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.

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Convalescent plasma therapy in the treatment of COVID-19: Practical considerations: Correspondence

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Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has infected approximately 6.5 million people, with a loss of over 383,000 lives across the globe (as of 03 June 2020). There is currently no cure for it. Convalescent plasma therapy (CPT) was used to treat a limited number of COVID-19 cases in China and South Korea, where five observational studies (involving 27 patients) reported recovery from illnesses and reduction in viral load (Table 1) [1–5], although this was not confirmed in another study involving six patients [6].

The development of immunity to a pathogen involves an innate response followed by an adaptive response, where the body makes specific antibodies to clear offending pathogens. Patients recovering from infections have variable antibody levels which can be used to treat other critically ill patients. Fully recovered donors can donate plasma by plasmapheresis, but where this is unavailable, whole blood is collected and plasma separated for transfusion to the patient maintaining optimum conditions of storage, defrosting and administration techniques (including 24 hours post thaw expiry rule) for fresh frozen plasma. Whole blood should be stored between 2 °C and 6 °C for a duration that depends on the anticoagulant and preservative used. Liquid plasma can be stored between 1 °C and 6 °C for up to 40 days, and plasma frozen at −18 °C or lower (stored within 24 hours after blood collection) can be stored for up to 12 months. Inactivation of plasma pathogens should be confirmed to minimise the risks of transfusion-transmitted infectious diseases and to rule out the possible risk of super-infection with SARS-CoV-2.

It is recommended that SARS-CoV-2 neutralising antibody (NAbs) titres should be greater than 1:320, but lower thresholds could also be effective. Plasma is released for transfusion without antibody testing in emergency situations, and archived samples tested later to confirm adequate levels of Nabs. Most people with high levels of antibody can donate plasma every two weeks as long as the titres remain adequate. A sample of donor plasma stored should be saved at −20 °C or lower for retrospective testing of total and anti-SARS-CoV-2 NAbs titres and other investigations dictated by the patient's status. Blood/serum/plasma samples of the recipient (both prior to, and after transfusion) should be collected for haemovigilance.

It is important to ensure ABO compatibility of plasma between donors and recipients to avoid Rhesus D (RhD) sensitisation when whole blood is transfused. Transfusion of plasma from at least two donors may be therapeutically beneficial to achieve more effective immune protection from delivery of diverse antibodies. Patients can receive an initial transfusion of 200 mL, followed by one or two additional transfusions of 200 mL according to disease severity and tolerance to the infusions. Although CPT is likely to have potential benefits and low risks, the complications of CPT (e.g., allergic transfusion reactions, transfusion-associated circulatory overload (TACO), and transfusion-related acute lung injury (TRALI) are not likely to be different from satndard transfusions particularly in developed nations. While the risk of TRALI is generally < 1/5000 units transfused, it is of particular concern in severe COVID-19 infections given the potential priming of the pulmonary endothelium (which can be mitigated by donor screening). Of note, risk factors for TACO (e.g., cardiorespiratory disease, advanced age, renal impairment etc.) are shared by those at risk of COVID-19, underscoring the need for careful attention to fluid volume management.

While the risk of transfusion-transmitted SARS-CoV-2 is mostly theoretical, there are no reports of transmission of a respiratory virus by blood transfusion. Nevertheless, donors still need to wait for 14 days following resolution of their symptoms in addition to first being tested negative for the virus. There is also the theoretical risk of antibody-dependent enhancement (ADE), where antibodies developed during a prior infection exacerbate clinical severity after infection with a different viral serotype following transfusion of human anti-SARS-CoV-2 plasma.

Finally, it is unclear if convalescent plasma can blunt the development of a natural immune response, especially when used prophylactically. There are multiple clinical trials taking place in several countries including in the UK (e.g., REMAP-CAP and RECOVERY Trials). People who have recovered from COVID-19 for more than 28 days, with no transfusion-transmitted diseases and who are not pregnant are eligible to participate. Recipients will be followed throughout their hospitalisation and a month after discharge. While we await trial

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Table 1
Observational studies that used CPT in the treatment of COVID-19.

Author [Ref]	Country	Sample size	Age range years	Outcome	Remarks
Duan et al. [3]	China	10	34–78	All recovered; viral load was undetectable in 7 patients	Received CPT at a median of 16.5 days after disease onset. Also received antivirals
Ye et al. [5]	China	6	28–75	All recovered	Received CPT > 4 weeks from disease onset
Ahn et al. [1]	Korea	2	67 and 71	Both recovered	Also received, systemic steroid.
Zhang et al. [2]	China	4	31–73	All patients became PCR negative for virus.	Received CPT about 2 weeks after disease onset. Also received antivirals, interferon α, antibiotics & antifungals. Two patients were treated with ECMO.
Shen et al. [4]	China	5	36–65	3 patients discharged from the hospital and 2 are in stable condition. All became negative for virus within 12 days after CPT.	CPT administered between 10 and 22 days after hospitalisation
Zeng et al. [6]	China	6	31.5–77.8	5 died, 1 survived. Reduced viral shedding	Received CPT 21.5 days after first detection

results, we recommend that CPT be considered for patients severely ill with COVID-19 upon hospitalisation.

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3. Hyperlink to your specific registration (must be publicly accessible and will be checked): Not relevant.

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