

Coronavirus

KEY FACTS

TERMINOLOGY

- RNA virus
- Order *Nidovirales*, family *Coronaviridae*, genus *Coronavirus*
- Human coronavirus
 - Alpha coronavirus (HCoV-229E and HCoV-NL63)
 - Beta coronavirus [HCoV-HKU1, HCoV-OC43, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), 2019 novel coronavirus (COVID-19)]

IMAGING

- Radiography
 - May be normal
 - Multifocal ill-defined opacities
- CT
 - Ground-glass opacities ± consolidation
 - Interlobular septal thickening ± crazy paving
 - Mixed central and peripheral distribution

TOP DIFFERENTIAL DIAGNOSES



- Pneumonia
- Acute respiratory distress syndrome

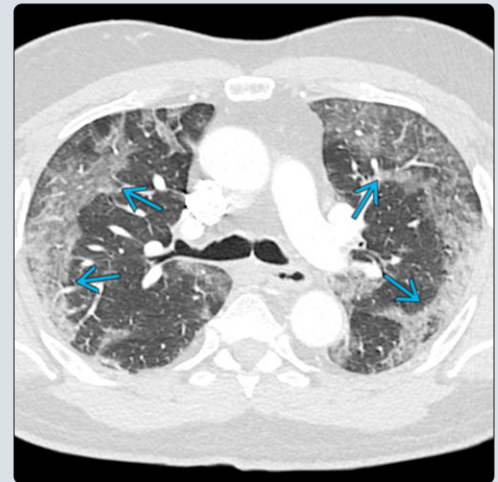
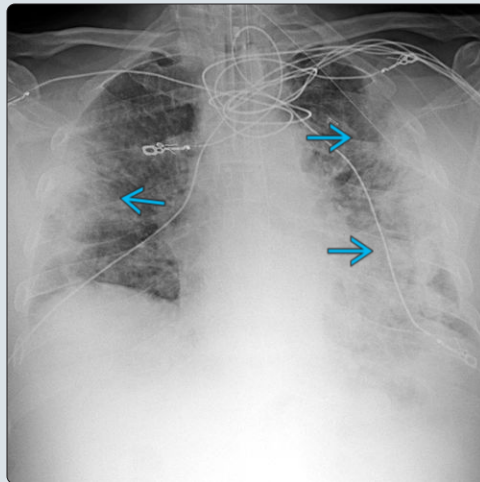
PATHOLOGY



- Acute diffuse alveolar damage
- Organizing pneumonia may occur after 10 days

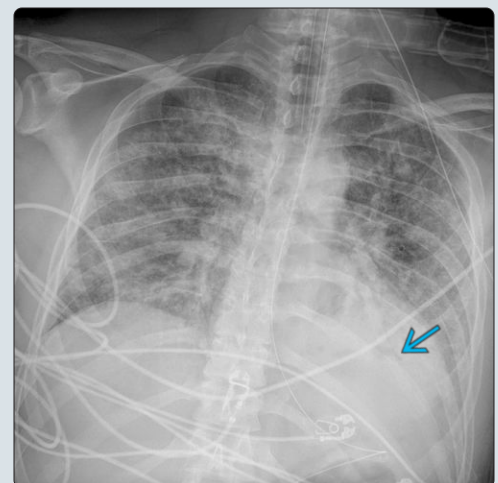
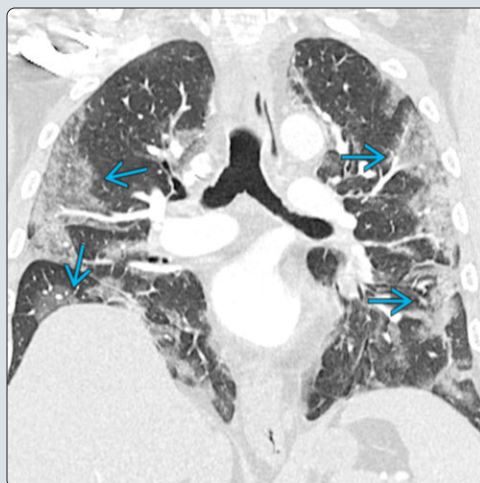
CLINICAL ISSUES

- Most common symptoms: Fever ± chills, shortness of breath, cough
- Epidemics: Zoonoses and human-to-human transmission
- Laboratory
 - Leukopenia, lymphopenia, thrombocytopenia
 - Reverse transcriptase PCR
 - Low procalcitonin
 - ↑ lactate dehydrogenase
 - ↑ alanine aminotransferase
- No specific antiviral treatment

(Left) AP chest radiograph of 58-yr-old patient with PCR-proven COVID-19 who presented with cough, fever, chills shows ill-defined peripherally predominant opacities bilaterally . Ferritin level: 551 ng/ml and C-reactive protein: 193 mg/l. **(Right)** Axial CECT of same patient shows peripheral, subpleural, well-demarcated ground-glass opacities interspaced with central areas of spared lung . Preliminary incidental pathologic reports have shown some features suggesting acute fibrinous organizing pneumonia (AFOP).



(Left) Coronal CECT of the same patient shows well-demarcated, peripheral, subpleural ground-glass opacities bilaterally , which are reminiscent of areas of organizing pneumonia. **(Right)** AP chest radiograph of a 44-year-old patient with PCR-proven COVID-19 who developed acute respiratory distress syndrome (ARDS) shows bilateral heterogeneous opacities and a dense left basilar consolidation . ARDS is a known complication of *Coronaviridae*-associated pulmonary infections.



TERMINOLOGY

Abbreviations

- Human coronavirus (HCoV)

Definitions

- RNA virus initially described in 1960s
 - Order: *Nidovirales*
 - Family: *Coronaviridae*
 - Genus: *Coronavirus*
- Respiratory and enteric disease in humans and other animals
- Genera: Alpha, beta, gamma, and delta
 - Human coronavirus
 - Alpha coronavirus: HCoV-229E, HCoV-NL63
 - Beta coronavirus: HCoV-HKU1, HCoV-OC43, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), 2019 novel coronavirus disease (COVID-19)
- Community-acquired coronavirus: HCoV-229E, HCoV-NL63, HCoV-HKU1, HCoV-OC43
- Epidemics: MERS-CoV, SARS-CoV, COVID-19

IMAGING

General Features

- Best diagnostic clue
 - Bilateral ground-glass opacities &/or consolidations
- Location
 - Diffuse, peripheral, lower lobe predominance

Radiographic Findings

- May be normal
- Multifocal ill-defined opacities, may be progressive

CT Findings

- Ground-glass opacities ± consolidation
 - Multifocal > focal
 - Bilateral > unilateral
 - Peripheral peribronchovascular
 - Mixed central and peripheral distribution
- Interlobular septal thickening ± crazy paving
- Pleural effusion, lymphadenopathy (rare)
- Cavitation (very rare)
- **Covid-19 common features**
 - Pulmonary opacities may predate real-time reverse transcription polymerase chain reaction (RT-PCR)
 - Subpleural or multifocal ground-glass opacities bilaterally 50–75% of patients; may exhibit "reversed halo" sign (rare)
 - Likely related to organizing pneumonia pattern (possibly acute fibrinous organizing pneumonia)
 - As disease progresses, diffuse crazy paving and consolidations [i.e., changes of acute respiratory distress syndrome (ARDS)]
- Survivors of severe disease (sequelae of ARDS)
 - Reticulation and traction bronchiectasis
 - Subpleural bands
 - Architectural distortion
 - Air trapping

DIFFERENTIAL DIAGNOSIS

Pneumonia

- Bacterial or viral
- Community-acquired pneumonia, health care-associated and nosocomial pneumonia
- Bacterial pneumonia: Elevated procalcitonin

Acute Respiratory Distress Syndrome

- Other pulmonary infection or diffuse inflammatory process

PATHOLOGY

General Features

- Spike (S) protein responsible for crown spikes; mediates receptor binding and fusion with host membrane
- Other proteins: Membrane (M), nucleocapsid (N), hemagglutinin-esterase (HE), small envelope (E)

Microscopic Features

- SARS
 - Acute diffuse alveolar damage
 - Hyaline membranes, interstitial edema, inflammatory interstitial infiltrates, bronchiolar injury
 - Organizing pneumonia may occur after 10 days
- MERS
 - Acute diffuse alveolar damage
 - Acute and chronic interstitial and alveolar inflammation
 - Hemorrhagic necrotizing pneumonia
 - Focal intimal arteritis

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
 - Community-acquired coronavirus
 - Ubiquitous
 - Upper respiratory tract infection
 - 3rd most common pulmonary infection after rhinovirus and influenza
 - Up to 1/3 of adult cases
 - HCoV-229E, HCoV-NL63, HCoV-HKU1, HCoV-OC43
 - Lower respiratory tract infection
 - Common viral community-acquired pneumonia
 - 2-3% of all community-acquired pneumonias
 - 4th most common viral pneumonia after influenza, human metapneumovirus, and parainfluenza
 - More common in COPD and immunocompromised patients (e.g., those with HIV, bone marrow transplant, cancer, etc.)
 - Mortality correlates with low hemoglobin, low monocyte count, low serum albumin, and low oxygen saturation
 - SARS-CoV
 - Criteria
 - Fever > 38°C
 - 1 or more of following: Cough, shortness of breath, difficulty breathing, hypoxia, radiographic findings of pneumonia or ARDS
 - Travel within 10 days to exposure area or contact with person who traveled to exposure area or had SARS

Coronavirus

- Most common symptoms
 - Fever, cough, chills, myalgia, dyspnea, headache
- Less common symptoms
 - Diarrhea
- MERS
 - Criteria
 - Confirmed: Laboratory confirmation ± symptoms
 - Probable: Febrile acute respiratory illness + pneumonia &/or ARDS + epidemiologic link
 - Most common symptoms: Fever ± chills, shortness of breath, cough
 - Less common symptoms: Hemoptysis, sore throat, myalgias, diarrhea, abdominal pain
 - More prominent gastrointestinal symptoms, acute kidney failure
 - Mechanical ventilation in 50-90% of infected patients
- 2019 novel coronavirus (COVID-19)
 - Criteria for testing: Clinical judgment; fever &/or upper respiratory infection symptoms + any of the following within prior 14 days
 - Close contact with confirmed or suspected case of COVID-19
 - Residence or travel in regions of widespread transmission
 - Attendance at events or settings with confirmed COVID-19 cases
 - Consider diagnosis in severe lower respiratory infection without alternative etiology
 - Common symptoms: Fever, fatigue, cough
 - Less common symptoms: Sputum production, headache, hemoptysis, diarrhea
 - Low or normal white blood cell count or low lymphocyte count
 - Spectrum of clinical features
 - No or mild disease in ~ 81%
 - Severe disease (dyspnea, hypoxia) in ~ 14%
 - Critical disease (respiratory failure, shock, multiorgan dysfunction) in ~ 5%
 - Affects older adults, with cardiopulmonary disease, weak immunity
 - Health care workers affected less proportionately than in SARS and MERS
 - Children less affected &/or less symptomatic
 - **Secondary hemophagocytic lymphohistiocytosis**
 - **Commonly triggered by viral infections**
 - **Hyperinflammatory syndrome with fulminant and fatal hypercytokinemia with multiorgan failure**
 - **Features: Unrelenting fever, cytopenias, and ferritin; pulmonary involvement (including ARDS) occurs in ~ 50%**
 - **Immunosuppression with corticosteroids may be beneficial**
- Other signs/symptoms
 - Occasional gastrointestinal symptoms: Vomiting, diarrhea, abdominal pain

Demographics

- SARS-CoV
 - Hong Kong, China, mid-March 2003
 - Spread to 37 countries

- Infected 8,098 persons, killed 774
- MERS-CoV
 - Saudi Arabia, 2012
 - Spread to 27 countries
 - Infected 2,494 persons, killed 858
- 2019 novel CoV (COVID-19)
 - Wuhan, China, 2019-2020
 - Spread to 184 countries and regions (as of 4/6/2020)
 - Preliminary data: Lower mortality than SARS-CoV and MERS-CoV, ~ 2-3%
 - >1,300,000 cases, 74,000 deaths
 - Risk factors: Middle-aged adults and elderly most commonly affected

Natural History & Prognosis

- Community-acquired coronavirus
 - More common in winter
 - Transmission through infected secretions and aerosol droplets
 - Immunity develops fast but wanes; reinfection common
- SARS-CoV
 - Incubation: 2-10 days
 - Zoonosis transmitted to humans; palm civets and raccoon dogs are intermediate hosts; horseshoe bats are natural hosts
 - Human-to-human transmission
 - Risk factors: Older age, diabetes, chronic hepatitis B, atypical symptoms, ↑ lactate dehydrogenase (LDH)
 - Pregnant women have higher mortality than nonpregnant women
 - Few reported infections and no mortality in children
 - Mortality: 10% of all infected
- MERS-CoV
 - Incubation: 2-10 days
 - Zoonosis transmitted to humans; dromedary camels are intermediate hosts, bats are reservoir
 - Human-to-human transmission (limited)
 - Risk factors: Diabetes, chronic cardiac disease, chronic renal disease, chronic lung disease, cancer
 - Mortality 35% of all infected
- 2019 novel CoV (COVID-19)
 - Incubation: Up to 14 days
 - Zoonosis, uncertain source (suspected bats and pangolins)
 - Human-to-human transmission
 - Overall case fatality rate of 2.3%

Treatment

- No specific antiviral treatment
- MERS
 - Individuals at risk should avoid camels
- 2019 novel CoV (COVID-19)
 - No specific treatment
 - **Corticosteroids may have role in secondary hemophagocytic lymphohistiocytosis**
- Prevention
 - Standard, contact, and airborne precautions, including eye protection

Laboratories

- Covid-19

- Reverse transcriptase PCR
- Elevated ferritin and C-reactive protein are inflammatory markers and usually elevated in secondary hemophagocytic lymphohistiocytosis
 - Often associated with ARDS and intubation
 - Corticosteroids may have role in treatment
- SARS
 - ↑ LDH (higher levels indicate poorer prognosis)
 - ↑ alanine aminotransferase
 - Thrombocytopenia
- MERS
 - Leukopenia, lymphopenia, thrombocytopenia
 - Lymphocytosis
 - ↑ alanine aminotransferase
 - ↑ LDH
- Procalcitonin typically low in viral infections


DIAGNOSTIC CHECKLIST

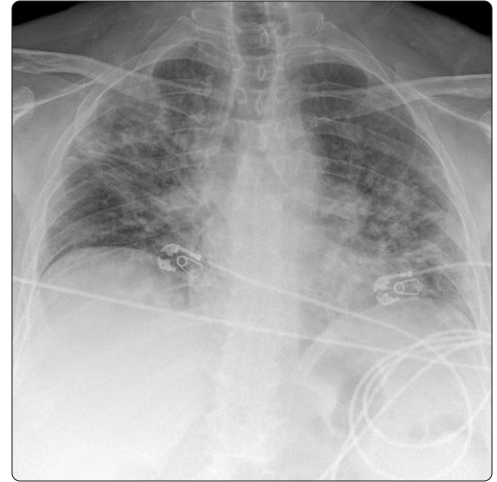
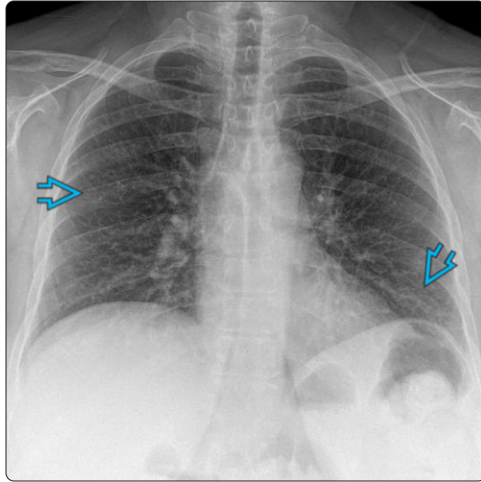
Consider


- As imaging findings are nonspecific, institutions may opt to avoid imaging in patients with suspected or confirmed COVID-19 to prevent disease transmission

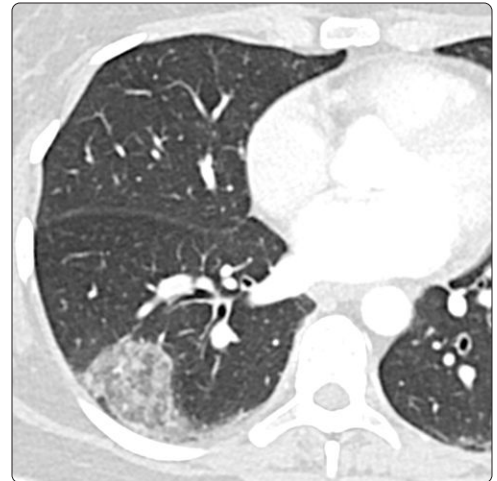
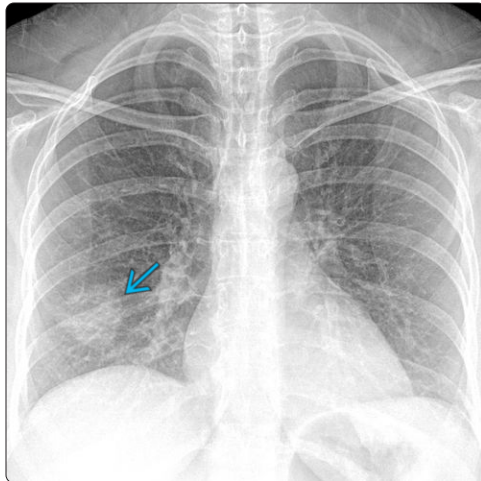
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(Left) PA chest radiograph of 55-year-old patient with mild dyspnea, low-grade fever shows subtle hazy opacities  in right upper and left lower lung zones. These findings can be easily overlooked but were new when compared to an old chest radiograph (not shown). **(Right)** AP chest radiograph of same patient 5 days later after PCR-proven COVID-19 shows extensive bilateral heterogeneous opacities in right upper and left mid to lower lung zones. Patient required intubation shortly thereafter due to severe dyspnea and hypoxemia.



(Left) AP chest radiograph of a 47-year-old patient with PCR-proven COVID-19 with history of gestational diabetes shows a right lower lobe mass . **(Right)** Axial CECT of the same patient shows subpleural mass-like area of ground-glass opacities and denser peripheral opacities (i.e., reversed halo sign). Features of organizing pneumonia (possibly acute fibrinous organizing pneumonia, AFOP) have been described as early histologic changes in COVID-19 infection.



(Left) Axial NECT of 77-yr-old man obtained 5 days after diagnosis of symptomatic COVID-19 shows subtle bilateral ill-defined peripheral ground-glass opacities . Two images published in *The Lancet Infectious Diseases*, Shi H et. al. *Radiological Findings of 81 Patients with COVID-19*. Copyright Elsevier (2020). **(Right)** Axial NECT of same patient obtained 15 days after the initial onset of symptoms shows progression of bilateral pulmonary involvement manifesting with bilateral peripheral consolidations and ground-glass opacities.

