

ADSORPTION SOLUTION SARS-CoV-2 INDUCED COVID-19

Since Dec. 2019, acute respiratory disease due to 2019 novel coronavirus (2019-nCoV) emerged in Wuhan city and rapidly spread throughout China.

On Jan 31, 2020, the WHO declared the outbreak to be a public health emergency of international concern.

Until Feb. 14th, 2020, the total clinical-confirmed cases are 64436 globally, 63929 cases in China and 507 cases out of China.

Thanks to the increasing medical resources of diagnosis and treatment received from all over the world, the spread of SARS-CoV-2 in Wuhan, China had almost under control.

National Health Commission has recently announced the National Recommendations for Diagnosis and Treatment of pneumonia caused by 2019-nCoV (the 5th edition)

National Recommendations for Diagnosis and Treatment of pneumonia caused by 2019-nCoV (The 5th Edition).

Since December 2019, a number of new cases of pneumonia caused by coronavirus have been found in Wuhan, Hubei. With the spread of the epidemic, other cases in China and other regions have also been found. As an acute respiratory infectious disease, the disease has been included in the class B infectious disease stipulated in the law of the People's Republic of China on the Prevention and Control of Infectious Diseases and is managed as class A infectious disease.

With the deepening of the understanding of the disease and the accumulation of experience in diagnosis and treatment, we revised the National Recommendations for Diagnosis and Treatment of pneumonia caused by 2019-nCoV (The 4th Edition).

III Treatment of severe and critical cases.

4. Other treatment measures

According to the degree of dyspnea and the progress of chest imaging, glucocorticoids can be used for a short time (3-5 days) as appropriate. It is recommended that the dosage should not exceed 1-2mg / kg / day of methylprednisolone. It should be noted that the large dose of glucocorticoids will delay the removal of coronavirus due to immunosuppression. Xuebijing can be given intravenously (100ml / time, twice a day) and enteroclysis can be used. The channel microecological regulator can maintain the microecological balance of the intestine and prevent the secondary bacterial infection. **If possible, the blood purification technology can be considered for the critically ill patients with high inflammatory response.** If possible, the recovery plasma treatment can be used.

The Story of Cytokine Storm

Is there cytokine storm in COVID-19?

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study

Nanshan Chen¹, Min Zhao², Xuan Dong³, Jierong Qu⁴, Fengguo Gong⁵, Yang Han⁶, Yong Qiu⁷, Jingli Wang⁸, Ying Liu⁹, Yuan Wei¹⁰, Jie Guo¹¹, Ying Yu¹², Zhen-Cheng Li¹³

Patients (n=99)	
(Continued from previous column)	
Infection-related biomarkers	
Procalcitonin (ng/ml; normal range 0.0-5.0)	0.5 (1.1)
Increased	6 (6%)
Interleukin-6 (pg/ml; normal range 0.0-7.0)	7.9 (6.1-10.6)
Increased	51 (52%)
Erythrocyte sedimentation rate (mm/h; normal range 0.0-15.0)	49.9 (23.4)
Increased	84 (85%)
Serum ferritin (ng/mL; normal range 21.0-274.7)	808.7 (490.7)
Increased	62 (63%)
C-reactive protein (mg/L; normal range 0.0-5.0)*	51.4 (41.8)
Increased	63/73 (86%)
Co-infection	
Other viruses	0
Bacteria	1 (1%)
Fungus	4 (4%)

Chen et al, 2020, Lancet

Nanshan Chen et al

Jan. 29th, 2020, **Chen et al** published the first retrospective analysis of 99 patients infected by SARS-CoV-2 on the Lancet. It reported 52% infected patients were observed increase of IL-6, indicated the potential existence of cytokine storm in COVID-19 progress.

Yinghui Jin et al

On Feb. 6th, 2020, the increase of IL-6 was again reported by **Jin et al** from China International Exchange and Promotive Association for Medical and Health Care (CPAM) on Military Medical Research.

CPAM

In the Rapid Advice Guideline for Diagnosis and Treatment of 2019 Novel Coronavirus Infected Pneumonia, CRP, PCT and organ function is strongly recommended to be carefully monitored.

Jin et al. Military Medical Research (2020) 7:4
https://doi.org/10.1186/s40779-020-0231-6

MMR MILITARY MEDICAL RESEARCH

POSITION ARTICLE AND GUIDELINE

Open Access

A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version)

Ying-Hui Jin¹, Lin Cai², Zhen-Shun Cheng³, Hong Cheng⁴, Tong Deng^{1,2}, Yi-Pin Fan^{1,2}, Cheng Fang¹, Di Huang¹, Lu-Qi Huang^{1,2}, Qiao Huang¹, Yong Han¹, Bo Hu¹, Fen Hu¹, Bing-Hui Li^{1,2}, Yi-Rong Li¹, Ke Liang^{1,2}, Li-Kai Lin^{1,2}, Li-Sha Luo¹, Jing Ma¹, Lin-Lu Ma¹, Zhi-Yong Peng¹, Yun-Bao Pan¹, Zhen-Yu Pan¹, Xue-Qun Ren¹, Hui-Min Sun^{1,2}, Ying Wang^{1,2}, Yun-Yun Wang¹, Hong Wang¹, Chao-Jie Wei¹, Dong-Fang Wu¹, Jian Xia^{1,2}, Yong Xiong^{1,2}, Hai-Bo Xu^{1,2}, Xiao-Mei Yao¹, Yu-Feng Yuan¹, Tai-Sheng Ye¹, Xiao-Chun Zhang^{1,2}, Ying-Wen Zhang¹, Yin-Gao Zhang¹, Hua-Min Zhang^{1,2}, Yan Zhao¹, Ming-Juan Zhao¹, Hao Zi^{1,2}, Xian-Tao Zeng^{1,10}, Yong-Yan Wang^{1,2}, Ying-Kuan Wang^{1,2}, for the Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team, Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care (CPAM)

6.2 Treatment plans

- (1) The patient should rest in bed, being monitored for vital signs (heart rate, pulse oxygen saturation, respiratory rate, blood pressure) and given supportive treatment to ensure sufficient energy intake and balance for water, electrolytes, acid-base levels and other internal environment factors (**Strong recommendation**).
- (2) The patient should be monitored for blood routine, CRP, PCT, organ function (liver enzyme, bilirubin, myocardial enzyme), creatinine, urea nitrogen, Urine volume, etc.), coagulation function, arterial blood gas analysis and chest imaging (**Strong recommendation**).
- (3) The patient should be given effective oxygen therapy, including nasal catheter, mask oxygen, high flow nasal oxygen therapy (HFNO), non-invasive ventilation (NIV) or invasive mechanical ventilation (**Strong recommendation**).

Jin et al, 2020, Military Medical Research

The role of cytokines in COVID-19?



Prof. Zhiyong Peng

Feb. 7th 2020, Wuhan University Zhongnan Hospital reported 138 hospitalized patients with COVID-19.

Totally 33 patients were tracked with the dynamic profile of laboratory findings. In the 5 non-survivors, the neutrophil counts is increased probably due to the cytokine storm induced by virus invasion, coagulation activation could have been related to sustained inflammatory response, and acute kidney injury could have been related to direct effects of the virus, hypoxia, and shock. The 3 pathologic mechanisms may be associated with the death of patients with NCIP.

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China

Dawei Wang, MD; Bo Hu, MD; Chang Hu, MD; Fangfang Zhu, MD; Xing Liu, MD; Jing Zhang, MD; Binbin Wang, MD; Hui Xiang, MD; Zhenshun Cheng, MD; Yong Xiong, MD; Yan Zhao, MD; Yirong Li, MD; Xinghuan Wang, MD; Zhiyong Peng, MD

and a minority of the patients needed invasive ventilation or even extracorporeal membrane oxygenation.

The data in this study suggest rapid person-to-person transmission of 2019-nCoV may have occurred. The main reason is derived from the estimation of the basic reproductive number (R_0) based on a previous study.¹⁵ R_0 indicates how contagious an infectious disease is. As an infection spreads to new people, it reproduces itself; R_0 indicates the average number of additional individuals that one affected case infects during the course of their illness and specifically applies to a population of people who were previously free of infection and have not been vaccinated. Based on the report, R_0 from nCoV is 2.2, which estimated that, on average, each patient has been spreading infection to 2.2 other people.¹⁵ One reason for the rapid

dia injury, hepatic injury, and kidney injury. These laboratory abnormalities are similar to those previously observed in patients with MERS-CoV and SARS-CoV infection.

The dynamic profile of laboratory findings was tracked in 33 patients with NCIP (5 non-survivors and 28 survivors). In the non-survivors, the neutrophil count, D-dimer, blood urea, and creatinine levels continued to increase, and the lymphocyte counts continued to decrease until death occurred. Neutrophilia may be related to cytokine storm induced by virus invasion, coagulation activation could have been related to sustained inflammatory response, and acute kidney injury could have been related to direct effects of the virus, hypoxia, and shock. The 3 pathologic mechanisms may be associated with the death of patients with NCIP.

Wang et al, 2020, JAMA

Solution to cytokine storm ?

Prof. Claudio Ronco & Prof. Jean-Louis Vincent

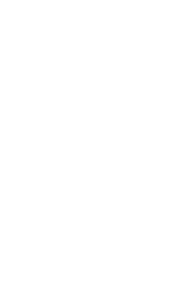
Feb. 6th, 2020, comments on Lancet Respir Med 2020.

•Hemoperfusion including new sorbent cartridges designed to remove cytokines and other circulating mediators should be considered facing the sepsis like syndrome induced by cytokines.



•CRRT can contribute to the AKI which could result from a systemic inflammatory syndrome involving combined myocardial and kidney function.

•Extracorporeal blood purification techniques might needed to support the liver dysfunction patient until hepatocyte recovery occurs.



Coronavirus epidemic: preparing for extracorporeal organ support in intensive care

Zoonotic viral infections are more frequently crossing species to infect human populations. In 2003, the severe acute respiratory syndrome (SARS) virus was transmitted to humans from exotic animals in wet markets in China, and in 2015, the Middle East respiratory syndrome (MERS) virus was transmitted from camels in Saudi Arabia. In both cases, and with the 2019 coronavirus outbreak in China, the original host of the virus is likely to be bats.

which might indicate, in the most severe forms, the need for venous-arterial ECMO support.

Extracorporeal CO₂ removal (ECCO2R) is a technique that can be performed in more ICUs due to the much lower level of complexity than is required for ECMO, but ECCO2R is not really helpful for severely hypoxaemic patients who actually need full ECMO treatment. **Acute kidney injury in these patients is not common, but it might result from a systemic inflammatory syndrome involving combined myocardial and kidney function. In these cases, continuous renal replacement therapies by haemofiltration and haemodiafiltration can contribute to resolution of organ failure. Liver dysfunction can also rarely occur in patients with severe viral infection and it might require extracorporeal blood purification techniques to support the patient until hepatocyte recovery occurs. Finally, a sepsis-like syndrome might occur frequently due to the virus itself or to a superimposed bacterial infection and in this case, since pharmacological approaches have shown poor results, new extracorporeal organ support therapies including haemoadsorption and haemoperfusion, with**

patients infected by coronavirus depends on the presence of comorbidities and immune status of the host. **On the one hand, anergic patients are likely to develop a severe clinical response; on the other hand, an excessive immune response might also add to severity through a generalised inflammatory status. In both cases, immune dysregulation can lead to a progressive cascade of pathophysiological events leading to critical illness with multiple organ dysfunction.**

new sorbent cartridges designed to remove cytokines and other circulating mediators, should be considered.

However, the 2019-nCoV epidemic evolves, ICU personnel must be prepared and trained to apply early and optimal interventions. Extracorporeal organ support therapies might represent an important part of the response and clinicians and other health-care professionals need to be familiar with this sophisticated therapy. A call to action should be made to raise awareness of the different extracorporeal techniques, each with specific criteria and modalities of prescription, delivery, and monitoring.

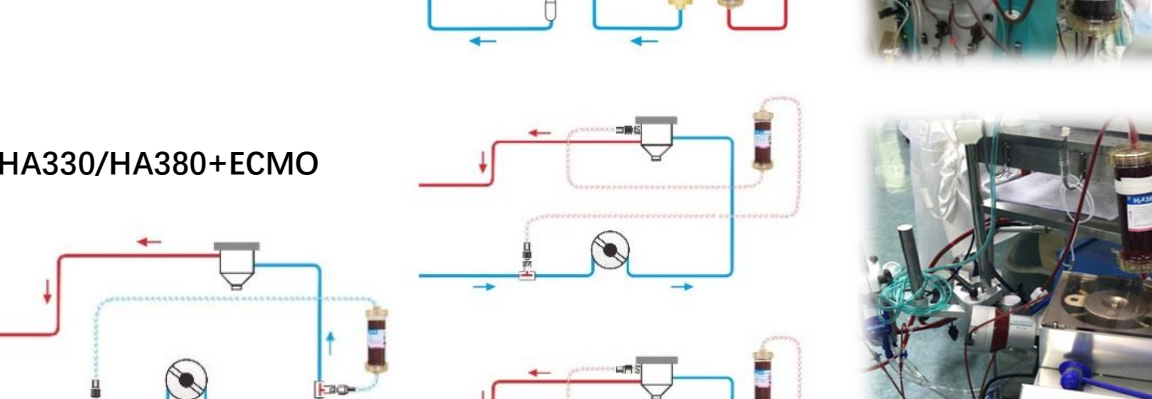
We declare no competing interests.

*Claudio Ronco, Paolo Navalesi, Jean Louis Vincent

ronco@goldnet.it
Department of Medicine, University of Padua, Padua, Italy (CR, PN); International Renal Research Institute, Vicenza, Italy (CR, PN); Division of Nephrology, Dialysis and Transplantation, San Bortolo Hospital, Vicenza, Italy (CR); Anesthesia and Intensive Care Unit, Padua University Hospital, Padua, Italy (PN); and Department of Intensive Care, Erasme University Hospital, Brussels, Belgium (JLV)

Ronco et al, 2020, Lancet Respir Med

HA330/HA380 Designed for Cytokine Adsorption



Neutral macroporous resin

3D network structure
Large specific surface area
Hydrophobic lipophilic skeleton

Relative specific adsorption

Medium-macromolecular substances
such as inflammatory mediators,
protein-bound toxins
Lipophilic hydrophobic metabolites

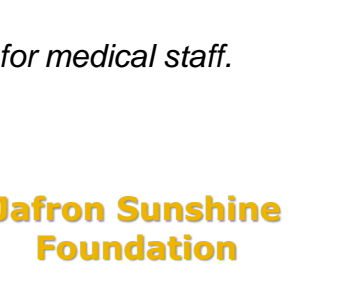
Advanced secondary cross-linked resin sorbent^{III}

Smoother surface
Higher biocompatibility
Higher safety

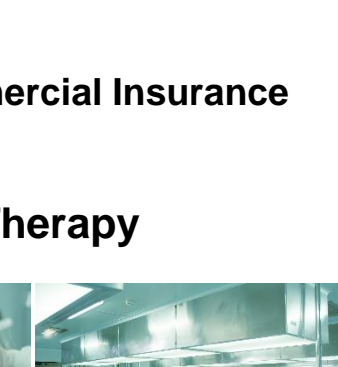
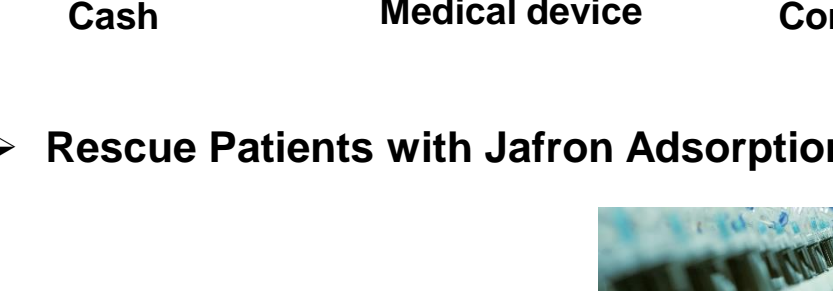
HA330/HA380 Adsorption Therapy

- Once a day for 3-5 consecutive days. 2-12 hours per treatment.
- Anticoagulant: Heparin or Citrate
- Compatible with various blood purification device.

HA330/HA380+CVVH



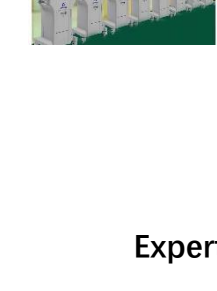
HA330/HA380+ECMO



Jafron in SARS-CoV-2 Epidemic

- **Donation: 2.5 million USD**

Cash, Medical device and consumables, Commercial Insurance for medical staff.



Cash

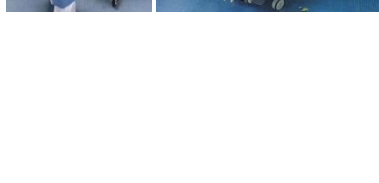


Medical device



Commercial Insurance

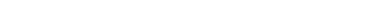
- **Rescue Patients with Jafron Adsorption Therapy**



Jan 20th 2020
Urgent Production



Feb 2nd 2020
Supplies Delivered from Jafron



Feb 3rd 2020
Experts Team and Supplies at Wuhan

Feb 4th 2020
Jafron Adsorption Therapy on Patients with Cytokine Storm

To be continued...

Jafron Biomedical Co., Ltd.

No. 98 Tech Six Road, Zhuhai, China, 519085
en.jafron.com
overseatrade@jafron.com