

# Expert Consensus by Qilu Hospital of Shandong University on the diagnosis, management, and treatment of suspected COVID-19 cases (English version)

Yuguo Chen\*, on behalf of Expert Consensus Group of Qilu Hospital of Shandong University on Diagnosis and Treatment for COVID-19

## Abstract

We devised a protocol to establish a standardized method of screening, diagnosing, and managing suspected cases of coronavirus disease (COVID-19) and to enhance the management of COVID-19 suspected cases. The protocol that included diagnostic criteria, preventive measures, and control measures against COVID-19 was developed based on new evidence regarding the epidemiological and clinical characteristics of COVID-19. A consensus document was subsequently formulated. The consensus focused on the clinical management of patients with suspected fever and reviewed the procedure for undergoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid testing. This consensus will contribute to the ongoing efforts worldwide for the prevention and control of COVID-19.

**Keywords:** COVID-19, Nucleic acid testing, Suspected cases

The outbreak of coronavirus disease (COVID-19) has had a tremendous impact on human health and the social economy worldwide. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus<sup>[1-3]</sup> with high contagiousness.<sup>[4,5]</sup> Effective vaccines are currently available against it. A more transmissible variant of SARS-CoV-2, which was first identified in Britain, is

associated with a higher degree of mortality than other variants.<sup>[6]</sup> While isolation of the source of infection, breaking the chain of transmission, and effectively treating infected patients are important for controlling the epidemic, the management of suspected cases also plays a pivotal role.<sup>[7]</sup> The diagnosis, management, prevention, and control of suspected cases of COVID-19 were discussed by Qilu Hospital of Shandong University to reach a consensus, which is summarized below.

*Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.*

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Emergency and Critical Care Medicine (2021) 1:1

Received: 8 June 2021; Accepted: 11 July 2021

Published online: 15 September 2021

<http://dx.doi.org/10.1097/EC9.000000000000011>

## Epidemiological characteristics of COVID-19

### The source of infection

At present, the source of infection mainly refers to patients infected with SARS-CoV-2 who are either symptomatic or asymptomatic.<sup>[8]</sup>

### The route of transmission

The main routes of transmission include the inhalation of respiratory droplets and contact with an infected person. Aerosol transmission can occur in closed environments where prolonged exposure to high aerosol concentrations occurs.<sup>[9,10]</sup>

### Susceptible population

Any person might be susceptible to infection.<sup>[11]</sup>

## Clinical characteristics of COVID-19

### Clinical manifestations

Epidemiological investigations have revealed an incubation period of COVID-19 to be 1–14 days, ranging between 3 and 7 days in most cases.<sup>[12,13]</sup> The main

symptoms of COVID-19 include fever (87.9%), fatigue (38.1%), and dry cough (67.7%). A small number of patients may present with nasal congestion (4.8%), sore throat (13.9%), and diarrhea (3.7%), among others.

Critically ill patients may develop dyspnea and/or hypoxemia 1 week after the onset of COVID-19. In severe cases, acute respiratory distress syndrome, septic shock, metabolic acidosis, and disorders of coagulation may occur. Patients with mild disease may only have low fever and slight fatigue.<sup>[14]</sup>

### Laboratory tests

In the early stages of COVID-19, the white blood cell count in peripheral blood is normal or decreased (94.1%) and the lymphocyte count is decreased (82.1%).<sup>[13,14]</sup> The levels of liver enzymes, lactate dehydrogenase, muscle enzymes, and myoglobin may be elevated in certain patients. Similarly, troponin levels may increase in critically ill patients. Most patients experience an increase in C-reactive protein (CRP) levels and erythrocyte sedimentation rate, while procalcitonin levels remain normal. In severe cases, D-dimer levels are increased, while the lymphocyte count in peripheral blood gradually declines.

Nucleic acid derived from SARS-CoV-2 can be detected in nasopharyngeal swabs, sputum, lower respiratory secretions, blood, stool, and other specimens collected from infected patients.

### Chest imaging

Chest computed tomography (CT) of patients with COVID-19 may reveal multiple ground-glass shadows, patchy shadows, and grid-like shadows in the subpleural regions, along the bronchial vascular bundles, or in a “bat wing” pattern. Bronchial vascular bundles may also have a thicker appearance.<sup>[15,16]</sup>

### Diagnostic criteria for suspected cases

The epidemiological history and clinical manifestations of suspected cases should be thoroughly investigated.

### Epidemiological history

- Contact with a confirmed case of COVID-19 (positive nucleic acid test) within 14 days prior to the onset of disease.
- Contact with patients with fever or respiratory symptoms from a community with positive cases reported, within 14 days prior to the onset of disease.

### Clinical manifestations

- Symptoms of fever and/or respiratory disturbance.
- Features of COVID-19 on imaging studies.
- Normal or decreased white blood cell count and decreased lymphocyte count in the early stages of disease.

Suspected cases should meet at least one of the criteria for epidemiological history and any two of the criteria for clinical manifestations. In the absence of an epidemiological history, all three clinical manifestations should be present for a patient to be diagnosed as a suspected case.

### Approach to screening, diagnosing, and managing suspected COVID-19 cases

#### Screening and diagnosis of patients with fever

**Outpatients and emergency patients.** Patients with fever (body temperature  $\geq 37.3^{\circ}\text{C}$ ) or obvious respiratory symptoms found during pre-examination, triage, or in the outpatient department shall be directed to the outpatient fever clinic for treatment.

As an independent unit attached to the emergency department (ED), the fever clinic is responsible for the screening of patients.

- In the presence of an identifiable cause of fever, the cause should be indicated in the patient’s medical record; if further treatment is required, the patient should be directed to the relevant department for treatment.
- Patients with fever of unknown origin should be isolated in a designated area for observation; the designated area should be determined in conformity with the criteria for observation.

Patients who meet the criteria for observation shall be observed in the isolation ward of the fever clinic and undergo laboratory tests, CT, and SARS-CoV-2 nucleic acid testing. It is recommended to test for the presence of SARS-CoV-2 even in patients who may have tested positive for common respiratory pathogens.

Patients who do not meet the criteria for observation shall undergo SARS-CoV-2 nucleic acid testing. After the collection of specimens for the test, the patients should be informed of precautions to be taken while awaiting the results. They should then sign the Home Observation Notice and return home for observation until the test results are made available. The corresponding medical institution should transmit each patient’s information to a designated team in the district or county where the patient resides for better management and control. For patients who test negative for SARS-CoV-2, no re-examination is required and home observation is automatically terminated.

- Critically ill patients who cannot be transferred to the fever clinic for observation shall be isolated without delay in the ED and shall be tested to determine the possible etiology. Meanwhile, medical staff, other patients in the ward, and any visitors to the ward should be fully protected.

The criteria for observation in the fever clinic are as follows:

- Patients meeting the diagnostic criteria for suspected COVID-19 cases.
- Fever of unknown origin (body temperature  $\geq 37.3^{\circ}\text{C}$ ), and inability to exclude viral pneumonia based on CT findings.

c. Key groups (close contacts of patients with fever in COVID-19 outbreak and surrounding areas or confirmed cases of COVID-19, in the previous 14 days). The isolation ward for observation should conform to the concept of “three zones and two passages,” which implies that a room should be occupied by a single person, visitors are not allowed, and all exits from the ward should be reported.

The criteria for termination of the observation period in the fever clinic are as follows (sampling time interval of at least 1 day):

- For suspected cases, two negative SARS-CoV-2 nucleic acid tests should be obtained.
- For low-risk patients with COVID-19, two negative SARS-CoV-2 nucleic acid tests should be obtained.
- For highly suspected cases with typical clinical manifestations, three negative SARS-CoV-2 nucleic acid tests are required, and no radiological worsening should be visible on repeat chest CT 3 days after the previous one.

**Inpatients.** Inpatients with unexplained fever or pneumonia should be immediately referred to the fever clinic for consultation. If the consultation cannot exclude SARS-CoV-2 infection, intervention by an expert group is required. If the expert group classifies those inpatients as suspected cases, the patients should be transferred to the isolation ward of the Department of Infectious Disease for observation and pathogenic testing. If a patient’s condition does not allow the transfer, the patient should be isolated in a single room in the original ward and should immediately undergo SARS-CoV-2 nucleic acid testing. Meanwhile, medical staff, other patients in the ward, and any visitors to the ward should be fully protected.

The criteria for the termination of isolation in the Department of Infectious Disease are listed below.

- For suspected cases, two negative SARS-CoV-2 nucleic acid tests should be obtained.
- For patients with typical clinical manifestations of SARS-CoV-2 infection and two negative SARS-CoV-2 nucleic acid tests, a third nucleic acid test is warranted. After three negative SARS-CoV-2 nucleic acid test results have been obtained, the patients shall be transferred back to the original department to which they were admitted, and the department shall not refuse the transfer. If all three nucleic acid tests are negative, but SARS-CoV-2 infection cannot be completely excluded, the patients should be transferred back to the temporary isolation ward of the original department. The medical staff should be effectively protected during any clinical interaction with these patients.

**Patients with fever and critical underlying chronic diseases.** After these patients have been observed in the isolation ward of the fever clinic or the Department of Infectious Disease, they should receive a consultation with a medical team from the departments involved in the treatment of their underlying chronic diseases. The medical team should aim to formulate a treatment plan to deal with

changes in the patients’ condition over time and should assist in therapy. The isolation ward of the fever clinic or the Department of Infectious Disease is responsible for providing isolation care, daily management, and symptomatic treatment.

### **Consultation procedure for patients with fever**

**Fever clinic consultation.** For inpatients with fever or pneumonia, it is necessary to exclude SARS-CoV-2 infection. The fever clinic will first conduct a preliminary consultation to rule out other causes of fever or pneumonia.

**Consultation with an expert group for the diagnosis and treatment of COVID-19.** If the patients are considered to be suspected cases after preliminary consultation, a consultation with the hospital’s expert group for the diagnosis and treatment of COVID-19 shall be requested by the fever clinic and arranged by the Medical Department. If confirmed to be suspected cases, they shall be reported as such and should follow the stipulated procedures.

### **Indications and procedure for SARS-CoV-2 nucleic acid testing**

#### **Test indications**

Indications for the test are as follows:

- Patients with fever of unknown origin (body temperature  $\geq 37.3^{\circ}\text{C}$ ).
- A decrease in the white blood cell or lymphocyte count for undetermined reasons.
- Patients with CT findings suggesting that viral pneumonia cannot be excluded.
- People in close contact with patients with COVID-19 (especially medical personnel).
- People with a history of having been to an area of COVID-19 outbreak.

#### **Operating rules for specimen collection**

**Protection requirements.** Personnel engaged in specimen collection for SARS-CoV-2 testing should undergo biosafety training and possess the relevant skills. Additionally, they should adopt level three personal protection measures that consist of the use of medical protective masks or N95 masks, double-layered latex gloves, goggles, overalls, double-layered medical protective caps, shoe covers, hand hygiene, and double masks (a medical protective mask on the outside with an N95 mask on the inside) if needed.

**Specimen types.** Upper respiratory tract specimens include pharyngeal swabs, nasal swabs, and nasopharyngeal swabs. Lower respiratory tract specimens include deep cough sputum, respiratory tract extracts, bronchial lavage fluid, and alveolar lavage fluid.

Stool specimens refer to fresh feces.

Conjunctival specimens refer to conjunctival swabs of the eyes.

**Method of specimen collection**

**Pharyngeal swab.** Using a plastic swab with a polypropylene fiber head, wipe both pharyngeal tonsils and the posterior pharyngeal wall. Next, immerse the swab head into a tube containing viral transport medium (isosmotic salt solution, tissue culture medium, or phosphate-buffered solution), discard the tail end, and tighten the cap.

**Nasal swab.** Gently insert a plastic swab with a polypropylene fiber head into one nostril, keep it inside for a while, and then withdraw it by slowly rotating it. Use another plastic swab with a polypropylene fiber head and repeat the steps mentioned above to collect a specimen from the other nostrils. Immerse both swabs in a tube containing viral transport medium, discard the tail ends, and tighten the cap.

**Nasopharyngeal or respiratory tract extract.** A collector connected to a negative pressure pump is used to extract mucus from the nasopharynx or respiratory secretions from the trachea. Insert the head of the collector into the nasal cavity or trachea, switch on the negative pressure, slowly rotate the head of the collector while withdrawing it to collect the extracted mucus, and flush the collector with 3 mL of sampling solution. The collector may also be replaced by a pediatric catheter connected to a 50-mL syringe.

**Sputum.** The coughed sputum must be collected in a sputum cup with the lid tightened after the specimen has been obtained.

**Bronchial and alveolar lavage fluid.** Bronchial and alveolar lavage are performed using an electronic bronchoscope, and the lavage fluid is collected in a collector.

**Fecal specimen.** In patients manifesting diarrheal symptoms at onset, 3–5 mL of a stool sample should be collected.

**Conjunctival swab.** Gently wipe the surface of the conjunctiva with a swab, insert the head of the swab into the sampling tube, discard the tail end, and tighten the cap.

**Specimen packaging and preservation**

**Specimen packaging.** The specimens should be packaged in three layers in accordance to guidelines regarding category A infectious substances. After the specimens are collected, the outer surface of the container is disinfected by wiping or spraying it with 1000 mg/L of chlorine-containing disinfectant. The specimen number and type, patient's name, and sampling date are then marked on the outer surface of the container. Afterward, each container is packaged in a special self-sealing bag with biosafety warning labels. The outer surface of each bag is disinfected using 1000 mg/L of chlorine-containing disinfectant. Numerous bags are then placed in designated sealed transport boxes, and the outer surface of each box is also disinfected by 1000 mg/L of chlorine-containing disinfectant.

**Specimen preservation.** Specimens collected for nucleic acid testing should be tested as soon as possible. Specimens that need to be tested within 24 h can be stored at 4°C, while those that cannot be tested within 24 h should be stored at –70°C or below. If a temperature of –70°C cannot be achieved, specimens should be temporarily stored at –20°C. Designated storehouses or cabinets should be set up for individual storage of these specimens.

**Procedures for specimen transportation and testing****Specimen transportation**

**In-hospital transportation.** The specimens shall be transported in designated boxes to the laboratory as soon as possible by biosafety-trained personnel who shall wear caps, disposable surgical masks, gloves, and isolation suits. During transportation, the specimens shall be placed vertically, and the transport boxes shall be kept stable to avoid violent bumps.

**Transportation outside of the hospital.** Contact the local Center for Disease Control and Prevention or an authorized and qualified third-party laboratory. Specimens that require transportation over long distances should be stored using dry ice or other refrigeration methods.

**Specimen testing.** Testing of SARS-CoV-2 should be performed in a qualified biosafety level two or above laboratory by professionals who have received adequate biosafety training and who possess the required laboratory skills. All personnel involved in testing should adopt level three biosafety measures according to standard operating procedures. All specimens used for SARS-CoV-2 nucleic acid testing shall be processed in a biosafety cabinet. Testing consist of the following three steps:

- a. Specimen receipt and inactivation,
- b. Nucleic acid extraction, and
- c. Nucleic acid testing using either the reverse transcription polymerase chain reaction (RT-PCR) or the sequencing method.

**Reporting and management of test results.** The test results should be reported within 24 h. If the test result is positive, the medical institution responsible for nucleic acid testing shall immediately notify the specimen submission unit. The cases recorded as “suspected cases” shall be modified to “confirmed cases” in the case of a positive laboratory test result.

**Protective measures**

Medical personnel should adopt personal protective measures according to the level of protection applicable to them.

Level one protection is applicable to medical technicians and medical assistance personnel involved in the pre-examination, triage, and general outpatient departments. They are required to wear disposable work caps, disposable surgical masks, overalls, and disposable latex gloves when necessary. Strict adherence to hand hygiene measures is also mandatory.

Level two protection is applicable to medical personnel allocated to the fever clinic, Department of Infectious Disease, and ED when they are engaged in the diagnosis and treatment of suspected or confirmed cases. They are required to wear disposable work caps, protective glasses or face shields (anti-fog type), medical protective masks, protective clothing, disposable latex gloves, and disposable shoe covers. Strict adherence to hand hygiene measures is obligatory.

Level three protection is applicable to medical personnel involved in aerosol-generating procedures performed on suspected or confirmed cases. These procedures include sputum specimen collection, respiratory tract sampling, tracheal intubation, and tracheotomy, which may result in the spraying or splashing of respiratory secretions and other fluids from patients. They are required to wear disposable work caps, facepiece respirators or positive pressure respirators, protective clothing, disposable latex gloves, and disposable shoe covers. Strict adherence to hand hygiene is mandatory.

All patients and people accompanying them are required to wear face masks.

Each ward should make provision of a room reserved for emergency use.

Asymptomatic infected patients should be isolated for 14 days, and they can be released from isolation if their nucleic acid test results are negative after 7 days of isolation.

## Monitoring and treatment

### Determination of the treatment site

The treatment site shall be determined in compliance with each patient's condition. Suspected and confirmed cases shall be treated in the isolation ward of the Department of Infectious Disease or in designated hospitals with effective isolation and protective measures in place. Each suspected case should receive treatment in isolation in a single room. However, multiple confirmed cases can be admitted to the same ward. Critically ill patients should be admitted to a single room in the intensive care unit for treatment in isolation as soon as possible.<sup>[16]</sup>

### Monitoring and treatment methods

- a. Routine tests performed on blood samples, including CRP, biochemical markers (liver enzymes, myocardial enzymes, and kidney function tests), coagulation function, and arterial blood gas analysis; tests performed on urine samples; and chest imaging can be monitored in accordance with each patient's condition. Cytokine testing is recommended if it is feasible.
- b. General treatment: Bed rest, strengthening supportive treatment, ensuring the intake of an adequate amount of calories, maintenance of the balance of water and electrolytes and the stability of the internal environment, and close monitoring of vital signs and oxygen saturation.
- c. Timely and effective oxygen therapy should be provided through nasal catheters, oxygen delivery masks, and nasal high-flow oxygen.

- d. Antiviral treatment: Currently, there is no proven effective antiviral treatment.
- e. Antibacterial treatment: Blind or inappropriate use of antibacterial drugs shall be avoided. Antibiotics can be prescribed when there is evidence of bacterial infection.
- f. Glucocorticoids: Glucocorticoids can be prescribed for a short period of time to reduce inflammation when the inflammatory response is severe.
- g. Respiratory support: Noninvasive ventilation, invasive ventilation, or extracorporeal membrane oxygenation can be used in critically ill patients.
- h. Adequate life-support treatment should be provided as needed.
- i. The treatment of underlying diseases should also be performed concomitantly.
- j. Traditional Chinese medicine (TCM) treatment: Vulnerable people and contacts of suspected cases can resort to TCM for energy restoration and strengthening of respiratory resistance.<sup>[17]</sup> Suspected cases of COVID-19 can be treated based on the applicability of TCM to their condition.

## Conflict of interest statement

Yuguo Chen is the Editor-in-Chief of *Emergency and Critical Care Medicine*. The authors declare no conflict of interest.

## Author contributions

This Consensus was jointly completed by Expert Consensus Group of Qilu Hospital of Shandong University on Diagnosis and Treatment for COVID-19.

## Funding

None.

## Ethical approval of studies and informed consent

Not applicable—not required for this study.

## Acknowledgements

None.

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**How to cite this article:** Chen Y. Expert Consensus by Qilu Hospital of Shandong University on the diagnosis, management, and treatment of suspected COVID-19 cases (English version). *Emerg Crit Care Med*. 2021;1:6–11. doi: 10.1097/EC9.0000000000000011