# Respiratory Viruses

Friday, September 19, 2025 7:27 PM

## Introduction

### Definition

- "Professional" respiratory viruses → Cause primary clinical manifestations in the upper &/or lower respiratory tract
- Other viruses (measles, mumps, rubella, varicella-zoster) enter via respiratory tract but cause systemic disease → studied separately

### General Properties

- Genome: Almost all are RNA viruses (only Adenovirus = DNA)
- Envelope:
  - Most are enveloped
  - Exceptions → Rhinovirus & Adenovirus (nonenveloped)

- Families involved:
  - Orthomyxoviruses → Influenza virus
  - Paramyxoviruses → Parainfluenza virus, RSV, Human metapneumovirus
  - Coronaviruses → Common cold, SARS, MERS, COVID-like diseases
  - Picornaviruses → Rhinovirus
  - Adenoviruses → DNA viruses causing respiratory + eye infections
- Key feature: All infect respiratory mucosal cells → Cause symptomatic respiratory illness

- Key feature: All infect respiratory mucosal cells → Cause symptomatic respiratory illness

📜 Laboratory Diagnosis

- Important in serious respiratory infections
- PCR-based assays on respiratory secretions → Rapid, sensitive
- Used for: Influenza, Parainfluenza, RSV, Rhinovirus, Metapneumovirus, Adenovirus

## Table 1 – Clinical Features of Respiratory Viruses

| Virus | Important Disease | Sero types | Epidemics/ Pandemics? | Main Clinical Findings | Vaccine | Treatment |
|---|---|---|---|---|---|---|
| Influenza virus | Influenza | Many | ✔ Yes | Sudden-onset headache, shaking chill, sore throat, cough, myalgias | ✔ Yes | Oseltamivir, Zanamivir, Amantadine, Rimantadine |
| Para influenza virus | Croup | 4 | ✕ No | Barking cough | ✕ None | ✕ None |
| Respiratory syncytial virus (RSV) | Bronchiolitis in infants | 2 | ✕ No | Cough, dyspnea, retractions, wheezing | ✕ None | Ribavirin |
| Human meta pneumo virus | Cold, bronchiolitis, pneumonia | 2 | ✕ No | Coryza, wheezing, cough | ✕ None | ✕ None |
| Corona Virus | Cold, SARS, MERS | 3 | ✕ No | Coryza, cough, severe pneumonia | ✕ None | ✕ None |
| Rhino virus | Common cold | Many | ✕ No | Coryza, sneezing, usually no fever | ✕ None | ✕ None |
| Adeno virus | Pharyngitis, pneumonia, conjunctivitis | Many | ✕ No | Sore throat, cough, pneumonia, "pink eye" | ✔ (military only) | ✕ None |

## 📊 Table 2 – Properties of Respiratory Viruses

| Property | Influenza virus | Parainfluenza, RSV, Metapneumovirus | Coronavirus | Rhinovirus | Adenovirus |
|---|---|---|---|---|---|
| Family | Ortho Myxo virus | Paramyxovirus | Coronavirus | Picornavirus | Adenovirus |
| Genome | Segmented ssRNA (–) | Nonsegmented ssRNA (–) | Non segmented ssRNA (+) | Non segmented ssRNA (+) | dsDNA |
| Virion RNA polymerase | ✅ Yes | ✅ Yes | ❌ No | ❌ No | ❌ No |
| Capsid | Helical | Helical | Helical | Icosahedral | Icosahedral |
| Envelope | ✅ Yes | ✅ Yes | ✅ Yes | ❌ No | ❌ No |
| Fusion protein | ❌ No | ✅ Yes | ❌ No | ❌ No | ❌ No |
| Giant cell formation | ❌ No | ✅ Yes | ❌ No | ❌ No | ❌ No |

---

# 🦠 Influenza Virus

### 🌍 Disease Importance

- Causes annual outbreaks → thousands sick, many deaths.

- Can cause pandemics (worldwide epidemics) when a new hemagglutinin variant emerges → no pre-existing immunity in humans.
- Influenza A → pandemics + major outbreaks.
- Influenza B → major outbreaks but no pandemics.
- Influenza C → only mild respiratory illness.

💡 *Example:* The 1918 pandemic killed more Americans than World War I, World War II, Korean War, and Vietnam War combined.

---

# Important Properties

- Family: Orthomyxovirus
- Genome: Segmented (–) ssRNA (usually 8 pieces) → unique ability to reassort → pandemics.

- Nucleocapsid: Helical
- Envelope: Lipoprotein with spikes
- Enzyme: RNA-dependent RNA polymerase (makes mRNA from negative RNA).

Surface Glycoproteins

- Hemagglutinin (HA) (16 subtypes):
  - Binds to sialic acid receptors → initiates infection.
  - Agglutinates RBCs → basis of hemagglutination inhibition test.
  - Target of neutralizing antibodies.
- Neuraminidase (NA) (9 subtypes):
  - Cleaves sialic acid → releases new virions.
  - Degrades mucus barrier → easier infection spread.
  - Target of neuraminidase inhibitor drugs (oseltamivir, zanamivir).

🔄 Antigenic Variation

The ability of influenza viruses to change HA and NA explains repeated epidemics and pandemics.

## 📊 Table: Antigenic Changes in Influenza

| Type of Change | Mechanism | Result | Example |
|---|---|---|---|
| Antigenic Drift 🌀 | Minor point mutations in RNA | New seasonal strains → annual epidemics | H3N2 seasonal variants |
| Antigenic Shift ⚡ | Major change by reassortment of genome segments | Completely new virus subtype → pandemics | 2009 H1N1 swine flu, 1968 H3N2 |

## 📝 Flowchart: Pathogenesis of Influenza

Inhalation of virus droplets

↓

Virus binds to sialic acid receptors via HA

↓

Entry → viral RNA released into cell

↓

RNA polymerase transcribes viral mRNA

↓

Synthesis of viral proteins

↓

Assembly of new virions

↓

NA cleaves sialic acid → virion release

↓

Spread → infection of more respiratory epithelial cells

↓

Destruction of ciliated epithelium → impaired clearance → secondary bacterial infection risk

🔬 Matrix Proteins

- M1 protein → beneath envelope; provides structural integrity.

- M2 protein → forms ion channel → transports protons into virion → disrupts envelope → releases nucleocapsid → allows uncoating.
  👉 *Target of amantadine/rimantadine (M2 inhibitors).*

🎯 Antigens

- Group-specific antigen:
  - Internal ribonucleoprotein in nucleocapsid.
  - Distinguishes Influenza A, B, C.
  - Antibody against it ❌ does not neutralize virus.

- Type-specific antigens (surface glycoproteins):
  1. Hemagglutinin (HA) → neutralizing antibody → prevents infection ✅.
  2. Neuraminidase (NA) → antibody reduces spread (by limiting release) but does not fully neutralize ❌.

⚡ Virulence Factor: NS-1 Protein

- NS-1 nonstructural protein → inhibits interferon mRNA production → ↓ innate immunity → ↑ virulence.

🐖 Animal Reservoirs & Antigenic Shift

- Many animals carry influenza A viruses → aquatic birds, chickens, swine, horses.

- Reassortment (mixing) occurs when:

  - Human + Avian influenza infect same cell → exchange genome segments.
  - Pigs act as mixing bowls 🐖 → new pandemic strains emerge.

- Subtype diversity:

  - In waterfowl → 16 H subtypes, 9 N subtypes.
  - In humans → mainly H1, H2, H3 and N1, N2.

👉 Influenza B virus has no animal reservoir → only antigenic drift, not shift.

🏷 Nomenclature of Influenza Strains

Format: Type / Location / Year / (Subtype)

Example: A/Philippines/82 (H3N2)

- A = Group antigen (Influenza A)
- Philippines = place of isolation
- 82 = year (1982)
- H3N2 = subtype (HA3, NA2)

Current common strains → H1N1 & H3N2.

🔄 Replicative Cycle (Step-by-Step)

📌 Flowchart: Influenza Virus Life Cycle

Attachment → HA binds sialic acid receptors

↓

Entry → virus enters via endocytosis in vesicles

↓

Uncoating → M2 ion channel pumps protons → envelope disrupted → nucleocapsid released

↓

Transport → nucleocapsid migrates to nucleus

↓

Transcription → RNA polymerase makes 8 mRNAs (requires cap-snatching from host nuclear RNAs)

↓

mRNAs → move to cytoplasm → translated into proteins

↓

Some mRNAs stay in nucleus → serve as template for negative-strand genome synthesis

↓

New genome segments bind NP + M1 proteins → transported to cytoplasm

↓

Assembly → helical nucleocapsid + envelope glycoproteins (HA, NA)

↓

Release → budding at cell membrane; NA cleaves sialic acid → virions released

📊 Exam Points

- M1 vs M2: structure vs ion channel/uncoating.
- HA antibody = neutralizing ✅ | NA antibody = reduces spread only.
- NS-1 = interferon inhibition → virulence factor.
- Antigenic shift requires animal reservoir (Influenza A only).
- Replication partly nuclear (rare for RNA viruses).
- Cap-snatching = unique transcription feature.

---

# Transmission & Epidemiology

- Mode of Transmission → airborne respiratory droplets 💨
- Antigenic Variation:

- Influenza A → Antigenic shift (major, infrequent, pandemics) + Antigenic drift (minor, yearly, epidemics).
- Influenza B → Antigenic drift only, less frequent and less severe.

- Pandemics → occur when new HA subtype emerges (no preexisting immunity).

- 1968 Pandemic → H3N2 emerged.

- Global Burden → up to 500,000 deaths/year worldwide (90% in elderly).

📅 Seasonality:

- Northern Hemisphere → Dec–Feb (winter)

- Southern Hemisphere → Jun–Aug (winter)

- Tropics → year-round circulation

---

# Pathogenesis

1. Virus inhaled → neuraminidase cleaves mucus → entry into epithelial cells.

2. Replication restricted to respiratory tract (proteases to cleave HA only present here).

3. Cytopathic effect → necrosis of superficial respiratory epithelium.

4. Cytokines → systemic symptoms (fever, myalgia, malaise).

5. Pneumonia → interstitial (viral) or secondary bacterial (Staph aureus, Strep pneumoniae).

☞ No significant viremia (systemic symptoms = cytokine mediated).

---

# Immunity

- Secretory IgA → main protection (mucosal).

- IgG → produced but less effective.
- Cytotoxic T cells (CD8+) → kill infected epithelial cells.
- Immunity is strain-specific (explains reinfections due to antigenic drift/shift).

🤒 Clinical Findings

- Incubation period → 24–48 hours.
- Abrupt onset 🚨
  - Fever 🌡️
  - Severe myalgias (muscle pain) 💪
  - Headache 🤕
  - Sore throat + cough 🤧
- Usually resolves in 4–7 days.
- Complications:
  - Viral pneumonia (interstitial).
  - Secondary bacterial pneumonia → Staph aureus, Strep pneumoniae 🦠.
  - Reye's syndrome (rare, children) → encephalopathy

+ liver degeneration; linked to aspirin use in viral illness.

📌 Key Clinical Clue → Severe myalgias + respiratory symptoms

---

# Laboratory Diagnosis

1. Clinical Diagnosis

- Most cases diagnosed based on classic symptoms during influenza season.

2. Rapid Diagnostic Tests (doctor's office)

- ELISA antigen detection (nasal/throat swabs, washings, sputum).

- Examples:

    - FLU OIA
    - QuickVue Influenza Test
    - ZstatFlu (detects neuraminidase activity → color change).

👉 Important: results within minutes, treatment decisions (NA inhibitors) within 48 hours.

3. Hospital Diagnosis

- PCR-based tests → detect viral RNA; high sensitivity; can differentiate A (H1, H3) and B.

4. Serology

- Retrospective diagnosis (epidemiology).
- ≥4-fold rise in antibody titer (Hemagglutination inhibition / CF test).
- Not useful for early clinical management.

5. Other Tests

- Direct fluorescent antibody staining (respiratory samples).
- Virus isolation in cell culture.

## 📊 Summary Table: Diagnosis of Influenza

| Test | Sample | Turnaround | Clinical Use |
| --- | --- | --- | --- |

| | | | |
|---|---|---|---|
| PCR | Respiratory secretions | Few hours | Hospital/serious cases |
| ELISA antigen | Nasal/ throat swabs | Minutes | Outpatient rapid diagnosis |
| Serology (HI/CF) | Serum | 10+ days | Epidemiology, retrospective |
| Fluorescent antibody | Respiratory samples | Few hours | Confirmation |
| Viral culture | Respiratory samples | Days | Research, reference labs |

## 📌 Exam Points

- Antigenic shift → pandemics (Influenza A only).
- Elderly & <2 yrs old = highest morbidity/mortality.
- Reye's syndrome → influenza B + aspirin 🚫.
- PCR = gold standard in serious hospital cases.
- Rapid antigen tests (ELISA) = for quick treatment decisions.

---

# Treatment

- Neuraminidase inhibitors (block release of virus from infected cells → limit spread)
    - Oseltamivir (Tamiflu) → Oral
    - Zanamivir (Relenza) → Inhaled powder
    - Peramivir (Rapivab) → Intravenous (available since 2015)
    - Effective against Influenza A & B
    - Must be taken within 48 hours of symptom onset for maximum benefit
    - Reduce illness duration by 1–2 days & limit transmission
    - Resistance:
        - Some H1N1 strains resistant to Tamiflu
        - H3N2 & all Influenza B strains remain susceptible to Tamiflu & Relenza

- M2 Ion Channel Blockers (block uncoating)
    - Amantadine (Symmetrel)
    - Rimantadine (Flumadine) – fewer side effects
    - ❌ Effective only against Influenza A
    - ❌ High resistance (>90% of H3N2 strains in US

resistant) → not recommended
  - Vaccine is preferred for prevention

---

# Prevention

- Main strategy: Annual Influenza vaccine (A & B strains)
- Reformulated yearly to match circulating strains

Types of Influenza Vaccines (US)

| 💉 Vaccine Type | Details |
|---|---|
| Killed (Inactivated) vaccine | Purified HA & NA proteins; inactivated with formaldehyde & lipid solvent. Given intramuscularly. High-dose version (4× HA) recommended for >65 yrs. Intradermal version also available. |
| Live, attenuated vaccine | Contains temperature-sensitive mutants (replicate at 33°C nasal mucosa → induce IgA; cannot replicate at 37°C lungs). Given intranasally. No reversion to virulence reported. |
| Non-egg based | (1) Virus grown in calf kidney cell culture → inactivated. (2) Recombinant insect virus |

| | |
|---|---|
| vaccines | expressing influenza HA grown in insect cells; purified HA used as antigen. |

## 📌 Flowchart – Influenza Prevention

Circulating Influenza Strains → Annual Vaccine Update

↓

Killed Vaccine (inactivated; IM / intradermal)
→ Induces neutralizing antibody (IgG) → Systemic protection

↓

Live Attenuated Vaccine (nasal; temp-sensitive mutant)
→ Replicates in nasal mucosa → Induces IgA → Mucosal protection

## ⚡ Exam Points

- HA = main antigen → elicits neutralizing antibodies 💡
- Oseltamivir & Zanamivir most effective if started within 48 hours
- Amantadine & Rimantadine obsolete due to resistance

- Vaccine preferred for prevention, antivirals used for treatment / outbreak control

💉 Influenza Vaccine – Key Points

- Live attenuated (nasal mist):
    - Recommended for children
    - ❌ Not for pregnant women or immunocompromised patients
    - 2016 FDA note: Live vaccine not recommended due to low efficacy (guidelines may change).
- Inactivated (killed) vaccine:
    - Recommended for adults
    - Safe in pregnancy → maternal IgG crosses placenta → protects newborn in first 6 months
    - Protection lasts ~6 months → yearly booster needed (preferably before flu season, e.g., October)
    - Induces IgG > IgA (systemic more than mucosal immunity)
- Special considerations:

- Made in chicken eggs → contraindicated in patients with severe egg allergy 🥚
- Alternatives for egg-allergic patients:
  - Flucelvax → inactivated vaccine from calf kidney cell culture
  - Flublok → recombinant vaccine (baculovirus in insect cells → purified HA protein)

📌 Flowchart – Influenza Vaccination

Circulating Influenza Strains (updated yearly)

↓

Killed vaccine (IM / intradermal)
→ Adults, elderly, pregnant women
→ IgG response → lasts ~6 months → yearly booster

↓

Live attenuated vaccine (nasal mist)
→ Children
→ IgA response in nasal mucosa
❌ Not for pregnancy / immunocompromised

### ⚠️ Side Effects

- Rare: Guillain-Barré Syndrome (GBS) associated with 1970s swine flu vaccine (ascending paralysis)
- Modern vaccines → No increased risk of GBS

### 🛡️ Additional Prevention

- Oseltamivir (Tamiflu):
  - Useful in elderly unvaccinated individuals exposed to influenza
  - 🚫 Not a substitute for vaccination (vaccine remains most reliable prevention)

---

## Avian Influenza Viruses in Humans

### 🐦 H5N1 Influenza Virus (Avian Flu)

- First human outbreak: 1997, Hong Kong
- Reservoir: Chickens 🐓

- Transmission: Direct from birds (respiratory secretions, guano) → rare person-to-person spread
- Cases (2003–2009): 408 cases → 254 deaths (62% mortality)
- Pathogenesis:
  - Infects chicken upper respiratory tract (receptor abundant)
  - Humans → receptor only in alveoli → requires intense exposure → severe pneumonia
  - High virulence due to:
    - Resistance to interferon
    - Excess cytokine induction (especially TNF) → pneumonia & ARDS
- Treatment: Sensitive to neuraminidase inhibitors (Oseltamivir = drug of choice). Resistant to amantadine/rimantadine.
- Vaccine available against H5N1 strain.

## 📌 Flowchart – H5N1 Pathogenesis

H5N1 infection in chickens → Upper respiratory tract (receptor abundant)

↓

Humans exposed (intense contact) → Virus reaches alveoli

↓

Severe pneumonia → ↑ TNF & cytokines → ARDS

↓

High mortality (~62%)

---

# H7N9 Influenza Virus

- First human outbreak: 2013 (China, Taiwan)
- Origin: Entirely avian genes
    - H7 gene → ducks
    - N9 gene → wild birds
    - Other genes → bramblings (Asian/European bird)

- Cases (2013–2017): 1258 infections → 41% mortality
- Transmission: Mostly from birds, no sustained person-to-person spread
- Treatment: Susceptible to neuraminidase inhibitors (Oseltamivir, Zanamivir)
- No approved vaccine yet (candidates under development).

## 📌 Comparison Table – Avian Influenza Strains

| Strain | Source | Human Cases | Mortality | Spread | Treatment | Vaccine |
|---|---|---|---|---|---|---|
| H5N1 | Chickens | 408 (2003–09) | 62% | Rare human-to-human | Oseltamivir, Zanamivir | Available |
| H7N9 | Ducks, wild birds, bramblings | 1258 (2013–17) | 41% | No sustained spread | Oseltamivir, Zanamivir | Not yet |

## ⚡ Exam Points

- Live vaccine → IgA (mucosal immunity) | Killed vaccine → IgG (systemic immunity)
- Pregnant women: Only killed vaccine ✅
- Egg allergy: Use Flucelvax or Flublok
- H5N1: High mortality, cytokine storm, Tamiflu effective
- H7N9: Bird origin, high mortality, no vaccine yet

---

# 🐖 Swine Influenza Virus Infection in Humans (H1N1, 2009)

🌍 Epidemiology

- First outbreak: April 2009 → Mexico → USA → spread to 208 countries by Dec 2009
- WHO: Pandemic alert level 6 (highest) on June 11, 2009
- By Aug 2010 → cases declined → pandemic warning rescinded

- As of 2016: cases significantly reduced
- Cases & deaths:
  - Millions worldwide
  - 9596 deaths globally (1445 in USA)

🧑 Affected Population

- Young people most affected → ~60% cases were ≤18 years
- Symptoms: generally mild
- Fatalities: rare → mostly in medically compromised patients
- ❌ No swine outbreaks in pigs before human pandemic
- ❌ Eating pork does not transmit virus

🧬 Genetics (Quadruple Reassortant Virus)

- Hemagglutinin, nucleoprotein, NS protein → North

American swine origin

- Neuraminidase, matrix protein → Eurasian swine origin
- 2 polymerase subunits → North American avian origin
- 1 polymerase subunit → Human H3N2 origin

📌 Triple reassortant strain (earlier in swine, rarely infected humans):

- All 5 non-polymerase genes → North American swine
- Polymerase genes → same as quadruple reassortant
- ❌ No Eurasian swine genes

🔍 Key Points

- Most humans lacked protective antibodies against the new swine hemagglutinin (H1)
- Even those previously infected/vaccinated with seasonal H1N1 had little protection

- Human-to-human spread: efficient
- Contrast → Avian H5N1: rarely spreads between humans

---

## Diagnosis

- PCR test available for detection of S-OIV RNA

---

## Treatment

- Sensitive: Oseltamivir (Tamiflu), Zanamivir (Relenza)
- Resistant: Amantadine, Rimantadine

💉 Prevention

- Both inactivated (killed) and live attenuated vaccines available by Nov 2009

📌 One-Liner Memory Aid

---

# Parainfluenza Virus

## Diseases

- Children:
    - Croup (acute laryngotracheobronchitis)
    - Laryngitis
    - Bronchiolitis
    - Pneumonia
- Adults:
    - Common cold-like illness

## Important Properties

- Family: Paramyxoviridae
- Genome: Negative-sense, ssRNA
- Structure:

- Surface spikes:
  - Hemagglutinin (H) + Neuraminidase (N) → on the same spike
  - Fusion (F) protein → separate spike, causes multinucleated giant cells (syncytia)

- Antigenic types: 4 (based on antigenicity, cytopathic effect, pathogenicity)

- Neutralizing immunity: Antibodies against H or F proteins

🔄 Replicative Cycle (Summary)

Parainfluenza Virus Replication →
Adsorption (via H protein)
→ Penetration + Uncoating
→ Viral RNA polymerase transcribes (–)RNA → mRNAs
→ Translation into multiple proteins (NO polyprotein, unlike poliovirus)
→ Assembly of helical nucleocapsid
→ Interaction with matrix protein + envelope
→ Budding → Release

🌍 Transmission & Epidemiology

- Mode: Respiratory droplets 💨
- Season: Winter (peak incidence)
- Distribution: Worldwide

---

# Pathogenesis & Immunity

- Causes upper & lower respiratory tract infections without viremia
- Large proportion are subclinical
- Types & Disease Association:

| Virus Type | Main Disease(s) | Notes |
|---|---|---|
| Parainfluenza 1 | Croup | Major cause |
| Parainfluenza 2 | Croup | Major cause |
| Parainfluenza 3 | Bronchiolitis, pneumonia | Most common isolated in children (US) |
| Parainfluenza 4 | Common cold | Rarely serious disease |

## 🧑‍⚕️ Clinical Findings

- Croup (most important) → Children < 5 yrs
  - Harsh, barking cough 🐶
  - Hoarseness
- Other conditions:
  - Common cold 🤧
  - Pharyngitis
  - Laryngitis
  - Otitis media
  - Bronchitis
  - Pneumonia

## 🔬 Laboratory Diagnosis

- Usually clinical diagnosis
- Laboratory confirmation:
  - PCR (detects viral RNA)
  - Viral isolation in cell culture
  - Fluorescent antibody test (viral antigens)
  - Serology → ≥ fourfold rise in antibody titer

💊 Treatment & Prevention

- No specific antiviral therapy
- No vaccine available
- Supportive care only

✅ Exam Point:

- Parainfluenza virus = main cause of croup in young children
- Fusion protein → multinucleated giant cells
- Antibodies to H or F proteins neutralize infection

---

# 🦠 Respiratory Syncytial Virus (RSV)

Diseases

- Infants 👶 → *Most important cause* of bronchiolitis & pneumonia

- Children → Otitis media
- Elderly & patients with cardiopulmonary disease → Severe pneumonia
- Healthy adults → Mild illness (common cold, bronchitis)

🔑 Important Properties

- Family: Paramyxoviridae
- Genome: Negative-sense ssRNA
- Surface proteins:
  - *Fusion protein only* (no hemagglutinin, no neuraminidase)
  - Fusion protein → causes cell fusion → multinucleated giant cells (syncytia) 🧬
- Natural host: Humans only
- Serotypes: Subgroup A & B

- Neutralization: Antibody against fusion protein

🔄 Replicative Cycle (Summary)

Same as Parainfluenza virus:

RSV Replication →
Attachment to host cell
→ Entry + uncoating
→ Transcription of (–) RNA → mRNAs
→ Translation into proteins
→ Nucleocapsid assembly
→ Budding → Release

🌍 Transmission & Epidemiology

- Mode: Respiratory droplets 💨 + direct contact (contaminated hands → nose/mouth)

- Seasonality: Winter epidemics ❄️ (annual, unlike other cold viruses)

- Age: Almost all children infected by age 3

- Hospitals: Nosocomial outbreaks common → controlled by handwashing & gloves 🧤

---

# Pathogenesis & Immunity

- Infants → More severe disease (lower respiratory tract involvement)

- Infection localized to respiratory tract only (no viremia)

- Immunopathogenesis theory:

  - Maternal antibodies may form immune complexes → damage respiratory tract cells
  - Killed vaccine trials worsened disease → supports immune-mediated mechanism ⚠

- Reinfections common (immunity incomplete, not due to antigenic variation)

- IgA → reduces reinfection risk with age

---

## 🧑‍⚕️ Clinical Findings

- Infants: Bronchiolitis, pneumonia
- Children: Otitis media
- Adults (healthy): Common cold, bronchitis
- Elderly & cardiopulmonary disease patients: Severe pneumonia

---

## 🔬 Laboratory Diagnosis

- PCR → Detects RSV RNA
- Rapid antigen test (EIA) → Detects RSV antigens in secretions
- Immunofluorescence → Viral antigens in respiratory epithelium
- Cell culture → CPE = syncytia (multinucleated giant cells)

- Serology → Fourfold rise in antibody titer

💊 Treatment

- Severe cases (hospitalized infants):
    - Aerosolized ribavirin (Virazole) 💊 (effectiveness debated)
    - Ribavirin + Hyperimmune globulins → more effective

🛡️ Prevention

- No vaccine available 🚫
- Killed vaccine trial → worsened disease → contraindicated
- Passive immunization:
    - Palivizumab (Synagis) → monoclonal antibody vs. fusion protein → for high-risk infants (premature, immunocompromised)
    - Hyperimmune globulin (RespiGam) → prophylaxis in infants with chronic lung disease

- Hospital prevention: Handwashing + gloves

📊 Quick Revision Table

| Feature | RSV | Parainfluenza Virus |
| --- | --- | --- |
| Major disease | Bronchiolitis, pneumonia in infants | Croup in children |
| Key protein | Fusion protein (syncytia) | H, N, and F proteins |
| Seasonality | Annual winter epidemics | Winter (but less consistent) |
| Viremia | ❌ Absent | ❌ Absent |
| Treatment | Ribavirin (severe cases) | Supportive |
| Vaccine | ❌ None (Palivizumab for prophylaxis) | ❌ None |

## ✅ Exam Points

- RSV = most important cause of pneumonia & bronchiolitis in infants 👶
- Causes syncytia (multinucleated giant cells) due to

fusion protein

- No vaccine (previous killed vaccine worsened disease)
- Palivizumab → prophylaxis for high-risk infants

---

## Human Metapneumovirus (HMPV)

### Important Properties

- Family: Paramyxoviridae
- Genome: (–) ssRNA, nonsegmented, enveloped
- Surface: Fusion protein (F) → mediates attachment + syncytia formation
- Antibody to F protein → neutralizes virus
- Genotypes: 2 major + subtypes

### Diseases

- Similar to RSV:
  - Mild URI → Bronchiolitis → Severe pneumonia
- Symptoms: Fever, coryza, cough, wheezing
- Epidemiology:
  - Most children infected by age 5
  - Immunity incomplete → reinfections common

🔬 Lab Diagnosis

- PCR assay → detects viral RNA in respiratory tract samples

💊 Treatment & Prevention

- Supportive only
- ❌ No antiviral drug
- ❌ No vaccine

---

# 🦠 Coronavirus

## 🩺 Diseases

- Common cold (second most common after rhinovirus)
- Severe emerging diseases:
  - SARS (2002) → Severe Acute Respiratory Syndrome (CoV-SARS)
  - MERS (2012) → Middle East Respiratory Syndrome (CoV-MERS)
  - (Later: COVID-19 (2019) → SARS-CoV-2)

## 🔑 Important Properties

- Genome: (+ )ssRNA, nonsegmented, enveloped
- Capsid: Helical nucleocapsid
- Virion: Club-shaped spikes → "corona/halo" appearance ✨
- No virion polymerase
- Human serotypes: 229E, OC43

- SARS-CoV receptor: ACE-2

## 🔄 Replicative Cycle (Summary)

1. Attachment via surface spikes → entry + uncoating
2. Genome (+RNA) → translated into 2 large polyproteins
3. Self-cleaved by viral protease → polymerase subunits
4. RNA polymerase → replicates genome + makes mRNAs
5. Proteins translated
6. Assembly in endoplasmic reticulum (ER) (NOT plasma membrane)
7. Release

## 📊 Quick Comparison (HMPV vs RSV vs Coronavirus)

| Feature | HMPV | RSV | Coronavirus |
|---|---|---|---|
| Family | Paramyxovirus | Paramyxovirus | Coronaviridae |
| Genome | (–) ssRNA | (–) ssRNA | (+) ssRNA |

| | | | |
|---|---|---|---|
| Surface proteins | Fusion (F) protein | Fusion protein | Spike glycoprotein |
| Syncytia | ✅ Yes | ✅ Yes | ❌ No |
| Main disease | Bronchiolitis, pneumonia (children) | Bronchiolitis, pneumonia (infants) | Cold, SARS, MERS |
| Seasonality | Winter epidemics | Winter Epidemics | Sporadic/epidemic |
| Diagnosis | PCR (RNA detection) | PCR, antigen, culture | PCR, serology |
| Vaccine | ❌ None | ❌ None (Palivizumab for prophylaxis) | ❌ None (except later COVID vaccines) |
| Treatment | Supportive | Ribavirin (severe infants) + supportive | Supportive/antivirals (newer for SARS/MERS/COVID) |

## ✅ Exam Points

- HMPV = RSV-like illness, but milder, incomplete immunity, PCR diagnosis, supportive Rx.
- Coronavirus = 2nd most common cold cause + severe syndromes (SARS, MERS, later COVID).
- Coronavirus genome is (+ ssRNA, enveloped, halo spikes, replicates in ER).

---

# Transmission & Epidemiology

- Transmission: Respiratory aerosols
- Global prevalence: Infection occurs worldwide, often early in life; >50% of children have antibodies
- Seasonality: Outbreaks mainly in winter, every 2–3 years
- SARS (2002–2003):
    - Origin: China
    - Cases: 8,300; Deaths: 785 → fatality ~9%
    - Human-to-human transmission: Yes (super-spreaders noted)
    - Reservoir: Horseshoe bat → intermediate host: civet cat
- MERS (2012–2013):
    - Cases: 1,879; Mortality: 35%
    - Reservoir: Bats → camel transmission to humans

- Human-to-human: Rare, mostly in hospitals with poor infection control

---

## Pathogenesis & Immunity

- Infection mostly limited to respiratory mucosal cells
- ~50% asymptomatic infections
- Immunity short-lived, reinfections possible
- SARS: binds ACE-2 → alveolar edema → hypoxia
- MERS: binds CD26 → pneumonia

---

## Clinical Findings

- Common cold: Coryza, sore throat, low-grade fever, lasts a few days
- SARS:

- Fever ≥38°C, nonproductive cough, dyspnea, hypoxia
- Chills, malaise, rigors, headache common
- Sore throat and rhinorrhea uncommon
- Chest X-ray: Interstitial "ground-glass" infiltrates, no cavitation
- Labs: Leukopenia, thrombocytopenia
- Incubation: 2–10 days (mean 5)

- MERS: Similar to SARS

---

## Lab Diagnosis

- PCR → detect viral RNA in blood or respiratory specimens

- Serology → antibody titer rise (epidemiology)

---

## Treatment & Prevention

- No proven antiviral therapy or vaccine
- Ribavirin + steroids used in life-threatening SARS, efficacy uncertain

---

# 🦠 Rhinovirus

🔑 Important Properties

- Genome: (+ )ssRNA, nonsegmented
- Structure: Nonenveloped, icosahedral capsid
    - 100 serotypes → explains high prevalence of common cold
- Replicates better at 33°C → primarily nasal & conjunctival infection
- Acid-labile → cannot survive stomach → no GI infection
- Host: Humans and chimpanzees only

## 🔄 Replicative Cycle

1. Attachment: ICAM-1 receptor
2. Entry & uncoating → RNA released into cytoplasm
3. Translation: Genome RNA acts as mRNA → large polypeptide
4. Cleavage: Virus protease → capsid + nonstructural proteins (including RNA polymerase)
5. Replication: Negative-strand synthesis → template for positive strands
6. Assembly: RNA + capsid proteins → progeny virions
7. Release: Cell death

## ✅ Exam Points

- SARS-CoV → ACE-2; MERS-CoV → CD26
- SARS: ~9% fatality; MERS: 35% fatality

- Rhinovirus: primary cause of common cold, multiple serotypes, prefers cooler temperatures (33°C)

---

## Transmission & Epidemiology

- Modes of transmission:

  1. Direct: Respiratory droplets from person to person

  2. Indirect: Droplets on hands/surfaces → contact with nose or eyes

- Global prevalence: Worldwide; most common human infection

- Seasonality: Fall and winter (likely due to crowding, not temperature)

- Population trends:

  - Frequent in childhood → decreases in adulthood (immunity acquired)

    - Seasonal serotype shifts → immunity to old serotypes, susceptibility to new ones

---

## Pathogenesis & Immunity

- Portal of entry: Upper respiratory tract
- Lower respiratory tract involvement: Rare (virus grows poorly at 37°C)
- Immunity:
    - Serotype-specific
    - Mainly nasal secretory IgA, not systemic antibodies

---

## Clinical Findings

- Incubation period: 2–4 days
- Symptoms: Sneezing, nasal discharge, sore throat,

cough, headache, chills

- Duration: ~1 week
- Other viruses causing similar cold-like illness: Coronaviruses, adenoviruses, influenza C, Coxsackie viruses

---

## Laboratory Diagnosis

- PCR → detection of rhinovirus RNA in respiratory specimens
- Serology: Not useful (too many serotypes)

---

## Treatment & Prevention

- No specific antiviral therapy or vaccine (impractical due to >100 serotypes)

- Preventive measures:
  - Paper tissues with citric acid + sodium lauryl sulfate → reduce virus transmission from fingers
- Symptomatic measures:
  - High-dose vitamin C: minimal preventive effect
  - Zinc gluconate lozenges: uncertain efficacy

✅ Exam Points

- Rhinovirus mainly affects upper respiratory tract; rarely lower tract
- Immunity is serotype-specific and IgA-mediated
- No vaccine available due to large serotype diversity
- Indirect contact (hands/surfaces) is an important mode of spread

---

# Diseases

- Respiratory: Pharyngitis, pharyngoconjunctival fever, bronchitis, atypical pneumonia, common cold
- Ocular: Conjunctivitis, keratoconjunctivitis
- Urinary: Hemorrhagic cystitis
- Gastrointestinal: Gastroenteritis (mainly <2 years old)
- Other: Some serotypes cause sarcomas in rodents (no evidence in humans)

---

# Important Properties

- Genome: dsDNA, linear, nonsegmented
- Capsid: Icosahedral, nonenveloped, with fiber at each vertex (organ of attachment/hemagglutinin)
- Antigenicity:
    - 41 serotypes

    - Fiber protein: main type-specific antigen
    - Hexon protein: group-specific antigen

- Replication:

    1. Virus attaches via fiber → uncoats → DNA enters nucleus

    2. Early genes → nonstructural proteins

    3. DNA replication → late genes → structural proteins

    4. Virus released by cell lysis (not budding)

---

## Transmission & Epidemiology

- Modes:

    1. Respiratory droplets

    2. Fecal-oral (common in children)

3. Direct inoculation of conjunctiva (fingers, instruments)

- Occurrence: Worldwide, endemic; outbreaks in military recruits (close quarters)

- Serotype-specific syndromes:

    - 3, 4, 7, 21 → respiratory disease
    - 8, 19 → epidemic keratoconjunctivitis
    - 11, 21 → hemorrhagic cystitis
    - 40, 41 → infantile gastroenteritis

---

## Pathogenesis & Immunity

- Infects mucosal epithelium (respiratory, GI tract, conjunctiva)

- Immunity: type-specific, lifelong

- Latent infection possible in adenoids & tonsils

---

## Clinical Findings

- Upper respiratory: Fever, sore throat, runny nose, conjunctivitis
- Lower respiratory: Bronchitis, atypical pneumonia
- Urinary: Hematuria, dysuria (hemorrhagic cystitis)
- GI: Nonbloody diarrhea (children <2)
- ~50% infections are asymptomatic

---

## Laboratory Diagnosis

- PCR → adenovirus DNA in respiratory samples
- Virus isolation in cell culture
- Fluorescent antibody detection
- Fourfold rise in antibody titer

---

## Treatment

- No specific antiviral therapy

---

## Prevention

- Military vaccines: Live, nonattenuated, serotypes 4, 7, 21
  - Monovalent, enteric-coated capsule → induces asymptomatic GI infection → immunity
  - Civilian use not available
- Keratoconjunctivitis prevention: Strict asepsis & handwashing in healthcare settings

✅ Exam Points

- Nonenveloped dsDNA virus → stable in environment → multiple transmission routes

- Fibers = viral attachment; serotype-specific immunity
- Causes respiratory, ocular, urinary, and GI disease
- Vaccines only available for military (serotypes 4, 7, 21)