
Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 6, Revised)

Since December 2019, multiple cases of novel coronavirus pneumonia (NCP) have been identified in Wuhan, Hubei. With the spread of the epidemic, such cases have also been found in other parts of China and abroad. As an acute respiratory infectious disease, NCP has been included in class B infectious diseases prescribed in the Law of the People's Republic of China on Prevention and Treatment of Infectious Diseases, and managed as an infectious disease of class A. With a better understanding of the epidemic and accumulation of diagnosis and treatment experience, we now release the *Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 6)*, which is based on the fifth trial version.

I. Etiological Characteristics

The novel coronaviruses belong to the β genus. They have envelopes, and the particles are round or oval, often polymorphic, with diameter being 60 to 140 nm. Their genetic characteristics are significantly different from SARS-CoV and MERS-CoV. Current research shows that they share more than 85% homology with bat SARS-like coronaviruses (bat-SL-CoVZC45). When isolated and cultured in vitro, the 2019-nCoV can be found in human respiratory epithelial cells in about 96 hours, however it takes about 6 days for the virus to be found if isolated and cultured in Vero E6 and Huh-7 cell lines.

Most of the know-how about the physical and chemical properties of coronavirus comes from the research on SARS-CoV and MERS-CoV. The virus is sensitive to ultraviolet and heat. Exposure to 56°C for 30 minutes and lipid solvents such as ether, 75% ethanol, chlorine-containing disinfectant, peracetic acid, and chloroform can effectively inactivate the virus. Chlorhexidine has not been effective in inactivating the virus.

II. Epidemiological Characteristics

1. Source of infection

Now, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source.

2. Transmission

Transmission of the virus happens mainly through respiratory droplets and close contact. There is the possibility of aerosol transmission in a relatively closed environment for a long time exposure to high concentrations of aerosol.

3. Susceptible groups

People are generally susceptible.

III. Clinical Characteristics

1. Clinical manifestations

Based on the current epidemiological investigation, the incubation period is one to 14 days, mostly three to seven days. Main manifestations include fever, fatigue and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases. Severe cases mostly developed dyspnea and/or hypoxemia after one week. In severe cases, patients progress rapidly to acute respiratory distress syndrome, septic shock, metabolic acidosis that is difficult to correct, coagulopathy, multiple organ failure and others. It is worth noting that for severe and critically ill patients, their fever could be moderate to low, or even barely noticeable.

The patients with mild symptoms did not develop pneumonia but only low fever and mild fatigue.

From current situations, most patients have good prognosis and a small number of patients are critically ill. The prognosis for the elderly and patients with chronic underlying diseases is poor. Children's symptoms are relatively mild.

2. Laboratory tests

In the early stages of the disease, peripheral WBC count is normal or decreased and the lymphocyte count decreases. Some patients see an increase in liver enzymes, lactate dehydrogenase (LDH), muscle enzymes and myoglobin. Elevated troponin is seen in some critically ill patients while most patients have elevated C-reactive protein and erythrocyte sedimentation rate and normal procalcitonin. In severe cases, D-dimer increases and peripheral blood lymphocytes progressively decrease. Severe and critically ill patients often have elevated inflammatory factors.

Novel coronavirus nucleic acid can be detected in nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces and other specimens. In order to increase the positive rate of nucleic acid detection, it is recommended to take as much sputum as possible, while lower respiratory tract secretions of patients undergoing tracheal intubation

should be collected, and the specimens should be submitted for examination as soon as possible after collection.

3. Chest imaging

In the early stage, imaging shows multiple small patchy shadows and interstitial changes, apparent in the outer lateral zone of lungs. As the disease progresses, imaging then shows multiple ground glass opacities and infiltration in both lungs. In severe cases, pulmonary consolidation may occur while pleural effusion is rare.

IV. Case Definitions

1. Suspect cases

Considering both the following epidemiological history and clinical manifestations:

1.1 Epidemiological history

1.1.1 History of travel to or residence in Wuhan and its surrounding areas, or in other communities where cases have been reported within 14 days prior to the onset of the disease;

1.1.2 In contact with novel coronavirus infected people (with positive results for the nucleic acid test) within 14 days prior to the onset of the disease;

1.1.3 In contact with patients who have fever or respiratory symptoms from Wuhan and its surrounding area, or from communities where confirmed cases have been reported within 14 days before the onset of the disease; or

1.1.4 A cluster of cases.

1.2 Clinical manifestations

1.2.1 Fever and/or respiratory symptoms;

1.2.2 The aforementioned imaging characteristics of NCP;

1.2.3 Normal or decreased WBC count and decreased lymphocyte count in the early stage of onset.

A suspect case has any of the epidemiological history plus any two clinical manifestations or all three clinical manifestations if there is no clear epidemiological history.

2. Confirmed cases

Suspect cases with one of the following etiological evidence:

2.1 Real-time fluorescent RT-PCR indicates positive for new coronavirus nucleic acid;

2.2 Viral gene sequence is highly homologous to known new coronaviruses.

V. Clinical Classification

1. Mild cases

The clinical symptoms were mild, and there was no sign of pneumonia on imaging.

2. Moderate cases

Showing fever and respiratory symptoms with radiological findings of pneumonia.

3. Severe cases

Cases meeting any of the following criteria:

3.1 Respiratory distress (≥ 30 breaths/ min);

3.2 Oxygen saturation $\leq 93\%$ at rest;

3.3 Arterial partial pressure of oxygen (PaO_2)/ fraction of inspired oxygen (FiO_2) $\leq 300\text{mmHg}$ (1 mmHg=0.133kPa).

PaO_2 , FiO_2 in high-altitude areas (at an altitude of over 1,000 meters above the sea level) shall be corrected by the following formula:

$$\text{PaO}_2, \text{FiO}_2 \times [\text{Atmospheric pressure (mmHg)}/760]$$

Cases with chest imaging that showed obvious lesion progression within 24-48 hours $>50\%$ shall be managed as severe cases.

4. Critical cases

Cases meeting any of the following criteria:

4.1 Respiratory failure and requiring mechanical ventilation;

4.2 Shock;

4.3 With other organ failure that requires ICU care.

VI. Differential Diagnosis

1. The mild manifestations of NCP need to be distinguished from upper respiratory tract infections caused by other viruses.

2. NCP is mainly distinguished from other known viral pneumonia and mycoplasma pneumoniae infections such as influenza virus, adenovirus and respiratory syncytial virus. Especially for suspect cases, methods such as rapid antigen detection and multiplex PCR nucleic acid detection should be adopted as much as possible for detection of common

respiratory pathogens.

3. It should also be distinguished from non-infectious diseases such as vasculitis, dermatomyositis and organizing pneumonia.

VII. Case Finding and Reporting

Health professionals in medical institutions of all types and at all levels, upon discovering suspect cases that meet the definition, should immediately put them in single room for isolation and treatment. If the cases are still considered as suspected after consultation made by hospital experts or attending physicians, it should be reported directly online within 2 hours; samples should be collected for new coronavirus nucleic acid testing and suspect cases should be safely transferred to the designated hospitals immediately. People who have been in close contact with patients who have been confirmed of new coronavirus infection are advised to perform new coronavirus pathogenic testing in a timely manner, even though common respiratory pathogens are tested positive.

VIII. Treatment

1. Treatment venue determined by the severity of the disease

1.1 Suspected and confirmed cases should be isolated and treated at designated hospitals with effective isolation, protection and prevention conditions in place. A suspect case should be treated in isolation in a single room. Confirmed cases can be treated in the same room.

1.2 Critical cases should be admitted to ICU as soon as possible.

2. General treatment

2.1 Letting patients rest in bed and strengthening support therapy; ensuring sufficient caloric intake for patients; monitoring their water and electrolyte balance to maintain internal environment stability; closely monitoring vital signs and oxygen saturation.

2.2 According to patients' conditions, monitoring blood routine result, urine routine result, c-reactive protein (CRP), biochemical indicators (liver enzyme, myocardial enzyme, renal function etc.), coagulation function, arterial blood gas analysis, chest imaging and cytokines detection if necessary.

2.3 Timely providing effective oxygen therapy, including nasal catheter and mask oxygenation, and if necessary, nasal high-flow oxygen therapy.

2.4 Antiviral therapy: Hospitals can try Alpha-interferon (5 million U or equivalent dose each time for adults, adding 2ml of sterilized water, atomization inhalation twice daily), lopinavir/ritonavir (200mg/50mg per pill for adults, two pills each time, twice daily, no longer than 10 days), Ribavirin (suggested to be used jointly with interferon or lopinavir/ritonavir, 500mg each time for adults, twice or three times of intravenous injection daily, no longer than 10 days), chloroquine phosphate (500mg for adults, twice daily, no longer than 10 days), Arbidol (200mg for adults, three times daily, no longer than 10 days). Be aware of such adverse reactions as lopinavir/ritonavir-related diarrhea, nausea, vomiting, liver damage, and pay attention to interactions with other drugs. Further evaluate the efficacy of those drugs currently being used. Do not recommend using three or more antiviral drugs at the same time; if an intolerable toxic side effect occurs, the respective drug should be discontinued.

2.5 Antibiotic drug treatment: Blind or inappropriate use of antibiotic drugs should be avoided, especially in combination with broad-spectrum antibiotics.

3. Treatment of severe and critical cases

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

3.2 Respiratory support:

3.2.1 Oxygen therapy: Patients with severe symptoms should receive nasal cannulas or masks for oxygen inhalation and timely assessment of respiratory distress and/or hypoxemia should be performed.

3.2.2 High-flow nasal-catheter oxygenation or noninvasive mechanical ventilation: When respiratory distress and/or hypoxemia of the patient cannot be alleviated after receiving standard oxygen therapy, high-flow nasal cannula oxygen therapy or non-invasive ventilation can be considered. If conditions do not improve or even get worse within a short time (1-2 hours), tracheal intubation and invasive mechanical ventilation should be used in a timely manner.

3.2.3 Invasive mechanical ventilation: Lung protective ventilation strategy, namely low tidal volume (4-8ml/kg of ideal body weight) and low inspiratory pressure (platform pressure <30cmH₂O) should be used to perform mechanical ventilation to reduce ventilator-related lung injury. There are many cases of human-machine asynchronization, therefore sedation and muscle relaxants should be used in a timely manner.

3.2.4 Rescue therapy: Pulmonary re-tensioning is recommended for patients with severe ARDS. With sufficient human resources, prone position ventilation should be performed for more than 12 hours per day. If the outcome of prone position ventilation is poor, extracorporeal membrane oxygenation (ECMO) should be considered as soon as possible.

3.3 Circulatory support: On the basis of adequate fluid resuscitation, hospitals should improve microcirculation, use vasoactive drugs and perform hemodynamic monitoring when necessary.

3.4 Rehabilitation plasma treatment: It is suitable for patients with rapid disease progression, severe and critically ill patients. Usage and dosage should refer to *Clinical Treatment Plan for Convalescent Patients with NCP during Recovery Phase (first trial version)*.

3.5 Other therapeutic measures

For patients with progressive deterioration of oxygenation indicators, rapid progress in imaging and excessive activation of the body's inflammatory response, glucocorticoids can be used in a short period of time (three to five days). It is recommended that dose should not exceed the equivalent of methylprednisolone 1-2 mg/kg/day. Note that a larger dose of glucocorticoid will delay the removal of coronavirus due to immunosuppressive effects. Xuebijing 100ml/time can be administered intravenously twice a day. Intestinal microecological regulators can be used to maintain intestinal microecological balance and prevent secondary bacterial infections. For critically ill patients with high inflammatory reactions, extracorporeal blood purification technology can be considered when conditions permit, such as plasma exchange, adsorption, perfusion, blood/plasma filtration.

Patients often suffer from anxiety and fear and they should be supported by psychological counseling.

4. Traditional Chinese Medicine treatment

This disease belongs to the category of plague in traditional Chinese medicine (TCM), caused by the epidemic pathogenic factors. According to the different local climate characteristic and individual state of illness and physical conditions, the following treatment Protocol may vary. The use of over-pharmacopoeia doses should be directed by a physician.

4.1 During medical observation

Clinical manifestation 1: fatigue and gastrointestinal discomfort

Recommended Chinese patent medicine: Huoxiang Zhengqi capsules (pills, liquid, or oral solution)

Clinical manifestation 2: fatigue and fever

Recommended Chinese patent medicine: Jinhua Qinggan granules, Lianhua Qingwen capsules (granules), Shufeng Jiedu capsules (granules), Fangfeng Tongsheng pills (granules)

4.2 During clinical treatment (confirmed cases)

4.2.1 Lung cleansing & detoxifying decoction

Scope of application: It is suitable for light, moderate and severe patients, and can be used reasonably in combination with the actual situation of patients in the treatment of critically ill patients.

Recommended prescription: Ephedra 9g, Zhigancao 6g, Almond 9g, Gypsum 15-30g (fried first), Guizhi 9g, Zixie 9g, Zhuling 9g, Baizhu 9g, Zhiling 15g, Bupleurum 16g, Scutellaria baicalensis 6g, and Pinellia 9g, Ginger 9g, aster 9g, winter flower 9g, shoot dry 9g, asarum 6g, yam 12g, coriander fruit 6g, tangerine peel 6g, aquilegia 9g.

Suggested use: Traditional Chinese medicine decoction pieces for decocting in water. One dose per day, twice in the morning and evening (forty minutes after a meal), take with warm water, and three doses a course.

If conditions permit, the patient can take half a bowl of rice soup each time after taking the medicine, and can take up to one bowl if the patient has a dry tongue and is deficient in bodily fluids. (Note: If the patient does not have a fever, the amount of gypsum should be little. If having a fever or strong heat, the amount of gypsum can be increased). If the symptoms improve but do not fully recover, then take the 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.

Source of prescription: *Notice on Recommending the Use of 'Lung cleansing & detoxifying decoction' in Treatment of NCP by Integrated Traditional Chinese and Western Medicine* by the Office of the State Administration of Traditional Chinese Medicine & the General Office of the National Health Commission. (2022 No.22)

4.2.2 Mild cases

4.2.2.1 Cold dampness and stagnation lung syndrome

Clinical manifestations: fever, fatigue, sore body, cough, expectoration, chest tightness, suffocation, loss of appetite, nausea, vomiting, sticky stools. Tongue has thin fat tooth mark or is faint red, and the coating is white thick rot or white greasy and the pulse is moisten or slippery.

Recommended prescription: Raw ephedra 6g, raw gypsum 15g, almond 9g, loquat 15g, gardenia 15g, Guanzhong 9g, Dilong 15g, Xu Changqing 15g, Huoxiang 15g, Peilan 9g, Cangzhu 15g, Yunling 45g, Atractylodes 30g, Jiao Sanxian 9g each , Magnolia officinalis 15g, betel coconut 9g, yarrow fruit 9g, ginger 15g.

Suggested use: one dose daily, boiled with 600ml water, take it three times at morning, noon and evening before meal.

4.2.2.2 Dampness and heat-accumulation lung syndrome

Clinical manifestations: low or no fever, slight chills, fatigue, heavy head and body, muscle soreness, dry cough, low phlegm, sore throat, dry mouth, do not want to drink more, or accompanied by chest tightness, no sweat or sweating, Or vomiting and loss of appetite, diarrhea or sticky stool. The tongue is reddish, and the coating is white, thick and greasy or thin yellow, and the pulse is slippery or sloppy.

Recommended prescription: Betel nut 10g, apple 10g, Magnolia 10g, Zhimu 10g, scutellaria baicalensis 10g, Bupleurum 10g, red peony 10g, forsythia 15g, artemisia annua 10g (decocted later), 10g of green leaves, 10g of green leaves, 5g of raw licorice.

Suggested use: one dose daily, boiled with 400ml water, take it twice at morning and evening.

4.2.3 Moderate cases

4.2.3.1 Dampness and stagnation lung syndrome

Clinical manifestations: fever, low cough and sputum, or yellow sputum, suffocation, shortness of breath, bloating, and constipation. The tongue is dark red and fat; the coating is greasy or yellow and the pulse is slippery or stringy.

Recommended prescription: raw ephedra 6g, bitter almond 15g, raw gypsum 30g, raw coix seed 30g, grass root 10g, patchouli 15g, artemisia annua 12g, Polygonum

cuspidatum 20g, verbena 30g, dried reed root 30g, gardenia 15g 15g of orange red, 10g of raw licorice.

Suggested use: one dose daily, boiled with 400ml water, take it twice at morning and evening.

4.2.3.2 Cold dampness lung syndrome

Clinical manifestations: low fever, low body temperature, or no heat, dry cough, low sputum, fatigue, chest tightness, nausea, or nausea. The tongue is pale or red, and the coating is white or greasy, and the veins are pulsating.

Recommended prescription: Atractylodes lancea 15g, Chenpi 10g, Magnolia 10g, Aquilegia 10g, grass fruit 6g, raw ephedra 6g, Zhihuo 10g, ginger 10g, betel nut 10g.

Suggested use: one dose daily, boiled with 400ml water, take it twice at morning and evening.

4.2.4 Severe cases

4.2.4.1 Plague poison and lung-closing syndrome

Clinical manifestations: fever, flushing, cough, yellowish phlegm, or blood in sputum, wheezing, shortness of breath, tiredness, fatigue, dryness and stickiness, nausea, food loss, poor stool, and short urination. Red tongue, yellow greasy coating, slippery pulses.

Recommended prescription: Raw ephedra 6g, almond 9g, raw gypsum 15g, licorice 3g, fragrant fragrant 10g (back), Magnolia 10g, atractylodes 15g, grass fruit 10g, pinellia 9g, Poria 15g, raw rhubarb 5g (back) 10g, gardenia 10g, red peony 10g.

Suggested use: one or two doses daily, boiled with 100-200ml water, take it 2-4 times, oral or nasal feeding.

4.2.4.2 Syndrome of flaring heat in qifen and yingfen

Clinical manifestations: Hot fever, thirst, shortness of breath, shortness of breath, blurred vision, or spotted rash, or vomiting blood, bleeding, or convulsions in the limbs. Tongue ridges have few or no moss, and the pulse sinks finely, or floats large and counts.

Recommended prescription: 30-60g gypsum (fried first), 30g of Zhimu, 30-

60g of raw land, 30g of buffalo horn (fried first), 30g of red sage, 30g of black ginseng, 15g of forsythia, 15g of paeonia, 6g of peony 12g, gardenia 15g, raw licorice 6g.

Suggested use: 1 dose per day, decoction, first decoct gypsum and buffalo horn, then apply other pieces, 100ml-200ml each time, 2-4 times a day, orally or nasally.

Recommended Chinese patent medicines: Xiyanping 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 traditional Chinese medicine decoction.

4.2.5 Critical cases (syndrome of inner blocking causing collapse)

Clinical manifestations: dyspnea, asthma or need mechanical ventilation, fainting, irritability, cold sweating, dark purple tongue, thick or dry moss, large floating roots.

Recommended prescription: 15g of ginseng, 10g of Heishun tablets (decoct first), 15g of dogwood, delivered with Suhexiang Pill or Angong Niuhuang Pill.

Recommended Chinese patent medicines: Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shengmai injection, Shenmai 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 traditional Chinese medicine decoction.

Note: Recommended usage of Chinese medicine injections for severe and critical cases

The use of traditional Chinese medicine injections follows the principle of starting from a small dose and gradually adjusting the dosage according to the instructions of the drug. The recommended usage is as follows:

Viral infection or combined mild bacterial infection: 0.9% sodium chloride injection 250ml plus Xiyanping injection 100mg bid, or 0.9% sodium chloride injection 250ml heated Duning injection 20ml, or 0.9% sodium chloride injection

250ml plus Tanreqing injection 40ml bid.

High fever with disturbance of consciousness: 250ml of 0.9% sodium chloride injection and 20ml bid of Xingnaojing injection.

Systemic inflammatory response syndrome or/and multiple organ failure: 250ml of 0.9% sodium chloride injection and 100ml of Xuebijing injection.

Immunosuppression: 250ml of 0.9% sodium chloride injection and 100ml bid of Shenmai injection.

Shock: 250ml of 0.9% sodium chloride injection plus 100ml bid of Shenfu injection.

4.2.6 Convalescent period

4.2.6.1 Lung and spleen qi deficiency syndrome

Clinical manifestations: shortness of breath, fatigue, anorexia, nausea, fullness, weak stool, and uneasiness. The tongue is pale and greasy.

Recommended prescription: French Pinellia 9g, Chenpi 10g, Codonopsis 15g, Sunburn Astragalus 30g, Stir-fried Atractylodes 10g, Poria 15g, Huoxiang 10g, Amomum villosum 6g (later), and Licorice 6g

Suggested use: 1 dose per day, boiled with 400ml of water, twice a day at morning and evening.

4.2.6.2 Qi and Yin deficiency syndrome

Clinical manifestations: Fatigue, shortness of breath, dry mouth, thirst, palpitations, sweating, poor appetite, low or no lever, dry cough and little sputum; dry tongue, fine or weak pulses.

Recommended prescription: North and south radix salviae 10g, 15g ophiopogonis, 6g American ginseng, 6g schisandra, 6g gypsum 15g, 10g light bamboo leaves, 10g mulberry leaves, 15g reed root, 15g salviae miltiorrhiza, 6g raw liquorice.

Suggested use: 1 dose per day, boiled with 400ml of water, twice a day at morning and evening.

IX. Isolation Removal and After-discharge Notice

1. Criteria for isolation removal and discharge
 - 1) Body temperature is back to normal for more than three days;
 - 2) Respiratory symptoms improve obviously;

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- 3) Pulmonary imaging shows obvious absorption of inflammation,
 - 4) Nuclei acid tests negative for respiratory tract pathogen twice consecutively (sampling interval being at least one day).

Those who meet the above conditions can be discharged from isolation.

2. After-discharge notice

2.1 The designated hospitals should contact the primary healthcare facilities where the patients live and share patients' medical record, to send the information of the discharged patients to the community committee and primary healthcare facility where the patients reside.

2.2. After discharge, due to their low immune function during the recovery phase, the patients have the risks of infection with other pathogens; it is recommended for patients to monitor their own health status for 14 days, wear a mask, live in well-ventilated single room if possible, reduce close contact with family members, separate dining, practice hand hygiene and avoid going out.

2.3 It is recommended for the patients to return to the hospitals for follow-up and re-visit in two and four weeks after discharge.

X. Patients Transportation Principles

Patients should be transported in accordance with the *Work Protocol for Transfer of the Novel Coronavirus Pneumonia Patients (Trial Version)* issued by the National Health Commission.

XI. 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 Novel Coronavirus in Medical Institutions (First Edition)* and the *Guidelines on the Usage of Common Medical Protective Equipment against Novel Coronavirus Infection (Trial Version)* formulated by the National Health Commission.

The General Office of National Health Commission

Office of State TCM Administration