



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Convalescent plasma as a treatment modality for coronavirus disease 2019 in Sudan

Mozan Osman Hassan<sup>a,\*</sup>, Asma Ahmed Osman<sup>b</sup>, Hana Elsir Abd Elbasit<sup>c</sup>,  
Hanan Elsamani Hassan<sup>c</sup>, Hala Rufai<sup>c</sup>, Maria M.M. Satti<sup>c</sup>, Musab Elnegoumi<sup>d</sup>, Roaa Idris<sup>e</sup>,  
Ashraf Musa<sup>f</sup>, Abdelhakam H. Ali<sup>g</sup>, Susan Ali Zroog<sup>h</sup>, Abduelbagi D.A. Altayb<sup>k</sup>, Amna Khairy<sup>d</sup>,  
Mushal Allam<sup>i</sup>, Asaad Tageldein Idris Abdelhalim<sup>j</sup>

<sup>a</sup> Faculty of Medical Laboratory Science, Omdurman Ahlia University, Sudan

<sup>b</sup> Faculty of Medicine and Health Science, Omdurman Islamic University, Sudan

<sup>c</sup> National Blood Transfusion Services, Federal Ministry of Health, Sudan

<sup>d</sup> Diseases Control Directorate, Federal Ministry of Health, Sudan

<sup>e</sup> University of Wolverhampton, United Kingdom

<sup>f</sup> Abeer Hospital, Muscat, Oman

<sup>g</sup> Faculty of Medical Laboratory Science, University of Al Butana, Sudan

<sup>h</sup> Faculty of Applied Medical Science, University of Al Butana, Sudan

<sup>i</sup> National Institute for Communicable Diseases, National Health Laboratory Service, South Africa

<sup>j</sup> Clinical Immunology Council, Sudan Medical Specialization Board, Sudan

<sup>k</sup> Intensive Care Unit, King Khalid Hospital, Saudi Arabia

### ARTICLE INFO

#### Keywords:

SARS-CoV-2

COVID-19

Treatment

Protocol

Convalescent plasma

### ABSTRACT

Coronavirus disease 2019 (COVID-19) is a disease spreading rapidly in Sudan, the rest of the African continent and the world with no known definitive treatment or vaccines. However, among many treatment interventions being tested globally, beneficial effects and clinical improvements have been reported when convalescent plasma is used for treating COVID-19 patients. We prepared a guiding protocol for treating early to moderate COVID-19 patients with plasma transfusion from convalescent COVID-19 patients. This protocol was deduced based on previously published reports and studies that evaluated and tested convalescent plasma as a prospective therapy for COVID-19 patients. The protocol covers instructions on patient and donor selection criteria, plasma harvesting, plasma product specifications, dosage and precautions for convalescent plasma collection and transfusion process. Altogether, we prepared a treatment protocol that is tailored to the context of Sudan to be adopted by Sudan's health authority. Moreover, it will also provide reference for researchers to design open label clinical trials for convalescent plasma transfusion.

### 1. Introduction

The pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that emerged in Wuhan, China in 2019 was called COVID-19 [1]. The virus emerged as a global pandemic which was declared by the World Health Organization (WHO) on the 11 of March 2020. Currently, the COVID-19 disease is threatening lives and livelihoods across the world, including Sudan [2]. On 13 March 2020 Sudan reported the first case of COVID-19, and as of the 13th of July, more than 10,000 cases have been confirmed with 657 resulting

fatalities [3].

While there is no proven vaccine or therapy for COVID-19, the clinical management protocol of the disease recommended by WHO focuses on infection prevention, monitoring and detection [4]. Convalescent whole blood or plasma was recommended by WHO as an empirical treatment in several viral outbreaks and pandemics: Middle East respiratory syndrome outbreak in 2015 [5], the hemorrhagic fevers such as Ebola West Africa outbreak in 2014 [6], as well as Human influenza-A (H1N1) in 2009 and avian influenza-A (H5N1) pandemics in 2019 [7,8].

\* Corresponding author.

E-mail address: [oh.mozan@gmail.com](mailto:oh.mozan@gmail.com) (M.O. Hassan).

<https://doi.org/10.1016/j.transci.2020.102918>

Received 11 May 2020; Received in revised form 17 August 2020; Accepted 18 August 2020

Available online 27 August 2020

1473-0502/© 2020 Elsevier Ltd. All rights reserved.

Recently, plasma collected from patients in the convalescent phase of infection has been used as an empirical treatment for COVID-19 in many countries [9]. For example, outcomes of an uncontrolled study carried out in China, following 5 severe COVID-19 cases showed clinical improvement after convalescent plasma transfusion [10]. Another study also conducted in China included 10 patients reported a significant progress after 3 days of convalescent plasma transfusion [11]. Furthermore, a study in South Korea showed 2 cases of COVID-19 patients treated with convalescent plasma exhibited good progress in oxygenation and chest X-rays with decrease in the viral load and inflammatory markers [12]. Another reported beneficial effect for convalescent plasma transfusion is improvement and normalization of hypercoagulable state and lowering the incidence of thrombosis that may be present in many of COVID-19 patients [13].

Despite the promising results of these studies some limitations should be considered like the absence of large scale randomized clinical trials with control groups and the fact that in some of these studies plasma transfusion was done concurrently with the administration of antiviral drugs, which may interfere with the outcomes [9].

Additionally, the safety of using convalescent plasma for treating COVID-19 patients has not been confirmed yet, notwithstanding the fact that convalescent plasma therapy can be associated with serious adverse events including circulatory overload, risk of infectious disease transmission, allergy and fever. Even though some propitious early safety results in 5000 patients with severe COVID-19 who received convalescent plasma showed that less than 1 % had serious adverse events, and the mortality rate in 7 days was 14 % which is not disturbing, providing that in some of these cases plasma transfusion was done as an attempt to save intensive care unit (ICU) patients with other critical mortality causes or multi-organ failure [14].

The effect of COVID-19 in Sudan will weaken the economic and health system which is responsible to provide the latest approved medication against COVID-19. Convalescent plasma transfusion is a promising and readily available therapy with low risk and good feasibility. The capacity of the National Blood Bank Service in Sudan is quite suitable with adequate numbers of Aphaeresis machines. Moreover, during the course of this pandemic blood transfusion service in Sudan have been urged by clinicians to provide convalescent plasma to treat COVID-19 patients. Consequently, we defined the requirements in donor selection, collection, preparation and transfusion of convalescent plasma from people who have fully recovered from COVID-19; and its administration to patients with active COVID-19. In this massive local transmission, convalescent plasma transfusion can be adapted as one of the treatment interventions and preparedness plans applicable to all health authorities and blood transfusion services in Sudan.

## 2. Ethical considerations

This paper is not a clinical trial; an approval from the national health ethics committee is required to design precise clinical trials and evaluate the safety and efficiency of convalescent plasma therapy.

The protocol also requires the patient or next of kin written informed consent to receive plasma from someone who has recovered from COVID-19 (see appendix A).

## 3. Donor eligibility

Criteria for recovered patients from COVID-19 to donate plasma should be based on the following:

- 1 Previously reported and confirmed positive infection with SARS-CoV-2 by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) based on nasopharyngeal Swabs obtained during the course of the disease, or detection of SARS-CoV-2 antibodies in the donor serum or plasma by validated antibodies testing.

- 2 Negative repeated SARS-CoV-2 RT-PCR based on nasopharyngeal swabs after recovery or at time of donation with symptoms resolution for at least 14 days. In the absence of repeated test, the donor must be symptoms free for at least 28 days. Pre-donation screening questions like onsets severity, date of symptoms resolution, donor general health must be assessed and documented by physician in the donor's data form to ensure that donor satisfies convalescent plasma donor criteria.
- 3 All donors must meet the WHO blood donor selection criteria in terms of age, weight, hemoglobin level (Hb) and blood pressure and subjected to pre-donation tests including ABO grouping compatibility, screening tests for HIV, HBV, HCV and syphilis [15]. To date, transmission of COVID-19 through blood products has not been reported and limited data have shown detection of SARS-CoV-2 RNA in plasma or serum samples with unclear possibility of COVID-19 transmission through plasma transfusion. Thus, further studies are needed to confirm this, therefore care must be taken to avoid transmission from pre-symptomatic and asymptomatic donors in the donation facilities [16].
- 4 Priority in convalescent plasma collection should be given to untransfused male donors or females who have never experienced pregnancy or abortion; this should be done to avert transfusion related acute lung injury (TRALI) and reduce the chance of transmission of human leukocytes antibodies that might cause TRALI. TRALI can be very serious and fatal and may appear within 6 h following plasma transfusion [17].

No changes should be allowed on the donor selection criteria except in extreme circumstances. Deviation in the donor selection criteria is allowed by WHO blood regulators network, for parameters such as; age limits, Hb level and donation intervals, provided that it will not result in harmful effect to the donor [18]. Male donors can undergo double or triple plasmapheresis donation and should be watched carefully during the process with medical care staff constantly available [13].

## 4. Plasma product specifications

### 4.1. Neutralizing antibody titer in donors plasma

Neutralizing antibodies produced by humoral immunity plays an important role in reducing disease severity and viral replication hence they can eliminate and treat viral infection [19]. Normally viral load peaks in the first week of infection and seroconversion in SARS-Cov-2 occurs by day 10–14 after onset [20]. Many studies demonstrated that SARS-CoV-2 seroreactivity will present in most recovered patients regardless of clinical and onsets severity during the infection. A study conducted in China showed that the seropositivity in 70 COVID-19 patients with different clinical presentation reached 100 % within 20 days of the onsets, 52 % had antibody titer between 1:64 -1:512 and 47 % had titer of 1:4000 - 1:40000, antibodies titers peaked at 31–40 days and remained till 41–53 days since onsets, then started to decrease slightly [21]. Another study found that among 40 donors recovered from COVID-19, 39 were suitable convalescent plasma donors and showed SARS-CoV-2 antibody titers >1:160, whereas only one had an antibody titer of 1:32 [11]. Additionally, Ling Li et al. found only one out of 64 convalescent plasma donors had SARS-CoV-2 antibody titer of 1:160, while the rest had titer >1: 320 [22].

Titration for SARS-CoV-2 neutralizing antibody in the donor serum or plasma should be done to identify the most suitable donor with efficient neutralizing antibody titer and to evaluate the efficacy of convalescent plasma transfusion. The optimal threshold of neutralizing antibody is still currently debated and further studies are needed to standardize the effective therapeutic titer. In this protocol we recommend SARS-CoV-2 neutralizing antibody titer of at least 1:160, as per the Food and Drug Administration (FDA, USA) recommendations and when not available a titer of 1:80 should be acceptable [23].

Since it is unknown whether the passive antibody protection will last for weeks or months preference in donation should be given to untransfused recovered donors [24]. More studies are needed to disclose the immunity timeline and when exactly the neutralizing antibody titer will start to decline. For SARS-CoV, the immunity lasted for 7 months in recovered patients before they began to decline again [25].

#### 4.2. Convalescence plasma harvesting

Plasma collection and handling should be done by experienced staff in certified facilities that use standard operating procedure in plasma collection according to international guidelines [26]. The plasma bag should be labelled as COVID-19 convalescent plasma and have the label (caution: new drug limited to investigational use) [27].

Where applicable pathogen reduction techniques like ultraviolet C (UVC) light should be applied to eliminate infectious agents and provide additional safety to the plasma product [13,28]. Unfortunately this technique is not applicable in Sudan and many developing countries moreover; routine plasma transfusion is performed normally without viral inactivation.

#### 4.3. Plasmapheresis

In plasmapheresis, the plasma is separated from the cellular component in a collection bag and retained then the cells are re-infused to the donor. The procedure can be used to collect immune plasma from donors with increased concentration of certain plasma immunoglobulins for patients who are immunosuppressed and have been exposed to varicella, herpes or other diseases [29]. To our knowledge, there are only five centers in Sudan equipped with Trima Accel aphaeresis machines. The National Blood Transfusion Services NBTS, and Omdurman Hospital Blood Bank (Awad Hussein Center), both have four machines each, then a single machine at each of the other 3 centers, namely; Radiation & Isotope Centre and Police Hospital in Khartoum, and Mac Nimir General Hospital in Shendi, in the River Nile State.

#### 4.4. Plasma distribution to hospital

Plasma should be distributed to the hospital by the blood bank only if the patient fulfils the eligibility criteria, and has given the informed consent. Also hospitals should agree to provide the blood bank with the outcome data and fill the patient's data collection and monitoring forms provided in the appendices [30].

### 5. Patient eligibility

- 1) Patients with laboratory confirmed diagnosis of SARS-CoV-2 infection by real-time PCR nasopharyngeal swab.
- 2) Aged 18 years old and above.
- 3) Has one of the following clinical symptoms for COVID-19 according to the Sudan national COVID-19 case treatment protocol (last update 16th March 2020): a) Mild disease: severity score of 0–4, tolerable upper respiratory tract infection, non- definite symptoms such as cough, fever, nasal congestion, headache, sore throat. b) Moderate disease: severity score 0–4, high clinical suspicion for pneumonia or evidence of pneumonia from the chest X-ray (Typical bilateral ground glass appearance) and Oxygen saturation < 94 %. [31].
- 4) Within day 3–10 from first signs of illness.

### 6. Patient exclusion criteria

- 1) Contraindication to transfusion (server volume overload, history of anaphylaxis to blood products).
- 2) Documented uncontrolled infections, severe disseminated intravascular coagulation needing factor replacement, on dialysis, active

intracranial bleeding, clinically significant myocardial ischemia, sever multi-organ failure and hemodynamic instability.

- 3) IgA deficient patient are not eligible due to sever anaphylactic reaction that may occur during plasma transfusion.
- 4) Pregnant or breast feeding females.
- 5) Under antiviral treatment or any other treatment targeting SARS-CoV-2 virus.

### 7. Dosage

Published peer-reviewed protocols in COVID-19 convalescent plasma transfusion applied a first dose of 200 ml, subsequently followed by two supplementary doses of 200 mL depending on the disease coarseness and patient's tolerance to multiple plasma infusion [11,12,18].

We recommend between 400–500 ml of ABO compatible plasma in 2 or 3 doses of 200 –250 ml for adult patients, for 1–4 h. Intravenous plasma transfusion should be observed during the first 15–20 min to check absence of transfusion reactions [11]. Premeditations other than antiviral agents may be administered prior to plasma administration according to individual acute care facility protocols [32].

### 8. Treatment commencement

Passive immunotherapy is generally more effective when given earlier and can be effective even with lower doses. In addition, plasma transfusion is more beneficial when done before clinical condition deterioration [28]. Previous literature indicated that transfusion of convalescent plasma as early as possible will have favorable outcomes. A study by Cheng et al. showed that convalescent plasma transfused after 14 days of the onset resulted in higher mortality rate (21 %) and longer hospital stay when compared to a group infused with plasma before 14 days in which mortality rate was (6 %) [33]. Another study showed that convalescent plasma treatment can contribute to longer survival duration and virus shedding but cannot reduce mortality in critically ill patients [34]. A randomized clinical trial also showed no significant difference in the mortality rate between sever and life-threatening COVID-19 patients treated with convalescent plasma and the control group [35].

### 9. Cost

The national blood transfusion service in Sudan is non-profitable and depends only on voluntary blood donation. The cost of consumables for apheresis machines will be covered completely by Sudan's National medical supplies fund. Compared to the superlative price of antiviral drugs that may reach more than \$3000-4000 per treatment course and given the scarceness of these drugs, convalescent plasma can represent a cheap and readily available potential treatment for COVID-19 in Sudan.

### 10. Patient safety and data collection

The issue of patient's safety is a prime concern in this protocol. Several measures should be taken to ensure optimal compliance with the protocol. Any serious adverse events should be reported immediately to the protocol project manager. A patient's data form should be filled by a physician before and after plasma transfusion with suggested follow up days (see appendices C and D).

### 11. Clinical and laboratory parameters before and after convalescent plasma transfusion

Patient monitoring is very important before and after the convalescent plasma transfusion to determine its safety, and efficacy, as well as to monitor the clinical outcomes and maximize the knowledge gain. To achieve this, a case report form should provide the following information (see appendix D).

### 11.1. Clinical parameters

Body temperature checking, sequential organ failure assessment (SOFA) score which contains several blood investigations to assess the functions of vital organs (range 0–24), with higher scores indicating more severe damage. PAO<sub>2</sub>/FIO<sub>2</sub> (ratio is the ratio of arterial oxygen partial pressure to fractional inspired oxygen). These clinical parameters will help to assess if there is any adverse reaction like hypersensitivity reaction type-1 as well as the improvement of health conditions [4].

### 11.2. Laboratory parameters

Complete blood count (CBC), clinical chemistry tests evaluating kidney and liver function, inflammatory factors: C-reactive protein (CRP), procalcitonin, and IL-6. In addition to chest X-ray radiograph; and reports on complications, such as acute respiratory distress syndrome (ARDS), bacterial infection and multiple organ dysfunction syndrome [11].

## 12. Conclusions

With an absence of other treatment options for COVID-19, convalescent plasma is now used widely as a therapy of COVID-19. Nevertheless, large-scale, randomized and well-designed clinical trials are urgently required to study the safety and effectiveness of COVID-19 convalescent plasma especially in Sudan.

## 13. Recommendations

We recommend health authorities to follow this protocol in mild to moderate cases to improve clinical outcomes as early as possible, decrease the need for ventilator support given the scarcity of intensive care units and the shortage of the medical supplies in our health facilities.

## Funding

Authors declare no financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

## CRediT authorship contribution statement

**Mozan Osman Hassan:** Conceptualization, Methodology, Investigation, Writing - original draft. **Asma Ahmed Osman:** Writing - original draft. **Hana Elsir Abd Elbasit:** Methodology. **Hanan Elsamani Hassan:** Data curation. **Hala Rufai:** Methodology. **Maria M.M. Satti:** Validation. **Musab Elnegoumi:** Writing - review & editing. **Roaa Idris:** Conceptualization. **Ashraf Musa:** Visualization. **Abdelhakam H. Ali:** Writing - review & editing. **Susan Ali Zroog:** Writing - review & editing. **Abduelbagi D.A. Altayb:** . **Amna Khairy:** Supervision. **Mushal Allam:** Supervision. **Asaad Tageldein Idris Abdelhalim:** Methodology, Supervision.

## Declaration of Competing Interest

The authors report no declarations of interest.

## Acknowledgements

We would like to express our most gratitude to those who offered their great assistance and support during all stages of this work particularly Sudan National Blood Transfusion Services (NBTS). We also would like to thank Dr. Stanford Kwenda for the professional proof-reading and his valuable comments and suggestions.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:[10.1016/j.transci.2020.102918](https://doi.org/10.1016/j.transci.2020.102918).

## References

- [1] Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis* 2020;20:398–400. [https://doi.org/10.1016/S1473-3099\(20\)30141-9](https://doi.org/10.1016/S1473-3099(20)30141-9).
- [2] World Health Organization. Coronavirus disease (COVID-2019) situation reports. WHO; 2020 (accessed July 14, 2020), <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports#>.
- [3] World Health Organization. WHO coronavirus disease (COVID-19) dashboard. WHO; 2020 (accessed July 14, 2020), <https://covid19.who.int/region/emro/country/sd>.
- [4] World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. 28 January 2020. WHO; 2020. <https://apps.who.int/iris/handle/10665/330893>.
- [5] Arabi Y, Balkhy H, Hajeer AH, Bouchama A, Hayden FG, Al-Omari A, et al. Feasibility, safety, clinical, and laboratory effects of convalescent plasma therapy for patients with Middle East respiratory syndrome coronavirus infection: a study protocol. *Springerplus* 2015;4:709. <https://doi.org/10.1186/s40064-015-1490-9>.
- [6] World Health Organization. Use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease for transfusion, as an empirical treatment during outbreaks: interim guidance for national health authorities and blood transfusion services. 2014.
- [7] Hung IFN, To KKW, Lee C-K, Lee C-K, Chan K, Yan W-W, et al. Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1) 2009 virus infection. *Clin Infect Dis* 2011;52:447–56. <https://doi.org/10.1093/cid/ciq106>.
- [8] Leider JP, Bruner PAR, Ness PM. Convalescent transfusion for pandemic influenza: preparing blood banks for a new plasma product? *Transfusion* 2010;50:1384–98. <https://doi.org/10.1111/j.1537-2995.2010.02590.x>.
- [9] Roback JD, Guarner J. Convalescent plasma to treat COVID-19: possibilities and challenges. *JAMA* 2020;323:1561–2. <https://doi.org/10.1001/jama.2020.4940>.
- [10] Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA* 2020;323:1582–9. <https://doi.org/10.1001/jama.2020.4783>.
- [11] Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proc Natl Acad Sci U S A* 2020;117:9490. <https://doi.org/10.1073/pnas.2004168117>. LP – 9496.
- [12] Ahn JY, Sohn Y, Lee SH, Cho Y, Hyun JH, Baek YJ, et al. Use of convalescent plasma therapy in two COVID-19 patients with acute respiratory distress syndrome in Korea. *J Korean Med Sci* 2020;35. <https://doi.org/10.3346/jkms.2020.35.e149>. e149–e149.
- [13] Seghatchian J, Lanza F. Convalescent plasma, an apheresis research project targeting and motivating the fully recovered COVID 19 patients: a rousing message of clinical benefit to both donors and recipients alike. *Transfus Apher Sci* 2020;59:102794. <https://doi.org/10.1016/j.transci.2020.102794>.
- [14] Joyner M, Wright RS, Fairweather D, Senefeld J, Bruno K, Klassen S, et al. Early safety indicators of COVID-19 convalescent plasma in 5,000 patients. *MedRxiv Prepr Serv Heal Sci* 2020. <https://doi.org/10.1101/2020.05.12.20099879>. 2020.05.12.20099879.
- [15] World Health Organization. Blood donor selection: guidelines on assessing donor suitability for blood donation. World Health Organization. WHO; 2020. <https://apps.who.int/iris/handle/10665/76724>. 2012.
- [16] European Centre for Disease Prevention and Control. Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA - First update. Stockholm. 2020.
- [17] Epstein J, Burnouf T. Points to consider in the preparation and transfusion of COVID-19 convalescent plasma. *Vox Sang* 2020. <https://doi.org/10.1111/vox.12939>. n/a.
- [18] World Health Organization Blood Regulators Network (BRN). Donor selection in case of pandemic situations. WHO; 2007. <https://www.who.int/bloodproducts/brn/DonorSelectioninCaseofPandemicSituations.pdf?ua=1>.
- [19] Pawar AY, Hiray AP, Sonawane DD, Bhambar RS, Derle DV, Ahire YS. Convalescent plasma: a possible treatment protocol for COVID-19 patients suffering from diabetes or underlying liver diseases. *Diabetes Metab Syndr* 2020;14:665–9. <https://doi.org/10.1016/j.dsx.2020.05.023>.
- [20] Zeng Q-L, Yu Z-J, Gou J-J, Li G-M, Ma S-H, Zhang G-F, et al. Effect of convalescent plasma therapy on viral shedding and survival in patients with coronavirus disease 2019. *J Infect Dis* 2020;222:38–43. <https://doi.org/10.1093/infdis/jiaa228>.
- [21] Wang X, Guo X, Xin Q, Pan Y, Hu Y, Li J, et al. Neutralizing antibody responses to severe acute respiratory syndrome coronavirus 2 in coronavirus disease 2019 inpatients and convalescent patients. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa721>.
- [22] Li L, Yang R, Wang J, Lv Q, Ren M, Zhao L, et al. Feasibility of a pilot program for COVID-19 convalescent plasma collection in Wuhan, China. *Transfusion* 2020. <https://doi.org/10.1111/trf.15921>. n/a.
- [23] US Food and Drug Administration. Recommendations for investigational COVID-19 convalescent plasma. FDA; 2020 (accessed June 14, 2020), <https://www.fda.gov>

- v/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma.
- [24] Casadevall A, Pirofski L. The convalescent sera option for containing COVID-19. *J Clin Invest* 2020;130:1545–8. <https://doi.org/10.1172/JCI138003>.
- [25] Chan KH, Cheng VCC, Woo PCY, Lau SKP, Poon LLM, Guan Y, et al. Serological responses in patients with severe acute respiratory syndrome coronavirus infection and cross-reactivity with human coronaviruses 229E, OC43, and NL63. *Clin Diagn Lab Immunol* 2005;12:1317–21. <https://doi.org/10.1128/CDLI.12.11.1317-1321.2005>.
- [26] World Health Organization expert committee on specifications for pharmaceutical preparations. WHO guidelines on good manufacturing practices for blood establishments. 2011. Geneva.
- [27] US Food and Drug Administration. Investigational COVID-19 convalescent plasma (Guidance for industry). FDA; 2020 (accessed June 14, 2020), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-covid-19-convalescent-plasma>.
- [28] Lanza F, Seghatchian J. Reflection on passive immunotherapy in those who need most: some novel strategic arguments for obtaining safer therapeutic plasma or autologous antibodies from recovered COVID-19 infected patients. *Br J Haematol* 2020;190:e27–9. <https://doi.org/10.1111/bjh.16814>.
- [29] Harmening DM. *Modern blood banking & transfusion practices*. seventh ed. F A DAVIS; 2018.
- [30] European commission, safety directorate-general for health and food. An EU programme of COVID-19 convalescent plasma collection and transfusion. Guidance on collection, testing, processing, storage, distribution and monitored use. Brussels. 2020.
- [31] Federal Ministry of health. COVID-19 case management committee. COVID-19 case management committee. Sudan national protocol for case treatment of COVID-19. 2020.
- [32] Mayo Clinic. Expanded access to convalescent plasma for the treatment of patients with COVID-19. 2020 (accessed July 13, 2020), <https://www.uscovidplasma.org/>.
- [33] Cheng Y, Wong R, Soo YOY, Wong WS, Lee CK, Ng MHL, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis* 2005;24:44–6. <https://doi.org/10.1007/s10096-004-1271-9>.
- [34] Erkurt MA, Sarici A, Berber İ, Kuku İ, Kaya E, Özgül M. Life-saving effect of convalescent plasma treatment in Covid-19 disease: clinical trial from eastern Anatolia. *Transfus Apher Sci* 2020:102867. <https://doi.org/10.1016/j.transci.2020.102867>.
- [35] Li L, Zhang W, Hu Y, Tong X, Zheng S, Yang J, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.10044>.