This report focuses on **use of Convalescent Plasma or Sera**

Immune (i.e. "convalescent") plasma refers to plasma that is collected from individuals, following resolution of infection and development of antibodies. Passive antibody therapy, through transfusion of convalescent plasma, may prevent clinical infection or blunt clinical severity in individuals with recent pathogen exposure. Antibody therapy can also be used to treat patients who are already manifesting symptoms of varying severity. However, passive antibody therapy is most effective when administered prophylactically or used early after the onset of symptoms.

Hoffman et al. (2020) show that the **sera from convalescent SARS patients cross-neutralized SARS-2-S-driven entry**. Convalescent SARS patients exhibit a neutralizing antibody response directed against the viral S protein (Liu et al., 2006). They investigated whether such antibodies block SARS-2-Sdriven entry. They showed that four sera obtained from three convalescent SARS patients inhibited SARS-S- but not VSV-G-driven entry in a concentration-dependent manner. In addition, these sera also reduced SARS-2-S-driven entry, although with lower efficiency compared to SARS-S. Similarly, rabbit sera raised against the S1 subunit of SARS-S reduced both SARS-S- and SARS-2-S-driven entry with high efficiency, and again inhibition of SARS-S-driven entry was more efficient. Thus, **antibody responses raised against SARS-S during infection or vaccination might offer some level of protection against SARS-CoV-2 infection**.

Source: Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. **SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor.** Cell. 2020 Apr 16;181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052 https://www.cell.com/cell/pdf/S0092-8674(20)30229-4.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420302294%3Fshowall%3Dtrue

---

In the UK, Prof David Tappin, a senior research fellow at the University of Glasgow, has applied to the National Institute for Health Research to run two clinical trials with convalescent plasma.

Prof Robert Lechler, said on Thursday 16th April on a COVID19@FoLSM/KCL TEAMS talk that St.Thomas' intended to conduct parallel trials of convalescent plasma and were looking to start this week.

In the US, **at least five clinical trials** have been proposed to evaluate human anti-SARS-CoV-2 plasma for the prevention and treatment of COVID-19:

1. First, is the use of human anti-SARS-CoV-2 plasma as **post-exposure prophylaxis**: a randomized, blinded Phase 2 trial will be undertaken to compare the efficacy and safety of human anti-SARS-CoV-2 plasma vs. control (SARS-CoV-2 nonimmune plasma) among adults (age ≥18yrs) who have had close contact exposure to COVID-19, but have not yet manifested symptoms.
2. The second trial will evaluate whether human anti-SARS-CoV-2 plasma can help patients initially presenting with **mild disease**. The target population would comprise symptomatic individuals with confirmed SARS-CoV-2. The endpoints would be resolution of symptoms, prevention of hypoxemia on room air or progression to severe disease, reflecting an interest in averting complications (and required hospitalization).
3. Third, the effect of human anti-SARS-CoV-2 plasma for **moderately ill patients** would be studied. The target population is hospitalized patients with COVID-19 who manifest symptoms—albeit—not of sufficient acuity to warrant ICU admission (and specifically mechanical ventilation). Staving off progression to critical illness could avoid overburdening of critical care resources, currently in shortage, such as mechanical ventilators.
4. A fourth trial will evaluate human anti-SARS-CoV-2 plasma treatment as a rescue intervention in **patients who require mechanical ventilation due to COVID-19.** This target group is important;

however, it is also a group for which data are most difficult to interpret given the likely presence of confounding variables including other putative therapies for COVID-19.

5. A fifth trial will examine safety and pharmacokinetics convalescent plasma in **high-risk pediatric patients.** Children of all ages are susceptible to COVID-19 infection; while comparatively rare, severe disease and even deaths have been described in children (32); underscoring the need to address risk to children.

Source: Evan M. Bloch, … , Jeffrey A. Bailey, Aaron A.R. Tobian. Deployment of convalescent plasma for the prevention and treatment of COVID-19. Published April 7, 2020. J Clin Invest. 2020. https://doi.org/10.1172/JCI138745

Table showing dosing of convalescent plasma in coronavirus epidemics

Disease	Location	Dose of CP	Titer	Summary finding	Reference
SARS1	Hong Kong, China	Mean volume 279.3±127.1 ml (range, 160–640 ml)	• Not performed	• Retrospective chart review of 80 patients who received CP • ~14 (range, 7–30 days) following the onset of symptoms • Good clinical outcome in 33 (41.3%) patients as defined by hospital discharge by day 22 • Improved outcome associated with early administration • No adverse events	(16)
SARS1	Taipei, Taiwan	500mL	• Serum antibody (IgG) titer was >640	• Uncontrolled case series of 3 severely ill patients • Improvement in clinical status of all 3 patients	(17)
SARS1	Hong Kong, China	200mL	• Not stated	• Case report of one patient • Improved clinical status • Other therapies also used • No adverse effect	(52)
SARS1	Shenzhen, China	2 units of 250mL each (total 500mL); transfused 12h apart	• Not stated	• Letter to editor/case report of one patient • Improvement in clinical status	(53)
MERS	Seoul, South Korea	4 transfusions of CP to 3 patients; volumes not stated	• PRNT negative (n=2), 1:40 (n=1) and 1:80 (n=1)	• Uncertain benefit although all 3 patients survived • ELISA IgG Optical density of 1.9 predictive of PRNT titer ≥1:80 with 100% specificity	(18)
MERS	Riyadh, Saudi Arabia	• (feasibility study) • 2 units (250–350 mL/unit) proposed for Phase 2	Of 196 individuals with suspected or confirmed MERS-CoV: • 8 (2.7%) reactive by ELISA; 6 of 8 reactive by MN Of 230 exposed healthcare workers: • 4 (1.7%) reactive by ELISA; 3 of 4 reactive by MN	• Feasibility study to assess proportion of convalescent donors that had antibodies against MERS-CoV • No transfusions of CP undertaken	(19)
MERS	Seoul, South Korea	250mL	• Not stated	• Case report (letter to editor) of 1 patient • Possible TRALI reported	(54)
COVID-19	Wuhan, China	200 mL	• Neutralizing Anti-SARS-CoV-2–antibody titer >1:640	• Uncontrolled case series of 10 severely ill patients • Other therapies included steroids, antimicrobials, antivirals • Median onset of symptoms to CP 16.5 days (IQR11.0–19.3 days) • Improvement in clinical status of all patients • No significant adverse effect	(22)
COVID-19	Shenzhen, China	2 consecutive transfusions of 200-250 mL (400mL total)	• ELISA Anti-SARS-CoV-2–antibody titer >1:1000 • Neutralizing antibody titer >40	• Uncontrolled case series of 5 critically ill patients • Administration of CP 10-22d post-admission • All had had steroids and antivirals • Improvement in clinical status of all patients	(21)

Abbreviations:
CP-Convalescent plasma TRALI- Transfusion related acute lung injury ELISA- Enzyme Linked Immunosorbent Antibody assay
PRNT-plaque reduction neutralization assay IFA- Indirect fluorescent antibody testing MN- Microneutralization assay

This report was contributed to by Georgina M. Ellison-Hughes