Translation: Diagnosis and Treatment Protocol for COVID-19 (Trial Version 9)

National Health Commission of the People’s Republic of China, National Administration of Traditional Chinese Medicine

In order to further strengthen the diagnosis and treatment of coronavirus disease 2019 (COVID-19), we revised the Diagnosis and Treatment Protocol for COVID-19 (Revised Trial Version 8) to Diagnosis and Treatment Protocol for COVID-19 (Trial Version 9).

1. Etiological characteristics

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the β-genus coronaviruses. It has an envelope, and the virus particle is round or oval, with a diameter ranging from 60 to 140 nm. The genome of SARS-CoV-2 contains five essential genes, which encode four structural proteins, namely, the nucleoprotein (N) protein, the envelope (E) protein the matrix protein (M), and the spike (S) protein and an RNA-dependent RNA polymerase (RdRp). The RNA genome is wrapped in the N protein, forming a nucleocapsid surrounded by lipid bilayer membrane, in which the E protein, the M protein and the S protein are embedded. The S protein interacts with angiotensin-converting enzyme 2 (ACE2) to enter cells. When isolated and cultured in vitro, SARS-CoV-2 can be found in human respiratory epithelial cells in approximately 96 hours; nevertheless, it takes approximately 4–6 days for the virus to be found if isolated and cultured in Vero E6 and Huh-7 cell lines.

Similar as observed for other viruses, mutations can occur in the genome of SARS-CoV-2, some of which may result in changes in the biological characteristics of the virus, thus attracting extensive attention. For instance, changes in the affinity of the S protein for ACE2 can affect the ability of the virus to invade host cells, the ability to replicate and spread, the production of antibodies in convalescent patients and vaccinated people, and the neutralization ability of antibody drugs. Five variants of concern, namely, alpha, beta, gamma, delta, and omicron, have been proposed by the World Health Organization. At present, the omicron variant has replaced delta variant as the main epidemic variant. Evidence has shown that compared with the delta variant, the omicron variant displays stronger transmissibility and weaker pathogenicity. For the omicron variant, the diagnostic accuracy of polymerase chain reaction (PCR) tests commonly used in China was not affected, but the neutralization efficacy of some monoclonal antibody-based drugs might be reduced.

The coronavirus is sensitive to ultraviolet light and heat. Exposure to 56 °C for 30 minutes and to lipid solvents, such as ether, 75% ethanol, chlorine-containing disinfectant, peracetic acid and chloroform, can effectively inactivate the virus, but chlorhexidine fails to inactivate the virus.

2. Epidemiological characteristics

2.1. Source of infection

SARS-CoV-2–infected patients are the main source of infection. The infection can be contagious at the incubation stage and is strongly infectious within 5 days after symptom onset.

2.2. Route of transmission

(i) Transmission of the virus happens mainly via respiratory droplets and close contact.
(ii) The virus can be spread by aerosols in a relatively enclosed environment.
(iii) Contact with objects contaminated with the virus can also cause infections.

2.3. Susceptible groups

People are generally susceptible. Immunity can be acquired after infection or vaccination.

3. Pathological changes

Pathological changes of major organs and results of SARS-CoV-2 detection based on earlier COVID-19 cases are summarized below (excluding underlying diseases).

3.1. Lungs

In early-stage or milder lesions, the alveoli are filled with fluid and fibrin with a hyaline membrane. Inflammatory cells are mainly monocytes and lymphocytes. There is congestion in the capillaries of alveolar septa. As the disease progresses and aggravates, the alveoli are filled with a large number of monocytes/macrophages and fibrin, with multinucleated syncytial cells observed and eosinophilic inclusion bodies occasionally seen. Pulmonary vasculitis, thrombogenesis (mixed thrombus, hyaline thrombus), and thromboembolism are observed. Detached epithelial cells and mucus are present in the bronchi, with exudate and mucus. Mucus plugs are often seen in bronchia and the bronchiole. Focal hemorrhage is often seen in lung tissues, and hemorrhagic infarction and bacterial and/or fungal infections are seen. Hyperventilation, interrupted alveolar interstitium, or cysts are seen in some alveoli. For cases with a long disease course,
By electron microscopy, SARS-CoV-2 virions are observed in the cytoplasm of bronchial epithelium and type II pneumocytes. Immunohistochemical staining reveals SARS-CoV-2 viral antigen immunoreactivity and positive SARS-CoV-2 nucleic acids in some bronchial epithelial cells, alveolar epithelial cells and macrophages.

3.2. Spleen, hilar lymph nodes, and bone marrow

The spleen shrinks. The white pulp is atrophic with a decreased number of lymphocytes and focal necrosis; the red pulp is congested with focal hemorrhage. Macrophage proliferation and phagocytosis are present in the spleen. Anemic infarct of the spleen can develop. Reduction of lymphocytes and focal necrosis are noted in lymph nodes. Immunohistochemistry highlights a decreased number of CD4+ and CD8+ T cells in the spleen and lymph nodes. The lymph node tissues can be positive for SARS-CoV-2 nucleic acids, and macrophages can be positive for SARS-CoV-2 viral antigen immunoreactivity. Hematopoietic cells are proliferated or decreased in bone marrow with an increased granulocyte-to-erythrocyte ratio. Hemophagocytosis develops occasionally.

3.3. Heart and blood vessels

Myocardial cells are partially degenerated or necrosed. Congestion and edema can be seen in the cardiac interstitium, along with infiltration of some monocytes, lymphocytes, and/or neutrophils. The cardiac tissue is occasionally positive for SARS-CoV-2 nucleic acids. Shedding of endothelial cells, endovasculitis and vasculitis are seen in small blood vessels across all major body parts. Formation of mixed thrombus, thromboembolism and infarction are present in vessels, and formation of hyaline thrombus is seen in the capillaries of major organs.

3.4. Liver and gallbladder

Degeneration and focal necrosis of hepatocytes are found, accompanied by infiltration of neutrophils. The hepatic sinusoids are congested. The portal areas are infiltrated by lymphocytes and monocytes. Microthrombi may develop. The gallbladder is prominently distended, and the gallbladder mucosal epithelia shows desquamation. The liver and gallbladder can be positive for SARS-CoV-2 nucleic acids.

3.5. Kidneys

Glomerular capillaries are congested, occasionally with segmental fibrinoid necrosis; proteinaceous exudates are found in the Bowman capsule. Degeneration of epithelial cells is seen in the proximal tubule, with partial necrosis and shedding; casts are seen in the distal tubule. The renal interstitium is congested along with microthrombi. The renal tissue is occasionally positive for SARS-CoV-2 nucleic acids.

3.6. Other organs

Cerebral hyperemia and edema are present, along with degeneration, ischemic changes and loss of some neurons, and neuronophagia and satellite phenomenon can be seen; infiltration of monocytes and lymphocytes is found in perivascular spaces. Necrotic foci are noted in the adrenal glands. Variable degrees of degeneration, necrosis, and desquamation of epithelial mucosa are observed in the esophagus, stomach, and bowel; infiltration of monocytes and lymphocytes is found in the lamina propria and submucosa. Degeneration, focal hemorrhage and necrosis of cortex cells are seen in adrenal glands.

A decreased number of spermatogenic cells and degeneration of Sertoli cells and Leydig cells are found in the testis.

SARS-CoV-2 is detected in nasopharyngeal and gastrointestinal mucosae and organs including testis and salivary glands.

4. Clinical characteristics

4.1. Clinical manifestations

The incubation period is 1–14 days, mostly 3–7 days. The main manifestations include fever, fatigue and dry cough. Some patients present symptoms such as nasal congestion, runny nose, sore throat, decrease in or loss of smell and taste, conjunctivitis, myalgia and diarrhea. Severe patients develop dyspnea and/or hypoxemia after 1 week and may progress rapidly to acute respiratory distress syndrome, septic shock, refractory metabolic acidosis, coagulopathy and multiple organ failure. Rare cases may manifest central nervous system involvement and avascular necrosis of the extremities. It is noteworthy that severe and critical cases may show only moderate to low fever, or even no fever at all.

Patients with mild symptoms usually do not develop pneumonia, but have low fever, mild fatigue and smell and taste disorders. Patients may show no obvious clinical symptoms after infection with SARS-CoV-2.

Asymptomatic and mild cases are predominant in those who have been vaccinated and those infected with the omicron variant. Among them, symptomatic patients mainly present with symptoms of upper respiratory tract infection such as moderate to low fever, dry pharynx, pharyngeal pain, nasal congestion and a runny nose.

Most patients have a good prognosis, and only a small percentage of patients become critically ill. The prognosis is poorer for the elderly, patients with chronic underlying diseases, women in the third trimester of pregnancy and in the perinatal period, and obese people.

Symptoms in children are relatively mild. Some children and neonatal patients may have atypical symptoms, presenting with gastrointestinal symptoms such as vomiting and diarrhea or manifesting only as low response and shortness of breath. Extremely rare cases of infected children develop multisystem inflammatory syndrome (MIS-C), present with Kawasaki syndrome or atypical Kawasaki syndrome, have toxic shock syndrome, or display macrophage activation syndrome, mostly occurring at the convalescence stage. The main manifestations are fever with rash, nonsuppurative conjunctivitis, mucosal inflammation, hypotension or shock, coagulation disorder and acute gastrointestinal symptoms. Once it happens, the disease can deteriorate rapidly within a short time.

4.2. Laboratory tests

4.2.1. General findings

In the early stages of the disease, the peripheral white blood cell count is normal or decreased, and the lymphocyte count is decreased. Some patients have elevated levels of liver enzymes, lactate dehydrogenase, muscle enzymes, myoglobin, troponin and ferritin. Most patients have elevated levels of C-reactive protein (CRP) and erythrocyte sedimentation rate and normal levels of procalcitonin (PCT). Among severe and critical cases, D-dimer increases, peripheral blood lymphocytes progressively decrease, and inflammatory factors increase.

4.2.2. Pathogenic and serological findings

(i) Pathogenic findings

SARS-CoV-2 nucleic acids can be detected in nasopharyngeal swabs, sputum and other lower respiratory tract secretions, feces and other specimens using nucleic acid amplification detecting methods.
SARS-CoV-2 nucleic acid detection can be affected by factors including the course of disease, specimen collection, detection process and detection reagents. To increase the accuracy of detection, specimen collection should be standardized, and the specimens should be submitted for testing as soon as possible after collection.

(ii) Serological findings
SARS-CoV-2–specific immunoglobulins M (IgM) and G (IgG) antibodies are positive. The positive rate is low within 1 week after onset. Because of the positive cutoff value of the reagent, the presence of interfering substances in patients (rheumatoid factors, heterophile antibodies, complement, lysozyme, etc), or the state of specimens (specimen hemolysis, contamination by bacteria, excessive storage time, incomplete solidification, etc), serological antibody tests can yield false-positive results. Diagnosis is normally not made according to serological findings alone, but in combination with epidemiological history, clinical manifestations, and underlying diseases.

4.3. Chest imaging
In the early stage, chest imaging shows multiple small patchy shadows and interstitial changes, more apparent in the lung periphery. As the disease progresses, imaging shows multiple ground-glass opacities and infiltrates in both lungs. In severe cases, pulmonary consolidation may occur. However, pleural effusion is rare. In cases of MIS-C, heart enlargement and pulmonary edema are seen in patients with cardiac dysfunction.

5. Diagnosis
5.1. Principle
Diagnosis should be made based on comprehensive analysis of epidemiological history, clinical manifestations and laboratory findings. A positive nucleic acid test for SARS-CoV-2 is the primary diagnostic criterion. For individuals not vaccinated with a COVID-19 vaccine, presence of SARS-CoV-2–specific antibodies can be used as an indication for diagnosis; for vaccinated individuals or individuals previously infected with SARS-CoV-2, diagnosis should not be based on serological antibodies.

5.2. Case definitions
5.2.1. Suspected cases
A suspected case has any of the epidemiological history criteria plus any two of the clinical manifestations.

If there is no clear epidemiological history, a suspected case has all three of the clinical manifestations, or two of the clinical manifestations plus positive SARS-CoV-2–specific IgM (except for individuals recently vaccinated with COVID-19 vaccine).

(i) Epidemiological history
a. History of travel to or residence in communities where cases have been reported within 14 days before the onset of the disease;
b. History of contact with SARS-CoV-2–infected people within 14 days before the onset of the disease;
c. In contact with patients who have fever or respiratory symptoms from communities where confirmed cases have been reported within 14 days before the onset of the disease; or
d. Clustered cases (two or more cases with fever and/or respiratory symptoms in a small area such as families, offices, schools, and so on within 14 days).

(ii) Clinical manifestations
a. Clinical manifestations related to COVID-19, such as fever and/or respiratory symptoms;
b. Presence of aforementioned imaging characteristics of COVID-19; or
c. Normal or decreased white blood cell counts or lymphocyte counts in the early stage of onset.

5.2.2. Confirmed cases
When suspected cases display one of the following etiological or serological evidence:
(i) Positive for SARS-CoV-2 nucleic acids; or
(ii) SARS-CoV-2–specific IgM and IgG are positive for individuals not vaccinated with a COVID-19 vaccine.

6. Clinical classification
6.1. Mild cases
The clinical symptoms are mild, and there is no sign of pneumonia on imaging.

6.2. Moderate cases
Showing aforementioned clinical symptoms with radiological findings of pneumonia.

6.3. Severe cases
Adult cases meeting any of the following criteria:
(i) High fever lasting >3 days;
(ii) Oxygen saturation ≤93% on fingertip pulse oximeter taken at resting state; or
(iii) Arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2) ≤300 mm Hg (1 mm Hg = 0.133 kPa). In high-altitude areas (at an altitude of >1000 m above the sea level), PaO2/FiO2 shall be corrected according to the following formula: PaO2/FiO2 = [760/atmospheric pressure (mm Hg)];
(iv) Cases with chest imaging that shows obvious lesion progression >50% within 24–48 hours shall be managed as severe cases.

Child cases meeting any of the following criteria:
(i) High fever lasting >3 days;
(ii) Tachypnea (RR ≥30 breaths/min for infants aged <2 months; RR ≥50 breaths/min for infants aged 2–12 months; RR ≥40 breaths/min for children aged 1–5 years, and RR ≥30 breaths/min for children aged >5 years old) independent of fever and crying;
(iii) Oxygen saturation ≤93% on fingertip pulse oximeter taken at resting state;
(iv) Labored breathing (nasal fluttering and three concave signs);
(v) Lethargy and convulsion; or
(vi) Difficulty in feeding and signs of dehydration.

6.4. Critical cases
Cases meeting any of the following criteria:
(i) Respiratory failure and requiring mechanical ventilation;
(ii) Shock; or
(iii) With other organ failure that requires intensive care unit management.

7. Populations at high risk of severe and critical conditions
(i) The elderly >60 years old;
8. Clinical early warning indicators of severe and critical cases

8.1. Adults

Adults with following indications are at risk of deterioration.
(i) Progressive exacerbation of hypoxemia or respiratory distress;
(ii) Deterioration of tissue oxygenation index (such as oxygen saturation on fingertip pulse oximeter and oxygenation index) or progressive elevation of lactic acid;
(iii) The peripheral blood lymphocytes decrease progressively or peripheral blood inflammatory factors, such as interleukin 6 (IL-6), CRP and ferritin, increase progressively;
(iv) Coagulation function-related indicators such as D-dimer significantly increase; and
(v) Chest imaging shows rapid development of lung lesions in a short period.

8.2. Children

(i) RR increases;
(ii) Poor mental reaction and drowsiness;
(iii) Lactate increases progressively;
(iv) Inflammation factors, such as CRP, PCT and ferritin, increase significantly.
(v) Imaging shows infiltration on both sides or multiple lobes, pleural effusion, or rapid progression of lesions in a short period; and
(vi) Children who have underlying diseases (congenital heart disease, bronchopulmonary dysplasia, respiratory tract deformity, abnormal hemoglobin and severe malnutrition, etc), immune deficiency, or hypoimmunity (long-term use of immunosuppressants) or neonates.

9. Differential diagnosis

(i) Mild manifestations of COVID-19 need to be distinguished from those of upper respiratory tract infections caused by other viruses.
(ii) COVID-19 is mainly distinguished from Mycoplasma pneumonia and other known viral pneumonias, such as influenza virus infection, adenovirus infection and respiratory syncytial virus infection. For suspected cases, efforts should be made to use methods such as rapid antigen detection and multiplex PCR nucleic acid testing for detection of common respiratory pathogens.
(iii) COVID-19 should also be distinguished from noninfectious diseases such as vasculitis, dermatomyositis and organizing pneumonia.
(iv) In children with rash and mucous membrane damage, COVID-19 should be distinguished from Kawasaki disease.
(v) People who have been in close contact with confirmed COVID-19 patients are advised to perform SARS-CoV-2 pathogen testing in a timely manner, even if common respiratory pathogens are tested positive.

10. Case finding and reporting

Medical institutions of all types and at all levels, upon discovering suspected cases that meet the suspected diagnosis definition or those who are tested positive for SARS-CoV-2, should immediately collect specimens for nucleic acid testing or transfer them in a closed loop manner to a qualified superior medical institution for nucleic acid testing, during which period the cases should be kept in a single room for isolation. If nucleic acid tests are positive, the cases should be placed under centralized isolation management or transferred to the designated hospital for treatment, and they should be reported directly online according to regulations.

If two nucleic acid tests, taken at least 24 hours apart, of a suspected COVID-19 case are negative, COVID-19 can be ruled out.

11. Treatment

11.1. Treatment venue and isolation management determined by the severity of the disease

(i) Centralized isolation management shall be implemented for mild cases, and people entering the country and close contacts shall not be isolated in the same centralized isolation site. Symptomatic treatment and condition monitoring should be performed well during isolation. If the conditions worsen, the patient should be transferred to a designated hospital for treatment.
(ii) Moderate, severe and critical cases and those with severe risk factors should be treated intensively in designated hospitals. Severe and critical cases should be admitted to the ICU as soon as possible. Patients with high risk factors and propensity for developing severe conditions should also be admitted to the ICU for treatment.

11.2. General treatment

(i) Let patients rest in bed and provide strengthening support therapy; ensure sufficient caloric intake for patients; and monitor their water and electrolyte balance to maintain internal environment stability.
(ii) Closely monitor vital signs, especially the oxygen saturation under resting and after activity.
(iii) According to patients’ conditions, monitor blood routine results, urine routine results, CRP, biochemical indicators (liver enzyme, myocardial enzyme, renal function, etc), coagulation function, arterial blood gas analysis and chest imaging. Cytokines can be detected if possible.
(iv) According to patients’ conditions, provide normative and effective oxygen therapy, including nasal catheter and mask oxygenation and nasal high-flow oxygen therapy.
(v) Antibiotic drug treatment: blind or inappropriate use of antibiotic drugs should be avoided, especially combined use of broad-spectrum antibiotics.

11.3. Antiviral therapy

11.3.1. PF-07321332/ritonavir tablets (Paxlovid)

Applicable for adults and adolescents (12–17 years of age, weight ≥40 kg) with mild and moderate conditions within 5 days of onset and with risk factors for progression to severe conditions.
Usage: 300 mg PF-07321332 combined with 100 mg ritonavir, once every 12 hours, for 5 consecutive days. The instructions should be read carefully before use, and it cannot be used in combination with drugs, such as pethidine and ranolazine, which are highly dependent on CYP3A for clearance and can cause serious and/or life-threatening adverse reactions at an elevated plasma concentration.
11.3.2. Monoclonal antibody: ambavirumab/remisvirumab injection
The combination therapy is applicable for adults and adolescents cases (12–17 years of age, weight ≥40 kg) with mild and moderate conditions and with risk factors for progression to severe conditions. Usage: the dosage of the two drugs is 1000 mg, respectively. Before administration, the two drugs are diluted with 100 mL 0.9% sodium chloride, respectively, and given by sequential intravenous infusion at a rate of no more than 4 mL/min, with 100 mL 0.9% sodium chloride flushing the tubing during the interval between administrations of the two drugs. Patients should be clinically monitored during the infusion and observed for at least 1 hour after the infusion is completed.

11.3.3. Intravenous injection of COVID-19 human immunoglobulin
This is applicable in the early stage of the disease for patients with high risk factors, high viral loads and rapid disease progression. The dosages of intravenous infusion are 100 mg/kg for mild cases, 200 mg/kg for moderate cases and 400 mg/kg for severe cases, respectively. The patients can be reinfused daily according to the improvement of the patient’s condition, no more than five times in total.

11.3.4. Convalescent plasma treatment
This is applicable in the early stage of the disease for patients with high risk factors, high viral loads, and rapid disease progression. The infusion dose is 200–500 mL (4–5 mL/kg). It can be decided to reinfuse or not in accordance with individual conditions of patients and their viral loads.

11.4. Immunotherapy

11.4.1. Glucocorticoid therapy
For patients with progressive deterioration of oxygenation indicators, rapid progress in imaging, and excessive activation of the body’s inflammatory responses, glucocorticoids can be used for a short period (no longer than 10 days). Dexamethasone 5 mg/d or methylprednisolone 40 mg/d is recommended; avoid long-term and high-dose glucocorticoid administration to reduce adverse effects.

11.4.2. IL-6 inhibitors: tocilizumab
For severe and critical cases with an increased level of IL-6 in laboratory testing, tocilizumab can be used for treatment. The initial dose is 4–8 mg/kg with the recommended dose of 400 mg, diluted with 0.9% sodium chloride to 100 mL. The infusion time should be >1 hour. If the initial medication is not effective, one extra administration can be given after 12 hours (same dose as before). No more than two administrations should be given with the maximum single dose no more than 800 mg. Watch out for allergic reactions. Administration of tocilizumab is prohibited for people with active infections such as tuberculosis.

11.5. Anticoagulation treatment
This is applicable for moderate, severe and critical cases with high risk factors and rapid disease progression. Low-molecular-weight heparin and unfractionated heparin are recommended in a manner of therapeutic dose for those without contraindications. When a thromboembolic event occurs, treatment should be performed according to corresponding guidelines.

11.6. Prone position treatment
Prone position treatment is recommended for moderate, severe and critical cases with high risk factors and rapid disease progression, no less than 12 hours a day.

11.7. Psychological intervention
Patients often suffer from anxiety and fear, and they should be supported by psychological counseling, supplemented by medication when necessary.

11.8. Support treatment of severe and critical cases

11.8.1. Treatment principle
On the basis of the aforementioned treatment, complications should be proactively prevented, underlying diseases should be treated, secondary infections should also be prevented, and organ function support should be provided timely.

11.8.2. Respiratory support
(i) Nasal cannulas or masks for oxygen inhalation
Severe cases with PaO2/FIO2 lower than 300 mm Hg should receive oxygen therapy immediately. The patients should be closely observed for a short time (1–2 hours) after receiving nasal cannulas or masks for oxygen inhalation. If respiratory distress and/or hypoxemia of the patient cannot be alleviated, high-flow nasal-catheter oxygenation (HFNC) or noninvasive ventilation (NIV) should be used.
(ii) HFNC or NIV
Patients with PaO2/FIO2 lower than 200 mm Hg should receive HFNC or NIV. For patients who are receiving HFNC or NIV without contraindications, prone position ventilation, namely, awake prone position ventilation, is recommended at the same time, and the treatment time in prone position should be >12 hours.
Some patients are at high risk of failure when treated with HFNC or NIV, and their symptoms and signs need to be closely monitored. If the condition does not improve after a short period of treatment (1–2 hours), especially if hypoxemia still does not improve or respiratory frequency or tidal volume is too large or respiratory effort is too strong after prone position treatment, it is likely that HFNC or NIV treatment is not effective. Invasive mechanical ventilation should be applied in time.

(iii) Invasive mechanical ventilation
In general, when PaO2/FIO2 is lower than 150 mm Hg, especially for those who have strong respiratory efforts, endotracheal intubation should be considered for invasive mechanical ventilation. However, in view of the atypical clinical manifestations of hypoxemia in patients with severe and critical COVID-19, PaO2/FIO2 should not be used as the only indication of endotracheal intubation and invasive mechanical ventilation. Real-time evaluation should be conducted based on the clinical manifestations and organ functions of patients. It is worth noting that delayed endotracheal intubation may be more harmful.

Early and appropriate invasive mechanical ventilation is an important treatment for critical cases. Pulmonary protective ventilation strategy should be used. Pulmonary retensioning is recommended for patients with moderate to severe acute respiratory distress syndrome, or when FIO2 of invasive mechanical ventilation is higher than 50%. Whether to repeatedly perform pulmonary retensioning techniques can be determined according to its reactiveness. It should be noted that some COVID-19 patients have poor reactiveness to pulmonary retensioning, and barotrauma caused by excessive positive end-expiratory pressure (PEEP) should be avoided.
(iv) Airway management
It is recommended to use an active heating humidifier for airway humidification and use a loop heating guide wire if possible to ensure the humidification effect. It is recommended to use closed sputum suction and bronchoscope suction if necessary and actively carry out airway clearance treatment, such as vibration expectoration, high-frequency thoracic oscillation, postural drainage and so on; in the case of stable oxygenation and hemodynamics,
passive and active activities should be carried out as soon as possible to promote sputum drainage and pulmonary rehabilitation.

(v) Extracorporeal membrane oxygenation (ECMO): if the outcome of protective ventilation and prone position ventilation is poor under optimal mechanical ventilation conditions ($FiO_2 \geq 80\%$, tidal volume of 6 mL/kg of ideal body weight, PEEP $\geq 5$ cm H$_2$O, and no contraindications) and one of the following indications is met, ECMO should be considered as soon as possible: a. $PaO_2/FiO_2 < 300$ mm Hg for $> 3$ hours; b. $PaO_2/FiO_2 < 80$ mm Hg for $> 6$ hours; c. Arterial blood pH $< 7.25$, $PaCO_2 > 60$ mm Hg for $> 6$ hours, and RR $> 35$ breaths/min; or d. RR $> 35$ breaths/min, arterial blood pH $< 7.2$, and platform pressure $> 30$ cm H$_2$O.

Critical cases that meet the ECMO indications and have no contraindications should start ECMO treatment as soon as possible to avoid delay in treatment and a poor prognosis.

Mode selection of ECMO: venovenous ECMO mode, which is the most frequently used mode, can be selected when only respiratory support is required; venoarterial ECMO (VA-ECMO) mode can be selected when both respiratory and circulatory support are required simultaneously; in case of brachiocephalic hypoxia during VA-ECMO, venous-arterial-venous ECMO can be applied. After the implementation of ECMO, lung protective ventilation strategy can be strictly administered. Recommended initial setup parameters are as follows: tidal volume $4-6$ mL/kg ideal body weight, platform pressure $\geq 25$ cm H$_2$O, generated pressure $< 15$ cm H$_2$O, PEEP 5–15 cm H$_2$O, RR 4–10 breaths/min, and $FiO_2 < 50\%$. Extracorporeal membrane oxygenation can be used in combination with prone ventilation for patients with difficulty in maintaining oxygenation or with strong respiratory effort, with significant consolidation of gravity-dependent region in both lungs, or requiring active secretion drainage from airways.

The cardiopulmonary compensation ability of children is weaker than for adults, and they are more sensitive to hypoxia. Therefore, more active oxygen therapy and ventilator support strategies and more relaxed indications should be applied for children than for adults. Routine application of pulmonary retensioning is not recommended.

11.8.3. Circulatory support
For critical cases complicated with shock, on the basis of adequate fluid resuscitation, vasoactive drugs should be used, and changes in blood pressure, heart rate and urine volume as well as lactate and base excess should be closely monitored. Hemodynamic monitoring should be performed when necessary.

11.8.4. Acute kidney injury and renal replacement therapy
Active efforts should be made to look for causes of acute kidney injury in critical cases, such as low perfusion and drugs. While actively eliminating the causes, the balance of fluid, acid-base and electrolyte should be maintained. The indications of continuous renal replacement therapy include the following: (a) hyperkalemia, (b) severe acidosis, and (c) pulmonary edema or water overload that does not respond to diuretics.

11.8.5. MIS-C
The treatment principle is multidisciplinary cooperation, including early anti-inflammatory management, correction of shock, correction of bleeding and coagulation dysfunction, organ function support, and anti-infection treatment when necessary. Intravenous infusion of $\gamma$-globulin (2 g/kg) shall be the first choice for MIS-C cases without shock, and methylprednisolone (1–2 mg/kg per day) or tocilizumab should be added for those without improvement. Intravenous infusion of $\gamma$-globulin combined with methylprednisolone 1–2 mg/kg per day is preferred for those with shock. Refractory severe children shall be treated with large doses of methylprednisolone (10–30 mg/kg per day) or tocilizumab.

11.8.6. Severe and critical cases in pregnancy
Multidisciplinary assessment for the risk of continuing pregnancy should be performed, and the pregnancy should be terminated preferably with cesarean section if necessary.

11.8.7. Nutritional support
Nutritional risk assessment should be strengthened. Enteral nutrition should be the first choice to ensure calories (25–30 kcal/kg per day) and protein intake (>1.2 g/kg per day), and parenteral nutrition should be added when necessary. Intestinal microecological regulators can be used to maintain intestinal microecological balance and prevent secondary bacterial infections.

11.9. Traditional Chinese medicine treatment
COVID-19 belongs to plague in traditional Chinese medicine (TCM), caused by epidemic pathogenic factors. According to the different local climate characteristics, individual state of illnesses and physical constitutions, treatment regimens should be selected referring to the following protocol. The use of over-pharmacopeial doses should be directed by a physician.

11.9.1. During medical observation
Clinical manifestation 1: fatigue with gastrointestinal discomfort
Recommended Chinese patent medicine: Huoxiang Zhengqi capsules (pills, liquid, or oral solution)
Clinical manifestation 2: fatigue with fever
Recommended Chinese patent medicines: Jinhua Qinggan granules, Lianhua Qingwen capsules (granules), Shufeng Jiedu capsules (granules)

11.9.2. During clinical treatment (confirmed cases)
(i) Qingfei Paidu decoction, Qingfei Paidu granules
Scope of application: According to the clinical observation of physicians from varied locations, it is suitable for mild, moderate and severe cases and can be used reasonably for the treatment of critically ill patients considering their actual situations.

Basic formula: Ephedrae Herba (Ma Huang) 9 g, prepared Glycyrrhizae Radix (Zhi Gan Cao) 6 g, Armeniaceae Semen (Xing Ren) 9 g, Natural Gypsum Fibrosum (Sheng Shi Gao) (decoked earlier) 15–30 g, Cinnamomi Ramulus (Gui Zhi) 9 g, Alismatis Rhizoma (Ze Xie) 9 g, Polypropus (Zhu Ling) 9 g, Atractylodis Macrocephalae Rhizoma (Bai Zhu) 9 g, Poria (Fu Ling) 15 g, Bupleuri Radix (Chai Hu) 16 g, Scutellariae Radix (Huang Qin) 6 g, Pinelliae Rhizoma Praeparatum (Jiang Ban Xia) 9 g, Zingiberis Rhizoma Recens (Sheng Jiang) 9 g, Asteris Radix (Zi Wai) 9 g, Farfarae Flos (Kuan Dong Hua) 9 g, Belamcandae Rhizoma (She Gan) 9 g, Asari Radix et Rhizoma (Xi Xin) 6 g, Dioscoreae Rhizoma (Shan Yao) 12 g, Aurantii Fructus Immaturus (Zhi Shu) 6 g, Citri Reticulatae Pericarpium (Chen Pi) 6 g, Pogostemonis Herba (Huo Xiang) 9 g.

Suggested use: traditional Chinese herbal pieces for decocting in water. One dose daily with half of the dose taken in the morning and half in the evening (40 minutes after meal) while the decoction is warm. Three doses constitute a course of treatment.

If possible, a half bowl of rice soup after taking the decoction is advised. For the patients with dry tongue due to fluid depletion, one bowl of rice soup is suggested. (Note: If no fever, the amount of Natural Gypsum Fibrosum should be little; in cases with fever or high fever, the amount can be increased.) If the symptoms improve but not totally recover, then take a second course of treatment. If the patient...
has special conditions or other underlying diseases, the prescription of the second course of treatment can be modified based on the actual situation, and the medicine should be discontinued when the symptoms disappear.

Suggested use of Qingfei Paifu granules: take after mixing it with boiled water, two bags each time, twice a day (BID); one treatment course duration lasts for 3–6 days.

(ii) Mild cases
a. Cold-dampness stagnation in lung syndrome
Clinical manifestations: fever, fatigue, sore body, cough, expectoration, chest tightness, suffocation, loss of appetite, nausea, vomiting, diarrhea and sticky stools. Tongue is pale and enlarged with teeth marks or is light red; the coating is white, thick, greasy and curdy or white and greasy; the pulse is soggy or slippery.

Recommended prescription: Hanshiyi formula

Basic formula: Raw Ephedrae Herba (Sheng Ma Huang) 6 g, Natural Gypsum Fibrosum (Sheng Shi Gao) 15 g, Armeniacae Semen (Xing Ren) 9 g, Notopterygii Rhizoma Seu Radix (Qiang Huo) 15 g, Lepidii/Descurainiae Semen (Ting Li Zi) 15 g, Cyrtomii Fructus, Jiao Bing Lang 9 g, Prepared Tsaoko Fructus, Wei Cao Guo 9 g, Arecae Semen (Bing Lang) 9 g, Prepared Crataegi Fructus, Massa Medicata Fermentata, and Hordei Fructus Germinatus (Jiao Shann Zha, Jiao Shen Qiu, and Jiao Mai Ya) 9 g each, Magnoliae Officinalis Cortex (Hou Po) 15 g, Prepared Arecae Semen (Jiao Bing Lang) 9 g, Prepared Tsaoko Fructus (Wei Cao Gao) 9 g, Zingiberis Rhizoma Recens (Sheng Jiang) 15 g.

Suggested use: one dose daily, 600 mL after decocting, taking one-third (200 mL) in the morning, afternoon and evening, respectively, before meals.

Hanshiyi formula is also applicable for moderate cases.

b. Dampness-heat accumulation in lung syndrome
Clinical manifestations: low or no fever, slight chills, fatigue, heavy head and body, muscle soreness, dry cough, sore throat, dry mouth without desire of drinking much water, or accompanied by chest tightness and gastric stuffiness, no sweat or difficulty in sweating, or vomiting and loss of appetite, diarrhea, or sticky stool. The tongue is reddish; the coating is white, thick, and greasy or thin and yellow; the pulse is slippery or soggy.

Recommended prescription: Arecae Semen (Bing Lang) 10 g, Tsaoko Fructus (Cao Guo) 10 g, Magnoliae Officinalis Cortex (Hou Po) 10 g, Anemarrhenae Rhizoma (Zhi Mu) 10 g, Scutellariae Radix (Huang Qin) 10 g, Bupleuri Radix (Chat Hu) 10 g, Paoniae Radix Rubra (Chi Shao) 10 g, Forsythiae Fructus (Lian Qiao) 15 g, Artemisiae Annuae Herba (Qing Hao) (decoced later) 10 g, Atractylodis Rhizoma (Cang Zhu) 10 g, Isatidis Folium (Da Qing Ye) 10 g, Raw Glycyrrhizae Radix (Sheng Gan Cao) 5 g.

Suggested use: one dose daily, 400 mL after decocting, take half of the dose in the morning and the other half in the evening.

Recommended Chinese patent medicine: Jinhua Qinggan granules, Lianhua Qingwen capsules (granules).

Suggested use of Jinhua Qinggan granules: take after mixing it with boiled water, one to two bags each time, three times a day (TID); one treatment course duration lasts for 5–7 days.

Suggested use of Lianhua Qingwen granule: oral administration, one bag each time, TID; one treatment course duration lasts for 7–10 days.

Suggested use of Lianhua Qingwen capsule: oral administration, four capsules each time, TID.

Recommended acupoints for acupuncture and moxibustion treatment: LI 4, SI 3, SP 9, KI 3, BL 13, BL 20. Acupuncture method: select three points at a time and apply neutral reinforcement and reduction until obtaining qi, retain needle for 30 minutes, once a day (QD).

(iii) Moderate cases

a. Dampness toxin stagnation in lung syndrome
Clinical manifestations: fever, cough and scanty sputum or yellow sputum, suffocation, shortness of breath, bloating and constipation. The tongue is dark red and enlarged; the coating is yellow and greasy or yellow and dry; the pulse is slippery and rapid or wiry and slippery.

Recommended prescription: Xuanfei Baidu formula

Basic formula: Ephedrae Herba (Ma Huang) 6 g, Fried Armeniacae Semen (Chao Ku Xing Ren) 15 g, Natural Gypsum Fibrosum (Sheng Shi Gao) 30 g, Cokisc Semen (Yi Yi Ren) 30 g, Fried Atractylodis Rhizoma (Fu Chao Cang Zhu) 15 g, Pogostemonis Herba (Guang Huo Xiang) 15 g, Artemisiae Annuae Herba (Qing Hao Cao) 12 g, Polygony Caspidati Rhizoma (Hu Zhang Polygonyi caspidati Rhizoma) 20 g, Verbenae Herba (Ma Bian Cao) 30 g, Phragmites Rhizoma (Lu Gen) 30 g, Lepidii/Descurainiae Semen (Ting Li Zi) 15 g, Citri Grandis Exocarpium (Hua Ju Hong) 15 g, Glycyrrhizae Radix (Gan Cao) 10 g.

Suggested use: one dose daily, 400 mL after decocting, take half of the dose in the morning and the other half in the evening.

Recommended Chinese patent medicine: Xuanfei Baidu granules.

Suggested use: take after mixing it with boiled water, one bag each time, BID; one treatment course duration lasts for 7–14 days, or follow the doctor’s advice.

b. Cold-dampness obstruction in lung syndrome
Clinical manifestations: low fever, unsurfaced fever or absence of fever, dry cough, scanty sputum, lassitude, chest tightness, gastric stuffiness, or nausea and loose stool. The tongue is pale or light red; the coating is white or white and greasy; the pulse is soggy.

Recommended prescription: Atractylodis Rhizoma (Cang Zhu) 15 g, Citri Reticulatae Pericarpium (Chen Pi) 10 g, Magnoliae Officinalis Cortex (Hou Po) 10 g, Pogostemonis Herba (Hu Xiang) 10 g, Tsaoko Fructus (Cao Guo) 6 g, Raw Ephedrae Herba (Sheng Ma Huang) 6 g, Notopterygii Rhizoma Seu Radix (Qiang Huo) 10 g, Zingiberis Rhizoma Recens (Sheng Jiang) 15 g, Arecae Semen (Bing Lang) 10 g.

Suggested use: one dose daily, 400 mL after decocting, take half of the dose in the morning and the other half in the evening.

c. Epidemic toxin with dryness syndrome
Clinical manifestations: aversion to cold, fever, muscular soreness, runny nose, dry cough, sore throat, itching throat, dry mouth, dry throat, constipation, light tongue with less fluid, thin-white or dry coating, floating and tight pulse.

Recommended prescription: Xuanfei Runzao Jiedu formula

Basic formula: Ma Huang (Ephedrae Herba) 6 g, Xing Ren (Armeniacae Semen) 10 g, Chai Hu (Bupleuri Radix) 12 g, Sha Shen (Adenophora stricata) 15 g, Bai Zhi (Angelicae Dahuricae Radix) 10 g, Paeoniae Radix Rubra (Chi Shao) 15 g, Forsythiae Fructus (Lian Qiao) 15 g, Artemisiae Annuae Herba (Qing Hao) (decoced later) 10 g, Atractylodis Rhizoma (Cang Zhu) 10 g, Isatidis Folium (Da Qing Ye) 10 g, Raw Glycyrrhizae Radix (Sheng Gan Cao) 5 g.

Suggested use: one dose daily, 400 mL after decocting, take half of the dose in the morning and the other half in the evening.

Recommended Chinese patent medicine: Jinhua Qinggan granules, Lianhua Qingwen capsules (granules).

Suggested use of Jinhua Qinggan granules: take after mixing it with boiled water, one to two bags each time, three times a day (TID); one treatment course duration lasts for 5–7 days.

Suggested use of Lianhua Qingwen granule: oral administration, one bag each time, TID; one treatment course duration lasts for 7–10 days.

Suggested use of Lianhua Qingwen capsule: oral administration, four capsules each time, TID.

Recommended acupoints for acupuncture and moxibustion treatment: LI 4, SI 3, SP 9, KI 3, BL 13, BL 20. Acupuncture method: select three points at a time and apply neutral reinforcement and reduction until obtaining qi, retain needle for 30 minutes, once a day (QD).
Suggested use of Lianhua Qingwen capsules: oral administration, four capsules each time, TID.

Recommended acupoints for acupuncture and moxibustion treatment: PC 6, LU 6, LI 11, CV 6, SP 9, CV 12. Acupuncture method: select three points at a time and apply neutral reinforcement and reduction until obtaining qi, retain needle for 30 minutes, QD.

(iv) Severe cases
a. Epidemic toxin blocking in lung syndrome
Clinical manifestations: fever, flushing, cough, scanty yellowish sputum or blood in sputum, wheezing, shortness of breath, tiredness, fatigue, dryness and bitterness, as well as stickiness in the mouth, nausea, loss of appetite, constipation and scanty dark urine. The tongue is red; the coating is yellow and greasy; the pulse is slippery and rapid.

Recommended prescription: Huashi Baidu formula

Basic formula: Raw Ephedrae Herba (Sheng Ma Huang) 6 g, Arseniicis Semen (Xing Ren) 9 g, Natural Gypsum Fibrosum (Sheng Shi Gao) 15 g, Glycyrrhizae Radix (Gan Cao) 3 g, Pogostemonis Herba (Huo Xiang) (decocted later) 10 g, Magnoliaceae Officinalis Cortex (Hou Po) 10 g, Atractylodis Macrocephala Radix (Zhi Huang Qi) 30 g, Prepared Atractylodis Macrocephala Radix Rubra (Chi Shao) 30 g, Scrophulariae Radix (Xuan Shen) 30 g, Forsythiae Fructus (Lian Qiao) 15 g, Moutan Cortex (Dan Pi) 15 g, Coptidis Rhizoma (Huang Lian) 6 g, Phyllostachys Nigrae Forsythiae Fructus (Lian Qiao) 15 g, Moutan Cortex (Dan Pi) 10 g, Paeoniae Radix (Sheng Huang Qi) 10 g, Lepidii/Descurainiae Semen (Ting Li Zi) 15 g, Poria (Fu Ling) 15 g, Raw Rhei Radix Praeparatum (Fa Ban Xia) 9 g, Poria (Fu Ling) 15 g, Raw Rhei Radix et Rhizoma (Sheng Da Huang) (decocted later) 5 g, Raw Astragali Radix (Sheng Huang Qi) 10 g, Lepidii/Descurainiae Semen (Ting Li Zi) 10 g, Paeoniae Radix Rubra (Chi Shao) 10 g.

Suggested use: one or two doses daily, decocting in water, take the dose(s) two to four times across the day, 100–200 mL each time, oral administration or nasal feeding.

b. Blazing of both qi and yin syndrome
Clinical manifestations: high fever, thirst, shortness of breath, delirium and unconsciousness, blurred vision, or spotted rash, or hematemesis, epistaxis, or convulsions in the limbs. The tongue is crimson with little or no coating. The pulse is deep, thready and rapid, or hollow and rapid.

Recommended prescription: Natural Gypsum Fibrosum (Sheng Shi Gao) (decocted earlier) 30–60 g, Anemarrhenae Rhizoma (Zhi Mu) 30 g, Raw Rehmanniae Radix (Sheng Di) 30–60 g, Bubali Cornu (Shui Niu Jiao) (decocted earlier) 30 g, Paonieae Radix Rubra (Chi Shao) 30 g, Scrophulariae Radix (Xuan Shen) 30 g, Forsythiae Fructus (Lian Qiao) 15 g, Moutan Cortex (Dan Pi) 15 g, Coptidis Rhizoma (Huang Lian) 6 g, Phyllostachys Nigrae Forsythiae Fructus (Zhu Ye) 12 g, Lepidii/Descurainiae Semen (Ting Li Zi) 15 g, Raw Glycyrrhizae Radix (Sheng Gan Cao) 6 g.

Suggested use: one dose per day, Raw Glycyrrhizae Radix and Bubali Cornu decocted earlier and other pieces decocted later, decoct in water, take the dose(s) two to four times across the day, 100–200 mL each time, oral administration, or nasal feeding.

Recommended Chinese patent medicines: Xiyinping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection. Drugs with similar efficacy can be selected according to individual conditions or can be used in combination according to clinical symptoms. Traditional Chinese medicine injection can be used in combination with TCM decoction.

Recommended acupoints for acupuncture and moxibustion treatment: Gv 14, Bl 13, Bl 20, KI 3, Lu 7, Lr 3. Acupuncture method: select three to five points at a time, combine back points and limb points, and apply neutral reinforcement and reduction, retain needle for 30 minutes, QD.

(v) Critical cases

a. Lung-spleen qi deficiency syndrome
Clinical manifestations: shortness of breath, fatigue, anorexia, nausea, vomiting, abdominal stuffiness and fullness, uneasiness of defecation and loose stool with sensation of incomplete defecation. The tongue is pale and enlarged, and the coating is white and greasy.

Recommended prescription: Sinensis Rhizoma Praeparatum (Fa Ban Xia) 9 g, Citri Reticulatae Pericarpium (Chen Pi) 10 g, Codonopsis Radix (Dang Shen) 15 g, Prepared Astragali Radix (Zhi Huang Qi) 30 g, Prepared Atractylodis Macrocephalae Rhizoma (Chao Bai Zhu) 10 g, Poria (Fu Ling) 15 g, Pogostemonis Herba (Huo Xiang) 10 g, Amomum Fructus (Sha Ren) (decocted later) 6 g, Glycyrrhizae Radix (Gan Cao) 6 g.

Suggested use: one dose per day, 400 mL after decocting, take half of the dose in the morning and the other half in the evening.

b. Deficiency of both qi and yin syndrome
Clinical manifestations: fatigue, shortness of breath, dry mouth, thirst, palpitations, profuse sweating, poor appetite, low or no fever, dry cough with little sputum, dry tongue with scanty fluid and thin or feeble and forceless pulse.

Recommended prescription: Adenophorae Radix (Nan Sha Shen) 10 g, Glehniae Radix (Bei Sha Shen) 10 g, Ophiopogonis Radix (Mai Dong) 15 g, Panacis quinquefolii Radix (Xi Yang Shen) 6 g, Schisandrae Fructus (Wu Wei Zi) 6 g, Natural Gypsum Fibrosum (Sheng Shi Gao) 15 g, Lophatheri Herba (Dan Zhu Ye) 10 g, Mori Foliolum (Sang Ye)
10 g, Phragmitis Rhizoma (Lu Gen) 15 g, Salviae Miltiorrhizae Radix (Dan Shen) 15 g, Raw Glycyrrhiza Radix (Sheng Gan Cao) 6 g. Suggested use: one dose per day, 400 mL after decocting, take half of the dose in the morning and the other half in the evening.

Recommended acupuncture points for acupuncture and moxibustion treatment: ST 36 (moxibustion), GV 20, KI 3. Acupuncture method: select the aforementioned points and apply neutral reinforcement and reduction, retain needle for 30 minutes, QD. Point selection of indirect moxibustion: GV 14, BL 13, BL 20, LU 6, moxibustion for 40 minutes each time, QD.

11.9.3. Chinese medicine treatment for pediatric patients
The characteristics of TCM syndromes and the core pathogenesis for pediatric patients are basically the same as those for adults. The TCM treatment plan for adults can be referred to and used according to the syndrome differentiation, combined with the clinical symptoms and physiological characteristics of pediatric patients. Chinese patent medicines can be chosen and differentially used for pediatric patients.

11.10. Early rehabilitation
Attention should be paid to early rehabilitation intervention of patients, and rehabilitation training and intervention should be actively carried out for COVID-19 patients with respiratory, physical and psychological disorders, to restore physical ability, constitution and immunity as much as possible.

12. Nursing
Identify the priorities of nursing and do basic nursing well according to the patient’s condition. In severe cases, patients’ vital signs and consciousness should be closely monitored, with emphasis on blood oxygen saturation. Continuous 24-hour electrocardiogram monitoring shall be performed for critical cases, with the heart rate, RR, blood pressure and SpO2 measured hourly, and the body temperature measured and recorded every 4 hours. Venous channel should be used rationally and correctly, and all kinds of tubing should be kept clear and properly fixed. Sickbed patients should change their position regularly to prevent stress injury. Those undergoing noninvasive mechanical ventilation, invasive mechanical ventilation, artificial airway, prone ventilation, sedation and analgesia, or ECMO treatment should receive care according to the nursing standards. Special attention should be paid to oral care and fluid intake and output volume management for patients with invasive mechanical ventilation to prevent aspiration. The psychological state of conscious patients should be assessed in time, and psychological nursing should be provided.

13. Criteria for ending isolation management and discharge and considerations for ending isolation and postdischarge management

13.1. Criteria for ending isolation management
For mild cases, Ct values for the N gene and Orf gene are ≥35 (fluorescence quantitative PCR method, cutoff value at 40, sampling interval ≥24 hours) in two consecutive SARS-CoV-2 nucleic acid tests, or nucleic acid tests are negative twice consecutively on respiratory tract samples (fluorescence quantitative PCR method, cutoff value <35, sampling interval ≥24 hours).

13.2. Discharge criteria
(i) Body temperature is back to normal for >3 days;
(ii) Respiratory symptoms improve obviously;
(iii) Pulmonary imaging shows obvious absorption of acute exudative inflammation;
(iv) Ct values for the N gene and Orf gene are ≥35 (fluorescence quantitative PCR method, cutoff value at 40, sampling interval ≥24 hours) in two consecutive nucleic acid tests, or nucleic acid tests are negative twice consecutively on respiratory tract samples (fluorescence quantitative PCR method, cutoff value <35, sampling interval ≥24 hours).

Those who meet the aforementioned criteria are allowed to discharge.

13.3. Considerations for ending isolation and postdischarge management
After ending isolation or discharge, it is recommended for patients to monitor their own health status at home for 7 days, wear a mask, live in a well-ventilated single room if possible, minimize close contacts with family members, separate dining, practice hand hygiene and avoid going out.

14. Patient transfer principles
Patients should be transferred in accordance with the Work Protocol for Transfer of the COVID-19 Patients (Second Version) issued by the Medical Treatment Group under the Joint Prevention and Control Mechanism of the State Council in Response to the Novel Coronavirus Pneumonia.

15. Nosocomial infection prevention and control
Measures to prevent and control nosocomial infection should be implemented in accordance with the requirements of the Technical Guidelines for the Prevention and Control of Infection by the SARS-CoV-2 in Medical Institutions (Third Edition) formulated by the National Health Commission.

16. Prevention
16.1. SARS-CoV-2 vaccination
SARS-CoV-2 vaccination can reduce the SARS-CoV-2 infection and morbidity, which is an effective means to reduce the incidence of severe illness and death. Anyone who meets the requirements should be vaccinated. Anyone who is eligible for strengthened immunization should be vaccinated timely for boosting immunization.

16.2. General precautions
Maintain a good personal and environmental hygiene, keep a balanced diet, get proper exercise and adequate rest, and avoid over fatigue. Improve health literacy and develop good hygienic habits and lifestyles, such as keeping “1-meter distance,” washing hands frequently, wearing masks, using communal chopsticks, and covering mouth and nose when coughing or sneezing. Keep indoor ventilation and apply scientific personal protection. Visit the fever clinic for medical treatment in time when having respiratory symptoms. For those who have recently traveled to high-risk areas or have a contact history with confirmed or suspected cases, nucleic acid tests should be carried out on their own initiative.

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