



Viral Infections - Comprehensive Medical Reference Guide

General Overview of Viral Infections

Viral infections represent a diverse category of diseases caused by obligate intracellular parasites known as viruses. Unlike bacteria and other microorganisms, viruses lack the cellular machinery necessary for independent metabolism and reproduction. They consist of genetic material (DNA or RNA) enclosed in a protein coat (capsid), and in some cases, an additional lipid envelope. Viruses can only replicate by hijacking the cellular machinery of living host cells, forcing them to produce new viral particles.

This fundamental dependency on host cells makes viral infections uniquely challenging from a therapeutic perspective and underscores the critical importance of prevention strategies. The relationship between viruses and their hosts ranges from acute self-limiting infections to chronic persistent infections, latent infections with potential for reactivation, and oncogenic transformations leading to cancer.



Critical Characteristics of Viral Infections

Antibiotic Ineffectiveness:

Antibiotics, which target bacterial cell walls, protein synthesis, or metabolic pathways unique to bacteria, are completely ineffective against viral infections. The inappropriate prescription of antibiotics for viral illnesses represents a major driver of antimicrobial resistance and exposes patients to unnecessary adverse effects without therapeutic benefit.

Treatment Approaches:

- **Supportive care** remains the cornerstone for most viral infections, focusing on symptom management, maintenance of hydration, nutritional support, and allowing the immune system to clear the infection
- **Antiviral medications** are available for specific viral infections, targeting various stages of viral replication including entry, uncoating, nucleic acid synthesis, or viral release
- **Immunomodulatory therapies** may be employed in severe cases to manage excessive inflammatory responses

Prevention Strategies:

Prevention assumes paramount importance in viral disease control:

- **Vaccination** - The single most effective public health intervention for vaccine-preventable viral diseases
- **Hygiene measures** - Hand hygiene, respiratory etiquette, surface disinfection
- **Behavioral modifications** - Avoiding exposure during peak transmission periods, social distancing during outbreaks
- **Vector control** - For vector-borne viral diseases
- **Screening and safe practices** - For blood-borne viruses

Viral Classification and Transmission

By Nucleic Acid Type:

- **DNA viruses** - Include herpesviruses, poxviruses, adenoviruses, hepatitis B
- **RNA viruses** - Include influenza, coronaviruses, rhinoviruses, dengue, measles, hepatitis A and C

By Transmission Route:

- **Respiratory transmission** - Influenza, COVID-19, common cold, measles
 - **Fecal-oral transmission** - Hepatitis A, norovirus, rotavirus
 - **Blood-borne transmission** - Hepatitis B and C, HIV
 - **Vector-borne transmission** - Dengue, Zika, yellow fever
 - **Direct contact transmission** - Herpes simplex, varicella-zoster
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1. Common Cold (Viral Upper Respiratory Infection)

Comprehensive Overview

The common cold represents the most frequent acute illness affecting humans, with adults experiencing an average of 2-3 episodes annually and children suffering 6-8 episodes per year. This self-limiting viral infection of the upper respiratory tract is caused by more than 200 different virus strains, with rhinoviruses accounting for 30-50% of cases. Other causative agents include coronaviruses (10-15%), respiratory syncytial virus, parainfluenza viruses, adenoviruses, and enteroviruses.

Despite its mild nature, the common cold exerts enormous socioeconomic impact through lost productivity, school absences, and healthcare costs. The high frequency of infection results from the large number of causative viruses, antigenic variation, and the lack of durable cross-protective immunity. Understanding that the common cold is a viral syndrome rather than a single disease entity is essential for appropriate management and patient education.

The term "cold" derives from the historical but incorrect belief that exposure to cold weather causes the illness. In reality, seasonal variation in cold incidence

relates more to behavioral factors (indoor crowding, reduced humidity affecting viral survival and mucosal defenses) than temperature per se.

Clinical Manifestations and Symptoms

The common cold typically presents with a constellation of upper respiratory symptoms that develop gradually:

- **Nasal symptoms** - The hallmark of the common cold:
 - **Rhinorrhea** (runny nose) - Initial clear, watery nasal discharge that may become thicker and mucopurulent (yellow-green) as illness progresses due to inflammatory cell infiltration, not bacterial superinfection
 - **Nasal congestion** - Mucosal edema and increased mucus production causing sensation of blocked nasal passages, often worse at night
 - **Postnasal drip** - Mucus drainage into throat causing throat clearing and cough
- **Sneezing** - Repeated, sudden expulsions of air through nose and mouth, triggered by viral irritation of nasal mucosa. Serves as major transmission mechanism for virus spread
- **Sore throat (pharyngitis)** - Scratchy or painful sensation in throat, typically most prominent in first 1-2 days of illness, often the initial symptom. Results from viral invasion and inflammation of pharyngeal mucosa
- **Cough** - Usually develops after nasal symptoms, may be dry initially then productive. Results from postnasal drip irritation and lower respiratory tract inflammation. May persist for 1-2 weeks after other symptoms resolve
- **Mild fever or subfebrile temperature** - Low-grade fever (37.5-38°C or 99.5-100.4°F) more common in children than adults. High fever suggests alternative diagnosis such as influenza
- **Malaise and fatigue** - General feeling of being unwell, mild body aches, reduced energy. Usually mild compared to influenza
- **Headache** - Mild to moderate, often related to sinus congestion and inflammation
- **Watery eyes** - Mild conjunctival irritation may occur

Symptom Timeline:

- Days 1-2: Sore throat, sneezing, nasal discharge begins
- Days 2-4: Peak nasal symptoms, congestion, possible cough development
- Days 5-7: Gradual improvement, though cough may persist
- Days 7-10: Most symptoms resolved, though minor symptoms may linger up to 2 weeks

Detailed Stages of Infection

1. **Viral Entry and Attachment** - Virus-containing respiratory droplets from coughs or sneezes of infected individuals, or from contaminated hands touching nasal or conjunctival mucosa, deliver virus to upper respiratory epithelium. Rhinoviruses bind to ICAM-1 (intercellular adhesion molecule-1) receptors on nasal epithelial cells. The high concentration of these receptors in nasal passages explains the predominant nasal symptoms
2. **Local Viral Replication and Epithelial Invasion** - Following receptor binding and cellular entry (typically within 15 minutes of inoculation), viruses uncoat and release their genetic material. Viral RNA is translated using host ribosomes, and new viral particles are assembled. Infected cells release progeny viruses that infect adjacent epithelial cells. Peak viral shedding occurs 2-3 days after infection onset. Notably, viral replication is confined to upper respiratory tract epithelium - rhinoviruses replicate optimally at 33-35°C, the temperature of nasal passages, explaining their anatomic restriction
3. **Innate and Adaptive Immune Response Activation** -
 - Infected cells release inflammatory mediators (bradykinin, histamine, prostaglandins, interleukins) causing vasodilation, increased vascular permeability, mucus hypersecretion, and stimulation of pain receptors - the physiologic basis of symptoms
 - Surprisingly, many symptoms result more from immune response than direct viral damage
 - Neutrophils infiltrate nasal mucosa, accounting for color change of nasal discharge

- Interferon production provides antiviral defense
- Cellular and humoral immunity develop, though strain-specific and short-lived

4. Symptom Resolution and Recovery - Immune clearance of virus typically occurs within 7-10 days. Mucosal healing follows. Temporary epithelial damage may increase susceptibility to bacterial superinfection, though true bacterial complication is uncommon. Post-viral cough may persist due to airway hyperreactivity. No lasting immunity develops to other rhinovirus strains

Comprehensive Preventive Measures

- **Hand hygiene** - The single most effective preventive measure:
 - Frequent handwashing with soap and water for at least 20 seconds, particularly after touching face, before eating, after using restroom
 - Alcohol-based hand sanitizers ($\geq 60\%$ alcohol) effective when handwashing unavailable
 - Rhinoviruses survive on hands for hours and on environmental surfaces for days; hand hygiene interrupts transmission
- **Respiratory etiquette** -
 - Covering coughs and sneezes with tissue or elbow, not hands
 - Immediate disposal of used tissues
 - Avoiding touching face, especially nose and eyes, which are primary entry portals
- **Avoidance of close contact** -
 - Maintaining distance from individuals with active cold symptoms
 - Infected individuals staying home, especially during first 2-3 days when viral shedding peaks
 - Avoiding sharing personal items (cups, utensils, towels)
- **Environmental measures** -

- Regular disinfection of frequently touched surfaces (doorknobs, keyboards, phones)
- Adequate ventilation in indoor spaces
- Maintaining indoor humidity at 40-60% (very low humidity impairs mucosal defenses; very high humidity promotes viral survival)
- **Lifestyle factors -**
 - Adequate sleep (sleep deprivation impairs immune function)
 - Stress management (chronic stress associated with increased cold susceptibility)
 - Regular physical activity (moderate exercise enhances immune function)
 - Balanced nutrition
- **No proven benefit from -**
 - Vitamin C supplementation (may slightly reduce duration in some studies but doesn't prevent infection)
 - Echinacea, zinc supplements (conflicting evidence)
 - "Boosting" immune system with supplements

Diagnostic Approaches

- **Clinical diagnosis -**
 - The common cold is diagnosed clinically based on characteristic symptom pattern
 - Key features: gradual onset, predominant nasal symptoms, mild or absent fever, absence of severe systemic symptoms
 - No laboratory testing required for typical presentation
- **Differential diagnosis considerations** - Distinguishing cold from other respiratory infections:
 - **Influenza** - More abrupt onset, high fever, severe myalgia, prostration

- **Bacterial sinusitis** - Symptoms >10 days or worsening after initial improvement, severe facial pain, high fever, purulent discharge
 - **Streptococcal pharyngitis** - Severe sore throat without cough, fever, tonsillar exudates, cervical lymphadenopathy
 - **Allergic rhinitis** - Seasonal pattern, itching, no fever, response to antihistamines
 - **COVID-19** - Loss of taste/smell, more severe systemic symptoms, epidemiologic factors
- **Viral identification** -
 - PCR testing can identify specific viruses but is not clinically indicated for uncomplicated common cold
 - May be useful in research settings or in immunocompromised patients with severe or prolonged symptoms
 - Multiplex respiratory viral panels can detect multiple viruses simultaneously

First Aid and Immediate Care Measures

- **Adequate rest** -
 - Allowing body to direct energy toward immune function
 - Avoiding strenuous exercise during acute illness
 - Sleep promotes immune system recovery
 - Staying home reduces transmission to others
- **Fluid intake** -
 - Maintaining hydration with water, warm liquids (tea, broth, warm lemon water)
 - Warm fluids may provide symptomatic relief for sore throat
 - Adequate hydration keeps mucus thin and easier to clear
 - Avoid excessive caffeine and alcohol which have diuretic effects

- **Symptomatic relief measures -**

For nasal congestion:

- Saline nasal irrigation or spray - mechanically clears mucus and moisturizes nasal passages
- Steam inhalation - temporarily relieves congestion
- Oral decongestants (pseudoephedrine, phenylephrine) - reduce nasal congestion but caution in hypertension, heart disease
- Topical decongestant sprays (oxymetazoline) - effective but limit use to 3 days to avoid rebound congestion

For sore throat:

- Warm salt water gargles (1/4 to 1/2 teaspoon salt in 8 oz warm water)
- Throat lozenges or hard candies stimulating saliva production
- Honey (not in infants <12 months) - may soothe throat and suppress cough

For fever and aches:

- Acetaminophen (paracetamol) or ibuprofen for fever and discomfort
- Avoid aspirin in children due to Reye's syndrome risk

For cough:

- Honey (age >1 year)
- Increased humidity
- Cough suppressants (dextromethorphan) or expectorants (guaifenesin) - limited evidence of benefit

- **Warning signs requiring medical evaluation -**

- Symptoms lasting >10 days without improvement
- High fever (>38.5°C or 101.3°F) or fever lasting >3 days
- Severe headache, facial pain, or sinus pain
- Difficulty breathing or wheezing

- Severe throat pain preventing swallowing
- Symptoms in high-risk individuals (infants, elderly, immunocompromised)

Antiviral and Drug Information (Educational Reference)

No Specific Antiviral Treatment:

- No antiviral medications are approved or indicated for treatment of common cold
- The large number of causative viruses and their rapid mutation rate has prevented development of effective antivirals
- Multiple experimental antivirals have been studied (pleconaril, vapendavir, BTA798) but none have achieved clinical approval
- Cost-benefit analysis argues against antiviral development given the self-limiting nature and low complication rate

Antibiotics are NOT Indicated:

- Antibiotics provide no benefit for viral upper respiratory infections
- Inappropriate antibiotic use leads to:
 - Adverse effects (diarrhea, allergic reactions, *Clostridioides difficile* infection)
 - Increased antimicrobial resistance
 - Unnecessary cost
 - False reassurance delaying recognition of complications

When to Consider Antibiotics:

Only if bacterial superinfection develops:

- Acute bacterial sinusitis - symptoms >10 days or worsening after initial improvement
- Streptococcal pharyngitis - confirmed by rapid strep test or culture
- Acute otitis media - ear pain with bulging tympanic membrane
- Bacterial pneumonia - persistent fever, dyspnea, focal chest findings

Over-the-Counter Combination Products:

- Many contain multiple ingredients (decongestant, antihistamine, cough suppressant, analgesic)
- May provide symptomatic relief but increased risk of side effects and drug interactions
- Avoid in young children - American Academy of Pediatrics recommends against use in children <4 years
- Read labels carefully to avoid duplicate ingredients and inadvertent overdose

Complementary Approaches:

- **Zinc lozenges** - Some evidence for reduced duration if started within 24 hours, though studies inconsistent
 - **Vitamin C** - Prophylactic supplementation does not prevent colds in general population (may benefit in extreme physical stress); treatment may marginally reduce duration
 - **Probiotics** - Some evidence for prevention of respiratory infections
 - **Herbal remedies** (echinacea, elderberry) - Inconsistent evidence, not routinely recommended
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2. Influenza (Flu)

Comprehensive Overview

Influenza is an acute viral respiratory infection caused by influenza viruses that results in seasonal epidemics and occasional pandemics with substantial morbidity and mortality worldwide. Unlike the common cold, influenza is characterized by abrupt onset of systemic symptoms, significant prostration, and higher risk of complications, particularly in vulnerable populations. The disease typically occurs in winter months in temperate climates, with annual epidemics affecting 5-15% of the population.

Influenza viruses belong to the *Orthomyxoviridae* family and are classified into types A, B, C, and D. Influenza A and B cause seasonal epidemics in humans, with

influenza A capable of causing pandemics due to its ability to undergo major genetic changes (antigenic shift). Influenza A viruses are further classified by two surface glycoproteins: hemagglutinin (H) and neuraminidase (N), with 18 H subtypes and 11 N subtypes identified. The segmented RNA genome of influenza viruses allows for genetic reassortment when two different viruses infect the same cell, potentially creating novel strains to which populations have little immunity.

The 20th and 21st centuries witnessed several devastating influenza pandemics: the 1918 "Spanish flu" (H1N1) killing an estimated 50 million people globally, the 1957 "Asian flu" (H2N2), the 1968 "Hong Kong flu" (H3N2), and the 2009 "swine flu" (H1N1). Seasonal influenza causes an estimated 290,000-650,000 respiratory deaths annually worldwide, with the elderly, young children, pregnant women, and those with chronic medical conditions at highest risk for severe disease.

Clinical Manifestations and Symptoms

Influenza presents with characteristic clinical features distinguishing it from common cold:

Cardinal Features:

- **Abrupt onset of high fever** - Temperature typically 38-40°C (100.4-104°F), appearing suddenly within hours. Fever usually lasts 3-4 days. Gradual onset or absence of fever suggests alternative diagnosis. Children may experience febrile seizures
- **Severe myalgia (muscle aches)** - Profound muscle and body aches, particularly in back and legs, often described as the most distressing symptom. May be incapacitating. Results from systemic inflammatory cytokine release rather than direct viral invasion of muscle
- **Headache** - Severe, often described as "like the worst headache ever experienced," typically frontal or diffuse. May be accompanied by photophobia (light sensitivity) and retro-orbital pain
- **Dry cough** - Nonproductive cough that may be severe and painful, resulting from tracheobronchitis. May persist for weeks after other symptoms resolve
- **Profound fatigue and weakness** - Extreme exhaustion and prostration disproportionate to other symptoms. Patients often describe feeling "too weak to get out of bed." Post-influenza fatigue may persist for weeks

Additional Symptoms:

- **Sore throat** - Less prominent than in common cold, may be present early
- **Nasal congestion and rhinorrhea** - Present but less prominent than systemic symptoms
- **Chills and rigors** - Shaking chills often accompany fever spikes
- **Anorexia** - Loss of appetite
- **Gastrointestinal symptoms** - Nausea, vomiting, and diarrhea more common in children ("stomach flu" is misnomer - true influenza is respiratory infection)

Complications:

- **Primary viral pneumonia** - Direct viral invasion of lung tissue, potentially fatal, especially in pregnant women and those with cardiopulmonary disease
- **Secondary bacterial pneumonia** - *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae* complicating influenza, presenting as worsening symptoms after initial improvement
- **Exacerbation of chronic conditions** - Worsening of asthma, COPD, heart failure, diabetes
- **Myocarditis and pericarditis** - Rare cardiac complications
- **Neurologic complications** - Encephalitis, seizures, Guillain-Barré syndrome (rare)
- **Multi-organ failure** - In severe cases

Detailed Stages of Infection

1. **Viral Inhalation and Exposure** - Influenza spreads primarily through respiratory droplets produced when infected individuals cough, sneeze, or talk. These droplets can travel up to 6 feet and land in mouths or noses of nearby people or be inhaled into lungs. The virus can also spread by touching surfaces contaminated with virus and then touching face. Influenza has a short incubation period of 1-4 days (average 2 days), with infected individuals contagious from 1 day before symptom onset until 5-7 days after symptom onset (longer in immunocompromised)

2. Rapid Viral Replication in Respiratory Epithelium -

- Following inhalation, viral hemagglutinin binds to sialic acid receptors on respiratory epithelial cells lining the upper and lower respiratory tract
- Virus enters cells through receptor-mediated endocytosis
- Viral RNA is released into cell nucleus where viral genome replication and mRNA transcription occur using viral RNA polymerase
- Newly synthesized viral proteins and RNA segments assemble at cell membrane
- Viral neuraminidase cleaves sialic acid, releasing progeny viruses to infect adjacent cells
- Rapid replication produces high viral loads within 48-72 hours of infection
- Infected epithelial cells undergo apoptosis, causing epithelial damage and loss of mucociliary clearance function

3. Systemic Immune Response and Cytokine Storm -

- Viral infection triggers robust innate immune response with production of interferons, tumor necrosis factor-alpha (TNF- α), interleukins (IL-1, IL-6, IL-8), and other inflammatory mediators
- This "cytokine storm" is responsible for systemic symptoms: fever (IL-1, IL-6, TNF- α acting on hypothalamic thermoregulatory center), myalgia, headache, fatigue
- Adaptive immune response develops with virus-specific antibodies and cytotoxic T-lymphocytes
- Antibodies to hemagglutinin provide strain-specific immunity preventing future infection
- In severe cases, excessive inflammatory response may cause acute respiratory distress syndrome (ARDS) and multi-organ dysfunction

4. Recovery or Development of Complications -

- In uncomplicated cases, symptoms peak at days 2-3, with gradual improvement over 3-7 days

- Fever typically resolves by day 3-4
- Cough, fatigue, and weakness may persist for 1-2 weeks or longer
- Epithelial repair occurs over weeks
- Damaged epithelium and impaired mucociliary clearance increase susceptibility to secondary bacterial pneumonia
- Full recovery in most healthy adults within 1-2 weeks, though elderly and those with complications may require months

Comprehensive Preventive Measures

Vaccination - The Cornerstone of Prevention:

- **Annual influenza vaccination** - The single most effective preventive measure:
 - Recommended for all individuals ≥ 6 months of age
 - Especially critical for high-risk groups: adults ≥ 65 years, young children, pregnant women, healthcare workers, individuals with chronic medical conditions
 - Vaccine composition updated annually based on WHO surveillance of circulating strains
 - Provides 40-60% efficacy in preventing infection when well-matched to circulating strains
 - Even when vaccine doesn't prevent infection, it reduces severity and complications
 - Available formulations: standard-dose inactivated vaccine, high-dose vaccine for elderly, adjuvanted vaccine, live attenuated intranasal vaccine (limited use), recombinant vaccine
 - Best administered before flu season begins (October-November in Northern Hemisphere) but beneficial throughout flu season
 - Takes 2 weeks to develop protective immunity

Respiratory Hygiene and Infection Control:

- **Cough etiquette** - Covering coughs and sneezes with tissue or elbow

- **Hand hygiene** - Frequent handwashing or use of alcohol-based sanitizers, especially after coughing/sneezing
- **Isolation of sick individuals** - Staying home when ill, avoiding contact with others for at least 24 hours after fever resolves
- **Avoiding touching face** - Limiting hand-to-face contact
- **Surface disinfection** - Regular cleaning of frequently touched surfaces
- **Mask wearing** - Particularly effective in healthcare settings and during outbreaks

Antiviral Chemoprophylaxis:

- **Post-exposure prophylaxis** - Antiviral medications (oseltamivir, zanamivir) can be given to high-risk individuals after exposure to prevent infection
- **Pre-exposure prophylaxis** - May be considered for high-risk individuals during outbreaks when vaccination is contraindicated or unavailable
- Not a substitute for vaccination
- Duration typically 7-10 days for post-exposure or throughout exposure period

Public Health Measures During Outbreaks:

- Social distancing
- School closures during severe outbreaks
- Postponement of mass gatherings
- Enhanced surveillance and reporting

Diagnostic Approaches

Clinical Diagnosis:

- During flu season, clinical diagnosis based on characteristic features (acute onset, fever, cough, myalgia) has reasonable positive predictive value
- Clinical diagnosis alone insufficient outside flu season or in hospitalized patients requiring specific management

Rapid Influenza Diagnostic Tests (RIDTs):

- Immunoassays detecting influenza viral antigens in respiratory specimens
- Results available in 10-15 minutes
- Can differentiate influenza A from B
- Moderate sensitivity (50-70%) but high specificity (90-95%)
- False negatives common; negative test does not rule out influenza
- Best used within first 3-4 days of symptom onset

Molecular Testing (RT-PCR):

- Reverse transcription polymerase chain reaction detecting viral RNA
- Gold standard with excellent sensitivity (>95%) and specificity (>98%)
- Can identify specific subtypes (H1N1, H3N2)
- Results typically available in hours to 1-2 days
- Recommended for hospitalized patients, severe cases, and when results will impact clinical management
- Multiplex PCR panels can simultaneously detect influenza and other respiratory viruses

Viral Culture:

- Rarely used clinically due to time required (3-7 days)
- Important for epidemiologic surveillance and antiviral resistance testing

When to Test:

- Hospitalized patients with acute respiratory illness
- Severely ill outpatients when results may guide antiviral treatment
- Institutional outbreaks requiring infection control measures
- Public health surveillance
- Testing not routinely necessary for outpatients with mild illness during flu season

First Aid and Immediate Care Measures

Rest and Activity:

- Complete bed rest during acute illness
- Gradual return to activities as symptoms improve
- Avoid strenuous exercise until fully recovered

Hydration:

- Aggressive fluid intake to prevent dehydration from fever and reduced oral intake
- Water, electrolyte solutions, warm liquids
- Monitor for dehydration signs (dark urine, dizziness, decreased urination)

Fever Management:

- Antipyretics for comfort:
 - Acetaminophen (paracetamol) 325-1000 mg every 4-6 hours (maximum 4 grams daily)
 - Ibuprofen 200-400 mg every 4-6 hours
 - Aspirin in adults (avoid in children)
- Physical cooling measures (tepid sponge bath, cool compress)
- Fever reduction improves comfort but does not accelerate recovery

Symptomatic Relief:

- Cough suppressants for severe cough interfering with sleep
- Analgesics for myalgia and headache
- Humidification for upper respiratory symptoms

Nutritional Support:

- Light, easily digestible foods as tolerated
- No need to "feed a fever" or "starve a fever" - eat based on appetite

Monitoring for Complications:

Seek immediate medical attention for:

- Difficulty breathing or shortness of breath
- Persistent chest pain or pressure
- Severe or persistent vomiting
- Confusion or altered mental status
- Seizures
- Severe weakness or dizziness
- Symptoms improving then worsening (suggesting secondary bacterial infection)
- High-risk individuals (very young, elderly, pregnant, chronic medical conditions) should have lower threshold for seeking care

Isolation Precautions:

- Stay home and avoid contact with others
- Remain isolated for at least 24 hours after fever resolves without antipyretics
- Wear mask if must be around others

Antiviral Drug Information (Educational Reference)

Neuraminidase Inhibitors:

Oseltamivir (Tamiflu)

- Oral antiviral inhibiting viral neuraminidase, preventing release of progeny viruses from infected cells
- Treatment: 75 mg twice daily for 5 days (dose adjustment for renal impairment; pediatric dosing weight-based)
- Prophylaxis: 75 mg once daily for 7-10 days (post-exposure) or duration of outbreak
- Most effective when started within 48 hours of symptom onset but benefits demonstrated up to 5 days in hospitalized patients
- Reduces symptom duration by approximately 1 day, reduces complications and hospitalizations

- Generally well-tolerated; nausea and vomiting most common side effects (reduced by taking with food)
- Resistance rare but reported

Zanamivir (Relenza)

- Inhaled neuraminidase inhibitor
- Treatment: Two inhalations (5 mg each) twice daily for 5 days
- Prophylaxis: Two inhalations once daily
- Similar efficacy to oseltamivir
- Contraindicated in individuals with reactive airway disease (may cause bronchospasm)
- Requires proper inhaler technique
- Preferred for oseltamivir-resistant strains

Peramivir

- Intravenous neuraminidase inhibitor
- Single 600 mg IV infusion for treatment
- Option for patients unable to take oral or inhaled medications

Baloxavir marboxil (Xofluza)

- Oral cap-dependent endonuclease inhibitor, blocking viral mRNA transcription
- Novel mechanism of action
- Single-dose treatment (weight-based): 40 mg for 40-79 kg, 80 mg for ≥ 80 kg
- Approved for age ≥ 12 years
- Rapid symptom relief (similar to oseltamivir)
- Concerns about emergence of resistance mutations

Adamantanes (M2 Inhibitors):

- Amantadine and rimantadine

- No longer recommended due to high rates of resistance in circulating influenza A strains
- No activity against influenza B

Treatment Recommendations:

Indications for antiviral treatment:

- All hospitalized patients with suspected or confirmed influenza
- Severely ill patients regardless of hospitalization status
- High-risk individuals:
 - Age <2 years or ≥ 65 years
 - Pregnant women or up to 2 weeks postpartum
 - Chronic medical conditions (pulmonary, cardiovascular, renal, hepatic, hematologic, metabolic disorders including diabetes, neurologic conditions, immunosuppression)
 - Residents of long-term care facilities
 - Morbid obesity ($BMI \geq 40$)

Timing:

- Greatest benefit when initiated within 48 hours of symptom onset
- Still recommended for hospitalized or severely ill patients beyond 48 hours
- Consider in high-risk outpatients even if presenting after 48 hours

Antibiotics:

- **NOT indicated for uncomplicated influenza**
- Antibiotics only appropriate if secondary bacterial infection develops:
 - Bacterial pneumonia (new fever after initial improvement, purulent sputum, focal infiltrate on chest X-ray)
 - Otitis media
 - Sinusitis

- Common bacterial pathogens: *S. pneumoniae*, *S. aureus* (including MRSA), *H. influenzae*
 - Empiric antibiotic selection should cover these organisms in suspected secondary bacterial pneumonia
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3. COVID-19 (Coronavirus Disease 2019)

Comprehensive Overview

COVID-19, caused by the novel coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), emerged in late 2019 in Wuhan, China, and rapidly evolved into a global pandemic that has fundamentally altered societies worldwide. As a member of the *Betacoronavirus* genus, SARS-CoV-2 is related to SARS-CoV (2003) and MERS-CoV (2012) but exhibits distinct biological and epidemiologic characteristics including higher transmissibility and broader clinical spectrum.

The virus spreads primarily through respiratory droplets and aerosols, with an estimated basic reproduction number (R_0) of 2-6 depending on the variant, meaning each infected person transmits to 2-6 others in a fully susceptible population without interventions. Key features distinguishing SARS-CoV-2 include presymptomatic and asymptomatic transmission (substantial transmission occurring before symptom onset), wide clinical variability (from completely asymptomatic to fatal), and continuing evolution through emergence of variants with altered transmissibility, virulence, and immune escape properties.

The pandemic has resulted in over 700 million confirmed cases and 7 million deaths globally as of 2024 (likely substantial underestimation due to testing limitations and unreported cases). Beyond acute illness, COVID-19 is associated with post-acute sequelae ("long COVID") affecting multiple organ systems and persisting for months after initial infection. The development of effective vaccines in unprecedented timeframes and antiviral therapeutics has substantially altered disease trajectory and outcomes.

Clinical Manifestations and Symptoms

COVID-19 exhibits remarkable clinical heterogeneity, ranging from asymptomatic infection (estimated 20-40% of cases) to critical illness requiring intensive care:

Common Symptoms:

- **Fever or chills** - Present in 43-98% of symptomatic patients, though absence of fever does not exclude COVID-19. Temperature typically 37.8-39°C (100-102°F)
- **Cough** - Usually dry, persistent cough in 60-86% of cases, though may become productive. Results from inflammation of bronchial epithelium
- **Fatigue and malaise** - Nearly universal in symptomatic patients, often profound and disproportionate, may persist long after viral clearance
- **Loss of taste (ageusia) or smell (anosmia)** - Distinctive feature of COVID-19, occurring in 40-84% of cases. Often occurs early, may be presenting symptom, can occur without nasal congestion. Results from viral infection of olfactory neurons and supporting cells. May persist for weeks to months, though most recover gradually
- **Shortness of breath (dyspnea)** - Occurs in 30-60% of hospitalized patients, reflecting lower respiratory tract involvement, pneumonia, or acute respiratory distress syndrome. May develop days after initial symptom onset. Warning sign requiring medical attention
- **Myalgia** - Muscle aches and body pain in 35-44% of cases
- **Headache** - Occurs in 10-14% initially, may be severe and persistent
- **Sore throat** - Present in 13-17% of cases
- **Nasal congestion or rhinorrhea** - Less common than with other respiratory viruses (5-10%)
- **Gastrointestinal symptoms** - Nausea, vomiting, diarrhea in 5-10% of cases, occasionally predominant

Severe Disease Manifestations:

- **Pneumonia** - Bilateral interstitial pneumonia visible on chest imaging (ground-glass opacities)

- **Acute respiratory distress syndrome (ARDS)** - Severe hypoxic respiratory failure requiring mechanical ventilation
- **Thromboembolic complications** - Deep vein thrombosis, pulmonary embolism, stroke (COVID-19 causes hypercoagulable state)
- **Cardiac complications** - Myocarditis, acute coronary syndrome, arrhythmias, heart failure
- **Acute kidney injury** - Direct viral injury and secondary to hypoxia
- **Neurologic manifestations** - Encephalopathy, encephalitis, seizures, Guillain-Barré syndrome
- **Multi-system inflammatory syndrome (MIS-C in children, MIS-A in adults)** - Post-infectious hyperinflammatory syndrome
- **Septic shock and multi-organ failure** - In critically ill patients

Post-Acute Sequelae of COVID-19 (PASC) / Long COVID:

- Symptoms persisting >4 weeks after initial infection
- Affects 10-30% of infected individuals
- Common symptoms: fatigue, cognitive impairment ("brain fog"), dyspnea, chest pain, palpitations, headache, sleep disturbances, anxiety, depression
- Mechanisms unclear; likely multifactorial including persistent viral reservoirs, immune dysregulation, autoimmunity, endothelial dysfunction

Detailed Stages of Infection

1. Viral Entry, Incubation, and Early Replication -

- SARS-CoV-2 transmitted through inhalation of virus-containing respiratory droplets/aerosols or touching contaminated surfaces then face
- Viral spike (S) protein binds to angiotensin-converting enzyme 2 (ACE2) receptors on respiratory epithelial cells, with TMPRSS2 facilitating viral entry
- ACE2 expressed throughout respiratory tract and in multiple organs (heart, kidneys, intestines, blood vessels) explaining multi-organ manifestations

- Incubation period: typically 2-14 days (median 4-5 days)
- Viral replication begins in upper respiratory tract (nasopharynx), then potentially spreads to lower respiratory tract
- Presymptomatic transmission: infected individuals contagious 1-3 days before symptom onset, accounting for substantial transmission

2. Symptomatic Phase - Local and Systemic Manifestations -

- Symptoms typically begin 4-5 days after exposure
- Viral load peaks around symptom onset
- Upper respiratory tract symptoms predominate initially
- In mild cases (80-85%), infection remains confined to upper respiratory tract with limited systemic inflammation; recovery over 7-14 days
- In moderate to severe cases, virus spreads to lower respiratory tract by days 5-8
- Infected cells undergo pyroptosis (inflammatory cell death), releasing damage-associated molecular patterns (DAMPs) triggering inflammatory cascade

3. Inflammatory Phase - Hyperinflammation in Severe Cases -

- Approximately 15-20% of symptomatic patients develop severe disease
- Excessive immune activation with "cytokine storm" - elevated IL-6, IL-1, TNF- α , and other inflammatory mediators
- Lymphopenia (low lymphocyte counts) characteristic finding
- Endothelial cell infection and inflammation leads to:
 - Vascular permeability and edema
 - Microthrombi formation throughout vasculature
 - Multiorgan hypoxic injury
- Pulmonary phase: diffuse alveolar damage with hyaline membrane formation
- D-dimer elevation reflects hypercoagulability

- This phase typically occurs 7-14 days after symptom onset

4. Recovery or Post-Viral Complications -

- **Uncomplicated recovery:** Gradual symptom improvement over 1-3 weeks with viral clearance. Median duration of viral shedding: 17-20 days but can persist longer, especially in immunocompromised
- **Severe disease recovery:** Prolonged hospitalization (weeks), often requiring rehabilitation for deconditioning, post-ICU syndrome
- **Long COVID:** Subset develops persistent symptoms for months
- **Immunity:** Natural infection provides protection against reinfection, though duration and degree of protection vary by variant. Vaccination after infection provides enhanced immunity
- **Post-COVID fibrosis:** Some severe cases develop pulmonary fibrosis

Comprehensive Preventive Measures

Vaccination - Most Effective Prevention:

- **COVID-19 vaccination** dramatically reduces risk of infection, severe disease, hospitalization, and death
- Multiple vaccine platforms available:
 - mRNA vaccines (Pfizer-BioNTech, Moderna) - highly effective, two-dose primary series
 - Viral vector vaccines (Johnson & Johnson, AstraZeneca)
 - Protein subunit vaccines (Novavax)
- Recommended for all individuals ≥ 6 months
- Boosters recommended to maintain protection, especially against evolving variants
- Updated variant-specific formulations released periodically
- Particularly critical for high-risk groups: elderly, immunocompromised, pregnant women, chronic medical conditions

- Vaccination safe and effective in pregnancy, protecting both mother and newborn

Non-Pharmaceutical Interventions:

Mask wearing:

- High-quality masks (N95, KN95, KF94) provide excellent protection by filtering viral particles
- Surgical masks provide moderate protection
- Cloth masks provide minimal protection but better than nothing
- Most effective in indoor settings, crowded spaces, high transmission periods
- Proper fit essential for effectiveness

Physical distancing:

- Maintaining 6 feet (2 meters) from others reduces droplet transmission
- Particularly important indoors and when unable to mask

Hand hygiene:

- Frequent handwashing with soap and water for ≥ 20 seconds
- Alcohol-based hand sanitizer ($\geq 60\%$ alcohol) when handwashing unavailable
- Avoid touching face, especially before hand hygiene

Ventilation:

- Improved indoor air quality through ventilation, air filtration (HEPA filters)
- Opening windows to increase air exchange
- Outdoor activities lower risk than indoor

Screening and testing:

- Testing when symptomatic, after exposure, or before high-risk gatherings
- Isolation when positive
- Contact tracing to identify and notify exposures

Population-level measures during surges:

- Capacity limits for indoor gatherings
- Remote work and learning when feasible
- Enhanced cleaning protocols

Diagnostic Approaches

Molecular Testing - Gold Standard:

RT-PCR (Reverse Transcription-Polymerase Chain Reaction):

- Detects viral RNA
- Highest sensitivity and specificity (>95%)
- Specimen types: nasopharyngeal swab (preferred), oropharyngeal swab, nasal mid-turbinate swab, anterior nasal swab, saliva
- Results typically available in hours to 2 days depending on laboratory
- Can detect infection from day of exposure through several weeks (though detection beyond 10 days often represents non-infectious viral fragments)
- Quantitative PCR can measure viral load though clinical utility debated

Rapid molecular tests:

- Near point-of-care PCR or isothermal amplification
- Results in 15-45 minutes
- Slightly lower sensitivity than laboratory PCR but adequate for most clinical purposes

Antigen Testing:

Rapid antigen tests (RATs):

- Detect viral nucleocapsid protein
- Results in 10-15 minutes
- Lower sensitivity than PCR (50-85% depending on timing and viral load)
- High specificity (>95%)
- Best performance when viral load high (first 5-7 days of symptoms)

- May miss early infection or asymptomatic cases with low viral loads
- Widely available for home use
- Serial testing (testing 2-3 times over several days) improves sensitivity
- Positive test highly specific and requires no confirmation; negative test should be interpreted cautiously and repeated if suspicion high

Antibody/Serologic Testing:

- Detects antibodies (IgM, IgG) to SARS-CoV-2
- Not useful for diagnosing acute infection (antibodies develop 1-3 weeks after infection onset)
- May identify prior infection or assess immune response to vaccination
- Cannot reliably determine degree of protection against reinfection

Imaging:

- **Chest X-ray:** May show bilateral infiltrates in pneumonia, though can be normal early
- **CT chest:** Ground-glass opacities, consolidation, typical patterns in COVID-19 pneumonia; useful in evaluating severity
- Not routinely necessary for mild outpatient disease

Laboratory Markers:

- Lymphopenia, elevated inflammatory markers (CRP, ferritin, IL-6), elevated D-dimer suggest severe disease
- Troponin elevation indicates cardiac involvement

When to Test:

- Symptomatic individuals
- Close contacts of confirmed cases
- Before gatherings or travel
- Surveillance in high-risk settings (healthcare facilities, nursing homes)

First Aid and Immediate Care Measures

Isolation:

- Isolate from household members and others to prevent transmission
- Use separate bedroom and bathroom if possible
- Duration: At least 5 days from symptom onset (or positive test if asymptomatic) AND symptoms improving AND no fever for 24 hours without antipyretics
- Mask around others for days 6-10
- Immunocompromised individuals may need longer isolation (up to 20 days)

Symptom Monitoring:

Monitor for warning signs requiring medical attention:

- Difficulty breathing or shortness of breath at rest
- Persistent chest pain or pressure
- New confusion or inability to wake/stay awake
- Bluish lips or face (cyanosis)
- Oxygen saturation <92% on pulse oximeter (if available)
- Inability to keep down fluids

Supportive Care at Home:

- **Rest:** Adequate sleep and minimize physical activity during acute illness
- **Hydration:** Drink plenty of fluids to prevent dehydration
- **Fever/pain management:** Acetaminophen or ibuprofen for fever and body aches
- **Cough:** Honey, cough drops, humidification
- **Positioning:** Prone positioning (lying on stomach) may help if short of breath, though seek medical care for significant dyspnea
- **Pulse oximetry:** Home pulse oximeter to monitor oxygen saturation if available (normal $\geq 95\%$)
- **Nutrition:** Eat as tolerated, focus on nutritious foods

When to Seek Medical Care:

- Emergency warning signs listed above
- High-risk individuals (age ≥ 65 , immunocompromised, significant comorbidities) should have lower threshold
- Worsening symptoms after initial improvement
- Inability to manage at home

Post-Infection:

- Gradual return to activities based on symptoms
- Avoid strenuous exercise during acute illness and for 2 weeks after
- Cardiac screening before returning to competitive sports if severe illness
- Monitor for symptoms of long COVID

Antiviral and Drug Information (Educational Reference)

Antiviral Medications:

Nirmatrelvir-Ritonavir (Paxlovid)

- Oral antiviral combination: nirmatrelvir (protease inhibitor) + ritonavir (CYP3A4 inhibitor boosting nirmatrelvir levels)
- Indications: High-risk patients with mild-to-moderate COVID-19 within 5 days of symptom onset
- Dosing: Nirmatrelvir 300 mg + ritonavir 100 mg twice daily for 5 days (dose reduction for renal impairment)
- Reduces risk of hospitalization/death by ~89% when started early
- Significant drug-drug interactions due to ritonavir; many medications contraindicated or require dose adjustment
- Caution in severe renal or hepatic impairment
- "Paxlovid rebound" phenomenon - recurrence of symptoms/positive test after treatment - described but not well understood

Remdesivir (Veklury)

- Intravenous nucleoside analog inhibiting viral RNA polymerase
- Indications:
 - Hospitalized patients requiring supplemental oxygen
 - High-risk outpatients within 7 days of symptom onset (as 3-day course)
- Dosing: 200 mg IV on day 1, then 100 mg daily for 4 more days (hospitalized) or 2 more days (outpatient)
- Modest reduction in time to recovery and mortality in hospitalized patients
- Generally well-tolerated; monitor liver enzymes and renal function

Molnupiravir (Lagevrio)

- Oral nucleoside analog causing viral error catastrophe
- Alternative option for high-risk patients when other antivirals unavailable/contraindicated
- Dosing: 800 mg twice daily for 5 days within 5 days of symptom onset
- Modest efficacy (~30% reduction in hospitalization/death)
- Avoided in pregnancy due to theoretical mutagenicity concerns

Immunomodulatory Therapies:

Dexamethasone

- Corticosteroid reducing harmful inflammatory response
- Indications: Hospitalized patients requiring supplemental oxygen
- Dosing: 6 mg daily (oral or IV) for up to 10 days
- Reduces mortality in severely ill patients
- Potentially harmful if given early in mild disease (interferes with viral clearance)

Baricitinib, Tofacitinib

- JAK inhibitors with immunomodulatory and potential antiviral effects
- Used in hospitalized patients requiring oxygen, often combined with dexamethasone

Tocilizumab

- IL-6 receptor antagonist
- May be used in hospitalized patients with severe disease and elevated inflammatory markers

Monoclonal Antibodies:

- Previously used monoclonal antibodies (bamlanivimab, casirivimab-imdevimab, sotrovimab) have lost activity against current Omicron variants and are no longer authorized
- Development continues for broadly neutralizing antibodies

Prophylaxis:

Evusheld (tixagevimab-cilgavimab)

- Monoclonal antibody combination for pre-exposure prophylaxis
- Previously authorized for immunocompromised unable to mount adequate vaccine response
- Revoked due to lack of activity against current variants

Antibiotics:

- **NOT indicated for COVID-19** as it is a viral infection
- Antibiotics only appropriate if bacterial co-infection or secondary bacterial pneumonia confirmed or strongly suspected
- Overuse of empiric antibiotics in hospitalized COVID-19 patients has been problematic contributor to antimicrobial resistance
- Procalcitonin levels may help distinguish bacterial from viral pneumonia

Supportive Care Remains Central:

- Oxygen therapy (nasal cannula, high-flow nasal oxygen, mechanical ventilation) as needed
- Prone positioning for ARDS
- Anticoagulation to prevent thromboembolism
- Nutritional support

- Management of complications
-

4. Dengue Fever

Comprehensive Overview

Dengue fever is an acute febrile illness caused by dengue virus (DENV), a mosquito-borne flavivirus transmitted primarily by *Aedes aegypti* and secondarily by *Aedes albopictus* mosquitoes. The disease represents the most rapidly spreading arboviral infection globally, with dramatic increases in incidence over recent decades. An estimated 390 million dengue infections occur annually across more than 100 countries in tropical and subtropical regions, placing approximately half the world's population at risk.

Dengue virus exists as four distinct but antigenically related serotypes (DENV-1, DENV-2, DENV-3, DENV-4). Infection with one serotype provides lifelong immunity to that serotype but only temporary and partial cross-immunity to the other three. This immunologic characteristic creates the concerning phenomenon whereby subsequent infection with a different serotype increases risk of severe dengue through antibody-dependent enhancement (ADE), where pre-existing non-neutralizing antibodies from prior infection facilitate viral entry into cells, leading to higher viral loads and more severe disease.

The clinical spectrum ranges from asymptomatic infection (estimated 75% of cases) to classic dengue fever to severe dengue (previously termed dengue hemorrhagic fever and dengue shock syndrome) characterized by plasma leakage, hemorrhage, and organ impairment. The transition from febrile to critical phase represents a particularly dangerous period requiring vigilant monitoring. Despite being a significant cause of morbidity and mortality, particularly in children in endemic areas, no specific antiviral treatment exists, and management relies entirely on supportive care and careful fluid management.

Clinical Manifestations and Symptoms

Dengue fever presents with variable severity:

Classic Dengue Fever:

- **High fever** - Abrupt onset of high-grade fever (39-40°C or 102-104°F), typically biphasic with initial fever lasting 2-7 days, brief defervescence, then potential recurrence. The dramatic temperature elevation distinguishes dengue from many other febrile illnesses
- **Severe headache** - Intense frontal or retro-orbital headache, often described as "pain behind the eyes," exacerbated by eye movement. This distinctive feature helps differentiate dengue from other tropical fevers
- **Muscle and joint pain (myalgia and arthralgia)** - Severe musculoskeletal pain, particularly affecting the back, legs, and large joints. The intensity of bone pain has led to the colloquial name "breakbone fever." Pain may be so severe as to limit movement
- **Retro-orbital pain** - Pain behind or around the eyes, worse with eye movement or pressure on eyeballs
- **Rash** -
 - Initial: Transient flushing or macular rash in first 24-48 hours
 - Later: Maculopapular or morbilliform rash appearing typically on days 3-5 of illness, starting on trunk and spreading to extremities and face. May be pruritic (itchy)
 - Characteristic pattern: "islands of white in a sea of red" - small areas of normal skin within the rash
 - Petechial rash may develop in severe cases
- **Facial flushing** - Erythema of face and neck
- **Gastrointestinal symptoms** - Nausea, vomiting, anorexia, abdominal pain. Vomiting may be persistent and contribute to dehydration
- **Hemorrhagic manifestations in mild disease** - Minor bleeding: petechiae, mucosal bleeding (epistaxis, gum bleeding), easy bruising. Positive tourniquet test (appearance of ≥ 20 petechiae in 1 square inch after blood pressure cuff inflation)
- **Mild hepatomegaly** - Tender liver enlargement may occur

Warning Signs of Severe Dengue (Require Urgent Medical Attention):

- Severe abdominal pain or persistent vomiting
- Clinical fluid accumulation (ascites, pleural effusion)
- Mucosal bleeding (hematemesis, melena, menorrhagia)
- Lethargy or restlessness
- Liver enlargement >2 cm
- Rapid decrease in platelet count with rising hematocrit (hemoconcentration indicating plasma leakage)

Severe Dengue (Life-Threatening):

- **Severe plasma leakage** - Leading to shock (dengue shock syndrome), fluid accumulation with respiratory distress
- **Severe hemorrhage** - Gastrointestinal bleeding, intracranial hemorrhage, other organ bleeding
- **Severe organ involvement** - Hepatic injury (AST/ALT >1000), neurologic complications (encephalopathy, seizures, encephalitis), myocarditis, acute kidney injury
- **Dengue shock syndrome** - Hypotension, narrow pulse pressure (<20 mmHg), cold clammy skin, altered mental status. Develops when plasma leakage reaches critical levels, typically during defervescence ("critical phase")

Detailed Stages of Infection

1. Febrile Phase (Days 1-3 to 1-7) -

- Following mosquito bite, incubation period of 4-10 days (average 5-7 days)
- Abrupt onset of high fever
- Patients develop the characteristic symptoms: severe headache, retro-orbital pain, myalgia, arthralgia
- Viremia (virus circulating in blood) peaks during first 2-3 days of fever, corresponding to peak infectivity to mosquitoes
- Face appears flushed; early rash may appear

- Leukopenia (low white blood cell count) develops
- Some patients experience gastrointestinal symptoms
- Mild cases may resolve after this phase without progression
- Duration typically 3-7 days

2. Critical Phase (Defervescence Period, Days 3-7) -

- The most dangerous period occurring around the time of fever resolution (defervescence)
- Temperature drops to normal or subnormal (37°C or 98.6°F)
- Many patients improve and recover without complications
- However, some patients (particularly those with secondary dengue infection) develop:
 - Increased vascular permeability causing plasma leakage from blood vessels into body cavities
 - Hemoconcentration: rising hematocrit (increasing blood viscosity as plasma volume decreases)
 - Thrombocytopenia: dramatic drop in platelet count
 - Fluid accumulation: pleural effusions, ascites, pericardial effusion
- If significant plasma leakage occurs: hypovolemic shock develops (dengue shock syndrome)
- Hemorrhagic manifestations more likely
- Organ impairment may develop
- This critical phase typically lasts 24-48 hours
- Close monitoring essential; aggressive but judicious fluid replacement can be life-saving

3. Recovery Phase (Days 7-10 and Beyond) -

- Gradual reabsorption of extravasated fluid from body cavities back into bloodstream
- Hematocrit stabilizes or decreases to normal

- White blood cell count begins to normalize, often with neutrophilia
- Platelet count begins to recover (may take several days to normalize)
- General well-being improves
- Appetite returns
- Rash may reappear or persist during early recovery
- Convalescent rash may develop: islands of white within the rash (characteristic finding)
- Pruritus (itching) common during recovery
- Complications during recovery:
 - Fluid overload if excessive IV fluids administered (pulmonary edema, heart failure)
 - Bradycardia (slow heart rate) common
- Full recovery may take weeks to months with persistent fatigue

Comprehensive Preventive Measures

Vector Control - Essential Strategy:

- **Elimination of mosquito breeding sites** - *Aedes aegypti* breeds in artificial water containers:
 - Removing or covering water storage containers (tanks, drums, buckets)
 - Emptying flower vases, plant pot saucers, and other water-holding receptacles weekly
 - Proper disposal or recycling of tires, bottles, cans
 - Cleaning rain gutters
 - Community-wide clean-up campaigns
 - These mosquitoes breed in small amounts of clean water, making elimination challenging
- **Larviciding** - Application of larvicides (temephos, *Bacillus thuringiensis israelensis*) to water containers that cannot be eliminated

- **Adult mosquito control -**

- Indoor residual spraying with insecticides
- Space spraying/fogging during outbreaks (limited effectiveness)
- Insecticide-treated materials

Personal Protective Measures:

- **Protective clothing -**

- Long-sleeved shirts and long pants, especially during peak biting times
- Light-colored clothing (mosquitoes attracted to dark colors)
- *Aedes* mosquitoes are day-biters, most active during early morning (7-9 AM) and late afternoon (4-6 PM)

- **Mosquito repellents -**

- DEET (20-30% concentration), picaridin, IR3535, oil of lemon eucalyptus
- Application to exposed skin and clothing
- Reapplication according to product directions

- **Mosquito nets and screens -**

- Bed nets (less useful than for malaria since *Aedes* bites during day)
- Window and door screens to prevent indoor mosquito entry
- Air conditioning reduces mosquito biting

Vaccination:

- **Dengvaxia (CYD-TDV)** - First licensed dengue vaccine:

- Live attenuated tetravalent vaccine
- Approved in some endemic countries
- WHO recommends use ONLY in individuals with prior documented dengue infection (seropositive)
- Risk: Increases severity of subsequent dengue in seronegative individuals (those without prior infection) due to ADE mechanism

- Requires pre-vaccination screening
- Three doses at 6-month intervals
- Limited global availability and uptake due to restrictions
- **TAK-003 (Qdenga)** - Newer vaccine with broader applicability:
 - Live attenuated tetravalent vaccine
 - Can be used in both seropositive and seronegative individuals
 - Approved in some countries
 - Two doses 3 months apart

Community-Based Prevention:

- Public health education about mosquito control
- Community participation in source reduction
- Surveillance for dengue cases and mosquito populations
- Rapid response to outbreaks

Diagnostic Approaches

Clinical Diagnosis:

- High suspicion in endemic areas during febrile illness with characteristic features
- WHO diagnostic criteria help categorize disease severity

Laboratory Confirmation:

Direct viral detection (Early phase, days 0-5):

- **NS1 antigen test** -
 - Detects dengue non-structural protein 1 in blood
 - Rapid diagnostic test available (15-20 minutes)
 - Can detect virus from day 1 of fever up to day 9
 - Sensitivity 50-90% depending on timing, serotype, and test
 - High specificity

- Does not distinguish between serotypes
 - Preferred early diagnostic test in many settings
 - **RT-PCR -**
 - Detects viral RNA
 - Gold standard for early diagnosis
 - Can identify specific serotype
 - High sensitivity and specificity
 - Usually positive days 1-5 of illness
 - Requires specialized laboratory, results take hours to days
 - **Viral isolation -**
 - Rarely performed due to technical complexity and time requirements
 - Mainly for research and surveillance
- Serologic testing (Later phase, day 5 onwards):**
- **IgM antibodies -**
 - Appear around day 5-7 of illness, peak at 2 weeks, persist for 2-3 months
 - IgM capture ELISA most common method
 - Single positive IgM suggests recent dengue infection
 - Cannot reliably distinguish between serotypes or between primary and secondary infection
 - May cross-react with other flaviviruses (Zika, yellow fever)
 - **IgG antibodies -**
 - Rise more slowly than IgM
 - In primary infection: IgG appears around day 7-10
 - In secondary infection: IgG rises rapidly from day 2-3 (diagnostic clue)
 - Paired serology showing 4-fold rise in IgG confirms recent infection
 - Ratio of IgM to IgG can help distinguish primary from secondary infection

Complete Blood Count (CBC):

- **Thrombocytopenia** - Platelet count <100,000/ μ L common, <20,000/ μ L suggests severe disease
- **Hemoconcentration** - Rising hematocrit (\geq 20% increase above baseline) indicates plasma leakage
- **Leukopenia** - Low white blood cell count typical in febrile phase

Liver Function Tests:

- Transaminase elevation (AST, ALT) common
- Severe elevation (>1000 U/L) indicates severe hepatic involvement

Other Tests:

- Coagulation profile if bleeding present
- Chest X-ray or ultrasound to detect pleural effusion or ascites
- Albumin (decreased with plasma leakage)

Tourniquet Test:

- Clinical test for capillary fragility
- Blood pressure cuff inflated to midpoint between systolic and diastolic pressure for 5 minutes
- Positive if \geq 20 petechiae per 1 square inch below cuff
- Suggests increased vascular permeability

First Aid and Immediate Care Measures

Home Management (Mild Cases Without Warning Signs):

Adequate hydration - Critical to prevent shock:

- Oral rehydration solutions (ORS) preferred
- Water, fruit juices, soup, coconut water
- Adults: 2-3 liters per day; children: encourage frequent fluids
- Maintain hydration despite vomiting

Fever management:

- Paracetamol (acetaminophen) only: 10-15 mg/kg every 6 hours
- **AVOID aspirin and NSAIDs** (ibuprofen, diclofenac, naproxen) - increase bleeding risk due to antiplatelet effects and gastric irritation
- Tepid sponging for comfort

Rest:

- Adequate bed rest during febrile illness
- Avoid strenuous activity

Monitoring for warning signs - Critical during days 3-7:

- Severe abdominal pain
- Persistent vomiting
- Bleeding from any site (nose, gums, vomitus, stool)
- Lethargy or restlessness
- Cold, clammy skin
- Decreased urine output

Seek immediate medical care if:

- Any warning signs develop
- Unable to maintain oral hydration
- Very young (<1 year), elderly, pregnant, or with comorbidities
- Living alone without someone to monitor

Hospital Management (Patients with Warning Signs or Severe Dengue):

- Admission for close monitoring
- Careful fluid management:
 - IV crystalloids (normal saline, Ringer's lactate)
 - Aggressive initial resuscitation if shock
 - Careful maintenance to prevent both hypovolemia and fluid overload

- Monitoring of hematocrit and urine output guides fluid therapy
- Frequent monitoring:
 - Vital signs every 1-4 hours
 - Hematocrit every 4-6 hours
 - Platelet count daily
 - Urine output monitoring
- Platelet transfusion only for active bleeding or very low counts (<10,000-20,000/ μ L) with high bleeding risk
- Fresh frozen plasma or blood transfusion for significant bleeding
- Intensive care for shock or organ dysfunction

Antiviral and Drug Information (Educational Reference)

No Specific Antiviral Therapy:

- Despite extensive research, no antiviral medications have proven effective against dengue virus
- Multiple candidates have been studied in clinical trials without demonstrable benefit
- Management remains entirely supportive
- Research continues for targeted antivirals

Supportive Treatment is Mainstay:

- Appropriate fluid management (as described above) is the most important intervention
- Timely fluid resuscitation dramatically reduces mortality from severe dengue
- The critical decision is recognizing which patients require IV fluids and hospitalization

Medications to Use:

- **Paracetamol (acetaminophen)** - Only safe antipyretic/analgesic in dengue

- Dose: 10-15 mg/kg/dose every 6 hours (not exceeding 4 grams/day in adults)
- Does not increase bleeding risk
- Provides symptomatic relief from fever and pain

Medications to AVOID:

- **Aspirin (acetylsalicylic acid)** - Absolutely contraindicated:
 - Antiplatelet effect increases bleeding risk
 - May worsen thrombocytopenia
 - Risk of Reye's syndrome in children
- **NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)** - Contraindicated:
 - Ibuprofen, naproxen, diclofenac, indomethacin, others
 - Antiplatelet effects
 - Gastric irritation may cause GI bleeding
 - May worsen renal function
- **Intramuscular injections** - Avoid due to bleeding risk from thrombocytopenia
- **Corticosteroids** - Not beneficial and may increase complications

Antibiotics:

- **NOT indicated** for dengue fever as it is a viral infection
- No benefit and contributes to antimicrobial resistance
- Only appropriate if bacterial co-infection confirmed or strongly suspected (rare)
- Signs suggesting bacterial infection: very prolonged fever beyond typical dengue course, specific focal infections, elevated procalcitonin

Prophylactic Platelet Transfusion:

- Not recommended in absence of bleeding
- Thrombocytopenia resolves spontaneously during recovery

- Transfusion carries risks (transfusion reactions, volume overload)
- Reserved for:
 - Active significant bleeding
 - Platelet count <10,000/ μ L with high bleeding risk
 - Planned invasive procedures with thrombocytopenia

Traditional and Alternative Medicines:

- Papaya leaf extract often used in some cultures for thrombocytopenia
 - Limited scientific evidence for efficacy
 - Not harmful if taken alongside appropriate medical care
 - Should never replace proper medical evaluation and treatment
-



5. Viral Hepatitis (A, B, C – Overview)

Comprehensive Overview

Viral hepatitis encompasses a group of infectious diseases causing inflammation of the liver (hepatitis), each caused by distinct hepatotropic viruses with different transmission routes, clinical courses, and long-term outcomes. While five main hepatitis viruses (A, B, C, D, and E) are recognized, hepatitis A, B, and C account for the vast majority of acute and chronic viral hepatitis cases globally. These infections represent a major public health burden, with an estimated 354 million people living with chronic hepatitis B or C worldwide, causing approximately 1.4 million deaths annually from acute hepatitis, cirrhosis, and hepatocellular carcinoma.

Hepatitis A and E are typically transmitted via the fecal-oral route, cause acute self-limiting hepatitis, and do not lead to chronic infection. In contrast, hepatitis B and C are blood-borne viruses that can establish persistent infection leading to chronic hepatitis, cirrhosis, and liver cancer. Hepatitis D (delta) is a defective virus requiring hepatitis B virus for replication, occurring only as co-infection or superinfection in hepatitis B patients.

The clinical presentation varies from asymptomatic or mild anicteric hepatitis to severe acute hepatitis with jaundice to fulminant hepatic failure. Chronic hepatitis develops insidiously, often remaining asymptomatic for decades while progressive liver damage occurs, eventually manifesting with complications of cirrhosis or hepatocellular carcinoma. The availability of effective vaccines for hepatitis A and B and curative antiviral treatments for hepatitis C represents major advances, though global elimination efforts face challenges including access, screening, and linkage to care.

Clinical Manifestations and Symptoms

Acute Viral Hepatitis (Common to HAV, HBV, HCV):

Many acute infections are asymptomatic or mildly symptomatic, particularly in children. When symptomatic:

Prodromal (Pre-icteric) Phase:

- **Fatigue and malaise** - Profound tiredness, one of the most prominent and persistent symptoms
- **Anorexia** - Loss of appetite, often striking
- **Nausea and vomiting** - May be severe
- **Low-grade fever** - More common in hepatitis A
- **Right upper quadrant pain** - Dull ache or discomfort in liver area
- **Myalgia and arthralgia** - Muscle and joint aches
- **Alterations in taste and smell** - Particularly aversion to cigarettes in smokers
- **Flu-like symptoms** - Headache, malaise
- Duration: Several days to 1-2 weeks

Icteric Phase:

- **Jaundice** - Yellowing of skin and sclera (whites of eyes) due to elevated bilirubin:
 - Typically appears when bilirubin exceeds 2.5-3 mg/dL
 - May be preceded by dark urine (1-5 days before)

- Sclerae often noticeably yellow before skin
- Intensity correlates roughly with disease severity
- **Dark urine ("tea-colored" or "cola-colored")** - Due to conjugated bilirubin excretion in urine; often the first sign noticed by patients
- **Clay-colored or pale stools (acholic stools)** - Due to reduced bile reaching intestines
- **Pruritus (itching)** - From bile salt deposition in skin, may be severe and distressing
- **Hepatomegaly** - Enlarged, tender liver palpable below right costal margin
- **Splenomegaly** - Mild splenic enlargement in some cases
- **Paradoxical improvement in systemic symptoms** - Anorexia, nausea often improve as jaundice appears
- Duration: 2-8 weeks typically

Convalescent Phase:

- Gradual resolution of jaundice
- Return of energy and appetite
- May take weeks to months for complete recovery
- Fatigue often persists longest

Severe/Fulminant Hepatitis:

- **Hepatic encephalopathy** - Confusion, altered consciousness, asterixis (flapping tremor), progressing to coma
- **Coagulopathy** - Prolonged prothrombin time, bleeding tendency
- **Hypoglycemia** - From impaired hepatic gluconeogenesis
- **Acute liver failure** - Multi-organ dysfunction, high mortality without liver transplantation

Chronic Hepatitis (HBV, HCV):

- Often **asymptomatic for decades** - "Silent" progression

- When symptoms present:
 - Chronic fatigue
 - Mild right upper quadrant discomfort
 - Non-specific symptoms: arthralgias, nausea

Extrahepatic Manifestations:

- **HBV:** Polyarteritis nodosa, glomerulonephritis, cryoglobulinemia
- **HCV:** Essential mixed cryoglobulinemia, membranoproliferative glomerulonephritis, porphyria cutanea tarda, lichen planus

Cirrhosis Complications (End-stage):

- **Portal hypertension:** Ascites, variceal bleeding, hepatic encephalopathy, splenomegaly
- **Hepatocellular carcinoma:** Primary liver cancer complicating chronic HBV and HCV
- **Hepatorenal syndrome, hepatopulmonary syndrome**

Disease-Specific Features:

Hepatitis A:

- Fecal-oral transmission (contaminated food/water)
- Incubation: 15-50 days (average 28 days)
- Acute infection only, NO chronic state
- Children often asymptomatic; adults typically symptomatic with jaundice
- Severity increases with age
- Complete recovery usual; fulminant hepatitis rare (<0.5%)
- Relapsing hepatitis occurs in ~10% (self-limited)
- Lifelong immunity after infection

Hepatitis B:

- Transmission: Blood/body fluids, sexual, mother-to-child (vertical)

- Incubation: 30-180 days (average 60-90 days)
- Acute phase may be more severe than HAV
- Chronicity depends on age at infection:
 - Newborns: 90% develop chronic infection
 - Children 1-5 years: 30-50% chronic
 - Adults: 5-10% chronic
- Chronic HBV: Risk of cirrhosis (15-40% over lifetime) and hepatocellular carcinoma
- Immune complex-mediated extrahepatic manifestations
- "Immune phases" in chronic infection (immune tolerant, immune active, inactive carrier, reactivation)

Hepatitis C:

- Transmission: Primarily blood-borne (IVDU, transfusions pre-1992, contaminated medical equipment)
- Sexual and vertical transmission less efficient than HBV
- Incubation: 14-180 days (average 45 days)
- Acute infection often mild or asymptomatic
- High chronicity rate: 55-85% develop chronic infection
- Genotypes 1-6 with varying geographic distribution and treatment response
- Progressive fibrosis over 20-30 years
- Cirrhosis develops in 10-20% after 20 years
- Annual HCC risk 1-5% in cirrhotic patients
- Cryoglobulinemia common extrahepatic manifestation

Detailed Stages of Infection

For Hepatitis A:

- 1. Fecal-Oral Transmission and Viral Entry** - Virus ingested via contaminated food (shellfish, unwashed produce, food handled by infected person) or water. Virus survives gastric acid, absorbed through intestinal epithelium, enters bloodstream (viremia), and reaches liver via portal circulation
- 2. Acute Hepatitis and Peak Viral Replication** - Virus infects hepatocytes, replicates in cytoplasm. Viral shedding in feces begins before symptom onset and continues through first 1-2 weeks of illness (peak infectivity period). Liver inflammation results primarily from cell-mediated immune response targeting infected hepatocytes. Transaminases rise dramatically (often >1000 U/L). Jaundice appears as damaged hepatocytes cannot process bilirubin
- 3. Immune Clearance and Resolution** - Strong cytotoxic T-cell response clears infected cells. Anti-HAV IgM antibodies appear early and persist for 3-6 months (diagnostic of acute infection). Anti-HAV IgG antibodies develop and provide lifelong immunity. Complete viral clearance typically within 6 months. Liver regenerates fully in most cases
- 4. Complete Recovery** - No chronic phase. Liver function normalizes. Lifelong immunity achieved

For Hepatitis B:

- 1. Exposure and Viral Entry** - Virus transmitted through blood, sexual contact, or perinatally. Virus enters bloodstream, circulates to liver, and infects hepatocytes via sodium taurocholate cotransporting polypeptide (NTCP) receptor
- 2. Acute Hepatitis Phase** - Incubation period followed by symptomatic acute hepatitis in 30-50% of adults. HBsAg (surface antigen) detectable before symptoms. High levels of viral replication. Immune response causes hepatocyte damage and symptoms. Peak transaminase elevation. Outcome depends on strength of immune response and age:
 - Strong immune response: Viral clearance, anti-HBs antibody development, recovery
 - Weak immune response (especially in infants): Chronic infection

3. Resolution or Progression to Chronic Infection:

- **If cleared:** HBsAg disappears, anti-HBs antibodies appear (indicating immunity), complete recovery
- **If chronic:** HBsAg persists >6 months, various phases follow:

4. Phases of Chronic Hepatitis B:

- **Immune-tolerant phase:** High viral replication, minimal liver inflammation (common in perinatal infection)
- **Immune-active (HBeAg-positive) phase:** Active liver inflammation, elevated transaminases, progressive fibrosis
- **Inactive carrier state:** Low/undetectable HBV DNA, normal transaminases, minimal disease progression
- **Reactivation (HBeAg-negative chronic hepatitis):** Viral mutations, renewed inflammation and fibrosis
- Over decades: Progressive fibrosis → cirrhosis → hepatocellular carcinoma risk

For Hepatitis C:

1. **Exposure and Acute Infection** - Virus transmitted through contaminated blood. Enters hepatocytes via multiple receptors. Acute infection typically mild or asymptomatic (80%). Only 20-30% develop jaundice. Diagnosis often missed
2. **Chronic Infection Development** - High chronicity rate (55-85%). Virus establishes persistent infection through:
 - High replication rate with error-prone RNA polymerase generating quasispecies
 - Immune evasion strategies
 - Lack of robust CD8+ T-cell response
3. **Progressive Chronic Hepatitis** - Ongoing hepatocyte damage and regeneration. Inflammatory infiltrates. Progressive fibrosis develops over 20-30 years. Rate influenced by age at infection, alcohol use, HIV or HBV co-infection, metabolic syndrome, male sex

- 4. Cirrhosis and Hepatocellular Carcinoma** - Approximately 10-20% develop cirrhosis after 20 years. Once cirrhotic: Annual risk of hepatic decompensation 3-6%, HCC 1-5%, death 2-5%

Comprehensive Preventive Measures

Hepatitis A Prevention:

Vaccination - Highly Effective:

- **Inactivated hepatitis A vaccine** (Havrix, Vaqta):
 - Two-dose series: Initial dose and booster at 6-18 months
 - >95% efficacy
 - Recommended for:
 - All children at age 12-23 months
 - Travelers to endemic areas
 - Men who have sex with men
 - Illicit drug users
 - Persons with chronic liver disease
 - Food handlers in some settings
 - Provides long-lasting (possibly lifelong) immunity

Hygiene and Food Safety:

- Handwashing after toilet use, before food preparation
- Safe water sources; boil water in endemic areas
- Proper sewage disposal
- Avoid raw shellfish from contaminated waters
- Wash fruits and vegetables
- Proper food handling practices

Post-exposure Prophylaxis:

- Hepatitis A vaccine or immune globulin within 2 weeks of exposure

Hepatitis B Prevention:

Vaccination - Cornerstone of Prevention:

- **Recombinant hepatitis B vaccine:**
 - Three-dose series: 0, 1, and 6 months (or accelerated schedules available)
 - ">95% protective efficacy in infants, children, and young adults
 - Recommended universally:
 - All infants at birth (within 24 hours)
 - All children and adolescents not previously vaccinated
 - High-risk adults: healthcare workers, household and sexual contacts of HBsAg-positive persons, dialysis patients, HIV-infected, men who have sex with men, IVDU, persons with multiple sexual partners, travelers to endemic areas
 - Immunity assessment (anti-HBs testing) recommended for healthcare workers and immunocompromised
 - Booster doses generally not needed in immunocompetent individuals

Prevention of Transmission:

- **Universal precautions** in healthcare: Safe injection practices, proper disposal of sharps, personal protective equipment
- **Blood supply screening** - All donated blood tested for HBsAg
- **Safe sex practices** - Condom use, reduction of partners
- **Needle exchange programs** - For injection drug users
- **Prevention of mother-to-child transmission:**
 - Screening all pregnant women for HBsAg
 - Infants born to HBsAg-positive mothers receive:
 - Hepatitis B vaccine within 12 hours of birth
 - Hepatitis B immune globulin (HBIG) within 12 hours
 - Complete vaccine series

- Post-vaccination serologic testing at 9-12 months
 - Antiviral therapy (tenofovir) for pregnant women with high viral loads (>200,000 IU/mL) in third trimester further reduces transmission

Post-exposure Prophylaxis:

- Unvaccinated exposed individuals: HBIG + vaccine series initiated
- Timing critical: Within 24 hours for perinatal exposure, within 7 days for sexual or needlestick exposure

Hepatitis C Prevention:

No Vaccine Available:

- Vaccine development challenging due to:
 - High viral genetic diversity (6 genotypes, multiple subtypes)
 - Rapid mutation rate and quasispecies
 - Lack of small animal models
 - Research ongoing

Prevention Through Risk Reduction:

Blood Safety:

- Universal screening of donated blood for anti-HCV and HCV RNA
- Heat treatment of plasma-derived products

Injection Safety:

- Safe injection practices in healthcare
- Single-use needles and syringes
- Proper sterilization of reusable medical equipment
- Needle exchange programs for IVDU
- Addiction treatment and harm reduction

Occupational Safety:

- Universal precautions in healthcare settings

- Post-exposure testing and monitoring (no effective post-exposure prophylaxis available)

Other Transmission Prevention:

- Avoid sharing personal items that might contact blood (razors, toothbrushes, nail clippers)
- Cover wounds
- Safe sex practices (though sexual transmission less efficient than HBV)

Screening and Treatment as Prevention:

- Identifying infected individuals through screening
- Linkage to curative treatment prevents ongoing transmission
- "Micro-elimination" strategies targeting high-prevalence populations

Diagnostic Approaches

Clinical Diagnosis:

- Suspicious symptoms: jaundice, dark urine, clay stools, right upper quadrant pain
- Risk factor assessment

Liver Function Tests (LFTs):

Transaminases (aminotransferases):

- **AST (aspartate aminotransferase) and ALT (alanine aminotransferase)** - Markers of hepatocyte injury:
 - ALT more specific for liver
 - Acute viral hepatitis: Often >1000 U/L, may exceed 3000 U/L
 - ALT typically higher than AST in viral hepatitis (AST:ALT ratio <1)
 - Degree of elevation does not correlate with prognosis
 - Elevation precedes jaundice

Bilirubin:

- **Total and direct (conjugated) bilirubin** elevated:
 - Peak usually lags behind transaminases
 - Direct hyperbilirubinemia predominates (conjugated >50%)
 - Levels vary from normal to >20 mg/dL

Alkaline phosphatase:

- Usually mildly elevated (<3 times normal)
- Greater elevation suggests cholestatic hepatitis or biliary obstruction

Albumin and prothrombin time:

- Usually normal in acute uncomplicated hepatitis
- Prolonged PT or low albumin suggests severe acute hepatitis or chronic liver disease
- PT >4-6 seconds prolonged is concerning for fulminant hepatitis

Complete Blood Count:

- Mild leukopenia common
- Atypical lymphocytes may be seen

Serologic Testing - Specific Diagnosis:

Hepatitis A:

- **Anti-HAV IgM** - Positive in acute infection, appears early, persists 3-6 months
- **Anti-HAV IgG** - Indicates past infection or vaccination, provides immunity
- **Total anti-HAV** - Screens for any prior exposure or immunity

Hepatitis B:

Screening:

- **HBsAg (hepatitis B surface antigen)** - Presence indicates active infection (acute or chronic)
- **Anti-HBc (hepatitis B core antibody) total** - Indicates current or past infection

- **Anti-HBs (antibody to surface antigen)** - Indicates immunity from infection or vaccination

Acute vs. Chronic:

- **Anti-HBc IgM** - High titer indicates acute infection or flare of chronic
- **HBsAg positive <6 months** = acute; **>6 months** = chronic

In Chronic HBV:

- **HBeAg/anti-HBe** - Markers of replication and infectivity
- **HBV DNA (viral load)** - Quantifies viral replication, guides treatment decisions
- **Genotype** - May influence treatment choice and prognosis

Hepatitis C:

- **Anti-HCV antibody (EIA)** - Screening test:
 - Positive indicates current or past HCV infection
 - May be negative early in acute infection (window period)
 - Remains positive for life even if infection cleared
 - Positive screen requires confirmatory testing
- **HCV RNA (quantitative PCR)** - Confirmatory and diagnostic:
 - Detects active viral replication
 - Distinguishes current from past infection
 - Quantifies viral load for treatment monitoring
 - Can be detected 1-2 weeks after exposure (before antibodies)
- **HCV genotype** - Essential for treatment planning:
 - Genotypes 1-6
 - Influences treatment regimen selection (though newer DAAs pan-genotypic)
 - Geographic distribution varies

Imaging:

- **Ultrasound** - Assess liver texture, size, rule out biliary obstruction, screen for HCC
- **Fibroscan (transient elastography)** - Non-invasive assessment of liver fibrosis/cirrhosis
- **MRI/CT** - If mass lesion or complications suspected

Liver Biopsy:

- Traditionally gold standard for assessing degree of inflammation and fibrosis
- Now less commonly needed due to:
 - Non-invasive alternatives (fibroscan, serum biomarkers)
 - Treatment decisions less dependent on biopsy with newer therapies
- Still may be performed for:
 - Diagnostic uncertainty
 - Assessing coexistent liver disease
 - Research purposes

First Aid and Immediate Care Measures

For Acute Viral Hepatitis (Outpatient Management):

Rest:

- Adequate rest based on symptoms and energy level
- Complete bed rest not necessary but avoid overexertion
- Gradual return to normal activities as symptoms improve
- May take weeks to months to regain full energy

Nutrition:

- Eat as tolerated; no special diet required
- Small frequent meals often better tolerated than large meals
- High-calorie breakfast often best tolerated (nausea worsens later in day)
- Adequate protein intake

- Fluid intake to maintain hydration

Alcohol Avoidance - Absolutely Critical:

- Complete abstinence from alcohol during acute hepatitis and for at least 6 months after
- Alcohol exacerbates liver injury
- May increase risk of fulminant hepatitis
- Continue abstinence if chronic hepatitis develops

Medication Precautions:

- Avoid hepatotoxic medications:
 - Acetaminophen (paracetamol) - avoid or use minimal doses only if essential
 - Many herbal supplements and traditional medicines
 - Unnecessary medications
- Review all medications with physician
- Some medications require dose adjustment in liver disease

Monitor for Complications:

Seek immediate medical attention for:

- **Severe vomiting** preventing oral intake
- **Confusion or altered mental status** (hepatic encephalopathy)
- **Easy bruising or bleeding** (coagulopathy)
- **Increasing abdominal distention** (ascites)
- **Worsening jaundice** instead of improvement
- **Prolonged course** without improvement

Isolation and Transmission Prevention:

Hepatitis A:

- Isolation from work/school during first 1-2 weeks of jaundice

- Strict hand hygiene, especially after toilet use
- Avoid food preparation for others
- Household contacts should receive HAV vaccine or immune globulin

Hepatitis B and C:

- No isolation from work/school necessary
- Cannot transmit through casual contact, food preparation, breastfeeding (HBV may transmit if cracked, bleeding nipples)
- Prevention:
 - Do not share items that may have blood (razors, toothbrushes, nail clippers)
 - Cover wounds
 - Clean blood spills with bleach solution
 - Disclose infection status to sexual partners; use condoms
 - Do not donate blood, organs, sperm, or ova
 - Household contacts should be vaccinated (HBV)
 - Sexual partners should be tested and vaccinated (HBV)

Follow-up:

- Regular monitoring of LFTs until normalization
- Repeat testing to confirm resolution or document chronicity
- Hepatitis B: Repeat HBsAg at 6 months to determine if chronic
- Hepatitis C: Repeat HCV RNA at 12 weeks and 6 months post-infection to determine if chronic

For Chronic Hepatitis:

- Regular monitoring for disease progression
- Screening for hepatocellular carcinoma (ultrasound +/- AFP every 6 months in cirrhosis or high-risk patients)
- Vaccination against hepatitis A and B if not immune

- Avoid alcohol, hepatotoxic medications
- Evaluation for antiviral treatment

Antiviral and Drug Information (Educational Reference)

Hepatitis A:

No Specific Antiviral Treatment:

- Acute hepatitis A is self-limiting
- Supportive care only
- Full recovery expected in >99% of cases
- Monitor for rare fulminant hepatitis

Hepatitis B:

Treatment Indicated For:

- Chronic HBV with active viral replication (HBV DNA >2000 IU/mL) AND either:
 - Persistently elevated transaminases (ALT elevation)
 - Significant liver fibrosis/cirrhosis on biopsy or non-invasive testing
- Cirrhotic patients regardless of ALT or HBV DNA level
- Acute severe or fulminant HBV
- HBV reactivation
- Certain special populations (pregnant women with high viral load, immunosuppressive therapy)

Goals of Treatment:

- Virologic suppression (HBV DNA undetectable or <2000 IU/mL)
- ALT normalization
- Prevention of progression to cirrhosis and HCC
- In some cases: HBeAg seroconversion or HBsAg loss ("functional cure")

Nucleos(t)ide Analogues - First-Line Therapy:

Tenofovir disoproxil fumarate (TDF) or Tenofovir alafenamide (TAF):

- **Dosing:** TDF 300 mg once daily; TAF 25 mg once daily
- High potency, high barrier to resistance
- Preferred first-line agents
- TAF has improved renal and bone safety profile compared to TDF
- Usually long-term/indefinite therapy required
- Cannot cure infection (cccDNA persists in hepatocytes)
- Minimal side effects
- Safe in pregnancy (TDF has most data)

Entecavir:

- **Dosing:** 0.5 mg once daily (1 mg if lamivudine-resistant)
- High potency, high barrier to resistance
- Alternative first-line agent
- Long-term therapy required
- Generally well-tolerated
- Limited pregnancy data; avoid if possible

Older agents (rarely used due to resistance):

- Lamivudine - high resistance rates
- Adefovir - inferior potency, renal toxicity
- Telbivudine - inferior to TDF/TAF

Interferon-alpha/Pegylated Interferon:

- Alternative for select patients (young, non-cirrhotic, high ALT, low HBV DNA, certain genotypes)
- **Dosing:** Subcutaneous injections weekly (pegIFN) for 48 weeks
- **Advantages:** Finite duration, possibility of HBsAg loss
- **Disadvantages:** Injectable, significant side effects (flu-like symptoms, depression, cytopenias), contraindicated in cirrhosis, autoimmune disease,

pregnancy

- Less commonly used now given excellent oral alternatives

Monitoring on Treatment:

- HBV DNA and ALT every 3-6 months
- Annual AFP and ultrasound for HCC screening in cirrhosis

Hepatitis C:

REVOLUTION IN HCV TREATMENT:

- Direct-Acting Antivirals (DAAs) introduced starting 2013 have transformed HCV from difficult-to-treat to curable in >95% of patients
- Short treatment duration (8-12 weeks typically)
- Oral medications
- Minimal side effects
- High efficacy across all genotypes

Treatment Indicated For:

- All patients with chronic HCV infection should be evaluated for treatment
- Priority: Advanced fibrosis/cirrhosis, high-risk occupations, HCV/HIV co-infection, transplant recipients/candidates

Goal of Treatment:

- **Sustained Virologic Response (SVR)** = Cure:
 - Defined as undetectable HCV RNA 12 or 24 weeks after treatment completion
 - SVR indicates viral eradication
 - Associated with improved outcomes: regression of fibrosis, reduced HCC risk, reduced mortality

Direct-Acting Antivirals (DAAs):

Multiple drug classes targeting different steps in HCV lifecycle:

- NS3/4A protease inhibitors (suffix: -previr)

- NS5A inhibitors (suffix: -asvir)
- NS5B polymerase inhibitors (suffix: -buvir)

Most commonly used **pan-genotypic combination regimens:**

Sofosbuvir/Velpatasvir (Epclusa):

- **Dosing:** One tablet (400/100 mg) once daily
- **Duration:** 12 weeks for most patients without cirrhosis or treatment-experienced; may extend to 24 weeks for decompensated cirrhosis
- **Genotypes:** All (1-6)
- **Efficacy:** >95% SVR
- **Side effects:** Minimal; fatigue and headache most common

Glecaprevir/Pibrentasvir (Mavyret):

- **Dosing:** Three tablets (100/40 mg each) once daily with food
- **Duration:** 8 weeks for treatment-naive without cirrhosis; 12-16 weeks for some patients
- **Genotypes:** All (1-6)
- **Efficacy:** >95% SVR
- **Side effects:** Minimal; fatigue, headache, nausea
- **Contraindication:** Decompensated cirrhosis (Child-Pugh B/C)

Ledipasvir/Sofosbuvir (Harvoni):

- **Dosing:** One tablet (90/400 mg) once daily
- **Duration:** 12 weeks typically; 8 weeks for some treatment-naive without cirrhosis
- **Genotypes:** 1, 4, 5, 6 (most commonly used for genotype 1)
- **Efficacy:** >95% SVR

Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi):

- **Dosing:** One tablet daily

- **Duration:** 12 weeks
- **Indication:** Salvage therapy for DAA treatment failures
- **Genotypes:** All

Treatment Selection:

- Based on genotype (though pan-genotypic regimens simplifying), prior treatment history, presence/severity of cirrhosis, renal function, drug interactions
- Individual regimens may have specific contraindications or dose adjustments

Monitoring:

- HCV RNA at baseline, end of treatment, and 12 weeks post-treatment (to confirm SVR)
- LFTs during treatment
- Drug interactions - careful review of concomitant medications

Post-SVR:

- Cured of HCV
- Anti-HCV antibodies remain positive (does not indicate active infection)
- Risk of reinfection if ongoing exposure (no immunity develops)
- Continue HCC surveillance if cirrhosis present (risk reduced but not eliminated)
- Lifestyle modifications (alcohol avoidance)

Antibiotics:

- **NOT indicated for any viral hepatitis** as they are viral infections
- Antibiotics have no role in treatment
- May cause additional hepatotoxicity
- Only use if confirmed bacterial infection develops

6. Measles

Comprehensive Overview

Measles (rubeola) is one of the most contagious infectious diseases known to humanity, caused by measles virus, a single-stranded RNA virus of the *Morbillivirus* genus in the *Paramyxoviridae* family. Before widespread vaccination, measles infected virtually every child by adolescence, causing millions of deaths annually. The disease is characterized by fever, cough, coryza (runny nose), conjunctivitis (the "three Cs"), and a distinctive maculopapular rash that spreads from head to trunk to extremities.

Measles virus is extraordinarily transmissible, with a basic reproduction number (R_0) of 12-18, meaning each infected person transmits to 12-18 susceptible contacts. The virus spreads through airborne respiratory droplets and aerosols, remaining infectious in the air and on surfaces for up to 2 hours. Up to 90% of susceptible contacts become infected after exposure. This extreme contagiousness necessitates very high vaccination coverage (>95%) to maintain herd immunity and prevent outbreaks.

While often dismissed as a benign childhood illness, measles causes significant morbidity and mortality, particularly in young children, malnourished individuals, and immunocompromised persons. Complications occur in up to 30% of cases and include diarrhea, otitis media, pneumonia (leading cause of measles deaths), and encephalitis. Notably, measles virus causes profound immunosuppression lasting weeks to months after acute illness ("immune amnesia"), increasing vulnerability to other infections. A rare but devastating late complication, subacute sclerosing panencephalitis (SSPE), manifests years after acute infection with progressive neurodegeneration and death.

The measles vaccine, introduced in 1963, is highly effective (97% efficacy after two doses), safe, and cost-effective. Global vaccination efforts through the Expanded Programme on Immunization have prevented an estimated 21 million deaths between 2000-2017. However, measles remains endemic in many countries, and outbreaks occur even in countries with high vaccination coverage due to pockets of unvaccinated individuals. Achieving measles elimination requires sustained high vaccination coverage, robust surveillance, and rapid outbreak response.

Clinical Manifestations and Symptoms

Measles follows a predictable clinical course progressing through distinct phases:

Incubation Period:

- 10-14 days (range 7-21 days) from exposure to symptom onset
- Asymptomatic
- Virus replicates in respiratory epithelium and local lymph nodes, then disseminates via bloodstream
- Patient not contagious during this period

Prodromal (Catarrhal) Phase (Days 1-4 of Illness):

The classic "**three Cs**":

- **Cough** - Hacking, persistent cough resulting from bronchial inflammation. One of the earliest symptoms
- **Coryza** - Profuse nasal discharge (runny nose). Clear initially, may become mucopurulent
- **Conjunctivitis** - Red, watery eyes, photophobia (light sensitivity), edema of eyelids. Produces characteristic "measles facies" with red eyes, swollen eyelids, and facial edema

Plus:

- **High fever** - Temperature typically 39-40.5°C (102-105°F), may reach 41°C (106°F). Fever rises in stepwise fashion
- **Malaise** - Irritability, restlessness, general ill appearance
- **Anorexia** - Loss of appetite
- **Pathognomonic Koplik's spots** - The pathognomonic (uniquely characteristic) finding of measles:
 - Tiny white spots (1-2 mm) with red halos on buccal mucosa (inside cheeks) opposite the molars
 - Described as "grains of salt on a red background"
 - Appear 1-2 days before rash, fade as rash appears

- Present in 60-70% of cases
- Diagnostic if recognized but transient nature means often missed

Enanthem - Red spots on soft palate and pharynx

Highly contagious: Patient infectious from 4 days before rash onset through 4 days after rash appearance (infectivity highest during prodrome)

Rash Phase (Eruptive Phase, Days 5-9 of Illness):

- **Characteristic rash:**
 - **Maculopapular** - Red, slightly raised blotchy spots, may become confluent
 - **Cephalocaudal (head-to-toe) progression:**
 - **Day 1:** Begins at hairline, forehead, behind ears
 - **Day 2:** Spreads to face, neck, upper trunk and arms
 - **Day 3:** Reaches lower trunk, thighs, lower legs and feet
 - As rash spreads downward, it becomes confluent on face and upper body
 - Individual lesions last 3-4 days
 - Blanches with pressure initially
 - May become hemorrhagic (petechial) in severe cases
- **Fever peaks** at 40-41°C (104-106°F) as rash appears, then begins to defervescence
- **Continued symptoms:** Cough, conjunctivitis, and coryza persist during rash phase but begin improving

Recovery Phase (Days 10-14):

- **Rash fades** in same cephalocaudal sequence, leaving brownish discoloration and desquamation (skin peeling)
- Fever resolves
- Symptoms gradually improve
- Cough may persist for 1-2 weeks

- Patient no longer contagious 4 days after rash onset

Complications (Occur in ~30% of Cases):

Common Complications:

- **Diarrhea** - Most common complication, contributes to malnutrition and mortality in developing countries
- **Otitis media** - Middle ear infection in 7-9% of cases
- **Pneumonia** - Leading cause of measles mortality:
 - Primary viral pneumonia - direct viral invasion of lungs
 - Secondary bacterial pneumonia - bacterial superinfection
 - Occurs in 1-6% of cases, higher in infants and immunocompromised
- **Laryngotracheobronchitis (croup)** - Inflammation of airways causing barking cough and stridor

Serious Complications:

- **Encephalitis** - Brain inflammation:
 - Occurs in approximately 1 per 1000 cases
 - Onset typically 2-14 days after rash
 - Presents with altered consciousness, seizures, focal neurologic signs
 - Mortality rate 10-15%; long-term neurologic sequelae in 25% of survivors
 - Acute disseminated encephalomyelitis (ADEM) - demyelinating disorder
- **Immune suppression** - Measles causes profound, prolonged immunosuppression:
 - "Immune amnesia" - loss of pre-existing immunologic memory to other pathogens
 - Lasts weeks to months after recovery
 - Increased susceptibility to other infections (bacterial, viral, parasitic)
 - Major contributor to post-measles mortality
- **Keratitis and blindness** - Corneal infection, particularly in vitamin A deficiency

- **Subacute sclerosing panencephalitis (SSPE)** - Rare, fatal late complication:
 - Progressive neurodegenerative disorder
 - Develops 7-10 years after acute measles infection (range 1 month to 27 years)
 - Occurs in 4-11 per 100,000 measles cases
 - Higher risk if measles contracted before age 2 years
 - Insidious onset: behavioral changes, cognitive decline, myoclonic seizures
 - Progressive deterioration leading to coma and death over months to years
 - No effective treatment
 - Caused by persistent measles virus infection in central nervous system with defective viral replication

High-Risk Groups for Complications:

- Children <5 years, especially infants <12 months
- Adults >20 years
- Pregnant women (risk of miscarriage, preterm labor, maternal mortality)
- Immunocompromised individuals
- Malnourished children, particularly vitamin A deficiency
- Chronic lung or heart disease

Detailed Stages of Infection

1. **Exposure and Viral Entry (Day 0)** - Measles virus transmitted through airborne respiratory droplets or aerosols from infected person's cough, sneeze, or breathing. Direct contact with respiratory secretions also transmits. Virus extremely contagious; 90% of susceptible contacts become infected. Virus enters through respiratory epithelium or conjunctiva
2. **Initial Replication and Primary Viremia (Days 1-4)** - Virus replicates in respiratory epithelium and spreads to regional lymph nodes (tonsils, adenoids, cervical nodes). Initial multiplication in respiratory tract and lymphoid tissue. Primary viremia (virus in bloodstream) begins around day 2-4, spreading to

reticuloendothelial system throughout body (lymph nodes, liver, spleen). Patient asymptomatic and not contagious during this period

3. **Amplification and Secondary Viremia (Days 5-7)** - Extensive viral replication in reticuloendothelial system. Secondary viremia begins around day 5-7 with much higher viral load. Virus disseminates widely to skin, respiratory tract, gastrointestinal tract, urinary tract, lymphoid tissue, and other organs. This marks transition from incubation to prodromal phase
4. **Prodromal (Catarrhal) Phase (Days 7-11, Clinical Days 1-4)** - Onset of symptoms coincides with secondary viremia. Virus replicates extensively in respiratory epithelium causing the three Cs: cough, coryza, conjunctivitis. High fever develops. Koplik's spots appear on buccal mucosa (1-2 days before rash) - diagnostic finding representing focal necrosis of oral epithelium. Peak viral shedding during this phase. Patient highly contagious (from 4 days before rash onset). Immune response begins with interferon production and cellular immunity activation
5. **Rash (Eruptive) Phase (Days 11-14, Clinical Days 4-7)** - Rash appears as cell-mediated immune response peaks. Rash represents immune response rather than direct viral damage - T-cells attacking virus-infected endothelial cells in small blood vessels. Cephalocaudal progression as described above. Fever peaks as rash appears then defervesces. Koplik's spots fade as rash appears. Antibody response (IgM then IgG) develops. Viral shedding decreases. Patient remains contagious through 4 days after rash onset
6. **Recovery Phase (Days 14-21, Clinical Days 7-14 and Beyond)** - Immune clearance of virus. Rash fades leaving brownish hyperpigmentation and desquamation. Symptoms gradually resolve though cough may persist. Patient no longer contagious. However, profound immunosuppression begins that lasts weeks to months, erasing previous immunologic memory and increasing vulnerability to other infections
7. **Development of Immunity or Late Complications** - Most patients develop lifelong immunity mediated by antibodies and cellular immunity. However, in rare cases (~1 in 10,000), persistent defective measles virus establishes CNS infection leading to SSPE years later

Comprehensive Preventive Measures

Vaccination - The Most Effective Prevention:

MMR Vaccine (Measles, Mumps, Rubella):

- **Live attenuated vaccine** - Contains weakened measles virus that replicates but causes minimal or no symptoms
- **Schedule:**
 - First dose at 12-15 months of age
 - Second dose at 4-6 years (before school entry)
 - Two doses required for optimal protection
- **Efficacy:**
 - One dose: 93% effective
 - Two doses: 97% effective
 - Duration: Lifelong immunity in most recipients
- **Safety:** Excellent safety profile; serious adverse events extremely rare
- **Benefits outweigh risks by enormous margin**

Contraindications to MMR vaccine:

- Severe immunodeficiency (HIV with CD4 <15%, chemotherapy, high-dose steroids)
- Pregnancy (theoretical risk; avoid pregnancy for 28 days after vaccination)
- Severe allergic reaction to previous dose or vaccine component
- Recent blood product administration (antibodies may interfere)

Catch-up vaccination:

- Unvaccinated children, adolescents, and adults should receive 2 doses separated by 28 days
- Particularly important for healthcare workers, international travelers

Herd Immunity:

- Requires >95% vaccination coverage to interrupt transmission

- Protects individuals who cannot be vaccinated (infants, immunocompromised)
- Outbreaks occur when vaccination coverage drops below threshold

Outbreak Response Vaccination:

- Rapid vaccination of susceptible contacts within 72 hours of exposure may prevent or attenuate disease

Post-Exposure Prophylaxis:

For Susceptible Contacts:

MMR vaccine:

- If administered within 72 hours of exposure, may provide protection or attenuate disease
- Preferred for children ≥ 6 months (off-label for 6-12 months), adolescents, and adults without contraindications

Immunoglobulin (IG):

- For individuals with contraindications to vaccine (immunocompromised, pregnant women, infants < 6 months)
- Must be administered within 6 days of exposure
- Provides passive antibodies
- Dose: 0.5 mL/kg IM (maximum 15 mL) for immunocompetent; 0.25 mL/kg for immunocompromised
- May prevent or modify disease severity

Isolation Measures:

- **Infected individuals:** Isolate from others (especially unvaccinated) from 4 days before rash through 4 days after rash onset
- **Airborne precautions** in healthcare settings - negative pressure room, N95 respirators for healthcare workers
- **School/work exclusion** for at least 4 days after rash onset
- **Susceptible exposed contacts:** Exclude from school/work from day 5 through day 21 after exposure if not vaccinated post-exposure

Vitamin A Supplementation in Endemic Areas:

- Vitamin A deficiency increases measles severity and mortality
- WHO recommends vitamin A supplementation for all children diagnosed with measles in areas where vitamin A deficiency prevalent
- Reduces severity and mortality

Diagnostic Approaches

Clinical Diagnosis:

- **Classic presentation** highly suggestive:
 - Prodrome of fever, cough, coryza, conjunctivitis
 - Koplik's spots (if observed)
 - Characteristic cephalo-caudal maculopapular rash
 - History of exposure
- **Case definition (WHO):**
 - Fever $\geq 38^{\circ}\text{C}$ (100.4°F) AND
 - Maculopapular (non-vesicular) rash AND
 - One of: cough, coryza, or conjunctivitis

Laboratory Confirmation (Essential for Surveillance):

Serology:

Measles-specific IgM antibodies:

- Most common confirmatory test
- Detected 3-4 days after rash onset
- Peak at 7-14 days
- Persist for 4-8 weeks
- Single positive IgM confirms acute infection
- False negatives if tested too early (<3 days after rash) - repeat testing recommended

- False positives rare (other viral infections, parvovirus B19, rheumatoid factor)

Measles-specific IgG antibodies:

- Appears shortly after IgM
- 4-fold rise in paired acute/convalescent titers (2-3 weeks apart) confirms recent infection
- Single positive IgG indicates past infection or vaccination (not diagnostic of acute infection)
- Used to assess immunity status

Viral Detection:

RT-PCR (Reverse Transcription-Polymerase Chain Reaction):

- Detects measles virus RNA
- Gold standard for confirmation
- Specimens: throat swab, nasal swab, nasopharyngeal aspirate, urine (first morning void)
- Most sensitive during first 3 days after rash onset
- Can determine viral genotype (important for outbreak investigation and distinguishing wild-type from vaccine virus)
- Rapid results (hours to days)

Viral culture:

- Rarely performed (labor-intensive, requires specialized facilities, takes 1-2 weeks)
- Mainly for research and genotyping

Specimen Collection Timing:

- **Optimal:** Collect within 5 days of rash onset
- Blood for serology: 3-28 days after rash onset (preferably after day 3)
- Respiratory specimens (throat/nasal swab) for PCR: Ideally within 7 days of rash onset

- Urine for PCR: Within 14 days of rash onset

Complete Blood Count:

- Leukopenia (low white blood cell count) common
- Lymphopenia (low lymphocyte count) due to viral-induced immunosuppression
- Not diagnostic but supportive

Chest X-ray:

- If pneumonia suspected
- May show interstitial or alveolar infiltrates

Public Health Reporting:

- Measles is a **nationally notifiable disease**
- All suspected and confirmed cases must be reported to public health authorities immediately
- Essential for outbreak detection, contact tracing, and containment

First Aid and Immediate Care Measures

Supportive Care - Mainstay of Treatment:

Rest:

- Complete bed rest during acute illness
- Dim lighting may help if photophobia present
- Quiet environment

Hydration:

- Adequate fluid intake crucial, especially if fever or diarrhea present
- Water, oral rehydration solutions, clear broths
- Monitor for dehydration (particularly in children)

Fever Management:

- Antipyretics for comfort:

- Paracetamol (acetaminophen): 10-15 mg/kg every 4-6 hours
- Ibuprofen: 5-10 mg/kg every 6-8 hours
- **AVOID aspirin in children** - Risk of Reye's syndrome
- Tepid sponging
- Light clothing

Symptomatic Relief:

- **For cough:** Humidification, honey (age >1 year), cough suppressants if severe
- **For conjunctivitis:** Wipe eyes gently with damp cloth, dim lighting, artificial tears
- **For photophobia:** Dim room lighting, avoid bright lights

Nutrition:

- Offer easily digestible, nutritious foods
- Small frequent meals if anorexia
- Soft foods if mouth sores present
- Continue breastfeeding in infants

Vitamin A Supplementation - CRITICAL:

WHO recommends vitamin A for ALL children with measles:

- **Age 6-11 months:** 100,000 IU orally once daily for 2 days
- **Age ≥12 months:** 200,000 IU orally once daily for 2 days
- **Infants <6 months:** 50,000 IU orally once daily for 2 days

Rationale:

- Measles depletes vitamin A stores
- Vitamin A deficiency increases severity, complications, and mortality
- Supplementation reduces mortality by 50% and reduces severity of complications
- Benefits even in well-nourished populations

- Particularly important for severe measles, immunodeficiency, malnutrition, vitamin A deficiency

Isolation:

- Isolate from others, especially unvaccinated individuals, pregnant women, immunocompromised
- Duration: From onset of symptoms through 4 days after rash appears
- Airborne precautions (N95 mask if must leave isolation)
- Remember: virus remains in air and on surfaces for 2 hours

Monitoring for Complications:

Seek immediate medical attention for:

- **Respiratory distress** - rapid breathing, difficulty breathing, chest retractions, cyanosis
- **Altered consciousness** - confusion, lethargy, seizures (possible encephalitis)
- **Severe dehydration** - decreased urination, dry mucous membranes, sunken eyes
- **Persistent high fever** >3 days after rash onset (may indicate bacterial superinfection)
- **Severe diarrhea**
- **Ear pain** (otitis media)
- **Visual changes** (keratitis)
- **Worsening after initial improvement** (bacterial pneumonia)

High-Risk Patients:

- Infants, immunocompromised, pregnant women, malnourished children should be monitored closely
- Lower threshold for hospitalization

Contact Management:

- Identify all contacts from 4 days before rash through 4 days after

- Assess vaccination and immunity status
- Provide post-exposure prophylaxis (vaccine or IG) as appropriate
- Monitor for 21 days after last exposure

Antiviral and Drug Information (Educational Reference)

No Specific Antiviral Treatment:

- No antiviral medications proven effective against measles virus
- Multiple agents have been studied without demonstrated benefit
- Ribavirin has been used in immunocompromised patients with severe measles but evidence limited
- Treatment remains entirely supportive

Vitamin A - The Most Important Intervention:

- As described above - reduces mortality and morbidity
- Should be given to ALL children with measles
- This is the single most evidence-based specific intervention for measles

Antibiotics:

NOT Indicated for Uncomplicated Measles:

- Measles is a viral infection
- Antibiotics provide no benefit and should not be given prophylactically
- Contribute to antimicrobial resistance
- May cause adverse effects

When Antibiotics ARE Indicated:

Only if bacterial complication develops:

- **Bacterial pneumonia:**
 - Suspected if: New fever after rash, purulent sputum, focal chest findings, infiltrate on chest X-ray

- Common organisms: *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, Group A Streptococcus
- Empiric antibiotic choice: Amoxicillin-clavulanate or cephalosporin, adjust based on local resistance patterns
- Severe cases may require hospitalization and IV antibiotics
- **Acute otitis media:**
 - Ear pain, bulging tympanic membrane
 - Standard treatment: Amoxicillin
- **Sinusitis:**
 - Prolonged symptoms, purulent nasal discharge, facial pain

Immunoglobulin:

- As post-exposure prophylaxis (described above)
- Not used for treatment of established disease

Corticosteroids:

- Not routinely recommended
- May be considered in severe croup causing airway obstruction
- Avoid in uncomplicated measles (may worsen immunosuppression)

Symptomatic Medications:

- Antipyretics (paracetamol, ibuprofen) for fever and discomfort
- Cough suppressants (dextromethorphan) for severe cough
- Antihistamines not particularly helpful

Management of Complications:

- **Pneumonia:** Oxygen, supportive care, antibiotics if bacterial
- **Encephalitis:** Hospitalization, supportive care, seizure control, no specific treatment
- **Severe diarrhea:** Oral rehydration, IV fluids if severe, zinc supplementation

- **Keratitis:** Ophthalmologic evaluation, vitamin A, topical antibiotics if secondary bacterial infection

Hospital Admission Indications:

- Age <12 months
- Immunocompromised
- Pregnant women
- Severe complications (pneumonia, encephalitis, severe dehydration)
- Inability to maintain hydration
- Social factors preventing adequate home care

Prevention of Secondary Cases:

- Rapid identification and vaccination of susceptible contacts
- Public health investigation and response
- Enhanced surveillance during outbreaks



7. Chickenpox (Varicella)

Comprehensive Overview

Chickenpox (varicella) is a highly contagious acute viral infection caused by varicella-zoster virus (VZV), a member of the *Herpesviridae* family. The disease is characterized by a distinctive pruritic vesicular rash that appears in successive crops, accompanied by fever and systemic symptoms. Before the introduction of varicella vaccine in 1995, chickenpox was a nearly universal childhood infection in the United States, affecting over 90% of individuals by adolescence, with approximately 4 million cases annually.

Varicella-zoster virus is a double-stranded DNA virus that establishes lifelong latent infection in dorsal root ganglia after primary infection. This latency allows the virus to reactivate years to decades later as herpes zoster (shingles), typically in older adults or immunocompromised individuals. The virus is transmitted through respiratory droplets and direct contact with vesicular fluid, with a

secondary attack rate of 61-100% among susceptible household contacts, reflecting its high contagiousness.

While typically a mild, self-limiting disease in healthy children, chickenpox can cause severe complications including bacterial superinfection of skin lesions (most common), pneumonia, encephalitis, cerebellar ataxia, and hemorrhagic complications. Certain populations face particularly high risk: neonates, adolescents, adults, pregnant women, and immunocompromised individuals. Maternal varicella infection during pregnancy can result in congenital varicella syndrome (if infected in first 20 weeks) or severe neonatal varicella (if infected around delivery).

The introduction of universal varicella vaccination has dramatically reduced disease burden in countries with vaccination programs. The vaccine is highly effective (two doses provide >90% protection against all varicella and >95% protection against severe disease) and has proven safe. However, breakthrough infections occur in vaccinated individuals, though these are typically much milder. Global implementation of varicella vaccination remains variable, with some countries adopting universal programs while others reserve vaccination for high-risk groups.

Clinical Manifestations and Symptoms

Incubation Period:

- 10-21 days after exposure (average 14-16 days)
- Asymptomatic period
- Virus replicates in respiratory mucosa and regional lymph nodes, then disseminates via bloodstream
- Not contagious during most of incubation period

Prodromal Phase (1-2 Days Before Rash):

Not always present, more common in older children and adults:

- **Low-grade fever** - Temperature 37.5-39°C (99.5-102.2°F)
- **Malaise** - General feeling of being unwell
- **Anorexia** - Loss of appetite

- **Headache** - Mild to moderate
- **Mild respiratory symptoms** - Occasional cough or sore throat

Infants and young children often have minimal or no prodrome, with rash being first sign.

Characteristic Rash (Hallmark of Disease):

Evolution of Individual Lesions:

Distinctive progression through stages ("dew drop on a rose petal" appearance):

1. **Macule** - Small flat red spot (few hours)
2. **Papule** - Raised red bump (few hours)
3. **Vesicle** - Clear fluid-filled blister on erythematous base (1-2 days):
 - Described as "dewdrop on rose petal"
 - Thin-walled, fragile, easily rupture
 - Contain highly infectious viral particles
4. **Pustule** - Vesicle fluid becomes cloudy (not indicating bacterial infection) (1 day)
5. **Crust/Scab** - Lesion dries and forms crust (several days to 1-2 weeks)
 - Crusts eventually fall off leaving temporary pink marks
 - Usually no scarring unless lesions scratched/infected

Distribution and Progression:

- **Centripetal distribution** - Highest concentration on trunk, face, and scalp; relatively fewer on extremities (opposite of smallpox which was centrifugal)
- **Successive crops** - New lesions appear in waves over 3-5 days
- **Lesions at different stages** - Characteristic finding: macules, papules, vesicles, and crusts all present simultaneously ("starry sky" pattern)
- Rash starts on face and trunk, then spreads to rest of body
- **Number of lesions** - Varies widely:
 - Typical chickenpox: 200-500 lesions

- Mild cases (including breakthrough in vaccinated): 10-50 lesions
- Severe cases: >1500 lesions

Mucosal Involvement:

- Vesicles can appear on mucous membranes:
 - Oral mucosa (mouth, palate, tongue) - rupture quickly forming shallow painful ulcers
 - Conjunctivae
 - Genital mucosa
 - Respiratory tract

Intense Pruritus (Itching):

- Most distressing symptom for patients
- Begins as vesicles appear
- May be severe, interfering with sleep
- Strong urge to scratch (leading to risk of bacterial superinfection and scarring)

Fever:

- Usually present but varies in severity
- Typically 38-39°C (100.4-102.2°F), may reach 40°C (104°F)
- Often peaks as new crop of lesions appear
- Usually resolves as new lesions stop appearing (by day 4-5)

General Symptoms:

- Irritability (especially in young children)
- Fatigue
- Decreased appetite

Contagious Period:

- **Highly contagious:** From 1-2 days BEFORE rash appears until ALL lesions are crusted (typically 5-7 days after rash onset)

- Cannot return to school/work until all lesions crusted
- Crusts are not infectious

Breakthrough Varicella (in Vaccinated Individuals):

- Milder presentation:
 - Fewer lesions (<50, often <10)
 - Less fever or no fever
 - More rapid resolution
 - Lesions may not progress through all classic stages (may remain maculopapular without vesiculation)
 - Still contagious but less so than unvaccinated cases

Complications:

Bacterial Skin Superinfection (Most Common):

- Secondary infection of scratched lesions
- Organisms: *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes* (Group A Strep)
- Presentations:
 - **Impetigo** - superficial infection with honey-colored crusts
 - **Cellulitis** - spreading infection of deeper skin layers
 - **Abscess** - localized collection of pus
 - **Lymphangitis** - red streaking
 - **Necrotizing fasciitis** - life-threatening deep soft tissue infection (rare but serious)
 - **Toxic shock syndrome** - from streptococcal or staphylococcal toxins

Pneumonia:

- **Varicella pneumonia** - primary viral pneumonia:
 - More common in adults, adolescents, pregnant women, immunocompromised

- Onset 1-6 days after rash
- Symptoms: cough, dyspnea, chest pain, hemoptysis
- Chest X-ray: diffuse nodular infiltrates
- Can be severe, potentially fatal (mortality 10-30% in adults without treatment)
- **Secondary bacterial pneumonia** - less common

Neurologic Complications:

- **Cerebellar ataxia:**
 - Most common CNS complication in children
 - Onset days to weeks after rash
 - Unsteady gait, incoordination, tremor
 - Usually self-limited with complete recovery
- **Encephalitis:**
 - Rare but serious (1-2 per 10,000 cases)
 - Altered consciousness, seizures, focal deficits
 - Mortality 5-20%; neurologic sequelae in survivors
- **Guillain-Barré syndrome, transverse myelitis, aseptic meningitis** - rare

Hemorrhagic Varicella:

- Vesicles fill with blood
- Bleeding into skin, mucous membranes, internal organs
- Occurs primarily in immunocompromised
- High mortality

Reye's Syndrome:

- Acute hepatic encephalopathy
- Associated with aspirin use during varicella
- Reason why aspirin absolutely contraindicated in children with varicella

Other Complications:

- **Hepatitis** - elevated liver enzymes common, clinical hepatitis rare
- **Thrombocytopenia** - low platelet count
- **Arthritis** - joint inflammation
- **Nephritis, myocarditis, orchitis** - rare

Maternal and Fetal Complications:

Congenital Varicella Syndrome:

- If mother infected at 8-20 weeks gestation
- Risk ~0.4-2%
- Features: limb hypoplasia, scarring of skin in dermatomal distribution, eye abnormalities (cataracts, chorioretinitis), neurologic abnormalities (microcephaly, cortical atrophy), low birth weight
- Severe outcomes including fetal death

Perinatal Varicella:

- If mother develops rash from 5 days before to 2 days after delivery
- Severe neonatal varicella in 17-30% (newborn lacks maternal antibodies)
- Mortality up to 30% without treatment
- Preventable with varicella-zoster immune globulin (VarIZIG)

Maternal varicella pneumonia - serious complication in pregnant women

Detailed Stages of Infection

1. Exposure and Viral Entry (Day 0) - Transmission occurs through:

- **Respiratory route:** Inhalation of airborne droplets from respiratory secretions of infected person
- **Direct contact:** Touching vesicular fluid from chickenpox lesions or shingles lesions
- Virus enters through respiratory mucosa or occasionally through conjunctivae

- Highly contagious with 61-100% secondary attack rate in susceptible household contacts
2. **Primary Replication (Days 1-4)** - Virus replicates in respiratory epithelium and regional lymph nodes of upper respiratory tract and oral cavity. Initial viral multiplication at entry site. Clinically silent. Patient not yet contagious
 3. **Primary Viremia and Reticuloendothelial Spread (Days 4-6)** - Virus enters bloodstream (primary viremia) and disseminates to liver, spleen, and other reticuloendothelial organs. Extensive replication in these organs over several days. Still asymptomatic. Not contagious
 4. **Secondary Viremia (Days 14-16)** - Massive viral replication in liver and spleen leads to secondary viremia with much higher viral load. Virus circulates throughout body and infects skin, causing characteristic vesicular rash. Virus also infects sensory nerve ganglia where it establishes latency for potential future reactivation as zoster. Prodromal symptoms begin 1-2 days before rash in some patients. Patient becomes contagious 1-2 days before rash appears
 5. **Rash Phase (Days 14-20, Clinical Days 0-6)** - Vesicular rash appears as virus infects skin epithelial cells. Successive crops of lesions appear over 3-5 days. Each lesion progresses through stages: macule → papule → vesicle → pustule → crust. Different stages present simultaneously. Immune response develops: interferon production, cellular immunity, antibody response (IgM then IgG). Peak infectivity during first few days of rash when active vesicles present. Patient highly contagious until all lesions crusted (typically 5-7 days after rash onset)
 6. **Crusting and Resolution (Days 19-28, Clinical Days 5-14)** - New lesion formation stops by day 4-6. Existing vesicles progress to crusting. Crusts persist for 1-2 weeks then fall off. Temporary pink marks remain for weeks to months but usually fade completely. Immunity develops: VZV-specific IgG provides lifelong protection against chickenpox. Patient no longer contagious once all lesions crusted
 7. **Latency Establishment** - After primary infection resolves, varicella-zoster virus remains dormant in dorsal root ganglia (sensory nerve ganglia) and cranial nerve ganglia for life. Virus persists in latent form, not replicating.

Reactivation later in life (typically age >50 or with immunosuppression) causes herpes zoster (shingles) - painful vesicular rash in dermatomal distribution

Comprehensive Preventive Measures

Vaccination - Highly Effective Prevention:

Varicella Vaccine:

- **Live attenuated vaccine** - Contains weakened varicella-zoster virus (Oka strain) that replicates minimally, inducing immunity without causing disease in most recipients
- **Schedule:**
 - **Two-dose series:**
 - **First dose:** 12-15 months of age
 - **Second dose:** 4-6 years of age (before school entry)
 - **Catch-up vaccination:** Unvaccinated older children, adolescents, and adults should receive 2 doses separated by 4-8 weeks (adults) or 3 months (children)
- **Efficacy:**
 - **One dose:**
 - 85% protection against any varicella
 - 95% protection against severe varicella
 - **Two doses:**
 - 90-95% protection against any varicella
 - 95% protection against severe varicella
 - Duration: Long-lasting immunity, possibly lifelong in most individuals
 - Breakthrough infections occur but are typically very mild (fewer lesions, less fever)
- **Safety:**
 - Excellent safety profile

- Mild reactions: injection site soreness, low-grade fever, mild rash at injection site or generalized (2-5 weeks post-vaccination)
 - Serious adverse events extremely rare
- **Benefits:**
 - Prevents chickenpox
 - Reduces risk of herpes zoster (shingles) later in life
 - Eliminates risk of severe complications
 - Prevents transmission to others
 - Cost-effective (saves healthcare costs and parental time off work)
 - **Priority Groups for Vaccination (if not universally vaccinated):**
 - Healthcare workers
 - Teachers and childcare workers
 - Household contacts of immunocompromised individuals
 - Non-pregnant women of childbearing age
 - International travelers
 - College students and military personnel

Contraindications to Varicella Vaccine:

- Severe immunodeficiency (HIV with CD4 <15%, active cancer treatment, high-dose immunosuppressive therapy)
- Pregnancy (defer vaccination; avoid pregnancy for 1 month after vaccination)
- Severe allergic reaction to previous dose or vaccine component (gelatin, neomycin)
- Recent blood product or immunoglobulin administration (wait 3-11 months depending on product)
- Moderate to severe acute illness

Special Populations:

- **Mild immunosuppression:** May be vaccinated under specialist guidance

- **HIV-infected children:** Can receive vaccine if CD4 ≥15%

Post-Exposure Prophylaxis:

For Susceptible Exposed Individuals:

Varicella Vaccine (Post-Exposure Vaccination):

- **Indications:** Healthy susceptible individuals (no history of varicella or vaccination) exposed to chickenpox
- **Timing:** Administer within 3-5 days of exposure (ideally within 72 hours)
- **Efficacy:** 70-90% effective in preventing disease or significantly modifying severity
- **Who should receive:** Healthy children, adolescents, and adults without contraindications

Varicella-Zoster Immune Globulin (VariZIG):

- **Indications:** Susceptible high-risk individuals with contraindications to vaccine:
 - Immunocompromised patients
 - Pregnant women without immunity
 - Newborns whose mothers developed varicella from 5 days before to 2 days after delivery
 - Premature infants (<28 weeks gestation or <1000 g)
 - Hospitalized premature infants whose mothers lack immunity
- **Timing:** Administer within 10 days of exposure (ideally within 96 hours)
- **Dose:** 125 units per 10 kg body weight IM (maximum 625 units)
- **Effect:** Passive antibodies may prevent or attenuate disease
- **Note:** Does not provide long-term immunity; patient remains susceptible to future exposures

If VariZIG unavailable: Intravenous immunoglobulin (IVIG) may be used as alternative

Antiviral Prophylaxis:

- Acyclovir or valacyclovir may be considered for high-risk exposed individuals when vaccine or VariZIG not available or not given within appropriate timeframe
- Begin 7-10 days after exposure, continue for 7 days
- Evidence limited

Isolation and Infection Control:

Infected Individuals:

- **Home isolation:** Stay home from school, work, daycare until all lesions crusted (typically 5-7 days after rash onset)
- **Avoid contact** with high-risk individuals: pregnant women without immunity, newborns, immunocompromised individuals
- **Hospital isolation:** Airborne and contact precautions (negative pressure room, healthcare workers wear N95 respirators and gloves)

Exposed Susceptible Individuals:

- If unvaccinated and did not receive post-exposure prophylaxis, consider excluding from school/work from day 10 through day 21 after exposure

Healthcare Settings:

- Healthcare workers should have documented immunity (history of varicella, vaccination, or serologic evidence)
- Susceptible healthcare workers exposed should be furloughed from day 10-21 after exposure

Prevention of Scratching-Related Complications:

- Keep fingernails short and clean
- Mittens for young children (especially at night)
- Cool compresses
- Distraction techniques

Diagnostic Approaches

Clinical Diagnosis:

- **Usually diagnosed clinically** based on characteristic features:
 - Pruritic vesicular rash
 - Lesions at different stages (macules, papules, vesicles, crusts present simultaneously)
 - Centripetal distribution (trunk > extremities)
 - History of exposure
 - Absence of varicella vaccination or history of previous chickenpox
- **Classic presentation** generally does not require laboratory confirmation

Laboratory Confirmation (When Indicated):

Indications for laboratory testing:

- Atypical presentation
- Severe or complicated cases
- Immunocompromised patients
- Pregnant women
- Public health surveillance
- Outbreak investigation
- Breakthrough varicella in vaccinated individuals
- Need to rule out other vesicular illnesses (smallpox in appropriate setting, disseminated herpes simplex)

Direct Viral Detection (Preferred):

PCR (Polymerase Chain Reaction):

- **Gold standard** for laboratory confirmation
- Detects VZV DNA
- **Specimen:** Vesicle fluid or vesicle scrapings preferred; can also use crusts or throat swab
- **Collection:** Unroof vesicle, swab base vigorously

- Highly sensitive and specific
- Rapid results (hours to days)
- Can distinguish wild-type VZV from vaccine strain (Oka strain) - important for investigating potential vaccine-related rash or transmission

Direct Fluorescent Antibody (DFA) Testing:

- Detects VZV antigens in clinical specimens
- Specimen: vesicle scrapings
- Less sensitive than PCR
- Rapid results
- Less commonly used now that PCR widely available

Viral Culture:

- Specimen: vesicle fluid
- Least sensitive method (VZV difficult to culture)
- Takes several days to weeks
- Rarely used clinically (mainly research)

Serology (Antibody Testing):

Less useful for diagnosis of acute infection but has specific applications:

IgM antibodies:

- Appear within days of rash onset
- Indicate recent infection
- **Problem:** Less reliable than direct detection; false positives and negatives occur
- Not routinely recommended for acute diagnosis

IgG antibodies:

- Appear about 1 week after rash, rise over weeks

- 4-fold rise in paired acute/convalescent titers (2-3 weeks apart) confirms recent infection
- **Primary use:** Assessing immunity status
 - Positive IgG = immune (past infection or vaccination)
 - Negative IgG = susceptible
- Important for:
 - Screening healthcare workers
 - Evaluating pregnant women for susceptibility
 - Determining need for vaccination or post-exposure prophylaxis

Commercial serologic assays vary in sensitivity; some may not reliably detect vaccine-induced immunity

Specimen Collection:

- **Best:** Fresh vesicle (ideally <3 days old) - unroof, collect fluid and scrape base with swab
- Place in viral transport medium
- Keep refrigerated, transport promptly
- If delayed, freeze at -70°C

Tzanck Smear:

- Historical test, rarely used now
- Scraping from vesicle base stained to look for multinucleated giant cells
- Cannot distinguish VZV from herpes simplex virus
- Less sensitive and specific than modern methods

First Aid and Immediate Care Measures

Supportive Care - Mainstay for Uncomplicated Chickenpox:

Pruritus (Itch) Relief - Most Important for Patient Comfort:

Topical measures:

- **Cool compresses or cool baths:**
 - Plain water or colloidal oatmeal (Aveeno) baths
 - Soak 15-20 minutes several times daily
 - Pat dry gently; do not rub
- **Calamine lotion** - apply to lesions for soothing effect
- **Topical anesthetics** (pramoxine) may provide relief
- **Avoid topical antihistamines** - risk of systemic absorption and toxicity

Oral medications:

- **Oral antihistamines** - for itch relief:
 - **First-generation antihistamines** (diphenhydramine, hydroxyzine) - sedating effect may help sleep
 - Dose: Diphenhydramine 12.5-25 mg every 6 hours in children; 25-50 mg in adults
- **Second-generation antihistamines** (cetirizine, loratadine) - non-sedating, may be less effective for itch

Prevent scratching:

- Keep fingernails short and clean
- Cotton gloves or mittens (especially at night in young children)
- Distraction, keeping hands occupied
- Cool environment (heat increases itching)
- Loose-fitting, soft cotton clothing

Fever Management:

- **Acetaminophen (paracetamol):**
 - Dose: 10-15 mg/kg every 4-6 hours (maximum 4 grams/day in adults)
 - Safe and effective
- **Ibuprofen:**

- Some concerns about increased risk of invasive Group A streptococcal infection, though evidence controversial
- If used: 5-10 mg/kg every 6-8 hours
- Many experts prefer acetaminophen as first choice
- **ABSOLUTELY AVOID ASPIRIN** in children and adolescents with chickenpox:
 - Risk of Reye's syndrome (acute hepatic encephalopathy)
 - Potentially fatal
 - Aspirin contraindicated in anyone <18 years with viral illness

Hydration:

- Encourage adequate fluid intake
- Water, clear fluids, oral rehydration solutions
- Important especially if fever present or oral lesions affecting intake

Nutrition:

- Offer easily digestible foods
- Soft, bland foods if oral lesions present (avoid acidic, salty, or spicy foods that cause pain)
- Cold foods may be soothing (ice cream, popsicles, smoothies)
- Continue breastfeeding in infants

Oral Hygiene:

- Gentle mouth care
- Rinse with salt water or baking soda solution for oral lesions
- Avoid citrus and acidic beverages if mouth sores painful

Skin Care:

- **Hygiene:** Daily gentle baths with mild soap
- Keep skin clean to prevent bacterial superinfection
- Pat dry gently

- **Do not pick or scratch lesions** - increases scarring and infection risk

Rest:

- Adequate rest and sleep
- Quiet activities
- Limited physical activity during acute illness

Monitoring:

When to Seek Medical Attention:

Contact healthcare provider if:

- **Bacterial superinfection signs:**
 - Increasing redness, warmth, swelling, tenderness around lesions
 - Pus or cloudy drainage
 - Red streaks from lesion
 - Fever persisting or increasing after first 4 days of rash
- **Respiratory symptoms:**
 - Difficulty breathing, rapid breathing, chest pain, persistent cough
 - May indicate pneumonia
- **Neurologic symptoms:**
 - Severe headache, stiff neck, vomiting
 - Altered consciousness, confusion, unusual behavior
 - Seizures
 - Difficulty walking, loss of coordination
 - May indicate encephalitis or cerebellar ataxia
- **Dehydration:**
 - Decreased urination, dry mouth, lethargy
- **Hemorrhagic lesions:**
 - Bleeding into vesicles, easy bruising, bleeding from other sites

- **Very young infants, pregnant women, immunocompromised:**
 - Should be evaluated early
 - Lower threshold for medical attention

Isolation:

- **Stay home** from school, work, daycare until all lesions crusted (typically 5-7 days after rash onset)
- **Avoid contact** with high-risk individuals:
 - Pregnant women without varicella immunity
 - Newborn infants
 - Immunocompromised individuals
 - Susceptible adults (higher risk of severe disease than children)
- Remember: contagious from 1-2 days before rash through all lesions crusted

School/Work Return:

- May return when ALL lesions have crusted
- Crusts alone are not infectious
- Usually 5-7 days after rash onset

Antiviral and Drug Information (Educational Reference)

Antiviral Medications - For Specific Indications:

Acyclovir:

Mechanism: Antiviral agent inhibiting VZV DNA polymerase, preventing viral replication

Indications for Treatment:

Antiviral therapy generally **NOT recommended** for routine uncomplicated chickenpox in healthy children due to modest benefit relative to natural disease course.

Treatment IS recommended for:

1. High-risk groups:

- **Age \geq 13 years** (adolescents and adults have more severe disease)
- **Immunocompromised patients** (HIV, cancer, transplant recipients, immunosuppressive therapy)
- **Pregnant women**
- **Neonates**
- **Chronic pulmonary or cutaneous disorders** (chronic lung disease, eczema)
- **Long-term aspirin or corticosteroid therapy**

2. **Secondary household cases** (tend to be more severe due to higher inoculum)

3. **Severe disease** regardless of age or risk factors

Dosing:

Oral acyclovir (for most outpatient cases):

- **Children:** 20 mg/kg/dose (maximum 800 mg/dose) 4 times daily for 5 days
- **Adults:** 800 mg 5 times daily for 5-7 days
- **Best if started within 24 hours of rash onset** (72 hours maximum); efficacy decreases if started later
- Poor oral bioavailability (~10-20%) but adequate for most cases

Intravenous acyclovir (for severe or complicated cases):

- **Indications:** Immunocompromised patients, varicella pneumonia, encephalitis, disseminated disease, severe disease requiring hospitalization
- **Dose:** 10-15 mg/kg IV every 8 hours
- **Duration:** 7-10 days or until no new lesions for 48 hours
- Requires adequate hydration to prevent nephrotoxicity

Valacyclovir:

- **Prodrug of acyclovir** with better oral bioavailability
- **Approved for age \geq 12 years**
- **Dose:** 1000 mg three times daily for 5-7 days

- More convenient dosing than acyclovir
- Increasingly used for adolescents and adults

Famciclovir:

- Alternative antiviral
- Less commonly used for varicella; more for zoster
- Dose: 500 mg three times daily

Efficacy of Antivirals:

- In healthy adolescents/adults: Reduces duration of fever by 1 day, reduces number of lesions by ~30%, shortens time to healing
- In immunocompromised: Reduces risk of dissemination, visceral complications, and mortality
- Most effective when started early (<24 hours after rash onset)

Considerations:

- Cost vs. benefit in healthy children often favors no treatment
- Significant benefit in high-risk groups
- Prevention through vaccination preferable to treatment

Antibiotics:

NOT Indicated for Uncomplicated Varicella:

- Chickenpox is a viral infection
- Antibiotics have no role in treating varicella itself
- Should not be given prophylactically
- Contribute to antimicrobial resistance
- May cause adverse effects

When Antibiotics ARE Indicated:

Only if **bacterial superinfection** develops:

Bacterial skin/soft tissue infection:

- Most common complication
- Organisms: *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes*
- Presentations: impetigo, cellulitis, abscess, lymphangitis

Treatment:

- **Mild impetigo:**
 - Topical mupirocin or
 - Oral antibiotics: cephalexin, dicloxacillin
- **Cellulitis/more extensive infection:**
 - Oral: cephalexin 25-50 mg/kg/day divided every 6-8 hours, or clindamycin 10-25 mg/kg/day divided every 6-8 hours
 - Consider MRSA coverage (clindamycin, trimethoprim-sulfamethoxazole) based on local prevalence
- **Severe infection (necrotizing fasciitis, toxic shock):**
 - Hospitalization
 - IV antibiotics: vancomycin + piperacillin-tazobactam (or clindamycin for toxin suppression)
 - Surgical debridement if necrotizing infection

Secondary bacterial pneumonia:

- Less common than viral pneumonia
- IV antibiotics covering *S. pneumoniae*, *S. aureus*

Other Medications:

Corticosteroids:

- **NOT recommended** for routine varicella
- May increase risk of dissemination and complications
- Avoid in chickenpox

VariZIG (Varicella-Zoster Immune Globulin):

- As described under prevention
- Post-exposure prophylaxis, not treatment

Management of Complications:

Varicella Pneumonia:

- Hospitalization
- IV acyclovir 10-15 mg/kg every 8 hours
- Oxygen support
- Mechanical ventilation if respiratory failure

Encephalitis:

- Hospitalization, ICU if severe
- IV acyclovir
- Supportive care
- Seizure management

Cerebellar Ataxia:

- Usually self-limited
- Supportive care
- Monitor for resolution

Hospital Admission Indications:

- Immunocompromised patients
- Varicella pneumonia
- Encephalitis or other neurologic complications
- Severe bacterial superinfection
- Inability to maintain hydration
- Neonatal varicella
- Pregnant women with severe disease

Prevention Remains Most Important:

- Vaccination is highly effective and safe
 - Prevents disease and eliminates risk of complications
 - Preferable to treating established infection
-

General Principles of Managing Viral Infections

Supportive Care as Foundation:

- Most viral infections are self-limiting
- Focus on symptom relief, hydration, nutrition, rest
- Antipyretics for fever and discomfort
- Allow immune system time to clear infection

Appropriate Use of Antivirals:

- Antivirals available for specific viral infections (influenza, COVID-19, herpes viruses, hepatitis B & C, HIV)
- Use when indicated based on evidence
- Early initiation often critical for efficacy (influenza, COVID-19)
- High-risk patients may benefit even when healthy individuals would not require treatment

Antibiotic Stewardship - Critical Principle:

- **Antibiotics are NEVER effective against viruses**
- Inappropriate antibiotic use for viral infections:
 - Provides zero therapeutic benefit
 - Exposes patients to adverse effects (allergic reactions, diarrhea, *C. difficile* infection)
 - Drives antimicrobial resistance - a major global health threat
 - Wastes healthcare resources

- Antibiotics only appropriate when bacterial complication develops

Prevention as Priority:

- Vaccination - single most effective public health intervention
- Hygiene measures - hand hygiene, respiratory etiquette
- Vector control - for vector-borne diseases
- Behavioral modifications - avoiding exposure, using protection
- Screening and safe practices - for blood-borne viruses

Transmission Prevention:

- Isolate infected individuals appropriately
- Use personal protective equipment when indicated
- Identify and manage contacts
- Public health reporting for notifiable diseases

Recognize and Manage Complications:

- Vigilant monitoring for warning signs
- Prompt evaluation and treatment of complications
- Lower threshold for intervention in high-risk populations

Public Health & Antibiotic Stewardship Note



Critical Message for Healthcare Providers and Patients

Prescribing Antibiotics for Viral Infections:

X Provides NO benefit - Antibiotics target bacteria, not viruses. They cannot cure or shorten viral illnesses.

X Increases antimicrobial resistance - Unnecessary antibiotic use is a primary driver of antibiotic resistance, creating "superbugs" that threaten the effectiveness of antibiotics for serious bacterial infections. This is one of the greatest threats to global health.

X Causes avoidable adverse effects - Patients experience side effects (allergic reactions, diarrhea, yeast infections, *Clostridioides difficile* infection) without any therapeutic benefit.

X Wastes resources - Unnecessary prescriptions burden healthcare systems and patients financially.

X Creates false expectations - Reinforces misconception that antibiotics are needed for viral illnesses.

Appropriate Antibiotic Use:

- Antibiotics should ONLY be prescribed when bacterial infection is confirmed or strongly suspected based on clinical and laboratory findings
- Common bacterial complications of viral infections that may require antibiotics: bacterial pneumonia, sinusitis, otitis media, skin superinfection
- Clinical judgment, appropriate diagnostic testing, and adherence to evidence-based guidelines should guide all antibiotic prescribing decisions

The Role of Public Health:

- Promoting vaccination to prevent viral diseases
- Educating patients and providers about appropriate antibiotic use
- Surveillance for antimicrobial resistance
- Infection prevention and control measures
- Rapid outbreak detection and response

Patient Education:

- Antibiotics will not help viral infections get better faster
 - Most viral illnesses resolve on their own with supportive care
 - Taking antibiotics when not needed increases personal risk of antibiotic-resistant infections in the future
 - Always complete prescribed antibiotic courses when they ARE appropriately prescribed
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Safety Disclaimer



Educational Purpose Only

This document is intended **strictly for educational and academic purposes**. The information provided serves as a comprehensive reference for understanding viral infections, their clinical presentations, pathophysiology, preventive measures, and general management principles.

Not a Substitute for Professional Medical Advice:

- This document does NOT constitute medical advice, diagnosis, or treatment recommendations for specific individuals
- Clinical decisions must ALWAYS be based on:
 - Direct patient evaluation and diagnostic confirmation
 - Individual patient factors, comorbidities, and circumstances
 - Current evidence-based clinical practice guidelines
 - Local antibiotic resistance patterns and epidemiology
 - Consultation with qualified healthcare professionals

For Healthcare Professionals:

- Use this reference in conjunction with clinical judgment and official treatment guidelines
- Verify current recommendations, as medical knowledge and guidelines evolve
- Consider local formularies, resistance patterns, and institutional protocols
- Document clinical reasoning for all therapeutic decisions

For Patients and General Public:

- Always consult qualified healthcare providers for medical concerns
- Do not self-diagnose or self-treat based on this information
- Seek immediate medical attention for emergency warning signs

- Follow your healthcare provider's specific instructions for your situation

Accuracy and Currency:

- While every effort has been made to ensure accuracy, medical knowledge continuously evolves
- Treatment recommendations may change as new evidence emerges
- Local guidelines may differ from general principles presented here

No Liability:

- The creators and distributors of this educational document assume no liability for any adverse outcomes resulting from use or misuse of this information
- This document does not establish a healthcare provider-patient relationship

When in Doubt:

- Contact a qualified healthcare provider
- For medical emergencies, call emergency services immediately
- Follow official public health guidance during outbreaks or public health emergencies