

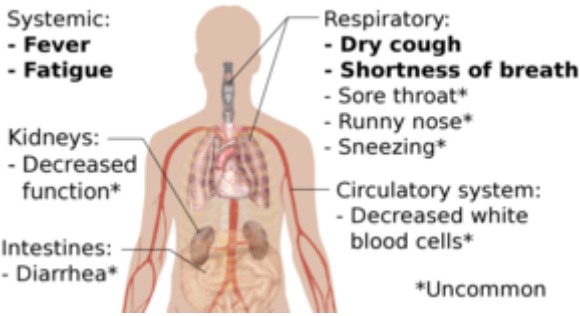
Coronavirus disease 2019

Coronavirus disease 2019 (**COVID-19**) is an infectious disease caused by SARS coronavirus 2 (SARS-CoV-2),^[8] a virus closely related to the SARS virus.^{[9][10][11]} The disease is the cause of the 2019–20 coronavirus outbreak.^{[12][13]} Those affected may develop a fever, dry cough, fatigue and shortness of breath.^{[7][14][15]} A sore throat, runny nose or sneezing is less common.^[16] Cases can progress to pneumonia and multi-organ failure in the most vulnerable.^{[12][13]}

Infection is spread from one person to others via respiratory droplets produced from the airways, often during coughing or sneezing.^{[17][18]} Time from exposure to onset of symptoms is generally between 2 and 14 days, with an average of 5 days.^{[19][20][21]} The standard method of diagnosis is by reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab or sputum sample, with results within a few hours to 2 days. Antibody assays can also be used, using a blood serum sample, with results within a few days.^[22] The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia.^{[23][24]}

Hand washing, maintaining distance from people who are coughing and not touching one's face with unwashed hands are measures recommended to prevent the disease.^[25] It is recommended to cover one's nose and mouth with a tissue or a bent elbow when coughing.^[25] The World Health Organization (WHO) and U.S. Centers for Disease Control and Prevention (CDC) recommend those who suspect that they are carrying the virus wear a surgical face mask and seek medical advice by calling a doctor rather than directly visiting a clinic in person. Masks are also recommended for those who are taking care of someone with a suspected infection but not for the general public.^{[26][27]} There is no vaccine or specific antiviral treatment, with management involving treatment of symptoms, supportive care, and experimental measures.^[28] The case fatality rate is estimated at between 1% and 3%.^{[29][30]}

The WHO has declared the 2019–20 coronavirus outbreak to be a Public Health Emergency of International Concern (PHEIC).^{[31][32]} As of 29 February 2020, China, Hong Kong, Iran, Italy, Japan, Singapore, South Korea and the United States are areas having evidence of community transmission of the disease.^{[33][34]}

Coronavirus disease 2019 (COVID-19)	
Other names	<ul style="list-style-type: none"> 2019-nCoV acute respiratory disease Novel coronavirus pneumonia^[1] Wuhan pneumonia^{[2][3][4][5]}
	
Symptoms	
Pronunciation	/kəˈroʊnə.vaɪrəs dɪˈziːz/
Specialty	Acute respiratory infection ^[6]
Symptoms	Fever, cough, shortness of breath ^[7]
Complications	Pneumonia, ARDS, kidney failure
Causes	SARS-CoV-2
Diagnostic method	rRT-PCR testing, immunoassay, CT scan
Prevention	Hand washing, cough etiquette
Treatment	Symptomatic and supportive

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Signs and symptoms

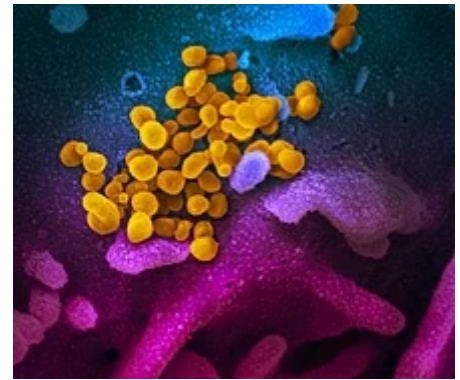
Those infected may either be asymptomatic or develop symptoms including fever, cough or shortness of breath.^{[7][14][15]} Diarrhea or upper respiratory symptoms (e.g. sneezing, runny nose, sore throat) are less frequent.^[16] Cases can progress to pneumonia, multi-organ failure, and death in the most vulnerable.^{[12][13]}

The incubation period ranges from 1 to 14 days with an estimated median incubation period of 5 to 6 days according to the World Health Organization.^{[35][36]}

A WHO review of 55,924 laboratory-confirmed cases in China indicated the following typical signs and symptoms: fever (87.9% of cases), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), hemoptysis (0.9%) and conjunctival congestion (0.8%).^[37] Another study of 1,099 Chinese patients found that CT scans showed ground-glass opacities in 56% of patients, but 18% had no radiological findings. 5% of patients were admitted to intensive care units, 2.3% needed mechanical support of ventilation, and 1.4% died.^[38] Bilateral and peripheral ground glass opacities are the most typical CT findings, according to researcher Bernheim et al. Consolidation, linear opacities, reverse halo sign are other radiological findings. Initially the lesions are located to one lung, but as the disease progress, indications manifest to both lungs at 88% of patients.^[39] Children seem to handle the disease better than adults as the symptoms are usually milder, but sufficient evidence is still lacking.^[40]

Cause

The disease is caused by the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), previously referred to as the 2019 novel coronavirus (2019-nCoV).^[10] It is primarily spread between people via respiratory droplets from coughs and sneezes.^[42]



Scanning electron microscope image of SARS-CoV-2 (centre, yellow)^[41]

The virus is thought to have an animal origin.^[43] There has been a "continuous common source" of the outbreak in December 2019, which would imply that several animal-to-human zoonotic events occurred at the Huanan Seafood Wholesale Market. The primary source of infection became human-to-human transmission in early January 2020.^{[44][45]}

Pathology

Histopathological examinations of post-mortem lung samples showed diffuse alveolar damage with cellular fibromyxoid exudates in both lungs. Viral cytopathic changes were observed in the pneumocytes. The lung picture resembled acute respiratory distress syndrome (ARDS).^[46]

Diagnosis

The WHO has published several testing protocols for the disease.^{[48][49]} The standard method of testing is real time reverse transcription polymerase chain reaction (rRT-PCR).^[50] The test can be done on respiratory samples obtained by various methods, including nasopharyngeal swab or sputum sample.^[51] Results are generally available within a few hours to 2 days.^{[52][53]} Blood tests can be used, but these require two blood samples taken two weeks apart and the results have little immediate value.^[54] Chinese scientists were able to isolate a strain of the coronavirus and publish the genetic sequence so that laboratories across the world could independently develop polymerase chain reaction (PCR) tests to detect infection by the virus.^{[12][55][56][57]}



CDC rRT-PCR test kit for COVID-19^[47]

COVID-19 testing can also be done with antibody test kits.^[58] Antibody assays use a blood serum sample and can provide a positive result even if the person has recovered and the virus is no longer present.^[22] The first antibody test was demonstrated by a team at the Wuhan Institute of Virology on 17 February 2020.^{[59][22]} On 25 February, a team from Duke–NUS Medical School in Singapore announced another antibody test for COVID-19 that can provide a result within a few days.^{[22][60]}

Diagnostic guidelines released by Zhongnan Hospital of Wuhan University suggested methods for detecting infections based upon clinical features and epidemiological risk. These involved identifying patients who had at least two of the following symptoms in addition to a history of travel to Wuhan or contact with other infected patients: fever, imaging features of pneumonia, normal or reduced white blood cell count, or reduced lymphocyte count.^[23] A study published by a team at the Tongji Hospital in Wuhan on 26 February 2020 showed that a chest CT scan for COVID-19 has more sensitivity (98%) than the polymerase chain reaction (71%).^[24]

Prevention

Global health organisations have published preventive measures to reduce the chances of infection. Recommendations are similar to those published for other coronaviruses: staying home, avoiding travel and public activities, frequent washing of hands with soap and water; not touching the eyes, nose, or mouth with unwashed hands; and practicing good respiratory hygiene.^{[61][62]}

The use of masks by healthy members of the public is not recommended outside of China.^{[63][64][65]}

To prevent transmission, the CDC recommends that infected individuals stay at home except to get medical care; call ahead before visiting a healthcare provider; wear a facemask (especially in public); cover coughs and sneezes with a tissue; regularly wash hands with soap and water; and avoid sharing personal household items.^[66]

In early 2020, the WHO said it was not expected that a vaccine against SARS-CoV-2 could be available in less than 18 months.^[67]

Management

There are no specific antiviral medications approved for this disease. Symptoms are managed with supportive care.^[68] Both the WHO and Chinese National Health Commission have published detailed treatment recommendations for hospitalized patients with severe acute respiratory infection (SARI) when a SARS-CoV-2 infection is suspected.^{[69][70]} WHO advises against the use of steroids and methylprednisolone unless the disease is complicated by acute respiratory distress syndrome.^[71] The WHO also recommended volunteers take part in randomized controlled trials for testing the effectiveness and safety of potential treatments.^[72]

Bruce Aylward, an assistant director-general of the World Health Organization (WHO), has stated "there is only one drug right now that we think may have real efficacy and that's remdesivir." It was reported on 25 February 2020 that clinical trials for this drug were in progress, with results possibly available within weeks.^[73]

The Beijing branch of China's National Health Commission suggested the use of lopinavir/ritonavir as part of treatment plans in the absence of an approved drug for this indication.^[74] The lopinavir/ritonavir combination and interferon can now be claimed for via health insurance in some countries.^[75]

Chloroquine was being trialed in China in February 2020, with preliminary results that seemed quite positive.^[76] The drug was enrolled in treatment guidelines.^[76]

Psychological

Infected individuals may experience distress from quarantine, travel restrictions, side effects of treatment, or fear of the infection itself. To address these concerns, the National Health Commission of China published a national guideline for psychological crisis intervention on 27 January 2020.^{[77][78]}

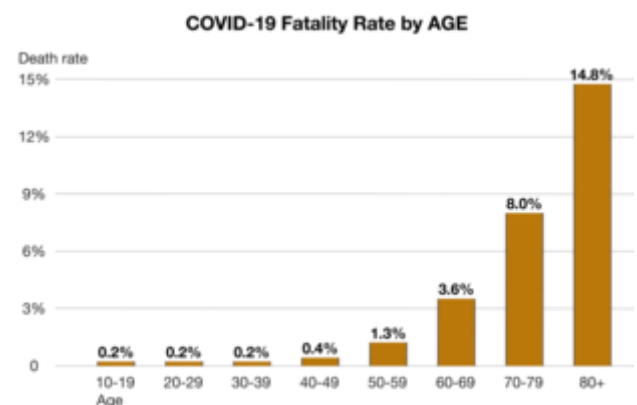
Alternative medicine

Chinese health authorities recommend the use of traditional Chinese medicine (TCM) in addition to standard medical supportive care to prevent or treat the disease. On 22 January, National Health Commission put TCM into the third issue of the COVID diagnostic and treatment plan.^[79] On 2 February, Wuhan officials ordered all patients to be put on a specific TCM treatment.^{[80][81]} On 14 February, Wuhan opened a TCM-oriented temporary hospital.^[82] The efficacy and safety of TCM has not been established in coronavirus infections.^{[83][84]}

Prognosis

According to WHO, based on analysis of 44,000 cases of COVID-19 in Hubei province, around 80% of people have a mild form of the disease, 14% developed more severe disease such as pneumonia, 5% have critical disease, and 2% of cases are fatal.^[85]

Among those who died, many had preexisting conditions, including hypertension, diabetes, or cardiovascular disease,^[87] and the median time from initial symptoms to death was 14 days (range 6–41 days).^[88] Males had a death rate of 2.8% while females had a death rate of 1.7%.^[89] In those under the age of 50 the risk of death is less than 0.5% while in those over the age of 70 it is more than 8%.^[89] No deaths had occurred under the age of 10 as of 26 February 2020.^[89]



Fatality rates by age group in China^[86]

Epidemiology

Overall mortality and morbidity rates due to infection are not well established; while the case fatality rate (CFR) changes over time in the current outbreak, the proportion of infections that progress to diagnosable disease remains unclear.^{[90][91]} However, preliminary research has yielded case fatality rate numbers between 2% and 3%;^[29] in January 2020 the WHO suggested that the case fatality rate was approximately 3%,^[92] and 2% in February 2020 in Hubei.^[93] Other CFR numbers, which adjust for differences in time of confirmation, death and/or cured, are 7%^[94] and 33% for Wuhan patients January 31st^[95]. An unreviewed preprint study by Imperial College London among 55 fatal cases noted that early estimates of mortality may be too high as asymptomatic infections are missed. They estimated a mean infection fatality ratio (IFR, the mortality among infected) ranging from 0.8% when including asymptomatic carriers to 18% when including only symptomatic cases from Hubei province.^[96] Other estimates of the IFR are between 0.5% to 0.8% and around 0.95%.^{[97][98]} Pauline Vetter, in an editorial in The BMJ noted that mortality outside of Hubei province seems to be lower than within Hubei.^[71] The outbreak in 2019–2020 has caused at least 89,769 confirmed infections and 3,118 deaths.

An observational study by Huijun Chen et al published at The Lancet of nine patients, found no intrauterine vertical transmission from mother to the newborn.^[99]

Research

Vaccine

Many organizations are using published genomes to develop possible vaccines against SARS-CoV-2.^{[100][101]} Bodies developing vaccines include the Chinese Center for Disease Control and Prevention,^{[102][103]} the University of Hong Kong,^[104] and Shanghai East Hospital.^[104] Three vaccine projects are being supported by the Coalition for Epidemic Preparedness Innovations (CEPI), including projects by the biotechnology companies Moderna^[105] and Inovio Pharmaceuticals and another by the University of Queensland.^[106] The United States National Institutes of Health (NIH) is cooperating with Moderna to create an RNA vaccine matching a spike of the coronavirus surface, and intends to start human trials by May 2020.^[100] Inovio Pharmaceuticals is developing a DNA-based vaccination and collaborating with a Chinese firm, planning human clinical trials in the summer of the Northern Hemisphere of 2020.^[107] In Australia, the University of Queensland is investigating the potential of a molecular clamp vaccine that would genetically modify viral proteins in order to stimulate an immune reaction.^[106] In Canada, the International Vaccine Centre (VIDO-InterVac), University of Saskatchewan, are working on a vaccine,^[108] aiming to start animal testing in March 2020 and human testing in 2021.^[108]

In January 2020, Janssen Pharmaceutical Companies began work on developing a vaccine, using the same technologies as for its experimental Ebola vaccine.^[109] In the following month, the U.S. Department of Health and Human Services' Biomedical Advanced Research and Development Authority (BARDA) announced that it would collaborate with Janssen and, later, Sanofi Pasteur to develop a vaccine.^{[110][111]} Sanofi has previously worked on a vaccine for SARS and it stated to expect to have a vaccine candidate within six months that could be ready to test in people within a year to 18 months.^[110]

On February 26, 2020, a U.S. health official from the National Institute of Allergy and Infectious Diseases, said that it will take "at least a year to a year and a half at best" to develop a vaccine for the coronavirus.^[112]

Antiviral

No drug has yet been approved to treat coronavirus infections in humans.^[113] Research into potential treatments for the disease was initiated in January 2020, and several antiviral drugs are already in clinical trials.^{[100][101]} Although completely new drugs may take until 2021 to develop,^[114] several of the drugs being tested are already approved for other antiviral indications, or are already in advanced testing.^[113]

Antivirals being tested include chloroquine,^[115] darunavir,^[116] galidesivir,^[113] interferon beta,^[117] the lopinavir/ritonavir combination,^{[101][115]} the RNA polymerase inhibitor remdesivir,^{[117][118][119]} and triazavirin.^{[120][121]} Umifenovir (Arbidol) and darunavir were proposed by the National Health Commission.^[122]

Remdesivir and chloroquine effectively inhibit the coronavirus in vitro.^[115]

Preliminary results from a multicentric trial, announced in a press conference and described by Gao, Tian, and Yang, suggested that chloroquine is effective and safe in treating COVID-19 associated pneumonia, "improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course".^[76]

Terminology

The process of naming the disease has been called "chaotic".^[123]


The World Health Organization announced on 11 February 2020 that "COVID-19" will be the official name of the disease. World Health Organization chief Tedros Adhanom Ghebreyesus said "co" stands for "corona", "vi" for "virus" and "d" for "disease", while "19" was for the year, as the outbreak was first identified on 31 December 2019. Tedros said the name had been chosen to avoid references to a specific geographical location (i.e. China), animal species, or group of people in line with international recommendations for naming aimed at preventing stigmatization.^{[124][125]}

See also

- Coronavirus diseases, a group of closely related syndromes
- Li Wenliang, a doctor at Wuhan Central Hospital and first to describe the syndrome

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