

Diagnosis and Treatment Protocols for Patients with Novel Coronavirus Pneumonia

(Trial Version 5, Revised)

Since December 2019, hospitals in the City of Wuhan, Hubei Province have identified multiple cases of novel coronavirus pneumonia (NCP). 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, although it is dealt with 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 Patients (Trial Version 5)*, which is based on the fourth 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 novel coronavirus infection patients are the main source of infection

although asymptomatic infected people can also be an infectious source.

2. Transmission

Transmission of the virus happens mainly through respiratory droplets and contact transmission while aerosol, digestive routes and other routes remain to be determined.

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 and diarrhea are found in a few cases. Severe cases mostly developed dyspnea and/or hyoxemia after one week. In severe cases, patients progress rapidly to acute respiratory distress syndrome, septic shock, metabolic acidosis difficult to correct, and coagulopathy. 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 disease 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, 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.

Novel coronavirus nucleic acid can be detected in nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces and other specimens.

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

For cases reported outside of Hubei province:

1. Suspected 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 pneumonia;

1.2.3 Normal or decreased WBC count or 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

Suspected cases with one of the following etiological evidence:

2.1 Respiratory tract specimens or blood samples were tested positive for the novel coronavirus nucleic acid by real-time fluorescent RT-PCR tests;

2.2 Sequencing of virus genes in respiratory or blood samples is highly

homologous to that of known novel coronavirus.

For cases reported in Hubei province:

1. Suspected cases

Assessing 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 with fever or respiratory symptoms from Wuhan or its surrounding areas or from communities where cases have been reported within 14 days prior to the onset of the disease; or

1.1.4 Cluster of cases.

1.2 Clinical manifestations

1.2.1 Fever and/or respiratory symptoms;

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

Suspect cases are those with or without epidemiological history and with both clinical manifestations.

2. Clinically diagnosed cases

Suspected cases with radiographic features of pneumonia.

3. Confirmed cases

Clinically diagnosed cases or suspected cases with one of the following etiological evidence:

3.1 Respiratory tract specimens or blood samples were tested positive for the novel coronavirus nucleic acid by real-time fluorescent RT-PCR tests;

3.2 Sequencing of virus genes in respiratory or blood samples is highly homologous to that of known novel coronavirus.

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 Finger 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);

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

Major candidate diseases to be distinguished from include the known viral pneumonia, for example, pneumonia caused by influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, SARS coronavirus; and mycoplasma pneumoniae and chlamydia pneumonia, and bacterial pneumonia. In addition, non-infectious diseases such as vasculitis, dermatomyositis and organizing pneumonia are also candidate diseases to be distinguished from.

VII. Case Finding and Reporting

In provinces outside Hubei:

Health professionals in medical institutions of all types and at all levels, upon discovering suspected cases that meet the definition, should immediately isolate and treat them. 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 patients should be immediately and safely transferred to the designated hospitals. 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.

Suspected cases can be released only after they test nuclei acid negative for respiratory pathogen twice consecutively (sampling interval being at least one day).

In Hubei province:

Health professionals in medical institutions of all types and at all levels, upon discovering suspected cases that meet the definition and clinically diagnosed cases, should immediately isolate and treat them. Suspected cases and clinically diagnosed cases should be separated and their samples should be collected as quickly as possible for pathogenic testing.

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 suspected 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 Monitoring blood routine result, urine routine result, c-reactive protein (CRP), biochemical indicators (liver enzyme, myocardial enzyme, renal function etc.), coagulation function according to patients' conditions, arterial blood gas analysis, chest imaging and cytokines texts 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: There are currently no effective antiviral drugs. Hospitals can try Alpha-interferon inhalation (5 million U each time for an adult, add 2 ml of sterilized water for injection twice daily); lopinavir/ ritonavir (200mg/50mg for each pill), 2 capsules a time and twice a day; or add Ribavirin (4g for the first time for adults, every 8 hours a time on the following day; or 8mg/kg iv. every 8 hours a time). Be aware of such adverse reactions as lopinavir/ritonavir-related diarrhea, nausea, vomiting, liver damage, and pay attention to interactions with other drugs.

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 Other therapeutic measures

Glucocorticoids can be used in a short period of time (three to five days) according to the degree of respiratory distress and the progress of chest imaging. It is recommended 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. Xuebing 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. Convalescent plasma treatment can be applied. For critically ill patients with high inflammatory reactions, extracorporeal blood purification technology can be considered when conditions permit.

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.

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

4.2.1 In the early stage when coldness and dampness are blocked in the lunges with the clinical manifestations: fever or no fever due to severe coldness, dry cough, dry pharynx, tiredness, fatigue, chest tightness, a dirty lump in the abdomen, vomiting, loose

stools, light or light red tongue with white and greasy coating and slow pulse

Recommended TCM prescription: atractylodis 15g, tangerine peel 10g, magnolia officinalis 10g, huoxiang 10g, grass fruit 6g, raw ephedra 6g, notopterygium 10g, raw ginger 10g and areca nut 10g

4.2.2 In the interim period when the epidemic pathogenic factors begin to infect the lungs with the clinical manifestations: persistent fever or alternative coldness and heat, cough with little phlegm or yellow phlegm, abdominal distension and constipation; stuffy chest, cough and asthmatic suffocating; red tongue with yellow greasy coating, rolling and rapid pulse

Recommended TCM prescription: almond 10g, raw gypsum 30g, Mongolian snake gourd 30g, raw rhubarb 6g (added later), raw and processed ephedra 6g each, pepperweed seed 10g, peach kernel 10g, grass fruit 6g, areca nut 10g and rhizoma atractylodis 10g

Recommended Chinese patent medicine: Xiyaping injection and XueBi Jing injection

4.2.3 In critical condition when inner blocking causes collapse externally with the clinical manifestations: breathing difficulties, frequent asthma or need to be supported with aided ventilation, occasional coma, dysphoria, sweating with cold limbs, dark purple tongue with thick and greasy or dry coating and floating pulse.

Recommended TCM prescription: ginseng 15g, black prepared lateral root of aconite 10g (boiled), cornus officinalis 15g, taking with styrax pills or Angong Niuhuang pills

Recommended Chinese patent medicine: XueBi Jing injection, Shenfu injection and Shengmai injection

4.2.4 In the restoration stage when lungs and spleen are deficient with the clinical manifestations: shortness of breath, tiredness and fatigue, poor appetite and vomiting, developed lump in the abdomen, defecating weakness, loose stool and light and swelling tongue with white greasy coating

Recommended prescription: prepared pinellia tuber 9g, dried orange peel 10g, codonopsis codonopsis 15g, prepared astragalus 30g, poria cocos 15g, agastache 10g, amomum fruit 6g (added later)

IX. Criteria for Isolation Removal and Discharge

Patients meeting the following criteria can be removed from medical isolation and discharged or be transferred to other departments to treat other medical conditions, if any: body temperature is back to normal for more than three days; respiratory symptoms improve obviously; pulmonary imaging shows obvious absorption of inflammation, and nuclei acid tests negative for respiratory tract pathogen twice consecutively (sampling interval being at least one day).

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

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