	2x100mg + 2x300mg PO	Neuroretinitis

Icu:

Drug	Dose	Note
Gentamicin + Doxycycline	3mg/kg/day IV + 2x100mg PO/IV	Endocarditis
Surgery	Valve replacement	Bartonella endocarditis

Targeted:

Typical CSD: Azithromycin (optional); Neuroretinitis/severe: Doxycycline±Rifampicin;
Endocarditis: Gentamicin+Doxycycline±surgery

Supportive:

- Surgical drainage (fluctuating lymph node)
- Analgesics
- Warm compresses
- NO INCISIONAL BIOPSY (scarring, sinus formation)

Prevention:

- Cat flea control
- Avoid scratches/bites (play)
- Hand washing after touching cat
- Wound disinfection
- Immunosuppressed: avoid cats

Q Fever

Pathogen: Bacterium - Coxiella burnetii (Gram-negative (intracellular))

Epidemiology:

- Incidence: Zoonosis, occupational disease
- Seasonality: Spring (birthing season)
- Transmission: Aerosol (placenta, amniotic fluid, milk, feces dust)
- Risk Groups: Livestock farmers, Slaughterhouse workers, Veterinarians

Pathomechanism:

Steps:

- Inhalation (a single bacterium can infect!)
- Infection of alveolar macrophages
- Replication in acidic phagosomes
- Hematogenous spread
- Granuloma formation (doughnut granuloma)

Virulence Factors:

- Spore-like form (resistant)
- LPS phase variation

Clinical Features:

- Incubation: 2-3 weeks
- Onset: Sudden

Symptoms:

- **Acute Q fever:** Flu-like: Fever, fatigue, severe headache (>90% in symptomatic)
- **Hepatitis:** 60-75% (granulomatous), hepatomegaly
- **Pneumonia:** 30-50% (atypical), often mild cough
- **Chronic Q fever:** <5% after acute case; Endocarditis (60-70% in chronic)

Physical Exam:

- Hepatomegaly
- Splenomegaly
- Relative bradycardia

Complications:

- Chronic Q fever (Endocarditis)

- Osteomyelitis
- Chronic hepatitis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Liver enzymes	Elevated	Hepatitis
Thrombocytopenia	Mild	Common

Imaging:

- **Chest X-ray:** Round opacities, multiple (*Pneumonia*)
- **Echo:** Vegetation (*Endocarditis (chronic)*)

Microbiology:

- **Serology (IF):** Phase II (acute), Phase I (chronic) (*Diagnostic*)
- **PCR:** From blood (*In early phase*)

Differential Diagnosis:

- **Brucellosis:** Undulant fever, dairy products
- **Influenza:** Seasonality, respiratory symptoms dominate
- **Viral hepatitis:** Serology

Therapy:

Outpatient:

Drug	Dose	Note
Doxycycline	2x100mg	Acute Q fever

Inpatient:

Drug	Dose	Note
Doxycycline	2x100mg	

Icu:

Drug	Dose	Note
Doxycycline + Hydroxychloroquine	Long-term	Chronic Q fever (endocarditis)

Targeted:

Doxycycline

Supportive:

- Antipyretics

Prevention:

- Protective equipment during birthing
- Pasteurization of milk

- Vaccine (Australia)

Rabies

Pathogen: Virus - Rabies lyssavirus (RNA virus)

Epidemiology:

- Incidence: Worldwide 59,000 deaths/year (mainly Asia, Africa)
- Seasonality: None
- Transmission: Bite (saliva), scratch, mucous membrane contact
- Risk Groups: Animal handlers, Travelers to endemic areas, Spelunkers (bat)

Pathomechanism:

Steps:

- Inoculation (muscle tissue)
- Entry into peripheral nerves (NMJ)
- Retrograde axonal transport to CNS
- Replication in brain (Negri bodies)
- Centrifugal spread (salivary glands, cornea)

Virulence Factors:

- Neurotropism
- Immune evasion

Clinical Features:

- Incubation: 1-3 months (days to years)
- Onset: Acute neurological after prodrome

Symptoms:

- **Prodrome:** Paresthesia/pain at bite site (50-80%)
- **Furious (Encephalitic) form:** 80%: Hydrophobia (50-80%), aerophobia, agitation
- **Paralytic (Dumb) form:** 20%: Ascending paralysis (Guillain-Barré like)
- **Hydrophobia:** Laryngeal spasm on drinking/seeing water (pathognomonic)
- **Coma:** End stage, death

Physical Exam:

- Autonomic instability (hypersalivation, piloerection)
- Mental status change
- Focal neurological signs
- Fever

Complications:

- Death (~100%)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
No early marker	-	Clinical suspicion!

Imaging:

- **MRI:** Non-specific encephalitis (*Exclusion*)

Microbiology:

- **PCR:** Saliva, nape skin biopsy (hair follicle) (*Diagnostic (ante mortem)*)
- **Antigen detection:** Corneal impression, skin (*DFA*)
- **Serology:** CSF/serum (*Late*)

Differential Diagnosis:

- **Tetanus:** Trismus, no hydrophobia/pleocytosis
- **Other encephalitis:** No bite history, hydrophobia
- **Psychiatric disorder:** Fever, progression

Therapy:**Outpatient:**

Drug	Dose	Note
Post-exposure prophylaxis (PEP)	IMMEDIATELY!	Life-saving!

Inpatient:

Drug	Dose	Note
Palliative sedation	Symptomatic	In case of clinical rabies

Icu:

Drug	Dose	Note
Milwaukee protocol	Experimental	Not recommended routinely (unsuccessful)

Targeted:

No effective therapy after symptom onset.

Supportive:

- Sedation
- Analgesia
- Isolation

Prevention:

- PEP: Wound cleaning + Vaccine (0, 3, 7, 14 days) + RIG (immunoglobulin)
- Animal vaccination
- Pre-exposure vaccine (travelers, professionals)

Anthrax

Pathogen: Bacterium - *Bacillus anthracis* (Gram-positive)

Epidemiology:

- Incidence: Rare, bioterrorism risk
- Seasonality: None
- Transmission: Spore inoculation (skin), inhalation, ingestion
- Risk Groups: Leather workers / Tanners, Livestock farmers, Lab workers

Pathomechanism:

Steps:

- Spore entry → germination
- Toxin production (Edema toxin, Lethal toxin)
- Capsule (phagocytosis inhibition)
- Tissue necrosis, edema, systemic toxicity

Virulence Factors:

- Poly-D-glutamic acid capsule
- Protective Antigen (PA)
- Edema Factor (EF)
- Lethal Factor (LF)

Clinical Features:

- Incubation: Skin: 1-7 days; Inhalational: 1-60 days
- Onset: Form dependent

Symptoms:

- **Cutaneous anthrax:** 95% of natural cases; Painless black eschar
- **Inhalational anthrax:** Rare; Biphasic: flu-like → fulminant mediastinitis/shock
- **GI anthrax:** Rare; Abdominal pain, bloody diarrhea, ascites
- **Meningitis:** Hemorrhagic meningitis (can complicate any form)

Physical Exam:

- Malignant pustule (black eschar, edematous halo)
- Massive mediastinal edema (inhalational)
- Meningeal signs

Complications:

- Septic shock
- Meningitis
- Mediastinitis
- Death

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis	Inflammation
Blood culture	Gram+ rods	Sepsis

Imaging:

- **Chest X-ray/CT:** Mediastinal widening (lymphadenopathy), pleural effusion (*Inhalational anthrax (pathognomonic)*)

Microbiology:

- **Gram stain:** Large Gram+ rods ("bamboo cane") (*From vesicle fluid*)
- **PCR:** Positive (*Rapid*)
- **DFA:** Capsule antigen (*Confirmation*)

Differential Diagnosis:

- **Spider bite:** Painful, no eschar
- **Tularemia:** Painful ulcer
- **Pneumonia:** Lack of mediastinal widening

Therapy:**Outpatient:**

Drug	Dose	Note
Ciprofloxacin	2x500mg	Cutaneous anthrax (60 days if bioterror suspicion)
Doxycycline	2x100mg	Alternative

Inpatient:

Drug	Dose	Note
Ciprofloxacin + Meropenem + Linezolid	IV combination	Inhalational/systemic (antitoxin also given)

Icu:

Drug	Dose	Note
Raxibacumab	Monoclonal antibody	Toxin neutralization

Targeted:

Ciprofloxacin, Doxycycline, Penicillin G (if sensitive)

Supportive:

- Fluid replacement
- Ventilation
- Pleural drainage

Prevention:

- Vaccine (soldiers, high risk)

- PEP (Ciprofloxacin 60 days)
- Burning animal carcasses

Bacterial Respiratory Infections

Bacterial Pneumonia

Pathogen: Bacterium - Streptococcus pneumoniae (Gram-positive)

Epidemiology:

- Incidence: Most common cause of community-acquired pneumonia (CAP) (30-40%)
- Seasonality: Winter-spring peak, often as influenza superinfection
- Transmission: Droplet infection, endogenous activation
- Risk Groups: Elderly (>65 years), Chronic patients (COPD, heart failure, diabetes), Immunosuppressed, Splenectomized, Alcoholics, Smokers

Pathomechanism:

Steps:

- Colonization: S. pneumoniae from the nasopharynx is aspirated into the lower airways
- Adherence: Pneumococcus surface protein A (PspA) and choline-binding proteins bind to epithelial cells
- Capsular polysaccharide: The capsule inhibits phagocytosis and complement activation
- Pneumolysin: Pore-forming toxin → cell damage, inflammation
- Consolidation: Alveoli fill with inflammatory exudate (red blood cells, fibrin, neutrophils)

Virulence Factors:

- Capsular polysaccharide (93 serotypes)
- Pneumolysin
- Autolysin (LytA)
- Neuraminidase
- IgA1 protease

Clinical Features:

- Incubation: 1-3 days
- Onset: Sudden, dramatic onset

Symptoms:

- **Cough:** Present in 90%; productive (66%), rusty sputum is classic but rare
- **Fever and chills:** Fever (80%), chills (40-50%)
- **Dyspnea:** Shortness of breath (66%)
- **Pleuritic pain:** Sharp, increases with inspiration (50%)
- **Other:** GI symptoms (10-20%), altered mental status (elderly)

Physical Exam:

- Tachypnea, tachycardia
- Dullness to percussion over the affected lobe
- Bronchial breath sounds, crepitation
- Increased bronchophony and tactile fremitus
- Cyanosis in severe cases

Complications:

- Empyema
- Lung abscess
- Meningitis
- Sepsis/septic shock
- ARDS
- Pericarditis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (15-30 G/L), left shift	Typical for bacterial infection
CRP	Significantly elevated (>100 mg/L)	Marker of active inflammation
PCT	>0.5 ng/mL	Suspicion of bacterial sepsis
Arterial blood gas	Hypoxemia, possibly hypocapnia	Respiratory failure
Blood culture	Positive in 20-30%	Pathogen identification

Imaging:

- **Chest X-ray (PA+lateral):** Lobar/segmental consolidation, air bronchogram (*Typical appearance*)
- **Chest CT:** Detailed parenchyma evaluation (*Exclusion of complications*)

Microbiology:

- **Sputum Gram stain:** Gram+ lancet-shaped diplococci, >25 neutrophils/field (*Quick orientation*)
- **Sputum culture:** *S. pneumoniae* isolation (*Antibiotic susceptibility*)
- **Urine antigen test:** Pneumococcal polysaccharide detection (*Fast, specific (>90%)*)
- **PCR:** lytA gene detection (*Most sensitive method*)

Differential Diagnosis:

- **Legionella pneumonia:** Hyponatremia, GI symptoms, atypical X-ray
- **Klebsiella pneumonia:** Alcoholics, currant jelly sputum, upper lobe
- **Mycoplasma pneumonia:** Young people, slow onset, atypical symptoms
- **Pulmonary embolism:** Risk factors, D-dimer, CTPA
- **Heart failure:** Cardiac history, BNP, bilateral infiltrates

Therapy:

Guidelines: NICE NG138 (Pneumonia in adults) 2024/2025, ATS/IDSA 2019 CAP Guidelines,

Hungarian Society of Infectology

CAP - Outpatient (Mild - CURB-65 0-1):

Drug	Dose	Note
Amoxicillin	3x500mg-1g PO	First choice (NICE). 5-day course is usually sufficient.
Doxycycline	200mg stat, then 1x100mg PO	For penicillin allergy.
Clarithromycin	2x500mg PO	Alternative.

CAP - Inpatient (Moderate - CURB-65 2):

Drug	Dose	Note
Amoxicillin + Clarithromycin	3x500mg-1g PO/IV + 2x500mg PO/IV	Atypical coverage may be needed. (NICE)
Doxycycline	200mg stat, then 1x100mg PO	Monotherapy for penicillin allergy.
Levofloxacin	1x500mg PO/IV	Alternative (NICE: respiratory fluoroquinolone).

CAP - Severe (CURB-65 3-5) / ICU:

Drug	Dose	Note
Co-amoxiclav + Clarithromycin	1.2g IV q8h + 500mg IV q12h	NICE recommendation for severe CAP.
Ceftriaxone + Clarithromycin	1x2g IV + 2x500mg IV	Common alternative (not NICE first-line, but widespread).
Levofloxacin	1x500mg IV	For beta-lactam allergy.

HAP - Not severe / Early:

Drug	Dose	Note
Co-amoxiclav	625mg PO TID or 1.2g IV TID	First choice (NICE NG191).
Doxycycline	100mg PO	Alternative.

HAP - Severe / VAP / High risk:

Drug	Dose	Note
Antipseudomonal beta-lactam	e.g., Piperacillin/tazobactam, Cefepime, Meropenem	1st component (Gram-negative coverage).
+ Antipseudomonal fluoroquinolone or	e.g., Ciprofloxacin, Amikacin	2nd component (double G- coverage if needed).

aminoglycoside		
+ MRSA coverage	Vancomycin or Linezolid	3rd component (if MRSA risk >10-20%).

Targeted:

Penicillin-sensitive: Penicillin G 4x4 million IU IV; Resistant: Ceftriaxone or Vancomycin

Supportive:

- O₂ therapy (SpO₂ >92%)
- Fluid resuscitation
- Antipyretics
- Chest drain for empyema

Prevention:

- PPSV23 (23-valent polysaccharide)
- PCV13/15/20 (conjugate)
- Influenza vaccine

Pulmonary Tuberculosis

Pathogen: Mycobacterium - Mycobacterium tuberculosis (Acid-fast (Ziehl-Neelsen+))

Epidemiology:

- Incidence: ~10 million new cases/year worldwide, ~500 cases/year in Hungary
- Seasonality: No seasonality
- Transmission: Droplet infection (< 5 µm aerosol), 8+ hours exposure in a closed space
- Risk Groups: HIV positive (20-30x risk), Diabetics, Immunosuppressed, Socially disadvantaged, Healthcare workers, Immigrants from endemic areas

Pathomechanism:**Steps:**

- Inhalation: Bacillus reaches the alveoli
- Phagocytosis: Alveolar macrophages engulf but cannot kill them
- Intracellular multiplication: Primary complex (Ghon focus + hilar lymph node) in 2-12 weeks
- Granuloma formation: T-cell mediated immune response → epithelioid cells, Langhans giant cells
- Latent infection: Granulomas encapsulate the bacilli (90%)
- Reactivation: Immunosuppression → caseating necrosis → cavity → spreads by coughing

Virulence Factors:

- Cord factor (trehalose dimycolate)
- Mycolic acid (cell wall)
- Lipoarabinomannan
- ESAT-6 and CFP-10 secreted antigens

Clinical Features:

- Incubation: Primary: 2-12 weeks; Reactivation: years-decades
- Onset: Slow, insidious

Symptoms:

- **Chronic cough:** >90% in active pulmonary TB; lasting >3 weeks
- **Fever:** 60-80%, often afternoon/evening subfebrility
- **Night sweats:** Profuse (50%)
- **Weight loss:** Significant weight loss (common)
- **Hemoptysis:** Bloody sputum (20-30%), usually a late sign
- **Chest pain:** Pleuritic or dull

Physical Exam:

- Cachexia
- Crepitation/bronchial breathing over upper lobes
- Decreased breath sounds over a cavity
- Pleural friction rub
- Lymphadenopathy (miliary/extrapulmonary)

Complications:

- Miliary TB
- TB meningitis
- Pleuritis
- Pericarditis
- Spontaneous pneumothorax
- Hemoptysis
- Amyloidosis

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Normocytic anemia, lymphopenia	Signs of chronic disease
CRP/ESR	Moderately elevated	Non-specific
Liver/kidney function	Baseline before treatment	Monitoring for drug toxicity
HIV serology	Mandatory	Exclusion of coinfection

Imaging:

- **Chest X-ray:** Upper lobe infiltrate, cavity, fibrotic scarring, calcification (*Screening and follow-up*)
- **Chest CT:** Tree-in-bud sign, cavities, miliary pattern (*More sensitive, extrapulmonary*)

Microbiology:

- **Sputum Ziehl-Neelsen stain:** Acid-fast bacilli (AFB) (*Fast, but only positive >10^4/mL*)
- **Sputum/BAL culture:** Löwenstein-Jensen/MGIT (*Gold standard, 2-8 weeks*)

- **GeneXpert MTB/RIF:** MTB DNA + rifampicin resistance (*Fast (<2 hours), sensitive*)
- **Tuberculin skin test (Mantoux):** >10mm induration (*Exposure, not active disease*)
- **IGRA (QuantiFERON/T-SPOT):** IFN- γ production to ESAT-6/CFP-10 (*Not affected by BCG*)

Differential Diagnosis:

- **Lung carcinoma:** Smoking, X-ray/CT, bronchoscopy, biopsy
- **Non-tuberculous mycobacteriosis (NTM):** Bronchiectasis, culture, MAC most common
- **Sarcoidosis:** Bilateral hilar lymphadenopathy, biopsy (non-caseating)
- **Fungal pneumonia:** Immunosuppression, culture/antigen
- **Actinomycosis:** Sulfur granules, chest wall penetration

Therapy:

Outpatient:

Drug	Dose	Note
Isoniazid (INH)	5 mg/kg (max 300mg) PO	Hepatotoxicity, peripheral neuropathy (B6!)
Rifampicin (RIF)	10 mg/kg (max 600mg) PO	Drug interactions (CYP450)
Pyrazinamide (PZA)	25 mg/kg PO	Hyperuricemia, hepatotoxicity
Ethambutol (EMB)	15 mg/kg PO	Optic neuritis

Inpatient:

Drug	Dose	Note
Same + isolation	Airborne isolation	Negative pressure room

Icu:

Drug	Dose	Note
IV formulations	If PO not tolerated	MDR-TB: individualized

Targeted:

MDR-TB: Bedaquiline, Linezolid, Fluoroquinolones, Aminoglycosides - expert center

Supportive:

- Vitamin B6 (neuropathy prevention)
- Nutrition
- Contact tracing

Prevention:

- BCG vaccine (newborns)
- LTBI treatment (INH 9 mo or RIF 4 mo)
- Contact screening

Legionella Pneumonia (Legionnaires' Disease)

Pathogen: Bacterium - Legionella pneumophila (Gram-negative (stains poorly))

Epidemiology:

- Incidence: 2-9% of CAP, up to 30% of nosocomial pneumonia
- Seasonality: Summer-autumn (air conditioning)
- Transmission: Inhalation (aerosol from contaminated water: cooling towers, showers, hot tubs). NOT transmitted person-to-person!
- Risk Groups: Elderly (>50 years), Smokers, COPD patients, Immunosuppressed, Chronic kidney disease, Diabetes

Pathomechanism:

Steps:

- Aerosol inhalation from contaminated water source
- Legionella enters alveolar macrophages
- Dot/Icm T4SS system: Inhibition of phagosome-lysosome fusion
- Intracellular replication in a special vacuole
- Cell lysis → infection of adjacent cells
- Severe necrotizing alveolitis, inflammatory infiltration

Virulence Factors:

- Dot/Icm secretion system
- Mip (macrophage infectivity potentiator)
- Flagellum
- Over 300 effector proteins

Clinical Features:

- Incubation: 2-10 days (average 5-6 days)
- Onset: Prodrome for 1-2 days, then rapid progression

Symptoms:

- **High fever:** >90%, often >39°C
- **Cough:** 90%; initially dry, later productive (50%)
- **GI symptoms:** Diarrhea (20-50%), nausea/vomiting (10-30%)
- **Neurological symptoms:** Confusion (25-50%), headache (40-50%)
- **Dyspnea:** Shortness of breath (25-60%)

Physical Exam:

- High fever with relative bradycardia (Faget's sign)
- Signs of consolidation on auscultation
- Mild hepatomegaly
- Cerebellar signs possible

Complications:

- Respiratory failure/ARDS

- Acute kidney injury
- Rhabdomyolysis
- Sepsis
- Endocarditis
- Encephalopathy

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (left shift)	Non-specific
Sodium	Hyponatremia (<130 mmol/L)	SIADH - characteristic!
Liver enzymes	Elevated AST, ALT, LDH	Common association
CK	Elevated	Myositis/rhabdomyolysis
CRP/PCT	Significantly elevated	Severe bacterial infection

Imaging:

- **Chest X-ray:** Rapidly progressing infiltrate, often unilateral, lobar (*Worse than clinical picture*)
- **Chest CT:** Ground-glass and consolidation, pleural effusion (*More sensitive*)

Microbiology:

- **Urine Legionella antigen:** L. pneumophila serogroup 1 (70%) (*Fast (< 15 min), specific >95%*)
- **Culture (BCYE agar):** Legionella isolation (*Gold standard, 3-5 days*)
- **PCR:** Legionella DNA (*Fast, detects all serotypes*)
- **Serology:** 4x titer rise (*Retrospective diagnosis*)

Differential Diagnosis:

- **Pneumococcal pneumonia:** Productive cough, no GI/neuro symptoms, normal Na
- **Mycoplasma pneumonia:** Younger patients, slower progression, cold agglutinins
- **Q fever:** Animal exposure, hepatitis dominates
- **Psittacosis:** Bird contact, hepatosplenomegaly
- **Influenza pneumonia:** Seasonality, rapid test, epidemiology

Therapy:

Outpatient:

Drug	Dose	Note
Azithromycin	1x500mg PO	First choice
Levofloxacin	1x750mg PO	Alternative

Inpatient:

Drug	Dose	Note

Levofloxacin	1x750mg IV	Better penetration
Azithromycin	1x500mg IV	Alternative

Icu:

Drug	Dose	Note
Levofloxacin + Azithromycin	In combination	In severe cases
Rifampicin may be added	2x300mg IV/PO	In immunosuppressed patients

Targeted:

Fluoroquinolones or macrolides (beta-lactams are ineffective!)

Supportive:

- Fluid resuscitation
- Electrolyte correction
- Ventilation for ARDS

Prevention:

- Water system maintenance (>60°C)
- Disinfection of cooling towers
- Nosocomial surveillance

Mycoplasma Pneumonia

Pathogen: Bacterium - Mycoplasma pneumoniae (No cell wall)

Epidemiology:

- Incidence: 15-20% of CAP, 50% in epidemics
- Seasonality: Autumn-winter, but occurs year-round
- Transmission: Droplet infection (close contact)
- Risk Groups: School-aged children, Young adults, Closed communities (dorms, barracks)

Pathomechanism:**Steps:**

- Adherence to respiratory epithelial cells (P1 adhesin)
- Ciliostasis and ciliary destruction (hydrogen peroxide)
- CARDS toxin production (inflammation, vacuolization)
- Immune-mediated lung injury

Virulence Factors:

- P1 adhesin
- CARDS toxin
- Hydrogen peroxide

Clinical Features:

- Incubation: 2-3 weeks
- Onset: Slow, gradual

Symptoms:

- **Cough:** >95%; dry, hacking, paroxysmal, lasts for weeks
- **General symptoms:** Headache, malaise (common)
- **Sore throat:** Common (non-exudative)
- **Fever:** Variable, can be high or absent
- **Extrapulmonary:** Hemolysis (subclinical common), rash (Stevens-Johnson <10%)

Physical Exam:

- Often sparse auscultation findings
- Possible rales, wheezing
- Bullous myringitis (eardrum blisters - rare but specific)
- Cervical lymphadenopathy

Complications:

- Stevens-Johnson syndrome
- Hemolytic anemia (cold agglutinin)
- Encephalitis
- Myocarditis

Diagnostics:**Laboratory:**

Test	Finding	Interpretation
CBC	Normal WBC, possibly mild leukocytosis	Non-specific
CRP	Moderately elevated	Atypical feature
Cold agglutinin	Positive (50%)	Non-specific, but characteristic

Imaging:

- **Chest X-ray:** Interstitial pattern, patchy infiltrates (*Worse than clinical picture ("Walking pneumonia")*)

Microbiology:

- **PCR:** DNA detection (throat/sputum) (*Gold standard, fast*)
- **Serology (IgM/IgG):** Titer rise (*Retrospective, often negative in acute phase*)

Differential Diagnosis:

- **Chlamydia pneumoniae:** Clinically difficult to distinguish, PCR
- **Viral pneumonia:** Epidemiology, PCR
- **Legionella:** More severe, older patients, hyponatremia

Therapy:**Outpatient:**

Drug	Dose	Note
Azithromycin	500mg D1, then 250mg D2-5	First choice
Doxycycline	2x100mg	Alternative (>8 years)
Clarithromycin	2x500mg	Alternative

Inpatient:

Drug	Dose	Note
Levofloxacin	1x500-750mg IV/PO	In severe cases
Moxifloxacin	1x400mg IV/PO	Alternative

Icu:

Drug	Dose	Note
Macrolide + Beta-lactam	Combination	To cover mixed infection

Targeted:

Macrolides (resistance increasing!), Tetracyclines, Fluoroquinolones

Supportive:

- Cough suppressants
- Antipyretics

Prevention:

- Droplet precautions
- No vaccine

Chlamydia pneumoniae

Pathogen: Bacterium - Chlamydophila pneumoniae (Gram-negative (intracellular))

Epidemiology:

- Incidence: 5-10% of CAP
- Seasonality: Year-round
- Transmission: Droplet infection
- Risk Groups: Elderly, Chronic patients, Closed communities

Pathomechanism:**Steps:**

- Inhalation of elementary body (EB)
- Intracellular transformation to reticulate body (RB)
- Replication, inclusion formation
- Cell lysis, EB release

- Ciliostasis

Virulence Factors:

- Intracellular survival
- Endotoxin-like substances

Clinical Features:

- Incubation: 3-4 weeks
- Onset: Gradual

Symptoms:

- **Biphasic course:** Upper respiratory symptoms followed by pneumonia
- **Hoarseness/Laryngitis:** Characteristic accompanying symptom
- **Cough:** Persistent, lasting for weeks-months

Physical Exam:

- Pharyngitis
- Rales
- Signs of sinusitis

Complications:

- Reactive arthritis
- Myocarditis
- Atherosclerosis (association)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Normal	Non-specific

Imaging:

- **Chest X-ray:** Small infiltrates (*Non-specific*)

Microbiology:

- **PCR:** DNA detection (*Most sensitive*)
- **Serology:** MIF (microimmunofluorescence) (*Gold standard serology*)

Differential Diagnosis:

- **Mycoplasma:** Practically identical clinical picture
- **Viruses:** PCR

Therapy:

Outpatient:

Drug	Dose	Note
Doxycycline	2x100mg	First choice
Azithromycin	500mg D1, 250mg D2-5	Alternative

Inpatient:

Drug	Dose	Note
Levofloxacin	1x750mg	In more severe cases

Icu:

Drug	Dose	Note
Levofloxacin	IV	

Targeted:

Tetracyclines, Macrolides, Quinolones

Supportive:

- Symptomatic treatment

Prevention:

- No vaccine

Ornithosis (Psittacosis)

Pathogen: Bacterium - Chlamydia psittaci (Intracellular)

Epidemiology:

- Incidence: Rare, occupational disease
- Seasonality: None
- Transmission: Inhalation of dust from bird droppings
- Risk Groups: Bird owners (parrots, pigeons), Veterinarians, Poultry workers

Pathomechanism:**Steps:**

- Inhalation
- Infection of the reticuloendothelial system (liver, spleen)
- Hematogenous spread to the lungs
- Interstitial pneumonia

Virulence Factors:

- Intracellular survival

Clinical Features:

- Incubation: 5-14 days
- Onset: Sudden

Symptoms:

- **Fever:** Almost 100%, sudden onset
- **Headache:** Severe, often with photophobia
- **Cough:** Dry (50-90%)

- **Splenomegaly:** Detected in 10-70%

Physical Exam:

- Relative bradycardia (Faget's sign)
- Splenomegaly (10-70%)
- Horder's spots (pink rash - rare)
- Sparse lung findings

Complications:

- Endocarditis
- Hepatitis
- Neurological symptoms
- ARDS

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Normal or leukopenia	Non-bacterial character
Liver enzymes	Elevated	Common

Imaging:

- **Chest X-ray:** Atypical pneumonia, fan-shaped hilar infiltrate (*Characteristic*)

Microbiology:

- **Serology:** MIF, complement fixation (*4x titer rise*)
- **PCR:** Respiratory sample (*Specific*)

Differential Diagnosis:

- **Q fever:** Similar, but no bird contact
- **Legionella:** Water exposure
- **Typhoid fever:** Travel, rash

Therapy:

Outpatient:

Drug	Dose	Note
Doxycycline	2x100mg	First choice

Inpatient:

Drug	Dose	Note
Doxycycline	2x100mg IV	In severe cases

Icu:

Drug	Dose	Note
Doxycycline	IV	

Targeted:

Tetracyclines (Doxycycline), Macrolides (less effective)

Supportive:

- Antipyretics

Prevention:

- Quarantine of birds
- Protective equipment
- Wet cleaning

Q Fever

Pathogen: Bacterium - Coxiella burnetii (Gram-negative (intracellular))

Epidemiology:

- Incidence: Zoonosis, occupational disease
- Seasonality: Spring (birthing season)
- Transmission: Aerosol (placenta, amniotic fluid, milk, feces dust)
- Risk Groups: Livestock farmers, Slaughterhouse workers, Veterinarians

Pathomechanism:**Steps:**

- Inhalation (a single bacterium can infect!)
- Infection of alveolar macrophages
- Replication in acidic phagosomes
- Hematogenous spread
- Granuloma formation (doughnut granuloma)

Virulence Factors:

- Spore-like form (resistant)
- LPS phase variation

Clinical Features:

- Incubation: 2-3 weeks
- Onset: Sudden

Symptoms:

- **Acute Q fever:** Flu-like: Fever, fatigue, severe headache
- **Pneumonia:** Variable, often mild cough, but radiological findings
- **Hepatitis:** Hepatomegaly, right upper quadrant pain
- **Chronic:** Endocarditis (main manifestation)

Physical Exam:

- Hepatomegaly
- Splenomegaly

- Relative bradycardia

Complications:

- Chronic Q fever (Endocarditis)
- Osteomyelitis
- Chronic hepatitis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Liver enzymes	Elevated	Hepatitis
Thrombocytopenia	Mild	Common

Imaging:

- **Chest X-ray:** Round opacities, multiple (*Pneumonia*)
- **Echo:** Vegetation (*Endocarditis (chronic)*)

Microbiology:

- **Serology (IF):** Phase II (acute), Phase I (chronic) (*Diagnostic*)
- **PCR:** From blood (*In early phase*)

Differential Diagnosis:

- **Brucellosis:** Undulant fever, dairy products
- **Influenza:** Seasonality, respiratory symptoms dominate
- **Viral hepatitis:** Serology

Therapy:

Outpatient:

Drug	Dose	Note
Doxycycline	2x100mg	Acute Q fever

Inpatient:

Drug	Dose	Note
Doxycycline	2x100mg	

Icu:

Drug	Dose	Note
Doxycycline + Hydroxychloroquine	Long-term	Chronic Q fever (endocarditis)

Targeted:

Doxycycline

Supportive:

- Antipyretics

Prevention:

- Protective equipment during birthing
- Pasteurization of milk
- Vaccine (Australia)

Viral Respiratory Infections

Influenza

Pathogen: Virus - Influenza A/B/C virus (RNA virus, Orthomyxoviridae)

Epidemiology:

- Incidence: Seasonal epidemic: 5-20% of population/year, pandemics: up to 50%
- Seasonality: November-March (northern hemisphere)
- Transmission: Droplet, contact (1-2 meters), fomites
- Risk Groups: Elderly (>65), Children (<5), Pregnant women, Chronic patients, Healthcare workers, Immunosuppressed

Pathomechanism:**Steps:**

- Hemagglutinin (HA) binds to sialic acid receptors on respiratory epithelium
- Receptor-mediated endocytosis
- Viral RNA replication in the nucleus
- Neuraminidase (NA) aids in the release of new viruses
- Epithelial cell apoptosis, ciliary damage
- Cytokine storm in severe cases (IL-6, TNF- α , IFN- γ)

Virulence Factors:

- Hemagglutinin (H1-18)
- Neuraminidase (N1-11)
- NS1 protein (IFN antagonist)
- PB1-F2 (pro-apoptotic)

Clinical Features:

- Incubation: 1-4 days (average 2 days)
- Onset: Sudden

Symptoms:

- **Fever:** Sudden onset, 38-41°C (95% of symptomatic cases)
- **Cough:** Dry, non-productive (>90%), often with chest pain
- **Myalgia:** Severe muscle pain (90%), especially back/limbs
- **Headache:** Severe, often retro-orbital (85%)
- **Sore throat:** Common accompanying symptom (60-70%)

- **Prostration:** Marked weakness, bedridden

Physical Exam:

- Febrile, ill-appearing
- Conjunctivitis
- Pharyngeal hyperemia
- Clear lung auscultation (uncomplicated)
- Tachycardia

Complications:

- Primary influenza pneumonia
- Secondary bacterial pneumonia
- Myocarditis
- Encephalitis
- Reye's syndrome (aspirin!)
- Myositis

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Leukopenia or normal, lymphopenia	Typical for viral infection
CRP	Moderately elevated	Lower than in bacterial
PCT	Normal (<0.25)	Exclusion of bacterial superinfection

Imaging:

- **Chest X-ray:** Normal or interstitial pattern (*Exclusion of pneumonia*)
- **CT:** Ground-glass opacities (*Viral pneumonia*)

Microbiology:

- **Rapid antigen test (RAT):** Influenza A/B (*Fast (15 min), low sensitivity (50-70%)*)
- **RT-PCR:** Viral RNA detection (*Gold standard, subtyping*)
- **Virus culture:** Isolation (*Epidemiological/surveillance*)

Differential Diagnosis:

- **COVID-19:** Loss of smell/taste, PCR
- **RSV infection:** Children, elderly, bronchiolitis
- **Adenovirus infection:** Conjunctivitis, pharyngitis, longer febrile period
- **Bacterial pneumonia:** Productive sputum, localized findings, high PCT

Therapy:

Outpatient:

Drug	Dose	Note
Oseltamivir	2x75mg PO	Within 48 hours of symptom onset!

Baloxavir	1x40-80mg PO	>80kg: 80mg
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Inpatient:

Drug	Dose	Note
Oseltamivir	2x75mg PO/NG	Longer in severe cases
Peramivir	1x600mg IV	If PO not tolerated

Icu:

Drug	Dose	Note
Oseltamivir	2x150mg PO/NG	Higher dose may be considered
+ Empiric AB	CAP coverage	Bacterial superinfection

Targeted:

Neuraminidase inhibitors (oseltamivir, zanamivir, peramivir) or cap-dependent endonuclease inhibitor (baloxavir)

Supportive:

- Antipyretics (paracetamol!)
- Fluid resuscitation
- Oxygen
- Ventilation for ARDS

Prevention:

- Annual influenza vaccine
- Hand hygiene
- Patient isolation
- Chemoprophylaxis (oseltamivir 1x75mg)

COVID-19

Pathogen: Virus - SARS-CoV-2 (RNA virus, Coronaviridae)

Epidemiology:

- Incidence: Pandemic from 2020, becoming endemic
- Seasonality: Winter peak, but year-round
- Transmission: Respiratory (aerosol + droplet), contact, fecal-oral rare
- Risk Groups: Elderly (>65), Obese (BMI>30), Diabetes, Cardiovascular disease, Immunosuppressed, Chronic lung disease

Pathomechanism:**Steps:**

- Spike protein binds to ACE2 receptor (lung, heart, vessels, gut)
- TMPRSS2 protease cleaves spike protein → fusion

- Viral replication and spread
- Endothelial dysfunction, microthrombosis
- Cytokine storm (IL-6, IL-1 β , TNF- α) in severe cases
- ARDS, multi-organ failure

Virulence Factors:

- Spike protein
- NSP1 (host shutdown)
- ORF8 (immunomodulation)
- Nucleocapsid

Clinical Features:

- Incubation: 2-14 days (median 5 days, Omicron 3 days)
- Onset: Variable

Symptoms:

- **Fever:** Common (70-90%), but may be absent (elderly)
- **Cough:** Dry (60-80%), persistent
- **Fatigue:** Pronounced (40-70%)
- **Dyspnea:** Shortness of breath (30-50% of hospitalized), hypoxia
- **Anosmia/Dysgeusia:** Loss of smell/taste (variant-dependent, 20-60%)
- **Myalgia:** Muscle pain (30-60%)

Physical Exam:

- Fever, tachypnea
- Decreased SpO₂ (silent hypoxia!)
- Bilateral crepitation
- Tachycardia
- No specific physical sign

Complications:

- ARDS
- Pulmonary embolism
- Myocarditis
- Acute kidney injury
- Stroke
- MIS-C (children)
- Long COVID

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Lymphopenia, normal/decreased platelets	Marker of severity
D-dimer	Elevated	Thrombotic risk, poor prognosis

Ferritin	Elevated	Marker of cytokine storm
CRP/IL-6	Elevated	Degree of inflammation
LDH, troponin	Elevated in severe cases	Tissue damage

Imaging:

- **Chest X-ray:** Bilateral peripheral infiltrates (*Less sensitive*)
- **Chest CT:** Ground-glass opacities, crazy paving, consolidation (*Characteristic pattern*)

Microbiology:

- **RT-PCR (nasopharynx/oropharynx):** SARS-CoV-2 RNA (*Gold standard, Ct value*)
- **Rapid antigen test:** Nucleocapsid protein (*Fast, indicates infectiousness*)
- **Serology:** Anti-S, Anti-N IgG/IgM (*Past infection, vaccine efficacy*)

Differential Diagnosis:

- **Influenza:** Faster course, myalgia dominates, PCR
- **Bacterial pneumonia:** High PCT, lobar infiltrate
- **Heart failure:** Cardiac history, BNP, bilateral
- **Pulmonary embolism:** D-dimer, CTPA

Therapy:**Outpatient:**

Drug	Dose	Note
Paxlovid (nirmatrelvir/ritonavir)	2x300/100mg PO	Early, high-risk, interactions!
Molnupiravir	2x800mg PO	Alternative if Paxlovid is contraindicated

Inpatient:

Drug	Dose	Note
Remdesivir	200mg IV D1, then 100mg/day	If O2 is needed
Dexamethasone	6mg/day IV/PO	Only with O2 need/ventilation!

Icu:

Drug	Dose	Note
Dexamethasone	6-20mg/day	Cytokine storm
Tocilizumab	8mg/kg IV single dose	IL-6 inhibitor, rapidly deteriorating
LMWH	Therapeutic dose	Thromboprophylaxis/therapy

Targeted:

Antiviral (Paxlovid, Remdesivir) early; Immunomodulatory (steroid, tocilizumab) in hypoxic phase

Supportive:

- Oxygen (prone positioning!)
- HFNC/NIV
- Invasive ventilation
- ECMO

Prevention:

- mRNA vaccines (Pfizer, Moderna)
- Hand hygiene
- Mask wearing
- Isolation

❤️ Cardiovascular Infections

Infective Endocarditis

Pathogen: Bacterium - *Staphylococcus aureus*, *Streptococcus viridans* (Gram-positive)

Epidemiology:

- Incidence: 3-10/100,000 per year
- Seasonality: None
- Transmission: Bacteremia (dental procedure, skin infection, catheter)
- Risk Groups: Valvular defects, Prosthetic valves, IV drug users, Congenital heart disease, Previous endocarditis

Pathomechanism:

Steps:

- Endothelial injury (turbulent flow)
- Sterile platelet-fibrin thrombus formation (NBTE)
- Bacteremia (pathogen adherence)
- Vegetation formation (bacteria + fibrin + platelets)
- Tissue destruction, embolization

Virulence Factors:

- Adhesins (MSCRAMM)
- Biofilm formation
- Toxins

Clinical Features:

- Incubation: Days (acute) or weeks (subacute)
- Onset: Variable

Symptoms:

- **Fever:** Most common symptom (>90%), often with chills
- **Heart murmur:** New or changed regurgitant murmur (85%)

- **Emolic symptoms:** Stroke, pulmonary embolism, spleen/kidney infarct (20-50%)
- **Heart failure:** Dyspnea, edema (40-60% - most common complication)
- **Skin manifestations:** Petechiae (20-40%), Osler/Janeway (5-10% - rarer today)

Physical Exam:

- Fever
- New heart murmur (especially regurgitant)
- Signs of heart failure (S3, congestion)
- Splenomegaly (15-30%)
- Peripheral signs (Splinter, Osler, Janeway, Roth - rare)

Complications:

- Heart failure (valve insufficiency)
- Septic embolism (brain, spleen, kidney)
- Abscess (ring)
- Glomerulonephritis

Diagnostics:

Criteria:

Major criteria (ESC 2023): Positive blood culture (typical pathogen: S. aureus, Enterococcus, Viridans strep, S. gallolyticus, HACEK) from 2 separate samples, Positive imaging (Echo/CT/PET-CT): Vegetation, abscess, pseudoaneurysm, fistula, perforation, new dehiscence, Paravalvular lesion on CT, Abnormal activity around prosthetic valve (PET/CT or SPECT/CT)

Minor criteria: Predisposition (heart defect, prosthetic valve, previous IE), Fever >38°C, Vascular phenomena (embolism, septic infarct, mycotic aneurysm, Janeway, imaging-confirmed lesions), Immunological phenomena (Osler's nodes, Roth spots, RF+, Glomerulonephritis), Microbiological evidence (positive culture not meeting major criteria)

Diagnosis (Definite): 2 Major, 1 Major + 3 Minor, 5 Minor

Laboratory:

Test	Finding	Interpretation
Blood culture	Positive (continuous bacteremia)	DUKE major criterion (3 sets!)
CBC	Anemia, leukocytosis	Chronic inflammation
CRP/ESR	Elevated	Inflammation

Imaging:

- **Echocardiography (TTE/TEE):** Vegetation, abscess, dehiscence (*Primary imaging*)
- **Cardiac CT / PET-CT:** Paravalvular spread, embolism (*Adjunctive (ESC 2023)*)

Microbiology:

- **Blood culture:** Pathogen identification (*Basis of therapy*)
- **Serology:** Coxiella, Bartonella (*If blood culture is negative*)

Therapy:

Guidelines: ESC 2023 Guidelines for the management of endocarditis

Empiric: Native valve or Late prosthetic valve (>12 mo):

Drug	Dose	Note
Ampicillin + (Flu)cloxacillin + Gentamicin	12g + 12g + 3mg/kg IV	IB recommendation. Gentamicin only for the first few days/until pathogen is known.
Vancomycin + Gentamicin	30-60mg/kg + 3mg/kg IV	IB recommendation. For penicillin allergy.
Daptomycin + Gentamicin	10mg/kg + 3mg/kg IV	IB recommendation. Alternative.

Empiric: Early prosthetic valve (<12 mo) or Nosocomial:

Drug	Dose	Note
Vancomycin + Gentamicin + Rifampicin	30-60mg/kg + 3mg/kg + 900-1200mg IV/PO	IB recommendation. Rifampicin only after bacteremia has cleared (to prevent resistance).

Targeted: Staphylococcus spp.:

Drug	Dose	Note
MSSA: (Flu)cloxacillin	12g/day IV	IB recommendation. Penicillin allergy (non-anaphylactic): Cefazolin 6g/day (IB).
MRSA: Vancomycin	30-60mg/kg/day IV	IB recommendation. Alternative: Daptomycin 10mg/kg (IB).
Prosthetic valve (PVE): + Rifampicin + Gentamicin	Adjunct	IB recommendation. Rifampicin 900-1200mg, Gentamicin 3mg/kg.

Targeted: Streptococcus spp. (Oral/Bowel):

Drug	Dose	Note
Penicillin G or Amoxicillin or Ceftriaxone	Standard high dose	IB recommendation. Penicillin-sensitive strains.
Combination with Gentamicin	Beta-lactam + 3mg/kg Gentamicin	IB recommendation. Can shorten course only for native valve, uncomplicated cases.
Penicillin allergy: Vancomycin	30mg/kg/day IV	IB recommendation.

Targeted: Enterococcus spp.:

Drug	Dose	Note
Amoxicillin + Ceftriaxone	200mg/kg + 4g/day IV	IB recommendation. Preferred for E. faecalis (less nephrotoxicity than with gentamicin).
Ampicillin + Gentamicin	12g + 3mg/kg IV	IB recommendation. Traditional therapy.
Vancomycin + Gentamicin	30mg/kg + 3mg/kg IV	IB recommendation. For beta-lactam resistance/allergy.

Culture-negative IE:

Drug	Dose	Note
Coxiella burnetii	Doxycycline + Hydroxychloroquine	IB recommendation. Q fever endocarditis.
Bartonella spp.	Doxycycline + Gentamicin (2 weeks)	IB recommendation.
Brucella spp.	Doxycycline + Streptomycin + Rifampicin	IB recommendation.

Targeted:

See detailed protocols above. In stable patients (left-sided IE), oral switch is possible after 10-14 days of IV therapy (POET trial, IB recommendation) if TEE has excluded abscess and patient is cooperative.

Supportive:

- Heart failure management (IB)
- Embolism prophylaxis (anticoagulation may be contraindicated due to bleeding risk!)
- Source control (full body CT/PET-CT)

Prevention:

- Antibiotic prophylaxis (Amoxicillin 2g or Clindamycin 600mg) ONLY in high-risk patients (prosthetic valve, previous IE, cyanotic congenital vitium) before dental procedures (IIa)
- Oral hygiene (IB)

Myocarditis

Pathogen: Virus - Coxsackie B, Adenovirus, Parvovirus B19 (RNA/DNA viruses)

Epidemiology:

- Incidence: Hard to estimate (many mild cases), 10-20% of sudden cardiac death in young people
- Seasonality: Virus-dependent (e.g., enterovirus summer-autumn)
- Transmission: Fecal-oral, droplet (pathogen-dependent)
- Risk Groups: Young adults, Men, Immunosuppressed

Pathomechanism:**Steps:**

- Virus entry into cardiomyocytes (receptor-mediated)
- Direct cytopathic effect (replication)
- Activation of immune response (T-cells, cytokines)
- Autoimmune reaction (molecular mimicry)
- Myocardial necrosis, fibrosis, dilation

Virulence Factors:

- Protease 2A (dystrophin cleavage)
- Receptor binding (CAR)

Clinical Features:

- Incubation: 1-2 weeks after viral infection
- Onset: Variable (from asymptomatic to fulminant)

Symptoms:

- **Chest pain:** Sharp, pericardial-like (85-95% in uncomplicated cases)
- **Dyspnea:** On exertion or at rest (19-49%)
- **Palpitations:** Sensation of arrhythmias (6-18%)
- **Prodromal symptoms:** Fever, respiratory/GI symptoms days before (60%)
- **Syncope:** Due to arrhythmia (rare, but dangerous)

Physical Exam:

- Tachycardia (disproportionate to fever)
- Signs of heart failure (S3, distended neck veins, edema)
- Pericardial friction rub (in myopericarditis)
- Arrhythmia (extrasystoles)

Complications:

- Dilated cardiomyopathy (DCM)
- Heart failure
- Fatal arrhythmias
- Sudden cardiac death

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Troponin (hs-cTn)	Elevated	Myocardial necrosis (high sensitivity)
NT-proBNP	Elevated	Heart failure / prognostic marker
CRP/ESR	Elevated	Inflammation

Imaging:

- **ECG:** ST-T changes, AV block, QRS widening (*Prognostic value*)
- **Echocardiography:** Global/regional wall motion abnormalities, decreased EF, pericardial effusion (*Basic examination*)
- **Cardiac MRI (CMR):** Lake Louise criteria (T1/T2 signals, LGE) (*Gold standard non-invasive diagnosis (ESC 2023)*)

Microbiology:

- **Endomyocardial biopsy (EMB):** Inflammation + Virus PCR (*Gold standard. Indicated in: fulminant course, non-responsive HF, specific suspicion (giant cell) (ESC 2023)*)
- **Virus serology:** Not routinely recommended (*Low diagnostic value (except hepatitis, HIV, Borrelia)*)

Differential Diagnosis:

- **Acute coronary syndrome (ACS):** Coronary angiography negative, young patient
- **Pericarditis:** Troponin less elevated, no wall motion abnormalities
- **Anxiety/panic:** ECG/Troponin negative

Therapy:**Outpatient:**

Drug	Dose	Note
Physical rest	No sports	Crucial! (ESC 2023)
NSAID (e.g., Ibuprofen)	Symptomatic	Only for chest pain if EF is preserved!

Inpatient:

Drug	Dose	Note
Heart failure therapy (GDMT)	ACEi/ARB/ARNI + BB + MRA + SGLT2i	If LVEF is reduced (ESC 2023)
Antiarrhythmic drugs	Amiodarone	In case of severe arrhythmia

Icu:

Drug	Dose	Note
Mechanical circulatory support (MCS)	VA-ECMO, Impella	In fulminant myocarditis / cardiogenic shock
High-dose steroids	Methylprednisolone	Only in proven autoimmune/giant cell forms (virus negative!)

Targeted:

Immunosuppression (Prednisolone + Azathioprine) ONLY in biopsy-proven virus-negative (PCR-) lymphocytic, giant cell, or sarcoidosis-related myocarditis (ESC 2023).

Contraindicated in active viral infection!

Supportive:

- Strict physical rest (3-6 months) until inflammation resolves
- Heart failure management
- ICD implantation (if inflammation has resolved and EF remains low)

Prevention:

- Vaccinations (Influenza, COVID, Measles)
- Hygiene

Acute Pericarditis

Pathogen: Virus/Idiopathic - Coxsackie, Echovirus, Adenovirus, CMV, EBV (Variable)

Epidemiology:

- Incidence: Common (0.1% of hospitalized)
- Seasonality: Virus-dependent
- Transmission: Droplet (viral)
- Risk Groups: Men (20-50 years), Post-cardiotomy, Autoimmune patients

Pathomechanism:Steps:

- Inflammation of the pericardium (viral, autoimmune, neoplastic)
- Fibrinous deposits (dry pericarditis)
- Exudate formation (pericardial effusion)
- Risk of tamponade (if fluid accumulates rapidly)

Virulence Factors:

- -

Clinical Features:

- Incubation: Variable
- Onset: Sudden

Symptoms:

- **Chest pain:** Sharp, pleuritic, worse when lying down, improves when leaning forward
- **Fever:** Usually low-grade
- **Dyspnea:** Due to pain or tamponade

Physical Exam:

- Pericardial friction rub (systolic and diastolic components)
- Muffled heart sounds (effusion)
- Beck's triad (in tamponade): hypotension, muffled heart sounds, distended neck veins

Complications:

- Pericardial tamponade
- Constrictive pericarditis
- Recurrent pericarditis (15-30%)

Diagnostics:Criteria:

Diagnosis (2 out of 4): Chest pain (typical), Pericardial friction rub, ECG changes (ST elevation, PR depression), Pericardial effusion (Echo)

Laboratory:

Test	Finding	Interpretation
CRP/ESR	Elevated	Inflammation activity (also for follow-up!)
Troponin	Normal or slightly elevated	Exclusion of myocarditis (if high: myopericarditis)
CBC	Leukocytosis	Inflammation

Imaging:

- **ECG:** Diffuse concave ST elevation, PR depression (elevation in aVR) (*Diagnostic*)
- **Echocardiography:** Pericardial effusion (*Exclusion of tamponade, diagnosis*)
- **Chest X-ray:** Normal or "water bottle heart" (large effusion) (*Exclusion of other causes*)

Microbiology:

- **Virus serology:** Not routine (*Only in special cases*)
- **Pericardiocentesis:** Culture/PCR (*Only in tamponade or suspicion of purulent/neoplastic cause*)

Differential Diagnosis:

- **Acute myocarditis:** Troponin elevation dominates, wall motion abnormalities
- **STEMI:** Convex ST elevation, reciprocal depression, regional
- **Pulmonary embolism:** Dyspnea dominates, D-dimer, CT

Therapy:

Outpatient:

Drug	Dose	Note
Aspirin	750-1000mg every 8 hours	First choice (ESC 2015)
Ibuprofen	600mg every 8 hours	Alternative
+ Colchicine	0.5mg once daily (<70kg) or twice (>70kg)	For prevention of recurrence (ESC 2015)!
PPI	Standard	Gastric protection

Inpatient:

Drug	Dose	Note
None	-	Only for high-risk cases (fever >38, subacute, large effusion, tamponade, anticoagulated patient)

Icu:

Drug	Dose	Note
Pericardiocentesis	Drainage	Life-saving in tamponade

Targeted:

Steroids (Prednisolone 0.2-0.5 mg/kg) ONLY if NSAID/Colchicine are contraindicated, unsuccessful, or for specific indications (autoimmune).

Supportive:

- Physical rest (no sports) until CRP normalizes (min. 3 months for athletes)

Prevention:

- Colchicine for the first episode

⚠️ Upper Respiratory Infections

Upper Respiratory Infections (Common Cold)

Pathogen: Virus - Rhinovirus (most common), Coronavirus, Adenovirus, Influenza (RNA viruses)

Epidemiology:

- Incidence: Most common infection, adults 2-3x/year, children 6-8x/year
- Seasonality: Year-round, peak in autumn-winter
- Transmission: Droplet, contact, fomites
- Risk Groups: Children, Elderly, Immunosuppressed

Pathomechanism:

Steps:

- Virus entry into nasal/pharyngeal mucosa
- Infection of epithelial cells
- Local inflammation (neutrophils, edema)
- Ciliostasis, increased mucus production
- Systemic response (fever, general symptoms)

Virulence Factors:

- Receptor binding (ICAM-1 for rhinovirus)
- Immunomodulation

Clinical Features:

- Incubation: 1-3 days
- Onset: Sudden

Symptoms:

- **Rhinorrhea:** Clear → mucopurulent
- **Sneezing:** Paroxysmal
- **Sore throat:** Mild
- **Cough:** Dry, irritative
- **Fever:** Mild or absent

Physical Exam:

- Nasal mucosa hyperemia, edema
- Mild pharyngeal redness
- Cervical lymphadenopathy
- Normal lung auscultation

Complications:

- Sinusitis
- Otitis media
- Bronchitis

- Pneumonia (rare)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
Not needed	-	Clinical diagnosis

Imaging:

- **undefined**: - (*undefined*)

Microbiology:

- **Virus PCR**: Etiology (*If needed (e.g., epidemic)*)

Differential Diagnosis:

- **Allergic rhinitis**: Pruritus, seasonality, eosinophilia
- **Bacterial sinusitis**: Persistent symptoms, fever, pain
- **Influenza**: High fever, myalgia, prostration

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Rest, fluids, symptomatic treatment
Decongestant	Oxymetazoline nasal	Not for longer!
Antihistamine	Loratadine	If allergy is suspected

Inpatient:

Drug	Dose	Note
Not needed	-	Rare

Icu:

Drug	Dose	Note
Not needed	-	Rare

Targeted:

No specific antiviral

Supportive:

- Rest
- Fluid intake
- Antipyretics

Prevention:

- Hand hygiene

- Mask wearing during epidemics

RSV Infection (Respiratory Syncytial Virus)

Pathogen: Virus - Human Respiratory Syncytial Virus (HRSV) (RNA virus, Pneumoviridae)

Epidemiology:

- Incidence: All children infected by age 2, adults reinfection
- Seasonality: Winter-spring
- Transmission: Droplet, contact (very contagious!)
- Risk Groups: Infants (<6 months), Elderly (>65), Chronic lung patients, Immunosuppressed

Pathomechanism:

Steps:

- Virus entry into airways
- Fusion with ciliated epithelial cells
- Syncytium formation
- Ciliary destruction, impaired mucociliary clearance
- Development of bronchiolitis or pneumonia

Virulence Factors:

- Fusion protein (F)
- G glycoprotein (adherence)

Clinical Features:

- Incubation: 4-6 days
- Onset: Gradual

Symptoms:

- **Rhinorrhea:** Clear
- **Cough:** Dry, then productive
- **Fever:** Mild-moderate
- **Dyspnea:** Severe in infants
- **Wheezing:** Sign of bronchiolitis

Physical Exam:

- Tachypnea, retractions
- Wheezing, crepitation
- Apnea in infants
- Hypoxia

Complications:

- Bronchiolitis obliterans
- Pneumonia
- Apnea

- Death (rare in infants, but possible)

Diagnostics:

Laboratory:

Test	Finding	Interpretation
CBC	Normal or mild leukocytosis	Non-specific

Imaging:

- **Chest X-ray:** Hyperinflation, atelectasis (*Bronchiolitis*)

Microbiology:

- **Nasopharyngeal aspirate PCR:** RSV RNA (*Gold standard*)
- **Immunofluorescence:** Antigen detection (*Fast*)

Differential Diagnosis:

- **Bronchiolitis other causes:** Virus PCR
- **Asthma:** History, atopy
- **Pertussis:** Whoop, lymphocytosis

Therapy:

Outpatient:

Drug	Dose	Note
Supportive	-	Oxygen, hydration
Bronchodilator	Salbutamol	If wheezing

Inpatient:

Drug	Dose	Note
Ribavirin	Aerosol	In severe cases, immunosuppressed

Icu:

Drug	Dose	Note
Ventilation	NIV or intubation	In case of apnea

Targeted:

Palivizumab prophylaxis for high-risk infants

Supportive:

- Oxygen
- Hydration
- Physiotherapy

Prevention:

- Hand hygiene
- Isolation

- Palivizumab (monoclonal Ab)

Tonsillitis

Pathogen: Bacterium - Streptococcus pyogenes (GAS, most common) (Gram-positive)

Epidemiology:

- Incidence: Common in childhood, 5-15 years
- Seasonality: Winter-spring
- Transmission: Droplet, contact
- Risk Groups: Children, Young adults

Pathomechanism:

Steps:

- Bacterial colonization of the tonsils
- Local inflammation, edema
- Toxin production (streptolysin O)
- Systemic response (fever, general symptoms)

Virulence Factors:

- M protein
- Streptolysins
- Hyaluronidase

Clinical Features:

- Incubation: 2-5 days
- Onset: Sudden

Symptoms:

- **Sore throat:** Severe, difficulty swallowing
- **Fever:** High
- **Dysphagia:** Pain on swallowing
- **Tonsillar exudate:** White, purulent

Physical Exam:

- Tonsillar hyperemia, swelling
- Exudate
- Cervical lymphadenitis
- Scarlet fever symptoms (rare)

Complications:

- Peritonsillar abscess
- Rheumatic fever
- Glomerulonephritis
- Lemierre's syndrome

Diagnostics:**Microbiology:**

- **Strep test:** Positive (*undefined*)
- **Throat swab culture:** GAS (*Confirmation*)

Differential Diagnosis:

- **Viral pharyngitis:** Mild symptoms, no exudate
- **Mononucleosis:** Lymphocytosis, hepatosplenomegaly

Therapy:**Outpatient:**

Drug	Dose	Note
Penicillin V	4x500mg PO	First choice
Amoxicillin	3x500mg PO	Alternative

Inpatient:

Drug	Dose	Note
Penicillin G	4x4 million IU IV	In severe cases

Icu:

Drug	Dose	Note
Surgical drainage	For abscess	

Targeted:

Penicillin

Supportive:

- Analgesics
- Fluids

Prevention:

- Hygiene

Sinusitis

Pathogen: Virus/Bacterium - Viruses (first 7-10 days), then Streptococcus pneumoniae, Haemophilus influenzae (Mixed)

Epidemiology:

- Incidence: Common, adults 1-2x/year
- Seasonality: Winter
- Transmission: Endogenous, complication of upper respiratory infection
- Risk Groups: Allergic individuals, Smokers, Immunosuppressed

Pathomechanism:**Steps:**

- Nasal mucosa inflammation (virus)
- Ostium obstruction
- Bacterial superinfection
- Purulent inflammation

Virulence Factors:

- Biofilm formation

Clinical Features:

- Incubation: After upper respiratory infection
- Onset: Gradual

Symptoms:

- **Facial pain:** Over forehead, sinuses
- **Nasal congestion:** Mucopurulent discharge
- **Headache:** Frontal
- **Fever:** In acute cases

Physical Exam:

- Facial tenderness
- Mucopurulent nasal discharge
- Postnasal drip

Complications:

- Orbital cellulitis
- Meningitis
- Osteomyelitis

Diagnostics:**Imaging:**

- **Sinus CT:** Fluid level, mucosal thickening (*If needed*)

Differential Diagnosis:

- **Migraine:** Unilateral headache, aura
- **Dental pain:** Dental examination

Therapy:**Outpatient:**

Drug	Dose	Note
Amoxicillin/Clavulanate	2x875/125mg PO	If bacterial is suspected
Decongestant	Pseudoephedrine	Symptomatic

Inpatient:

Drug	Dose	Note

IV antibiotics

If complicated

Icu:

Drug	Dose	Note
Surgical drainage	If abscess	

Targeted:

Antibiotics if bacterial

Supportive:

- Decongestants
- Steam inhalation

Prevention:

- Allergy treatment

Otitis Media

Pathogen: Bacterium - Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis (Mixed)

Epidemiology:

- Incidence: Common in childhood, 80% experience by age 3
- Seasonality: Winter
- Transmission: Complication of upper respiratory infection
- Risk Groups: Infants, Children, Passive smoking

Pathomechanism:**Steps:**

- Eustachian tube obstruction (adenoid hyperplasia, rhinitis)
- Bacterial ascent
- Purulent inflammation in the middle ear
- Possible eardrum perforation

Virulence Factors:

- Biofilm
- Toxins

Clinical Features:

- Incubation: After upper respiratory infection
- Onset: Sudden

Symptoms:

- **Ear pain:** Severe, children cry
- **Fever:** Common
- **Hearing loss:** Temporary

- **Rhinorrhea:** Associated

Physical Exam:

- Eardrum hyperemia, bulging
- Discharge if perforated
- Tympanocentesis if needed

Complications:

- Mastoiditis
- Meningitis
- Labyrinthitis

Diagnostics:

Imaging:

- **Otoscopy:** Eardrum examination (*Diagnostic*)

Differential Diagnosis:

- **Otitis externa:** Pinna is affected
- **Pharyngitis:** No ear pain

Therapy:

Outpatient:

Drug	Dose	Note
Amoxicillin	3x40mg/kg PO	First choice
Cefuroxime	2x250mg PO	Alternative

Inpatient:

Drug	Dose	Note
IV antibiotics	If complicated	

Icu:

Drug	Dose	Note
Surgical drainage	If abscess	

Targeted:

Antibiotics

Supportive:

- Analgesics
- Decongestants

Prevention:

- Vaccines (Pneumococcus, Hib)

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