COVID-19

KEY FACTS

TERMINOLOGY

- SARS-CoV-2
- Beta coronavirus first reported in Wuhan, China in 2019
- Reverse transcriptase polymerase chain reaction (RT-PCR)

IMAGING

- **Radiography**: Patchy peripheral (subpleural) predominant hazy opacities ± consolidations
- **CT**
  - Early (~ 7-14 days after onset of symptoms)
    - Bilateral peribronchovascular and peripheral predominant ground-glass opacities ± consolidations
  - ARDS (late phase; > 14 days)
    - Diffuse consolidations &/or ground-glass opacities
- Complications: Bacterial pneumonia, pneumothorax, pneumomediastinum, acute pulmonary thromboembolic disease
- Sequela: Peribronchovascular fibrosis with reticulation and traction bronchiectasis, constrictive bronchiolitis

TOP DIFFERENTIAL DIAGNOSES

- Other viral pneumonia
- Organizing pneumonia
- E- cigarette or vaping product use-associated lung injury

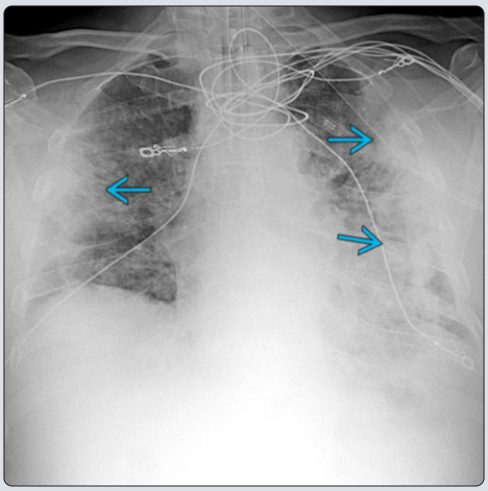
PATHOLOGY

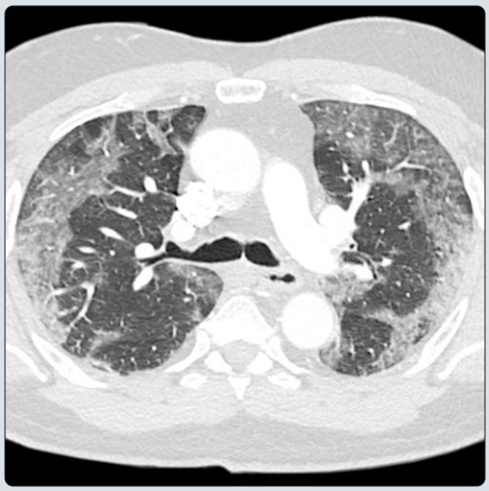
- Organizing pneumonia
- Acute fibrinous and organizing pneumonia
- Diffuse alveolar damage

CLINICAL ISSUES

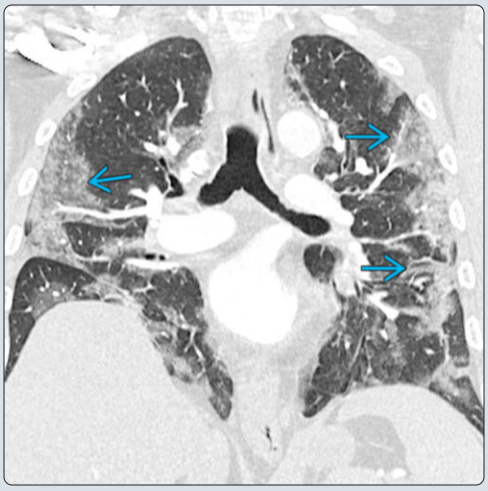
- Fever, chills, cough, shortness of breath, fatigue, muscle/body aches, headache, loss of taste/smell, sore throat, congestion, runny nose, nausea, vomiting, diarrhea
- Transmission: Person to person via respiratory droplets
- Diagnosis: RT-PCR in nasopharyngeal swab or other respiratory secretions
- Treatment: Prone ventilation, corticosteroids, convalescent serum

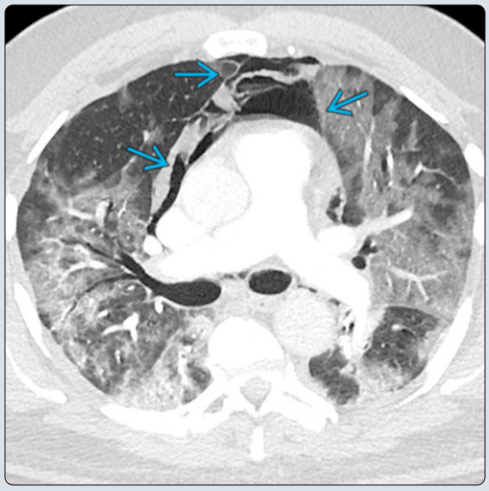
(Left) *AP chest radiograph of a 58-year-old patient with PCR-proven COVID-19 who presented with cough, fever, and chills shows bilateral ill-defined, peripheral, predominant opacities (ferritin: 551 ng/mL, C-reactive protein: 193 mg/L.).* **(Right)** *Axial CECT of the same patient shows peripheral, subpleural, well-demarcated ground-glass opacities with central areas of spared lung. Early pathologic reports have shown some features suggestive of acute fibrinous organizing pneumonia (AFOP).*





(Left) *Coronal CECT of the same patients shows bilateral well-demarcated, peripheral, subpleural ground-glass opacities, which are reminiscent of areas of organizing pneumonia.* **(Right)** *Axial CECT of a patient with COVID-19 shows extensive bilateral ground-glass opacities with peribronchial and subpleural distribution and a spontaneous pneumomediastinum. Pneumomediastinum and pneumothorax may occur in the context of the disease itself or as a consequence of barotrauma.*





TERMINOLOGY

Abbreviations

- Human coronavirus (HCoV)
- Organizing pneumonia (OP)
- Acute fibrinous and organizing pneumonia (AFOP)
- Diffuse alveolar damage (DAD)
- Acute respiratory distress syndrome (ARDS)
- Reverse transcriptase polymerase chain reaction (RT-PCR)

Synonyms

- SARS-CoV-2

Definitions

- Coronavirus
  - RNA virus initially described in 1960s
  - COVID-19: Beta coronavirus first reported in Wuhan, China in 2019

IMAGING

General Features

- Best diagnostic clue
  - Bilateral peripheral predominant opacities

Radiographic Findings

- May be normal
- Patchy peripheral (subpleural) predominant hazy opacities ± consolidations
- Diffuse lung opacities ± reticular opacities
  - Severe/advanced disease
  - May be indistinguishable from ARDS from other etiologies

CT Findings

- Early findings (~7-14 days after onset of symptoms)
  - Bilateral peribronchovascular and peripheral predominant ground-glass opacities ± consolidations
    - Often sharply demarcated from spared lung
    - "Crazy paving": Interlobular septal thickening and intralobular lines within areas of ground-glass opacities
  - Perilobar distribution
    - Bowed or polygonal opacities, surrounded by or surrounding aerated lung
  - Bronchial or bronchiolar &/or peripheral vascular dilation in affected areas
  - Reversed halo sign
    - Peripheral subpleural consolidation surrounding central ground-glass opacity
  - Small rounded or ill-defined scattered ground-glass opacities
- ARDS (late phase; > 14 days)
  - Diffuse consolidations &/or ground-glass opacities
- Complications
  - Bacterial pneumonia (rare)
  - Pneumothorax (rare)
    - May occur in absence of mechanical ventilation
  - Pneumomediastinum (rare); spontaneous or associated with barotrauma
  - Acute pulmonary thromboembolic disease (controversial whether incidence is increased)
- Chronic findings (after resolution)
  - Still early in pandemic to establish with certainty
  - Peribronchovascular fibrosis with reticulation and traction bronchiectasis described in some patients
  - Mosaic attenuation and air-trapping suggestive of constrictive bronchiolitis described in some patients

Imaging Recommendations

- Best imaging tool
  - CT superior to radiography for detection of pulmonary abnormalities, but not required for diagnosis, does not replace RT-PCR as diagnostic gold standard
  - CT not required for diagnosis, should be reserved to evaluate complications

DIFFERENTIAL DIAGNOSIS

Viral Pneumonia

- Various viral infections may exhibit imaging abnormalities similar to those of COVID-19, e.g., influenza

Organizing Pneumonia

- Typically subacute or chronic course
- AFOP
  - Histologic variant of OP with overlapping features of DAD
  - May be acute or subacute
  - Acute AFOP often has clinical presentation similar to that of typical ARDS/DAD
- OP and AFOP may be idiopathic or secondary (e.g., infection, connective tissue disease, autoimmunity, drug toxicity, etc.); often exhibit imaging findings similar to those seen in COVID-19

E-Cigarette or Vaping Product Use-Associated Lung Injury (EVALI)

- Various pathologic patterns: DAD, OP, hypersensitivity pneumonitis, acute eosinophilic pneumonia, chronic eosinophilic pneumonia, lipoid pneumonia
- Diffuse ground-glass opacities ± consolidations, centrilobular ground-glass micronodules

Desquamative Interstitial Pneumonia

- Within spectrum of smoking-related pulmonary diseases
- Multifocal subpleural ground-glass opacities &/or consolidations
- Often coexists with emphysema &/or other smoking-related disease

PATHOLOGY

Microscopic Features

- AFOP
  - Subtype of OP
  - Predominant pattern of acute lung injury
    - Extensive intraalveolar fibrin deposition (a.k.a. fibrin balls) rather hyaline membranes
    - Intraluminal loose connective tissue within alveolar ducts and bronchioles
    - Fibroblastic bodies and fibroblasts surrounding intraalveolar fibrin

- Moderate interstitial T-cell lymphocytic and plasma cells infiltrate and type 2 pneumocyte hyperplasia with cytologic atypia
- Vascular injury: Endothelial injury with cytoplasmic vacuolization and cell detachment in small to medium-sized pulmonary arteries

- Histological overlap with DAD
  - Different from DAD: Predominant feature is organizing intraalveolar fibrin

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - Fever or chills, cough, shortness of breath, fatigue, muscle/body aches, headache, loss of taste/smell, sore throat, congestion, runny nose, nausea, vomiting, diarrhea
  - 2 clinical phenotypes
    - Type L: 70 - 80%
      - Low: Elastance (near normal compliance), ventilation:perfusion (VA/Q) ratio, lung weight, lung recruitability
    - Type H (ARDS): 20-30%
      - High: Elastance (abnormal compliance), right-to-left shunt, lung weight, lung recruitability
  - Children
    - Most asymptomatic or with mild symptoms; may spread disease even if asymptomatic
    - Some may develop severe illness
    - Mortality rare
    - Multisystem inflammatory syndrome in children (MIS-C)
      - Symptoms: Fever, abdominal pain, vomiting, diarrhea, neck pain, rash, red eyes, asthenia
      - May involve heart, lungs, kidneys, brain, skin, eyes, gastrointestinal organs
- Other signs/symptoms
  - RT-PCR in nasopharyngeal swab or other respiratory secretions
  - Laboratory
    - Lymphopenia
    - Thrombocytopenia
    - ↑ liver enzymes
    - ↑ lactate dehydrogenase (LDH)
    - ↑ inflammatory markers [e.g., C-reactive protein (CRP), ferritin)], inflammatory cytokines [i.e., interleukin 6 (IL-6) and tumor necrosis factor (TNF)-alpha]
    - ↑ D-dimer (> 1 mcg/mL)
    - ↑ prothrombin time (PT)
    - ↑ troponin
    - ↑ creatine phosphokinase (CPK)
    - Acute kidney injury
    - Procalcitonin is usually normal or mildly elevated; marked elevation suggest bacterial coinfection
- Clinical profile
  - Incubation period
    - 4-5 days; may be as long as 14 days
  - Protective factors: Prior BCG vaccination

Demographics

- Sex
  - Males have reported higher mortality rate
- Ethnicity
  - Black, Hispanic, and South Asian subject more likely to develop disease and have higher mortality rates
- Epidemiology
  - > 55 million cases worldwide
  - Transmission
    - Airborne via respiratory droplets (most common)
    - Contaminated surfaces
    - Low risk of transmission 7-10 days following symptom onset
- Risk factors for severe illness
  - Cancer
  - Chronic kidney disease
  - Chronic obstructive pulmonary disease (COPD)
  - Heart conditions (e.g., heart failure, coronary artery disease, cardiomyopathy)
  - Immunocompromised state (weakened immune system) from solid organ transplant
  - Severe obesity (BMI ≥ 40 kg/m2)
  - Pregnancy
  - Sickle cell disease
  - Smoking
  - Type 2 diabetes mellitus
  - A+ ABO blood group
- Mortality
  - Increases with age
  - Crude mortality 2-3%; improved after corticosteroids and other measurements implemented
  - > 1.3 million deaths (> 240,000 in the USA)

Natural History & Prognosis

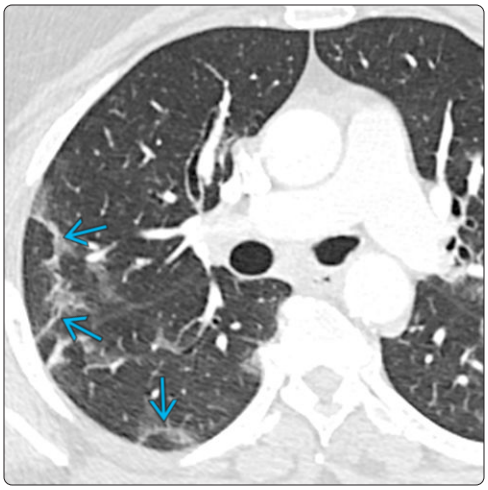
- Complications
  - ARDS
    - 8 days after symptom onset in 20% of patients with severe disease
    - 12-24% require intubation
  - Cardiovascular
    - Cardiomyopathy: 1/3 of patients admitted to ICU
    - Arrhythmia
  - Acute thromboembolic disease
  - Secondary hemophagocytic lymphohistiocytosis
    - Hyperinflammatory syndrome with fulminant and fatal hypercytokinemia with multiorgan failure
    - Features: Unremitting fever, cytopenia, ↑ ferritin; pulmonary involvement in ~ 50% (including ARDS)

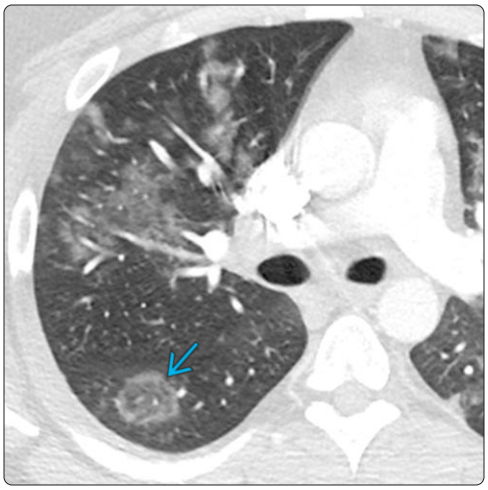
Treatment

- Prone ventilation (whether patient intubated or not)
- Corticosteroids
- Convalescent serum
- Vaccination soon available

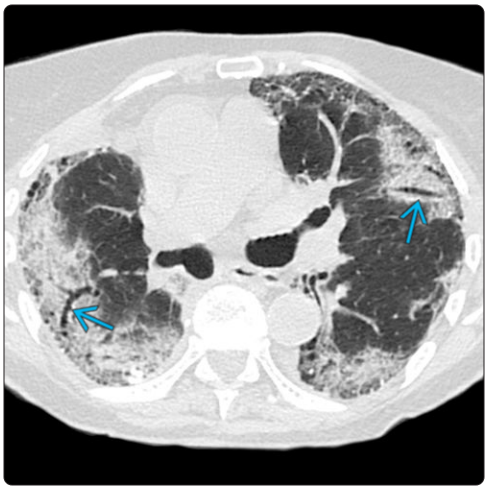
SELECTED REFERENCES

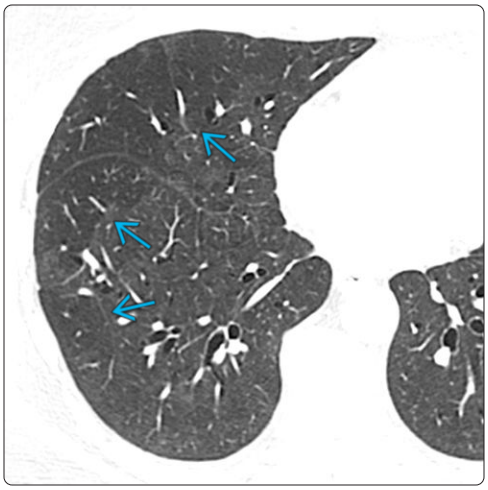
1. Copin MC et al: Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection. Intensive Care Med. 46(6):1124-6, 2020
2. Gattinoni L et al: COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 46(6):1099-102, 2020



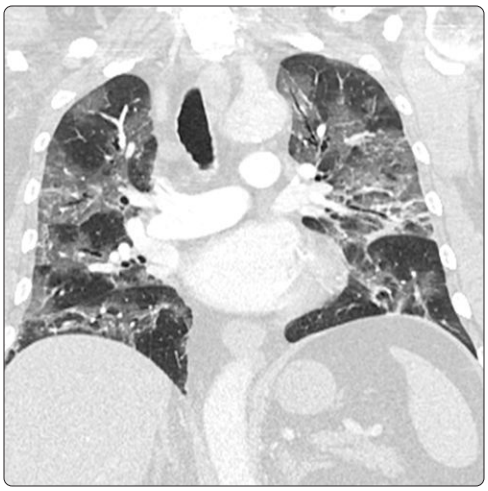


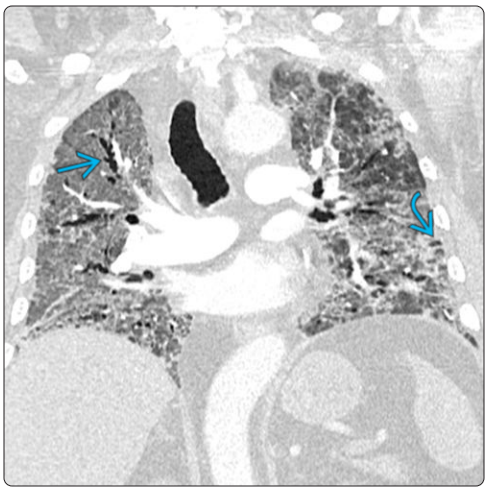
(Left) *Axial CECT of a patient with COVID-19 and pulmonary involvement shows bilateral patchy ground-glass opacities. Note arc-like opacities, the so-called perilobular pattern (a.k.a. the atoll sign), a characteristic pattern seen in organizing pneumonia.* **(Right)** *Axial CECT of a patient with COVID-19 shows multifocal bilateral ground-glass opacities, including a right lower lobe nodule that exhibits the reversed halo sign (i.e., denser peripheral opacities surrounding central ground-glass opacities), typical of organizing pneumonia.*





(Left) *Axial NECT of a patient with pulmonary involvement secondary to COVID-19 shows bilateral subpleural ground-glass opacities that exhibit intrinsic mild bronchial dilatation, a finding that has been described in the context of organizing pneumonia.* **(Right)** *Axial NECT of a patient who recovered from a COVID-19 infection but remained sort of breath shows bilateral scattered areas of mosaic attenuation, consistent with small airways disease, presumably constrictive bronchiolitis.*





(Left) *Coronal CECT of a patient with pulmonary involvement due to COVID-19 shows diffuse bilateral patchy ground-glass opacities secondary to organizing pneumonia.* **(Right)** *Coronal CECT of the same patient obtained 2 months later shows interval development of decreased lung volume and diffuse reticular opacities with extensive traction bronchiectasis and bronchiolectasis secondary to postinflammatory fibrosis. The pulmonary sequela of COVID-19 infection are still not well established.*