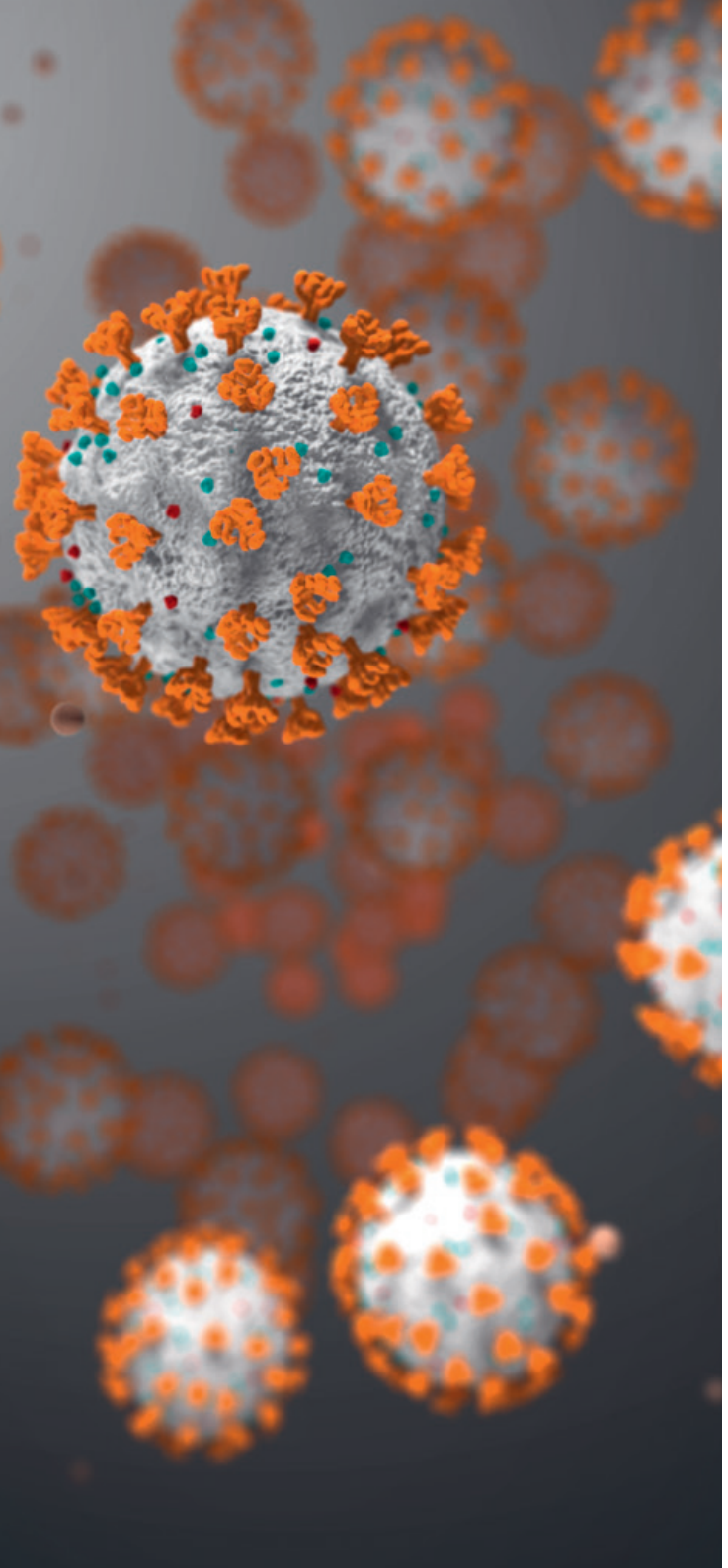


COVID-19 Laboratory Testing Guide

siemens-healthineers.com/covid-19

What is COVID-19?

COVID-19 (coronavirus disease 2019) is the disease resulting from infection with a newly emerged coronavirus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).[1] Coronaviruses are a family of RNA viruses usually found in animals. Mutations in the virus can result in human infection and subsequent spread.[2]

SARS-CoV-2 is closely related to the SARS virus identified in 2003 (SARS-CoV-1) and (to a lesser degree) the MERS-CoV virus from 2012. All three can produce a severe respiratory syndrome and associated mortality.[2-4] While both SARS-CoV-1 and the MERS- CoV viruses seem to have a higher comparative rate of mortality (especially MERS-CoV), the newly emerged SARS-CoV-2 appears much more infectious, with significant human-to human transmission.[5-7] Asymptomatic individuals may transmit the virus, challenging infection control.[8,9] Its rapid spread has produced a true global pandemic.

Diagnosis of COVID-19:

Diagnosis cannot be made solely on signs or symptoms as these overlap with other respiratory illness, so confirmation of the presence of the virus is essential. Table 1 describes the range and percent of symptoms seen in confirmed COVID-19 infections.

Sign or symptom	% of patients
Fever	83–99
Cough	59–82
Fatigue	44–70
Sputum production	28–33
Shortness of breath	31–40
Myalgia (muscle aches)	11–35

Table 1. Range and percent of symptoms seen in confirmed COVID-19 infections.[13]

In some populations, a loss of taste or smell is also a widely reported symptom.[10] Molecular testing specific for the SARS-CoV-2 RNA is used to confirm presence of the virus, and serology testing can identify antibodies to the virus.[11,12] Both testing modalities can aid a diagnosis of COVID-19. In addition, antibody testing is a promising approach to assess prevalence of infection and potentially identify immunity. It remains to be confirmed whether antibodies to SARS-CoV-2 offer protection (immunity) from subsequent exposure.

Conclusion:

Testing is critical to differentiate COVID-19 from other respiratory disease such as influenza or RSV (respiratory syncytial virus). Widespread testing will both inform a COVID-19 diagnosis and aid a greater understanding of disease prevalence, especially in infections that are asymptomatic.

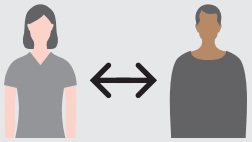
SIEMENS Healthineers

Clinical classification and transmission of COVID-19[14-26]

Clinical classification

Incubation period median 5 days, range 1–27 days → Patients with mild symptoms in week 1... → ...may progress in week 2 → **Progression may be rapid and sudden.**

Human-to-human transmission

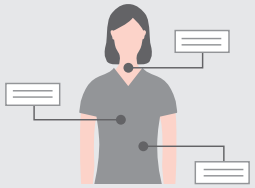


Possible transmission during asymptomatic phase 4–6 days before the onset of symptoms.

Possible transmission after remission of the symptoms

Possible transmission	Highest risk of transmission during symptomatic phase	Possible transmission

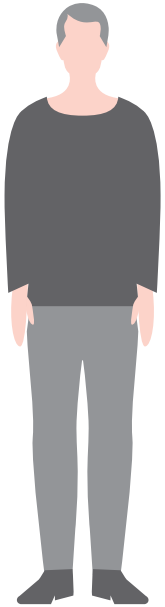
Disease spectrum



Asymptomatic	Symptomatic			Remission
No symptoms	Mild to Moderate	Severe	Critical	
1.2–17.6%	80%	10–15%	2–5%	
Infectious virus can be shed, viral loads may be comparable to symptomatic patients	No signs (mild) or some signs (moderate) of pneumonia on imaging	• Respiratory distress of ≥30 breath per minute • Oxygen saturation ≤93% at rest • PaO2/FiO2 ≤300 mmHg • Lung lesion progression >50% in 24–48h	• Respiratory failure requiring mechanical ventilation • Shock • Any organ failure requiring ICU care • Case/fatality rate current estimation 0.3 to 4%	

Course of patients at risk and/or infected by COVID-19[14-26]

Identification of high risk patients



- Age >55 years
- Any age with severe obesity BMI >40
- Pre-existing pulmonary disease (chronic lung disease or moderate to severe asthma, COPD, lung cancer, pulmonary hypertension, emphysema (smoking, A1AT deficiency))
- Chronic kidney disease
- Diabetes
- History of:
  - hypertension (treated and untreated)
  - cardiovascular disease
  - liver disease
  - transplants or other immunosuppression (ex. cancer treatment)
- All patients with HIV
- Patients with endocrine pathologies
- Use of biologic drugs

Patient triage[2,3,4]

Epidemiologic surveillance

Laboratory testing:

- RT-PCR
- Anti-SARS-CoV-2 antibodies

Diagnosis

Virus detection:

- Molecular testing (RT-PCR)

Imaging:

- Chest CT

Recovery

Epidemiologic surveillance

Laboratory testing:

- Anti-SARS-CoV-2 antibodies (IgG, IgM)

Confirm immunization

Therapeutic monitoring

Laboratory testing:

- Arterial blood gas
- Complete blood count
- Acute phase proteins, inflammation & coagulation
- Liver, kidney, cardiac function biomarkers
- Additional testing related to comorbidities

Imaging:

- Chest CT (ground glass opacification)

The essential role of laboratory diagnostics in SARS-CoV-2 infection[14-26]

Current recommended lab testing (WHO, ESICM)

Recommended daily labs	CBC with differential (trend total lymphocyte count) Comprehensive metabolic panel: • Electrolytes: Na, K, Total CO_2, Chloride • Total protein and Albumin • Creatinine • Bilirubin, ALT, AST CPK (total creatine kinase) Lactate
Risk stratification	D-dimer, Ferritin, CRP, ESR, LDH, Cardiac troponin
Viral serologies	HBV, HCV, HIV 1/2/O

Frequent laboratory abnormalities in patients with COVID-19*

Decreased

Blood lymphocyte count (35–75%)

Albumin (50–98%)

Hemoglobin (41–50%)

Increased

Neutrophil count

Erythrocyte sedimentation rate (ESR; up to 85%)

C-reactive protein (CRP; 75–93%)

Lactate dehydrogenase (LDH; 27–92%)

Alanine aminotransferase (ALT)

Aspartate aminotransferase (AST)

Total bilirubin

Cardiac troponin

Procalcitonin (6–25%)

Prothrombin time (PT)

D-dimer (36–43%)

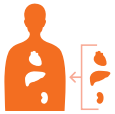
**Approximate percentage of patients*

Additional essential lab testing	Test	Potential clinical significance
Arterial blood gas	pH, PaCO2, PaO2, and aHCO3	For ventilator adjustments
Hematology	Lymphopenia with atypical lymphocytes Leukocytosis, Neutrophilia, low eosinophils Thrombocytopenia: Platelet count	Decreased immunological response to the virus Bacterial (super) infection Consumption (disseminated) coagulopathy
Hemostasis	Prothrombin time, D-Dimer	Activation of blood coagulation and/or disseminated coagulopathy PT and D-dimer are significant predictors of disease severity
Inflammation/Infection	CRP, Ferritin, IL6, TNFα, SAA Procalcitonin	Severe viral infection/viremia Bacterial (super) infection
Cardiac	High-sensitivity troponin, CK-MB, BNP/NT-proBNP	Increased levels may be associated with higher mortality†
Liver	Albumin, ALT, AST, Bilirubin	Impairment of liver function, Liver injury
Renal	Creatinine, Cystatin C	Kidney injury

†This information represents a potential novel clinical utility. Data have not been reviewed by FDA or any other regulatory agency

Impact of Comorbidities on COVID-19 Patients

Patients with comorbidities (like diabetes mellitus, hypertension, cardiovascular, chronic lung and chronic kidney disease) are particularly susceptible to COVID-19 infection and are likely to have more severe illness[14-26]

	Comorbidities	Additional testing	Impact of COVID-19
	**Cardiovascular disease**	Troponin, Natriuretic peptides, CKMB	Precipitates cardiac complications like: acute heart failure, myocardial infarction, myocardial injury, cardiac arrest.
	**Chronic kidney disease**	Blood: Creatinine, Cystatin C, eGFR Urine: Albumin	Challenges for patients on dialysis, in particular, in-center hemodialysis; uremic patients are particularly vulnerable to infection and may exhibit greater variations in clinical symptoms and infectivity.
	**Heart/liver/kidney transplant**	Immunosuppressant Drugs: Mycophenolate, Cyclosporine, Tacrolimus, Sirolimus, Everolimus	Patients may be more vulnerable due to immunocompromised status.
	**Viral co-infection**	Hepatitis B serologies (anti-HBs, anti-HBc, and HBsAg) Hepatitis C serology (anti-HCV), unless positive in past HIV 1/2/O, CD4 count	Viral serologies assist in interpretation of ALT elevations, present in ~25% of COVID-19 patients. HIV patients may get severe side effects when taking Tocilizumab (drug being used for COVID-19 pneumonia).‡ Hepatitis patients are at higher risk for liver complications.
	**Diabetes**	Blood glucose	Patients with diabetes who are infected with COVID-19 may see their glycemic control deteriorate during the illness.
	**Chronic lung disease**	LDH	Patients may be more vulnerable due to lung function insufficiency.
	**Chronic liver disease**	Albumin, AST, ALT, Total Protein, Bilirubin, PT INR	Patients may be more vulnerable due to liver function insufficiency.

‡PDR Tocilizumab https://www.pdr.net/drug-summary/Actemra-tocilizumab-2359#1

At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

References:

1. Lai CC, Shih TP, Ko WC, et al. Int J Antimicrob Agents. 2020 Mar;55(3):105924.
2. Chen, Y. et al. J Med Virol. 2020 Apr;92(4):418-423
3. Guarner J. Am J Clin Pathol. 2020 Mar 9;153(4):420-421.
4. Liu J. et al. J Med Virol. 2020;92:491–494
5. Riou J, Althous CL. Euro Surveill. 2020;25(4):2000058. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.4.2000058
6. Liu Y, Gayle AA, Wilder-Smith A, et al. J Travel Med. 2020;27(2). https://doi.org/10.1093/jtm/taaa021
7. Guo YR et al. Mil Med Res. 2020;7(1):11. https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-00240-0
8. Bai Y. et al. JAMA. Published online February 21, 2020. doi:10.1001/jama.2020.2565
9. https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html#transmission. Accessed April 6, 2020.
10. https://www.the-hospitalist.org/hospitalist/article/219556/coronavirus-updates/reports-increasingly-suggest-anosmia/hyposmia-can Accessed April 6, 2020.
11. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html Accessed April 6, 2020.
12. https://www.cdc.gov/coronavirus/2019-ncov/about/testing.html Accessed April6, 2020.
13. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html
14. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 44. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
15. https://www.ifcc.org/ifcc-news/2020-03-26-ifcc-information-guide-on-covid-19/
16. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)
17. March 22, 2020 Content source: National Cent Immunization and Respiratory Diseases (NCIRD) Division of Viral Diseases
18. JAMA.2020 Feb7. doi:10,1001/jama,20201585
19. Ann Transl Med 2020;8(3):48 | http://dx.doi.org/10.21037/atm.2020.02.06
20. Lippi G, PlebaniM. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020 Mar 3. doi: 10.1515/cclm-2020-0198.
21. https://www.massgeneral.org/news/coronavirus/coronavirus-latest-updates
22. Jingyuan Liu, https://doi.org/10.1101/2020.02.10.20021584
23. Hematologic parameters in patients with COVID-19 infection 10.1002/ajh.25774
24. Ruan et al: https://doi.org/10.1007/s00134-020-05991-x
25. Boettler T et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID Position Paper. https://easl.eu/wp-content/uploads/2020/04/EASL-ESCMID-Position-Paper-on-COVID-19-and-the-liver-2-April-2020.pdf April 2, 2020.
26. ifcc.org/ifcc-news/2020-03-26-ifcc-information-guide-on-covid-19/

Siemens Healthineers Headquarters
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen, Germany
Phone: +49 9131 84-0
siemens-healthineers.com

Published by
Siemens Healthcare Diagnostics Inc.
Laboratory Diagnostics
511 Benedict Avenue
Tarrytown, NY 10591-5005
USA
Phone: +1 914-631-8000

Published by Siemens Healthcare Diagnostics Inc. · Order No. 31-20-14365-01-76 · 04-2020 ·