Guidance for Corona Virus Disease

Prevention, Control, Diagnosis and Management

Edited by
National Health Commission (NHC) of the PRC
National Administration of Traditional Chinese Medicine of the PRC

Compiled and Translated by
Chinese Preventive Medicine Association

Translators in Chief
Xiaofeng LIANG Zijian FENG Liming LI

PEOPLE'S MEDICAL PUBLISHING HOUSE

WHO COLLABORATION CENTRE FOR HEALTH INFORMATION AND PUBLISHING

Book edited by Daniel Weber PhD, DSc

Characteristics of Coronavirus Pathogens

The coronavirus subfamilies are categorized into four genera: α , β , γ , and δ . Coupled with this newly discovered coronavirus, seven types of coronaviruses are known to infect humans. Most coronaviruses cause upper respiratory tract infections, but Middle East respiratory syndrome coronavirus (MERSr-CoV), severe acute respiratory syndrome associated coronavirus (SARSr-CoV) and novel coronavirus 2019 (2019-nCoV) can cause mild and even severe pneumonia, and can be transmitted from person to person.

The 2019-nCoV belongs to the genus β coronavirus and has distinct genetic characteristics from SARSr-CoV and MERSr-CoV. Coronaviruses are sensitive to ultraviolet rays and heat, and can be effectively inactivated when environmental temperature is 56 °C and lasts for 30 min, and lipid solvents such as ether, 75% ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except chlorhexidine.

Based on current epidemiological investigations, the incubation period of COVID-19 is 1 to 14 days, and generally within 3 to 7 days. At present, the major source of infection is the COVID-19 patients, and asymptomatic 2019-nCoV carriers can also be the source of infection. The main routes of transmission are respiratory droplets and contact, while aerosol and fecal-oral transmission routes are yet to be verified. Humans of all ages are generally susceptible.

Epidemiological Characteristics

The source of infection is changed to "The major source of infection currently is the patients with COVID-19, and asymptomatic 2019-nCoV carriers can also be the source of infection".

Clinical Manifestations

Based on current epidemiological investigations, the incubation period of COVID-19 is ranged between 1 to 14 days, and generally within 3 to 7 days.

Fever, fatigue and dry coughing are considered the main clinical manifestations, but symptoms such as stuffy nose, runny nose, pharyngalgia, myalgia and diarrhea are relatively less common. In severe cases, dyspnea and/or hypoxemia usually occurs after one week of disease onset, and the worse can rapidly progresses to acute respiratory distress syndrome, septic shock, metabolic acidosis hard to correct, and hemorrhage and coagulation dysfunction, multiple organ failure, etc. It's worth noting that patients with severe or critical illness may have a moderate to low fever, or no fever at all.

Mild cases only present with light fever, mild fatigue and so on without manifestation of pneumonia.

From the cases treated currently, most of the patients have a favorable prognosis. The elderly and people with chronic underlying diseases usually have poor prognosis while cases with relatively mild symptoms are common in children.

In terms of laboratory examination, this edition adds the following descriptions, "Increased values of liver enzymes, LDH, muscle enzymes and myoglobin can occur in some patients; and raised level of troponin can be seen in some critical patients" and "The nucleic acid of 2019-nCoV can be detected in biological specimens such asnasopharyngeal swabs, sputum, secretions of lower respiratory tract, blood and feces".

Chest Imaging. In the early stage of COVID-19, the images show that there are multiple small patched shadows and interstitial changes, especially in the lung periphery. As the disease progresses, the images of these patients further develop into multiple ground glass

shadows and infiltration shadows in both lungs. In severe cases, lung consolidation may occur. It is seldom to find pleural effusion in patients with COVID-19.

Differential Diagnosis

The mild manifestations caused by COVID-19 should be distinguished from respiratory infections caused by other viruses.

Treatment - Determine the Treatment Place According to the Severity of the Disease Suspected and confirmed cases should be isolated and treated in designated hospitals with effective isolation and protective conditions. Suspected cases should be treated in single rooms, while confirmed cases can be admitted to the same ward. Critical cases should be admitted to ICU as soon as possible.

General Treatment

Rest patients in bed, strengthen supportive treatment, and ensure adequate nutrition. Keep the balance of water and electrolyte to maintain the stability of the internal environment. Closely monitor vital signs, oxygen saturation, etc.

Monitor blood routine, urine routine, CRP, biochemical indicators (liver enzyme, myocardial enzyme, renal function, etc.), coagulation function, arterial blood gas analysis, chest imaging, etc. according to the patient's condition. If possible, cytokine testing should be conducted. Give effective oxygen therapy measures in time, including nasal cannula, mask oxygen, high-flow nasal oxygen therapy.

Antiviral Treatment: Give alpha-interferon nebulization (5 million units or equivalent per time for adult, add 2 mL of sterile water for injection, aerosol inhalation twice per day); lopinavir/ritonavir (200 mg/50 mg per capsule, 2 capsules each time, twice per day for adults, the course of treatment should be ≤ 10 days); ribavirin (combining with interferon or lopinavir/ritonavir are recommended, 500 mg for adults per time, inject 2–3 times per day intravenously, the course of treatment should be ≤ 10 days). Chloroquine phosphate (500 mg for adult, twice per day, the course of treatment should be ≤ 10 days), Arbidol (200 mg for adults, three times per day, the course of treatment should be ≤ 10 days). Keep alert on side effects such as diarrhea, nausea, vomiting, and liver damage related to lopinavir/ ritonavir, as well as harmful interaction with other drugs. Effects of current trial drugs should be further evaluated during clinical usage. Simultaneously use of three or more types of antiviral drugs is not recommended and relevant drug treatment should stop if unbearable side effects occur. Antibacterial Drug Treatment: unselective or inappropriate use of antibiotics should be avoided, especially in combination with broad- spectrum antibiotics.

Treatment of Severe and Critical Cases

Treatment Principles: On the basis of symptomatic treatment, actively prevent complications, treat accompanying diseases, prevent secondary infections, and provide organ function support in time.

Respiratory Support

Oxygen Therapy: Severe patients should be provided inhalation oxygen with facemask or nasal catheter. Timely assess whether respiratory distress and/or hypoxemia are relieved. High-Flow Nasal Catheter Oxygen Therapy or Non-Invasive Mechanical Ventilation: When respiratory distress and/or hypoxemia cannot be relieved after standard oxygen therapy, high-flow nasal catheter oxygen therapy or noninvasive ventilation should be considered. If the condition does not improve or even worsen within a short period of time (1–2 hours), endotracheal intubation and invasive mechanical ventilation should be performed promptly.

Invasive Mechanical Ventilation: Use lung protective ventilation strategies, which means small tidal volume (4–8 mL/kg ideal weight) and low inspiratory pressure (platform pressure <30 cmH2O) for mechanical ventilation to reduce ventilator-related lung injuries. For several patients, human-machine synchronization is not available, and sedative and muscle relaxants should be used in time.

Salvage Treatment: For patients with severe ARDS, it is recommended to perform lung expansion. If possible, prone position ventilation should be performed for more than 12 hours per day. For those with poor prone position ventilation, extracorporeal membrane oxygenation (ECMO) should be considered as soon as possible if conditions permit. Circulation Support: On the basis of adequate fluid resuscitation, improve microcirculation, use vasoactive drugs, and perform hemodynamic monitoring when necessary. Convalescent plasma therapy: suitable for treating rapidly developed cases, severe cases and critical cases. Administrations and dosage refer to Clinical Plasma Therapy Plan for Corona Virus Disease 2019 Convalescents during Recovery (Tentative First Edition).

Other Treatments

According to the severity of respiratory distress and the progress of chest imaging, glucocorticoids can be used within a short period of time (3–5 days) as appropriate. Dose does not exceed the equivalent of 1–2 mg/ kg/day of methylprednisolone is recommended. It should be noted that higher doses of glucocorticoids would delay coronavirus clearance due to immunosuppressive effects; Xuebijing Injection (a traditional Chinese medicine) can be given intravenously 100 mL/day, twice a day for treatment; microecological preparation can be used to keep the equilibrium for intestinal microecology and prevent secondary bacterial infection; Plasma exchange, adsorption, perfusion, blood/plasma filtering and other extracorporeal blood purification technologies should be considered if possible for critical cases with severe inflammatory reactions.

Anxiety and fear usually occur in many patients, therefore psychological counseling should be strengthened.

Traditional Chinese Medicine Treatment

COVID-19 can also be treated with traditional Chinese medicine, which considers it caused by epidemic pathogenic factors located in the lungs. Different regions can refer to the following schemes for dialectical treatment according to the disease condition, local climate characteristics, and different physical conditions. Use drugs under the guidance of doctors if the dose of drug exceeds the pharmacopoeia.

Clinical Treatment Period (For Confirmed Cases) Lung-Clearing and Detoxification Soup

Application Scope: suitable for mild, general and severe cases; reasonable for treating critical cases according to clinical symptoms.

Basic Prescription: Herba Ephedrae 9 g, roasted Radix Glycyrrhizae 6 g, Semen Armeniacae Amarum 9 g, raw Gypsum Fibrosum 15–30 g (decocted first), Ramulus Cinnamomi 9 g, Rhizoma Alismatis 9 g, Polyporus Umbellatus 9 g, Rhizoma Atractylodis Macrocephalae 9 g, Poria 15 g, Radix Bupleuri 16 g, Radix Scutellariae 6 g, Rhizoma Pinelliae Preparata 9 g, Rhizoma Zingiberis Recens 9 g, Radix Asteris 9 g, Flos Farfarae 9 g, Rhizoma Belamcandae 9 g, Herba Asari 6 g, Rhizoma Dioscoreae 12 g, Fructus Aurantii Immaturus 6 g, Pericarpium Citri

Reticulatae 6 g, Herba Pogostemonis 9 g.

Mild Type

1) Cold Dampness Stagnating Lungs

Clinical Manifestations: fever, fatigue, soreness, coughing, expectoration, chest tightness, suffocation, nausea, vomiting and sticky stools. Pale or red tongue with fat tooth marks, moss white thick rotten or greasy fur, and soft and floating or slippery pulse.

Recommended Prescription: Raw Herba Ephedrae 6 g, raw Gypsum Fibrosum 15 g, Semen Armeniacae Amarum 9 g, Rhizoma et Radix Notopterygii 15 g, Semen Lepidii 15 g, Rhizoma Cyrtomii 9 g, Lumbricus 15 g, Radix Cynanchi Paniculati 15 g, Herba Pogostemonis 15 g, Herba Eupatorii 9 g, Rhizoma Atractylodis 15 g, Poria 45 g, raw Rhizoma Atractylodis Macrocephalae 30 g, charred Fructus Hordei Germinatus, charred Fructus Crataegi and charred Massa Medicata Fermentata 9 g each, Cortex Magnoliae Officinalis 15 g, charred Semen Arecae 9 g, Fructus Tsaoko 9 g, Rhizoma Zingiberis Recens 15 g.

Administrations and Dosage: One dose per day, decocted with 600 mL water, taken in the morning, noon and evening respectively before meals.

2) Damp-Heat Accumulated Lung

Clinical Manifestations: low fever or normal body temperature, slight chills alternate, head and body heaviness, muscle soreness, dry cough and less sputum, sore throat, dry mouth and no desire to drink, or chest tightness, epigastric fullness, no sweat or unsmooth sweating, or vomiting, nausea, loose stool or constipation. Pale or red tongue with white, thick, greasy or thin yellow fur, and smooth or moist pulse.

Recommended Prescription: Semen Arecae 10 g, Fructus Tsaoko 10 g, Cortex Magnoliae Officinalis 10 g, Rhizoma Anemarrhenae 10 g, Radix Scutellariae 10 g, Radix Bupleuri 10 g, Radix Paeoniae Rubra 10 g, Fructus Forsythiae 15 g, Herba Artemisiae Annuae 10 g (decocted later), Rhizoma Atractylodis 10 g, Folium Isatidis 10 g, raw Radix Glycyrrhizae 5 g.

Administrations and Dosage: One dose per day, decocted with 400 mL water, taken once in the morning and once in the evening.

General Type

1) Damp-Poison Stagnating Lung

Clinical Manifestations: fever, cough with less sputum or yellow

sputum, chest tightness, shortness of breath, abdominal distension. Dark red and fat tongue with yellow greasy or dry fur, rapid and/or slippery pulses.

Recommended Prescription: raw Herba Ephedrae 6 g, Semen Armeniacae 12

Amarum 15 g, raw Gypsum Fibrosum 30 g, raw Semen Coicis 30 g, Rhizoma Atractylodis 10 g, Herba Pogostemonis 15 g, Herba Artemisiae Annuae 12 g, Rhizoma Polygoni Cuspidati 20 g, Herba Verbenae 30 g, Dry Rhizoma Phragmitis 30 g, Semen Lepidii 15 g, Exocarpium Citri Grandis 15 g, Radix Glycyrrhizae 10 g.

Administrations and Dosage: one dose per day, decocted with 400 ml water, taken once in the morning and once in the evening.

2) Cold Dampness Obstructing Lung

Clinical Manifestations: Low fever, hiding fever, or no fever, dry cough, little sputum, fatigue, chest tightness, nausea, or vomiting, loose stools. Pale or red tongue, white greasy fur, soft and floating pulse.

Recommended Prescription: *Rhizoma Atractylodis* 15 g, *Pericarpium Citri Reticulatae* 10 g, *Cortex Magnoliae Officinalis* 10 g, *Herba Pogostemonis* 10 g, *Fructus Tsaoko* 6 g, *raw*

Herba Ephedrae 6 g, Rhizoma et Radix Notopterygii 10 g, Rhizoma Zingiberis Recens 10 g, Semen Arecae 10 g.

Administrations and Dosage: One dose per day, decocted with 400 mL water, taken once in the morning and once in the evening.

Severe Type

1) Lung Blocked by Epidemic Toxin

Clinical Manifestations: fever, flushing, cough, less yellow sticky sputum with or without blood, wheezing and shortness of breath, fatigue, bitter and sticky dry mouth, nausea with anorexia, poor stool movements, less brown urine. Red tongue with yellow greasy, slippery pulse.

Recommended Prescription: Raw Herba Ephedrae 6 g, Semen Armeniacae Amarum 9 g, Gypsum Fibrosum 15 g, Radix Glycyrrhizae 3 g, Herba Pogostemonis 10 g (decocted later), Cortex Magnoliae Officinalis 10 g, Rhizoma Atractylodis 15 g, Fructus Tsaoko 10 g, Rhizoma Pinelliae Preparatum 9 g, Poria 15 g, raw Radix et Rhizoma Rhei 5 g (decocted later), raw Radix Astragali seu Hedysari 10 g, Semen Lepidii 10 g, Radix Paeoniae Rubra 10 g.

Administrations and Dosage: One or two doses per day, decocted with 100–200 mL water, taken 2–4 times a day, oral or nasal feeding.

2) Flaring Heat in Qi and Ying

Clinical Manifestations: severe fever and polydipsia, dyspnea and anhelation, delirium, blurred vision, rash, or hematemesis and epistaxis, or convulsion of the limbs. Tongue with little or no fur, deep and count pulse, or large and rapid pulse.

Recommended Prescription: Raw *Gypsum Fibrosum* 30–60 g (decocted first), *Rhizoma Anemarrhenae* 30 g, *Radix Rehmanniae* 30–60 g, *Cornu Bubali* 30 g (decocted first), *Radix Paeoniae Rubra* 30 g, *Radix Scrophulariae* 30 g, *Fructus Forsythiae* 15 g, *Cortex Moutan* 15 g, *Rhizoma Coptidis* 6 g, *Folium Phyllostachydis Henonis* 12 g, *Semen Lepidii* 15 g, *Radix Glycyrrhizae* 6 g.

Administrations and Dosage: One dose per day, decocted with 100 mL to 200 mL water, decoct Gypsum Fibrosum and Cornu Bubali firstly, taken 2 to 4 times per day, oral or nasal feeding.

Recommend Chinese Medicine: Xiyanping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection. Drugs with similar effects may be selected according to individual conditions or may be used jointly according to clinical symptoms. Traditional Chinese medicine injection can be used in combination with decoction.

Critical Type (Internal Block and Outward Desertion)

Clinical Manifestations: dyspnea, asthma requires assisted ventilation, dizziness, irritability, cold sweaty limbs, purple tongue, thick or dry fur, large floating and rootless pulse. Recommended Prescription: *Radix Ginseng* 15 g, *Radix Aconiti Lateralis Preparata*10 g (decocted first), *Fructus Corni* 15 g, drinking with Suhexiang Pills or Angong Niuhuang Pills.

Recommended Chinese Medicine: Xuebijing Injection, Reduning Injection, Tanreqing Injection, Xingnaojing Injection, Shenfu Injection, Shengmai Injection 1, Shengmai Injection 2. Drugs with similar effects may be selected according to individual conditions or may be used jointly according to clinical symptoms. Traditional Chinese medicine injection can be used in combination with decoction.

Notes: Recommended Usage of Traditional Chinese Medicine Injections for Severe and Critical Cases

The use of traditional Chinese medicine injections should follow the principle of starting with low dose and modifying gradually and dialectically according to the drug instructions. The recommended usage is as follows:

Viral Infection or Combined with Mild Bacterial Infection: 0.9% Sodium Chloride Injection 250 mL and Xiyanping Injection 100 mg bid, or 0.9% Sodium Chloride Injection 250 mL and Reduning Injection 20 mL, or 0.9% Sodium Chloride Injection 250 mL and Tanreqing Injection 40 mg bid.

Severe Fever with Consciousness Disturbance: Xingnao Injection 20 mL and 0.9% Sodium Chloride Injection 250 mL, bid, twice daily.

Systemic Inflammatory Response Syndrome (SIRS) and/or multiple organ failure: Xuebijing Injection 100 mL and 0.9% Sodium Chloride Injection 250 mL, bid, twice daily.

Immunosuppression: Shengmai Injection 100 mL and 0.9% Sodium

Chloride Injection 250 mL, bid, twice daily.

Shock: Shenfu Injection 100 mL and 0.9% Sodium Chloride Injection

250 mL, bid, twice daily.

Recovery Period

1) Lung Deficiency and Spleen Qi

Clinical Manifestations: shortness of breath, tiredness, anorexia,

distention and fullness, constipation, loose stool, pale tongue, whitish greasy fur.

Recommended Prescription: *Rhizoma Pinelliae Preparatum* 9 g, *Pericarpium Citri Reticulatae* 10 g, *Radix Codonopsis* 15 g, roasted *Radix Astragali seu Hedysari* 30 g, roasted *Rhizoma Atractylodis Macrocephalae* 10 g, *Poria* 15 g, *Herba Pogostemonis* 10 g, *Fructus Amomi Villosi* 6 g (decocted later), *Radix Glycyrrhizae* 6 g.

Administrations and Dosage: One dose per day, decocted with 400 mL water, take once in the morning and once in the evening.

2) Deficiency of Qi and Yin

Clinical Manifestations: fatigue, shortness of breath, dry mouth, thirst, hyperhidrosis, anorexia, low fever or no fever, dry cough, less sputum, dry tongue, thin or weak pulse. Recommended Prescription: *Radix Adenophorae* 10 g, *Radix Glehniae* 10 g, *Radix Ophiopogonis* 15 g, *Radix Panacis Quinquefolii* 6 g, *Fructus Schisandrae Chinensis* 6 g, raw *Gypsum Fibrosum* 15 g, *Herba Lophatheri* 10 g, *Folium Mori* 10 g, *Rhizoma Phragmitis* 15 g, *Radix Salviae Miltiorrhizae* 15 g, *Radix Glycyrrhizae* 6 g.

Administrations and Dosage: One dose per day, decocted with 400 mL water, intake once in the morning and once in the evening.

Release of isolation should meet with the following four standards

- 1) Having normal body temperature for more than 3 days;
- 2) With significantly recovered respiratory symptoms;
- 3) Lung imaging shows obvious absorption and recovery of acute exudative lesion;
- 4) With negative results of the nucleic acid tests of respiratory pathogens for consecutive twice (sampling interval at least 1 day).