

# Diagnosis and Treatment Protocol for COVID-19 Patients (Tentative 8th Edition): Interpretation of Updated Key Points

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Coronavirus Disease 2019 (COVID-19) has become a major global public health pandemic. China was the first country to report the epidemic situation, which quickly identified the pathogen, and released the novel coronavirus gene sequence globally. Thus, China has played an essential role in the global fight against COVID-19. Since the outbreak of the epidemic, the Chinese government and citizens have pursued robust prevention and control measures, including wearing masks, hand hygiene, social distancing, etc. Large-scale nucleic acid testing has been fully implemented and has resulted in early detection, reporting, quarantine, and treatment. China's epidemic situation has been generally brought under control, and the fatality rate has been effectively controlled.<sup>[1-4]</sup> Recently there are sporadic cases of COVID-19 in China. Of the locally transmitted cases reported at January 20, 2021, 68 were reported in Heilongjiang, 33 in Jilin, 20 in Hebei, two each in Beijing and Shanxi, and one in Shandong, the National Health Commission reported.<sup>[5]</sup>

For further COVID-19 medical treatment, the National Health Commission and the State Administration of Traditional Chinese Medicine have organized national experts of infection, respiratory and intensive medicine, pediatrics, and traditional Chinese medicine to revise the seventh edition of China's diagnosis and treatment plan. The appointed national experts have summarized prior clinical experience and referred to the diagnosis and treatment guidelines of WHO as well as other countries to produce the eighth edition of the diagnosis and treatment of COVID-19.<sup>[6]</sup> Currently, it has been updated, and the interpretation is as follows:

## I. Epidemiological characteristics

Asymptomatic infected individuals or patients have been recognized as an important source of further infection. Current research has shown that the asymptomatic are similarly as

infectious as COVID-19 patients. Simultaneously, since asymptomatic infected individuals or patients do not take the initiative to seek medical treatment, their infectivity is more insidious. In this regard, large-scale active nucleic acid screening is an essential means to eliminate the potential transmission of the asymptomatic, and it is an effective measure in clinical practice. Moreover, following novel coronavirus infection, the infectivity during the incubation period is similar to that after the onset of illness, thus the statement that "infectivity occurs during the incubation period, but is highly infectious within five days after the onset of illness" was added. During the incubation period, transmission risk control is the key to quickly control the epidemic. Therefore, monitoring the mobility of the high-risk population and actively using nucleic acid detection are effective ways to eliminate the risk of latent infection.

Imported frozen food and outer packaging has tested positive for the SARS-CoV-2 nucleic acid, thus was added to the transmission route that included "contact with virus-contaminated items can also cause infection", which is a reminder that epidemiological information should be paid attention to in clinical diagnosis. Furthermore, regular nucleic acid screening for employees can detect infected persons early and help control transmission before spread.

## II. Pathological characteristics

The new guidelines give an update on pathological characteristics of COVID-19. Anatomical features and microscopic findings of the main affected organs, such as the lungs, spleen, hilar lymph nodes, bone marrow, heart, blood vessels, liver, gallbladder, kidneys, brain tissue, esophagus, stomach, intestinal mucosa, and testes were described in detail, which provides a basis for understanding the clinical manifestations and therapeutic interventions of COVID-19. For example, the characteristics of extensive thrombosis provide a basis for clinical anti-coagulation therapy, and the decrease of lymphocytes in the spleen and lymph nodes is consistent with the appearance of peripheral blood, which provides a basis for clinical immunological intervention.

## III. Clinical characteristics

### 1. Clinical manifestations

A new guideline adds that "in some patients, decrease or loss of smell and taste is the first symptom." Since decrease of smell and

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taste is common in upper respiratory diseases, this chief complaint is often neglected if not carefully questioned. Simultaneously, “a small number of patients can also have central nervous system involvement and avascular necrosis of the extremities” and other manifestations, prompting clinicians to pay attention to the monitoring and intervention of consciousness change and coagulation mechanisms. A multi-system inflammatory syndrome in children (MIS-C) has been reported by many countries worldwide, and the clinical manifestations of MIS-C were generalized in the new guideline. Thus, clinicians should be aware of this new addition.

## 2. Laboratory examination

The updated guidelines added that “SARS-CoV-2-specific IgM and IgG antibodies have a low positive rate within 1 week of onset”. It was suggested that patients who are clinically suspected to have COVID-19 and those in convalescence with a negative nucleic acid result should be diagnosed by the antibody test to offset the false-negative nucleic acid result.

## IV. Diagnostic criteria

Given the possibility of a false negative in nucleic acid detection and to further strengthen the screening of cases, which will effectively control the epidemic situation, “those who have no clear epidemiological history and meet any two clinical manifestations, and who are positive for novel coronavirus specific IgM antibody” should be added to “suspected cases”. However, attention should be paid to the false-positive results of the IgM antibody test.

## V. Clinical classification

The diagnostic criteria for severe cases in adults and children have been appropriately modified. For example, some ordinary patients may not experience fever or respiratory symptoms, but have the appearance of pneumonia in image.

## VI. Criteria for high-risk of severe and critical cases

The people who have been identified as high-risk of severe and critical cases are as follows: (1) elderly people, age >65; (2) Patients with cardiovascular and cerebrovascular diseases (including hypertension), chronic lung diseases (chronic obstructive pulmonary disease, moderate to severe asthma), diabetes, chronic liver, kidney diseases, tumors, and other primary diseases; (3) Immunodeficiency (eg, AIDS patients, people treated by chronic use of corticosteroids or other immunosuppressive drugs); (4) Obesity (BMI  $\geq$  30); (5) Women in the third trimester of pregnancy and perinatal period; and (6) Heavy smokers. Thus, identifying high-risk groups provides the basis for early clinical intervention. For the high-risk patients, more active disease observation and timely oxygen therapy are needed to reduce the risk of disease progression. It is crucial to discern the signs of severe or critical cases and transfer patients to the ICU in time to minimize the fatality rate.

## VII. “Severe/critical early warning indicators” for adults and children

Through the analysis and summary of a large number of cases, studies have shown that many indicators can predict the

occurrence of severe/critical cases, such as lymphocyte count, inflammation indicators, etc. It is worth noting that those indicators differ among children and adults, which provides evidence for early clinical intervention. In addition, some indicators, such as lactate dehydrogenase level and troponin, can be used as warning indicators. In clinical practice, it is necessary to dynamically monitor the patient to discover changes in disease for timely intervention and quickly transfer patients into ICU for treatment.

## VIII. Discovery and reporting of cases

In clinical practice, suspected cases are often negative for nucleic acid detection, but due to false-negative results of nucleic acid detection, SARS-CoV-2 infection cannot be ruled out for such patients. Therefore, patients may be excluded from a COVID-19 diagnosis when (i) the nucleic acid test results of suspected cases were negative for two consecutive novel coronavirus nucleic acid tests (the sampling time was at least 24 hours apart) and (ii) the specific IgM and IgG antibodies remain negative seven days after onset. This information provides criteria for exclusion of suspected cases, avoiding the problem of indefinite detention.

## IX. Treatment

### 1. Antiviral therapy

Currently, there are no recognized specific antiviral drugs. Some antiviral drugs with safety data have been reserved for clinical trial use for the treatment of pneumonia in patients with COVID-19. However, the necessity of further randomized, double-blind, placebo-controlled studies has been emphasized. Lopinavir/ritonavir and ribavirin alone, hydroxychloroquine, or azithromycin in combination are clearly not recommended.

### 2. Glucocorticoid therapy

A low dose of hormone and a short course of treatment have been recommended for patients with progressive deterioration of oxygenation index, rapid imaging progression, and excessive activation of inflammatory reaction.

### 3. Treatment of severe and critical patients

- (1) The timely assessment of improvement in respiratory distress and/or hypoxemia should be performed. If no signs of improvement, additional respiratory support measures should be taken. The treatment using prone position ventilation has been emphasized for patients receiving oxygen therapy. If there are no complications, prone position ventilation (ie, awake in the prone position) should be simultaneously recommended. The treatment time while in the prone position should be more than 12 hours.
- (2) The contents related to airway management were added and include the initiation timing, extracorporeal membrane oxygenation (ECMO) indications, ECMO mode selection, and recommended initial setting of ECMO.
- (3) Indications for preventive “anticoagulant therapy” have been added, and in the event of a thromboembolic event, anticoagulant therapy should be administered using the appropriate guidelines.

- (4) Principles of the treatment in MIS-C have been added, such as the usage of intravenous gamma globulin (IVIG), glucocorticoids, and aspirin.

#### 4. Early rehabilitation

Because pulmonary fibrosis may occur in COVID-19 patients with severe pneumonia and patients generally have emotional states, such as anxiety and tension, it has been recommended to “pay attention to early rehabilitation intervention of patients, actively carry out rehabilitation training and intervention for respiratory function, physical function and psychological dysfunction of patients with pneumonia in COVID-19, and restore physical fitness, physique, immunity and mental health as much as possible”.

#### 5. Treatment by Traditional Chinese Medicine (TCM)

TCM plays an important role in the treatment of pneumonia in COVID-19 patients. The eighth-edition guidelines have refined the TCM treatment principle based on syndrome differentiation and highlighted the “three drugs and three schemes” for clinical treatment.

#### X. “Nursing”

The nursing of critically-ill patients is a vital link to improve prognosis. Therefore, “nursing” has been added to the eighth-edition of the guidelines, which has stressed the importance of “closely monitoring vital signs and state of consciousness, emphasizing oxygen saturation” in severe/critical patients with COVID-19. Nursing is necessary to prevent pressure injury in bedridden patients and strengthen the prevention and management of pressure injury in prone ventilation patients. Moreover, reducing nosocomial infection is the key to decreasing critically-ill patients’ mortality rate due to prevention and control of hospital infection.

#### XI. “Prevention”

The eighth-edition of the guidelines has suggested to keep good personal and environmental hygiene, improve health literacy, keep adequate indoor ventilation, perform personal protection that has been scientifically proven, and visit the doctor when illness is suspected.

#### Conflicts of Interest

None.

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