

Post-Covid Syndrome: Involvement of the Respiratory Tract in COVID-19

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Abstract. Coronavirus disease 2019 (COVID-19) is an infection caused by a novel coronavirus. On March 11, 2020, the World Health Organization (WHO) declared the outbreak of a new type of coronavirus COVID-19 a pandemic. The public health response to the COVID-19 pandemic is a comprehensive response to reduce morbidity and mortality, minimize disease transmission, protect healthcare workers, and keep the healthcare system running smoothly. The methodological recommendations are intended for practicing physicians, paramedical personnel, healthcare organizers. For radiologists, sections on semiotics, the COVID-19 diagnostic algorithm, and standards for describing studies of patients with suspected viral pneumonia are useful. Nursing staff will be interested in sections on the rules for using personal protective equipment and organizing work in the radiology department during a pandemic. For healthcare organizers, this manual includes links to current regulatory documents (standards), describes in detail the organization of the work of the radiology department in the context of the coronavirus pandemic, and provides a scheme for optimizing business processes in the radiology department to ensure personnel safety in the current epidemiological situation.

1 Introduction

In the modern world, civilization is faced with viral infections that no one knew about before. The climate has changed, the population of the planet has increased, the migration activity of the population has increased, and the processes of urbanization of the population have intensified. All these factors contribute to the rapid spread of infection around the world [10]. At the moment, many infectious diseases have been studied. Reproduction of the model of the course of infectious diseases makes it possible to develop measures for their prevention, spread and prevention. Data on the course, clinical manifestations, prevention and treatment of a new coronavirus infection COVID-19 have not yet been fully studied. Scientists from all over the world are working on these questions. New information about coronavirus infection is updated regularly [1]. The relevance of this topic is due to the rapid spread, high morbidity and mortality of the New Coronavirus infection. According to the WHO, as of October 30, 2021, the number of people infected with

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coronavirus in Russia is 8,472,797, 7,358,539 have recovered and 237,380 deaths have been recorded [11]. At autopsy, the macroscopic picture of lung tissue has no specific changes. The nature of morphological changes in the uncomplicated course of COVID-19 is still unknown [2]. The spread of COVID-19 has posed challenges for the medical community to create a rapid diagnosis and effective treatment of this pathology (fig.1).

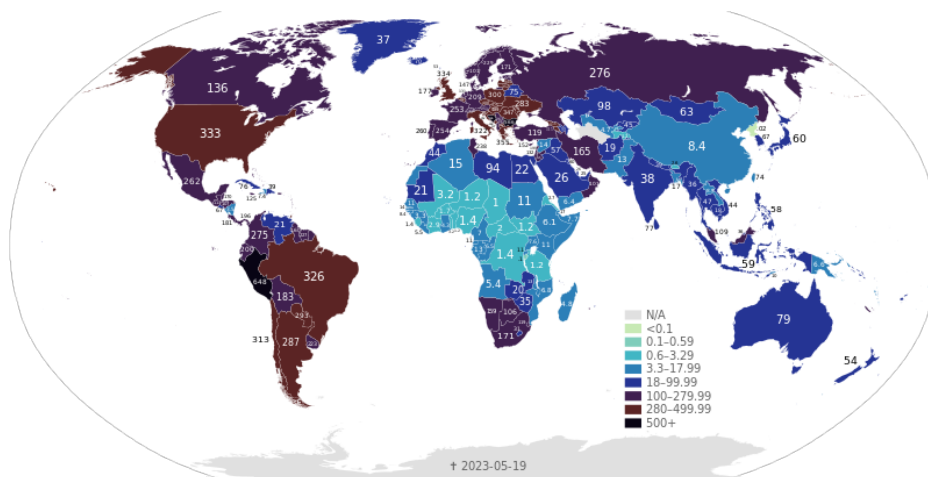


Fig. 1. COVID-19 pandemic by country and territory

Given the speed of the spread of a new coronavirus infection, the involvement of the entire population of the planet in the problem, regardless of gender, age, a deep and detailed study of the pathogenesis of this infection is necessary, in particular: 1) the study of the pathogenesis of new strains of this virus, mutations; 2) study of the nature of morphological changes in organs and tissues in the uncomplicated course of coronavirus infection; 3) study of additional and preferential pathways for penetration into the cell [2, 8]. These data are necessary for the development of new means of its prevention and treatment. Coronaviruses are RNA viruses. This virus is characterized by instability in the environment. Dies under the influence of various factors: UV radiation, disinfectants, heating. On the surface of various objects at 18–25 °C, it remains viable from 2 to 72 hours [2]. Each virus consists of a unique specific DNA or RNA sequence, i.e. genome. Sometimes, when a virus replicates, minor changes to its genome can occur. These changes are called "mutations". Using the word "strain", scientists mean a genetically distinct branch of the virus that differs in one or more mutations from its "parent" [11]. As the pandemic evolves, COVID-19 is mutating. This phenomenon poses a high danger to the population, since the virus acquires new properties due to mutation. Several thousand strains of the SARS-CoV-2 virus circulate in nature. But the main ones that require close attention are only seven. They are usually grouped into large groups - clades. To date, the following coronavirus clades are known: GR, G, GH, O, S, L, and V [5]. Until 2002, coronavirus infection was isolated as an infection that did not cause concern, along with SARS, and did not lead to death. But in 2002, the SARS-CoV coronavirus of the genus Betacoronavirus caused an epidemic of SARS, which killed 774 people. Since 2004, no new cases of this infection have been detected. In 2012, a new epidemic caused by the MERS-CoV coronavirus was registered. The reservoir of this infection are one-humped camels. Until 2020, 866 deaths from the MERS-CoV coronavirus were detected. Today, MERS-CoV continues to cause new cases [2, 12]. The Delta strain (India strain) is now of increasing concern. Currently, the share of the delta strain in the structure of coronavirus variants in the world is about 100%, while almost completely replacing the alpha strain.

The delta strain of the coronavirus has the T19R, Δ 157-158, L452R, T478K, D614G, P681R, and D950N mutations in the spike protein. This is the reason for intensive replication, high viral load and increased contagiousness of the virus [2]. In June 2021, a mutated variant of the delta strain was discovered in India. It is called AY.1 or "delta plus". "Delta plus" is distinguished by the presence of the K417N mutation in the spike protein, which leads to a decrease in antibody activity in recovered and vaccinated people. In terms of contagiousness: one patient infected with the Delta Plus strain can approximately infect nine healthy people; one patient infected with the "Delta" strain infects eight healthy ones. For comparison, one infected with the original strain from Wuhan could infect three healthy ones [2, 5].

2 Research Methodology

A post-COVID-19 syndrome (or "long-term effects of COVID-19 exposure") is a condition in which a person has symptoms and problems after exposure to COVID-19. Research methods in this area include Epidemiological studies:

1. Studying large groups of people to determine how many people experience post-COVID-19 syndrome, which symptoms are most common, and how long these symptoms persist.

2. Clinical Research: Controlled research aimed at better understanding the symptoms, pathogenesis, and treatment of post-COVID-19 syndrome.

3. Biomarker studies: The study of biomarkers that can help determine the presence or nature of the post-COVID syndrome.

4. Brain Activity Studies: Study changes in brain activity in patients with postcysticercosis syndrome using methods such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI).

5. History taking and examination: A detailed history taking and various examinations are carried out to assess the condition and identify symptoms. Immune System Studies: To study the response of the immune system to infection with COVID-19 and the changes that occur after infection with COVID-19.

6. Psychological Research: Examining the psychological aspects of post-COVID-19 syndrome, including depression, anxiety, and quality of life.

Molecular genetic studies: study of genetic factors and potential molecular mechanisms that may influence the development of post-COVID-19 syndrome. Treatment and management research: an evaluation of different approaches to the treatment and management of symptoms of post-Covid-19 syndrome.

Through these approaches, we will be able to better understand the nature and pathogenesis of Post-Covidien syndrome and develop more effective treatments and support for patients.

Respiratory involvement following COVID-19 can take many forms and severity, including inflammation, dysfunction, and long-term consequences. Possible lesions are detailed below:

1. Pneumonia and pulmonary fibrosis: One of the most common lesions is pneumonia (pneumonia) caused by coronaviruses. In some cases, it leads to scarring of the lung tissue (fibrosis), a decrease in its elasticity and gas exchange capacity.

2. Acute Respiratory Distress Syndrome (ARDS): This is a serious condition characterized by severe respiratory distress; in severe cases, COVID-19 infection can be caused by pneumonia requiring mechanical ventilation.

3. Bronchitis and bronchiectasis: Coronaviruses can cause inflammation of the bronchial tubes and small bronchi, leading to bronchitis and bronchiectasis. This may lead to impaired respiratory function.

4. Long-term symptoms: People infected with COVID-19 may continue to have long-term symptoms such as fatigue, shortness of breath, and difficulty breathing even after the infection ends. This may be due to inflammatory changes in the respiratory organs.

5. Decreased physical activity: Exposure to COVID-19 may lead to reduced physical activity, which can lead to respiratory problems and poor overall health.

6. Chronic disease risk: Patients with severe COVID-19 have an increased risk of developing chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma.

Medical investigations such as clinical examination, lung examinations (such as spirometry and computed tomography), and biomarker analysis are needed to obtain a more detailed and accurate picture of respiratory disease after COVID-19.

3 Results and Discussions

The source of the new coronavirus infection is a sick person. The most contagious person is considered in the first 2 days of the disease. The infection is transmitted by the fecal-oral, airborne, contact and airborne routes. A number of authors recognize the possibility of fetal damage during transplacental infection [5]. As of October 30, 2021, 247,251,168 cases of infection were detected worldwide, deaths: 5,007,342. Among all countries of the world, the United States is in the top position, where about 40% of the total number of infections in the world is registered [11]. Every country in the world has been affected by the coronavirus. But it is worth noting that the epidemiological situation in different countries of the world is extremely heterogeneous. In Italy, the USA, Great Britain, a high incidence rate is noted due to the late introduction of anti-epidemic measures. Conversely, Singapore, South Korea, and Japan are experiencing low incidence rates due to the introduction of quarantine measures and their strict enforcement at the very beginning of the pandemic. In terms of the number of cases of infection, Russia is in 5th place in global statistics [1, 11]. Clinically, a new coronavirus infection is characterized by severe weakness, headache and muscle pain, impaired sense of smell and loss of taste, fever, dry cough or cough with scanty discharge, shortness of breath, a feeling of congestion in the chest, diarrhea, skin rash and sore throat [2, 5].

The pathogenesis of COVID-19 is under active investigation. It is known that the penetration of the virus into the cell occurs by the fusion of the viral envelope with the membrane of the host cell. Angiotensin-converting enzyme 2 is one of the main cell receptors, which binds to the S-protein of the SARSCoV-2 viral envelope. The S protein is activated by transmembrane serine protease 2 [7]. The main target of the SARS-CoV-2 virus is alveolocytes of the 1st and 2nd types, vascular endothelium. This is the reason for the dysfunction of the air-blood barrier and the surfactant alveolar complex [5]. The most popular pathogenetic concept of COVID-19 is immune dysregulation resulting in macrophage activation syndrome (MAS) [5] (fig.2).

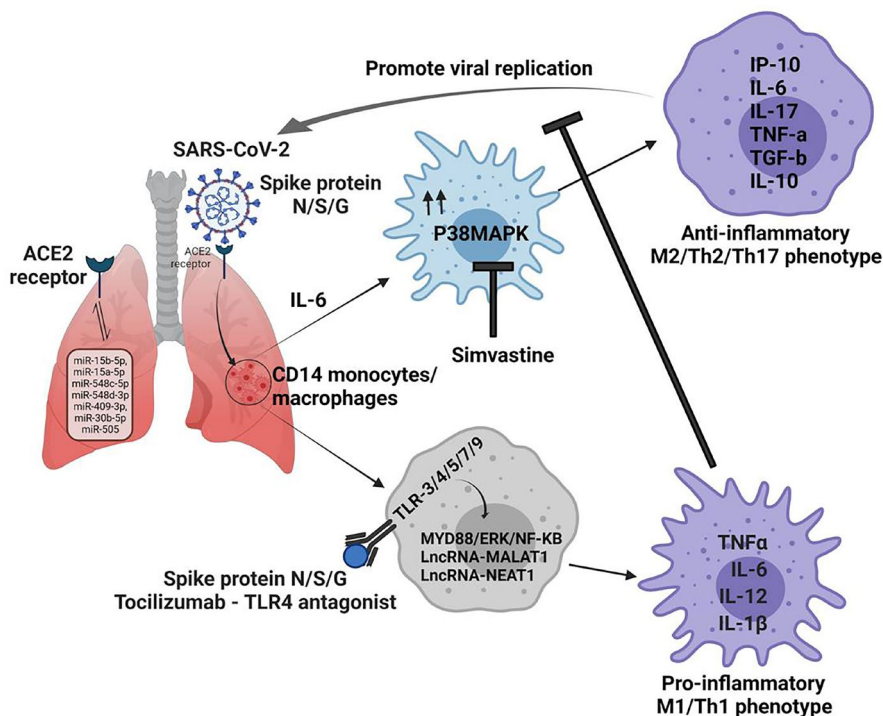


Fig. 2. Macrophage Activation Syndrome and COVID 19

In patients with a severe course of coronavirus infection, a hyperimmune response is detected, which is characterized by dysregulatory activation of monocytic phagocytes, followed by a massive release of cytokines [5]. An elevated serum level of IL 6, 8, 18, 1B and TNF is a marker of a complicated course of coronavirus infection. An increase in the level of IL-6 indicates a high risk of death. The consequence of ARDS is a hyperergic immune response [7]. One of the mechanisms of cell death in coronavirus infection is pyroptosis. Pyroptosis is a type of cell death in which the enzyme caspase-1 is activated, due to which damage to the cell membrane occurs with the formation of pores and the release of contents to the outside. In the center of inflammation, inflammatory mediators are actively produced, and growth factors that activate fibroblasts are synthesized [5]. In the early period of the disease, neutrophils are activated as a reaction to a violation of homeostasis in the respiratory system. There is a violation of the integrity of the endothelium and a slowdown in blood flow, which leads to damage to the microvasculature. The outcome of the disease depends on the extent of damage to the microvasculature [2, 4]. Currently, scientists believe that in addition to ACE2 receptors, there are other receptors for the invasion of the coronavirus into the cell. CD147 receptors attract the most attention for discussion [4]. In a morphological study in the trachea, the microscopic picture was described by desquamation of the epithelium, edema, erythrostatics in the vessels, infiltration of the mucosa by macrophages, lymphocytes, and neutrophils [3]. The microscopic picture in the morphological examination of the bronchi is similar to changes in the trachea. In the walls of the bronchi, desquamation, edema, erythrostatics in the vessels and infiltration by macrophages, lymphocytes and neutrophils were also detected. But in some cases, squamous metaplasia was noted in the bronchial lumen [3, 8]. Macroscopically, the picture of the lungs was characterized by a bilateral decrease in the airiness of the lung tissue, a doughy consistency of the lung tissue in the lower sections

with a color change to purple-bluish. The visceral layers of the pleura are smooth, varnish-like. Marked plethora of lung tissue was noted.

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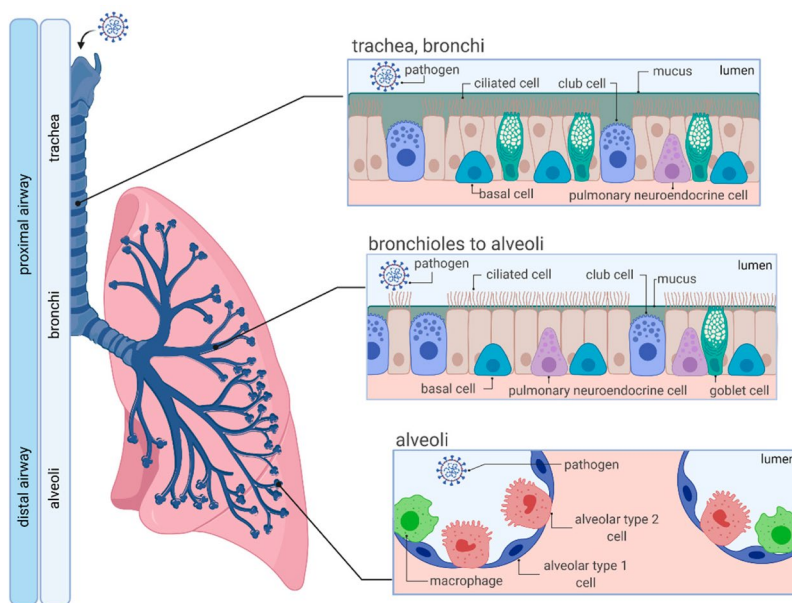


Fig. 3. Organization and cellular characteristics of the human respiratory airway

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In more rare cases, along with thickening of the interalveolar membranes against the background of edema, uneven lymphocytic infiltration of vessel walls and their thrombosis were observed. In the lumen of such alveoli, there was a large amount of fibrin, alveolar macrophages, irregularly shaped cells with severe nuclear hyperchromia. Such areas of lung tissue are macroscopically airless. They alternated with emphysematous foci. Rarely, in the proliferative stage, squamous metaplasia of the alveolar epithelium was detected [7, 8].

There is little evidence in the medical literature about extrapulmonary lesions in coronavirus infection. Disorders of the cardiovascular system, disorders of the gastrointestinal tract, lesions of the urinary system, neurological diseases, skin lesions, visual impairment, hepatocellular damage are described [2]. In a study conducted on the basis of 22 autopsy cases of deaths with infection caused by SARS-CoV-2, it was found that there are left ventricular myocardial infarctions - in 50% of cases, infarctions of the renal cortex - in 72.3% of cases, centrilobular necrosis liver - in 31.8% of cases. Also, in 18.2% of cases, lymphopenia was clinically detected [8]. Edema and infiltration by phagocytes in the area of inflammation were observed in the myocardium of the dead [8]. Electron microscopy of preparations from patients who recovered from COVID-19 revealed lymphocytic infiltration in the squamous epithelium of the esophagus and

infiltration of plasma cells and plasmocytes of the gastric, duodenal and rectal mucosa [8]. In histological preparations of the liver, in most cases, centrilobular steatosis and mononuclear infiltration were observed [7]. In the kidneys, signs of necrosis of the epithelium of the renal tubules were observed. In some cases, these changes were accompanied by exudation in extracapillary spaces [8]. An analysis of data in modern literature on a new coronavirus infection confirms that the CNS also suffers from this pathology. Myalgias, rhabdomyolysis, polyneuropathies may manifest damage to the cranial and peripheral nerves [9]. Acute hemorrhagic necrotizing encephalopathy may be characteristic of COVID-19 [3]. Neuroimaging (CT, MRI of the brain) shows damage to the white matter of the brain with microhemorrhages and local encephalomaliation [5]. Neuroimaging signs of leukoencephalopathy with multiple juxtacortical and callosal hemorrhages are found mainly in patients with respiratory failure of the 2nd degree, with stable hemodynamics, and the absence of blood clotting disorders [5]. In morphological assessment, in addition to microhemorrhages, foci of necrosis, axonal damage in the form of loss of myelin, lacunar infarcts, perivascular inflammatory infiltrates, arteriolosclerosis and endotheliitis are visualized. Such changes are not observed in the gray matter of the spinal cord, basal ganglia, leptomeninges, and brainstem [3, 5]. Additionally, acute hemorrhagic posterior reversible encephalopathy is considered to be one of the options for morphological changes in the brain when it is affected by a new coronavirus infection. It is manifested by headache, disturbed consciousness, behavioral disorders, convulsions. It is characterized by subcortical vasogenic edema, bilateral lesions of the white matter, and petechial hemorrhages of the cerebral cortex [4, 8]. During autopsy, RNA-coronavirus is detected in sputum, saliva, nasopharynx, lung parenchyma, bronchial washings, lacrimal fluid and in the conjunctival sac. This indicates the defeat of the virus mucous eyes, nose and mouth, respiratory tract. COVID-19 is characterized by selective damage to the white and gray matter of the cerebral cortex in the form of necrotizing hemorrhagic encephalopathy. Similar brain damage is also characteristic of sepsis, shock, and Still's disease [9]. An analysis of the literature data indicates the likelihood of placental damage in COVID-19. Placental disease in COVID-19 is characterized by decidual vasculopathy, villous hypoplasia, perivillous fibrin, and villous infarcts [2, 9]. In pregnant women with complicated forms of a new coronavirus infection, compared with pregnant women with asymptomatic course, there are differences in the morphological changes in the placenta according to the degree of damage. In cases of asymptomatic course, choriitis, amnionitis, fetal vascular disorders and villusitis were noted. In severe and moderate course of the disease, villus infarcts and thrombus formation in the intervillous space were detected [2, 3, 9].

4 Conclusions

The main factor in the development of lethal outcomes in a new coronavirus infection is interstitial pneumonia [8]. Infiltration of the lung tissue by macrophages, generalized damage to the microcirculatory bed with the development of thromboembolic complications, fibrosis of the lung parenchyma, and the addition of a secondary bacterial infection are considered as factors of an unfavorable outcome [5]. Morphological signs of a severe course of a new coronavirus infection, ending in death up to 10 days, are a monocyte-macrophage hyperimmune reaction with the subsequent development of thromboinflammatory processes in the microvasculature. Morphological signs of a severe course of a new coronavirus infection, ending in death up to 20 days, are the development of widespread thrombosis in larger vessels. Severe course of COVID-19-interstitial pneumonia, leading to death on the 21st–45th day of the disease, is accompanied by severe fibrosis of the lung parenchyma [3, 5, 8].

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