

# Infectious Diseases Textbook

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**Version:** 2.8.0 | **Date:** 2026. 02. 08.

## 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), Patients with chronic diseases (COPD, heart failure, diabetes), Immunocompromised, Asplenic patients, Patients with alcohol use disorder, Smokers

#### Pathomechanism:

##### Steps:

- The infection usually begins with microaspiration of bacteria colonizing the upper airways. The pathogen's virulence factors (e.g., capsule) help evade host defense mechanisms (e.g., phagocytosis).
- The bacteria multiply in the alveoli, triggering a vigorous inflammatory response. Released toxins (e.g., pneumolysin) damage epithelial cells.
- Inflammatory cells (neutrophils), red blood cells, and fibrin fill the alveoli, leading to the consolidation of lung tissue. This process is responsible for the characteristic picture of lobar pneumonia.

##### Virulence Factors:

- Capsular polysaccharide (93 serotypes)
- Pneumolysin
- Autolysin (LytA)
- Neuraminidase
- IgA1 protease

##### Clinical Features:

- Incubation: 1-3 days
- Onset: Sudden, dramatic onset

##### Symptoms:

- **Sudden Onset:** Characterized by high fever, chills, and malaise.

- **Respiratory Symptoms:** Initially a dry cough, which later becomes productive, classically with rust-colored sputum. Pleuritic, sharp chest pain and shortness of breath are common.
- **Atypical Presentation:** In the elderly, fever may be absent, and altered mental status can be the leading symptom.

#### 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
<b>Amoxicillin</b>	3x500mg-1g PO	First choice (NICE). 5-day course is usually sufficient.
<b>Doxycycline</b>	200mg stat, then 1x100mg PO	For penicillin allergy.
<b>Clarithromycin</b>	2x500mg PO	Alternative.

#### CAP - Inpatient (Moderate - CURB-65 2):

Drug	Dose	Note
<b>Amoxicillin + Clarithromycin</b>	3x500mg-1g PO/IV + 2x500mg PO/IV	Atypical coverage may be needed. (NICE)
<b>Doxycycline</b>	200mg stat, then 1x100mg PO	Monotherapy for penicillin allergy.
<b>Levofloxacin</b>	1x500mg PO/IV	Alternative (NICE: respiratory fluoroquinolone).

#### CAP - Severe (CURB-65 3-5) / ICU:

Drug	Dose	Note
<b>Co-amoxiclav + Clarithromycin</b>	1.2g IV q8h + 500mg IV q12h	NICE recommendation for severe CAP.
<b>Ceftriaxone + Clarithromycin</b>	1x2g IV + 2x500mg IV	Common alternative (not NICE first-line, but widespread).
<b>Levofloxacin</b>	1x500mg IV	For beta-lactam allergy.

#### HAP - Not severe / Early:

Drug	Dose	Note
<b>Co-amoxiclav</b>	625mg PO TID or 1.2g IV TID	First choice (NICE NG191).
<b>Doxycycline</b>	100mg PO	Alternative.

#### HAP - Severe / VAP / High risk:

Drug	Dose	Note

<b>Antipseudomonal beta-lactam</b>	e.g., Piperacillin/tazobactam, Cefepime, Meropenem	1st component (Gram-negative coverage).
<b>+ Antipseudomonal fluoroquinolone or aminoglycoside</b>	e.g., Ciprofloxacin, Amikacin	2nd component (double G- coverage if needed).
<b>+ MRSA coverage</b>	Vancomycin or Linezolid	3rd component (if MRSA risk >10-20%).

**Targeted:**

Penicillin-sensitive: Penicillin G 4x4 million IU IV; Resistant: Ceftriaxone or Vancomycin

**Supportive:**

- O<sub>2</sub> therapy (SpO<sub>2</sub> >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: People living with HIV (20-30x risk), Patients with diabetes, Immunocompromised, Socially disadvantaged, Healthcare workers, Immigrants from endemic areas

**Pathomechanism:****Steps:**

- Infection occurs by inhaling aerosol droplets containing the pathogen. The bacteria are phagocytosed by alveolar macrophages but survive and multiply within them.
- A primary lesion (Ghon focus) develops at the site of infection, and the bacteria spread to regional lymph nodes, forming the primary complex.
- The cellular immune response (T-cells) is activated, leading to granuloma formation. These granulomas encapsulate the bacteria, establishing a latent infection (LTBI) in 90% of cases.

- In case of immunosuppression, the bacteria can reactivate. The center of the granuloma undergoes caseous necrosis, which can liquefy and form a cavity, leading to an open, infectious form of the disease.

### 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:

- Respiratory Symptoms:** Chronic cough lasting more than 3 weeks, which may initially be dry and later become productive. Bloody sputum (hemoptysis) may appear later.
- Constitutional (B) Symptoms:** Insidious onset with prolonged symptoms: low-grade fever (especially in the afternoon), profuse night sweats, and significant unintentional weight loss.
- Other:** Fatigue, loss of appetite, chest pain.

### 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
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**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, Immunocompromised, Chronic kidney disease, Diabetes

#### **Pathomechanism:**

#### Steps:

- Infection occurs by inhaling aerosols (e.g., from showers, cooling towers, air conditioners) containing the bacteria.
- Once in the lungs, Legionella enters alveolar macrophages, where a special secretion system (Dot/Icm) prevents the fusion of phagosomes and lysosomes.
- The bacteria replicate within a protected vacuole inside the macrophage, then lyse the cell to infect new ones.
- This process triggers a severe, necrotizing pneumonia and a strong inflammatory response.

#### 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:

- **Atypical Pneumonia:** High fever, chills, and an initially dry, non-productive cough.

- **Extrapulmonary Symptoms:** Multisystem involvement is characteristic: gastrointestinal (diarrhea, nausea) and neurological (headache, confusion, delirium).
- **Characteristic Signs:** Relative bradycardia (low pulse rate despite high fever) and hyponatremia in lab tests are common.

### 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 ( $>60^{\circ}\text{C}$ )
- 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-age children, Young adults, Closed communities (dorms, barracks)

### **Pathomechanism:**

#### Steps:

- The pathogen adheres tightly to the cilia of respiratory epithelial cells using its P1 adhesin.
- Hydrogen peroxide and the CARDs toxin produced by the bacterium damage the cilia (ciliostasis), leading to impaired mucociliary clearance.
- The inflammatory response and cellular damage cause the prolonged cough and pneumonia.

#### Virulence Factors:

- P1 adhesin
- CARDs toxin
- Hydrogen peroxide

#### **Clinical Features:**

- Incubation: 2-3 weeks
- Onset: Slow, gradual

#### Symptoms:

- **Atypical Pneumonia:** Gradual onset with low-grade fever, headache, and malaise. The leading symptom is a dry, hacking, paroxysmal cough that lasts for weeks.
- **"Walking Pneumonia":** Physical findings (sparse auscultation) are often much milder than the extensive inflammation seen on the chest X-ray.
- **Extrapulmonary Symptoms:** Rashes (e.g., erythema multiforme), hemolytic anemia (cold agglutinin disease), or neurological complications can occur.

#### 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
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**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
<b>Azithromycin</b>	500mg D1, then 250mg D2-5	First choice
<b>Doxycycline</b>	2x100mg	Alternative (>8 years)
<b>Clarithromycin</b>	2x500mg	Alternative

**Inpatient:**

Drug	Dose	Note
<b>Levofloxacin</b>	1x500-750mg IV/PO	In severe cases
<b>Moxifloxacin</b>	1x400mg IV/PO	Alternative

**Icu:**

Drug	Dose	Note
<b>Macrolide + Beta-lactam</b>	Combination	To cover mixed infection

**Targeted:**

Macrolides (resistance increasing!), Tetracyclines, Fluoroquinolones

**Supportive:**

- Cough suppressants
- Antipyretics

**Prevention:**

- Droplet precautions
- No vaccine

## **Chlamydia pneumoniae**

**Pathogen:** Bacterium - *Chlamydia pneumoniae* (Gram-negative (intracellular))

### **Epidemiology:**

- Incidence: 5-10% of CAP
- Seasonality: Year-round
- Transmission: Droplet infection
- Risk Groups: Elderly, Patients with chronic diseases, Closed communities

### **Pathomechanism:**

#### Steps:

- Infection begins with the inhalation of infectious elementary bodies (EBs). Inside the cell, EBs transform into reticulate bodies (RBs), the replicating form.
- After replication, RBs convert back to EBs, the cell lyses, and the new elementary bodies infect more cells.
- This cycle leads to damage of the respiratory epithelium and inflammation.

#### Virulence Factors:

- Intracellular survival
- Endotoxin-like substances

### **Clinical Features:**

- Incubation: 3-4 weeks
- Onset: Gradual

#### Symptoms:

- **Biphasic Course:** Often occurs in two phases: initially pharyngitis and laryngitis (hoarseness is characteristic), followed 1-3 weeks later by the development of atypical pneumonia.
- **Prolonged Cough:** The most characteristic feature of the pneumonia is a dry, irritative cough that persists for weeks to months.

#### Physical Exam:

- Pharyngitis
- Rales
- Signs of sinusitis

#### Complications:

- Reactive arthritis
- Myocarditis
- Atherosclerosis (association)

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation

CBC	Normal	Non-specific
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**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
<b>Doxycycline</b>	2x100mg	First choice
<b>Azithromycin</b>	500mg D1, 250mg D2-5	Alternative

**Inpatient:**

Drug	Dose	Note
<b>Levofloxacin</b>	1x750mg	In more severe cases

**Icu:**

Drug	Dose	Note
<b>Levofloxacin</b>	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:

- Infection occurs by inhaling dust contaminated with the dried droppings of birds (especially parrots, pigeons).
- The pathogen spreads from the lungs to the reticuloendothelial system (liver, spleen), where it multiplies.
- During a secondary viremia, the bacteria return to the lungs, causing an atypical, interstitial pneumonia.

#### Virulence Factors:

- Intracellular survival

#### **Clinical Features:**

- Incubation: 5-14 days
- Onset: Sudden

#### Symptoms:

- **Typhoid-like Symptoms:** Sudden onset of high fever, chills, and a severe, debilitating headache.
- **Respiratory Symptoms:** A dry, non-productive cough. Physical findings are often sparse compared to the chest X-ray.
- **Systemic Signs:** Hepatosplenomegaly and relative bradycardia (Faget's sign) are common.

#### Physical Exam:

- Relative bradycardia (Faget's sign)
- Splenomegaly (10-70%)
- Horder 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
<b>Doxycycline</b>	2x100mg	First choice

**Inpatient:**

Drug	Dose	Note
<b>Doxycycline</b>	2x100mg IV	In severe cases

**Icu:**

Drug	Dose	Note
<b>Doxycycline</b>	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:**

- Infection occurs by inhaling highly infectious aerosols from animal birth products (placenta, amniotic fluid).
- The pathogen enters alveolar macrophages, where it not only survives but also replicates within acidic phagosomes.
- It spreads via the bloodstream to the liver and bone marrow.
- The body attempts to contain the infection by forming characteristic "doughnut-shaped" granulomas.
- The disease can be acute or chronic (mainly manifesting as endocarditis).

**Virulence Factors:**

- Spore-like form (resistant)
- LPS phase variation

**Clinical Features:**

- Incubation: 2-3 weeks
- Onset: Sudden

**Symptoms:**

- **Acute Q Fever:** Presents with a sudden onset of high fever, severe retro-orbital headache, and flu-like symptoms. Atypical pneumonia (mild cough) and granulomatous hepatitis (elevated liver enzymes) are common.
- **Chronic Q Fever:** Develops months to years later, mainly in patients with pre-existing heart valve defects or immunosuppression. The most common manifestation is culture-negative endocarditis.

**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
<b>Doxycycline</b>	2x100mg	Acute Q fever

**Inpatient:**

Drug	Dose	Note
<b>Doxycycline</b>	2x100mg	

**Icu:**

Drug	Dose	Note
<b>Doxycycline + Hydroxychloroquine</b>	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, Patients with chronic diseases, Healthcare workers, Immunocompromised

### **Pathomechanism:**

#### Steps:

- The virus uses its hemagglutinin (HA) to bind to respiratory epithelial cells and enter them.
- It replicates within the cell and then uses neuraminidase (NA) to be released and infect new cells.
- The viral infection leads to the destruction of respiratory epithelial cells and damage to the cilia, impairing airway clearance.
- The body's strong immune response (cytokine storm) causes systemic symptoms like fever and muscle pain.

#### Virulence Factors:

- Hemagglutinin (H1-H18)
- Neuraminidase (N1-N11)
- NS1 protein (IFN antagonist)
- PB1-F2 (pro-apoptotic)

#### **Clinical Features:**

- Incubation: 1-4 days (average 2 days)
- Onset: Sudden

#### Symptoms:

- **Sudden Onset:** Begins with a high fever (>38°C), chills, severe headache, and muscle pain (myalgia).
- **Respiratory Symptoms:** A dry, hacking cough and sore throat are characteristic.
- **Constitutional Symptoms:** Marked weakness, malaise (prostration), and loss of appetite.

#### 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
<b>Oseltamivir</b>	2x75mg PO	Within 48 hours of symptom onset!
<b>Baloxavir</b>	1x40-80mg PO	>80kg: 80mg

**Inpatient:**

Drug	Dose	Note
<b>Oseltamivir</b>	2x75mg PO/NG	Longer in severe cases
<b>Peramivir</b>	1x600mg IV	If PO not tolerated

**Icu:**

Drug	Dose	Note
<b>Oseltamivir</b>	2x150mg PO/NG	Higher dose may be considered
<b>+ Empiric AB</b>	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), Patients with obesity (BMI>30), Diabetes, Cardiovascular disease, Immunocompromised, Chronic lung disease

#### **Pathomechanism:**

##### Steps:

- The virus uses its Spike (S) protein to bind to the ACE2 receptor on the surface of cells, which is found in many organs (lungs, heart, vessels, gut).
- After entry, the virus replicates within the cell (viral phase).
- In severe cases, an excessive immune response, the so-called cytokine storm, can develop in the second week of the disease.
- This hyperinflammation leads to systemic endothelial damage, microthrombosis, and, in the lungs, acute respiratory distress syndrome (ARDS), which is the basis of the severe course.

#### 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:

- **Common Symptoms:** Fever, dry cough, fatigue, and muscle pain (myalgia).

- **Characteristic Symptoms:** Loss of smell and taste (anosmia, dysgeusia) can be an early, specific sign.
- **Severe Symptoms:** Shortness of breath (dyspnea), chest pain, and hypoxemia (low blood oxygen), which can lead to ARDS.

### Physical Exam:

- Fever, tachypnea
- Decreased SpO<sub>2</sub> (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
<b>Paxlovid (nirmatrelvir/ritonavir)</b>	2x300/100mg PO	Early, high-risk, interactions!
<b>Molnupiravir</b>	2x800mg PO	Alternative if Paxlovid is contraindicated

#### Inpatient:

Drug	Dose	Note
<b>Remdesivir</b>	200mg IV D1, then 100mg/day	If O2 is needed
<b>Dexamethasone</b>	6mg/day IV/PO	Only with O2 need/ventilation!

#### Icu:

Drug	Dose	Note
<b>Dexamethasone</b>	6-20mg/day	Cytokine storm
<b>Tocilizumab</b>	8mg/kg IV single dose	IL-6 inhibitor, rapidly deteriorating
<b>LMWH</b>	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*, *Viridans group streptococci* (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, People who inject drugs (PWID), Congenital heart disease, Previous endocarditis

### Pathomechanism:

#### Steps:

- The process begins with injury to the heart valve endothelium, to which a sterile thrombus (nonbacterial thrombotic endocarditis, NBTE) adheres.
- During a transient bacteremia (e.g., dental procedure), circulating pathogens adhere to this damaged surface.
- The bacteria multiply, form a biofilm, and create a vegetation composed of bacteria, fibrin, and platelets.
- This vegetation damages the valve (causing insufficiency), and fragments can break off, causing septic emboli to various parts of the body (e.g., brain, spleen).

#### Virulence Factors:

- Adhesins (MSCRAMM)
- Biofilm formation
- Toxins

#### **Clinical Features:**

- Incubation: Days (acute) or weeks (subacute)
- Onset: Variable

#### Symptoms:

- **General Symptoms:** The most common are fever, chills, night sweats, and weight loss. The presentation is often that of a fever of unknown origin (FYO).
- **Cardiac Symptoms:** Appearance of a new or changed heart murmur, or symptoms of heart failure (shortness of breath, edema) due to valve damage.
- **Embolic Phenomena:** Fragments breaking off from the vegetation can cause septic emboli: stroke, splenic or renal infarction, skin manifestations (Janeway lesions, splinter hemorrhages).

#### 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
<b>Ampicillin + (Flu)cloxacillin + Gentamicin</b>	12g + 12g + 3mg/kg IV	IB recommendation. Gentamicin only for the first few days/until pathogen is known.
<b>Vancomycin + Gentamicin</b>	30-60mg/kg + 3mg/kg IV	IB recommendation. For penicillin allergy.
<b>Daptomycin + Gentamicin</b>	10mg/kg + 3mg/kg IV	IB recommendation. Alternative.

**Empiric: Early prosthetic valve (<12 mo) or Nosocomial:**

Drug	Dose	Note
<b>Vancomycin + Gentamicin + Rifampicin</b>	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
<b>MSSA: (Flu)cloxacillin</b>	12g/day IV	IB recommendation. Penicillin allergy (non-anaphylactic): Cefazolin 6g/day (IB).
<b>MRSA: Vancomycin</b>	30-60mg/kg/day IV	IB recommendation. Alternative: Daptomycin 10mg/kg (IB).
<b>Prosthetic valve (PVE): + Rifampicin + Gentamicin</b>	Adjunct	IB recommendation. Rifampicin 900-1200mg, Gentamicin 3mg/kg.

**Targeted: *Streptococcus* spp. (Oral/Bowel):**

Drug	Dose	Note
<b>Penicillin G or Amoxicillin or Ceftriaxone</b>	Standard high dose	IB recommendation. Penicillin-sensitive strains.
<b>Combination with Gentamicin</b>	Beta-lactam + 3mg/kg Gentamicin	IB recommendation. Can shorten course only for native valve, uncomplicated cases.
<b>Penicillin allergy: Vancomycin</b>	30mg/kg/day IV	IB recommendation.

**Targeted: *Enterococcus* spp.:**

Drug	Dose	Note
<b>Amoxicillin + Ceftriaxone</b>	200mg/kg + 4g/day IV	IB recommendation. Preferred for <i>E. faecalis</i> (less nephrotoxicity than with gentamicin).
<b>Ampicillin + Gentamicin</b>	12g + 3mg/kg IV	IB recommendation. Traditional therapy.
<b>Vancomycin + Gentamicin</b>	30mg/kg + 3mg/kg IV	IB recommendation. For beta-lactam resistance/allergy.

**Culture-negative IE:**

Drug	Dose	Note
<b>Coxiella burnetii</b>	Doxycycline + Hydroxychloroquine	IB recommendation. Q fever endocarditis.
<b>Bartonella spp.</b>	Doxycycline + Gentamicin (2 weeks)	IB recommendation.
<b>Brucella spp.</b>	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, Immunocompromised

### **Pathomechanism:**

#### Steps:

- The infection begins with a viral infection, during which the virus can directly damage heart muscle cells.
- The later, more severe phase of the disease is caused by the body's excessive immune response. T-cells and autoantibodies attack the heart muscle cells (molecular mimicry), resulting in extensive inflammation, necrosis, and myocardial dysfunction.
- During healing, scarring (fibrosis) can develop, leading to dilated cardiomyopathy (DCM) and chronic heart failure.

#### 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:

- **Viral Prodrome:** Cardiac symptoms are often preceded by a febrile, respiratory, or gastrointestinal infection a few days earlier.

- **Heart Failure Symptoms:** Fatigue, shortness of breath on exertion, then at rest, and edema.
- **Chest Pain and Arrhythmia:** Atypical, sharp chest pain (myopericarditis) and palpitations (due to arrhythmias) are common.

### 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

<b>Physical rest</b>	No sports	Crucial! (ESC 2023)
<b>NSAID (e.g., Ibuprofen)</b>	Symptomatic	Only for chest pain if EF is preserved!

**Inpatient:**

Drug	Dose	Note
<b>Heart failure therapy (GDMT)</b>	ACEi/ARB/ARNI + BB + MRA + SGLT2i	If LVEF is reduced (ESC 2023)
<b>Antiarrhythmic drugs</b>	Amiodarone	In case of severe arrhythmia

**Icu:**

Drug	Dose	Note
<b>Mechanical circulatory support (MCS)</b>	VA-ECMO, Impella	In fulminant myocarditis / cardiogenic shock
<b>High-dose steroids</b>	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 patients, Autoimmune patients

**Pathomechanism:****Steps:**

- Inflammation of the pericardial layers, most commonly as a result of a viral infection.

- Due to inflammation, fibrin is deposited between the layers, causing the characteristic friction rub (dry pericarditis).
- Fluid can also accumulate (pericardial effusion), which, if it accumulates rapidly or in large amounts, can compress the heart and cause cardiac tamponade.

### Virulence Factors:

- -

### **Clinical Features:**

- Incubation: Variable
- Onset: Sudden

### Symptoms:

- **Characteristic Chest Pain:** Sharp, stabbing chest pain that worsens with inspiration and lying down, and improves when leaning forward.
- **Other Symptoms:** Often accompanied by low-grade fever, malaise, and shortness of breath.

### 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
<b>Aspirin</b>	750-1000mg every 8 hours	First choice (ESC 2015)
<b>Ibuprofen</b>	600mg every 8 hours	Alternative
+ <b>Colchicine</b>	0.5mg once daily (<70kg) or twice (>70kg)	For prevention of recurrence (ESC 2015)!
<b>PPI</b>	Standard	Gastric protection

#### Inpatient:

Drug	Dose	Note
<b>None</b>	-	Only for high-risk cases (fever >38, subacute, large effusion, tamponade, anticoagulated patient)

#### Icu:

Drug	Dose	Note
<b>Pericardiocentesis</b>	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, Immunocompromised

### Pathomechanism:

#### Steps:

- Viruses enter through the mucous membranes of the upper respiratory tract, where they replicate in epithelial cells.
- The infection triggers local inflammation, edema, and increased mucus production.
- This causes the characteristic symptoms: rhinorrhea, nasal congestion, and sore throat.

#### Virulence Factors:

- Receptor binding (ICAM-1 for rhinovirus)
- Immunomodulation

#### **Clinical Features:**

- Incubation: 1-3 days
- Onset: Sudden

#### Symptoms:

- **Typical Symptoms:** Typically presents with rhinorrhea, nasal congestion, sneezing, sore throat, and a dry cough. Fever is usually mild or absent. Symptoms generally resolve on their own within 7-10 days.

#### 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
<b>Supportive</b>	-	Rest, fluids, symptomatic treatment
<b>Decongestant</b>	Oxymetazoline nasal	Not for longer!
<b>Antihistamine</b>	Loratadine	If allergy is suspected

#### Inpatient:

Drug	Dose	Note
<b>Not needed</b>	-	Rare

#### Icu:

Drug	Dose	Note
<b>Not needed</b>	-	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), Patients with chronic lung disease, Immunocompromised

### **Pathomechanism:**

#### Steps:

- The virus infects respiratory epithelial cells and, using its fusion (F) protein, causes the cells to merge, forming so-called syncytia.
- This process leads to epithelial cell destruction, ciliary damage, and increased mucus production.
- In infants, the small airways (bronchioles) become narrowed due to mucus and edema, creating the characteristic picture of bronchiolitis (wheezing, shortness of breath).

#### Virulence Factors:

- Fusion protein (F)
- G glycoprotein (adherence)

#### **Clinical Features:**

- Incubation: 4-6 days
- Onset: Gradual

#### Symptoms:

- **Initial Symptoms:** Begins with mild, upper respiratory symptoms (rhinorrhea, low-grade fever).
- **Bronchiolitis (Infants):** The most severe form in infants. Characterized by shortness of breath, wheezing, tachypnea, and intercostal retractions. In severe cases, apnea and respiratory failure can occur.

#### Physical Exam:

- Tachypnea, retractions
- Wheezing, crepitant
- 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
<b>Supportive</b>	-	Oxygen, hydration
<b>Bronchodilator</b>	Salbutamol	If wheezing

**Inpatient:**

Drug	Dose	Note
<b>Ribavirin</b>	Aerosol	In severe cases, immunocompromised

**Icu:**

Drug	Dose	Note
<b>Ventilation</b>	NIV or intubation	In case of apnea

**Targeted:**

Palivizumab prophylaxis for high-risk infants

**Supportive:**

- Oxygen
- Hydration
- Physiotherapy

**Prevention:**

- Hand hygiene
- Isolation
- Passive immunization: Nirsevimab, Clesrovimab (long-acting), Palivizumab
- Vaccination: Elderly (>60 years) and pregnant women (maternal)

**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:

- Bacteria colonize the pharyngeal mucosa, triggering a strong local inflammatory response.
- This causes swelling and redness of the tonsils and the formation of purulent exudate (follicles).
- Bacterial toxins (e.g., streptolysin) are responsible for systemic symptoms like fever, and erythrogenic toxin for the rash in scarlet fever.

#### Virulence Factors:

- M protein
- Streptolysins
- Hyaluronidase

#### **Clinical Features:**

- Incubation: 2-5 days
- Onset: Sudden

#### Symptoms:

- **Local Symptoms:** Sudden onset of severe sore throat and difficulty swallowing. The tonsils are swollen, red, and often covered with a white, purulent exudate (follicles).
- **Systemic Symptoms:** Accompanied by high fever, chills, headache, and painful swelling of the cervical lymph nodes.

#### 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:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Penicillin V</b>	4x500mg PO	First choice
<b>Amoxicillin</b>	3x500mg PO	Alternative

**Inpatient:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Penicillin G</b>	4x4 million IU IV	In severe cases

**Icu:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Surgical drainage</b>	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: Patients with allergies, Smokers, Immunocompromised

**Pathomechanism:****Steps:**

- Following a viral upper respiratory infection (common cold), the nasal and sinus mucosa become swollen.
- The edema blocks the sinus ostia (openings), leading to mucus retention.

- The stagnant mucus provides an ideal breeding ground for bacterial superinfection, resulting in purulent inflammation.

### Virulence Factors:

- Biofilm formation

### **Clinical Features:**

- Incubation: After upper respiratory infection
- Onset: Gradual

### Symptoms:

- **Characteristic Symptoms:** Facial pain or pressure that worsens when bending forward. It is accompanied by nasal congestion, purulent nasal discharge, and often a headache.
- **Signs of Bacterial Superinfection:** Symptoms lasting more than 10 days, worsening symptoms ("double sickening"), or high fever ( $>38^{\circ}\text{C}$ ) and unilateral facial pain suggest a bacterial origin.

### 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
<b>Amoxicillin/Clavulanate</b>	2x875/125mg PO	If bacterial is suspected
<b>Decongestant</b>	Pseudoephedrine	Symptomatic

#### **Inpatient:**

Drug	Dose	Note
<b>IV antibiotics</b>	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, Exposure to 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:**

- **Main Symptoms:** Sudden onset of severe, throbbing ear pain, fever, and hearing loss.
- **Signs in Infants:** In infants, irritability, inconsolable crying, poor feeding, and pulling at the ear are characteristic.

**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
<b>Amoxicillin</b>	3x40mg/kg PO	First choice
<b>Cefuroxime</b>	2x250mg PO	Alternative

**Inpatient:**

Drug	Dose	Note
<b>IV antibiotics</b>	If complicated	

**Icu:**

Drug	Dose	Note
<b>Surgical drainage</b>	If abscess	

**Targeted:**

Antibiotics

**Supportive:**

- Analgesics
- Decongestants

**Prevention:**

- Vaccines (Pneumococcus, Hib)

 **Gastrointestinal Infections**

## Differential Diagnosis of Gastrointestinal Infections

**Epidemiology:**

**Pathomechanism:**

**Clinical Features:**

**Diagnostics:**

**Therapy:**

### 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 treatment disrupts the normal gut flora, allowing *C. difficile* spores to germinate and multiply.
- The bacterium produces toxins: Toxin A (enterotoxin) causes fluid secretion and inflammation, while Toxin B (cytotoxin) directly damages intestinal epithelial cells.
- Severe inflammation and cell death lead to the formation of characteristic pseudomembranes on the colonic mucosa.

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:** Frequent (3-15x/day), characteristically greenish, foul-smelling, watery diarrhea.
- **Abdominal Pain:** Diffuse, crampy abdominal pain and tenderness.

- **Fever:** Often accompanied by fever and leukocytosis.

### 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
- **Medication-induced diarrhea (e.g., laxatives, PPIs):** Medication history, resolution after stopping

**Therapy:****Outpatient:**

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

**Inpatient:**

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

**Icu:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Vancomycin</b>	4x500mg PO + rectal	Fulminant: higher dose
<b>+ Metronidazole</b>	3x500mg IV	In case of ileus (IV penetration)
<b>Surgery</b>	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:

- After ingestion (high bacterial load required), the pathogens survive gastric acid and reach the small intestine.
- In the small intestine, they enter Peyer's patches and deeper layers of the intestinal wall via M-cells.
- Bacterial multiplication triggers a strong inflammatory response, leading to neutrophil infiltration and fluid secretion.

#### Virulence Factors:

- Type III secretion system (T3SS)
- Enterotoxin

#### **Clinical Features:**

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

#### Symptoms:

- **Diarrhea:** Sudden onset of profuse, watery, sometimes mucoid or bloody diarrhea.
- **Fever:** May be accompanied by high fever, chills, headache, and myalgia.
- **Abdominal Cramps:** Periumbilical or diffuse abdominal cramps.

#### 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*)

#### **Differential Diagnosis:**

- **Campylobacteriosis:** Culture, similar clinical picture

- **Shigellosis:** Bloody-mucoid stool more common
- **Viral gastroenteritis:** Vomiting dominates, watery diarrhea
- **IBD (Crohn's/Colitis):** Chronic, non-infectious, endoscopy

**Therapy:****Outpatient:**

Drug	Dose	Note
<b>Supportive</b>	-	Healthy adults do NOT need antibiotics (may prolong carriage!)

**Inpatient:**

Drug	Dose	Note
<b>Ceftriaxone</b>	1-2g IV	In severe/invasive cases
<b>Ciprofloxacin</b>	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:**

- Bacteria invade colonic epithelial cells and spread from cell to cell, evading the immune system.
- Bacterial multiplication and produced toxins (e.g., Shiga toxin) cause mucosal necrosis, ulceration, and bleeding.
- Shiga toxin entering the bloodstream can damage renal endothelial cells, causing Hemolytic Uremic Syndrome (HUS).

**Virulence Factors:**

- Shiga toxin (Stx)
- Invasion plasmid antigens

**Clinical Features:**

- Incubation: 1-3 days
- Onset: Sudden

**Symptoms:**

- **Dysentery:** Frequent, small-volume, bloody-mucoid-purulent stools.
- **Tenesmus:** Painful, ineffective urge to defecate.
- **Fever:** Characterized by high fever and a toxic state.

**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*)

**Differential Diagnosis:**

- **EIEC (E. coli):** Clinically identical, microbiology decides
- **Amoebiasis:** *E. histolytica* detection, less febrile
- **Campylobacteriosis:** Culture
- **C. difficile:** Antibiotic history, toxin test

**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:

- Bacteria colonize and invade the mucosa of the small and large intestines.
- They produce toxins (e.g., CDT) that inhibit cell division and trigger inflammation.
- The infection can trigger Guillain-Barré syndrome via an autoimmune mechanism.

#### Virulence Factors:

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

#### **Clinical Features:**

- Incubation: 2-5 days
- Onset: Sudden

#### Symptoms:

- **Diarrhea:** Profuse, watery, often bloody diarrhea.
- **Abdominal Pain:** Severe, crampy abdominal pain that can mimic appendicitis (pseudoappendicitis).
- **Fever:** Diarrhea is often preceded by fever, headache, and myalgia.

#### 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*)

**Differential Diagnosis:**

- **Salmonellosis:** Culture, epidemiology
- **Shigellosis:** More severe dysentery, culture
- **Appendicitis:** US/CT, surgical consultation

**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, EPEC, EIEC)**

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

**Epidemiology:**

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

**Pathomechanism:****Steps:**

- ETEC: Bacteria adhere in the small intestine and produce enterotoxins, causing massive fluid secretion.
- EHEC: Produce Shiga toxin in the large intestine, causing bloody diarrhea and potentially renal failure (HUS) upon systemic absorption.
- EPEC/EIEC: Adhere to or invade intestinal epithelial cells, causing mucosal damage and inflammation.

### Virulence Factors:

- Enterotoxins
- Shiga-toxin (Stx1, Stx2)
- Adhesins (EPEC)
- Invasins (EIEC)

### **Clinical Features:**

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

### Symptoms:

- **Watery Diarrhea (ETEC/EPEC):** Sudden onset of profuse watery diarrhea, without fever (traveler's diarrhea).
- **Bloody Diarrhea (EHEC/EIEC):** Bloody stools with severe abdominal cramps, often afebrile (EHEC) or with fever (EIEC).

### Physical Exam:

- Dehydration
- Abdominal tenderness (EHEC/EIEC: marked)
- Fever (common in EIEC, rare in EHEC)

### Complications:

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

### **Diagnostics:**

#### Laboratory:

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

#### Microbiology:

- **Stool culture:** Sorbitol-MacConkey (EHEC) (*EHEC screening*)
- **Shiga-toxin detection:** PCR or EIA (*EHEC diagnosis*)
- **PCR panel:** Virulence genes (*Differentiation of EPEC/EIEC/ETEC*)

### **Differential Diagnosis:**

- **Shigellosis:** EIEC clinically identical, culture decides

- **Campylobacteriosis:** Culture, GBS risk
- **TTP:** Adults, neurological symptoms, ADAMTS13

**Therapy:****Outpatient:**

Drug	Dose	Note
<b>ETEC: Rifaximin</b>	2x200mg PO	Traveler's diarrhea
<b>EHEC: ANTIBIOTICS CONTRAINDICATED!</b>	-	Increases risk of HUS (toxin release)!
<b>EIEC: Ciprofloxacin/Azithromycin</b>	Standard dose	Severe cases (like Shigella)

**Targeted:**

ETEC/EIEC: Ciprofloxacin or Azithromycin (in severe cases). EHEC: ONLY supportive! EPEC: 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:**

- Bacteria enter Peyer's patches and mesenteric lymph nodes via M-cells in the ileum.
- They cause inflammation and microabscesses in the lymph nodes (mesenteric lymphadenitis).
- The infection can trigger reactive arthritis via immunological mechanisms.

**Virulence Factors:**

- *Yersinia* outer proteins (Yops)
- T3SS

- Invasin

### **Clinical Features:**

- Incubation: 4-7 days
- Onset: Gradual

### **Symptoms:**

- **Enterocolitis:** Fever, diarrhea (possibly bloody), vomiting.
- **Pseudoappendicitis:** Right lower quadrant pain and tenderness mimicking appendicitis.

### **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*)

### **Differential Diagnosis:**

- **Appendicitis:** US/CT, surgical consultation
- **Crohn's disease:** Chronic, endoscopy, biopsy
- **Other bacterial enteritis:** Culture

### **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:**

- Trophozoites are released from ingested cysts in the duodenum.
- Parasites attach to the villi of the small intestine with their sucking discs but do not invade tissues.
- Damage to intestinal villi and deficiency of disaccharidase enzymes cause malabsorption and osmotic diarrhea.

**Clinical Features:**

- Incubation: 1-3 weeks
- Onset: Gradual

**Symptoms:**

- **Diarrhea:** Prolonged, foul-smelling, greasy, non-bloody diarrhea.
- **Bloating:** Marked gas production, abdominal bloating, sulfurous burping.
- **Weight Loss:** Significant weight loss may occur due to malabsorption.

**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*)

**Differential Diagnosis:**

- **Lactose intolerance:** Breath test, effect of diet
- **IBS:** Chronic, negative parasite test
- **Cryptosporidiosis:** Acid-fast stain, immunosuppression

**Therapy:****Outpatient:**

Drug	Dose	Note
<b>Metronidazole</b>	3x250mg PO	First choice
<b>Tinidazole</b>	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:**

- Trophozoites develop from ingested cysts in the large intestine and invade the mucosa.
- Parasites produce tissue-dissolving enzymes, creating characteristic flask-shaped ulcers.
- Entering the bloodstream, parasites can reach the liver and form abscesses.

**Clinical Features:**

- Incubation: 2-4 weeks
- Onset: Gradual

Symptoms:

- **Amoebic Dysentery:** Bloody, mucoid diarrhea with abdominal pain.
- **Amoebic Liver Abscess:** Right upper quadrant pain, fever, weight loss, even without diarrhea.

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)*)

Differential Diagnosis:

- **Bacterial dysentery:** Culture, fever more common
- **Pyogenic liver abscess:** Bacterial culture, more septic
- **Echinococcus cyst:** Serology, imaging (daughter cysts)

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:**

- After ingestion of oocysts, sporozoites attach to the surface of small intestinal epithelial cells (intracellular but extracytoplasmic).
- Infection causes villus atrophy and crypt hyperplasia.
- This leads to severe malabsorption and secretory diarrhea.

**Virulence Factors:**

- Adhesins
- Proteases

**Clinical Features:**

- Incubation: 7-10 days
- Onset: Sudden

**Symptoms:**

- **Watery Diarrhea:** Profuse, watery diarrhea with abdominal cramps.
- **Persistent Diarrhea:** In immunosuppressed patients (e.g., AIDS), diarrhea can become chronic and cause severe fluid loss.

**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/ $\mu$ L	Risk of severe course (HIV)
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**Microbiology:**

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

**Differential Diagnosis:**

- **Giardiasis:** Stool exam, bloating dominates
- **Isosporiasis:** Larger oocysts, TMP-SMX effective
- **Microsporidiosis:** Smaller spores, special stain

**Therapy:****Outpatient:**

Drug	Dose	Note
<b>Nitazoxanide</b>	2x500mg PO	For immunocompetent
<b>ART (Antiretroviral therapy)</b>	-	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:**

- Viruses replicate in the epithelial cells of small intestinal villi, destroying them.
- Shortening of villi reduces the absorptive surface and digestive enzymes.
- Unabsorbed nutrients draw water into the intestinal lumen (osmotic diarrhea).

**Virulence Factors:**

- Capsid stability
- NSP4 (Rota)

**Clinical Features:**

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

**Symptoms:**

- **Vomiting:** Sudden, repeated vomiting (especially with Norovirus).
- **Watery Diarrhea:** Large volume watery stools accompanied by fever and myalgia.

**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*)

**Differential Diagnosis:**

- **Bacterial gastroenteritis:** Fever, bloody stool, culture
- **Food poisoning (toxin):** Shared meal, shorter incubation
- **Drug side effect:** History

**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:

- Bacteria adhering in the small intestine produce cholera toxin.
- The toxin activates adenylate cyclase, leading to increased cAMP levels.
- This causes massive efflux of chloride ions and water into the intestinal lumen, leading to severe, life-threatening diarrhea.

#### 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 diarrhea resembling rice water.
- **Dehydration:** Rapidly developing severe dehydration, muscle cramps, shock.

#### 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*)

#### Differential Diagnosis:

- **ETEC:** Travel, less severe
- **Viral gastroenteritis:** Vomiting may dominate, less severe dehydration

#### Therapy:

##### Outpatient:

Drug	Dose	Note
<b>Doxycycline</b>	300mg PO	For adults
<b>Azithromycin</b>	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:

- Infection is most commonly caused by enterotoxin-producing E. coli (ETEC) or invasive bacteria (Campylobacter, Shigella).
- Pathogens trigger inflammation or fluid secretion in travelers encountering a microbiome different from local hygiene conditions.

#### Virulence Factors:

- Variable

#### **Clinical Features:**

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

#### Symptoms:

- **Diarrhea:** Watery diarrhea with abdominal cramps occurring during or after travel.
- **Fever:** Fever and bloody stool suggest an invasive pathogen.

#### 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*)

#### **Differential Diagnosis:**

- **IBD flare:** History, endoscopy
- **Giardiasis:** Prolonged, greasy stool

#### **Therapy:**

#### **Outpatient:**

Drug	Dose	Note
<b>Azithromycin</b>	1000mg PO once or 500mg for 3 days	Southeast Asia (Campy resistance) or dysentery
<b>Rifaximin</b>	2x200mg PO	In non-invasive (afebrile) cases
<b>Ciprofloxacin</b>	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, Immunosuppressed

**Pathomechanism:****Steps:**

- Pathogens (*Shigella*, *EIEC*, *EHEC*, *Campylobacter*, *Entamoeba*) invade the colonic mucosa.
- Tissue invasion causes severe inflammation, ulceration, bleeding, and mucus production.

**Virulence Factors:**

- Invasins
- Cytotoxins

**Clinical Features:**

- Incubation: Variable
- Onset: Acute

**Symptoms:**

- **Bloody-mucoid Diarrhea:** Frequent, small-volume, bloody-mucoid-purulent stools.
- **Tenesmus:** Painful, ineffective urge to defecate.

**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*)

### **Differential Diagnosis:**

- **Inflammatory bowel disease (IBD):** Chronic history, endoscopy, biopsy
- **Ischemic colitis:** Older age, vascular risk factors, CT

### **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

## Differential Diagnosis of Viral Hepatitis

**Epidemiology:**

**Pathomechanism:**

**Clinical Features:**

**Diagnostics:**

**Therapy:**

## Interpretation of Hepatitis B Serologic Patterns

**Epidemiology:**

**Pathomechanism:**

**Clinical Features:**

**Diagnostics:**

**Therapy:**

## 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: The virus is absorbed from the gut and reaches the liver via the portal circulation.
- Hepatocyte Infection: The virus enters hepatocytes via the HAVCR-1 receptor, replicates in the cytoplasm, but does not cause direct cell death (non-cytopathic).
- Immune Response: Hepatocyte damage is caused by the host's own cellular immune response (CD8+ cytotoxic T-cells and NK cells) killing infected hepatocytes.
- Excretion: The virus is excreted into bile and stool, often before symptoms appear.

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:**

- **Prodrome:** Flu-like symptoms (fever, headache, myalgia), anorexia, aversion to smoking/fatty foods.
- **Icteric Phase:** Dark urine (bilirubinuria), pale stool, followed by jaundice (skin, sclera). Fever often subsides by this time.
- **Abdominal Symptoms:** Dull right upper quadrant pain, hepatomegaly, nausea.

**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 (HBV, HCV, HEV):** Serology (HBsAg, Anti-HCV, Anti-HEV)
- **Toxic/Drug-induced hepatitis:** History (acetaminophen, mushroom), toxicology
- **Biliary obstruction (Choledocholithiasis):** Abdominal US (dilated ducts), ALP/GGT dominance, colic
- **EBV/CMV mononucleosis:** Sore throat, lymphadenopathy, monospot/serology
- **Autoimmune hepatitis:** Autoantibodies (ANA, ASMA), elevated IgG

**Therapy:****Outpatient:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Supportive</b>	-	Rest, adequate calories, no alcohol

**Inpatient:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Supportive</b>	-	In case of severe vomiting, dehydration, or coagulopathy

**Icu:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Liver transplant</b>	Listing	In case of fulminant liver failure

**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 and Replication: The virus enters hepatocytes via the NTCP receptor. It forms cccDNA (covalently closed circular DNA) in the nucleus, which is the basis for persistence.

- Immune Pathogenesis: The virus itself is not cytopathic. Liver damage is caused by the cytotoxic T-cell immune response against infected cells.
- Chronicity: If the immune response is insufficient (e.g., in neonates), the virus persists. Viral DNA can integrate into the host genome, increasing the risk of hepatocellular carcinoma (HCC).

### Virulence Factors:

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

### **Clinical Features:**

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

### Symptoms:

- **Acute Phase:** Often asymptomatic. If symptomatic: serum sickness-like prodrome (rash, joint pain), then jaundice, fatigue, RUQ pain.
- **Chronic Phase:** Mostly asymptomatic ("silent killer"). In late stages, signs of liver cirrhosis (ascites, variceal bleeding, encephalopathy) dominate.
- **Extrahepatic Symptoms:** Polyarteritis nodosa, glomerulonephritis.

### 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:

- **Other viral hepatitis (HAV, HCV, HDV):** Serology (Anti-HAV IgM, Anti-HCV, Anti-HDV)
- **Autoimmune hepatitis:** Autoantibodies (ANA, ASMA, LKM-1), hypergammaglobulinemia
- **Alcoholic liver disease:** History, AST > ALT (2:1 ratio), elevated GGT
- **Drug-induced liver injury (DILI):** Medication history, improvement after withdrawal
- **Wilson's disease:** Young age, low ceruloplasmin, Kayser-Fleischer ring

### Therapy:

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

### Outpatient:

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

### Inpatient:

Drug	Dose	Note
<b>Tenofovir (TDF/TAF) or Entecavir</b>	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:**

- Replication: The virus replicates in the cytoplasm of hepatocytes (no nuclear phase, hence curable).
- Immune Evasion: The viral RNA polymerase is error-prone, leading to constant mutation (quasispecies) and evasion of immune recognition.
- Fibrosis: Chronic inflammation activates stellate cells, which produce collagen, leading to liver fibrosis and eventually cirrhosis.

**Virulence Factors:**

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

**Clinical Features:**

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

**Symptoms:**

- **Acute Phase:** Rarely diagnosed (80% asymptomatic). Mild fatigue, anorexia may occur.
- **Chronic Phase:** Can be asymptomatic for decades. The leading symptom is chronic fatigue. Often only complications of cirrhosis or lab findings draw attention.
- **Extrahepatic Symptoms:** Cryoglobulinemia (vasculitis), porphyria cutanea tarda, lichen planus, diabetes.

**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:**

- **Hepatitis B:** HBsAg positive
- **Alcoholic liver disease:** History, AST > ALT, macrocytosis
- **Non-alcoholic fatty liver disease (NAFLD/NASH):** Metabolic syndrome, US (steatosis), biopsy
- **Autoimmune hepatitis:** Autoantibodies, histology (plasma cell infiltration)
- **Hemochromatosis:** High ferritin, transferrin saturation, HFE gene mutation

**Therapy:**

**Guidelines:** EASL Recommendations on Treatment of Hepatitis C 2020

**Outpatient:**

Drug	Dose	Note
<b>Glecaprevir / Pibrentasvir (Maviret)</b>	3 tabs (300/120mg) PO 1x	Pangenotypic. 8 weeks in both non-cirrhotic and compensated cirrhotic patients.
<b>Sofosbuvir / Velpatasvir (Epclusa)</b>	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](http://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)
- Seasonality: None
- Transmission: Parenteral, sexual (like HBV). Only infects in the presence of HBV!

- Risk Groups: HBV infected, IV drug users, Sexual partners, Healthcare workers

### **Pathomechanism:**

#### Steps:

- Defective Virus: Requires Hepatitis B virus surface antigen (HBsAg) for replication and packaging of infectious particles.
- Coinfection: Simultaneous infection with HBV and HDV. Usually causes severe acute hepatitis, but chronicity is rare (<5%).
- Superinfection: Chronic HBV carrier infected with HDV. This is the most severe form, often leading to fulminant course or rapidly progressive cirrhosis.

#### Virulence Factors:

- Delta antigen (HDAg)

#### **Clinical Features:**

- Incubation: 30-60 days
- Onset: Sudden

#### Symptoms:

- **Exacerbation:** Sudden deterioration of a known HBV patient's condition (acute flare).
- **Decompensation:** Rapidly developing liver failure, jaundice, coagulopathy.

#### Complications:

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

#### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
ALT/AST	elevated	Acute flare

#### Microbiology:

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

#### **Differential Diagnosis:**

- **HBV coinfection:** HDV RNA positive, Anti-HDV positive
- **Acute HBV flare:** HDV RNA negative, Anti-HDV negative

#### **Therapy:**

**Guidelines:** EASL Clinical Practice Guidelines on hepatitis delta virus 2023

#### **Outpatient:**

Drug	Dose	Note
<b>Bulevirtide</b>	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:**

- Entry: Fecal-oral (contaminated water - Genotype 1,2) or zoonosis (raw meat - Genotype 3,4).
- Pregnancy: In pregnant women (especially 3rd trimester), the virus can cause fulminant liver failure, likely due to hormonal and immunological changes (20% mortality).
- Chronicity: In immunosuppressed patients (e.g., transplant recipients), the virus is not eliminated, causing chronic hepatitis and fibrosis.

**Virulence Factors:**

- ORF3 protein (release)
- Capsid protein

**Clinical Features:**

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

**Symptoms:**

- **Acute Hepatitis:** Similar to HAV (fever, jaundice, vomiting).
- **Neurological Symptoms:** More frequently associated with neurological complications (Guillain-Barré syndrome, neuralgic amyotrophy).
- **In Pregnancy:** Signs of severe, life-threatening liver failure.

**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 (Anti-HAV IgM)
- **Drug-induced liver injury (DILI):** History (e.g., antibiotics, NSAIDs)
- **Ischemic hepatitis:** History of shock/hypotension, extreme LDH elevation
- **Wilson's disease (in fulminant cases):** Hemolysis, low ALP, high urine copper

### **Therapy:**

**Guidelines:** EASL Clinical Practice Guidelines on hepatitis E virus infection

#### **Outpatient:**

Drug	Dose	Note
<b>Supportive</b>	-	In immunocompetent acute infection (self-limiting).

#### **Inpatient:**

Drug	Dose	Note
<b>Ribavirin</b>	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*)

#### **Differential Diagnosis:**

- **Other viral hepatitis:** Serology (HBV, HCV)
- **Non-infectious liver diseases:** Diagnosis of exclusion

### **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*)

**Differential Diagnosis:**

- **Other viral hepatitis:** Serology (HBV, HCV)
- **Non-infectious liver diseases:** Diagnosis of exclusion

**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*)

**Differential Diagnosis:**

- **Other viral hepatitis:** Serology (HBV, HCV)
- **Non-infectious liver diseases:** Diagnosis of exclusion

**Therapy:****Targeted:**

None

**Prevention:**

- -

## Urinary Tract Infections

### Localised Urinary Tract Infection: 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:**

- Colonization: Gut bacteria (mainly *E. coli*) colonize the periurethral area and vaginal introitus.
- Ascension: Bacteria ascend through the urethra into the bladder (shorter urethra in women predisposes).
- Adherence and Invasion: Bacteria adhere to the bladder urothelium using P-fimbriae, avoiding washout by urine, and then invade cells.
- Inflammation: Bacterial multiplication and toxins (e.g., hemolysin) trigger an inflammatory response, causing mucosal hyperemia, edema, and symptoms.

**Virulence Factors:**

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

**Clinical Features:**

- Incubation: Variable
- Onset: Sudden

**Symptoms:**

- **Dysuria:** Burning, stinging sensation during urination caused by irritation of the inflamed urethra and bladder neck.
- **Frequency:** Frequent voiding of small amounts of urine due to bladder wall irritation and reduced capacity.
- **Urgency:** Sudden, compelling urge to urinate that is difficult to defer (risk of urge incontinence).
- **Suprapubic pain:** Pressure or pain felt in the lower abdomen, above the pubic bone.
- **Hematuria:** Macroscopic bloody urine (approx. 30%), often at the end of urination (terminal hematuria), due to bleeding from the hyperemic mucosa.

**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

## Localised Urinary Tract Infection: 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:

- Ascending Infection: Bacteria ascend from the bladder up the ureter to the renal pelvis (often facilitated by vesicoureteral reflux).
- Parenchymal Invasion: Pathogens invade the renal parenchyma, primarily the medulla.
- Inflammatory Response: A vigorous acute inflammatory reaction (neutrophil infiltration) is triggered against the bacteria, causing tissue edema, microabscesses, and tubular damage.
- Systemic Effect: Inflammatory mediators entering the circulation cause fever and systemic symptoms.

#### Virulence Factors:

- P-fimbriae
- Endotoxin
- Capsule

#### **Clinical Features:**

- Incubation: Days after cystitis
- Onset: Sudden

#### Symptoms:

- **Fever and Chills:** Sudden onset of high fever ( $>38^{\circ}\text{C}$ ), often accompanied by shaking chills, indicating systemic bacteremia or toxemia.
- **Flank Pain:** Dull, continuous, unilateral or bilateral pain in the kidney area (flank pain), caused by stretching of the renal capsule.
- **Gastrointestinal Symptoms:** Nausea, vomiting, and loss of appetite are common accompanying symptoms due to peritoneal irritation.
- **Lower Urinary Tract Symptoms:** Dysuria and frequency often precede fever but 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
<b>Cefuroxime axetil</b>	2x500mg PO	no activity against Enterococcus
<b>Levofloxacin</b>	1x750mg PO	Only an alternative if E. coli resistance <10% (EAU 2025)
<b>Ceftibuten/Cefixime</b>	PO	If quinolone cannot be given (less effective)

**Inpatient:**

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

**Icu:**

Drug	Dose	Note
<b>Piperacillin/tazobactam</b>	4x4.5g IV	Urosepsis, obstruction
<b>Meropenem</b>	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

## Systemic 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:

- Predisposing Factor: Anatomical (e.g., stricture, stone) or functional (e.g., neurogenic bladder) abnormality, or presence of a foreign body (catheter) impedes urine flow and bacterial washout.
- Biofilm Formation: Bacteria (e.g., *Proteus*, *Pseudomonas*) form a biofilm layer on the catheter or stone, protecting them from antibiotics and the immune system.
- Persistence: Infection is difficult to eradicate; selection of resistant strains and recurrent infection are common.

#### Virulence Factors:

- Biofilm
- Multidrug resistance
- Urease (*Proteus*)

#### **Clinical Features:**

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

#### Symptoms:

- **Mixed Symptoms:** Symptoms of cystitis and pyelonephritis may coexist, but the clinical picture is often atypical.
- **Systemic Signs:** Fever, chills, tachycardia. In the elderly, confusion or deterioration of general condition may be the only symptom.

- **Oligosymptomatic:** In catheterized patients or those with spinal cord injury, classic pain and voiding complaints may be absent.
- **Urine Changes:** Cloudy, foul-smelling, sedimentous urine, possibly bloody.

#### 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 bacteruria
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*)

#### **Differential Diagnosis:**

- **Shigellosis:** Similar to EIEC/EHEC, culture
- **Cholera:** In ETEC (rice-water stool), travel
- **Viral gastroenteritis:** No blood, vomiting may dominate
- **Campylobacteriosis:** Culture

#### **Therapy:**

##### **Outpatient:**

Drug	Dose	Note
<b>Cefuroxime axetil</b>	2x500mg PO	no activity against Enterococcus
<b>Ciprofloxacin</b>	2x500-750mg PO	Only if no fluoroquinolone treatment in the last 6 months and E. coli resistance <10%

		(EAU 2025)
<b>Levofloxacin</b>	1x750mg PO	Alternative if <i>E. coli</i> resistance <10% (EAU 2025)
<b>Ceftibuten/Cefixime</b>	PO	If quinolone cannot be given

**Inpatient:**

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

**Icu:**

Drug	Dose	Note
<b>Broad spectrum (Carbapenem + Amikacin)</b>	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:**

- Route of Infection: Most commonly, bacteria enter the prostatic ducts via intraprostatic reflux of infected urine.
- Inflammation: In acute cases, edema and microabscesses develop in the glands, causing swelling and tension of the prostate.
- Chronicity: Bacteria can form biofilms on prostatic stones or in ductal channels, maintaining recurrent infections.

**Virulence Factors:**

- Biofilm
- Anatomical location (poor AB penetration)

**Clinical Features:**

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

**Symptoms:**

- **Acute: Systemic Symptoms:** Sudden onset of high fever, chills, myalgia, malaise (flu-like onset).
- **Pain:** Characteristic perineal, rectal, lower abdominal pain, radiating to testes and penis.
- **LUTS (Lower Urinary Tract Symptoms):** Marked dysuria, frequency, urgent need to void.
- **Obstruction:** The swollen prostate compresses the urethra, which can cause difficulty voiding, weak stream, or complete urinary retention.
- **Chronic Symptoms:** Milder, recurrent complaints: pelvic discomfort, recurrent urinary tract infections, painful ejaculation.

**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
<b>Levofloxacin</b>	1x500-750mg PO	EAU 2025: First choice (good penetration)
<b>Ciprofloxacin</b>	2x500mg PO	EAU 2025: First choice
<b>Cotrimoxazole</b>	2x960mg PO	Alternative

**Inpatient:**

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

**Icu:**

Drug	Dose	Note
<b>Meropenem</b>	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 Bacteruria**

**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:**

- Colonization: Bacteria colonize the urinary tract but lack virulence factors (e.g., specific fimbriae) that would trigger tissue invasion or inflammation.
- Commensalism: A state of equilibrium develops between the bacteria and the host, without symptoms.
- Protective Effect: Colonizing strains may compete with more virulent pathogens, potentially having a protective effect.

**Virulence Factors:**

- Reduced virulence

**Clinical Features:**

- Incubation: -
- Onset: Asymptomatic

**Symptoms:**

- **Asymptomatic:** The patient has no urinary complaints (no dysuria, no fever, no pain). Bacteriuria is an incidental finding.

**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
<b>NO treatment</b>	-	General rule (not even in elderly, diabetics, catheterized patients!)

**Inpatient:**

Drug	Dose	Note
<b>NO treatment</b>	-	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

## Skin and Soft Tissue Infections

### Necrotizing Fasciitis

**Pathogen:** Bacterium - Polymicrobial (Type I) or Monomicrobial (Type II) (Mixed)

**Epidemiology:**

- Incidence: Rare (0.4-1/100,000), but high mortality
- Seasonality: None

- Transmission: Endogenous (skin breach) or direct inoculation
- Risk Groups: Type I: Diabetes, immunosuppression, obesity, PVD, Type II: Healthy young, trauma, surgery, IV drug use, Type III: Seawater exposure, liver disease (*Vibrio*)

### **Pathomechanism:**

#### Steps:

- Entry: Infection enters the subcutaneous tissue through a breach in the skin (even minor). Bacteria spread rapidly along the superficial fascial planes, which are poorly vascularized.
- Toxin Effect: Pathogens (especially GAS and Clostridium) produce potent toxins that cause direct tissue necrosis, thrombosis of small blood vessels, and inhibition of the local immune response.
- Tissue Necrosis: Thrombosis and inflammatory edema further compromise blood supply, leading to extensive tissue death. The process also destroys subcutaneous nerves, leading to anesthesia of the area (a late sign).
- Systemic Toxicity: Toxins entering the circulation cause systemic toxic shock syndrome and multi-organ failure.

#### Virulence Factors:

- Strep: M protein, exotoxins (SpeA/B/C)
- Staph: PVL, TSST-1
- Clostridium: alpha-toxin
- Anaerobes: gas production

#### **Clinical Features:**

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

#### Symptoms:

- **Early Signs:** The most important early sign is excruciating pain, which is disproportionate to the clinical findings. The skin may only show mild erythema or swelling, but the patient is systemically ill and febrile.
- **Late Signs:** The skin turns dark purple or black, blisters (bullae) appear, and gas (crepitus) can be felt in the subcutaneous tissues. Pain may subside due to nerve death, which is a poor prognostic sign. Septic shock develops rapidly.

#### Physical Exam:

- Pain disproportionately SEVERE to findings (early sign!)
- Tense, "woody" edema extending beyond erythema
- Skin: erythema → violaceous/grey → bullae → necrosis
- Anesthesia in the area (nerve damage)
- Crepitus (mainly Type I and Clostridium)
- Systemic signs: fever, tachycardia, hypotension, confusion

#### Complications:

- Septic shock
- Multi-organ failure (MODS)

- Limb loss
- Death (20-40%, 100% without treatment)

## Diagnostics:

### Laboratory:

Test	Finding	Interpretation
LRINEC score	$\geq 6$ : suspicion, $\geq 8$ : high probability (but low sensitivity!)	CRP, WBC, Hb, Na, creatinine, glucose
CBC	Leukocytosis ( $> 15 \text{ G/L}$ ), left shift	Severe infection
Sodium	Hyponatremia ( $< 135 \text{ mmol/L}$ )	Common indicator
Lactate	Elevated ( $> 2-4 \text{ mmol/L}$ )	Tissue hypoperfusion/necrosis
CK	Elevated	Muscle involvement (myositis/necrosis)

### Imaging:

- **CT:** Fascial thickening, fluid, gas in soft tissues (specific!) (*Best imaging, but DO NOT delay surgery!*)
- **MRI:** High sensitivity, low specificity (*Time consuming, avoid in unstable patients*)

### Microbiology:

- **Surgical tissue sample:** Gram stain and culture (*Gold standard (aerobe + anaerobe)*)
- **Blood culture:** Positive (mainly Type II) (*Systemic spread*)
- **Finger test:** Fascia easily separated, no bleeding, "dishwater" pus (*Bedside diagnosis*)

### **Differential Diagnosis:**

- **Cellulitis:** No disproportionate pain, no systemic toxicity, slower
- **Pyomyositis:** Muscle abscess, more localized, MRI helps
- **Gas gangrene (Clostridium):** Muscle necrosis dominates, faster, crepitus more pronounced
- **Deep Vein Thrombosis (DVT):** Swelling, but no fever/toxicity, Doppler negative

### **Therapy:**

#### **Outpatient:**

Drug	Dose	Note
<b>No outpatient treatment!</b>	IMMEDIATE HOSPITAL/SURGERY!	Surgical emergency!

#### **Inpatient:**

Drug	Dose	Note
<b>Piperacillin/tazobactam</b>	4x4.5g IV	Broad spectrum (G+, G-, anaerobe)
<b>+ Vancomycin</b>	2x15-20 mg/kg IV	MRSA coverage
<b>+ Clindamycin</b>	3x900 mg IV	Toxin inhibition (GAS/Staph)

**Icu:**

Drug	Dose	Note
<b>Meropenem</b>	3x1g IV	Alternative (Type I)
<b>+ Vancomycin + Clindamycin</b>		Standard triple therapy
<b>IVIG</b>	1g/kg day 1, then 0.5g/kg	Consider in Strep toxic shock syndrome

**Targeted:**

Based on culture. Type I: broad spectrum. Type II (GAS): Penicillin G + Clindamycin. Type III (Vibrio): Doxycycline + Ceftriaxone.

**Supportive:**

- IMMEDIATE aggressive surgical debridement (crucial!)
- Fluid resuscitation
- Vasopressors
- Re-look surgery within 24h
- Hyperbaric oxygen (controversial, adjunctive)

**Prevention:**

- Wound care
- Management of chronic diseases

## 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:**

- Entry: The pathogen (most commonly *Streptococcus pyogenes*) enters the upper dermis and superficial lymphatics through a minor break in the skin.
- Lymphatic Spread: The bacteria spread rapidly through the lymphatic system, resulting in the characteristic, sharply demarcated, flame-like advancing edge.
- Inflammation: Bacterial toxins cause a brisk local inflammation and systemic symptoms (fever, chills).

**Virulence Factors:**

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

### **Clinical Features:**

- Incubation: 2-5 days
- Onset: Acute

### Symptoms:

- **Skin Manifestations:** Sudden onset of a sharply demarcated, flame-like spreading, bright red, swollen, warm, and painful skin lesion. Most commonly affects the face or lower limbs.
- **Systemic Symptoms:** The skin manifestations are often preceded or accompanied by high fever, chills, and malaise.

### 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:** - (*Clinical diagnosis*)

#### Microbiology:

- **Skin swab culture:** *Streptococcus pyogenes* (*Confirmation*)
- **ASO titer:** Elevated (*undefined*)

#### **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
<b>Penicillin V</b>	4x500 mg PO	First choice
<b>Amoxicillin</b>	3x500 mg PO	Alternative
<b>Clindamycin</b>	3x300 mg PO	In case of penicillin allergy, 30% resistance rate

**Inpatient:**

Drug	Dose	Note
<b>Penicillin G</b>	4x4-6 million IU IV	In severe cases
<b>Cefazolin</b>	3x1g IV	Alternative
<b>Ceftriaxone</b>	1x2 g IV	In case of penicillin allergy

**Icu:**

Drug	Dose	Note
<b>Broad-spectrum antibiotics</b>	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, Immunocompromised, Skin injuries, Lymphedema

### **Pathomechanism:**

#### Steps:

- Entry: Pathogens (*S. pyogenes*, *S. aureus*) enter the deeper dermis and subcutaneous fat through a break in the skin.
- Diffuse Spread: The infection spreads diffusely through the tissues, not confined to the lymphatics as in erysipelas. This results in a less sharply demarcated but deeper inflammation.

#### Virulence Factors:

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

#### **Clinical Features:**

- Incubation: 1-3 days
- Onset: Acute

#### Symptoms:

- **Skin Manifestations:** Compared to erysipelas, it is a less sharply demarcated, diffuse erythema, swelling, and warmth. The skin is tense and painful.
- **General Symptoms:** May be accompanied by fever and chills, but not always as pronounced as in erysipelas.

#### Physical Exam:

- Red, warm, swollen skin
- Diffuse, poorly demarcated 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
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**Imaging:**

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

**Microbiology:**

- **Skin aspirate/culture:** Pathogen identification (*If possible*)
- **Wound exudate:** Often contaminated (*Not reliable*)

**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
<b>Amoxicillin/Clavulanate</b>	3x875/125 mg PO	First choice
<b>Cephalexin</b>	4x500 mg PO	Alternative

**Inpatient:**

Drug	Dose	Note
<b>Amoxicillin/Clavulanate</b>	3x500 mg PO	Alternative
<b>Cefazolin</b>	3x1g IV	Alternative
<b>Ceftriaxone</b>	1x2 g IV	In severe cases
<b>+ Vancomycin</b>	2x15-20 mg/kg IV	If MRSA is suspected

**Icu:**

Drug	Dose	Note
<b>Piperacillin/Tazobactam</b>	3x4.5 g 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

## 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, People who inject drugs (PWID), Hemodialysis

### Pathomechanism:

#### Steps:

- Entry: Pathogens reach the bone via the bloodstream (hematogenous), from adjacent soft tissues (contiguous), or by direct inoculation from trauma/surgery.
- Inflammation and Ischemia: In the bone, they cause inflammation, leading to edema and increased pressure in the bone marrow. This compromises blood supply, leading to bone death (sequestrum).
- Chronicity: The body attempts to wall off the dead bone with new bone formation (involucrum). In chronic cases, bacteria persist by forming a biofilm.

#### Virulence Factors:

- Biofilm formation
- Adhesins (MSCRAMM)
- Toxins

#### **Clinical Features:**

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

#### Symptoms:

- **Acute Osteomyelitis:** Sudden onset of localized pain, swelling, erythema, and fever. The patient is often unable to bear weight on the affected limb.
- **Chronic Osteomyelitis:** More insidious, with a dull, deep pain, and often a draining sinus tract to the skin. Fever is rare.

#### 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 (may be normal in chronic)
CRP/ESR	Elevated	Excellent for monitoring (response to therapy)
Blood culture	Positive (50%)	In hematogenous origin (important in vertebral OM)

**Imaging:**

- **X-ray:** Negative in early phase (10-14 days)! Later periosteal reaction, lytic lesions (*Late sign, but baseline*)
- **MRI:** Bone marrow edema, abscess, sequestrum (*Gold standard (sensitivity >90%)*)
- **Bone scintigraphy/PET-CT:** Increased uptake (*If MRI cannot be performed or multifocal suspicion*)

**Microbiology:**

- **Bone biopsy culture:** Pathogen identification (*Gold standard diagnosis (before antibiotics!)*)
- **Sinus tract discharge:** Often contaminated (*Correlates well with bone only for S. aureus*)

**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
<b>None</b>	-	Hospital investigation/sampling required

**Inpatient:**

Drug	Dose	Note
<b>Vancomycin</b>	15-20 mg/kg IV	MRSA coverage
<b>+ Ceftriaxone/Cefepime</b>	2g IV	Gram-negative coverage (e.g. Pseudomonas)

**Icu:**

Drug	Dose	Note
Broad-spectrum antibiotics	IV	In case of sepsis

**Targeted:**

Based on bone biopsy! S. aureus: Cefazolin/Flucloxacillin. MRSA: Vancomycin. Implant-associated: Rifampicin adjunct (biofilm).

**Supportive:**

- Surgical debridement (removal of necrotic bone) - CRITICAL!
- Implant removal (if possible)
- Early oral switch possible (OVIVA study)

**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, People who inject drugs (PWID), Sexually active young people (Gonococcus)

**Pathomechanism:****Steps:**

- Entry: Pathogens reach the joint space via the bloodstream (hematogenous) or direct injury.
- Inflammatory Response: They colonize the synovial membrane, triggering a massive inflammatory response, leading to a large purulent effusion.
- Cartilage Damage: Enzymes released from neutrophils and inflammatory cytokines cause irreversible damage to the articular cartilage within hours to days.

**Virulence Factors:**

- Adhesins
- Toxins
- Cartilage-damaging enzymes

**Clinical Features:**

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

Symptoms:

- **Acute Monoarthritis:** Sudden onset of extremely painful swelling, redness, and warmth of a single large joint (most commonly knee, hip).
- **Loss of Function:** The patient is unable to move the joint, either actively or passively, due to pain. High fever and chills are common.

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
Synovial fluid	>50,000 WBC/ $\mu$ L (>90% PMN)	Typical for septic arthritis

Imaging:

- **X-ray:** Initially negative/soft tissue swelling, later joint space narrowing (*Baseline*)
- **Ultrasound:** Joint fluid, synovial thickening (*Guiding puncture, early diagnosis*)
- **MRI:** Joint effusion, bone marrow edema, abscess (*Exclusion of osteomyelitis, complications*)

Microbiology:

- **Joint aspiration (Arthrocentesis):** Purulent, Gram stain positive (50%) (*Perform IMMEDIATELY!*)
- **Culture (Synovial + Blood):** Positive (*Gold standard*)
- **PCR (16S rRNA):** Pathogen DNA (*If culture is negative (pre-treated patient)*)

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:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>None</b>	-	Emergency hospital admission!

**Inpatient:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Vancomycin</b>	15-20 mg/kg IV	Gram+ (MRSA) coverage
<b>+ Ceftriaxone</b>	2 g IV once daily	Gram- (Gonococcus/G- rods) coverage

**Icu:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Vancomycin + Meropenem</b>	IV	In case of sepsis/immunosuppression

**Targeted:**

S. aureus: Cefazolin/Flucloxacillin; MRSA: Vancomycin/Daptomycin; Gonococcus: Ceftriaxone. Duration: 2-6 weeks (IV then PO switch possible - OVIVA).

**Supportive:**

- Joint drainage (daily needle aspiration, arthroscopy or open washout) - CRUCIAL!
- Analgesics
- Early mobilization after inflammation subsides

**Prevention:**

- Sterility in prosthesis surgeries
- Prevention of gonorrhea
- Treatment of skin infections

## Spondylodiscitis

**Pathogen:** Bacterium - *Staphylococcus aureus* (most common), *Streptococcus* spp., Gram-negative bacteria (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, Immunocompromised, People who inject drugs (PWID), Post-spine surgery, Urogenital infections

**Pathomechanism:****Steps:**

- Hematogenous Spread: Pathogens most commonly reach the highly vascularized vertebral bodies via the bloodstream (hematogenous route), often from a distant

infection (e.g., urinary tract, skin).

- Progression: The infection spreads from the vertebral body to the adjacent intervertebral disc and the next vertebra, causing inflammation and tissue destruction.
- Complications: The process can lead to the formation of an epidural or paravertebral abscess, causing spinal cord compression and neurological symptoms.

#### Virulence Factors:

- Adhesins (MSCRAMM)
- Biofilm formation
- Toxins

#### **Clinical Features:**

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

#### Symptoms:

- **Back Pain:** The leading symptom (>90%) is a gradually worsening, localized back pain that is present even at rest and tender to percussion.
- **Fever and Neurological Symptoms:** Fever is often low-grade or absent. Neurological symptoms (radicular pain, limb weakness) suggest an epidural abscess and represent an emergency.

#### 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
<b>None</b>	-	Hospitalization required

#### Inpatient:

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

#### Icu:

Drug	Dose	Note
<b>Broad-spectrum antibiotics</b>	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



## Central Nervous System Infections

## Differential Diagnosis of CSF Findings

**Epidemiology:**

**Pathomechanism:**

**Clinical Features:**

**Diagnostics:**

**Therapy:**

## 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: Neonates (<1 month), Children, Adults >65 years, Asplenic patients, Complement deficiency, Cochlear implant recipients

**Pathomechanism:**

Steps:

- Colonization and Invasion: Pathogens (e.g., Meningococcus, Pneumococcus) colonize the nasopharyngeal mucosa and invade the bloodstream (bacteremia).
- Crossing the Blood-Brain Barrier: Bacteria cross the endothelium of the choroid plexus or cerebral capillaries to enter the subarachnoid space.
- Replication and Inflammation: Bacteria multiply rapidly in the CSF (which lacks humoral immunity). Bacterial cell wall components (LPS, teichoic acid) trigger a massive inflammatory response via PRRs (cytokines: TNF- $\alpha$ , IL-1 $\beta$ ).
- Cerebral Edema and ICP: Inflammation increases BBB permeability (vasogenic edema), reduces CSF absorption (interstitial edema), and causes cell swelling (cytotoxic edema).
- Consequence: The resulting cerebral edema raises intracranial pressure (ICP), reducing cerebral perfusion pressure (CPP), leading to ischemia and neuronal damage.

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:** The classic triad (fever, nuchal rigidity, altered mental status) is present in <50% of patients. Headache (severe, diffuse) and fever are the most common (95%).
- **Meningeal Signs:** Nuchal rigidity (chin cannot touch chest), Kernig's sign (pain on leg extension with hip flexed), and Brudzinski's sign (legs lift when head is raised).
- **Systemic "Red Flags":** Especially in Meningococcus: leg pain, cold hands/feet, mottled skin - these are early signs of sepsis preceding meningitis symptoms.
- **Rash:** In Meningococcemia: petechiae (tiny bleeds) or purpura (larger bleeds) that do not fade under pressure (non-blanching rash).
- **Neurological Symptoms:** Altered mental status (confusion to coma), seizures (20-30%), cranial nerve palsies (III, IV, VI, VII, VIII), and focal signs.

### Physical Exam:

- Meningeal signs: Kernig (+), Brudzinski (+), nuchal rigidity
- Fever (often >39°C)
- Altered mental status (decreased GCS)
- Focal neurological deficits (cranial nerve palsy, paresis)
- Petechiae/purpura (Meningococcemia)
- Papilledema (late sign)

### Complications:

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

### Diagnostics:

#### Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (15-30 G/L) with 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 profile	Signs of DIC ( $\downarrow$ fibrinogen, $\uparrow$ D-dimer)	Meningococcus

### Imaging:

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

### Microbiology:

- **CSF Analysis:** WBC >1000/ $\mu$ L (PMN), Protein >1 g/L, Glucose <40% of serum (*Typical for bacterial meningitis*)
- **CSF Lactate:** Elevated (*Helps differentiate from viral*)
- **CSF Gram Stain:** 60-90% positive (*Quick orientation*)
- **CSF/Blood Culture:** Pathogen isolation (*Antimicrobial susceptibility testing*)
- **CSF PCR (Multiplex):** DNA detection (*Fast, sensitive, useful in pre-treated patients*)
- **CSF Latex Agglutination:** Antigen detection (*Fast, less sensitive*)

### Differential Diagnosis:

- **Viral Meningitis:** Milder course, 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
- **Meningeal Carcinomatosis:** Malignancy history, cytology

### Therapy:

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

### Outpatient:

Drug	Dose	Note
<b>Benzylpenicillin or Ceftriaxone</b>	IM/IV stat	Only if hospital transfer is significantly delayed (NICE)

### Inpatient:

Drug	Dose	Note
<b>Ceftriaxone</b>	2 g IV every 12 hours (or 4 g once daily)	First choice (NICE). Alternative: Cefotaxime.
<b>+ Ampicillin</b>	2 g IV every 4 hours	If Listeria risk (>60 years, immunocompromised, pregnancy).
<b>Dexamethasone</b>	10 mg IV every 6 hours	Administer BEFORE or WITH the first antibiotic dose. Avoid in septic shock without meningitis.

### Icu:

Drug	Dose	Note
<b>Supportive Care</b>	-	Airway protection, fluid resuscitation, vasopressors

### Targeted:

N. meningitidis: 7 days; S. pneumoniae: 14 days; L. monocytogenes: 21 days; H. influenzae: 10 days; S. agalactiae (GBS): 14-21 days.

#### Supportive:

- Fluid and electrolyte management
- Intracranial pressure (ICP) monitoring
- Seizure management
- Droplet isolation (for Meningococcus, until 24h of effective antibiotics)

#### Prevention:

- Meningococcal vaccines (MenACWY, MenB)
- Pneumococcal vaccines (PCV, PPSV)
- Hib vaccine
- Chemoprophylaxis for close contacts (Rifampicin, Ciprofloxacin, or Ceftriaxone)

## Meningococcal Meningitis

**Pathogen:** Bacterium - *Neisseria meningitidis* (Gram-negative)

#### Epidemiology:

- Incidence: Can be epidemic
- Seasonality: Winter-Spring
- Transmission: Droplet (close contact)
- Risk Groups: Infants, Adolescents, Closed communities (dorms), Asplenia

#### Pathomechanism:

##### Steps:

- The bacterium colonizes the nasopharynx and enters the bloodstream.
- Rapid replication in blood releases massive amounts of endotoxin (LOS) (meningococcemia).
- Endotoxin triggers systemic inflammation, vasculitis, and disseminated intravascular coagulation (DIC).
- This leads to small vessel occlusion (skin necrosis, adrenal hemorrhage - Waterhouse-Friderichsen syndrome) and septic shock, often before meningitis develops.

#### Virulence Factors:

- Capsule (A,B,C,W,Y)
- LOS (Lipooligosaccharide)
- IgA protease

#### Clinical Features:

- Incubation: 1-10 days
- Onset: Hyperacute

#### Symptoms:

- **Hyperacute Onset:** Patient condition deteriorates dramatically within hours. Fever, vomiting, headache are early signs.
- **Hemorrhagic Rash:** Initially blanching macules, rapidly evolving into petechiae and purpura that DO NOT fade under pressure (non-blanching rash). Sign of meningococcemia.
- **Septic Shock:** Cold extremities, cyanosis, low blood pressure, rapid pulse, anuria.

#### Physical Exam:

- Meningeal signs
- Purpura
- Signs of shock

#### Complications:

- Limb necrosis/amputation
- Deafness
- Death (within hours)

#### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CSF	Purulent	-
PCR	Positive	undefined

#### Microbiology:

- **Gram stain:** Gram-negative diplococci (*Rapid*)

#### **Therapy:**

#### **Inpatient:**

Drug	Dose	Note
Ceftriaxone	2g IV every 12 hours	NICE NG240 recommendation

#### Targeted:

Ceftriaxone for 7 days. Prophylaxis for contacts: Ciprofloxacin (single 500mg PO) or Rifampicin.

#### Prevention:

- Vaccination (MenACWY, MenB)

## Pneumococcal Meningitis

**Pathogen:** Bacterium - *Streptococcus pneumoniae* (Gram-positive)

#### **Epidemiology:**

- Incidence: Most common adult meningitis

- Seasonality: Winter
- Transmission: Endogenous spread or droplet
- Risk Groups: Elderly, Alcoholics, Splenectomy, Otitis/Sinusitis/Pneumonia, CSF leak

### **Pathomechanism:**

#### Steps:

- Infection often spreads to meninges from an adjacent focus (otitis media, sinusitis, mastoiditis) or via bacteremia accompanying pneumonia.
- The pneumococcal capsule inhibits phagocytosis, and pneumolysin toxin directly damages cells and stimulates inflammation.
- This pathogen causes the most severe purulent meningitis, with frequent coma and permanent sequelae.

#### Virulence Factors:

- Capsule
- Pneumolysin

#### **Clinical Features:**

- Incubation: Short
- Onset: Acute

#### Symptoms:

- **Severe Meningitis:** Characterized by rapid onset of altered consciousness, coma, and seizures. Mortality and sequelae rates are highest in this type.
- **Predisposing Signs:** Concurrent pneumonia, otitis media, or sinusitis is often found.

#### Physical Exam:

- Meningeal signs
- Signs of otitis media
- Altered mental status

#### Complications:

- Deafness
- Hydrocephalus
- Brain abscess

#### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CSF	Purulent, very high protein, low sugar	-

#### Microbiology:

- **Gram stain:** Gram-positive diplococci (-)

#### **Therapy:**

#### **Inpatient:**

Drug	Dose	Note

<b>Ceftriaxone</b>	2g IV every 12 hours	NICE NG240 recommendation
<b>Dexamethasone</b>	10mg IV every 6 hours	Continue if Pneumococcus is confirmed!

**Targeted:**

Ceftriaxone for 14 days. If resistance confirmed: + Vancomycin/Rifampicin.

**Prevention:**

- Pneumococcal vaccine (PCV, PPSV)

## **Listeria Meningitis**

**Pathogen:** Bacterium - *Listeria monocytogenes* (Gram-positive)

**Epidemiology:**

- Incidence: Rare but dangerous
- Seasonality: None
- Transmission: Food (soft cheese, cold cuts)
- Risk Groups: Neonates, Elderly (>50 years), Pregnant women, Immunocompromised (transplant, alcoholic)

**Pathomechanism:****Steps:**

- Bacteria enter via contaminated food, penetrate the gut wall, and enter the bloodstream.
- It has a specific tropism for the brainstem (rhombencephalon) and meninges.
- As an intracellular pathogen, it spreads cell-to-cell, evading antibodies. Cellular immunity is crucial (which is weaker in infants, elderly, pregnant).
- Forms microabscesses and granulomas in the brainstem.

**Virulence Factors:**

- Intracellular survival
- Listeriolysin O

**Clinical Features:**

- Incubation: 1-4 weeks
- Onset: Subacute

**Symptoms:**

- **Subacute Course:** Symptoms may develop more slowly over days to weeks, not as stormy as other bacterial meningitides.
- **Rhombencephalitis:** Signs of brainstem involvement: cranial nerve palsies (e.g., facial weakness, swallowing difficulty), ataxia, nystagmus, and respiratory distress.
- **Lack of Signs:** Nuchal rigidity is often absent; only fever and confusion may be noted.

**Physical Exam:**

- Meningeal signs (may be absent)
- Focal signs

**Complications:**

- Brain abscess
- Hydrocephalus

**Diagnostics:****Laboratory:**

Test	Finding	Interpretation
CSF	Can be lymphocytic! (not always PMN)	Misleading

**Microbiology:**

- **Gram stain:** Often negative or Gram+ rods (can be mistaken for diphtheroids) (-)

**Therapy:****Inpatient:**

Drug	Dose	Note
<b>Amoxicillin / Ampicillin</b>	2g IV every 4 hours	NICE NG240 recommendation. Cephalosporins are INEFFECTIVE!
+ <b>Gentamicin</b>	5mg/kg IV once daily	Synergistic effect

**Targeted:**

Amoxicillin/Ampicillin (21 days) + Gentamicin (first 7 days). In penicillin allergy: Cotrimoxazole (Trimethoprim/Sulfamethoxazole).

**Prevention:**

- Food hygiene in risk groups

## Aseptic (Viral) Meningitis

**Pathogen:** Virus - Enteroviruses (*Coxsackie, Echo*), HSV-2, VZV (RNA/DNA)

**Epidemiology:**

- Incidence: Most common form of meningitis
- Seasonality: Summer-Autumn (Enterovirus)
- Transmission: Fecal-oral (Enterovirus), Sexual (HSV-2)
- Risk Groups: Children, Young adults

**Pathomechanism:****Steps:**

- The virus (e.g., Enterovirus) enters the bloodstream from the gut or respiratory tract (viremia).
- It crosses the blood-brain barrier to infect the meninges and choroid plexus.
- It triggers an inflammatory response (mainly lymphocytic), but unlike bacterial infection, no purulent exudate forms, and the brain parenchyma is usually spared (hence clear consciousness).

- The process is usually self-limiting; the immune system clears the infection.

### Virulence Factors:

- 

### **Clinical Features:**

- Incubation: 3-7 days
- Onset: Sudden

### Symptoms:

- Meningeal Syndrome:** Headache (frontal/retro-orbital), fever, photophobia, and nuchal rigidity.
- Clear Consciousness:** The most important differential sign: the patient is alert, oriented, with no focal neurological deficits (unlike encephalitis or bacterial meningitis).
- Systemic Symptoms:** Rash, sore throat, diarrhea may accompany Enterovirus; genital lesions with HSV-2.

### Physical Exam:

- Meningeal signs (milder)
- Consciousness clear (difference from encephalitis!)

### Complications:

- Rare (Meningoencephalitis)

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CSF	Lymphocytic pleocytosis (tens-hundreds), normal glucose, slightly elevated protein	Viral profile

### Microbiology:

- CSF PCR:** Enterovirus/HSV/VZV (*Diagnostic*)

### **Therapy:**

#### **Outpatient:**

Drug	Dose	Note
Supportive	-	Pain relief, Rest

### Targeted:

Consider Acyclovir for HSV-2/VZV (especially in immunocompromised). Enterovirus: symptomatic.

### Prevention:

- Hygiene

## 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: Year-round
- Transmission: HSV: Reactivation/Primary; Enterovirus: Fecal-oral; Arbovirus: Vector-borne (Mosquito/Tick)
- Risk Groups: Neonates (HSV-2), Immunocompromised patients, Elderly (VZV reactivation), Travelers to endemic areas (Arboviruses)

### Pathomechanism:

#### Steps:

- Entry: Viruses reach the CNS via hematogenous spread (e.g., Arboviruses) or neural pathways (e.g., HSV, Rabies).
- Neurotropism: Viruses directly infect neurons and glial cells. HSV-1 specifically targets the temporal and frontal lobes (via olfactory or trigeminal routes).
- Mechanism of Injury: Neuronal death is caused by direct viral cytopathic effects and the host's cytotoxic T-cell immune response.
- Histology: Perivascular lymphocytic infiltration, neuronophagia, and microglial nodules. HSV causes hemorrhagic necrosis.
- Consequence: Cerebral edema, inflammation, hemorrhage, and extensive neuronal death leading to focal deficits and altered consciousness.

### Virulence Factors:

- HSV: Glycoproteins (gB, gC, gD) for cell entry
- VZV: Latency in sensory ganglia
- Enterovirus: Capsid proteins

### Clinical Features:

- Incubation: HSV variable; Enterovirus 3-7 days; Arbovirus 4-14 days
- Onset: Acute to Subacute

### Symptoms:

- **Altered Mental Status (Hallmark):** The key distinguishing feature from meningitis: the patient is not alert/oriented. Manifests as confusion, lethargy, personality changes, or coma.
- **Fever and Headache:** Almost always present (>90%), often accompanied by nausea and vomiting.
- **Focal Neurological Deficits:** Depending on the affected area: hemiparesis, aphasia, ataxia, cranial nerve palsies.
- **Seizures:** Common (especially in HSV and autoimmune causes), can be focal or generalized.
- **Psychiatric Symptoms:** Hallucinations, agitation, psychosis, memory loss - especially in forms affecting the limbic system (e.g., HSV).

**Physical Exam:**

- Decreased level of consciousness (GCS)
- Focal signs (Hemiparesis, CN palsies)
- Seizures (Focal or Generalized)
- Meningeal signs (often mild/moderate)
- Papilledema (signs of raised ICP)

**Complications:**

- Permanent neurological sequelae
- Post-encephalitic epilepsy
- Motor/Cognitive deficits
- Death (Untreated HSV mortality ~70%)

**Diagnostics:****Laboratory:**

Test	Finding	Interpretation
CBC	Variable (Leukocytosis or Normal)	Non-specific
CRP	Normal or Moderately elevated	Usually lower than in bacterial meningitis
Renal/Liver function	Baseline assessment	Monitor for Acyclovir nephrotoxicity

**Imaging:**

- MRI Brain:** HSV: Asymmetric hyperintensity in temporal/frontal lobes (T2/FLAIR) (*Gold standard imaging. Perform early.*)
- CT Head:** Often normal in early stages (*To exclude mass effect before LP*)

**Microbiology:**

- CSF PCR:** HSV-1/2, VZV, Enterovirus, Arbovirus (*Gold standard. False negative possible in first 24-48h.*)
- CSF Analysis:** Lymphocytic pleocytosis (10-500 cells/ $\mu$ L), Protein normal/mildly elevated, Glucose normal (*Viral profile*)
- CSF Erythrocytes:** Elevated RBCs, Xanthochromia (*Suggests hemorrhagic necrosis (HSV)*)
- Serology (Serum/CSF):** IgM or 4-fold IgG rise (Arboviruses) (*Often retrospective*)

**Differential Diagnosis:**

- Bacterial Meningitis:** More acute, CSF: PMN predominance, Hypoglycorrachia
- Autoimmune Encephalitis:** Subacute, psychiatric features, Anti-NMDA-R antibodies
- Brain Abscess:** Imaging: Ring-enhancing lesion
- Toxic-Metabolic Encephalopathy:** Metabolic derangements, Toxins, No fever/pleocytosis
- Non-convulsive Status Epilepticus:** EEG diagnostic

**Therapy:****Outpatient:**

Drug	Dose	Note

<b>No outpatient treatment</b>	Immediate hospitalization	High mortality without treatment
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**Inpatient:**

Drug	Dose	Note
<b>Acyclovir</b>	10 mg/kg IV every 8 hours	Start empirically if HSV suspected

**Icu:**

Drug	Dose	Note
<b>Acyclovir</b>	10 mg/kg IV every 8 hours	For immunocompromised or severe cases
<b>Anticonvulsants</b>	e.g., Levetiracetam	For seizure control

**Targeted:**

HSV/VZV: Acyclovir; CMV: Ganciclovir/Foscarnet; Enterovirus: Supportive

**Supportive:**

- ICP Management
- Seizure Control
- Fluid/Electrolyte Balance
- Rehabilitation

**Prevention:**

- VZV Vaccination
- Vector control (Arboviruses)
- C-section for active genital herpes to prevent Neonatal HSV

## Herpes Simplex Encephalitis

**Pathogen:** Virus - *Herpes Simplex Virus 1* (HSV-1) (dsDNA)

**Epidemiology:**

- Incidence: Most common sporadic fatal encephalitis
- Seasonality: None
- Transmission: Reactivation (trigeminal ganglion) or Primary infection
- Risk Groups: Anyone (no seasonality)

**Pathomechanism:****Steps:**

- Latent virus reactivates in the trigeminal ganglion and travels retrogradely via nerve fibers back to the brain.
- It selectively attacks the temporal and frontal lobes and the limbic system.

- Viral replication and immune response cause severe, asymmetric, necrotizing, hemorrhagic inflammation in these areas.
- Resulting cerebral edema and temporal lobe swelling can lead to uncal herniation.

### Virulence Factors:

- Neurovirulence genes

### **Clinical Features:**

- Incubation: Variable
- Onset: Acute (days)

### Symptoms:

- **Prodrome:** Fever, headache, malaise for a few days.
- **Behavioral Changes:** Sudden onset of bizarre behavior, personality changes, psychosis, hallucinations (olfactory/gustatory). Often initially mistaken for a psychiatric condition.
- **Neurological Deficits:** Aphasia (speech disturbance), hemiparesis, memory loss (especially short-term).
- **Seizures:** Common, often with focal onset.

### Physical Exam:

- Altered mental status
- Focal neurological signs
- Memory impairment

### Complications:

- Uncal herniation
- Permanent cognitive impairment
- Death

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CSF	Lymphocytic, elevated RBCs (xanthochromia), elevated protein	Hemorrhagic necrosis

#### Imaging:

- **MRI:** Asymmetric hyperintensity in temporal lobe (T2/FLAIR) (*Pathognomonic*)

#### Microbiology:

- **CSF PCR:** HSV-1 DNA (*Gold standard*)

### **Therapy:**

#### **Inpatient:**

Drug	Dose	Note
<b>Acyclovir</b>	10 mg/kg IV every 8 hours	Start immediately upon suspicion!

#### Targeted:

Acyclovir IV. Repeat if relapse occurs.

#### Supportive:

- Seizure control
- Cerebral edema management

#### Prevention:

- None

## Tick-Borne Encephalitis (TBE)

**Pathogen:** Virus - *Tick-Borne Encephalitis Virus* (RNA, Flaviviridae)

#### **Epidemiology:**

- Incidence: Endemic in Central Europe
- Seasonality: Spring-Autumn
- Transmission: Tick bite, unpasteurized milk
- Risk Groups: Forest goers, Tick bite

#### **Pathomechanism:**

#### Steps:

- The virus enters via the saliva of an infected tick.
- Phase 1 (Viremia): The virus replicates in lymph nodes and spleen, causing flu-like symptoms.
- Phase 2 (Neuroinvasion): In some patients, the virus crosses the blood-brain barrier and attacks the meninges (meningitis), brain parenchyma (encephalitis), or spinal cord (myelitis).
- Spinal cord involvement typically destroys anterior horn motor neurons, leading to flaccid paralysis.

#### Virulence Factors:

- -

#### **Clinical Features:**

- Incubation: 7-14 days
- Onset: Biphasic

#### Symptoms:

- **Phase 1 (Flu-like):** Fever, headache, muscle pain, fatigue lasting 2-7 days. Followed by a 1-3 week symptom-free interval.
- **Phase 2 (Neurologic):** Fever returns in 20-30% of patients, with neurological symptoms. Forms: Meningitis (milder), Meningoencephalitis (confusion, ataxia), Meningoencephalomyelitis (paralysis).
- **Paralysis:** Asymmetric flaccid paralysis of the shoulder girdle and upper limbs is characteristic (due to anterior horn damage).

#### Physical Exam:

- Ataxia
- Tremor
- Flaccid paralysis of shoulder girdle (myelitis)
- Altered mental status

**Complications:**

- Permanent paralysis
- Post-encephalitic syndrome

**Diagnostics:****Laboratory:**

Test	Finding	Interpretation
CSF	Lymphocytic pleocytosis	-

**Microbiology:**

- **Serology (IgM/IgG):** Blood and CSF (*Diagnostic (PCR often negative in phase 2!)*)

**Therapy:****Inpatient:**

Drug	Dose	Note
Supportive	-	No specific therapy

**Targeted:**

Symptomatic treatment (edema reduction, rehabilitation).

**Prevention:**

- Vaccination (FSME-Immun, Encepur)
- Tick protection

## Cryptococcal Meningitis

**Pathogen:** Fungus - *Cryptococcus neoformans* (Yeast (encapsulated))

**Epidemiology:**

- Incidence: Most common fungal meningitis in HIV/AIDS patients
- Seasonality: None
- Transmission: Inhalation (pigeon dropping dust) -> lung -> hematogenous spread
- Risk Groups: HIV (CD4 <100), Transplant recipients, Steroid treatment

**Pathomechanism:****Steps:**

- Fungus enters lungs via inhalation, causing primary infection (often asymptomatic).
- In immunosuppression (e.g., AIDS), it disseminates via blood to the brain.
- Its thick polysaccharide capsule protects it from phagocytosis.

- Accumulation in arachnoid villi blocks CSF absorption, leading to extremely high intracranial pressure without purulent inflammation.

### Virulence Factors:

- Polysaccharide capsule
- Melanin production

### **Clinical Features:**

- Incubation: Unknown (reactivation)
- Onset: Subacute/Chronic (weeks)

### Symptoms:

- **Slow Progression:** Symptoms develop over weeks. Leading symptoms are worsening headache and fever.
- **High ICP Symptoms:** Due to blocked CSF absorption: visual disturbances (diplopia, blurriness), nausea, altered mental status.
- **Absence of Meningeal Signs:** Since inflammatory response is weak (few WBCs), nuchal rigidity is often absent!

### Physical Exam:

- Meningeal signs often absent!
- Papilledema (high ICP)
- Skin symptoms (molluscum-like)

### Complications:

- High intracranial pressure (blindness, herniation)
- Cryptococcoma
- IRIS (at therapy start)

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CD4	<100/ $\mu$ L	Risk

#### Imaging:

- **CT/MRI:** Often normal, or dilated perivascular spaces, cryptococcoma (*Exclusion*)

#### Microbiology:

- **CSF CrAg (antigen):** Positive (*Gold standard (also from blood!)*)
- **India ink stain:** Encapsulated yeasts (*Rapid, but less sensitive*)
- **CSF culture:** C. neoformans (*Diagnostic*)
- **CSF pressure:** Often extremely high (>25 cmH<sub>2</sub>O) (*Therapeutic tap required*)

### **Therapy:**

#### **Inpatient:**

Drug	Dose	Note

<b>Amphotericin B + Flucytosine</b>	IV + PO	Gold standard
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**Targeted:**

Induction (AmB+5FC) -> Consolidation (Fluconazole 400mg 8 weeks) -> Maintenance (Fluconazole 200mg 1 year/CD4>200).

**Supportive:**

- Repeated LP to lower pressure (vital!)

**Prevention:**

- Fluconazole prophylaxis (if blood CrAg positive)
- Start ART (but carefully due to IRIS)

## Primary Amoebic Meningoencephalitis (PAM)

**Pathogen:** Protozoan - *Naegleria fowleri* (-)

**Epidemiology:**

- Incidence: Very rare, but fatal
- Seasonality: Summer (warm water)
- Transmission: Water entering nose -> olfactory nerve -> brain
- Risk Groups: Children/young adults, Freshwater swimmers

**Pathomechanism:****Steps:**

- Water enters the nose during swimming in warm fresh water.
- The amoeba penetrates the nasal mucosa and cribriform plate.
- It migrates along the olfactory nerve directly to the frontal lobes of the brain.
- Multiplying in brain tissue, it enzymatically dissolves and "eats" brain tissue, causing massive hemorrhagic necrosis and edema.

**Virulence Factors:**

- Tissue-degrading enzymes
- Amebostome (feeding apparatus)

**Clinical Features:**

- Incubation: 1-9 days (average 5)
- Onset: Fulminant

**Symptoms:**

- **Initial Symptoms:** Sudden onset of excruciating frontal headache, fever, nausea. Often preceded by smell/taste disturbances (parosmia/ageusia).
- **Progression:** Rapid development of stiff neck, hallucinations, seizures, and coma. Death occurs within 3-7 days due to cerebral edema and herniation.

**Physical Exam:**

- Meningeal irritation
- Coma
- Rapid deterioration

### Complications:

- Herniation
- Death (within 3-7 days)

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CSF	Purulent (PMN), RBCs, low sugar	Looks bacterial!

#### Microbiology:

- **CSF microscopy (wet mount):** Motile amoebas (*Diagnostic (but experience needed)*)
- **PCR:** Naegleria DNA (*CDC/Reference lab*)

### **Therapy:**

#### Icu:

Drug	Dose	Note
<b>Miltefosine + Amphotericin B + Rifampicin + Fluconazole + Azithromycin</b>	Combination	Experimental, few survivors

#### Targeted:

Miltefosine is the key drug. Cooling (hypothermia) may help.

#### Prevention:

- Nose clip in warm fresh water
- Nasal irrigation only with sterile water

## **Brain Abscess**

**Pathogen:** Bacterium - *Streptococcus* spp., *Staphylococcus aureus*, Anaerobes (Mixed)

#### **Epidemiology:**

- Incidence: Rare but serious (0.4-1.3/100,000/year)
- Seasonality: None
- Transmission: Endogenous spread (contiguous or hematogenous)
- Risk Groups: Immunocompromised, Chronic otitis/sinusitis, Dental infection, Endocarditis, Head trauma/surgery

#### **Pathomechanism:**

#### Steps:

- Direct spread: Infection spreads from adjacent structures (e.g., middle ear, sinus, teeth) to the brain parenchyma (40-50%).
- Hematogenous spread: Bacteria reach the brain via the bloodstream from a distant focus (e.g., lung, heart - endocarditis) (25-35%).
- Trauma/Surgery: Direct entry following open skull fracture or neurosurgical procedure.
- Abscess formation: Bacterial multiplication causes local inflammation (cerebritis), then necrosis. The body attempts to isolate the process with capsule formation.

### Virulence Factors:

- Synergism of mixed flora
- Capsule formation

### **Clinical Features:**

- Incubation: Variable (days-weeks)
- Onset: Subacute

### Symptoms:

- **Headache:** Most common symptom (>70%), often localized, dull, constant, and progressive.
- **Focal neurological deficits:** Depending on abscess location (e.g., hemiparesis, aphasia, visual field defect).
- **Fever:** Present in only 50% of cases! Absence does not rule it out.
- **Altered mental status:** Drowsiness, confusion, then coma may develop due to increased intracranial pressure.

### Physical Exam:

- Papilledema (high ICP)
- Focal neurological signs
- Fever (may be absent)

### Complications:

- Herniation
- Abscess rupture into the ventricular system (ventriculitis - high mortality)
- Epilepsy

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CBC	Leukocytosis (in 60%)	Unreliable
CRP	Elevated	Inflammation
Blood culture	Positive	undefined

#### Imaging:

- **Head CT/MRI:** Ring enhancement, perifocal edema (*Gold standard (MRI is more sensitive)*)

**Microbiology:**

- **Stereotactic aspiration:** Pus culture (*Basis for etiological diagnosis and therapy*)
- **Lumbar puncture:** CONTRAINDICATED! (*Forbidden due to risk of herniation if mass effect exists!*)

**Differential Diagnosis:**

- **Brain tumor (Glioblastoma, Metastasis):** Imaging (DWI sequence helps), biopsy
- **Stroke:** Sudden onset, vascular risk factors
- **Encephalitis:** More diffuse, no encapsulated abscess

**Therapy:****Inpatient:**

Drug	Dose	Note
<b>Ceftriaxone</b>	2g IV every 12 hours	Base therapy
<b>+ Metronidazole</b>	500mg IV every 8 hours	Anaerobic coverage
<b>+ Vancomycin</b>	15-20mg/kg IV	If <i>S. aureus</i> suspected (e.g., trauma, endocarditis)

**Targeted:**

Based on culture. Prolonged (6-8 weeks) IV, then PO therapy.

**Supportive:**

- Neurosurgical aspiration/drainage (if >2.5 cm)
- Steroids (Dexamethasone) only if significant edema/risk of herniation
- Anticonvulsants

**Prevention:**

- Treatment of ENT infections
- Endocarditis prophylaxis

## Tuberculous Meningitis

**Pathogen:** Mycobacterium - *Mycobacterium tuberculosis* (Acid-fast)

**Epidemiology:**

- Incidence: Most common form of extrapulmonary TB
- Seasonality: None
- Transmission: Hematogenous spread from a primary lung focus
- Risk Groups: Immunocompromised (HIV), Individuals from endemic areas, Infants, Alcoholics

**Pathomechanism:****Steps:**

- Hematogenous Spread: Bacteria spread from a primary lung focus via the bloodstream to the brain/meninges.
- Rich Foci: Small, caseating foci (tuberculomas) form in the subcortical or meningeal space.
- Rupture: The foci rupture, releasing bacteria and antigens into the subarachnoid space.
- Basal Exudate: A thick, gelatinous, inflammatory exudate forms at the base of the brain, encasing cranial nerves and cisterns.
- Consequence: Communicating hydrocephalus (impaired CSF absorption), cranial nerve palsies (III, IV, VI, VII), vasculitis, and cerebral infarcts.

#### Virulence Factors:

- Cord factor
- Intracellular survival

#### **Clinical Features:**

- Incubation: Weeks-months
- Onset: Subacute

#### Symptoms:

- **Prodromal Phase (1-2 weeks):** Slow, insidious onset: apathy, personality changes, low-grade fever, headache, nausea.
- **Meningeal Phase (2-3 weeks):** Nuchal rigidity, altered mental status, lethargy, cranial nerve palsies (especially VI, III, IV, VII).
- **Paralytic Phase:** Rapid progression to coma, hemiplegia, decerebrate rigidity. Fatal without treatment.

#### Physical Exam:

- Nuchal rigidity
- Altered mental status
- Cranial nerve palsies
- Papilledema

#### Complications:

- Hydrocephalus
- Cerebral infarction
- Permanent neurological damage
- SIADH

#### **Diagnostics:**

##### Laboratory:

Test	Finding	Interpretation
CSF	Lymphocytic pleocytosis, VERY high protein ( $>1$ g/L), VERY low glucose ( $<2.2$ mmol/L)	Characteristic triad!
CSF ADA	Elevated	Adenosine deaminase, aids in diagnosis

Imaging:

- **MRI/CT with contrast:** Basal meningeal enhancement, hydrocephalus, tuberculomas (*Diagnostic*)

Microbiology:

- **CSF Ziehl-Neelsen:** Acid-fast bacilli (*Low sensitivity (<20%)*)
- **CSF Culture:** M. tuberculosis (*Gold standard, but slow (weeks)*)
- **CSF PCR (GeneXpert):** MTB DNA (*Rapid, sensitive*)

**Differential Diagnosis:**

- **Cryptococcal meningitis:** CrAg test, lower protein
- **Meningeal carcinomatosis:** Cytology, known tumor
- **Neurosypilis:** Serology, CSF VDRL

**Therapy:****Inpatient:**

Drug	Dose	Note
<b>RIPE (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol)</b>	Standard dose	Longer treatment required
<b>+ Dexamethasone</b>	IV/PO	Reduces mortality! Mandatory!

Targeted:

Therapy modified based on susceptibility testing.

Supportive:

- ICP management
- VP shunt (for hydrocephalus)

Prevention:

- BCG vaccine
- LTBI treatment



## 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:

- Entry and Dissemination: *T. pallidum* enters through micro-abrasions in skin or mucous membranes. It disseminates via lymphatics and bloodstream within minutes/hours, becoming systemic before the primary lesion appears.
- Immune Evasion: The bacteria use a "stealth" strategy with low outer membrane protein density to evade antibody binding and complement activation, allowing persistence.
- Tissue Damage: Pathology is based on obliterative endarteritis (inflammation and occlusion of small vessels) accompanied by perivascular plasma cell infiltration.
- Consequence: Ischemia caused by vessel occlusion leads to ulceration of the primary chancre and formation of gummas (necrotic granulomas) in the tertiary stage.

Clinical Features:

- 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:** A painless, indurated ulcer with a clean base at the site of inoculation (genitals, mouth, anus) approx. 3 weeks post-infection. Accompanied by painless regional lymphadenopathy. It heals spontaneously, but the bacteria remain.
- **Secondary: Rash & Lesions:** Sign of hematogenous spread (6-8 weeks later). Generalized, non-pruritic, copper-colored rash typically involving palms and soles. Infectious, weeping papules (condyloma lata) may appear in skin folds.
- **Secondary: Systemic Symptoms:** Fever, malaise, generalized lymphadenopathy ("micropolyadenopathy"), patchy "moth-eaten" alopecia, and mucous patches.
- **Tertiary: Late Complications:** Develops years later. Gumma (destructive granulomas in skin/bone/liver), cardiovascular syphilis (aortitis, aneurysm), and neurosyphilis (tabes dorsalis, general paresis/dementia).

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↑ (*Neurosyphilis 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
<b>Benzathine Penicillin G</b>	2.4 million IU IM	Early syphilis (primary, secondary, early latent <1 year)
<b>Penicillin allergy:</b> <b>Doxycycline</b>	2x100mg PO	Alternative (compliance!)

##### Inpatient:

Drug	Dose	Note
<b>Benzathine Penicillin G</b>	2.4 million IU IM	Late latent (>1 year) or unknown duration

#### Icu:

Drug	Dose	Note
<b>Aqueous Crystalline Penicillin G</b>	3-4 million IU IV every 4 hours	Neurosypilis!

**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, People who inject drugs (PWID), Sex workers, Transfusion recipients (developing countries), Partners

**Pathomechanism:****Steps:**

- Entry and Binding: Viral gp120 binds to CD4 receptor and CCR5/CXCR4 co-receptors on T-helper cells and macrophages.
- Replication and Integration: Viral RNA is reverse transcribed to DNA (prone to errors/resistance), then integrated into host DNA (provirus) by integrase, where it can remain latent.
- Immune Destruction: Infected CD4+ T-cells die due to viral replication (pyroptosis), cytotoxic T-cell attack, and syncytium formation. Early depletion of gut-associated lymphoid tissue (GALT) drives chronic systemic inflammation.
- Consequence: Critical decline in CD4+ count (<200/ $\mu$ L) leads to immune collapse and opportunistic infections/malignancies (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 Retroviral Syndrome (ARS):** Mononucleosis-like illness occurring 2-4 weeks post-infection: fever, sore throat, lymphadenopathy, muscle pain, and maculopapular rash. High viral load and transient CD4 drop.
- **Clinical Latency:** Asymptomatic or mild period lasting 8-10 years without treatment. The virus actively replicates in lymph nodes. Persistent generalized lymphadenopathy (PGL) may occur.
- **AIDS Stage:** When CD4 count falls below 200/ $\mu\text{L}$ . Appearance of opportunistic infections (e.g., Pneumocystis pneumonia, esophageal candidiasis, Toxoplasma encephalitis, CMV retinitis) and malignancies (Kaposi sarcoma, Lymphoma).

### 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 ( $<200/\mu\text{L}$ = 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
<b>Bictegravir / Tenofovir alafenamide (TAF) / Emtricitabine (FTC)</b>	1 tab (50/25/200mg) PO 1x	Preferred first-line (STR). Does not require HLA testing.
<b>Dolutegravir + Tenofovir (TDF/TAF) + Emtricitabine (FTC) / Lamivudine (3TC)</b>	Combination	Preferred first-line.
<b>Dolutegravir / Lamivudine (3TC)</b>	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, knowlesi* (-)

### 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, Immunocompromised

**Pathomechanism:****Steps:**

- During the bite of an infected Anopheles mosquito, sporozoites enter the bloodstream and migrate to liver cells within minutes.
- Liver phase (exoerythrocytic): Inside hepatocytes, the parasites multiply asexually, forming schizonts. This phase is asymptomatic. *P. vivax* and *P. ovale* can form hypnozoites (dormant forms), which can lead to relapses.
- Blood phase (erythrocytic): Merozoites released from the liver infect red blood cells (RBCs). Inside the RBCs, they develop into ring-stage trophozoites and then into schizonts, which release new merozoites upon RBC rupture.
- The cyclical rupture of RBCs (every 48-72 hours) causes the characteristic, periodic fever paroxysms due to the release of inflammatory cytokines (TNF-alpha, IL-1).
- RBCs infected with *P. falciparum* adhere to the walls of small blood vessels via the PfEMP1 protein (cytadherence), obstructing microcirculation and leading to severe organ damage (brain, kidneys, lungs).

**Virulence Factors:**

- PfEMP1 (adhesion)
- Antigenic variation
- Hemozoin pigment

**Clinical Features:**

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

**Symptoms:**

- **Uncomplicated Malaria:** Characterized by febrile paroxysms: chills, high fever (40-41°C), followed by sweating and defervescence. The cycle repeats every 48 (*P. falciparum*, *vivax*, *ovale*) or 72 hours (*P. malariae*). Accompanying symptoms include headache, myalgia, nausea, and splenomegaly.
- **Severe Malaria (*P. falciparum*):** A life-threatening condition. Manifestations include cerebral malaria (impaired consciousness, coma, seizures), severe anemia, ARDS (pulmonary edema), renal failure (blackwater fever), metabolic acidosis, hypoglycemia, and shock.

**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 and thin blood smears:** 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
<b>Artemether-Lumefantrine</b>	PO (weight-based)	First-line ACT for uncomplicated P. falciparum.
<b>Dihydroartemisinin-Piperaquine</b>	PO	Alternative ACT.
<b>Artesunate-Pyronaridine</b>	PO	Alternative ACT.
<b>Chloroquine</b>	PO	Only for P. vivax/ovale/malariae if from a chloroquine-sensitive area.

#### Inpatient:

Drug	Dose	Note
<b>Artesunate</b>	2.4 mg/kg IV/IM	First choice for severe malaria (adult/child/pregnant). Follow with a full course of ACT!

<b>Artemether</b>	3.2 mg/kg IM	Alternative if artesunate is not available.
<b>Quinine</b>	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 (hypnozoiticide). 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: Fecal-oral (cat feces), raw meat (cyst), vertical
- Risk Groups: Immunocompromised (HIV/AIDS, transplant), Pregnant women (fetus!), Cat owners

**Pathomechanism:****Steps:**

- Infection can occur via three routes: 1. Ingestion of oocysts from soil/food contaminated with cat feces. 2. Consumption of tissue cysts in raw or undercooked meat. 3. Vertical transmission (from mother to fetus).
- In the intestine, parasites released from cysts transform into tachyzoites (rapidly dividing form), which penetrate the intestinal wall and can spread to any part of the body via the bloodstream.
- In response to an intact immune system, tachyzoites convert into bradyzoites (slowly dividing form) and form tissue cysts, primarily in the brain, muscles, and eyes. This establishes a latent, lifelong infection.
- In cases of immunosuppression (e.g., AIDS, transplantation), these latent cysts can reactivate. Bradyzoites convert back to tachyzoites, leading to severe, often fatal disease

(e.g., encephalitis).

### Virulence Factors:

- Intracellular survival
- Cyst formation
- Immunomodulation

### **Clinical Features:**

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

### Symptoms:

- **Immunocompetent Infection:** 80-90% of cases are asymptomatic. When symptoms occur, they are mild and mononucleosis-like: painless cervical lymphadenopathy, fever, and fatigue.
- **Ocular Toxoplasmosis:** The most common cause of chorioretinitis. It causes blurred vision, eye pain, and floaters. It can be a result of primary infection or reactivation.
- **Cerebral Toxoplasmosis (AIDS):** The most common CNS opportunistic infection in AIDS (CD4<100). Characterized by headache, confusion, fever, and focal neurological signs (seizures, hemiparesis). MRI typically shows multiple ring-enhancing lesions.
- **Congenital Toxoplasmosis:** A consequence of primary maternal infection during pregnancy. The classic Sabin's tetrad includes hydrocephalus, intracranial calcifications, chorioretinitis, and seizures. It can cause severe and permanent damage.

### 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/ $\mu$ 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
<b>None</b>	-	Asymptomatic immunocompetent individuals do not require treatment

**Inpatient:**

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

**Icu:**

Drug	Dose	Note
<b>Steroid</b>	Dexamethasone	In case of mass effect (cerebral edema)

**Targeted:**

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

**Supportive:**

- Leucovorin (Folinic acid) supplementation 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: Fecal-oral (soil/vegetables contaminated with eggs)
- Risk Groups: Children, People in poor hygienic conditions

**Pathomechanism:**

Steps:

- Infection occurs via the fecal-oral route from soil, vegetables, or water contaminated with eggs.
- Ingested eggs hatch in the small intestine, and the larvae penetrate the intestinal wall, migrating through the portal circulation to the liver and then the lungs.
- In the lungs, the larvae cause inflammation (Löffler's syndrome), are coughed up, and then swallowed, returning to the small intestine.
- In the small intestine, they mature into adult worms (15-35 cm), where they absorb nutrients. In heavy infections, a bolus of worms can cause intestinal or biliary obstruction.

Virulence Factors:

- Protease inhibitors
- Migration ability

**Clinical Features:**

- Incubation: 4-8 weeks
- Onset: Slow

Symptoms:

- **Pulmonary Phase (Löffler's Syndrome):** A transient syndrome during larval migration: dry cough, shortness of breath, low-grade fever, and marked eosinophilia in the blood count.
- **Intestinal Phase:** Mild infections can be asymptomatic. In more severe cases, abdominal pain, bloating, nausea, and in children, malnutrition and growth retardation may occur.
- **Obstructive Complications:** In massive infections, a worm bolus can cause mechanical intestinal obstruction (ileus). Worms migrating into the bile ducts or pancreatic duct can cause jaundice, cholangitis, or pancreatitis.

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 examination 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: People who consume raw meat

**Pathomechanism:**

**Steps:**

- **Taeniasis (Intestinal Tapeworm):** Occurs by consuming raw or undercooked beef (*T. saginata*) or pork (*T. solium*) containing larvae (cysticerci). In the intestine, the larva develops into an adult tapeworm, several meters long.
- **Cysticercosis (Tissue Form):** Caused EXCLUSIVELY by *T. solium*! The worm eggs are ingested via the fecal-oral route (e.g., contaminated food, autoinfection). Larvae hatch from the eggs in the intestine, enter the bloodstream, and travel to tissues (brain, muscle, eye), where they encyst (cysticercus).

**Virulence Factors:**

- Scolex (hooks/suckers)

**Clinical Features:**

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

**Symptoms:**

- **Taeniasis (Intestinal Infection):** Often asymptomatic. Mild abdominal discomfort, bloating, or changes in appetite may occur. The diagnosis is often made by observing motile tapeworm segments (proglottids) passed in the stool.
- **Neurocysticercosis (NCC):** The most severe form, occurring after ingestion of *T. solium* eggs. Cysts in the central nervous system cause seizures (most common), headaches, increased intracranial pressure, hydrocephalus, or focal neurological symptoms, depending on their location.

**Physical Exam:**

- Unremarkable (intestinal infection)
- 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: Fecal-oral: ingestion of eggs from dog/fox feces
- Risk Groups: Dog owners, shepherds, People who consume wild berries (fox - *E. multilocularis*)

**Pathomechanism:****Steps:**

- Infection occurs by ingesting eggs from soil or vegetables contaminated with the feces of dogs (*E. granulosus*) or foxes (*E. multilocularis*). Humans are an intermediate host for the parasite.
- In the intestine, oncospheres (larvae) hatch from the eggs, penetrate the intestinal wall, enter the portal circulation, and most commonly settle in the liver (70%), or less frequently in the lungs (20%) or other organs.
- *E. granulosus*: The larva slowly grows (over years) into a fluid-filled, thick-walled hydatid cyst, which can contain thousands of new larvae (protoscolices). The mass effect of the cyst causes symptoms.
- *E. multilocularis*: The larva grows in a tumor-like, infiltrative manner, destroying liver tissue. It has no clear border, making it difficult to remove surgically.
- Cyst rupture can cause severe anaphylactic shock due to the release of its antigenic contents, and dissemination of the infection.

**Virulence Factors:**

- Laminated layer (immune protection)
- Protoscolices

**Clinical Features:**

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

**Symptoms:**

- **Symptoms:** The disease is asymptomatic for years. Symptoms depend on the cyst's size and location. Liver cyst: right upper quadrant pain, feeling of fullness, hepatomegaly, jaundice (biliary compression). Lung cyst: chest pain, cough, hemoptysis.
- **Cyst Rupture:** Sudden abdominal or chest pain, fever, urticaria, eosinophilia, and in severe cases, anaphylactic shock. The cyst contents can spread within the body, leading to the formation of new cysts.
- **Alveolar Echinococcosis (*E. multilocularis*):** Behaves like liver cancer: jaundice, abdominal pain, weight loss, hepatomegaly. Poor prognosis.

#### 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:

- **Ultrasound/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: Fecal-oral, autoinfection (scratching → mouth), inhalation (dust)
- Risk Groups: Small children, Institutionalized settings (daycare, school), Family members

### Pathomechanism:

#### Steps:

- Infection occurs by ingesting the sticky eggs, which can be found under fingernails, on bedding, and in dust. Autoinfection (hand-to-mouth after scratching) is common.
- Larvae hatch from the eggs in the small intestine, migrate to the cecal area, and mature into adult worms.
- The fertilized female worm (approx. 1 cm) migrates to the perianal folds at night, lays her eggs, and then dies. The egg-laying and movement of the worm cause the characteristic, intense itching.

#### Virulence Factors:

- -

### Clinical Features:

- Incubation: 2-6 weeks
- Onset: Gradual

#### Symptoms:

- **Perianal Pruritus (Itching):** The leading symptom, typically most intense at night, causing sleep disturbance and restlessness. Scratching can lead to secondary bacterial skin infections.
- **Other Symptoms:** Rarely, mild abdominal pain. In young girls, the worm can migrate into the vagina, causing vulvovaginitis. Most infections are mild or asymptomatic.

#### Physical Exam:

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

#### Complications:

- Bacterial superinfection (scratching)
- Salpingitis (rare)

### Diagnostics:

#### Microbiology:

- **Cellophane 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	

**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: People who consume raw/smoked pork, wild boar

**Pathomechanism:****Steps:**

- Infection occurs by consuming raw or undercooked meat (especially pork, wild boar) containing larvae.
- Enteral phase: In the intestine, larvae mature into adult worms, which burrow into the intestinal wall and produce new larvae. This causes diarrhea and nausea.
- Parenteral phase: The newborn larvae enter the blood and lymphatic circulation, disseminate throughout the body, and specifically migrate to highly oxygenated, active striated muscles (masticatory muscles, diaphragm, tongue, eye muscles).
- In the muscle cells, the larvae encyst, creating a "nurse cell" complex, which causes chronic inflammation and the characteristic muscle pain.

**Virulence Factors:**

- Nurse cell formation in muscle

**Clinical Features:**

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

**Symptoms:**

- **Enteral Phase (1st week):** Diarrhea, nausea, vomiting, and abdominal pain occurring a few days after infection.

- Parenteral Phase (from 2nd week):** Larval migration causes the classic triad of symptoms: 1. High fever. 2. Severe muscle pain (myalgia), especially in the chewing and eye muscles. 3. Characteristic bilateral periorbital edema (swelling around the eyes). Extreme eosinophilia is seen in the blood count.
- Complications:** Larvae can also affect the heart muscle (myocarditis) or the central nervous system (encephalitis), which can be life-threatening.

### 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
<b>Mebendazole</b>	3x200-400mg PO	More effective in early phase
<b>Albendazole</b>	2x400mg PO	

#### **Inpatient:**

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

**Targeted:**

Antihelminthic + 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: Fecal-oral: ingestion of soil contaminated with eggs (not direct animal contact!)
- Risk Groups: Small children (sandbox, geophagia), Dog owners

**Pathomechanism:****Steps:**

- Infection occurs by accidental ingestion of eggs from soil contaminated with dog (*T. canis*) or cat (*T. cati*) feces (e.g., sandboxes). Humans are accidental, or paratenic, hosts for the parasite.
- In the intestine, larvae hatch from the eggs, penetrate the intestinal wall, and migrate via the bloodstream to various organs (liver, lungs, brain, eyes).
- Because humans are not the natural host, the larvae cannot mature into adult worms. Instead, they wander through the tissues (larva migrans), and the body forms granulomatous inflammation around them, which causes tissue damage.

**Virulence Factors:**

- Tissue migration
- Excretory-secretory antigens (TES)

**Clinical Features:**

- Incubation: Weeks-months
- Onset: Slow

**Symptoms:**

- **Visceral Larva Migrans (VLM):** Typically occurs in young children (1-5 years). Symptoms include prolonged fever, hepatomegaly, cough, and wheezing. Lab tests show extremely high eosinophilia and leukocytosis.
- **Ocular Larva Migrans (OLM):** More common in older children and adults. A larva migrating to the eye can cause unilateral vision loss, strabismus, and leukocoria (white pupil), which can be mistaken for retinoblastoma. Systemic symptoms and eosinophilia are usually absent.

- **Covert Toxocariasis:** A form with mild, non-specific symptoms such as abdominal pain, headache, and cough, with moderate eosinophilia.

#### 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 Ultrasound:** 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 via urine of rodents/animals
- Risk Groups: Agricultural workers, Veterinarians, Slaughterhouse workers, Sewer workers, Participants in water sports/extreme sports, Soldiers (jungle environment)

#### **Pathomechanism:**

##### Steps:

- Leptospira bacteria survive in water or soil contaminated with the urine of infected animals (especially rodents). The pathogen enters the body through broken skin or mucous membranes (eyes, nose, mouth).
- After entry, the bacteria rapidly enter the bloodstream (hematogenous spread) and reach almost all organs, particularly the liver, kidneys, lungs, and central nervous system.
- The pathogen damages the endothelial cells of blood vessels, leading to increased vascular permeability, fluid leakage, and hemorrhages.
- The severe form, Weil's disease, is characterized by the triad of liver and kidney failure, jaundice (icterus), and severe hemorrhagic complications (e.g., pulmonary hemorrhage).
- Some clinical symptoms are caused by the host's intense, immune-mediated inflammatory response rather than the direct toxic effect of the bacterium.

##### 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:

- **Acute/Septic Phase (First Week):** Sudden onset of high fever with chills, intense headache, and characteristic, excruciating muscle pain, especially in the calves and lower back. Conjunctival suffusion (redness of the eyes without purulent discharge) is common.
- **Immune Phase (Second Week):** A brief improvement may follow the first phase, then symptoms return due to the immune response. This is when aseptic meningitis, uveitis, and organ manifestations can appear.
- **Weil's Disease (Severe Form):** Develops in 5-10% of patients. It is characterized by jaundice, renal failure (acute tubular necrosis), and hemorrhagic complications like pulmonary hemorrhage, which has a high mortality rate.

#### 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):**  $\geq 1:400$  titer or  $4 \times \uparrow$  (*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
<b>Doxycycline</b>	100 mg PO twice daily	First choice in mild cases
<b>Amoxicillin</b>	500 mg PO 3 times daily	Alternative (pregnant, child)

#### Inpatient:

Drug	Dose	Note
<b>Penicillin G</b>	1.5 million IU IV every 4 hours	Severe/Weil's disease
<b>Ceftriaxone</b>	1-2 g IV once daily	Alternative

#### Icu:

Drug	Dose	Note
<b>Penicillin G</b>	1.5 million IU IV every 4 hours	Severe Weil's disease
<b>Dialysis</b>	If renal failure	Supportive
<b>Ventilation</b>	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, Occupations with rodent contact, Cleaning poorly ventilated buildings

### Pathomechanism:

#### Steps:

- Infection occurs through inhalation of aerosolized dust contaminated with dried urine, feces, or saliva of rodents (e.g., bank vole). Person-to-person transmission does not occur.
- The virus enters the bloodstream via the lungs and specifically infects endothelial cells lining the blood vessels, without causing direct cell death.
- The main damage is caused by the body's excessive immune response. Activated T-cells and cytokines (TNF-alpha) loosen the junctions between endothelial cells, leading to capillary leak.
- HFRS (Hemorrhagic Fever with Renal Syndrome): The capillary leak primarily occurs in the kidneys, leading to acute renal failure, proteinuria, and hemorrhages.
- HPS (Hantavirus Pulmonary Syndrome): The leak is dominant in the lungs, leading to rapidly progressing, non-cardiogenic pulmonary edema and cardiogenic shock. Thrombocytopenia and hemoconcentration are key laboratory signs.

#### 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:

- **Prodromal Phase (3-5 days):** Sudden onset of high fever, chills, severe headache, and muscle pain (especially back and thighs). Facial flushing and conjunctival injection are common.
- **HFRS (Renal Involvement):** The febrile phase is followed by hypotension, then oliguria/anuria. Severe flank pain, massive proteinuria, and thrombocytopenia are characteristic. Polyuria occurs during the recovery phase.
- **HPS (Pulmonary Involvement):** After the prodromal phase, a rapidly progressing cough and shortness of breath develop, leading to severe, non-cardiogenic pulmonary edema and cardiogenic shock within hours. High mortality rate.

#### 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

##### 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	33 mg/kg IV loading, then 16 mg/kg every 6 hours	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:** Spirochaete - *Borrelia burgdorferi sensu lato* (Gram-negative)

### Epidemiology:

- Incidence: USA: 476,000 cases/year; Europe: 232,000 cases/year. Common and endemic in Hungary.
- Seasonality: From spring to autumn (tick activity)
- Transmission: Ixodes ricinus tick bite (usually >24 hours of feeding required)
- Risk Groups: Visitors to wooded areas, Hikers, campers, Foresters, hunters, Gardeners, Children

### Pathomechanism:

#### Steps:

- During the feeding of an infected Ixodes tick, *Borrelia* spirochetes are transmitted from the tick's salivary glands into the host's skin (usually requires >24 hours of attachment).
- The bacteria replicate locally in the skin and spread centrifugally, creating the characteristic Erythema migrans (EM) rash.
- The pathogens disseminate via the bloodstream (hematogenous) and lymphatic system to distant organs (heart, nervous system, joints, skin).
- The bacteria can evade the immune system (antigenic variation, complement inhibition), allowing for persistence and the development of chronic inflammation.
- Tissue damage is primarily caused not by toxins but by the host's inflammatory response (cytokines, immune complexes).

#### Virulence Factors:

- Osp (Outer surface proteins)
- VlsE (antigenic variation)
- Motility

#### **Clinical Features:**

- Incubation: EM: 3-30 days (average 7-14 days)
- Onset: Staged

#### Symptoms:

- **Early Localized Stage (Erythema Migrans):** A painless, slowly expanding (>5 cm) rash at the site of the tick bite, often target-like (but can be uniform). This is the most common symptom and allows for a clinical diagnosis. It may be accompanied by general flu-like symptoms (fever, headache, myalgia).
- **Early Disseminated Stage (Organs):** Occurs weeks to months after bacterial spread. Nervous system: Bannwarth syndrome (nocturnal radicular pain, facial palsy, meningitis).

Heart: Lyme carditis (AV block, arrhythmia). Skin: Lymphocytoma (bluish-red nodule).

- **Late Stage (Chronic):** Months to years later. Lyme arthritis: intermittent swelling and pain of large joints (especially the knee). Skin: Acrodermatitis chronica atrophicans (ACA) - livid discoloration and atrophy of the extensor surfaces of the limbs.

### Physical Exam:

- Erythema migrans: >5 cm in diameter, expanding erythema
- Facial paresis (can be bilateral)
- Meningeal signs (mild)
- Joint swelling (knee)
- ACA: cigarette paper-like skin

### Complications:

- Chronic arthritis
- Post-Lyme disease syndrome (subjective complaints)
- Chronic neuroborreliosis

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
Two-tier serology (ELISA + Western blot)	IgM (2-4 weeks), IgG (4-6 weeks)	Two-tier! NOT recommended in EM stage (clinical dx, may still be negative). Indicated in disseminated/late stages.
CSF	Lymphocytic pleocytosis, intrathecal antibody synthesis (AI > 1.5)	Confirmation of neuroborreliosis

#### Imaging:

- **ECG:** AV block (*In case of suspected carditis*)

#### Microbiology:

- **Tick testing:** NOT recommended (*No clinical relevance for treatment*)
- **PCR:** Borrelia DNA (*May be useful from synovial fluid or skin biopsy (ACA). Low sensitivity from blood/CSF.*)

### **Differential Diagnosis:**

- **Erysipelas/Cellulitis:** Fever, pain, rapid spread, leukocytosis
- **Tinea corporis:** Scaling border, itching, KOH positive
- **Other arthritis:** Septic (fever, pus), RA (symmetrical, serology)
- **Multiple sclerosis:** MRI, CSF oligoclonal bands

### **Therapy:**

#### **Outpatient:**

Drug	Dose	Note

<b>Doxycycline</b>	100 mg BID PO	First choice (EM, Neuroborreliosis, Carditis, Arthritis, ACA). Can also be given to children.
<b>Amoxicillin</b>	500-1000 mg TID PO	Alternative (EM, Arthritis, ACA, pregnancy)
<b>Cefuroxime axetil</b>	500 mg BID PO	Alternative

**Inpatient:**

Drug	Dose	Note
<b>Ceftriaxone</b>	2 g QD IV	Severe neuroborreliosis (e.g., encephalitis), carditis (high-grade block), refractory arthritis

**Targeted:**

Early localized (EM): Doxycycline 10 days. Neuroborreliosis (Bannwarth): Doxycycline PO (as effective as IV Ceftriaxone!) 14 days. Arthritis: Doxycycline 28 days.

**Supportive:**

- Symptomatic treatment
- Physiotherapy

**Prevention:**

- Prompt tick removal
- Protective clothing
- Prophylactic antibiotics after a bite are NOT recommended (Hungarian guideline)

## 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, Tanners, Agricultural workers, Lab workers, Foresters, Veterinarians

**Pathomechanism:****Steps:**

- *Francisella tularensis* is a highly infectious bacterium (<10 organisms are sufficient), which enters the body via tick bites, direct contact with infected animals (e.g., rabbits), or inhalation of contaminated dust.
- At the site of entry, the bacterium is phagocytosed by macrophages, but it can escape from the phagosome into the cytoplasm, where it multiplies.
- Infected macrophages migrate to regional lymph nodes, where the bacterium continues to replicate, causing painful, necrotizing granulomas and lymphadenitis.
- Different clinical forms develop depending on the portal of entry (e.g., ulceroglandular, pulmonary).

- The bacteria can spread from the lymphatic system into the bloodstream, causing systemic infection (typhoidal form) and involvement of distant organs (lungs, liver, spleen).

### Virulence Factors:

- Capsule
- Phagosome escape (igA-D locus)
- LPS (toxic)
- Siderophores
- Intracellular survival

### **Clinical Features:**

- Incubation: 3-5 days (1-14 days)
- Onset: Sudden

### Symptoms:

- Ulceroglandular Form (75-85%):** The most common form. A painful ulcer with a black eschar develops at the portal of entry (e.g., bite site), accompanied by painful swelling of regional lymph nodes (bubo).
- Glandular Form (5-10%):** Similar to the ulceroglandular form, but the primary skin ulcer is absent; only painful lymph node swelling is present.
- Typhoidal Form (5-15%):** A severe, systemic illness with high fever, chills, and headache, but without a primary site of infection (ulcer, lymph node). Often associated with pneumonia.
- Other Forms:** Oculoglandular (conjunctivitis and lymph node swelling if it enters the eye), Oropharyngeal (tonsillitis if ingested), Pulmonary (atypical pneumonia if inhaled).

### 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  $4\times$ ↑ (*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
<b>Doxycycline</b>	100 mg PO twice daily	Mild form first choice
<b>Ciprofloxacin</b>	500 mg PO twice daily	Alternative

**Inpatient:**

Drug	Dose	Note
<b>Streptomycin</b>	7.5-10 mg/kg IM twice daily	Gold standard in severe cases
<b>Gentamicin</b>	5 mg/kg IV once daily	Streptomycin not available
<b>Doxycycline</b>	100 mg IV twice daily	In combination

**Icu:**

Drug	Dose	Note
<b>Gentamicin + Doxycycline</b>	Combination	Typhoidal/pulmonary severe
<b>Ciprofloxacin</b>	400 mg IV twice daily	Better penetration in meningitis

**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, Immunocompromised (HIV), Veterinarians, shelter workers

#### Pathomechanism:

#### Steps:

- The bacterium *Bartonella henselae* is most commonly transmitted to human skin by a scratch or bite from an infected (but asymptomatic) cat, especially a kitten. Cats infect each other via fleas.
- A primary lesion, a red papule or pustule, develops at the site of entry within 3-10 days.
- The bacteria migrate via the lymphatic vessels to the regional lymph nodes (e.g., axillary, cervical).
- In the lymph nodes, the pathogen creates characteristic, stellate (star-shaped) necrotizing granulomas, causing painful enlargement of the lymph nodes.
- In immunocompetent individuals, the infection is usually self-limiting. In the immunosuppressed (e.g., HIV), the bacterium can disseminate and cause systemic disease, such as bacillary angiomatosis (vascular proliferation) or peliosis hepatitis.

#### 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:

- **Typical Form:** Following a primary papule at the scratch site, unilateral, painful regional lymph node swelling develops after 1-3 weeks (most commonly in the axilla or neck). It may be accompanied by mild fever and malaise. The lymph node may suppurate.
- **Parinaud Oculoglandular Syndrome:** The pathogen enters through the conjunctiva, causing unilateral conjunctivitis and swelling of the preauricular lymph node.
- **Atypical/Disseminated Forms:** Less commonly, especially in the immunosuppressed, the infection can disseminate. It can cause neuroretinitis (vision loss), encephalitis, hepatosplenic disease (liver and spleen abscesses), or bacillary angiomatosis (vascular tumors on the skin and internal organs).

### 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 hepatitis

### **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
<b>Azithromycin</b>	500 mg on day 1, then 250 mg daily	First choice, reduces lymph node size
<b>Doxycycline</b>	100 mg PO twice daily	Alternative in adults
<b>OBSERVATION</b>	Self-limiting disease	Antibiotics not necessarily needed in mild cases

#### Inpatient:

Drug	Dose	Note
<b>Azithromycin</b>	500 mg IV daily	If PO not tolerated
<b>Doxycycline + Rifampicin</b>	100 mg twice daily + 300 mg twice daily PO	Neuroretinitis

#### Icu:

Drug	Dose	Note
<b>Gentamicin + Doxycycline</b>	3 mg/kg IV daily + 100 mg PO/IV twice daily	Endocarditis
<b>Surgery</b>	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:

- *Coxiella burnetii* is a highly infectious, obligate intracellular bacterium. Infection most commonly occurs by inhaling aerosol containing spore-like particles from the birthing products of infected animals (sheep, goats, cattle).
- After entering the lungs, the pathogen is phagocytosed by alveolar macrophages.
- The bacterium not only survives but also replicates within the acidic phagosomes of macrophages, creating a specialized vacuole.
- Upon release from infected cells, the pathogen spreads via the bloodstream (hematogenous spread) to various parts of the body, mainly the liver and bone marrow.
- The body attempts to contain the infection by forming characteristic "doughnut-shaped" granulomas. The disease can be acute or chronic (endocarditis).

##### Virulence Factors:

- Spore-like form (resistant)
- LPS phase variation

#### **Clinical Features:**

- Incubation: 2-3 weeks
- Onset: Sudden

#### Symptoms:

- Acute Q Fever:** About 60% of cases are asymptomatic. The symptomatic form presents with a sudden onset of high fever, severe retro-orbital headache, and flu-like symptoms. Atypical pneumonia (mild cough) and granulomatous hepatitis (elevated liver enzymes) are common.
- Chronic Q Fever:** Develops months to years after the acute infection, mainly in patients with pre-existing heart valve defects or immunosuppression. The most common manifestation is culture-negative endocarditis. Other forms include vascular (aneurysm) and bone infections.

#### 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	100 mg twice daily	Acute Q fever

##### **Inpatient:**

Drug	Dose	Note

<b>Doxycycline</b>	100 mg twice daily	
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**Icu:**

Drug	Dose	Note
<b>Doxycycline + Hydroxychloroquine</b>	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:**

- The rabies virus is transmitted through the saliva of an infected animal (e.g., dog, fox, bat) via a bite, typically into muscle tissue.
- The virus initially replicates in muscle cells, then enters peripheral nerves at the neuromuscular junction (NMJ).
- It travels via retrograde axonal transport within nerve cells towards the central nervous system (CNS), i.e., the spinal cord and brain.
- In the CNS, the virus replicates rapidly, causing severe, fatal encephalitis. Characteristic inclusions, known as Negri bodies, appear in infected nerve cells.
- From the brain, the virus spreads centrifugally along nerves to other organs, most importantly the salivary glands, which allows for further transmission.

**Virulence Factors:**

- Neurotropism
- Immune evasion

**Clinical Features:**

- Incubation: 1-3 months (days to years)
- Onset: Acute neurological after prodrome

**Symptoms:**

- **Prodromal Stage:** The first signs are non-specific: fever, headache, malaise. Pain, itching, or paresthesia at the bite site can be characteristic.
- **Acute Neurological Stage:** Two main forms exist. The "furious" (encephalitic) form (80%) involves agitation, confusion, hydrophobia (fear of water due to painful laryngeal spasms on attempting to swallow), and aerophobia (fear of drafts). The "dumb" (paralytic) form (20%) is characterized by ascending flaccid paralysis starting from the bite site.
- **Coma and Death:** Both forms ultimately progress to coma and death from respiratory/circulatory failure, usually within 7-10 days of symptom onset.

**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
<b>Post-exposure prophylaxis (PEP)</b>	IMMEDIATELY!	Life-saving!

**Inpatient:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Palliative sedation</b>	Symptomatic	In case of clinical rabies

**Icu:**

<b>Drug</b>	<b>Dose</b>	<b>Note</b>
<b>Milwaukee protocol</b>	Experimental	Not recommended routinely (unsuccessful)

**Targeted:**

No effective therapy after symptom onset.

**Supportive:**

- Sedation
- Analgesia
- Isolation

**Prevention:**

- PEP: Wound cleaning + Vaccine (days 0, 3, 7, 14) + 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: Tanners, Livestock farmers, Lab workers

**Pathomechanism:****Steps:**

- *Bacillus anthracis* spores can survive in the soil for decades. Infection occurs through entry of the spores: via the skin (cutaneous), inhalation, or ingestion (gastrointestinal).
- In the body, spores are taken up by macrophages, where they germinate into vegetative bacteria and then travel to the lymph nodes.
- The bacteria have two main virulence factors: an antiphagocytic capsule that protects them from the immune system, and a three-component exotoxin.
- The components of the anthrax toxin are: Protective Antigen (PA), which binds to cells; Edema Factor (EF), which causes edema; and Lethal Factor (LF), which causes cell death and disrupts the cytokine response.

- The toxins induce massive tissue necrosis, edema, hemorrhage, and systemic shock, which is responsible for the high mortality of the disease.

### 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%):** An itchy papule appears at the site of entry, which develops into a vesicle and then a painless ulcer with a black center (eschar), surrounded by characteristic non-inflammatory edema. Without treatment, mortality is 20%.
- Inhalational (Pulmonary) Anthrax:** Has a biphasic course. Initially, mild, flu-like symptoms (fever, cough). After 1-3 days, a sudden deterioration occurs: high fever, shortness of breath, shock. A characteristic finding on chest CT is mediastinal widening (hemorrhagic mediastinitis). Almost always fatal without treatment.
- Gastrointestinal Anthrax:** Develops after consuming infected meat. It causes nausea, vomiting, bloody diarrhea, and severe abdominal pain. High mortality rate.

### 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
<b>Ciprofloxacin</b>	500 mg twice daily	Cutaneous anthrax (60 days if bioterror suspicion)
<b>Doxycycline</b>	100 mg twice daily	Alternative

**Inpatient:**

Drug	Dose	Note
<b>Ciprofloxacin + Meropenem + Linezolid</b>	IV combination	Inhalational/systemic (antitoxin also given)

**Icu:**

Drug	Dose	Note
<b>Raxibacumab</b>	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

**Brucellosis (Malta Fever)**

**Pathogen:** Bacterium - *Brucella spp.* (*melitensis*, *abortus*, *suis*) (Gram-negative)

**Epidemiology:**

- Incidence: Endemic in Mediterranean, Middle East
- Seasonality: Spring-Summer

- Transmission: Direct contact, inhalation, unpasteurized dairy products
- Risk Groups: Veterinarians, Shepherds, Abattoir workers, Consumers of unpasteurized dairy

### **Pathomechanism:**

#### Steps:

- Entry: Bacteria enter through broken skin, conjunctiva, respiratory tract, or GI tract.
- Phagocytosis: Macrophages engulf them, but bacteria survive and replicate intracellularly.
- Dissemination: Infected macrophages travel to regional lymph nodes and bloodstream (bacteremia).
- Organ involvement: Granulomas form in reticuloendothelial organs (liver, spleen, bone marrow, lymph nodes).

#### Virulence Factors:

- LPS (smooth)
- T4SS secretion system
- Intracellular survival

#### **Clinical Features:**

- Incubation: 2-4 weeks (1 week to months)
- Onset: Gradual or sudden

#### Symptoms:

- **Undulant Fever:** Wavelike fever pattern (low in morning, high in afternoon) with profuse, moldy-smelling sweat.
- **Musculoskeletal:** Joint pain (arthralgia), back pain (sacroiliitis), myalgia.
- **Constitutional:** Fatigue, headache, depression, weight loss.

#### Physical Exam:

- Hepatomegaly
- Splenomegaly
- Lymphadenopathy
- Spinal tenderness

#### Complications:

- Osteomyelitis (vertebral)
- Endocarditis
- Neurobrucellosis
- Epididymo-orchitis

#### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CBC	Leukopenia, relative lymphocytosis	-

Liver enzymes	Mild elevation	Granulomatous hepatitis
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**Imaging:**

- **Spine MRI:** Spondylodiscitis (*If back pain present*)

**Microbiology:**

- **Blood culture:** Brucella spp. (*Slow growth (up to 3-4 weeks), notify lab!*)
- **Serology (Wright):** Titer  $\geq 1:160$  or 4x rise (*Standard diagnosis*)

**Differential Diagnosis:**

- **Typhoid fever:** Rose spots, bradycardia
- **Tuberculosis:** Respiratory symptoms, sputum
- **Malaria:** Periodicity, travel

**Therapy:****Outpatient:**

Drug	Dose	Note
<b>Doxycycline + Rifampicin</b>	100mg BID + 600-900mg QD PO	Standard therapy

**Targeted:**

Doxycycline + Rifampicin (6 weeks). Alternative: Doxycycline + Streptomycin (2-3 weeks).

Neurobrucellosis/Endocarditis: Doxy + Rif + Ceftriaxone/Cotrimoxazole (months).

**Supportive:**

- Symptomatic treatment

**Prevention:**

- Pasteurization of milk
- Protective gear
- Animal vaccination

## ⚡ 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), Immunocompromised, Patients with chronic diseases, Patients with invasive devices

## **Pathomechanism:**

### Steps:

- During infection, pathogen-associated molecular patterns (PAMPs) are recognized by receptors of the innate immune system (e.g., Toll-like receptors), triggering a massive inflammatory response.
- A pro-inflammatory cytokine storm (TNF- $\alpha$ , IL-1, IL-6) develops, leading to systemic endothelial activation and damage, increasing vascular permeability (capillary leakage).
- Activation of the coagulation cascade and inhibition of fibrinolysis lead to disseminated intravascular coagulation (DIC) and formation of microthrombi.
- Microcirculatory dysfunction, tissue hypoxia, and mitochondrial dysfunction ultimately lead to multiple organ dysfunction syndrome (MODS) and death.

### Clinical Features:

- Endotoxin (LPS)
- Superantigens
- Exotoxins
- Capsule

### **Clinical Features:**

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

### Symptoms:

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

### Physical Exam:

- Fever or hypothermia
- Tachycardia ( $>90/\text{min}$ )
- Tachypnea ( $>20/\text{min}$ )
- Prolonged capillary refill time ( $>3 \text{ sec}$ )
- 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
<b>Antibiotics</b>	Broad-spectrum IV	After taking blood cultures. Source-dependent choice (e.g., Pip/Tazo, Meropenem).
<b>Fluid resuscitation</b>	30 ml/kg crystalloid	If hypotension or lactate $\geq 4$ mmol/L.

**Icu:**

Drug	Dose	Note
<b>Norepinephrine</b>	Maintain MAP $>65$ mmHg	First choice vasopressor.
<b>Vasopressin</b>	max 0.03 U/min	Can be added to norepinephrine to reduce dose or if dose is high.
<b>Hydrocortisone</b>	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:**

- During local infection or colonization by *Staphylococcus aureus* or *Streptococcus pyogenes*, exotoxins (e.g., TSST-1, SpeA) are produced.
- These toxins act as superantigens: binding to MHC II molecules on antigen-presenting cells and T-cell receptors, they non-specifically activate up to 20% of T-cells (normally <0.01%).
- This massive T-cell activation leads to an uncontrolled cytokine storm (TNF- $\alpha$ , IL-1, IL-6).
- The cytokines cause severe capillary leakage, vasodilation, and hypotension, rapidly leading to shock and 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
<b>None</b>	-	Immediate ICU admission!

**Inpatient:**

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

**Icu:**

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

**Targeted:**

Staph (MSSA): Flucloxacillin (Cefazolin) + Clindamycin; MRSA: Vancomycin + Clindamycin.  
 Strep: Penicillin G + Clindamycin (toxin inhibition). IVIG in severe cases. Source control (tampon removal, surgical exploration) is essential!

**Supportive:**

- Massive fluid resuscitation
- Ventilation
- Dialysis
- Wound care

**Prevention:**

- Tampon hygiene (frequent change)
- Wound disinfection

## Fungal Infections

### **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 antibiotics, 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%)
- **Hepatosplenic 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
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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
<b>None</b>	-	Hospital treatment

**Inpatient:**

Drug	Dose	Note
<b>Fluconazole</b>	800 mg loading, then 400 mg	Only for stable patients with no prior azole exposure

**Icu:**

Drug	Dose	Note
<b>Echinocandin (Caspofungin)</b>	70 mg loading, then 50 mg	First choice in unstable/severe patients

**Targeted:**

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

**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
<b>None</b>	-	Hospital treatment

#### **Inpatient:**

Drug	Dose	Note
<b>Voriconazole</b>	6 mg/kg followed by 4 mg/kg IV/PO	GOLD STANDARD (therapeutic drug monitoring required!)

#### **Icu:**

Drug	Dose	Note
<b>Isavuconazole</b>	200 mg IV/PO	Fewer side effects
<b>Liposomal Amphotericin B</b>	3-5 mg/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

## 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: Travelers to tropical regions, People living in endemic areas

#### Pathomechanism:

##### Steps:

- After the bite of an infected mosquito, the virus infects dendritic cells and monocytes in the skin, then migrates to lymph nodes.
- Entry: After the bite of an infected mosquito, the virus infects dendritic cells and monocytes in the skin, then migrates to lymph nodes.
- Viremia: The virus multiplies and enters the bloodstream (viremia), causing high fever and systemic symptoms.
- ADE Phenomenon: In secondary infection, if the patient has previously encountered another serotype, Antibody-Dependent Enhancement (ADE) occurs: non-neutralizing antibodies facilitate virus entry into cells, leading to increased replication.
- Consequence: This triggers a severe cytokine storm and increased vascular permeability (capillary leakage), leading to plasma loss, hemoconcentration, and shock.

##### Virulence Factors:

- NS1 protein
- ADE (Antibody-Dependent Enhancement)

#### Clinical Features:

- Incubation: 4-10 days
- Onset: Sudden

#### Symptoms:

- **Febrile Phase:** Sudden onset of high fever ( $40^{\circ}\text{C}$ ), accompanied by severe headache and retroorbital pain.
- **"Breakbone Fever":** Extremely severe muscle and joint pain (myalgia, arthralgia) making movement difficult.

- **Critical Phase:** May occur when fever subsides (days 3-7). Warning signs: intense abdominal pain, persistent vomiting, fluid accumulation (ascites, pleural effusion), mucosal bleeding, lethargy or restlessness.
- **Rash:** Maculopapular rash appearing after fever, often with "white islands in a red sea" pattern.

### Physical Exam:

- Fever
- Facial flushing
- Positive tourniquet test (capillary fragility)
- Hepatomegaly
- Hemorrhagic signs (petechiae, ecchymosis)
- Signs of shock (cold extremities, weak pulse) in critical phase

### Complications:

- Dengue hemorrhagic fever (DHF)
- Dengue shock syndrome (DSS)
- Severe organ impairment (liver, kidney, heart)

### **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
<b>Supportive</b>	-	Fluids, antipyretics (Paracetamol). NSAIDs are contraindicated (bleeding risk)!

#### Targeted:

No specific antiviral agent.

#### Supportive:

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

#### Prevention:

- Mosquito repellent

- Vaccine (Qdenga)

## Zika Virus Infection

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

### Epidemiology:

- Incidence: Epidemic
- Seasonality: Mosquito season
- Transmission: Aedes mosquito, sexual, vertical
- Risk Groups: Pregnant women (risk of fetal defects), Travelers

### Pathomechanism:

#### Steps:

- Entry: The virus enters via mosquito bite, sexual route, or vertically. Skin cells (keratinocytes, dendritic cells) are infected first.
- Spread: The virus spreads to lymph nodes and bloodstream (viremia). It can cross the blood-brain barrier and the placental barrier.
- Neurotropism: It has strong neurotropism: during fetal development, it specifically infects and destroys neural progenitor cells, leading to brain developmental defects (microcephaly).
- Complication: In adults, it can trigger Guillain-Barré syndrome through an autoimmune mechanism.

#### Virulence Factors:

- Neurotropism
- Placental permeability

#### **Clinical Features:**

- Incubation: 3-14 days
- Onset: Mild

#### Symptoms:

- **Asymptomatic:** About 80% of infected individuals show no symptoms.
- **Rash and Itching:** The most common symptom is a maculopapular rash, often itchy, spreading from face to trunk.
- **Fever and Pain:** Low-grade fever, joint pain (especially small joints of hands/feet), muscle pain, and headache.
- **Conjunctivitis:** Non-purulent conjunctivitis (red eyes).

#### Physical Exam:

- Diffuse maculopapular rash
- Non-purulent conjunctivitis
- Joint swelling (hands/feet)
- Low-grade fever

**Complications:**

- Guillain-Barré syndrome (adults)
- Congenital Zika syndrome (fetal microcephaly, brain calcifications, vision/hearing loss)

**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 practices (virus can persist 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:**

- Entry: After mosquito bite, the virus replicates in the skin, then enters the bloodstream.
- Tropism: It infects tissues widely but shows specific tropism for joint capsules, muscles, and skin fibroblasts.

- Inflammation: It triggers an intense inflammatory response in joints (infiltration of monocytes, macrophages), causing acute arthritis.
- Chronicity: The virus or antigens can persist in joint tissues for months, maintaining chronic, rheumatoid arthritis-like complaints.

### Virulence Factors:

- Joint tropism

### **Clinical Features:**

- Incubation: 3-7 days
- Onset: Sudden

### Symptoms:

- **Acute Phase:** Sudden onset of high fever ( $>39^{\circ}\text{C}$ ) and excruciating, severe joint pain (polyarthralgia), often causing incapacitation. The joint pain is usually symmetrical and affects distal joints.
- **Rash:** Maculopapular rash on trunk and limbs (approx. 50%).
- **Chronic Phase:** In a significant proportion of patients (30-60%), joint pain and stiffness may recur or persist for months or years, significantly impairing quality of life.

### Physical Exam:

- High fever
- Symmetrical joint swelling and tenderness (hands, wrists, ankles)
- Tenosynovitis
- Maculopapular rash

### Complications:

- Chronic, disabling arthritis
- Rarely: myocarditis, encephalitis, hepatitis

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CBC	Lymphopenia	-

#### Microbiology:

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

### **Therapy:**

#### **Outpatient:**

Drug	Dose	Note
<b>Supportive</b>	-	NSAIDs may be used (once Dengue is excluded)

#### Targeted:

None.

**Supportive:**

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

**Prevention:**

- Mosquito protection
- Vaccine (Ixchiq - FDA approved)

## Emerging Pathogens

### **Mpox (Monkeypox)**

**Pathogen:** Virus - *Mpox virus* (MPXV)

**Epidemiology:**

- Incidence: Global outbreak (2022–), endemic in Central and West Africa
- Seasonality: None
- Transmission: Close skin-to-skin contact, respiratory droplets, fomites, zoonotic (rodents)
- Risk Groups: MSM (Men who have sex with men), Healthcare workers, Household contacts

**Pathomechanism:****Steps:**

- Entry: Virus enters through broken skin, mucous membranes, or respiratory tract.
- Replication: Initial replication occurs at the inoculation site and in regional lymph nodes.
- Viremia: The virus spreads via the bloodstream to the skin and internal organs.
- Lesion formation: Viral replication in the skin causes inflammation, necrosis, and characteristic pox-like lesions (macule-papule-vesicle-pustule-scab).

**Virulence Factors:**

- Immunomodulatory proteins (host immune evasion)

**Clinical Features:**

- Incubation: 5–21 days
- Onset: Acute

**Symptoms:**

- **Prodrome:** Fever, intense headache, lymphadenopathy, back pain, myalgia, and intense asthenia.
- **Lymphadenopathy:** Distinctive feature (cervical, inguinal), distinguishing it from smallpox and chickenpox.
- **Rash:** Appears 1-3 days after fever. Starts on face, spreads centrifugally (palms/soles involved). Stages: Macule → Papule → Vesicle → Pustule (umbilicated) → Scab. Lesions are often painful, then itchy.

- **Mucosal symptoms:** Oral, genital, and perianal lesions. Proctitis (rectal pain) is common in sexual transmission.

#### Physical Exam:

- Centrifugal distribution of rash (including palms and soles)
- Tender lymphadenopathy
- Anogenital lesions
- Fever

#### Complications:

- Secondary bacterial infection
- Bronchopneumonia
- Sepsis
- Encephalitis
- Keratitis (leading to corneal scarring)

#### **Diagnostics:**

##### Laboratory:

Test	Finding	Interpretation
CBC	Non-specific (leukocytosis or leucopenia)	-

##### Microbiology:

- **NAAT (PCR):** MPXV DNA (*Gold standard (swab from lesion base/roof)*)
- **Electron microscopy:** Poxvirus morphology (*Research/Public health labs*)

#### **Therapy:**

##### **Outpatient:**

Drug	Dose	Note
Supportive care	-	Analgesia, hydration, wound care, strict isolation

##### Targeted:

Tecovirimat (TPOXX) indicated for severe disease or immunocompromised patients.

##### Supportive:

- Analgesics (NSAIDs/Opioids)
- Fluid resuscitation

##### Prevention:

- Vaccination (JYNNEOS - modified vaccinia Ankara)
- Infection control
- Contact tracing

## Nipah Virus (NiV)

**Pathogen:** Virus - *Nipah virus* (NiV)

### Epidemiology:

- Incidence: Sporadic outbreaks (South and Southeast Asia)
- Seasonality: December–May (Bangladesh)
- Transmission: Direct contact with bats (*Pteropus*), consumption of contaminated date palm sap, pigs (intermediate host), human-to-human
- Risk Groups: Pig farmers, Date palm sap collectors/consumers, Close contacts of cases

### Pathomechanism:

#### Steps:

- Entry: Ingestion of contaminated food (e.g., date palm sap) or direct contact with infected animals (pigs, bats).
- Dissemination: The virus enters the bloodstream (viremia), either free or bound to leukocytes.
- Vasculitis: It infects endothelial cells (via Ephrin-B2 receptor), causing systemic vasculitis, thrombosis, and tissue ischemia.
- Tropism: High affinity for the CNS (crossing the blood-brain barrier) and lungs, causing severe inflammation and necrosis.

### Virulence Factors:

- Fusion (F) and Attachment (G) proteins
- Interferon antagonists (P/V/W proteins)

### Clinical Features:

- Incubation: 4–14 days (up to 45 days recorded)
- Onset: Acute

### Symptoms:

- **Prodrome:** Fever, headache, myalgia, sore throat, and vomiting.
- **Respiratory symptoms:** Cough, dyspnea, progressing to atypical pneumonia and acute respiratory distress syndrome (ARDS).
- **Encephalitis:** Dizziness, altered consciousness, rapidly progressing to coma (within 24–48h). Brainstem signs (areflexia, hypotonia) are common.

### Physical Exam:

- Hyperpyrexia
- Nuchal rigidity
- Altered mental status (GCS)
- Segmental myoclonus
- Hyporeflexia

### Complications:

- Fulminant encephalitis
- ARDS

- Relapsed/Late-onset encephalitis
- Death

### Diagnostics:

#### Laboratory:

Test	Finding	Interpretation
CBC	Thrombocytopenia, leukopenia	-

#### Imaging:

- **Brain MRI:** Small, confluent T2-hyperintense lesions (*Vascular encephalitis*)

#### Microbiology:

- **RT-PCR:** NiV RNA (throat swab, blood, urine, CSF) (*Diagnostic during acute phase*)
- **Serology (ELISA):** IgM/IgG seroconversion (*Confirmatory*)

#### Therapy:

#### Outpatient:

Drug	Dose	Note
N/A	-	Medical emergency; requires immediate isolation and ICU care

#### Targeted:

No approved antiviral. Monoclonal antibody (m102.4) and Ribavirin (limited evidence).

#### Supportive:

- Mechanical ventilation
- Seizure management
- Correction of electrolyte imbalances

#### Prevention:

- Avoid Pteropus bat habitats
- Boil raw date palm sap
- Culling of infected livestock
- Standard, contact, and droplet precautions



## 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, Immunocompromised

### **Pathomechanism:**

#### Steps:

- Entry and Replication: The virus enters via respiratory epithelium and immune cells (CD150 receptor), replicating in regional lymph nodes.
- Viremia: Following primary viremia, the virus multiplies in the reticuloendothelial system (liver, spleen, bone marrow), leading to a massive secondary viremia that spreads to skin, conjunctiva, and respiratory tract.
- Tissue Damage: Fusion of infected cells creates Warthin-Finkeldey giant cells. The rash is a result of the T-cell immune response against virus-infected endothelial cells.
- Immunosuppression: The virus causes transient but severe immunosuppression (anergy) lasting weeks to months, predisposing to secondary bacterial infections (e.g., pneumonia, otitis).

#### Virulence Factors:

- Hemagglutinin
- Fusion protein

#### **Clinical Features:**

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

#### Symptoms:

- **Prodrome (3C):** High fever ( $>40^{\circ}\text{C}$ ), Cough, Coryza, and Conjunctivitis are present in almost 100% of cases before the rash appears.
- **Koplik spots:** Pathognomonic salt-grain-like white spots on the buccal mucosa (60-70%), appearing before the rash and fading within 1-2 days.
- **Rash:** Maculopapular rash starting behind the ears, spreading to the face, trunk, and limbs (cranio-caudal). Lesions often become confluent and fade in the order of appearance, leaving brownish pigmentation and fine desquamation.

#### Physical Exam:

- Koplik spots
- Exanthema
- Fever
- Conjunctivitis

#### Complications:

- Otitis media
- Giant cell pneumonia
- 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:**

- The virus enters the upper respiratory tract via droplet transmission and replicates in epithelial cells.
- Viremia spreads the virus to target organs: salivary glands (mainly parotid), CNS, testes, pancreas, and ovaries.
- It causes swelling, interstitial edema, and lymphocytic infiltration in the affected glands.

**Virulence Factors:**

- -

**Clinical Features:**

- Incubation: 16-18 days
- Onset: Acute

**Symptoms:**

- **Parotitis:** Painful swelling of the parotid gland (95% of symptomatic cases), initially unilateral, often becoming bilateral. The earlobe is lifted, and chewing is painful.

- **Fever:** Moderate fever, headache, and myalgia during the prodromal phase.
- **Orchitis:** Testicular inflammation (20-30% of postpubertal males), characterized by painful swelling, rarely leading to sterility.

#### 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:

- Entry: The virus enters through the nasopharyngeal mucosa, migrates to regional lymph nodes, and replicates.
- Viremia: The virus spreads via the bloodstream to the skin and joints. The rash and joint symptoms are immune complex-mediated.
- Teratogenicity: During pregnancy, the virus crosses the placenta, inhibits mitosis in fetal cells, and induces apoptosis, leading to severe congenital defects (Congenital Rubella Syndrome).

### Virulence Factors:

- -

### **Clinical Features:**

- Incubation: 14-21 days
- Onset: Mild

### Symptoms:

- **Rash:** Fine, pink maculopapular rash starting on the face and spreading rapidly downwards, disappearing without a trace within 3 days.
- **Lymphadenopathy:** Characteristic painful swelling of occipital and retroauricular lymph nodes.
- **Arthralgia/Arthritis:** Joint pain or inflammation, common in adult women (up to 70%).
- **Forchheimer spots:** Petechiae on the soft palate (non-specific but can occur).

### 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:

- Colonization: *Streptococcus pyogenes* (GAS) colonizes the pharynx via droplet transmission, causing pharyngitis.
- Toxin Production: The bacterium produces erythrogenic toxin (superantigen) if infected by a bacteriophage.
- Systemic Effect: The toxin enters the bloodstream, causing generalized capillary dilation and an inflammatory skin reaction in individuals lacking antitoxin immunity.

#### Virulence Factors:

- Erythrogenic toxin (SpeA, B, C)

### Clinical Features:

- Incubation: 2-5 days
- Onset: Sudden

#### Symptoms:

- **Sore throat:** Sudden onset of severe sore throat, difficulty swallowing, often accompanied by vomiting.
- **Fever:** High fever and chills.
- **Rash:** Diffuse red rash with a "sandpaper" texture that blanches on pressure. Darker lines appear in skin folds (Pastia lines). Desquamation (peeling) of palms and soles is characteristic during recovery.
- **Tongue:** Initially white coated ("white strawberry tongue"), becoming red and papillated ("red strawberry tongue") after the coating peels off.

#### Physical Exam:

- Pharyngeal hyperemia
- Strawberry 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
<b>Penicillin V</b>	PO	First choice
<b>Amoxicillin</b>	PO	Alternative
<b>Macrolide (e.g., Azithromycin)</b>	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:**

- EBV spreads via saliva and infects the epithelial cells of the oropharynx.
- It subsequently infects B-lymphocytes, establishing latent infection and immortalizing them.
- The body mounts a strong cellular immune response (CD8+ T-cells), leading to atypical lymphocytes ("virocytes") in the blood and enlargement of lymphoid organs.

**Virulence Factors:**

- LMP, EBNA proteins

**Clinical Features:**

- Incubation: 4-6 weeks
- Onset: Gradual

**Symptoms:**

- **Sore throat:** Severe pharyngitis, often with pseudomembranous exudate on the tonsils.
- **Fever:** Prolonged fever, lasting up to 10-14 days.
- **Lymphadenopathy:** Generalized, symmetrical lymph node swelling, particularly affecting the posterior cervical chain.
- **Fatigue:** Pronounced weakness and fatigue that can persist 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

## Mononucleosis Syndrome (CMV, Toxoplasma, HIV)

**Pathogen:** Mixed - *Cytomegalovirus (CMV), Toxoplasma gondii, HIV (-)*

### Epidemiology:

- Incidence: Common, heterophile-negative mononucleosis cases
- Seasonality: None
- Transmission: Body fluids (CMV, HIV), fecal-oral/meat (Toxo)
- Risk Groups: Sexually active young adults (CMV, HIV), Cat owners/raw meat consumers (Toxo)

### Pathomechanism:

#### Steps:

- Pathogens (CMV, Toxoplasma, HIV) cause systemic infection triggering an immune response.
- Similar to EBV, they activate T-lymphocytes (atypical lymphocytes), but do not immortalize B-cells (unlike EBV).
- Symptoms result from the host immune response.

#### Virulence Factors:

- -

### Clinical Features:

- Incubation: Variable (CMV 20-60 days, HIV 2-4 weeks, Toxo 5-23 days)
- Onset: Gradual

#### Symptoms:

- **Fever:** Prolonged fever (can last weeks), often the leading symptom.
- **Lymphadenopathy:** Generalized lymph node swelling, but less pronounced than in EBV.
- **Absence/Mild Pharyngitis:** Unlike EBV, sore throat and tonsillitis are often absent or very mild (except acute HIV, where ulcers may occur).
- **Hepatomegaly/Splenomegaly:** Can occur, but rarer and milder than in EBV.

#### Physical Exam:

- Fever
- Mild lymphadenopathy
- Exanthema (common in HIV)
- Absence of pharyngitis (CMV/Toxo)

#### Complications:

- Hepatitis
- Pneumonia
- Guillain-Barré syndrome
- Congenital infection (in pregnancy!)

**Diagnostics:****Laboratory:**

Test	Finding	Interpretation
CBC	Lymphocytosis, atypical mononuclear cells	Similar to EBV
Liver enzymes	Mild elevation	Common

**Microbiology:**

- **Monospot test:** NEGATIVE (*Key difference from EBV!*)
- **CMV serology:** IgM positive (*CMV confirmation*)
- **Toxoplasma serology:** IgM positive (*Toxoplasma confirmation*)
- **HIV test:** Ag/Ab positive / PCR (*Acute HIV exclusion mandatory!*)

**Differential Diagnosis:**

- **EBV Mononucleosis:** Severe pharyngitis, Monospot positive
- **Streptococcal pharyngitis:** Purulent tonsils, leukocytosis (not lymphocytosis)
- **Lymphoma:** Fever, weight loss, night sweats, fixed lymph nodes

**Therapy:****Outpatient:**

Drug	Dose	Note
Supportive	-	Symptomatic treatment

**Targeted:**

CMV/Toxo: usually no treatment in immunocompetent. HIV: Start ART. Special treatment in pregnancy!

**Prevention:**

- Hygiene
- Safe sex
- Cooking meat thoroughly

## 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:**

- HHV-6 spreads via droplets and establishes lifelong latent infection.
- During primary infection, the virus replicates in salivary glands and lymphocytes.
- Viremia causes high fever, and the rash appears via an immune-mediated mechanism when the fever abruptly subsides.

### Virulence Factors:

- -

### **Clinical Features:**

- Incubation: 5-15 days
- Onset: Sudden

### Symptoms:

- **High fever:** Sudden onset of high fever (39-40°C) lasting 3-5 days, while the child's general condition remains surprisingly good.
- **Rash:** Pink, maculopapular rash appears on the trunk and then the neck simultaneously with or immediately after the fever drops.
- **Nagayama spots:** Ulcers or papules on the soft palate and 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, Immunocompromised, Pregnant women, Adults (more severe)

### Pathomechanism:

#### Steps:

- Entry: VZV enters through the respiratory tract and replicates in regional lymph nodes.
- Viremia: Following primary viremia, the virus replicates in the liver and spleen, then a secondary T-cell associated viremia spreads it to the skin and mucous membranes.
- Skin Lesions: The virus infects epithelial cells in the skin, causing intraepidermal vesicles and necrosis.
- Latency: After infection, the virus retreats along sensory nerves to the dorsal root ganglia, where it remains latent.

### Virulence Factors:

- -

### Clinical Features:

- Incubation: 10-21 days
- Onset: Sudden

### Symptoms:

- **Rash:** Itchy, polymorphic rash (macules, papules, vesicles, crusts) appearing in waves, so all stages are visible simultaneously ("starry sky"). Fresh vesicles resemble "a dewdrop on a rose petal".
- **Fever:** Moderate fever accompanying the appearance of the rash.
- **Enanthema:** Painful vesicles on the oral mucosa.

### 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, immunocompromised).

#### Prevention:

- Varicella vaccine (mandatory)

## Shingles (Herpes Zoster)

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

### Epidemiology:

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

### Pathomechanism:

#### Steps:

- Latent VZV reactivates in sensory ganglia (e.g., due to immunosuppression or aging).
- The virus travels along sensory nerve axons to the skin.
- It causes inflammation, pain, and a vesicular rash in the corresponding dermatome.

#### Virulence Factors:

- -

### Clinical Features:

- Incubation: -
- Onset: Starts with pain

#### Symptoms:

- **Pain:** Prodromal burning, shooting pain in the affected dermatome, which may precede the rash by days.
- **Rash:** Grouped, painful vesicles on an erythematous base, strictly unilateral and not crossing the midline.

#### 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
<b>Acyclovir</b>	5x800mg PO	Started within 72 hours
<b>Valacyclovir</b>	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:

- HSV-1 infects mucous membranes or broken skin via direct contact.
- Replication in epithelial cells causes cell death, vesicle formation, and ulcers.
- The virus enters sensory nerve endings and travels retrogradely to ganglia, where it becomes latent.

## Virulence Factors:

- -

## **Clinical Features:**

- Incubation: 2-12 days
- Onset: Sudden

## Symptoms:

- **Gingivostomatitis:** Primary infection in young children. High fever, painful, swollen, bleeding gums, and numerous ulcers in the mouth. Eating/drinking is painful.
- **Herpes labialis:** Recurrent infection (cold sore), preceded by prodromal tingling.
- **Eczema herpeticum:** Superinfection of atopic dermatitis, a severe condition with extensive vesicular rash and fever.

## 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<sub>0</sub>=12-17)
- Risk Groups: Infants (<6 months), Unvaccinated children, Adults (milder)

### Pathomechanism:

#### Steps:

- Adhesion: *Bordetella pertussis* adheres to ciliated respiratory epithelial cells (filamentous hemagglutinin).
- Toxin Effect: It produces toxins (pertussis toxin, tracheal cytotoxin) that paralyze cilia, inhibit mucociliary clearance, and cause local inflammation and necrosis.
- Systemic Effect: Pertussis toxin inhibits lymphocyte extravasation into lymph nodes, leading to extreme lymphocytosis in the blood.

#### 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). This is the most contagious phase but difficult to distinguish from a common cold.
- **Paroxysmal phase:** Paroxysmal, spasmodic coughing fits followed by a deep, inspiratory "whoop". Vomiting often occurs after the fit. Apnea may be the leading symptom in infants.
- **Convalescent phase:** Cough slowly subsides but may recur for months ("100-day cough").

#### Physical Exam:

- Coughing fits (whoop characteristic in children)
- Apnea (infants)
- Lymphocytosis (>20,000/ $\mu$ 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 ( $>20,000/\mu\text{L}$ )	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 contraindicated (mucus retention!)

**Prevention:**

- DTP vaccine (mandatory, 3+1 doses)
- Adult booster
- Vaccination of pregnant women in 3rd trimester

## Hand, Foot, and Mouth Disease (HFMD)

**Pathogen:** Virus - *Coxsackie A16, Enterovirus 71* (ssRNA, Picornaviridae)

**Epidemiology:**

- Incidence: Common in childhood (<5-10 years)
- Seasonality: Summer-Autumn
- Transmission: Fecal-oral, droplet infection, vesicle fluid
- Risk Groups: Young children, Communities

**Pathomechanism:****Steps:**

- The virus enters the oral cavity and replicates in the lymphoid tissues of the pharynx and intestine.
- Viremia spreads the virus to the skin and mucous membranes.
- It causes inflammation and vesicle formation on the skin and oral mucosa.

### Virulence Factors:

- 

### **Clinical Features:**

- Incubation: 3-7 days
- Onset: Sudden

### Symptoms:

- Prodrome:** Fever, sore throat, anorexia, malaise.
- Enanthema:** Painful vesicles and ulcers on the tongue, buccal mucosa (herpangina-like).
- Exanthema:** Non-itchy vesicles or papules with a red halo on palms, soles, and possibly the diaper area.

### Physical Exam:

- Vesicles on palms/soles
- Ulcers in mouth
- Fever

### Complications:

- Dehydration (painful swallowing)
- Nail shedding (onychomadesis - weeks later)
- Aseptic meningitis (rare, EV71)
- Encephalitis (EV71)

### **Diagnostics:**

#### Laboratory:

Test	Finding	Interpretation
CBC	Normal	-

### Microbiology:

- Clinical picture:** Characteristic (*Diagnostic*)
- PCR:** Enterovirus RNA (throat, stool) (*In severe cases*)

### **Therapy:**

#### **Outpatient:**

Drug	Dose	Note
Supportive	-	Pain relief, fluids

### Targeted:

None.

### Prevention:

- Hygiene
- Hand washing

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