

Providing vital guidance in a time of crisis: COVID-19 research support



What was achieved?

Research supported by Canadian Blood Services led to key discoveries at a crucial time in the COVID-19 pandemic that made it possible to improve patient care.

An international team that included Canadian Blood Services and our research partners led the largest Canadian clinical trial on COVID-19 convalescent plasma, CONCOR-1. This essential research, which investigated the effects of convalescent plasma on acute COVID-19 infections, utilized insights from past viral infections. However, it revealed a lack of effectiveness for most COVID-19 patients (Bégin et al., 2021).

And thanks to a groundbreaking research project by researchers at the McMaster Centre for Transfusion Research, we now know why a previously unknown clotting reaction — vaccine-induced thrombocytopenia (VITT) (Bourguignon et al., 2021) — happens and how it can be diagnosed and treated. Together, these research findings provided new, urgently needed guidance in a time of crisis.



How was this achieved?

At the start of the COVID-19 pandemic, there were good reasons to think that convalescent plasma could be a lifesaving treatment for COVID-19. COVID-19 convalescent plasma is plasma collected from donors who have recovered from COVID-19 or who have been vaccinated or both, which means they have developed antibodies to fight off the virus. In previous epidemics caused by viruses, convalescent plasma showed some promise in saving lives, but there was not enough data to conclude it was an effective therapy.

In May 2020, an international collaboration that included Canadian Blood Services and our research partners at the McMaster Centre for Transfusion Research, the University of Toronto's Quality in Utilization, Education and Safety in Transfusion (QUEST) program, and the University of Montreal, launched the CONCOR-1 clinical trial. The research team evaluated whether COVID-19 convalescent plasma could be used safely and effectively to reduce the risk of intubation or death in hospitalized patients with COVID-19. The findings provided clear evidence that COVID-19 convalescent plasma does not help seriously ill COVID-19 patients. The study also found that higher-titre plasma (plasma with a lot of antibodies) had differential effects compared to low-titre plasma. This finding informed the design of an ongoing international trial (called REMAP-CAP) on convalescent plasma for immunocompromised patients.

Around this same time, a rare and sometimes fatal clotting reaction associated with a specific type of COVID-19 vaccine was emerging called VITT. A research team from McMaster University studied the effects of high-dose intravenous immunoglobulin (IVIg) given to three Canadian patients who developed VITT after receiving the AstraZeneca vaccine (Bourguignon et al., 2021). As part of this work, the team uncovered the likely cause of clotting in these patients (Huynh et al., 2021).



What was the impact and outcome?

Findings from the CONCOR-1 trial provided much-needed guidance for health-care professionals who had been grappling with treatment options for COVID-19. Shortly after the publication of the CONCOR-1 findings, hospitals around the world stopped routinely using convalescent plasma to treat COVID-19. These findings have implications not just for recipients of convalescent plasma, but for all plasma recipients.

Conducting the CONCOR-1 trial at 68 centres in Canada also inspired the transfusion community to develop a unique transfusion medicine research collaborative, the Canadian Transfusion Trials Group. With funding from Canadian Blood Services, this group will collaborate on large definitive transfusion trials, drawing on what they've learned from doing research during a pandemic (Callum et al., 2023). Future studies are planned to better understand the antibody functions linked to COVID-19 convalescent plasma.

The VITT research findings were significant because at the time, nothing was known about this clotting reaction in some vaccine recipients. This work enabled researchers to provide vital guidance to the medical community on diagnosing VITT (Nazy et al., 2021), as well as recognizing, managing and reporting VITT cases (Sholzberg et al., 2021). Improving our understanding of how clots develop in VITT patients has led to better diagnosis and treatment of patients with VITT and can lead to safer vaccines by preventing VITT from happening in the first place. Researchers at the McMaster Centre for Transfusion Research are also pursuing follow-up studies of patients diagnosed with VITT to better understand the complications or conditions resulting from the disorder.

Bibliographies

Arnold, D., Callum, J., & Bégin, P. (n.d.). [CONCOR-1 clinical trial website](#).

Bégin, P., Callum, J., Jamula, E., Cook, R., Heddle, N. M., Tinmouth, A., Zeller, M. P., Beaudoin-Bussi eres, G., Amorim, L., Bazin, R., Cadogan Loftsgard, K., Carl, R., Chass e, M., Cushing, M. M., Daneman, N., Devine, D. V., Dumaresq, J., Fergusson, D. A., Gabe, C., ... Arnold, D. M. (2022). [Convalescent plasma for hospitalized patients with COVID-19: An open-label, randomized controlled trial](#). *Nature Medicine*, 27(11), 2012–2024.

Bourguignon, A., Arnold, D. M., Warkentin, T. E., Smith, J. W., Pannu, T., Shrum, J. M., Al Maqrashi, Z. A. A., Shroff, A., Lessard, M. -C., Blais, N., Kelton, J. G., & Nazy, I. (2021). [Adjunct immune globulin for vaccine-induced immune thrombotic thrombocytopenia](#). *New England Journal of Medicine*, 385, 720–728.

Callum, J., Bégin, P., Jamula, E., Liu, Y., Kron, A.T., Auclair, M.-C., Cushing, M., & Arnold, D.M. (2023). [Lessons learned from the CONCOR-1 trial](#). *Transfusion Medicine*, 33(1), 21–25.

Huynh, A., Kelton, J.G., Arnold, D.M., Daka, M., & Nazy, I. (2021). [Antibody epitopes in vaccine-induced immune thrombotic thrombocytopenia](#). *Nature*, 596, 565–569.

Nazy, I., Sachs, U.J., Arnold, D.M., McKenzie, S.E., Choi, P., Althaus, K., Ahlen, M.T., Sharma, R., Grace, R.F., & Bakchoul, T. (2021). [Recommendations for the clinical and laboratory diagnosis of VITT against COVID-19: Communication from the ISTH SSC Subcommittee on Platelet Immunology](#). *Journal of Thrombosis and Haemostasis*, 19(6), 1585–1588.

Sholzberg, M., Arnold, D.M., & Laupacis, A. (2021). [Recognizing, managing and reporting vaccine-induced immune thrombotic thrombocytopenia](#). *Canadian Medical Association Journal*, 193(24), E913–E915.