KEY FACTS

TERMINOLOGY

- Viruses typically affect respiratory epithelium

IMAGING

- **Radiography**
  - May be normal at presentation (20%)
  - Focal or multifocal consolidation
- **CT/HRCT**
  - Mosaic attenuation and expiratory air-trapping
  - Ground-glass opacity and consolidation
  - Nodules, micronodules, and tree-in-bud opacities
- Interlobular septal thickening
- Bronchial &/or bronchiolar wall thickening

TOP DIFFERENTIAL DIAGNOSES

- Bacterial pneumonia
- Aspiration
- Diffuse alveolar hemorrhage
- Organizing pneumonia

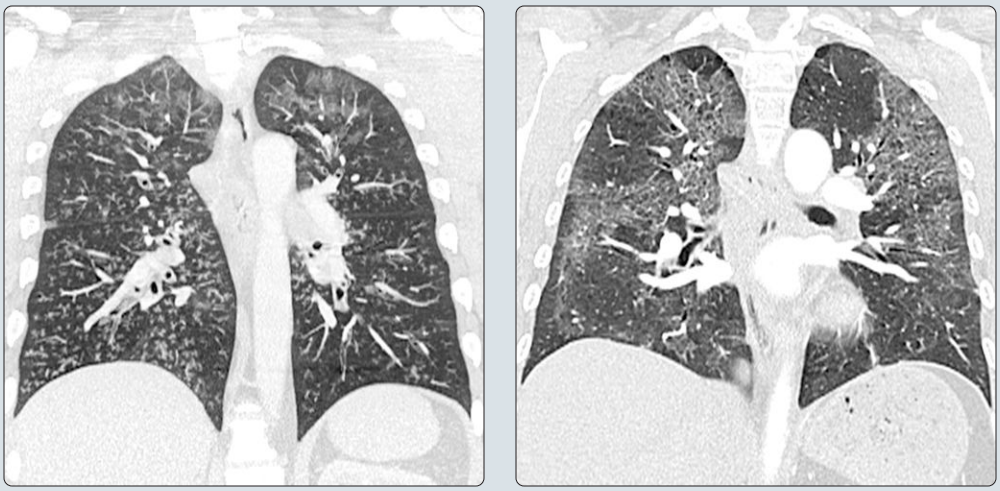
CLINICAL ISSUES

- Cold: Upper respiratory tract symptoms (tonsillopharyngitis, pharyngitis, epiglottitis, sinusitis, otitis media, and conjunctivitis)
- Influenza syndrome: Abrupt fever, headache, myalgias, and malaise
- Acute bronchiolitis in infants and children: Wheezing with concomitant signs of respiratory viral infection
- High rate of viral infection in patients with community-acquired pneumonia (2-35%)

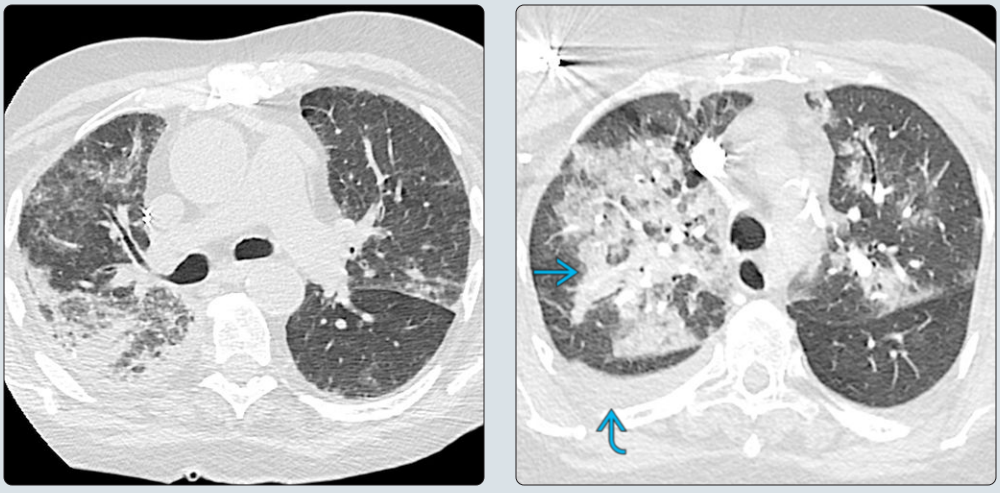
DIAGNOSTIC CHECKLIST

- Diagnosis relies on clinical suspicion: Host risk factors, presentation, and exposure history
- Lobar consolidation uncommon in viral pneumonia
- Nodules < 10 mm, may exhibit CT halo sign, and do not exhibit cavitation
- Branching or centrilobular nodules and mosaic perfusion common in viral bronchiolitis

(Left) *Coronal HRCT of a patient with acute infectious bronchiolitis secondary to respiratory syncytial virus (RSV) shows diffuse bilateral tree-in-bud nodules and upper lobe ground-glass opacities. RSV is a common cause of infectious bronchiolitis and has been linked to asthma in children.* **(Right)** *Coronal HRCT of a 52-year-old woman with rhinovirus pneumonia shows multifocal ground-glass opacities bilaterally. Rhinoviruses are the predominant cause of the common cold but occasionally cause viral pneumonia.*



(Left) *Axial NECT of a 75-year-old man with herpes simplex virus pneumonia shows multifocal ground-glass opacities and consolidations. Herpes pneumonia is rare but may occur in the setting of burns, transplantation, pregnancy, malignancy, and human immunodeficiency virus infection.* **(Right)** *Axial CECT of a 71-year-old woman with human metapneumovirus pneumonia shows bilateral consolidations and a small right pleural effusion. Human metapneumovirus is a common cause of viral pneumonia.*



TERMINOLOGY

Definitions

- Pulmonary viral infection typically affects respiratory epithelium from trachea to terminal bronchioles
  - Alveolar involvement less common, but often severe and rapidly progressive

RNA Virus-Related Diseases

- Influenza
  - Seasonal community infections, endemic infections, and unpredictable pandemics
  - Influenza type A: Most important respiratory virus affecting general population with regards to morbidity and mortality
  - Major cause of respiratory illness in immunocompromised hosts
- Avian influenza (H5N1)
  - Contact with infected birds; usually poultry
  - Overall case fatality rate exceeds 60%
- Swine influenza (H1N1)
  - 1st pandemic of 21st century, originally reported in Mexico (spring of 2009)
  - High transmission among humans, but virulence not greater than that observed with seasonal influenza
- Parainfluenza virus
  - Common cause of seasonal upper respiratory tract infection in adults and children
  - Parainfluenza virus type 3: Respiratory illness in immunocompromised hosts and solid organ transplant recipients
- Respiratory syncytial virus (RSV)
  - Ubiquitous cause of respiratory infection
  - Most frequent viral cause of lower respiratory tract infection in infants
- Human metapneumovirus (hMPV)
  - Implicated in 4-21% of infants with acute bronchiolitis
    - Symptoms clinically indistinguishable from those elicited by RSV
  - 4% of cases among patients with community-acquired pneumonia (CAP) or chronic obstructive pulmonary disease (COPD) exacerbations
- Measles
  - One of 3 major infectious diseases worldwide
    - 1.5 million childhood deaths per year
- Coxsackievirus, echovirus, and enterovirus
  - Lower respiratory tract infection may occur sporadically and is not always associated with pneumonia
- Human T-lymphotropic virus type 1 (HTLV-1)
  - Etiologic retrovirus of adult T-cell leukemia or lymphoma
    - Associated with myelopathy, Sjögren syndrome, and lymphocytic pneumonitis
- Hantavirus
  - Rodent-borne zoonotic disease
    - Hantavirus pulmonary syndrome: Severe acute respiratory distress syndrome (ARDS), rapid clinical progression, and high mortality
- Severe acute respiratory syndrome (SARS)
  - Atypical pneumonia caused by newly discovered SARS-associated coronavirus (SARS-CoV) in 2002 (Guangdong, China)
- Middle east respiratory syndrome (MERS)
  - Acute viral respiratory disease caused by novel virus currently named MERS coronavirus (MERS-CoV)

DNA Viruses

- Adenovirus
  - 5-10% of acute respiratory infections in infants and children, but < 1% of respiratory illnesses in adults
  - Swyer-James-MacLeod syndrome: Acquired constrictive bronchiolitis due to childhood adenovirus infection
- Varicella virus
  - Common contagious infection in childhood, increasing frequency in adults
    - Varicella pneumonia: 1 of every 400 cases of adulthood chickenpox infection
- Cytomegalovirus (CMV)
  - CMV infection: > 70% of hematopoietic stem cell transplant (HSCT) recipients; ~ 1/3 develop CMV pneumonia
    - Infection during postengraftment period (30-100 days after transplantation)
- Epstein-Barr virus (EBV)
  - Primary infection manifests as infectious mononucleosis
  - EBV pneumonia: Rare in immunocompetent or immunocompromised subjects
  - Associated with development of Burkitt lymphoma, Hodgkin lymphoma, nasopharyngeal carcinoma

IMAGING

Radiographic Findings

- Variable and overlapping appearance
  - Normal at presentation (20%)
- Tracheobronchitis
  - Bronchial wall thickening
  - Atelectasis: Discoid to segmental (mucus plugs)
- Pneumonia
  - Focal consolidation: Peripheral, mid, and lower lung zones (40%)
  - Unilateral or patchy bilateral areas of consolidation
  - Diffuse consolidation
- Complications
  - Bacterial superinfection: Sudden worsening, cavitation, or enlarging pleural effusion
- Uncommon findings
  - Hilar or mediastinal lymphadenopathy: Measles and infectious mononucleosis
  - Splenomegaly: Infectious mononucleosis
- Cardiac enlargement (pericardial effusion): Hantavirus
- Pleural effusion
  - Rare except for adenovirus, measles, hantavirus, HSV-1

CT Findings

- Alterations of parenchymal attenuation
  - Patchy heterogeneous pulmonary attenuation (mosaic attenuation pattern)
    - Bronchiolar obstruction (inflammation or cicatricial scarring) and secondary vasoconstriction
      - Inspiratory/expiratory CT: Differentiation of bronchiolar from pulmonary vascular disease

        - Bronchiolar disease (air-trapping): Decreased attenuation on inspiration, accentuated on expiration
        - Vascular disease: Little increase in attenuation or decrease in volume
- Ground-glass opacity and consolidation
    - Coexistence of interstitial thickening and partial airspace filling
    - Consolidation: Patchy and poorly defined (bronchopneumonia) vs. focal and well-defined (lobar pneumonia)
- Nodules, micronodules, and tree-in-bud opacities
    - Nodules 1-10 mm in diameter common in viral infections
        - Centrilobular nodules
            - Inflammation, infiltration, or fibrosis of surrounding interstitium and alveoli
        - Tree-in-bud opacities: Indicative of small airways disease
            - Dilatation of centrilobular bronchioles with lumina impacted with mucus, fluid, or pus
        - Branching or centrilobular nodules and mosaic perfusion: Common in viral bronchiolitis
        - Miliary nodules
            - Nearly any organism; typically tuberculosis, fungi, varicella-zoster virus
- Interlobular septal thickening
    - Widespread with associated ARDS
- Bronchial &/or bronchiolar wall thickening
    - Inflammatory exudates and bronchiolar wall thickening from edema and smooth muscle hyperplasia

DIFFERENTIAL DIAGNOSIS

Bacterial Pneumonia

- Consolidation, cellular bronchiolitis
- May exhibit cavitation

Aspiration

- Basilar predominant cellular bronchiolitis
- Esophageal abnormalities, neurological and deglutition disorders

Diffuse Alveolar Hemorrhage

- Ground-glass opacities ± interlobular septal thickening (crazy-paving pattern)
- No signs and symptoms of infection

Organizing Pneumonia

- Peripheral or peribronchial consolidation
- Migratory pulmonary opacities
- Reversed halo sign

PATHOLOGY

Microscopic Features

- Nodules contain infected cells with cytoplasmic inclusions: Cytomegalovirus, adenovirus, herpesvirus
- Necrotizing bronchitis &/or bronchiolitis and diffuse alveolar damage (DAD): Influenza, RSV, parainfluenza viruses
- Bronchiolitis and bronchiectasis: Adenovirus
- Necrotizing bronchopneumonia, multicentric areas of hemorrhage (centered on airways): Herpes simplex virus
- Acute interstitial pneumonia
    - Diffuse alveolar thickening by edema and mononuclear cells, airspace fibrinous exudate &/or hyaline membranes
    - CMV, hantaviruses (hantavirus pulmonary syndrome), SARS, and MERS
- Endothelial damage to small vessels (focal hemorrhagic necrosis, mononuclear infiltration of alveolar walls, and alveolar fibrinous exudates): Varicella-zoster virus

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
    - Clinical syndromes
        - Cold: Upper respiratory tract symptoms (tonsillopharyngitis, pharyngitis, epiglottitis, sinusitis, otitis media, and conjunctivitis)
        - Influenza syndrome: Abrupt fever, headache, myalgias, and malaise
    - Acute bronchiolitis in infants and children: Wheezing with concomitant signs of respiratory viral infection
        - RSV (most common), adenovirus, influenza, and parainfluenza
    - CAP: Cough, sputum, or dyspnea with fever or abnormalities at physical examination (rhonchi and rales)
        - Influenza and RSV
            - Comorbidities or risk factors: Smoking, COPD, asthma, diabetes mellitus, malignancy, heart failure, neurologic diseases, narcotic and alcohol use, and chronic liver disease
- Clinical profile
    - Role of biomarkers
        - **Procalcitonin: ↓ with viral infection**, ↑ with bacterial infection,
    - Better quality of diagnostic tests have improved ability to detect multiple viruses

Demographics

- Increasingly frequent cause of pulmonary disease worldwide
- High rate of viral infection in CAP (2-35%)
    - Influenza, hMPV, and RSV: 2/3 of all viral pathogens in patients with CAP

Natural History & Prognosis

- Variable prognosis
    - Complete resolution in immunocompetent individuals

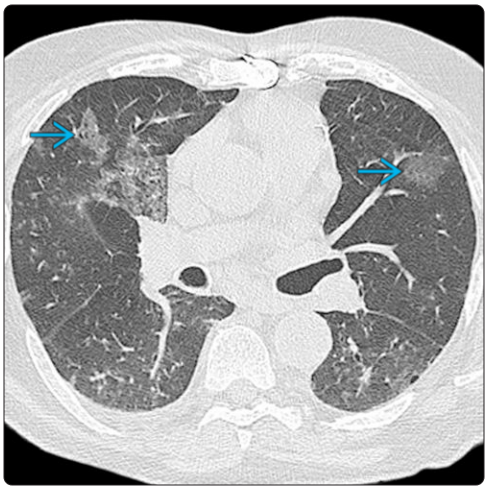
DIAGNOSTIC CHECKLIST

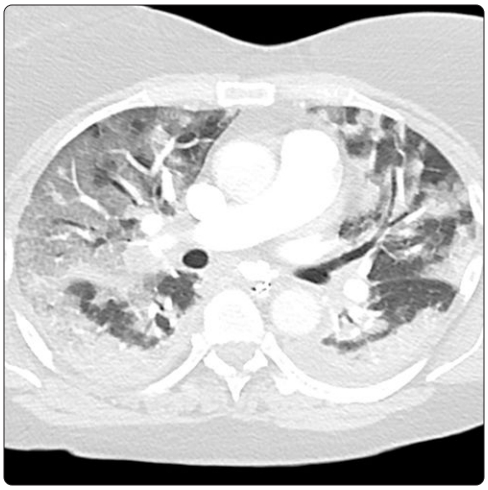
Image Interpretation Pearls

- Lobar consolidation uncommon in viral pneumonia
- Nodules < 10 mm, may exhibit CT halo sign; do not exhibit cavitation
- Branching or centrilobular nodules and mosaic perfusion/attenuation common in viral bronchiolitis

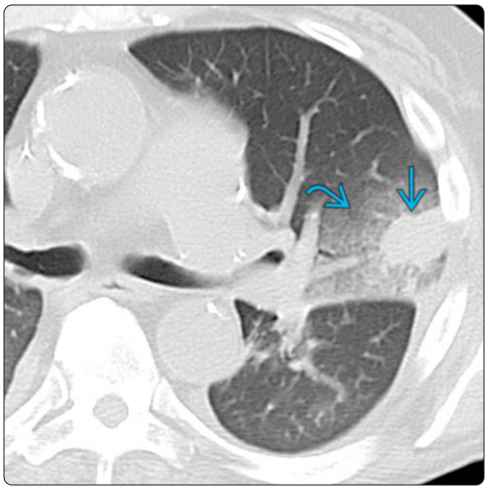
SELECTED REFERENCES

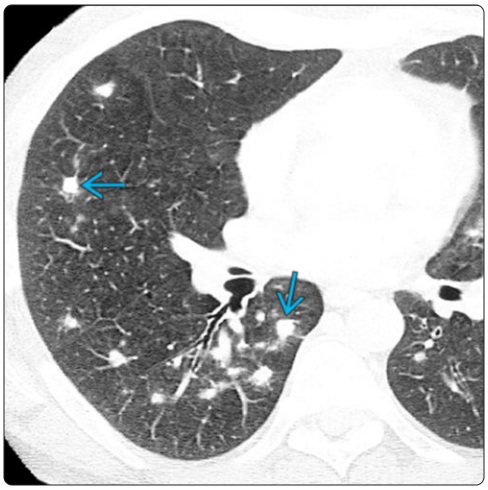
1. Franquet T: Imaging of pulmonary viral pneumonia. Radiology. Jul;260(1):18-39, 2011
2. Kim EA et al: Viral pneumonias in adults: radiologic and pathologic findings. Radiographics. 22 Spec No:S137-49, 2002



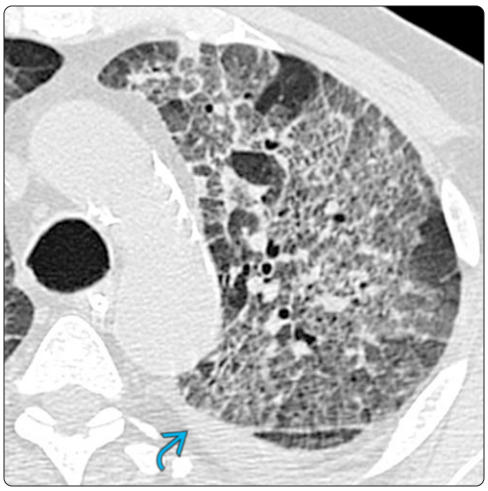


(Left) *Axial HRCT of a bone marrow transplant recipient who developed parainfluenza virus 3 pneumonia shows scattered bilateral ground-glass opacities. Influenza, respiratory syncytial virus, rhinovirus, and parainfluenza virus are the most common pathogens in this patient population.* **(Right)** *Axial CECT of a woman with influenza virus A pneumonia shows extensive, bilateral, peripheral ground-glass opacities and consolidations. The pattern is reminiscent of organizing pneumonia, which is often present histologically.*





(Left) *Axial NECT of a patient with cytomegalovirus pneumonia and a history of bilateral lung transplantation shows a left upper lobe nodule with surrounding ground-glass opacity, the so-called CT halo sign, which often correlates with perilesional hemorrhage.* **(Right)** *Axial NECT of a hematopoietic stem cell transplant recipient with cytomegalovirus infection shows multiple random lung nodules measuring < 10 mm, with surrounding ground-glass opacity. These findings are highly suggestive of a viral infection.*



(Left) *Axial CECT of a 28-year-old man with fever and a skin rash due to varicella-zoster virus infection shows profuse, miliary, 1- to 2-mm nodules scattered throughout the lung.* **(Right)** *Axial NECT of a patient with hantavirus pulmonary syndrome shows diffuse symmetric ground-glass opacities with superimposed linear and reticular opacities exhibiting the crazy-paving pattern and small bilateral pleural effusions. The findings were related to diffuse alveolar damage. (Courtesy A.S. Sousa, MD.)*