Diagnosis & Management of COVID-19

Pathophysiology, Transmission, Diagnosis, and treatment of Coronavirus Disease 2019 (COVID-19)
A Review

Case Presentation

- A 53-year-old man was admitted for hypoxemic respiratory distress.
- The patient had been well until 6 days before.
- Dry cough, fever, and worsening fatigue developed.
- Two days later, his symptoms had not resolved, and he presented to the emergency department.

Case Presentation

- No history of contacts.
- No family members were ill.
- He had not traveled recently.
- He did not use tobacco, drink alcohol, or use illicit substances.
- No history of coronary artery disease
- No history of pulmonary disease.

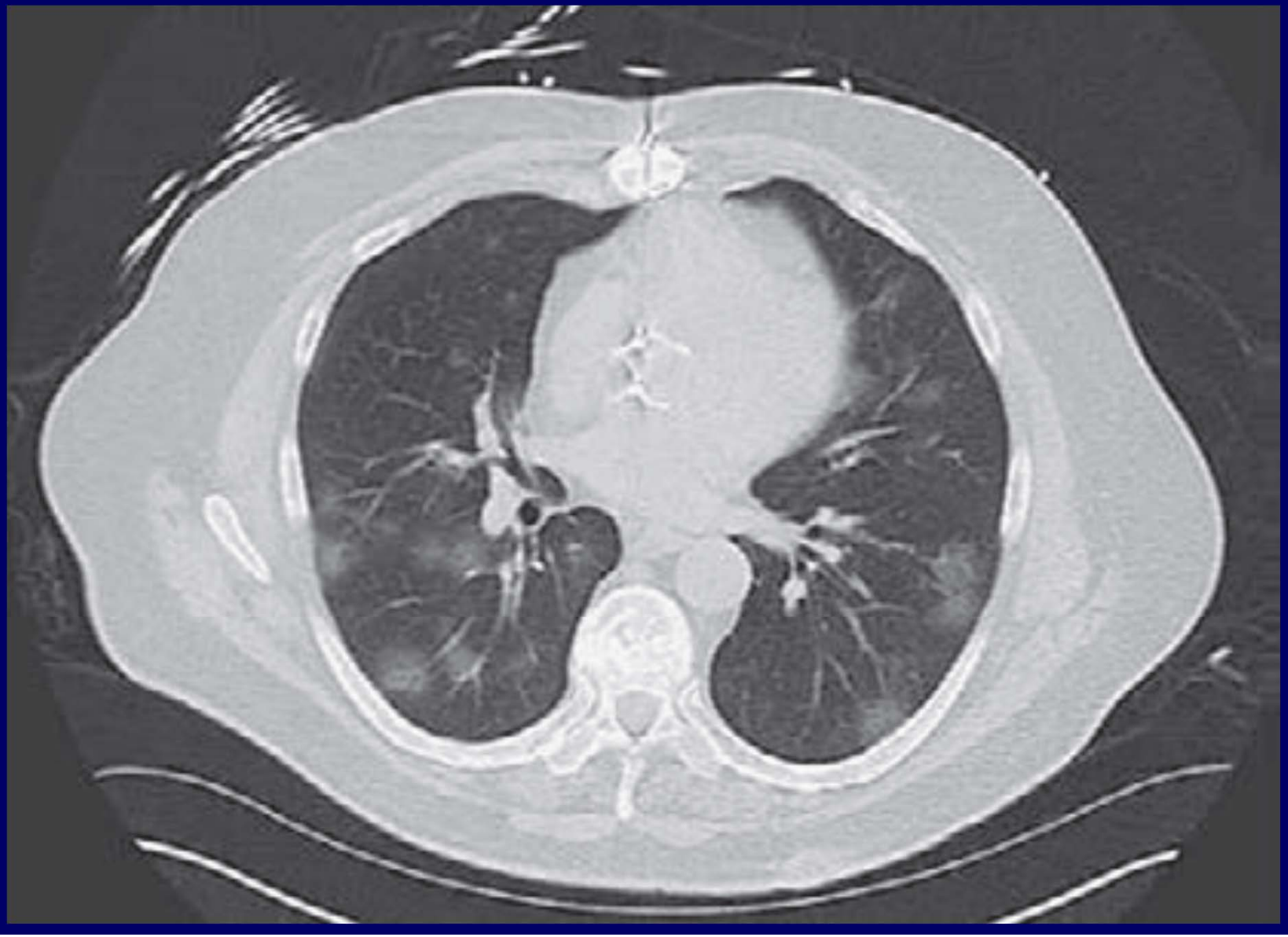
Case Presentation

- **P/E:**
- T = 38.8°C
- BP =100/60 mm Hg
- HR= 91 / minute
- RR=25 / minute
- The oxygen saturation 86% while he was breathing ambient air

Case Presentation

- He appeared ill with respiratory distress & the lung sounds were clear.
- WBC = 7600 /microliter
  - Neutrophils = 86%
  - Lymphocytes = 9%(ALC=684)
  - Monocyte = 5%

Chest CTScan: shows scattered, confluent central and peripheral ground glass opacities in both lungs.



Diagnosis

- Epidemiologic criteria
- Clinical characteristic
- Imaging
- Laboratory findings

Diagnosis

- CBC→ with a focus on the total lymphocyte count
- Complete metabolic panel
- Creatine kinase (CK)
- C-reactive protein (CRP)
- Ferritin

Routine laboratory abnormalities

- Lymphopenia (most common)
- Elevated serum:
  - CRP
  - LDH
  - ALT
  - AST

Routine laboratory abnormalities

- LDH , repeated daily if elevated
- Troponin, repeated every two to three days if elevated
- ECG with at least one repeat test after starting any QTc-prolonging agent

Routine laboratory abnormalities

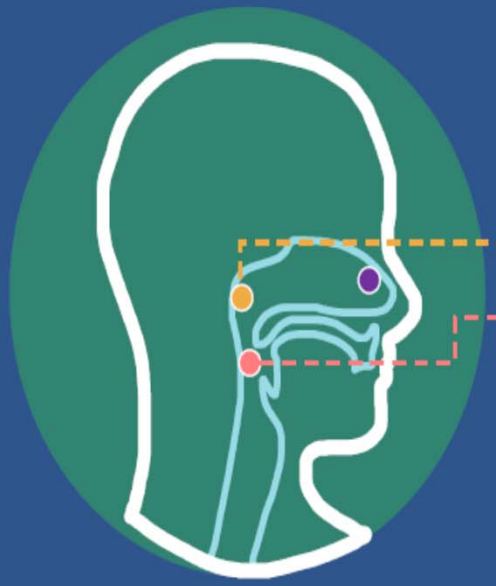
- Coagulopathy:
  - Prolongation of PT
  - Mild Thrombocytopenia
  - Elevated D-dimer values
- D-dimerand & lymphopenia seem to have the largest prognostic associations

Viral RNA by RT-PCR

- Nasopharyngeal swabs
- pharyngeal swab
- Upper respiratory tract specimens:
  - Saliva
  - Sputum

PCR testing for COVID-19: where to swab?

A swab audit at the National Centre for Infectious Diseases (NCID) showed that **nasopharynx** is the single sampling source with the highest sensitivity



	Sensitivity*†‡ (%)			
	Day of illness < 8	Day of illness ≥ 8	URTI	Pneumonia
Nasopharynx (NP)	95	64	92	60
Oropharynx (OP)	88	61	88	52
Combination of NP and OP	98	76	96	72
Combination of OP and mid-turbinate nasal (MT)	98	70	94	68

Scan the QR code for a video on how to collect a nasopharyngeal swab to test for COVID-19. While the video outlines the general principles, please follow the prevailing guidelines or protocols at your institution.

Marty FM, Chen K, Verrill KA. How to obtain a nasopharyngeal swab specimen. NEJM. 2020. DOI:10.1056/NEJMvcm2010260

PCR, polymerase chain reaction; URTI, upper respiratory tract infection

* Sensitivity refers to the proportion of individuals infected with COVID-19 who are found to have a positive test result

† Specificity: 100% (specificity refers to the proportion of individuals not infected with COVID-19 who are found to have a negative test result)

‡ NP + MT showed similar sensitivity to OP + MT; other sampling sources showed lower sensitivity, including MT alone and saliva (alone or in combination with OP or MT)

National Centre for Infectious Diseases
ACE agency for care effectiveness
MINISTRY OF HEALTH SINGAPORE

Viral RNA by RT-PCR

- In a study of 205 patients with confirmed COVID-19 infection, RT-PCR positivity was highest in:
  - Bronchoalveolar lavage 93%
  - Sputum 72%
  - Nasal swab 63%
  - Pharyngea swab 32%

Antibodies to SARS-CoV-2

- Serological diagnosis is especially important in mild to moderate illness & present late, beyond the first 2 wks of illness onset
- An important tool to understand the extent of COVID-19 in the community
- Identify individuals who are immune & potentially “protected” from becoming infected

Antibodies to SARS-CoV-2

- Begin to increase from the 2nd week of symptom onset.
- Although IgM & IgG ELISA have been found to be positive even as early as the 4th day after symptom onset.
- Higher levels occur in the 2nd & 3rd week of illness

Antibodies to SARS-CoV-2

- IgM begins to decline and reaches lower levels by week 5 and almost disappears by week 7.[7]
- IgG persists beyond 7 weeks
- In a study of 140 patients, combined sensitivity of PCR and IgM ELISA directed at NC Ag was 98.6% vs 51.9% with a single PCR test.

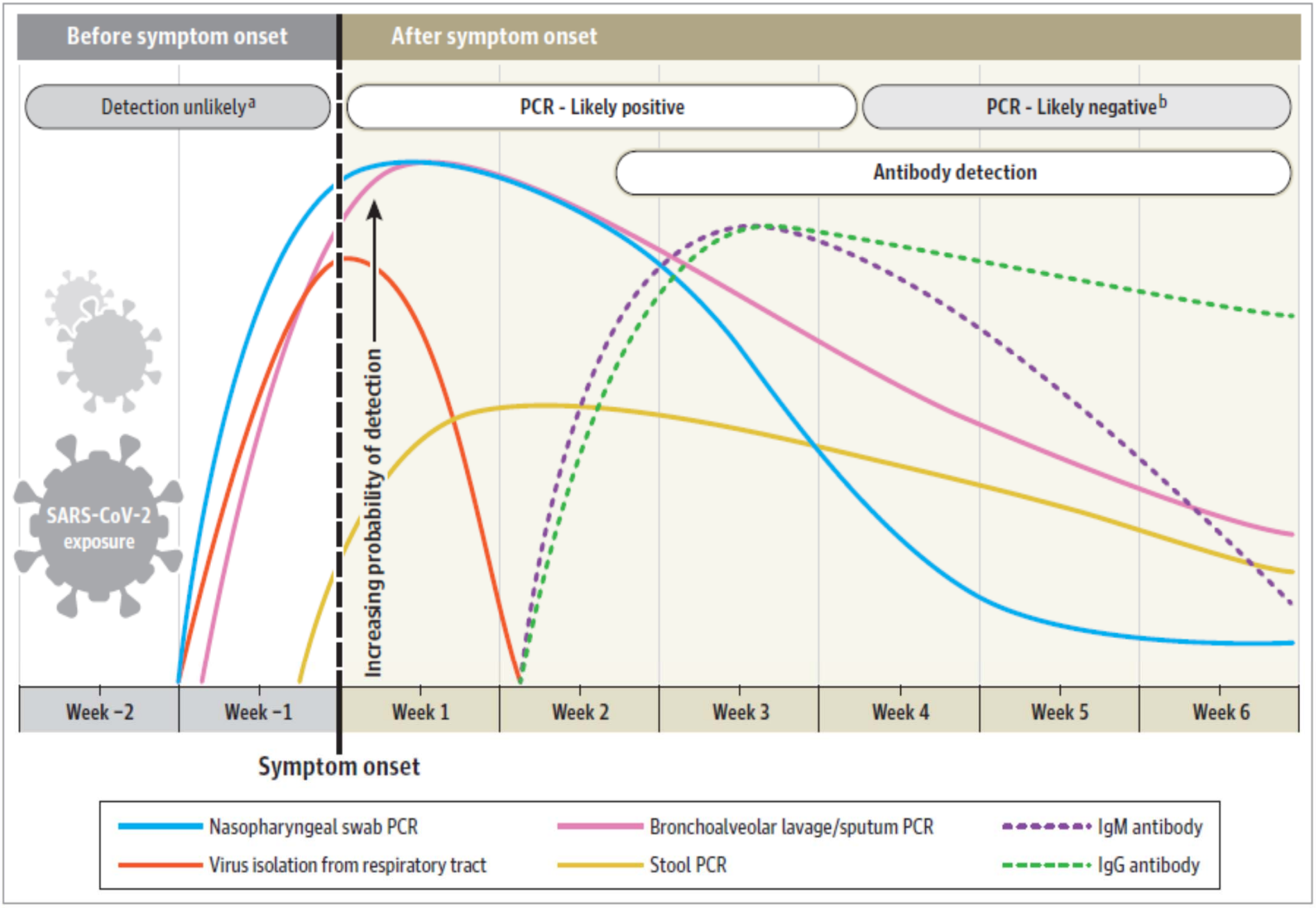
Antibodies to SARS-CoV-2

- ELISA-based IgM & IgG antibody tests have > 95% specificity for diagnosis of COVID-19.
- Therefore, tests that detect antibodies to NC would be the most sensitive
- antibodies to RBD-S would be more specific and are expected to be neutralizing.
- Using one or both antigens for detecting IgG & IgM would result in high sensitivity

Antibodies to SARS-CoV-2

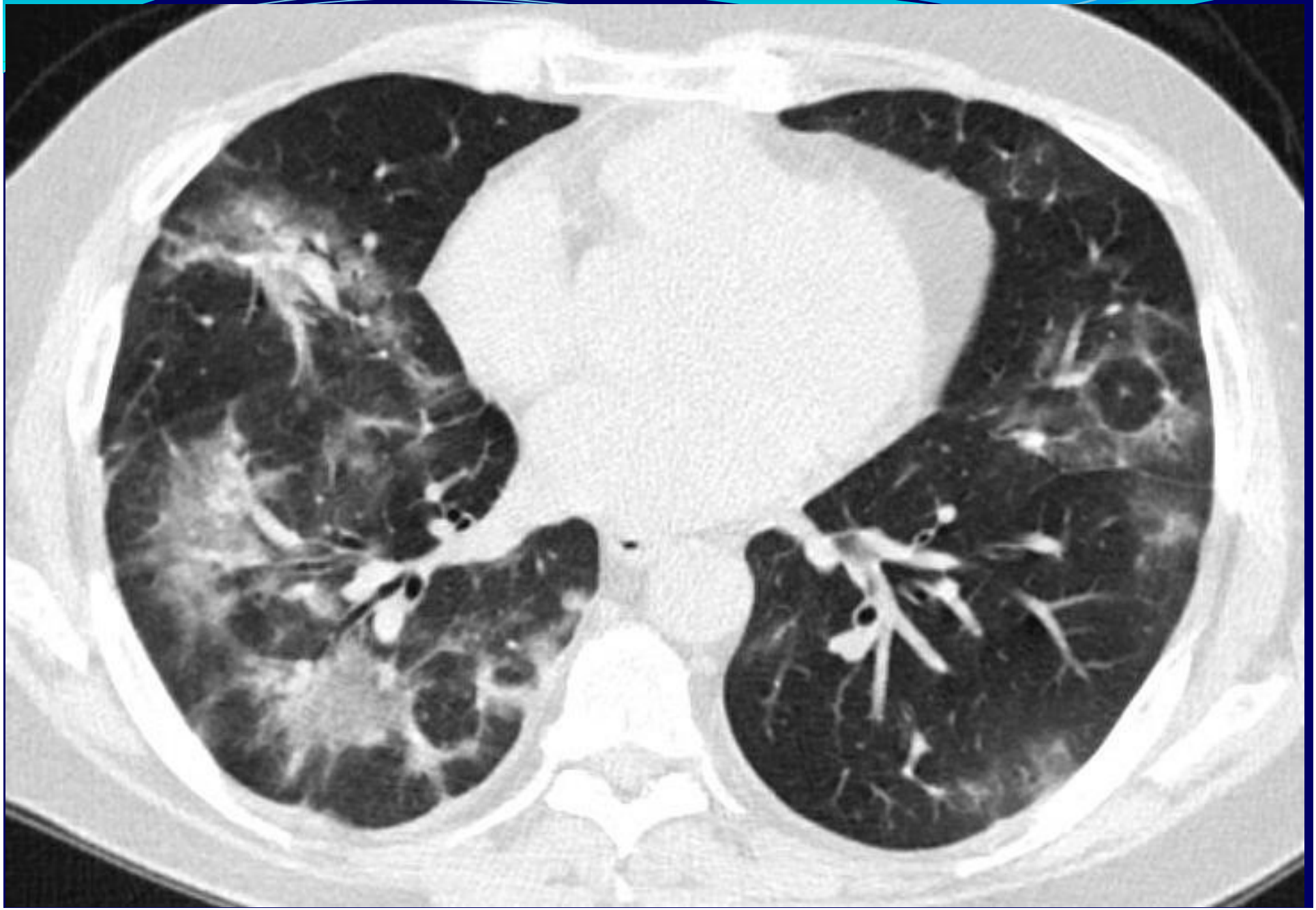
- Antibodies may have cross-reactivity with SARS-CoV and possibly other coronaviruses.
- However, high titers of IgG Ab detected by ELISA have been shown to positively with neutralizing antibodies.
- The long-term persistence and duration of protection conferred by the neutralizing antibodies remains unknown.

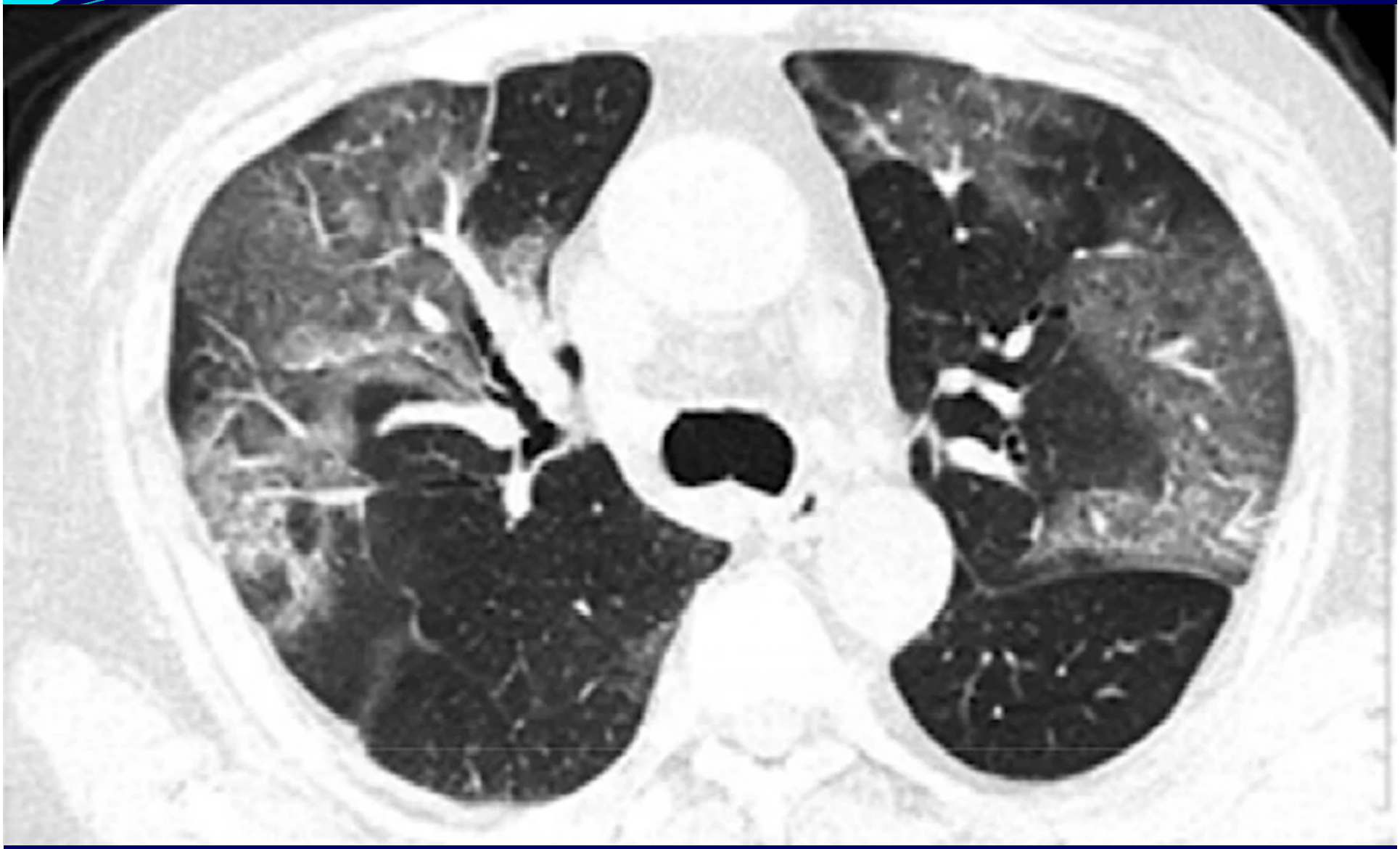
Figure. Estimated Variation Over Time in Diagnostic Tests for Detection of SARS-CoV-2 Infection Relative to Symptom Onset

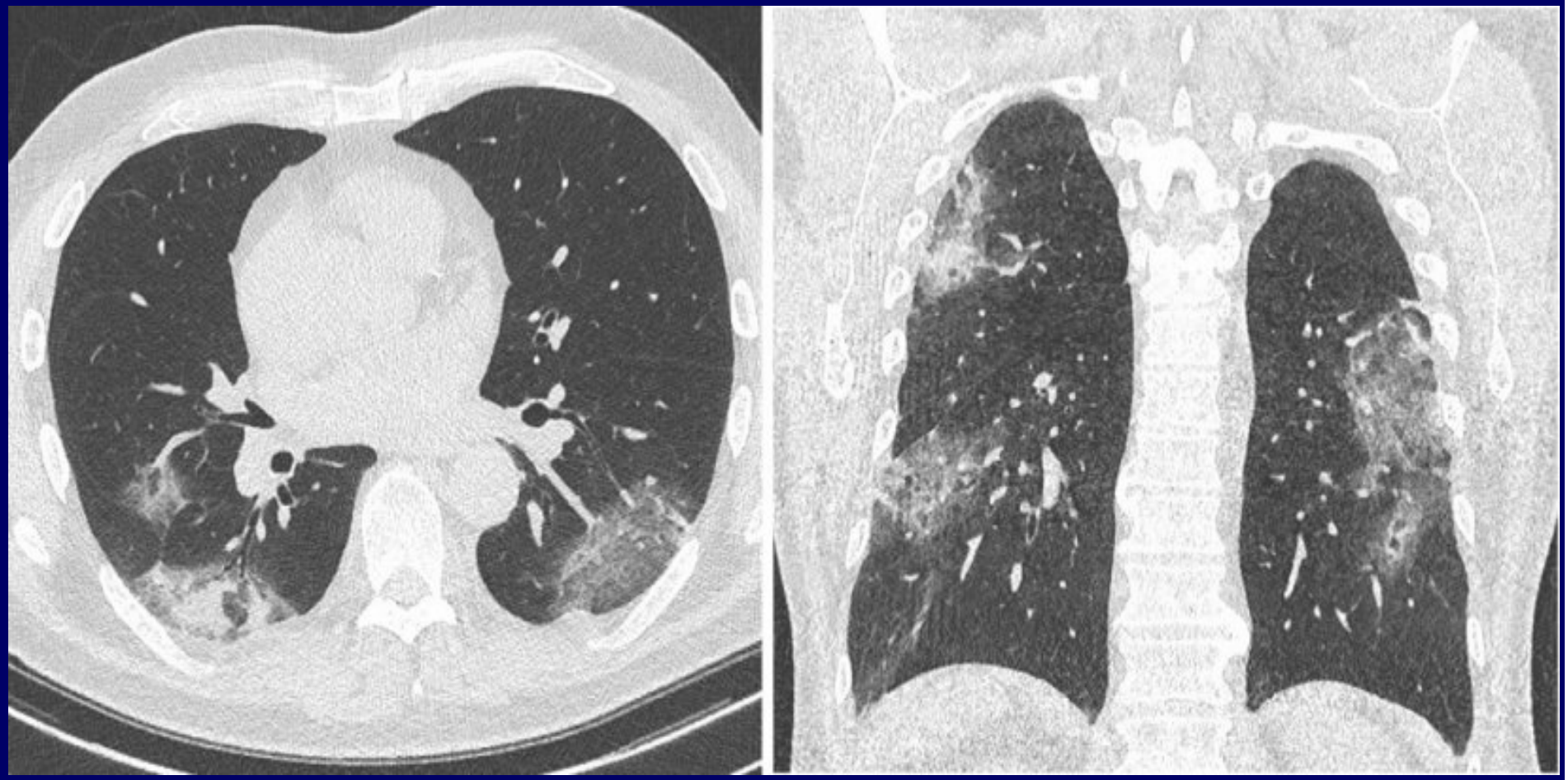


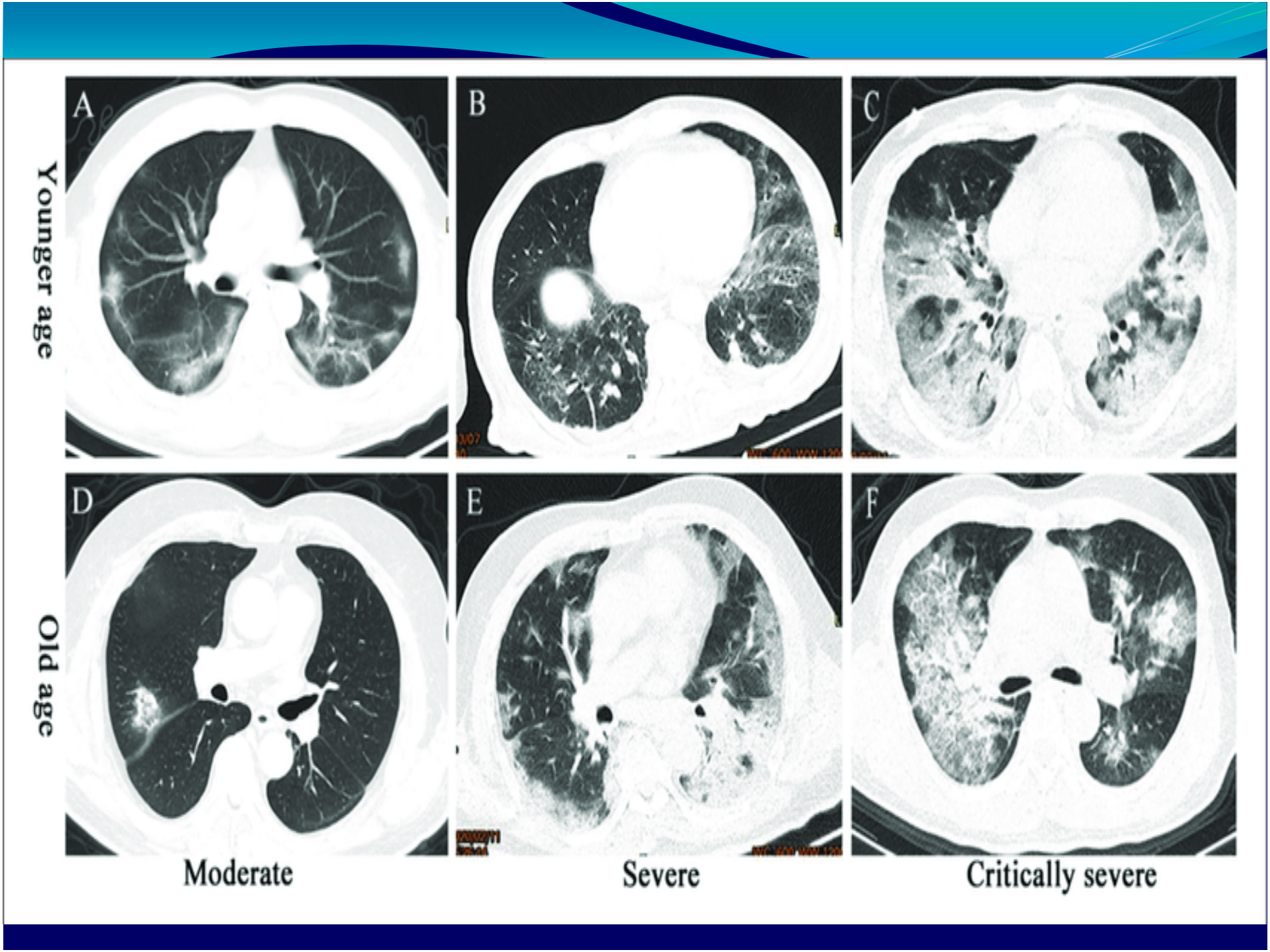
Imaging

- Characteristic chest CT-SCAN abnormalities:
- Peripheral ground-glass opacities
- Ground-glass opacities have:
  - Ill-defined margins
  - Air bronchograms
  - Smooth or irregular interlobular Septal thickening
  - Thickening of The adjacent pleura








A
B
C
D
E
F
Younger age
Old age
Moderate
Severe
Critically severe

General Mangement

- Supportive Care
- General activity
- Respiratory Support
- Targeting the Virus
- Prevention of and evaluation for venous thromboembolism

General Mangement

- Immunomodulatory agents (Dexamethasone & other glucocorticoids

- Approximately 8%of hospitalized patients with COVID-19 experience a bacterial or fungal co-infection, but up to 72% are treated with broad-spectrum

Targeting the Virus & the Host Response

- COVID-19-Spefic THERAPY
  - Remdesivir
  - Favipiravir
- Antibodies:
  - Convalescent plasma
  - Hyperimmune immunoglobulins

Targeting the Virus

- Interferon beta-1a
- Ivermectin
- Chloroquine or Hydroxychloroquine
- Lopinavir/Ritonavir Other HIV PIs
- Azithromycin

Targeting the Virus

- Interferon beta-1a
- Ivermectin

Adjunctive Therapy

- Nonsteroidal Anti-Inflammatory Drugs
- Vitamin C
- Vitamin D
- Zinc Supplementation
- Concomitant Medications

Care of Critically Ill Patients

- Infection Control
- Hemodynamic Support
- Ventilatory Support

Targeting the Virus & the Host Response

- Anti-inflammatory agents:
  - Dexamethasone
  - Statins
- Targeted Immunomodulatory therapies:
  - Tocilizumab
  - Sarilumab
  - Anakinra
  - Ruxolitinib

Targeting the Virus & the Host Response

- Anticoagulants:
  - Heparin
  - Low-molecular-weight heparin
- Antifibrotics:
  - Tyrosine kinase inhibitors

References

- Joost Wiersinga, MD, PhD; Andrew Rhodes, MD, PhD; Allen C. Cheng, MD, PhD; Sharon J. Peacock, PhD; Hallie C. Prescott, MD, MSc pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19) A Review JAMA July 10, 2020
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