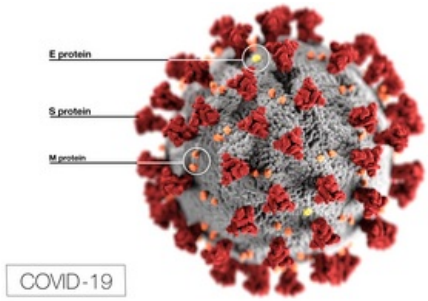
Covid-19

The **COVID-19** disease (***co**rona**vi**rus **d**isease 20**19***) is caused by the **coronavirus SARS-CoV-2'** (*severe acute respiratory syndrome coronavirus 2'*, initially working title *2019-nCoV*). The disease usually manifests like an upper respiratory tract infection, with some patients developing pneumonia with a potentially serious, in some cases fatal, course. Infection may be associated with coagulopathy. Due to the global spread of the disease, the WHO declared COVID-19 a pandemic on March 11, 2020[1].

Virology

The SARS-CoV-2 virus was first identified in China in early 2020 as the causative agent of an epidemic of pneumonia in the city of Wuhan. By sequencing epithelium from the respiratory tract of patients, it was possible to prove that the causative agent of the disease is the hitherto unknown β-coronavirus from the subgenus *sarbecovirus* subfamily *Orthocoronaviridae*. It is the seventh representative of the family coronaviruses, which causes human diseases. [2]. The first cases of this coronavirus at the end of 2019 were linked to a visit to seafood and live animal market in the city of Wuhan. The probable source is a bat, e.g. *Rhinolopus affinis*, *sinicus* or *ferrumequinum*. Some authors believe that transmission to humans may have occurred directly, as excrement and dried parts of bat bodies are used in Chinese folk medicine. However, the virus isolated from bats differs from viruses that are transmitted interhuman in several amino acids crucial for binding to human cells. It is, therefore, more likely that the transmission to humans occurred through intermediate hosts, which could be, for example, some snakes, turtles or minks. Especially discussed are pangolins, whose meat is consumed in China and whose body parts are also used in folk medicine. The sequence RNA isolated from pangolin coronaviruses differed more from SARS-CoV-2 than from bats coronaviruses, but it was identical in the domain responsible for binding to human cells. [3][4]. Therefore, it is speculated that SARS-CoV-2 arose from recombination of a very similar bat coronavirus with a scavenger coronavirus [5][6]

One of the glycoproteins of the virion envelope (*corona*), the **S-protein'** (*spike-protein*), is crucial for the entry of SARS-CoV-2 into the host cell. This binds to angiotensin-converting enzyme 2 (ACE2) expressed on the surface of susceptible cells and uses it as a receptor [7].



SARS-CoV-2 coronavirus virion model.

Analysis of the *spike protein* of coronavirus identified two variants caused by the substitution of glycine (G) for aspartate (D) at position 614. The G614 variant was associated with higher viral loads in vitro and may therefore indicate higher infectivity. No effect on disease course and risk of hospitalization was demonstrated. [8].

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Transfer path data is not yet complete. **The basic mode of transmission is direct interpersonal contact**, it is assumed that it occurs mainly by droplet infection. Droplets usually do not spread further than 2 meters and do not remain in the air [8]. The risk of direct transmission through the air is also discussed, especially in aerosol-producing procedures, but its significance is debatable and the impact on the spread of the pandemic is rather questionable. The possibilities of transmission over longer distances are likely to increase in enclosed, unventilated areas (restaurants, buses,...). [8].

Viral RNA has also been demonstrated in the blood, faeces and urine of patients, although these routes of transmission are probably not very epidemiologically significant [8]. The epidemiological significance of transmission by touching contaminated areas and subsequent contact with eyes, mouth or nose is still unclear, but extensive contamination of areas near patients with viral particles that can be a source of infection has been repeatedly described. The risk of infection from surfaces is higher in the case of massive contamination, for example, in the house of an infected person [8].

The risk of infection depends on the course of the disease – an infected patient with a mild course of the disease usually becomes infectious approximately 2.5 days before the onset of symptoms, the highest risk is around the onset of symptoms and gradually decreases approximately by the 7th–10th day after the onset of symptoms [8]. The risk of transmission after day 10 is small in immunocompetent patients with a mild course of the disease [8][9]. In severe or critical illness (dyspnea, pneumonia), the patient is usually infectious for no longer than 20 days [9]. However, PCR positivity can persist significantly longer even when non-infectious due to the presence of non-vital viral particles on mucous membranes. The median time to a negative mucosal PCR result is 18.4 days, but the positivity of PCR detection of viral RNA can persist for up to 3 months[9][10].

The degree of risk of transmission of infection also depends on the time of contact, the protective equipment used and epidemiological measures, or the number of viral particles in the secretion of the upper respiratory tract. The most common secondary transmission has been described between members of the same household or in

healthcare facilities where personal protective equipment was not used [8]. Infection is also possible from asymptomatic carriers of the virus, who are likely to be infectious for a similar length of time as symptomatic patients, but the importance of this type of transmission for the spread of the epidemic is still unknown [8].

Animal infections have been described in a case-by-case manner, but there is no evidence that transmission from animals to humans is present in a significant percentage. It is assumed only at the beginning of the epidemic, the further meaning is not confirmed [8].

The basic reproductive constant R_0 is around 3 [11].

Clinical course

The clinical course of the disease can be varied, with manifestations ranging from asymptomatic or very mild to a critical course ending in the death of the patient [12].

The frequency of **asymptomatic infections** is questionable. Some studies estimate their incidence to be around 40%, but for now, there are no analyses with a long enough follow-up to assess whether the symptoms did not manifest themselves later [12]. Thus, the number of purely asymptomatic cases is probably lower.

According to the current concept, no symptom is downright pathognomonic and diagnosis solely based on clinical signs can be difficult.

Symptoms of ongoing COVID-19 may include [12][13][14]:

- **fever** – the estimated incidence and height of which fluctuates significantly between studies (often only sub febrile is reported),
- **fatigue**,
- dry **cough**,
- muscle pain, headache,
- sore throat,
- nausea, vomiting, diarrhea,
- **loss or disturbance of smell or taste** – various studies report the incidence of these disorders in the range of 5–98%, but appears to be more common in the early stages of the disease than in other respiratory tract diseases,
- **shortness of breath** – occurs in approximately one-third of patients, typical is its onset approximately 5 days after the onset of the disease,
- stuffy nose or runny nose.

Complications

In the course of the disease, even with an initially mild course, a spectrum of complications may develop. Originally mild pneumonia can progress, as mentioned in the previous chapter, to a more severe state with shortness of breath approximately 5 days after the onset of symptoms. Other complications include [12]:

- ***respiratory insufficiency*** to image failure ***ARDS***;
- ***cardiac and cardiovascular complications***, including arrhythmias, acute coronary syndrome or shock;
- ***thromboembolic complications***, such as CMP or pulmonary embolism, may occur in younger patients without risk factors for complicated disease;
- dysregulation inflammatory responses;
- secondary infections.

Risk factors for the course of the disease, prognosis

More than 80% of symptomatic COVID-19 cases have a mild course. Approximately 15% of patients develop clinically severe pneumonia with dyspneas, hypoxia, and extensive bilateral infiltrates on radiographs 24 to 48 hours after onset. About 5% of patients require intensive care for respiratory distress, shock, or multiorgan failure [12]. A critical to the fatal course of the disease can occur even in young, otherwise healthy persons, but is usually associated with one or more of the following risk factors.

Risk factors for severe COVID-19 [12]

Cardiovascular disease	Smoking
Diabetes mellitus	Chronic kidney disease
Arterial hypertension	Obesity
Chronic lung disease	Cancer (especially hematological malignancies, lung cancer or metastatic disease)

Mortality in clinically manifested disease is estimated at 2.3%, with no deaths reported in patients with mild initial symptoms. According to the WHO-China *fact-finding mission*, the mortality rate in China ranged from 0.7% to 4%, depending on location [8].

Deaths most commonly occur in patients with significant comorbidities (cardiovascular disease, lung disease, diabetes mellitus, cancer or high blood pressure). Higher mortality is associated with higher age, with 80% of deaths due to COVID-19 occurring at age ≥ 65 years according to Chinese data[8]. The mortality rate under 19

years is 0.1% and 14.8% over 80 years [15].

Recovery occurs after approximately two weeks in patients with a mild course, in 3-6 weeks in a severe course [16].

Some patients who have had COVID-19 have one or more symptoms that persist after the acute phase of the disease (*long COVID*, *long-haul COVID*, *chronic post-COVID syndrome*). The most common symptoms are fatigue, shortness of breath, chest pain, cough or cognitive impairment. Preliminary data suggest that full recovery occurs after about three additional weeks if the course of COVID-19 has been mild. In the case of a moderate or severe course, symptoms persist for more than two months after hospital discharge. [17]

Memory impairment 18 %

Memory impairment|| 18 %

Persistent symptoms after COVID-19 [12]

Symptom	Proportion of patients	Time to recovery
Somatic		
Fatigue	15–87 %	3 months
Dyspnoea	10–71 %	2–3 months
months		
17-26 %	2-3 months	
Loss of smell	13 %	1 month
Psychic and cognitive		
Post-traumatic stress disorder	24 %	6 weeks to 3 months
Impaired concentration	16 %	
Anxiety, depression	22 %	

There are increasing data that some patients have long-term respiratory or cardiac damage.

Treatment

The treatment strategy depends on the severity of the manifestations. In mild cases, the patient can be left in **home isolation**, where the basis is **the prevention of the further spread of the virus** e.g. by wearing a mask when close to another person or by frequently disinfecting surfaces. Such a patient should be regularly monitored for symptoms to worsen and there is no need for hospitalization. Home isolation is terminated according to valid hygiene regulations, always insufficient time after the symptoms subside (reduction of fever without the use of antipyretics and improvement of respiratory symptoms).

(See rules of isolation according to valid regulations of the Ministry of Health of the Czech Republic (https://covid.gov.cz/situace/onemocneni-obecne-o-opatrenich/izolace))

Therapy of complicated cases requires treatment during hospitalization, often with varying degrees of **oxygen therapy** from a simple half mask with a reservoir, through high-flow oxygen therapy to artificial lung ventilation when developing **Acute respiratory distress syndrome (ARDS)**. In carefully indicated cases with refractory hypoxia, **extracorporeal membrane oxygenation (ECMO)** may be indicated.

🔎 *For more information see ARDS.*

Pharmacotherapy

- **Corticosteroids** – dexamethasone is most commonly used
  - indication: Patients with a severe disease whose treatment requires oxygen therapy or ventilation support are recommended to receive **dexamethasone**[18]. Administration of dexamethasone leads to a reduction in mortality, especially in the group of patients requiring mechanical ventilation or ECMO.

NSAIDs (non-steroidal anti-inflammatory drugs) are the mainstay of fever therapy in COVID-19 and should be dosed according to current recommendations. Single case reports of deterioration after NSAID use in younger patients have been published, but other observational studies have not confirmed an association between NSAID use and disease severity. According to current recommendations, NSAIDs should be used according to the usual clinical indications. [18]

- **Anticoagulation**

Due to the risk of thromboembolic complications, **antithrombotic prophylaxis** should be administered according to recommendations depending on the severity of the condition and the patient's history.

- **Nebulization**

Drugs under investigation

A list of ongoing trials for COVID-19 therapy can be viewed on this WHO website (http://apps.who.int/trialsearch/AdvSearch.aspx?SearchTermStat=117&ReturnUrl=~%2fListBy.aspx%3fTypeListing%3d0).

Drugs under investigation include[18]:

- **Remdesivir** - a nucleotide analogue with proven in vitro efficacy against SARS-CoV-2 confirmed in animal models. It is used for moderate and severe disease, and its efficacy in previous studies shows benefit when used in patients with a severe disease with low need for oxygen supplementation. In the general population, available data suggest that it does not reduce mortality, but new research is being analysed.
- **Convalescent plasma** - data on the provision of passive immunization by plasma administration to cured patients are still insufficient. The effect is mainly expected in patients in the early phase of the disease (before sufficient self-titre of antibodies is formed), in patients with immunosuppressive conditions or when plasma with high titres of neutralising antibodies is used.
- **Tocilizumab**, an IL-6 monoclonal antibody, is being evaluated for efficacy in the treatment of severe forms of COVID-19 with IL-6 elevation in systemic inflammation.
- **Favipiravir** - an RNA polymerase inhibitor that preliminary data suggest may accelerate viral clearance.
- **Ivermectin** – antiparasitic, which also has antiviral effects. An *in vitro* effect on SARS-CoV-2 has been demonstrated, but its concentration was much higher than the safe doses of this substance. [19]. In one retrospective study, ivermectin was associated with lower mortality in COVID-19 patients, but more patients treated with ivermectin required corticosteroids. [20]. In a recently published double-blind intervention study of fewer than 500 subjects, administration of 300 µg of ivermectin per kilogram body weight for 5 days compared to placebo had no significant effect either on recovery time or on the number of deaths [21].

Thus, there is not enough data for the use of ivermectin in COVID-19, and further studies are ongoing.

- **Chloroquine/hydroxychloroquine** - these antimalarials have been shown to inhibit SARS-CoV-2 in vitro. Despite initially promising study results, treatment is no longer recommended either alone or in combination with **azithromycin**. No sufficient benefit has been demonstrated and all these drugs are not recommended because of their side effects.
- **Lopinavir-ritonavir** - this drug has also not been shown to be effective.
- Many other agents are being tested in clinical trials without widespread use. An example is Famotidine, a histamine receptor antagonist used for the treatment of gastric ulcer disease. [22]

Other notes on selected drugs

- ACEi, statins, aspirin etc.

Diagnostics

The laboratory finding most often describes lymphopenia, may also be present leukopenia or vice versa leukocytosis. Lymphopenia below 1000 µl $^{-1}$ was associated with a severe course of illness [23].

Other non-specific laboratory findings include elevation of CRP and high erythrocyte sedimentation rate with normal procalcitonin concentration. Elevation of ALT, AST, creatinine, D-dimers, creatine kinase, lactate dehydrogenase, and prolongation of prothrombin time may occur. More marked abnormalities in these parameters tend to be associated with a more severe course [23].

X-ray findings of bilateral pulmonary infiltrate, cariated opacities, or a "ground glass" image on chest CT are frequent. Infiltrates are usually bilateral, peripheral and more commonly in the lower lobes [8].

Laboratory diagnosis is based on the detection of the viral genome by **RT-PCR** in nasopharyngeal or oropharyngeal swabs, sputum, or respiratory aspirate [24].

Confirmation is performed using RT-PCR with a different set of primers or sequencing. When taking material, sputum induction is not recommended. For safety reasons, virological culture is not performed in patients with suspected COVID-19. The WHO does not recommend approaches other than the detection of viral RNA for the diagnosis of COVID-19. However, **rapid diagnostic tests** based on evidence of IgG and IgM against SARS-CoV-2 are also available from auxiliary laboratory examination methods [25].

They have the advantage of the speed of execution (on the order of minutes compared to several hours required for RT-PCR) and low cost. The main disadvantage is the several-day diagnostic window. The sensitivity and specificity of rapid diagnostic tests are around 85-90% and 90% respectively in symptomatic individuals [25].

Other laboratory procedures that detect viral RNA are also being tried. These include procedures using rapid amplification of a section of viral nucleic acid using RT-RPA and detection based on specific cleavage using **CRISPR**. The advantage should be faster execution (on the order of tens of minutes) and less demanding laboratory equipment compared to classically performed RT-PCR while maintaining high sensitivity and specificity. [26]

Specific cases of infection

Pregnancy

Data for outcomes of infections in pregnancy are still very limited. Pregnancy appears to be a risk factor for a more severe course of maternal illness[27]. For now, there has been no evidence of an increased risk of fetal birth defects[28], however, there may be an increased risk of preterm delivery and associated complications, or complications of inadequate uterine perfusion in the critical course of the mother's illness [29]. Limited data suggest that the risk of spontaneous abortion is not increased.

The significance of vertical transmission is still uncertain; neonatal infections may be largely due to postnatal close contact between mother and child. The course of the disease in newborns is mild in the vast majority of cases, with complications usually due to premature birth. [29]

Infections in children

During the Chinese epidemic, the SARS-CoV-2 virus spread rapidly among children, so children are considered to be strong carriers. Infection in these children can range in severity from asymptomatic to severe respiratory failure. Respiratory failure has been described mainly in children with pre-existing chronic diseases. In general, however, COVID-19 disease usually has a mild course in children. The most common manifestations include fever, malaise and dry cough. A few patients have had symptoms of upper respiratory tract inflammation, such as feeling stuffy, nasal secretions and sore throat. Gastrointestinal symptoms include abdominal discomfort, vomiting, abdominal pain and diarrhea. Mycoplasma pneumoniae, influenza A, influenza B, RSV and EB virosis may coexist with SARS-CoV-2 infection. The clearance time of SARS-CoV-2 nucleic acid from nasopharyngeal swabs was monitored in 3 children - 9 days in 2 children and 12 days in 1 child. [30][31]

In Wuhan, 6 children were caught positive for SARS-CoV-2 in January 2020. They were aged 1 to 7 years old, previously quite healthy. All had a fever above 39°C, a cough and (4 of the 6) vomited. They had decreased lymphocytes (all), leukocytes (2/3) and neutrophils (1/2). 4 of these children had radiographic evidence of pneumonia, with CT scans showing a typical picture of viral pneumonia. One of the children was admitted to the intensive care unit and received immunoglobulins from healthy donors. All of these children were treated empirically with antivirals, antibiotics, and supportive care and recovered in 5 to 13 days. [31]

The treatment of COVID-19 in children is based on the experience of adult treatment. Of the antiviral agents, remdesivir or lopinavir-ritonavir is used. The pharmacology of i.v. remdesivir is unknown, while lopinavir-ritonavir has been shown to be safe in pregnancy but is only available in tablets. [32]

In an analysis of 72 314 cases from China, there were no confirmed deaths in the age category ≤ 9 years (0/416) and 1 death in the age category ≤ 19 years (1/549)[15].

A rare complication of SARS-CoV-2 infection in children is **pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2, PIMS-TS**.

🔎 *For more information see PIMS-TS.*

Prevention

Several types of vaccines can be vaccinated against SARS-CoV-2 infection. The development of this active immunization was based on earlier research conducted during the MERS-CoV and SARS-CoV-1 epidemics.

🔎 *For more information see COVID-19 vaccination.*

Pharmacological prophylaxis is currently unknown.

Thus, **non-pharmacological preventive practices** are the basis for preventing and limiting the spread of SARS-CoV-2. These include **limitation of close social contact**, **isolation of ill persons**, **hand hygiene** or **use of protective equipment**, especially to cover the mouth and nose in areas with a high risk of transmission according to current recommendations. The development of the current recommendations issued by health organisations can be followed, for example, on the WHO website (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications) or the Ministry of Health of the Czech Republic (https://koronavirus.mzcr.cz/).

Video library

Ministry of Health information spot

Added 31. 03. 2020

Summary video by Osmosis

Added 12 Aug 2020

PIMS-TS

Added 21 Jan 2021

A rare complication of Covid 19 in children

Etiopathogenesis, diagnosis, and treatment of covid-19-associated multisystem inflammatory response syndrome (PIMS-TS). Webinar. Paediatric Clinic of the 2nd Faculty of Medicine of Charles University and Motol University Hospital, Prague, 7 January 2021.

Links

External links

- **Trvale aktualizované postupy Eastern Virginia Medical School** (https://www.evms.edu/covid-19/covid_care_for_clinicians/)
- Doporučený postup PL 10/2020 (https://vseobecnylekar.cz/wp-content/uploads/2020/11/Doporu%C4%8Den%C3%BD-postup-ordinace_akt.4.11..pdf)
- COVID - kuchařka (na webu stefajir.cz) (https://www.stefajir.cz/covid-kucharka)
- Web Společnosti infekčního lékařství (https://www.infekce.cz/)
- SZÚ: Onemocnění COVID-19, nový koronavirus SARS-CoV-2 (http://www.szu.cz/tema/prevence/2019ncov)
- MZ ČR: Aktuálně o koronaviru (https://koronavirus.mzcr.cz/)
- European Centre for Disease Prevention and Control (ECDC) (https://www.ecdc.europa.eu/en)
- World Health Organization (WHO) (https://www.who.int/)

- Mapa výskytu (https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6) spravovaná *Center for System Science and Engineering* na *John Hopkins University* (průběžně aktualizováno).
- The Global Health Network knowledge hub for 2019 Novel Coronavirus (2019-nCoV) (https://coronavirus.tghn.org/)
- Anglicko-český slovník pojmů využívaných v souvislosti s pandemií COVID-19 (https://www.czechtrans.com/covid-19-glossary-english-czech-part-3/)
- časopis Vesmír 6/20230 Paradoxy Covid 19 (https://vesmir.cz/cz/casopis/archiv-casopisu/2020/cislo-6/paradoxy-infekce-zpusobene-sar-cov-2.html) vědecko-populární článek, rozdíly v průběhu nemoci
- MIS-C neboli PIMS-TS (webinář FN Motol) (https://www.lf2.cuni.cz/fakulta/clanky/audio-a-video/syndrom-multisystemove-zanetlive-odpovedi-spojene-s-covid-19-u-deti)

Related Articles

- Coronaviruses
- Pneumonia

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