

Novel Coronavirus Pneumonia diagnosis and treatment protocol

(revised 5th version for trial implementation)

Issued by National Health Commission
and National Administration of Traditional Chinese Medicine

Since December 2019, multiple cases of patients with Novel Coronavirus Pneumonia have been successively detected in Wuhan City of Hubei Province. With the spread of the epidemic, other cases in other regions both at home and abroad have also been found. Hence, the disease has been included as an acute respiratory infectious disease under the Class B Infectious Diseases specified in the *Law of the People's Republic of China on the Prevention and Control of Infectious Diseases*, subject to the management as a Class A Infectious Diseases.

With the deeper understanding of the disease and growing buildup of experiences in diagnosis and treatment, we have developed the “*Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Revised 5th Version for Trial Implementation)*” based on the revisions of the previous version, namely “*Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (5th Version for Trial Implementation)*”.

I. Pathogenic characteristics

As a betacoronavirus, the 2019-nCoV has an envelope and round or oval particles with a diameter of 60-140nm, and is often polymorphic. The genetic characteristics of the 2019-nCoV are significantly different from SARSr-CoV and MERSr-CoV. Current researches have shown that it has a homology of more than 85% with bat SARS-like coronavirus (bat-SL-CoVZC45). When isolated and cultured in vitro, 2019-nCoV can be found in human

respiratory epithelial cells in about 96 hours, while it takes about 6 days for the virus strain to be isolated and cultured from Vero E6 and Huh-7 cell lines.

The researches on SARSr-CoV and MERSr-CoV have contributed to the most of the understanding of the physical and chemical properties of the 2019-nCoV. 2019-nCoV is sensitive to ultraviolet rays and heat, and can be effectively inactivated at 56°C for 30 minutes and lipid solvents such as ether, 75% ethanol, chlorine-containing disinfectants, peracetic acid, and chloroform. Chlorhexidine cannot effectively inactivate the virus.

II. Epidemiological characteristics

1) Source of infection.

Based on the findings so far, the source of infection is mainly patients with 2019-nCoV infection. Patients with asymptomatic infection may also become the source of infection.

2) Routes of transmission.

The main routes of transmission are transmissions via respiratory droplets and contact. Other routes of transmission such as aerosol and digestive tract transmission are yet to be confirmed.

3) Susceptible groups.

The entire population is susceptible.

III. Clinical features

A. Clinical manifestations

Based on the current epidemiological investigations, the incubation period ranges from 1 to 14 days, mostly between 3-7 days.

The main clinical manifestations of 2019-nCoV infection are fever, fatigue and dry cough. A few patients also develop other symptoms such as nasal obstruction, runny nose, sore throat and diarrhea. In many severe patients, dyspnea and/or hypoxemia occurs after one week, and those critical cases can quickly progress to acute respiratory distress syndrome,

septic shock, and metabolic acidosis and coagulation dysfunction that are difficult to be corrected. Notably, severe and critical patients may have moderate to low-grade fever or even no obvious fever during the course of the disease.

Mild cases only show low-grade fever, mild fatigue, and no signs of pneumonia.

Judging from the cases being treated, most patients have good prognosis, and a few patients are critically ill. Poor prognosis is more common in the elderly and those with underlying chronic conditions, and pediatric cases have relatively mild symptoms.

B. Laboratory examinations

The peripheral white blood cell count is normal or decreases in the early stage of onset, and the lymphocyte count decreases. Some patients may develop elevated liver enzymes, lactate dehydrogenase (LDH), creatase, and myoglobin; some critical cases can have elevated troponin. Most patients have elevated C-reactive protein (CRP) and erythrocyte sedimentation, and normal procalcitonin. In severe cases, D-dimer is elevated and peripheral blood lymphocytes are progressively reduced.

The RNA of 2019-nCoV can be detected through the specimen of nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood and feces.

C. Chest CT scan

Multiple patchy shadows and interstitial changes are found in the early stage, especially in the lung periphery. And then the conditions develop into multiple ground-glass opacifications (GGO) and infiltration shadows. Severe cases may develop consolidation of lung tissue, with incidence of hydrothorax being rare.

IV. Diagnostic criteria

Provinces outside Hubei

A. Suspected cases.

Comprehensive analysis based on the following epidemiological history and clinical manifestations:

1. Epidemiological history

- 1) Travel or residence history in Wuhan and its surrounding areas or other communities with reported cases within 14 days before the onset of the disease.
- 2) History of contact with 2019-nCoV infected patients (the result of nucleic acid test showing positive) within 14 days before the onset of the disease.
- 3) Contact with patients with fever or respiratory symptoms from Wuhan and its surrounding areas or other communities with reported cases within 14 days before the onset of the disease.
- 4) Cluster infection.

2. Clinical manifestations:

- 1) Fever and/ or respiratory symptoms;
- 2) Having the aforementioned imaging features of Novel Coronavirus Pneumonia;
- 3) The total leukocyte count is normal or decreases, or the lymphocyte count decreases in the early stage of the disease.

Cases that meet any one condition of the epidemiological history and have any two conditions of the clinical manifestations. If there is no clear history of epidemiology, then the case should meet three conditions of the clinical manifestations.

B. Confirmed case

Suspected case with one of the following pathogenic evidences:

1. The result of RT-PCR used to detect the nucleic acid of 2019-nCoV in respiratory or blood samples is positive;
2. The result of virus gene sequencing analysis of respiratory or blood samples is highly homologous with the known 2019-nCoV.

Hubei Province:

A. Suspected cases

Comprehensive analysis based on the following epidemiological history and clinical manifestations:

1. Epidemiological history

- 1) Travel or residence history in Wuhan and its surrounding areas or other communities with reported cases within 14 days before the onset of the disease.
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2. Clinical manifestations:

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- 3) The total leukocyte count is normal or decreases, or the lymphocyte count decreases in the early stage of the disease.

Cases that meet any one condition of the epidemiological history and have any two conditions of the clinical manifestations. If there is no clear history of epidemiology, then the case should meet three conditions of the clinical manifestations.

B. Clinically diagnosed cases

Suspected cases with chest CT features of Novel Coronavirus Pneumonia.

C. Confirmed case

Clinically diagnosed cases or suspected case with one of the following pathogenic evidences:

1. The result of RT-PCR used to detect the nucleic acid of 2019-nCoV in respiratory or blood samples is positive;
2. The result of virus gene sequencing analysis of respiratory or blood samples is highly homologous with the known 2019-nCoV.

V. Clinical classification

1) Mild cases

Those cases which have mild clinical symptoms and no imaging features of Novel Coronavirus Pneumonia.

2) Normal cases

3) Cases with fever, respiratory tract and other symptoms and imaging features of Novel Coronavirus Pneumonia.

4) Severe cases

Cases that meet any of the following:

1. Respiratory distress, with RR> 30 times/minute;
2. Oxygen saturation in the resting state <93%;
3. Partial arterial oxygen pressure (PaO₂) / oxygen concentration (FiO₂) <300mmHg (1mmHg=0.133kPa)

5) Critical cases

Cases that meet one of the following:

1. Have respiratory failure and require mechanical ventilation;

2.Event of shock;

3.Combined with other organ failures that requires ICU monitoring and treatment.

VI. Differential diagnosis

The infection should be mainly distinguished from other known pneumonia caused by viruses such as influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, and SARS coronavirus. In addition, it should be distinguished from non-infectious diseases such as vasculitis, dermatomyositis, and organizing pneumonia.

VII. Case detection and reporting

Provinces outside Hubei:

Health workers at various levels and various types of facilities should immediately admit the cases for isolation treatment when they detect suspected cases that meet the case definition. If the cases are still considered as suspected cases upon the expert consultation or consultation with the attending physician in the hospital, they should be reported through the online reporting channel within 2 hours, with specimens of the cases to be collected for 2019-nCoV nucleic acid testing. The suspected cases should be immediately transferred to designated hospitals through safe transportation. For patients who have close contact with 2019-nCoV infected patients, even if they are tested positive for common respiratory pathogens, it is recommended to sample them for the 2019-nCoV pathogenic test in a timely manner.

Suspected cases can be ruled out only if they show negative results for two consecutive respiratory pathogenic nucleic acid tests (at least one day apart between the two specimen collections).

Hubei Province:

Health workers at various levels and various types of facilities should immediately isolate and treat suspected cases and clinically diagnosed cases that meet the case definition. Suspected cases and clinically diagnosed cases should be isolated in single rooms. Specimens of both types of cases should be collected as soon as possible for pathogenic testing.

VIII. Treatment

A. Treatment venue determined according to the conditions of the cases.

1. Suspected and confirmed cases should be isolated and treated in designated hospitals with effective isolation and protection conditions. Suspected cases should be treated in isolation and in a single room. Multiple confirmed cases can be admitted to the same ward.
2. Critical cases should be admitted to ICU for treatment as soon as possible.

B. General treatment.

1. Patients should rest on the bed and receive strengthened supportive care to ensure sufficient energy intake; attention should be paid to water and electrolyte balance to maintain the stability of the internal environment; and vital signs and finger oxygen saturation should be closely monitored.
2. Complete blood count, urinalysis, CRP, biochemical indicators (liver enzyme, myocardial enzyme, renal function, etc.), blood coagulation function, arterial blood gas analysis, chest imaging should be monitored according to the conditions of the cases. Cytokines testing should be performed if conditions permit.
3. Effective oxygen therapy measures should be provided in time, including nasal cannula, oxygen masks and high-flow nasal cannula oxygen therapy.
4. Anti-virus treatment: currently, no effective anti-virus treatment options have been confirmed so far, but doctors may administer atomization inhalation of interferon- α (for adults: 5 million U or equivalent dose, added with 2 ml sterile injection water, twice a day), Lopinavir/Ritonavir (200mg/50mg per pill) 2 capsules per serving, twice a day, or added with Ribavirin (500mg each injection, iv. two to three times a day). Attention should be paid to the adverse reaction associated with Lopinavir/ Ritonavir such as diarrhea, nausea, vomiting, and liver function impairment and also the interaction with other drugs.
5. Antibiotics treatment: avoid inappropriate use of antibiotics, especially the combination with broad-spectrum antibiotics.

C. Treatment of severe and critical cases.

1. Treatment principle: On the basis of symptomatic treatment, efforts should be made to

actively prevent complications, treat the underlying diseases, prevent secondary infections, and provide organ function support in a timely manner.

2. Respiratory support:

1) Oxygen therapy: severe patients should receive nasal cannula or mask oxygen inhalation, and receive prompt assessment on whether the respiratory distress and/or hypoxemia has been relieved.

2) High-flow nasal cannula oxygen therapy or non-invasive mechanical ventilation: when respiratory distress and/or hypoxemia of the patients cannot be relieved after they have received standard oxygen therapy, high-flow nasal cannula oxygen therapy or non-invasive ventilation can be considered. If their conditions do not improve or even worsen within a short span of time (one to two hours), tracheal intubation and invasive mechanical ventilation should be performed in time.

3) Invasive mechanical ventilation: lung protective ventilation strategy should be adopted, that is, small tidal volume (4-8ml/kg ideal weight) and low inspiratory pressure (platform pressure <30cmH₂O) for mechanical ventilation are used to reduce ventilator-related lung injury. In the event of patient-ventilator dyssynchrony cases, sedatives and muscle relaxants should be administered in a timely manner.

4) Rescue treatment: For patients with severe ARDS, it is recommended to perform lung re-expansion. In the case of sufficient human resources, prone ventilation should be performed for more than 12 hours per day. Those with poor effects from the prone ventilation should consider extracorporeal membrane oxygenation (ECMO) as soon as possible.

3. Circulation support: based on adequate fluid resuscitation, microcirculation should be improved by administering vasoactive drugs, and hemodynamic monitoring should be performed when necessary.

4. Other treatments.

Glucocorticoids can be administered for a short period of time (3 to 5 days) as appropriate according to the progression of the patient's dyspnea and chest imaging. The recommended dose should not exceed the equivalent dose of methylprednisolone at 1 ~ 2mg / kg /day. It should be noted that larger doses of glucocorticoids will delay the clearance of coronavirus

due to the immunosuppressive effects; intravenous administration of Xuebijing 100ml/ injection twice daily can be provided; microecological regulating agents in intestinal tract can be administered to maintain the intestinal micro-ecological balance and prevent secondary bacterial infections; convalescent plasma treatment can be adopted; for critical cases with high inflammatory response, extracorporeal blood purification can be performed if conditions permit.

Patients who often develop anxiety and fear should receive psychological counselling.

D. Traditional Chinese medicine (TCM) treatment.

This disease is classified by the traditional Chinese medicine as one of the epidemic infectious diseases, with the etiology as exposed to epidemic pathogen. Thus, different regions can refer to the following protocols for differentiated treatment according to the patient's conditions, local climate and different physical constitutions of the patients.

1. Medical observation period

Clinical manifestation 1: fatigue with gastrointestinal upset

Recommended Chinese patent medicine: Huoxiang Zhengqi Capsules (pills, liquid, and oral liquid)

Clinical manifestation 2: fatigue with fever

Recommended Chinese patent medicine: Jinhua Qinggan Granules, Lianhua Qingwen Capsules (granules), Shufeng Jiedu Capsules (granules), and Fangfeng Tongsheng Pills (granules).

2. Clinical treatment period

1) Early-stage: cold-dampness encumbering the lung

Clinical manifestations: fever or no fever, dry cough, dry throat, fatigue, chest congestion, epigastric stuffiness, or vomiting and nauseous, and loose stool. Pale or pink tongue with white and greasy tongue coating and soggy pulse.

Recommended formula: 15g of Cang Zhu (*Atractylodes rhizoma*), 10g of Chen Pi (dried orange peel), 10g of Hou Po (*Magnolia officinalis*), 10g of Huo Xiang (*Agastache rugosa*), 6g of Cao Guo (*Amomum tsaoko*), 6g of Sheng Ma Huang (raw ephedra), 10g of Qiang

Huo (*Notopterygium incisum*), 10g of Sheng Jiang (Fresh Ginger rhizome), and 10g of Bin Lang (Areca nuts).

2) Medium-term: pestilence-toxin blocking the lung

Clinical manifestations: persistent fever or alternative chill and fever, cough and scanty sputum, or yellow sputum, abdominal distension and constipation, chest tightness and shortness of breath, coughing and dyspnea, dyspnea after moving. Red tongue with yellow greasy or yellow dry coating, and slippery-rapid pulse.

Recommended formula: 10g of Xing Ren (almond log), 30g of Sheng Shi Gao (raw Gypsum Fibrosum), 30g of Gua Lou (snakegourd fruit), 6g of Sheng Da Huang (raw rhubarb) (decoct later), 6g of Sheng Zhi Ma Huang (raw and honey-fried ephedra), 10g of Ting Li Zi (Pepperweed seed), 10g of Tao Ren (peach kernel), 6g of Cao Guo (*Amomum tsaoko*), 10g of Bin Lang (Areca nuts), and 10g of Cang Zhu (*Atractylodes lancea*).

Recommended Chinese patent medicine: Xiyanping (XYP) injection, Xuebijing injection.

3) Severe conditions period: internal block and external collapse

Clinical manifestations: dyspnea, panting when moving, or in need of assisted ventilation, accompanied by unconsciousness, irritability, sweating and cold limbs, dark purple tongue with thick and greasy or dry coating, and floating, large and rootless pulse.

Recommended formula: take Su He Xiang Pill or Angong Niu Huang Pill with the decoction of 15g of Ginseng, 10g of Hei Shun Pian (black sliced aconite lateral root, decoct first), and 15g of Shan Zhu Yu (*Cornus officinalis*).

Recommended Chinese patent medicine: Xuebijing injection, Shenfu injection, and Shengmai injection.

4) Recovery period: lung-spleen qi deficiency

Clinical manifestations: shortness of breath, fatigue and lack of energy, poor appetite, vomiting and nausea, epigastric fullness, torpid bowel movement, sticky stools, pale and swollen tongue, and white and greasy tongue coating.

Recommended formula: 9g of Fa Ban Xia (*Rhizoma pinellinae praepa*), 10g of Chen Pi (dried orange peel), 15g of Dang Shen (*Codonopsis pilosula*), 30g of Zhi Huang Qi

(honey-fried Radix Astragali), 15g of Fu Ling (*Wolfiporia extensa*), 10g of Huo Xiang (*Agastache rugosa*), and 6g of Sha Ren (*Amomum villosum*) (decoct later).

IX. Isolation and hospital discharge standard

When the patients' body temperature returns to normal for more than 3 days, their respiratory symptoms have improved significantly, the chest imaging shows inflammation has been obviously absorbed, and two consecutive negative results are shown for the respiratory pathogen nucleic acid tests (with at least 1 day apart between the two sample collections), the patients can be discharged from the hospital or transferred to the corresponding department for the treatment of other diseases.

X. Transfer principle

Cases should be transferred in accordance with the "*Work Plan for the Transfer of Novel Coronavirus Pneumonia Cases (for Trial Implementation)*".

XI. Infection prevention and control in hospitals

Requirements should be strictly followed in the "*Technical Guide for the Prevention and Control of Novel Coronavirus Infection in Hospitals (First Edition)*" and the "*Guidelines for the Scope of Use of Common Medical Protective Products in the Prevention of Novel Coronavirus Pneumonia (for Trial Implementation)*".

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