

Expert consensus on comprehensive treatment of coronavirus disease in Shanghai 2019

By **admin** - March 4, 2020



Source: [Weixin](#)

On March 1st, the Chinese Journal of Infectious Diseases, which was hosted by the Shanghai Medical Association, pre-published the "Expert Consensus on Comprehensive Treatment of Coronavirus in Shanghai 2019" (<http://rs.yiigle.com/m/yufabiao/1183266.htm>), which has attracted widespread attention in the industry.

Corona virus disease 2019 (COVID-19) was first reported on December 31, 2019 in Wuhan, Hubei Province. COVID-19, as a respiratory infectious disease, has been included in the Class B infectious diseases stipulated in the Law of the People's Republic of China on the Prevention and Control of Infectious Diseases and managed as a Class A infectious disease.

With the deepening of understanding of the disease, COVID-19 has accumulated a certain amount of experience in the prevention and control of COVID-19. The Shanghai New Coronary Virus Disease Clinical Treatment Expert Group follows the National New Coronary Virus Pneumonia Diagnosis and Treatment Program and fully draws on the treatment experience of colleagues at home and abroad to improve the success rate of clinical treatment and reduce the mortality rate of patients, prevent the progress of the disease, and gradually reduce the disease. The proportion of patients with severe disease improves their clinical prognosis. Based on the continuous optimization and refinement of the treatment plan, expert consensus has been formed on the relevant clinical diagnosis and treatment.

I. Etiology and epidemiological characteristics

2019 novel coronavirus (2019-nCoV) is a new coronavirus belonging to the genus β. On February 11, 2020, the International Committee on Taxonomy of Viruses (ICTV) named the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Patients with COVID-19 and asymptomatic infection can transmit 2019-nCoV. Respiratory droplet transmission is the main route of transmission and can also be transmitted through contact. There is also the risk of aerosol transmission in confined enclosed spaces. COVID-19 patients can detect 2019-nCoV in stool, urine, and blood; some patients can still test positive for fecal pathogenic nucleic acid after the pathogenic nucleic acid test of respiratory specimens is negative. The crowd is generally susceptible. Children, infants, and young children also develop disease, but the condition is relatively mild.

Clinical characteristics and diagnosis

(A) clinical characteristics

The incubation period is 1 to 14 d, mostly 3 to 7 d, with an average of 6.4 d. Main symptoms are fever, fatigue, and dry cough. May be accompanied by runny nose, sore throat, chest tightness, vomiting and diarrhea. Some patients have mild symptoms, and a few patients have no symptoms or pneumonia.

The elderly and those suffering from basic diseases such as diabetes, hypertension, coronary atherosclerotic heart disease, and extreme obesity tend to develop severe illness after infection. Some patients develop symptoms such as dyspnea within one week after the onset of the disease. In severe cases, they can progress to acute respiratory distress syndrome (ARDS) and multiple organ damage. The time to progression to severe illness was approximately 8.5 days. It is worth noting that in the course of severe and critically ill patients, there may be moderate to low fever, even without obvious fever. Most patients have a good prognosis, and deaths are more common in the elderly and those with chronic underlying disease.

The early CT examination showed multiple small patches or ground glass shadows, and the internal texture of the CT scans was thickened in the form of grid cables, which was obvious in the outer lung zone. A few days later, the lesions increased and the scope expanded, showing extensive lungs, multiple ground glass shadows, or infiltrating lesions, some of which showed consolidation of the lungs, often with bronchial inflation signs, and pleural effusions were rare. A small number of patients progressed rapidly, with imaging changes reaching a peak on days 7 to 10 of the course. Typical "white lung" performance is rare. After entering the recovery period, the lesions are reduced, the scope is narrowed, the exudative lesions are absorbed, part of the fiber cable shadow appears, and some patients' lesions can be completely absorbed.

In the early stage of the disease, the total number of white blood cells in the peripheral blood was normal or decreased, and the lymphocyte count was reduced. Some patients may have abnormal liver function, and the levels of lactate dehydrogenase, muscle enzyme, and myoglobin may be increased; Most patients had elevated CRP and ESR levels and normal procalcitonin levels. In severe cases, D-dimer levels are elevated, other coagulation indicators are abnormal, lactic acid levels are elevated, peripheral blood lymphocytes and CD4 + T lymphocytes are progressively reduced, and electrolyte disorders and acid-base imbalances are caused by metabolic alkalosis See more. Elevated levels of inflammatory cytokines (such as IL-6, IL-8, etc.) may occur during the disease progression stage.

(Two) diagnostic criteria

1. Suspected case: Combined with the following epidemiological history and clinical manifestations. Suspected cases were diagnosed as having any one of epidemiological history and meeting any two of the clinical manifestations, or having no clear epidemiological history but meeting three of the clinical manifestations. ① Epidemiological history: travel history or residence history of Wuhan City and surrounding areas, or other communities with case reports within 14 days before the onset; history of contact with 2019-nCoV infection (positive nucleic acid test) within 14 days before the onset ; Patients with fever or respiratory symptoms from Wuhan and surrounding areas or from communities with case reports within 14 days before the onset of the disease; cluster onset. ② Clinical manifestations: fever and / or respiratory symptoms; with the above-mentioned imaging features of the new coronavirus pneumonia; the total number of white blood cells is normal or decreased in the early stage of onset, and the lymphocyte count is reduced.

2. Confirmed cases: Those with one of the following etiology evidence are diagnosed as confirmed cases. ① Real-time fluorescent reverse transcription PCR detected 2019-nCoV nucleic acid positive. ② Viral gene sequencing revealed high homology with the known 2019-nCoV. ③ Except for nasopharyngeal swabs, take sputum as much as possible. Patients undergoing tracheal intubation can collect lower respiratory tract secretions and send viral nucleic acid test positive.

(Three) differential diagnosis

It is mainly distinguished from other known viral pneumonias such as influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, severe acute respiratory syndrome (SARS) coronavirus, etc. , Different from Mycoplasma pneumoniae, Chlamydia pneumonia and bacterial pneumonia. In addition, it must be distinguished from non-infectious diseases such as pulmonary interstitial lesions and organizing pneumonia caused by connective tissue diseases such as vasculitis and dermatomyositis.

(Four) clinical classification

1. Mild: The clinical symptoms are slight, and no pneumonia manifestations on imaging examination.
2. Ordinary type: fever, respiratory tract symptoms, etc. Pneumonia manifestations on imaging examination.

Early warning of severe cases of common patients should be strengthened. Based on current clinical studies, elderly (aged > 65 years) with underlying diseases, CD4 + T lymphocyte counts <250 / μ L, blood IL-6 levels significantly increased, and lesions were found on lung imaging on 2 to 3 days Significant progress > 50%, lactic dehydrogenase (LDH) > 2 times the upper limit of normal value, blood lactic acid \geq 3 mmol / L, metabolic alkalosis, etc. are all early warning indicators of severe disease.

3. Heavy: Any one of the following. ① Shortness of breath, respiratory rate \geq 30 beats / min; ② In resting state, refers to arterial oxygen saturation (SaO_2) \leq 93%; ③ arterial partial pressure of oxygen, PaO_2 / fraction of inspired oxygen (FiO_2) \leq 300 mmHg (1

mmHg = 0.133 kPa). At high altitudes (above 1 000 m), PaO₂ / FiO₂ should be corrected according to the following formula: PaO₂ / FiO₂ × [Atmospheric Pressure (mmHg) / 760].

Pulmonary imaging examination showed that the lesions progressed significantly within 24 to 48 hours, and those with more than 50% of the lesions were managed as severe.

4. Dangerous: A person who meets any of the following conditions can be judged as critical. ① Respiratory failure occurs and requires mechanical ventilation; ② Shock occurs; ③ Combined failure of other organs requires ICU monitoring and treatment.

(5) Clinical monitoring

The clinical manifestations, vital signs, fluid volume, gastrointestinal function and mental state of the patients were monitored dynamically daily.

All patients were dynamically monitored for terminal blood oxygen saturation. For critically ill and critically ill patients, timely blood gas analysis is performed according to the changes in the condition; blood routine, electrolytes, CRP, procalcitonin, LDH, blood coagulation function indicators, blood lactic acid, etc. are tested at least once every 2 days; liver function, kidney function, ESR, IL-6, IL-8, lymphocyte subsets, at least once every 3 days; chest imaging examination, usually every 2 days. For patients with ARDS, routine ultrasound examination of the heart and lungs at the bedside is recommended to observe extravascular lung water and cardiac parameters. For monitoring of extracorporeal membrane oxygenation (ECMO) patients, refer to the implementation section of ECMO.

Treatment plan

(A) antiviral treatment

You can try hydroxychloroquine sulfate or chloroquine phosphate, or Abidol for oral administration, interferon nebulization and inhalation, interferon κ is preferred, and interferon α recommended by the national scheme can also be applied. It is not recommended to use 3 or more antivirals at the same time. The viral nucleic acid should be stopped in time after it becomes negative. The efficacy of all antiviral drugs remains to be evaluated in further clinical studies.

For patients with severe and critical viral nucleic acid positives, recovery patients can be tested for recovery plasma. For detailed operation and management of adverse reactions, please refer to the "Clinical Treatment Program for Recovery of New Coronary Pneumonia Patients During Recovery Period" (trial version 1). Infusion within 14 days of the onset may be more effective. If the viral nucleic acid is continuously detected at the later stage of the disease, the recovery period of plasma treatment can also be tried.

(Two) treatment of light and ordinary patients

Supportive treatment needs to be strengthened to ensure sufficient heat; pay attention to water and electrolyte balance to maintain internal environment stability; closely monitor patient vital signs and finger oxygen saturation. Give effective oxygen therapy in time. Antibacterials and glucocorticoids are not used in principle. The patient's condition

needs to be closely monitored. If the disease progresses significantly and there is a risk of turning into severe, it is recommended to take comprehensive measures to prevent the disease from progressing to severe. Low-dose short-course glucocorticoids can be used with caution (see the application section of glucocorticoids for specific protocols). Heparin anticoagulation and high-dose vitamin C are recommended. Low-molecular-weight heparin 1 to 2 per day, continued until the patient's D-dimer level returned to normal. Once fibrinogen degradation product (FDP) $\geq 10 \mu\text{g} / \text{mL}$ and / or D-dimer $\geq 5 \mu\text{g} / \text{mL}$, switch to unfractionated heparin. Vitamin C is administered at a dose of 50 to 100 mg / kg per day, and the continuous use time is aimed at a significant improvement in the oxygenation index. If lung lesions progress, it is recommended to apply a large-dose broad-spectrum protease inhibitor, ulinastatin, at 600 to 1 million units / day until the pulmonary imaging examination improves. In the event of a "cytokine storm", intermittent short veno-venous hemofiltration (ISVVH) is recommended.

(III) Organ function supportive treatment for severe and critically ill patients

1. Protection and maintenance of circulatory function: implement the principle of early active controlled fluid replacement. It is recommended to evaluate the effective volume and initiate fluid therapy as soon as possible after admission. Severe patients can choose intravenous or transcolonic fluid resuscitation depending on the conditions. The preferred supplement is lactated Ringer's solution. Regarding vasoactive drugs, noradrenaline and dopamine are recommended to maintain vascular tone and increase cardiac output. For patients with shock, norepinephrine is the first choice. It is recommended to start low-dose vasoactive drugs at the same time as fluid resuscitation to maintain circulation stability and avoid excessive fluid infusion. Cardioprotective drugs are recommended for severe and critically ill patients, and sedative drugs that inhibit the heart are avoided as much as possible. For patients with sinus bradycardia, isoprenaline can be used. For patients with sinus rhythm, a heart rate of < 50 beats / min and hemodynamic instability, intravenous pumping of low-dose isoproterenol or dopamine is recommended to maintain the heart rate at about 80 beats / min.

2. Reduce pulmonary interstitial inflammation: 2019-nCoV leads to severe pulmonary interstitial lesions that can cause pulmonary function deterioration. It is recommended to use a large dose of a broad-spectrum protease inhibitor ulinastatin.

3. Protection of renal function: Reasonable anticoagulant therapy and appropriate fluid therapy are recommended as soon as possible. See chapter "Cytokine storm" for prevention, protection and maintenance of circulatory function.

4. Protection of intestinal function: Prebiotics can be used to improve the intestinal microecology of patients. Use raw rhubarb (15-20 g plus 150 ml warm boiling water) or Dachengqi decoction for oral administration or enema.

5. Nutritional support: parenteral nutrition is preferred, via nasal feeding or via jejunum. The whole protein nutrient preparation is preferred, and the energy is 25 to 35 kcal / kg (1 kcal = 4.184 kJ) per day.

6. Prevention and treatment of cytokine storm: It is recommended to use large doses of vitamin C and unfractionated heparin. Large doses of vitamin C are injected intravenously at a dose of 100 to 200 mg / kg per day. The duration of continuous use is to significantly improve the oxygenation index. It is recommended to use large doses. Dose of the broad-spectrum protease inhibitor ulinastatin, given 1.6 million units, once

every 8 h, under mechanical ventilation, when the oxygenation index > 300 mmHg can be reduced to 1 million units / d. Anticoagulation can be taken. The treatment protects endothelial cells and reduces the release of cytokines. When $\text{FDP} \geq 10 \mu\text{g} / \text{mL}$ and / or $\text{D-dimer} \geq 5 \mu\text{g} / \text{mL}$, anticoagulation is given to unfractionated heparin (3 to 15 IU / kg per hour). Heparin is used for the first time. The patient's coagulation function and platelets must be re-examined 4 h later. ISVVH is used for 6 to 10 h every day.

7. Sedation and artificial hibernation: Patients undergoing mechanical ventilation or receiving ECMO need to be sedated on the basis of analgesia. For patients with severe man-machine confrontation during the establishment of an artificial airway, short-term application of low-dose muscle relaxants is recommended. Hibernation therapy is recommended for severe patients with oxygenation index < 200 mmHg. Artificial hibernation therapy can reduce the body's metabolism and oxygen consumption, and at the same time dilate the pulmonary blood vessels to significantly improve oxygenation. It is recommended to use continuous intravenous bolus medication, and the patient's blood pressure should be closely monitored. Use opioids and dexmedetomidine with caution. Because severely ill patients often have elevated IL-6 levels, which can easily lead to bloating, opioids should be avoided; 2019-nCoV can still inhibit sinus node function and cause sinus bradycardia, so it should be used with caution on the heart. Inhibitory sedatives. In order to prevent the occurrence and exacerbation of lung infections, and to avoid prolonged excessive sedation, try to withdraw muscle relaxants as soon as possible. It is recommended to monitor the depth of sedation closely.

8. Oxygen therapy and respiratory support: ① nasal cannula or mask oxygen therapy, $\text{SaO}_2 \leq 93\%$ under resting air condition, or $\text{SaO}_2 < 90\%$ after activity, or oxygenation index ($\text{PaO}_2 / \text{FiO}_2$) $200-300$ mmHg; With or without respiratory distress; continuous oxygen therapy is recommended. ② High-flow nasal cannula oxygen therapy (HFNC), receiving nasal cannula or mask oxygen therapy for 1 to 2 hours, oxygenation fails to meet treatment requirements, and respiratory distress does not improve; or hypoxemia during treatment And / or exacerbation of respiratory distress; or an oxygenation index of 150 to 200 mmHg; HFNC is recommended. ③ Noninvasive positive pressure ventilation (NPPV), receiving 1 to 2 h of HFNC oxygenation does not achieve the treatment effect, and there is no improvement in respiratory distress; or hypoxemia and / or exacerbation of respiratory distress during treatment; or When the oxygenation index is $150 \sim 200$ mmHg; NPPV can be selected. ④ Invasive mechanical ventilation, HFNC or NPPV treatment does not meet the treatment requirements for 1 to 2 hours of oxygenation, and respiratory distress does not improve; or hypoxemia and / or exacerbation of respiratory distress during treatment; or oxygenation index < 150 mmHg; invasive ventilation should be considered. Protective ventilation strategies with a small tidal volume (4-8 mL / kg ideal body mass) as the core are preferred.

9. Implementation of ECMO: Those who meet one of the following conditions may consider implementing ECMO. ① $\text{PaO}_2 / \text{FiO}_2 < 50$ mmHg for more than 1 h; ② $\text{PaO}_2 / \text{FiO}_2 < 80$ mmHg for more than 2 h; ③ Arterial blood pH < 7.25 with $\text{PaCO}_2 > 60$ mmHg for more than 6 h. ECMO mode is preferred for intravenous-venous ECMO.

(4) Special problems and treatment in treatment

1. Application of glucocorticoids: Use glucocorticoids with caution. Imaging showed significant progress in pneumonia. Patients with $\text{SaO}_2 \leq 93\%$ or shortness of breath (respiratory frequency ≥ 30 breaths / min) or oxygenation index ≤ 300 mmHg in the state of no oxygen inhalation. Glucocorticoids can be added at the risk of

intubation. Patients are advised to withdraw promptly from glucocorticoid use when intubation or ECMO support can maintain effective blood oxygen concentrations. For non-severe patients using methylprednisolone, the recommended dose is controlled at 20 to 40 mg / d, severe patients are controlled at 40 to 80 mg / d, and the course of treatment is generally 3 to 6 days. Can be increased or decreased according to the body weight.

2. Use of immunoregulatory drugs: Subcutaneous injection of thymosin 2 to 3 times per week has certain effects on improving patients' immune function, preventing the disease from becoming worse, and shortening the time of detoxification. Due to the lack of specific antibodies, high-dose intravenous immunoglobulin therapy is currently not supported. However, some patients have low levels of lymphocytes and the risk of co-infection with other viruses. Human immunoglobulin can be infused intravenously at 10 g / d for 3 to 5 days.

3. Accurate diagnosis and treatment of combined bacterial and fungal infections: clinical microbiological monitoring of all severe and critically ill patients. The sputum and urine of the patients are kept daily for culture, and the patients with high fever should be cultured in time. All patients with suspected sepsis who have indwelling vascular catheters should be sent for peripheral venous blood culture and catheter blood culture at the same time. All patients with suspected sepsis may consider collecting peripheral blood for molecular diagnostic tests for etiology, including PCR-based molecular biology testing and next-generation sequencing.

Elevated procalcitonin levels have implications for the diagnosis of sepsis / septic shock. When patients with new type of coronavirus pneumonia become more severe, there is an increase in CRP levels, which is not specific for the diagnosis of sepsis caused by bacterial and fungal infections.

Critically ill patients with open airways are often prone to bacterial and fungal infections at a later stage. If sepsis occurs, empirical anti-infective treatment should be given as soon as possible. For patients with septic shock, empirical antibacterial drugs can be used in combination before obtaining an etiological diagnosis, while covering the most common Enterobacteriaceae, Staphylococcus and Enterococcus infections. Patients with infection after hospitalization can choose β -lactamase inhibitor complex. If the treatment effect is not good, or the patient has severe septic shock, it can be replaced with carbapenem drugs. If considering enterococci and staphylococcal infections, glycopeptide drugs (vancomycin) can be added for empirical treatment. Daptomycin can be used for bloodstream infections, and linezolid can be used for lung infections. Attention should be paid to catheter-related infections in critically ill patients, and treatment should be empirically covered with methicillin-resistant staphylococci. Glycopeptide drugs (vancomycin) can be used for empirical treatment. Candida infection is also more common in critically ill patients. Candida should be covered empirically when necessary. Echinocin drugs can be added. With the length of hospitalization of critically ill patients, drug-resistant infections have gradually increased. At this time, the use of antibacterial drugs must be adjusted according to drug sensitivity tests.

4. Nosocomial infection prevention and control: ① In accordance with the Basic System for Infection Prevention and Control of Medical Institutions (Trial) of the National Health and Health Commission in 2019, actively implement evidence-based infection prevention and control clustering intervention strategies to effectively prevent ventilator-related pneumonia and intravascular Multidrug-resistant bacteria and fungal infections such as

catheter-related bloodstream infections, catheter-related urinary tract infections, carbapenem-resistant gram-negative bacilli. ② Strictly follow the National Health and Health Commission's "Technical Guide for the Prevention and Control of New Coronavirus Infection in Medical Institutions (First Edition)", "Guidelines for the Use of Common Medical Protective Products in the Prevention and Control of Pneumonia of New Coronavirus Infection (Trial)" and "New Coronary Pneumonia" During the epidemic period, the technical guidelines for protection of medical personnel (trial implementation), strengthened process management, correctly selected and used personal protective equipment such as masks, gowns, protective clothing, eye masks, protective masks, gloves, and strict implementation of various disinfection and isolation measures. Minimize the risk of nosocomial infections and prevent 2019-nCoV infections in hospitals by medical staff.

5. Treatment of infants and young children: Only mild symptomatic oral treatment is needed for mild children. In addition to symptomatic oral administration for children with common type, treatment with syndrome differentiation can be considered. If combined with bacterial infection, antibacterial drugs can be added. Severely ill children are mainly symptomatic and supportive treatment. Ribavirin injection was given antiviral therapy empirically at 15 mg / kg (2 times / day). The course of treatment did not exceed 5 days.

(V) Treatment plan of integrated traditional Chinese and western medicine

The combination of traditional Chinese and western medicine for the treatment of new coronavirus pneumonia can improve the synergistic effect. For adult patients, the condition can be improved through TCM syndrome differentiation. For light patients, those with a syndrome of wind-heat type are given the traditional Chinese medicine Yinqiaosan plus and minus treatment; those with gastrointestinal symptoms and those with damp-wetting and yang-type syndrome are given the addition and subtraction of Zhipu Xialing Decoction and Sanren Decoction. For ordinary patients, those with syndromes of hot and evil stagnation of lungs can be treated with Chinese medicine Ma Xing Shi Gan Decoction; those with syndromes of dampness and stagnation of lungs can be treated with traditional Chinese medicine Da Yuan Yin, Gan Lu Fang Dan, etc., which can be controlled to some extent Progression of the disease, reducing the occurrence of common to severe; for anorexia, nausea, bloating, fatigue, anxiety and insomnia, the addition and subtraction of Chinese medicine Xiao Chai Hu Tang can significantly improve symptoms. For severe patients, if the fever persists, or even the high fever, bloating, and dry stools are closed, and those who are heat-tolerant and the lungs are closed, give the Chinese medicine Dachengqi Decoction enema to relieve fever or reduce fever, or use Chinese medicine. The treatment of Baihu Decoction, Shengjiang San and Xuanbai Chengqi Decoction were added and subtracted to cut off the condition and reduce the occurrence of heavy to critical illness. Children with light patients, when the disease belongs to the defender, can be added or subtracted from Yinqiaosan or Xiangsusun. Ordinary children, those with damp heat and closed lungs, are given Ma Xing Shi Gan Decoction and Sanren Decoction; those with moderate scorching dampness and heat such as bloating and vomiting with abdominal distension can be added or subtracted without changing Jinzhengqi San. For severe patients with epidemic and closed lung (currently rare in the country), please refer to adult Xuanbai Chengqi Decoction and Manna Disinfection Danjiao; if the poison is hot, the gas can't pass, and the medicines are not good, the Rhubarb Decoction is given to enema for emergency.

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