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) 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 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.\(^6\)\(^8\) 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.

### Table 1. Range and percent of symptoms seen in confirmed COVID-19 infections.\(^13\)

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>83–99</td>
</tr>
<tr>
<td>Cough</td>
<td>59–82</td>
</tr>
<tr>
<td>Fatigue</td>
<td>44–70</td>
</tr>
<tr>
<td>Anorexia</td>
<td>40–84</td>
</tr>
<tr>
<td>Sputum production</td>
<td>28–33</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>31–40</td>
</tr>
<tr>
<td>Myalgia (muscle aches)</td>
<td>11–35</td>
</tr>
</tbody>
</table>

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.\(^11\)\(^12\) 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 diseases 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.
### Clinical classification and transmission of COVID-19

#### Clinical classification

- **Human-to-human transmission**
- **Disease spectrum**

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

#### Highest risk of transmission during symptomatic phase
- Patients with mild symptoms in week 1...
- ...may progress in week 2
- Progression may be rapid and sudden.

#### Possible transmission after remission of the symptoms

#### Asymptomatic
- No symptoms*
- 1.2–17.6%
- Infectious virus can be shed, viral loads may be comparable to symptomatic patients

#### Mild to Moderate
- 80%
- No signs (mild) or some signs (moderate) of pneumonia on imaging

#### Severe
- 10–15%
- • Respiratory distress of ≥30 breath per minute
  • Oxygen saturation ≤93% at rest
  • PaO2/FiO2 ≤300 mmHg
  • Lung lesion progression >50% in 24–48h

#### Critical
- 2–5%
- • Respiratory failure requiring mechanical ventilation
  • Shock
  • Any organ failure requiring ICU care
  • Case/fatality rate current estimation 0.3 to 4%

#### Remission

*Recent SARS-CoV-2 testing studies demonstrate a wide variety of asymptomatic patients between 1% and >80% partially due to different stages of outbreak, testing availability and population studied*
Course of patients at risk and/or infected by COVID-19

Identification of high risk patients
- Age >65 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)
- Patients with HIV or other immunocompromised conditions
- Patients with endocrine pathologies
- Use of biologic drugs

Population triage

Epidemiologic surveillance
- Laboratory testing:
  - RT-PCR
  - Anti-SARS-CoV-2 antibodies

Diagnosis and Determination of Disease Status
- Disease detection:
  - Molecular testing (RT-PCR)
- Immune Response:
  - Anti-SARS-CoV-2 antibodies (IgG, Total)
- Imaging:
  - Chest CT
  - Ultrasound
  - X-ray

Recovery
- Laboratory testing:
  - Anti-SARS-CoV-2 antibodies (IgG, Total)
- Confirm immunization (under investigation)

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)
  - Ultrasound
The essential role of laboratory diagnostics in SARS-CoV-2 infection

### Essential lab testing

<table>
<thead>
<tr>
<th>Daily labs</th>
<th>Test</th>
<th>Potential clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC with differential (trend total lymphocyte count)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive metabolic panel:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Electrolytes: Na, K, Total CO₂, Chloride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Total protein and Albumin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Creatinine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Bilirubin, ALT, AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPK (total creatine kinase)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk stratification</td>
<td>Test</td>
<td>Potential clinical significance</td>
</tr>
<tr>
<td>D-dimer, Ferritin, CRP, ESR, LDH, Cardiac troponin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral serologies</td>
<td>HBV, HCV, HIV Ab/Ag</td>
<td></td>
</tr>
</tbody>
</table>

### Frequent laboratory abnormalities in patients with COVID-19†

<table>
<thead>
<tr>
<th>Decreased</th>
<th>Increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood lymphocyte count (35–75%)</td>
<td>Neutrophil count</td>
</tr>
<tr>
<td>Hemoglobin (41–50%)</td>
<td>Erythrocyte sedimentation rate (ESR; up to 85%)</td>
</tr>
<tr>
<td>Lactate dehydrogenase (LDH; 27–92%)</td>
<td>C-reactive protein (CRP; 75–93%)</td>
</tr>
<tr>
<td>Procalcitonin (6–25%)</td>
<td>Aspartate aminotransferase (AST)</td>
</tr>
<tr>
<td>D-dimer (36–43%)</td>
<td>Total bilirubin</td>
</tr>
<tr>
<td>Cardiac troponin</td>
<td>Cardiac troponin</td>
</tr>
<tr>
<td>Procalcitonin (6–25%)</td>
<td>Prothrombin time (PT)</td>
</tr>
<tr>
<td>D-dimer (36–43%)</td>
<td></td>
</tr>
</tbody>
</table>

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

†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.  

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Additional testing</th>
<th>Impact of COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>Troponin, Natriuretic peptides, CKMB</td>
<td>Precipitates cardiac complications like: acute heart failure, myocardial infarction, myocardial injury, cardiac arrest.</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Blood: Creatinine, Cystatin C, eGFR Urine: Albumin</td>
<td>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.</td>
</tr>
<tr>
<td>Heart/liver/kidney transplant</td>
<td>Immunosuppressant Drugs: Mycophenolate, Cyclosporine, Tacrolimus, Sirolimus, Everolimus</td>
<td>Patients may be more vulnerable due to immunocompromised status.</td>
</tr>
<tr>
<td>Viral co-infection</td>
<td>Hepatitis B serologies (anti-HBs, anti-HBc, and HBsAg) Hepatitis C serology (anti-HCV), unless positive in past HIV 1/2/O, CD4 count</td>
<td>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.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Blood glucose</td>
<td>Patients with diabetes who are infected with COVID-19 may see their glycemic control deteriorate during the illness.</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>LDH</td>
<td>Patients may be more vulnerable due to lung function insufficiency.</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>Albumin, AST, ALT, Total Protein, Bilirubin, PT INR</td>
<td>Patients may be more vulnerable due to liver function insufficiency.</td>
</tr>
</tbody>
</table>

§Tocilizumab [https://www.pdr.net/drug-summary/Actemra-tocilizumab-2359#:~:text=PDR%20Tocilizumab](https://www.pdr.net/drug-summary/Actemra-tocilizumab-2359#)
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.

Siemens Healthineers’ SARS-CoV-2 molecular and serology tests have not been FDA cleared or approved. These tests have been authorized by FDA under an EUA for use by authorized laboratories. The molecular test has been authorized only for detecting the presence of antibodies against SARS-CoV-2, not for any other viruses or pathogens. The serology test has been authorized only for detecting the presence of antibodies against SARS-CoV-2, not for any other viruses or pathogens. These tests are only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

---

**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

---

**References:**

17. March 22, 2020 Content source: National Cent Immunization and Respiratory Diseases (NCIRD) Division of Viral Diseases
24. Ruan et al: https://doi.org/10.1007/s00134-020-05991-x