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# Translation: Expert consensus on the application of artificial liver blood purification system in the treatment of severe and critical COVID-19

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**Abstract**
The prevention and treatment of COVID-19 nationwide has entered a tackling phase. Effective treatment of severe and critically ill patients is the key to reducing the fatality of the disease. The artificial liver blood purification system can remove inflammatory factors, alleviate the damage of the inflammatory response to the body, and has important value for the treatment of severe COVID-19. Led by Academician Lanjuan Li, based on the experience of treating patients across the country, integrating the opinions of experts from all over the country, the center summarized and formulated the consensus including the basic principles, treatment indications, relative contraindications, mode selection, monitoring indicators, and efficacy evaluation of artificial liver, which provides reference for treatment of severe COVID-19 patients.
**Keywords:** Coronavirus infections；Liver, artificial；COVID-19；Expert consensus

At present, the prevention and treatment of COVID-19 has entered a critical stage. Effective treatment of severe and critical patients is the key to reduce the fatality of this disease.[1] The acute severe respiratory infectious diseases have common clinical characteristics: rapidly progressing inflammation of the lungs, severe hypoxemia and multiple organ failure. The respiratory failure, shock, multiple organ failure and uncontrollable secondary infection are the main causes of death finally.[2-3] Studies have revealed that severe cases of SARS, avian influenza H5N1 and H7N9 virus infections all present a "cytokine storm", which is the main factor of disease progression.[4-6] Therefore, blocking the "cytokine storm" is a key intervention for the treatment of shock, hypoxemia and multiple organ failure. Studies have shown that the artificial liver support system (ALSS) can remove inflammatory factors and block the "cytokine storm", thus reducing damage to the body caused by the inflammatory response, which is of great value for the treatment of severe and critical patients.[7-9] Clinical practices have shown that Li's ALSS has played an important role in the treatment of patients with severe H7N9 viral infection.[8-9] After discussions by the expert panel, the consensus has been reached on the principles, indications, contraindications, monitoring indicators and efficacy evaluation of ALSS for the treatment of severe and critical COVID-19 patients.[10]

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## 1. Basic principle

ALSS integrates plasma replacement, adsorption, perfusion, blood/plasma filtration and other techniques, to remove inflammatory mediators, endotoxins, and small and medium molecules of toxic and harmful substances, to supplement albumin, coagulation factors and other beneficial substances, and to regulate water electrolytes, acids and bases balance. It can block "cytokine storm", reduce pulmonary inflammation and improve respiratory function. At the same time, it can help to restore immune homeostasis, improve metabolic spectrum disorder in the body, facilitate accurate volume management, improve functions of liver, kidney and other organs, so as to increase the rescue success rate and reduce the fatality rate of severe and critical COVID-19 patients.[10]

## 2. Indications

Patients should receive ALSS treatment if they meet criteria (1) & (2), or only (3).

(1) The inflammatory factors (such as IL-6, *etc*.) are no less than 5 times the upper limit of the normal value, or the daily increase is greater than 1 times;
(2) Pulmonary imaging shows rapid progression, CT or X-rays indicate that the percentage of lung involvement progresses 10% or more per day;
(3) Patients with basic diseases that require ALSS for treatment.

## 3. Relevant contraindications

There are no absolute contraindications for ALSS during the rescue of patients with critical illnesses. But prudent use is necessary in the following situations:

(1) Patients with serious active bleeding or disseminated intravascular coagulation;
(2) Patients who have serious allergies for the blood products or drugs used in the treatment, such as plasma, heparin, protamine, *etc*.;

(3) Patients with acute cerebrovascular accidents or severe head injury;
(4) Patients with cardiac dysfunctions or cardiac function grade III and above;
(5) Patients with uncorrected hypotension or shock;
(6) Patients with severe arrhythmias.

## 4. Selection of treatment mode

After fully evaluating the patients, the appropriate treatment mode may be selected as following:

(1) When plasma is available, it is recommended to conduct plasma exchange in combination with plasma adsorption or double plasma molecular adsorption, perfusion and filtration; plasma exchange volume (L) = body mass (kg)×(1/13)×(1-Hematocrit/100); if plasma is in short supply, it is recommended to exchange more than 2000mL of plasma at least.
(2) When plasma is not available or less than 2000mL, it is recommended to carry out plasma adsorption or double plasma molecular adsorption, perfusion and hemo-filtration combination treatment.

In case of renal insufficiency, sequential combined hemo-dialysis and/or continuous hemofiltration should be performed.

## 5. Monitoring indicators

### *5.1 Pre-treatment monitoring indicators*

(1) Clinical symptoms and signs: vital signs, pulmonary manifestations, *etc*.; oxygen supply mode, flow rate and concentration;
(2) Blood type, blood routine test (BRT), C-reactive protein (CRP), procalcitonin (PCT), coagulation function, biochemical indexes, immunoglobulin, arterial blood gas analysis + lactic acid, peripheral blood IL-6, arterial oxygen partial pressure ($PaO_2$)/oxygen absorption concentration ($FiO_2$), and pulmonary imaging (X-ray or CT) examinations;
(3) The detection of cytokines such as IL-8, IL-10, tumor necrosis factor-α (TNF-α) and peripheral blood lymphocyte subsets can be added if the tests are available;
(4) Pneumonia severity index (PSI) score.

### *5.2 Post-treatment monitoring indicators*

(1) Daily record of clinical signs and symptoms: vital signs, lung performance, *etc*.; oxygen supply pattern, flow and concentration;
(2) Daily monitor BRT, CRP, PCT, coagulation function, biochemical indexes, arterial blood gas analysis + lactic acid, IL-6 and $PaO_2/FiO_2$; testing for IL-8, IL-10 and TNF-α may be added if available;
(3) Daily record PSI scores;
(4) Monitor immunoglobulin levels every 3 days; and lymphocyte subsets may be monitored if available;
(5) Complete lung imaging (X-ray or CT) examinations every 3 days.

## 6. Efficacy evaluation

Includes the efficacy evaluation of each treatment and survival rate.

### *6.1 Evaluation of the efficacy of each treatment*

Based on the changes of monitoring indicators before and after each treatment, mainly the cytokines (IL-6, *etc*.) and PSI scores.

### *6.2 Evaluation of survival rate*

Includes 28-day and 12-week survival rate.

## 7. Criteria for terminating treatment

If criterion (1) in combination with any of the criteria (2) to (5) is met, treatment termination could be considered, except for the condition that patients need continued treatment for basic diseases.

(1) Temperature has been normal for 3 days, and respiratory symptoms improve significantly;
(2) Inflammatory cytokines (such as IL-6) have dropped below 2 times the normal level for 3 days;
(3) Disengaged from respiration supporting therapy;
(4) Blood lactate has been below 2.0 mmol/L for 3 days;
(5) Pulmonary imaging shows significant improvement for one week, and the pulmonary lesion area is absorbed by more than 30% compared with before.

It should be noted that the current ALSS expert consensus for the treatment of severe and critical COVID-19 patients are based on the empirical data from several centers in Zhejiang, Hubei, Henan and Shaanxi provinces.[11] This consensus can be used as a treatment recommendation for implementation of effective treatment measures during the COVID-19 pandemic. We should make every effort to reduce the fatality rate of COVID-19.

## Expert panel

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