

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic and Transfusion Medicine: reflections from Italy

Luca Mascaretti^{1,2}, Vincenzo De Angelis^{3,4}, Pierluigi Berti^{5,6}



¹Blood Transfusion
Editor-in-Chief;

²Transfusion Medicine Department,
Azienda Sanitaria Universitaria
"Giuliano Isontina", Trieste;

³European School of Transfusion
Medicine (ESTM);

⁴Transfusion Medicine Department,
Azienda Sanitaria Universitaria
"Friuli Centrale", Udine;

⁵Italian Society of Transfusion
Medicine and Immunohaematology
(SIMTI), Rome;

⁶Immunohaematology and Transfusion
Medicine, "Umberto Parini" Hospital,
Aosta, Italy

Just over three months after the diagnosis of the first cases in the city of Wuhan, in the Hubei province of China, the SARS-CoV-2 pandemic has become one of the most serious global health crises of modern times. As of March 31, according to the World Health Organization, 750,890 novel Coronavirus Disease (COVID-19) cases have been diagnosed worldwide. The death toll has reached the alarming figure of 36,405¹, and numbers are continuing to rise at a dramatic rate. As we write, the COVID-19 outbreak seems to be under control in China, thanks to the measures adopted by the Chinese Government, which led to the lockdown of entire cities, and the management of the crisis by the Chinese National Health System. The main increase in new cases is now being observed in other countries, especially, but not only, in Western Europe and North America. In Italy, the number of infections has risen exponentially since the end of February²; by the end of March, a decrease in the rate of new cases had been observed, though it is too early to confirm a favourable trend¹.

It is very complex and perhaps inconclusive to write about COVID-19 while the pandemic is in progress. Nevertheless, we believe it is necessary to include in the second issue of Blood Transfusion 2020 two brief commentaries on COVID-19 and Transfusion Medicine, the most relevant of which from our Chinese colleagues Xiaohong Cai, Ming Ren, *et al.*³.

What is the impact of the SARS-CoV-2 pandemic on Transfusion Medicine?

The principal clinical issue, blood safety, has been discussed by Le Chang and colleagues in a recent review⁴. The authors report knowledge gained during the previous human Coronavirus epidemics, SARS-CoV and MERS-CoV, and highlight the differences with the present pandemic, the main difference being that COVID-19 patients seem to be infectious during the asymptomatic incubation period. This implies that blood donors must be carefully evaluated to prevent a potential blood-borne transmission. The Italian National Blood Center (Centro Nazionale Sangue, CNS⁵) has, therefore, recommended deferring donors who, in the 14 days prior to donation, have had a fever ($>37.5^{\circ}\text{C}$), symptoms of respiratory tract infection (cough, dyspnoea, sore throat, rhinorrhoea), or who have had contact with a suspected or confirmed case of COVID-19. The CNS has also emphasised the importance of setting up procedures to collect Post Donation Information (PDI) for all donations. Should a Transfusion Centre receive a PDI concerning a confirmed COVID-19 donor within 14 days of donation, all non-transfused blood components will be eliminated, and, in case of transfusion, the reference physician will be immediately informed to allow follow up of their patients. Moreover, safety of the Donor Center staff must also be addressed.

Preliminary data indicate that viraemia is present in 15% of patients, although with low

RNA concentrations⁴, meaning that, in principle, the risk of transmitting the virus through transfusion cannot be excluded. The efficacy of pathogen reduction techniques on the inactivation of SARS-CoV-2 is being evaluated⁴ and this could become part of a solution aimed at lowering the risk for transfusion of platelets and plasma (but not for red cells).

In the past, plasma from convalescent patients has been used to treat SARS of viral etiology; the treatment is safe and may have a clinically relevant effect if initiated early⁶⁻⁸. Convalescent plasma therapy has been used in China for COVID-19 patients, as reported by Cai *et al.*³. There are a number of ongoing clinical trials aimed at verifying how this therapeutic approach may improve the prognosis of COVID-19 patients⁹. Meanwhile, transfusion organisations need to prepare themselves to respond by defining the blood components' characteristics, the resources needed to enroll donors, and the criteria for product qualification (in compliance with Good Manufacturing Practices), storage and issue to patients, according to the appropriate safety measures.

A working group of the Italian Society of Haemapheresis and Cell Manipulation (SIdEM) and the Italian Society of Transfusion Medicine and Immunohaematology (SIMTI), has written a position paper on convalescent plasma therapy for COVID-19 patients^{11,12}.

The Italian Health System is being deeply affected by the pandemic, with a high percentage (9-11%) of infected patients being admitted to Intensive Care Units (ICUs), and in many institutes, strained ICU capacity has rapidly been reached². Hospitals have responded by drastically reducing all non-urgent surgical and medical admittance and, where possible, by increasing the number of sub-intensive Critical Care Unit and ICU beds. After the courageous measures taken by the Government aimed at enforcing social distancing, a worrying decrease in the number of blood donations became apparent. In the week 2-8 March, 44,297 whole blood units were collected and 46,183 red cell units were transfused in Italy, with a negative balance of 1,886 units (CNS, 2020, personal communication). A national media campaign on the importance and safety of blood donation, together with the above-mentioned reorganisation of hospital activity, led, in the following week, to a harvest of 53,538 whole blood units while red cell transfusions fell to 39,745 units (positive balance of 13,793 units). Apart from the excess in blood

inventory, common to many past disasters¹⁰, the highest and most characteristic risk has been the overcrowding observed in some donor centres, which jeopardises safe social distancing. The response of Italian blood donors and donor associations is highly commendable, but it is now the responsibility of the transfusion organisations to implement better planning by inviting donors to schedule their donation. This will allow a more organised flux of people, promoting donor and staff safety, as well as a more rational management of the blood inventory. The latter is of pivotal importance, since we still do not know how long the pandemic will last.

The SARS-CoV-2 pandemic is imposing a major strain on the Italian Health System and Transfusion Medicine professionals are doing their part. Once the pandemic has been overcome, more thorough considerations can be made, and we will be able to compare the approaches adopted by transfusion organisations in different countries around the world.

REFERENCES

1. WHO [Internet]. Coronavirus disease 2019 (COVID-19) Situation Report – 71. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200331-sitrep-71-covid-19.pdf?sfvrsn=4360e92b_4. Accessed on 01/04/2020.
2. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *Lancet*. 2020; doi: 10.1016/S0140-6736(20)30627-9. [Epub ahead of print].
3. Cai X, Ren M, Chen F, et al. Blood transfusion during the COVID-19 outbreak. *Blood Transfus* 2020; **18**: 79-82.
4. Chang L, Yan Y, Wang L. Coronavirus Disease 2019: coronaviruses and blood safety. *Transfus Med Rev* 2020; doi:10.1016/j.tmr.2020.02.003. [Epub ahead of print].
5. Centro Nazionale Sangue [Internet]. [Coronavirus, precautionary measures updated]. Available at: <https://www.centronazionalesangue.it/node/831>. Accessed on 31/03/2020. [In Italian].
6. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, et al. Convalescent Plasma Study Group. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. *J Infect Dis* 2015; **211**: 80-90.
7. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis* 2020; doi: 10.1016/S1473-3099(20)30141-9. [Epub ahead of print].
8. Marano G, Vaglio S, Pupella S, et al. Convalescent plasma: new evidence for an old therapeutic tool? *Blood Transfus* 2016; **14**: 152-7.
9. World Health Organization. International Clinical Trials Registry Platform. Available at: <https://apps.who.int/trialsearch/>. Accessed on: 31/03/2020.
10. Schmidt PJ. Blood and disaster--supply and demand. *N Engl J Med* 2002; **346**: 617-20.
11. SIdEM [Internet]. [Position paper on the production of hyperimmune plasma for the treatment of SARS-CoV-2 disease.] Available at: <http://www.emaferesi.it/2020/03/position-paper-sulla-produzione-di-plasma-iperimmune-da-utilizzare-nella-terapia-della-malattia-da-sars-cov2/>. Accessed on: 27/03/2020. [In Italian].
12. SIMTI [Internet]. [Position paper on the production of hyperimmune plasma for the treatment of SARS-CoV-2 disease.] Available at: http://www.simti.it/news_rec.aspx?id=30755&prec=0. Accessed on: 27/03/2020. [In Italian].