

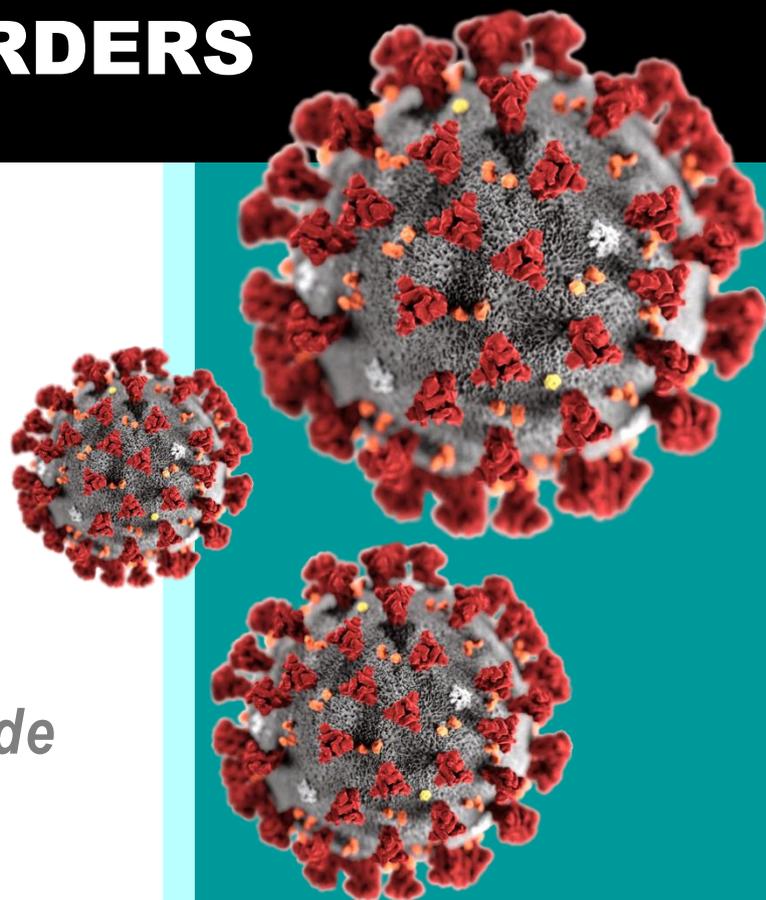
THE COVID-19 PANDEMIC AND HAEMOGLOBIN DISORDERS

BLOOD & COVID-19

*An Informational Guide
from the
Thalassaemia
International Federation
(TIF)*



**THALASSAEMIA
INTERNATIONAL
FEDERATION**



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Updated information marked in red

Introduction

In December 2019 in Wuhan China, a new coronavirus (COV), preliminary called by the World Health Organisation (WHO) in January 2020 a novel coronavirus, was found in a cluster of pneumonia patients.

Subsequently, the virus was named SARS Coronavirus 2 (SARS-COV-2) and the disease it causes was named Coronavirus Disease 2019 or COVID-19.

Diversity of coronaviruses

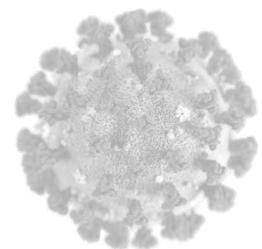
Largest RNA viruses are divided into four genera: α -CoVs, β -CoVs, γ -CoVs and δ -CoVs

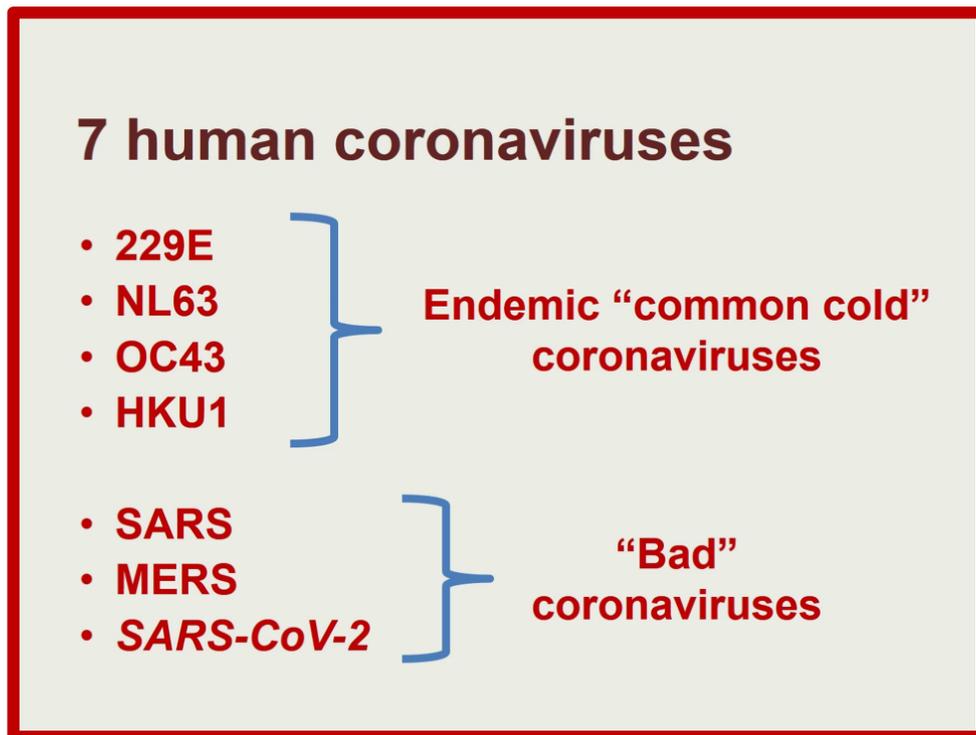
- α -CoVs and β -CoVs infecting mammals and
- γ -CoVs and δ -CoVs infecting birds and mammals

Seven coronaviruses have been found to infect humans and cause respiratory disease. Four out of these are common HCoVs (229E, OC43, NL63, HKU1) causing self-limited upper respiratory disease with more severe symptoms occasionally in young, elderly and immunosuppressed.

HCoV-229E and –OC43 were known since 1960. SARS in 2002 as novel β -coronavirus, came to attention and HCoV-NL63 and HKU1 were identified in 2004 and 2005 respectively. MERS-CoV isolated in 2012, is similar to SARS-CoV, both are infections of the lower respiratory tract causing severe respiratory syndromes in human with 35.5% and 10% fatality rate respectively.

SARS-CoV2 identified in January 2020 is a new member of β -CoVs.





(International Society of Blood Transfusion (ISBT) – Webinar: Update on the COVID-19 Coronavirus Outbreak: Blood Collection and Safety Implications, ISBT Education. Michael Busch, Louis M Katz & Hua Shan, 03/04/20; 289245 Topic: Emerging infections)

Context: case-fatality rates

Virus	Case fatality rate (%)
2009 H1N1	0.02-0.4
SARS-CoV-2	Evolving understanding (2-3%)
SARS	9.6
MERS	34.4
H7N9	39
West Afr. Ebola	63

After Munster VJ et al. NEJM. 2020

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Transfusion transmitted risks of SARS-COV-2

Although coronaviruses cause primarily mild to severe respiratory infections and no evidence exists to date of transfusion transmission from either SARS-CoV or MERS-Cov, COVID-19 caused by SARS-CoV2 virus on the contrary might be infectious during an asymptomatic incubation period.

A number of health related bodies including the World Health Organisation (WHO), the European Union, the Council of Europe, the European Centre for Disease Prevention and Control (ECDC), the European Directorate for the Quality of Medicines & HealthCare (EDQM) the European Blood Alliance (EBA), the AABB (formerly known as the American Association of Blood Banks), the International Society of Blood Transfusion (ISBT), the Centers for Disease Control and Prevention (USA), the European Medicines Agency (EMA), the Food and Drug Administration (FDA) health programmes and many other academic and industry bodies, have worked for decades to provide support and guidance to National Competent Authorities on every aspect related to safety and adequacy of blood and products. Most of these, have focused recently on providing guidance in relation to the COVID-19 pandemic.

The ECDC and the AABB published in January 2020 the RAPID RISK ASSESSMENTS recommendations e.g ECDC: precautionary deferral of donation of blood for 21 days following exposure to a confirmed patient or anyone who referred travelling from China (same applied for SARS-Cov and MERS-CoV).

Recovery confirmed COVID-19 patients should be deferred for at least 28 days after symptoms resolution and completion of therapy.

The WHO, the AABB, the FDA and the US CDC, mention that competent authorities and blood establishments **DO NOT currently require to take any actions** as there are no data suggesting a risk of transmission of SARS-CoV2 through transfusion.

The potential for transmission by transfusing however is worthy of consideration particularly for the patients TIF represents. A number of questions in this context must be asked and answered with two key ones:

1. **Is the virus transfusion transmittable?**
2. **IF YES, is there an asymptomatic but Viremic period that would pose a risk?**

What it takes to be a TTID

- **Asymptomatic blood-borne phase**
 - Chronic and/or acute
- **Infectiousness by parenteral route**
- **Survival of agent in contemporary components**
- **Susceptible recipients**
- **Recognized disease in transfusion recipients**

Our level of concern (should be) dependent on

- Incidence and prevalence, **especially** of pre- or asymptomatic infection
- Clinical severity
- Rate of growth of an epidemic

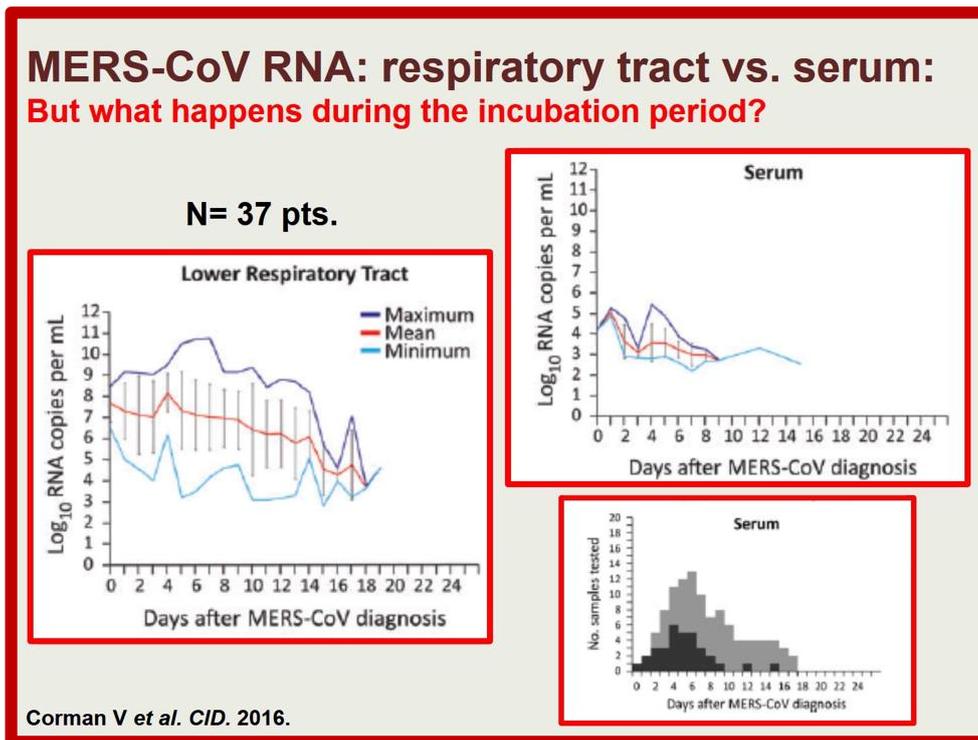
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SARS-CoV-2 as TTID?

- **Theoretically possible?**
 - Its RNA can be amplified from patient blood
 - Presence of infectious virus not established
 - No respiratory viruses, including human coronaviruses, provide a precedent for TTI
- **Routine donor screening practices will prevent symptomatic donors from giving**
- **Asymptomatic donors are our main concern**
- **Plasma derivatives should be safe**

So, how precautionary must we be??

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In China, most blood centres or blood banks have taken the following measures during the outbreak:

- i. Check body temperature before donation
- ii. Add extra questions in donor's questionnaire
- iii. Follow up with the donors asking them and their families about their current physical condition after the donation.

Given the differences between SARS-CoV, MERS CoV and SARS-CoV2, it is NOT KNOWN if prior recommendations used for the former two coronaviruses are sufficient, as we all know and agree that **with SARS-CoV2 we are all facing many unknowns.**

Perhaps stricter measures in donor questionnaires, viral RNA and virus related antibody screening of blood donations or the use of PRT (Pathogen Reduction Technology) may be the solution in some cases or in some patient populations such as regular, lifelong users of blood and blood products and heavily immunosuppressed patients that need blood/blood products for their medical care.

Moreover, although different methods of inactivation of platelets and plasma may be effective for coronavirus as well as for other similar lipid-enveloped pathogens, yet for Red Blood Cells, a safe and effective PRT is still lacking.

Nucleic Acids (RNA) have been detected in the serum or plasma of patients with SARS-CoV and in one instance (at least until Feb 2020) in lymphocytes of patients with clinical disease. Even faecal transmission was considered possible in the case of SARS-CoV. It is NOT CLEAR however, whether these findings establish infectivity status of blood.

It remains unknown if there is viraemia (i.e. infectious virus in plasma) prior to clinical disease during the period of asymptomatic infection. And if viraemia does occur, even for a duration of more than 20 days, is viral load of sufficient quantity to result in human infection? And if so under what conditions?

In individuals with COVID-19, plasma or serum viral RNA could also be detected as with SARS-CoV infection. Viraemia was found at very low RNA concentration with no differences between patients with severe symptoms and those with milder ones. For MERS-CoV, RNA signal was found in serum with viral load 2.1×10^2 to 2.5×10^5 copies/ml in Middle Eastern patients and 2×10^3 in Korean patients. This is consistent with the study of the first 41 cases of COVID-19 in Wuhan where SARS-CoV-2 RNA was detected in only 6/41. Researchers failed to isolate the virus suggesting that presence of RNA may not indeed render the blood infectious.

In addition, in a study of a familial COVID-19 cluster, viral RNA was detected in the serum of 1 of 5 infected family members, who had symptoms. For MERS-CoV infection, serum RNA levels decline as neutralising antibodies become detectable, between 10–20 days after symptom onset. This occurs with other viral infections as well, and would be expected to be demonstrated with SARS-CoV-2 too.

The transfusion-transmissibility of SARS-CoV-2 thus has not been determined to date. The primary risk to blood safety would be associated with infectious viraemic but asymptomatic donors, either acute infections prior to symptom onset or infections that do not result in symptoms. As noted, the blood phase of SARS-CoV-2 infections has not been defined, and the proportion of SARS-CoV-2 infections that result in symptoms is not known.

A pivotal point is that no respiratory virus, including SARS-CoV, MERS-CoV, and influenza viruses have ever been confirmed as transfusion-transmissible by any blood product.

Risks posed

All respiratory viruses normally attach to receptors in the airways (except adenoviruses) and their blood-borne transmission therefore is unknown or at least very confined. **Low to very low viraemia has been detected in some symptomatic patients, although viraemia in the incubation period, asymptomatic course of infection and after symptoms' resolution has NOT BEEN DOCUMENTED (at least until 20th March 2020).**

Both in China and South Korea, SARS-CoV-2 has been identified in 2430 routine blood donations (1656 platelets and 774 whole blood donations) between January – March 2020 by real time reverse transcription PCR as well as by retrospective analysis of 4995 samples of blood donors collected between December 2019 – January 22nd 2020. Four (4) samples in total were positive for SARS-CoV-2 from fully asymptomatic (at the time of collection/donation. Their prior donations in December 2019 were negative for viral RNA) and only two (2) of them developed fevers the day after donation which however resolved within a short period of time. Very low viral load was detected in all and transmission could not be confirmed.

In South Korea seven (7) donors who were tested at the time of donation, were positive to the SARS-CoV-2, 6-15 days post donation. 6 whole blood and 1 source plasma. From these donations, 6 platelets units and 3 RBCs units had been transferred to 9 patients. However, 8 of the recipients did not develop symptoms related to COVID-19 and the 9th died of causes unrelated to COVID-19.

A useful action taken by the Korean National Blood Services to prevent transmission of blood products at the earliest possible stage, was to request from the health authorities to receive the details of all confirmed COVID-19 cases and not to solely rely on post-donation information provided by blood donors. As from March 9th 2020, the Korean Red Cross Blood Services (KRCBS) is receiving the list of all COVID-19 cases identified for cross referring to donors to trace recipients or recall any blood products not transferred and to apply a 3-month deferral for future donation.

Although most likely viral load in blood plasma may be very weak to transmit and cause infection, further research and very meticulous monitoring and reporting, in the context of haemovigilance programmes, are needed to confirm the presence or absence of virions in blood and blood products and whether these are infectious.

Transmission of other 'similar' viruses, SARS-CoV, MERS-CoV and other coronaviruses through transfusion or transplantation has not been reported to date, neither vertical nor perinatal transmission (the latter only suspected).

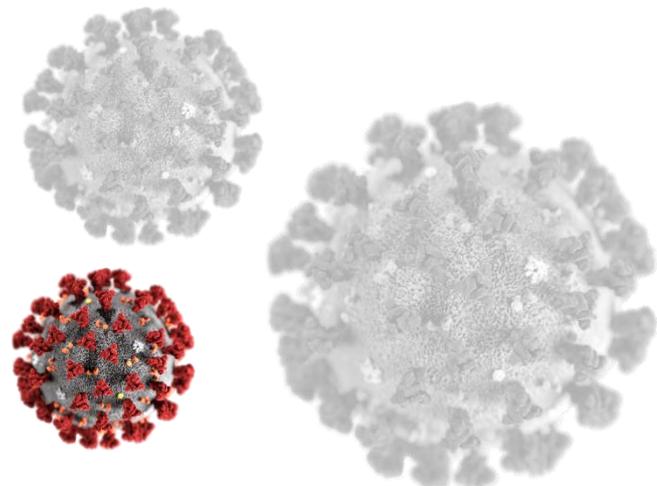
Strengthening of donor selection criteria and implementing routine donor screening measures, should prevent most individuals from donating Substances of Human Origin (soHO) i.e. blood, plasma, platelets.

For plasma derivatives on the other hand, regular screening of plasma donors showing clinical symptoms and the established processes of virus inactivation and removal during manufacturing, as has been demonstrated with other large size lipid-enveloped RNA viruses, should be sufficient to mitigate COVID-19 transmission through plasma derivatives. **Therefore, the COVID-19 outbreak is not considered a threat to the safety of plasma protein therapies when of course such methods are in place.**

COVID-19 has not been described in organs or haematopoietic stem cell transplant (HSCT) recipients to date. One fatal case of liver transplant recipient, one recipient of allogenic HSCT for acute myeloid leukemia with SARS-CoV infection and two renal transplant recipients with MERS-CoV infection have been reported to date.

An additional challenge in these patients (transplanted) is that due to their immunosuppression status, they may have prolonged shedding of the virus and thus potentially increasing the risk of transmission of the virus to their contacts including health care professionals.

Conversely immunosuppressed transplant recipients who regularly visit hospital settings may be exposed to the SARS-CoV2 in hospital settings and develop severe illnesses and it is thus anticipated that COVID-19 may increase mortality in transplant patients.



The Response of some countries to COVID-19 and Blood (Safety and adequacy)

Further to the official regulatory bodies and a number of professional NGOs at national and international level, almost every country across the six WHO regions - African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, and Western Pacific Region – have issued and adopted guidelines regarding transfusion safety and blood adequacy during the COVID-19 pandemic.

Below is some information, selected by TIF, from various official transfusion/blood related bodies and establishments in countries with large haemoglobinopathies patients' populations:

- ✓ **Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC), National Blood Transfusion Committee**

Recommendations for a number of aspects affected by the pandemic including:

1. Red cell shortage plan, March 2020
2. Appropriate use of blood and components. Emergency Blood management plan
3. Meticulous monitoring of blood STOCK LEVELS aiming to maintain a 6 days stock of RBCs with RBC shortage plan if stock falls to less than 2 days and maintain a minimum 1 day of stock for platelets and platelet shortage plan if stock falls to 1/5 days or less.

- ✓ **Asian Association of Transfusion Medicine** issued a very useful AIDE-MEMOIRE COVID-19 for members, blood banks, transfusion services and hospitals.
- ✓ **Asia Pacific Blood Network (APBN)** published on the 17th of February 2020, a very comprehensive paper on the 'expected challenges and risks to blood safety'
- ✓ **The Chinese Society of Blood Transfusion** prepared and published Recommendations for Blood Establishments Regarding the Novel Coronavirus Disease (COVID-19) Outbreak.(v1.0)

- ✓ **The National Blood Centre (NBC) Malaysia has issued Guidelines for Blood Donation Activity and Donor Selection Criteria for the Current COVID-19 Outbreak Situation in Malaysia**

Similarly, Hong Kong, India, Pakistan and almost every country across the globe focused considerable attention and issued directions and guidelines specifically focused on the aspect of blood, its adequacy and safety.

Risks posed to the sufficiency and sustainability of SoHO supplies

Blood Supply Challenges During Pandemics

The influenza A virus subtype H1N1 (H1N1) pandemic had a significant impact on the blood supply due to donors' fear of exposure to the virus at a hospital or a free-standing donor facility. Similarly, the COVID-19 pandemic has already led to significantly reduced blood supplies due to the cancellation of numerous community-based and mobile blood drives, as well as a marked reduction in donors arriving for scheduled appointments. For instance, as a result of the current pandemic and restrictions on congregating through social distancing, to date in the U.S., nearly 4000 American Red Cross blood drives have been canceled across the country. Hospital-based collections have been cancelled due to institutional concerns regarding donors spreading COVID-19 to hospitalized patients or vice versa. These cancellations have resulted in some 130,000 fewer blood donations in only a few weeks. More than 80% of the blood the American Red Cross collects comes from drives held at non-permanent collection locations. According to the Chief Executive Officer of New York Blood Center, the main blood supplier for New York City, around 75% of their incoming blood supply was interrupted during the week of March 16, 2020, when schools, businesses and religious institutions closed due to the coronavirus outbreak.

It is thus inevitable that the number of eligible donors in the course of a pandemic will inevitably decrease, due to a growing number of individuals being infected or in self-quarantine after exposure to infected persons or persons under investigation.

In addition, blood collection facilities have put additional selection criteria in place, declining donors with history of travel in the preceding 14 days. Finally, older persons, who often represent the most reliable donor pool, are also apparently among the most vulnerable to the COVID-19 pandemic.

The default response to reduced blood supplies and the limited capacity of health care facilities is the suspension of elective surgical procedures regardless of the lack of uniform definitions for “elective.” Yet, blood utilization for urgent and emergent interventions that can actually represent a greater demand on the blood supply is likely to remain unchanged. The same will likely be true for chronically transfusion-dependent patients, including those with malignancies, hematological conditions (e.g., sickle cell, thalassemia, myelodysplastic syndrome) and chemotherapy-induced anaemia. In some cases, cancellation of elective surgeries may permit disease progression resulting in more complex and urgent situations, as the pandemic further progresses.

Calls from blood centers for more donors do not sufficiently alleviate this problem. In the context of pandemics, the pressure on blood collection facilities and hospital transfusion medicine services and their staff is also increased, as more and more staff members are required to self-isolate, self-quarantine or become ill. In addition, the effort to continue standard blood donor recruitment will be diverted in part by the growing initiative to manufacture convalescent plasma from patients who have recovered from COVID-19. While this treatment option remains under investigation on a limited basis and is not currently a major source of demand for blood donations, the rapidly evolving nature of the pandemic might quickly change the landscape, creating a substantial new demand.

It should also be noted that supply chains are often affected by travel restrictions, factory closings, and decreased manufacturing output, which may in turn affect the ability of blood services to maintain their testing and production facilities in times of increasing need. Another remote but significant issue is possible virus transmission via donated blood.

At some stage of the pandemic, we expect that a considerable percentage of the population will be unknowingly infected by SARS-CoV-2, including the young blood donor population in which asymptomatic cases will be common. In the absence of nucleic acid testing (NAT) for blood donor screening for SARS-CoV-2, **we cannot exclude, albeit theoretical at this time, the possible transmission via a blood transfusion, if some of the donated blood may be contaminated.** Thus, we are facing significant unknowns,

and only future studies will elucidate the true risks of transfusion-transmitted SARS-CoV-2 if any.

In conclusion, COVID-19 pandemic may pose a significant risk in maintaining a sufficient and sustainable supply of SoHO because SARS-CoV2 may affect:

- The donor populations
- The recipient populations

In addition, COVID-19 amongst health care professionals and staff in SoHO establishments may cause delays and ineffectiveness in providing SoHO to chronic and/or acute patients in need.

In general, such a pandemic may cause significant disturbance in the coordination and control of all crucial activities involved in the complex processes with regards to blood transfusion therapy in chronic long term users of blood or its products and very importantly to the transplantation of solid organs and HSCT with dramatic consequences to the health of individuals in need.

Based on previous pandemic experiences or severe infectious diseases outbreaks, during the pandemic with COVID-19, the Blood Transfusion system of every country may experience:

- Decreased availability of donors (contacts of confirmed cases being in isolation, not being able to move i.e. in quarantine, etc.)
- Living donors may be unable to donate (blood or organ) because of having COVID-19 and being in isolation
- COVID-19 specific donor selection criteria contributes to the decrease in donor numbers (in Singapore during SARS epidemic for example a 60% decrease in donor's population was reported)
- Absenteeism among staff working in blood establishments

Many recommendations for alleviating blood shortages, have been put forward by official health and blood related institutions, including the WHO, the CDC (USA), the ECDC, the EMA, the FDA, the AABB, the ISBT, the EBA and many others at the international and national level. Many of these recommendations have been adopted by and are common in most countries worldwide. Each country however, may have either adjusted these to a

certain extend and/or included additional ones according to national blood services' infrastructure, economic recourses and medical/disease burden including the prevalence of multiply transfused patient populations.

FDA for example have issued four 'brave' blood donor eligibility guidelines on April 2nd, 2020: one on alternative procedure for blood and blood components collected during the COVID-19 public health emergency and three others on HIV malaria and CJD including briefly:

- Donation intervals shortened (where possible)
- 72 hours instead of 24 hours for blood establishments to clarify donor's responses or omitted information after collection.
- Source plasma released 45 days after collection from paid donors instead of 60 days
- Deferral of blood donors to 3 months instead of 12 months for those traveling to malaria endemic areas and for men who have sex with men (MSM) and female partners of MSM, drug users and sex workers

The grave fear of every national competent blood authority is to avoid reaching the point of very severe blood shortages and having as a consequence to take measures that could potentially jeopardize the safety of blood/components/products (Ref. 19-22)

Pathogen inactivation

This methodology is indeed invaluable particularly in such serious pandemic infectious disease outbreak, if of course cost and technological challenges could be overcome and if RBCs, in addition to plasma and platelets could be safely included into the equation, since to date pathogen inactivation covers only platelets and plasma.

For example, pathogen reduction methods including Amotosalen or riboflavin, ultraviolet light, methylene and light and ultraviolet C light alone can be effective in causing inactivation of SARS-CoV2 when applied only to platelets and fresh frozen plasma.

Transplant recipients

These patients should be tested for the presence of SARS-CoV-2 in the nasopharyngeal specimens before proceeding with the transplant procedure (organ and HSCT). Management protocols should be in place for organ recipients with COVID-19 in cases of transplant unit closing temporarily and recipients need to be isolated during a potential incubation period or in an area with sustained community transmission in order to protect the patient, his/her family and the hospital personnel.

Every attempt should be made so that national and international activities related to the transplant of organs, cells and tissues remains uninterrupted.

The World Health Organization (WHO)

The WHO mainly (but also other relevant official stakeholders) has issued a number of resolutions and recommendations since the 1970s regarding safety and adequacy of blood and published through the years, a plethora of reports. With regards to infectious outbreaks, an interim guidance was published and made available to the public, in March 2020: "Maintaining a safe and adequate blood supply during the pandemic outbreak of COVID-19".

Some major points/recommendations raised in this report include:

i. Post donation measures

A system must be in place for donors to report their health status consistent with COVID-19 or contact with a case that is confirmed positive, post-donation for at least 14 days and until 4 weeks after donation. In this context, a well-structured, simple post donation questionnaire is probably essential to be adopted and implemented during such crises.

ii. Recalling blood and blood components.

Blood and components collected within 14 to 28 days of disease onset in the donor or after contact exposure may be recalled as a precautionary measure.

iii. Testing for SARS-CoV2

Testing of the blood supply for SARS-CoV2, as mentioned in the WHO guidance, is premature in the absence of cases of documented transfusion transmission or demonstrated infectivity of the COVID-19 virus in blood collected from asymptomatic persons.

iv. Laboratory screening

In addition, there is no licensed test for the screening of blood, plasma for fractionation or cell and tissue donors/donations to-date. Laboratory screening of donors/donations of blood, plasma for the manufacture of medicinal products, and cells and tissues is currently not recommended. This is because transmission of COVID-19 through SoHO has not been reported; levels of detected RNA in plasma coinciding with clinical symptoms are very low and a screening policy has not been implemented for other viral respiratory illnesses for which transfusion transmission remains theoretical, including influenza. Testing of donors and recipients may be considered in organ and HSC transplantation settings.

v. Pathogen Reduction Technologies

As mentioned previously, Pathogen Reduction technologies (PRT) are demonstrated to be effective against SARS-CoV and MERS-CoV in plasma and platelets and are likely to be equally effective for SARS-CoV2. Such methods however, although available, they require significant logistical and financial investment and on the other hand for RBCs are still not available.

vi. Haemovigilance programmes

Robust haemovigilance programmes are in place only in a small number of countries around the globe and mainly in the Western World. A haemovigilance system should be in place to capture any possible cases of transmission while at the same time such a

system is invaluable in facilitating the understanding the behavior of the virus, its clinical impact on vulnerable group of patients, across ages etc., of the risk from blood and components and certainly the overall effectiveness of the measures taken by the blood service and the national health and other authorities of a country.

vii. Blood Donation Interval

Routine practices for donor management and infectious disease testing should not be changed. However, in extreme blood shortages, reduction of whole blood donation intervals may be considered for donors with robust haemoglobin levels who are able to tolerate more frequent donations

viii. Re-entry of infected donors

WHO in addition mentions that systems should be in place to enable re-entry of infected donors after recovery. Accordingly, most can donate 28 days AFTER FULL RECOVERY. This can also support the collection of convalescent plasma for treatment of COVID-19 patients.

ix. Convalescent plasma

Experience suggests that empirical use of convalescent plasma (CP) may be a potentially useful treatment for COVID-19. Detailed risk assessment must always be conducted to ensure that the blood service has sufficient capability to safely collect, process and store these specific blood components in a quality-assured manner. WHO has previously released interim guidance for the use of CP collected from patients recovered from Ebola Virus Disease. Additionally, the WHO Blood Regulators Network Position Paper on Use of Convalescent Plasma, Serum or Immune Globulin Concentrates as an Element in Response to an Emerging Virus (2017) provides helpful considerations.

The EBA also started a study group on convalescent plasma for parties interested in sharing information on how to best advance both the knowledge and practice in this field. Several European countries, members of EBA have initiated protocols to start collecting convalescent plasma and EBA is mapping the current initiatives on convalescent plasma for COVID-19 in a view to developing common approaches to donor selection criteria and collection and processing, wherever possible.

x. A potential 'benefit' for chronically transfused patients amongst the tragedy of the pandemic.

During widespread transmission, demand for blood and components may decrease as road accidents may decrease consequent to isolation measures as well as in other society related accidents, and as the health care systems shift towards treating an inevitably increasing number of COVID-19 patients. In this context, elective surgeries and non-urgent clinical interventions are deferred, compensating to a certain extent the anticipated reduction of blood supplies made for lifelong dependents on blood transfusion and other mainly haematological and oncological malignancies.

Certainly, for trauma, post-partum haemorrhage, severe infant anaemia, blood dyscrasias, and urgent surgeries, adequate blood supply remain very much needed and for COVID-19 patients with severe sepsis, or those requiring extracorporeal membrane oxygenation support, increased stocks may be needed.

xi. Patient management policies

Very importantly in such crises, strengthening patient management programmes or more prudent clinical use of blood will certainly help safeguard blood stocks and this has been scientifically documented.

What can we learn from patient blood management?

A shift is underway in many areas of the world to optimise patient outcomes while reducing perioperative blood use based on the concept of patient blood management. This is an evidence-based bundle of care to optimise patient outcomes by managing and preserving a patient's blood. PBM is based on three pillars: optimising the patient's own blood volume, minimising blood loss and bleeding, and harnessing and optimising the physiological reserve of anaemia.

Patient blood management reduces the need for transfusions, together with complication and mortality rates, length of hospital stay, and costs. Endorsed by the World Health Organization, it has been led by Australia, USA and within Europe in the Netherlands and Austria. Further efforts are underway to widen its implementation. We would argue that approaches to optimizing blood use in chronic diseases warrant similar policy attention.

EU guidance recommends that initiatives should increasingly focus on PBM in medical patients, especially haematology patients. It encourages transfusion stakeholders “to take a fresh look at their professional fields and discover new opportunities for safely reducing the transfusion rate in their hospitals”.

xii. Information and updating material

Updating and upgrading informational material focused on the daily progress of the national/country situation helps to empower people to donate. It is important to make arrangements to facilitate donors to give blood through the use of mobile units, **albeit the use of automatic apheresis procedures for the collection of platelets, plasma and in some cases red cells, is difficult to be applied in non-hospital for example mobile units' environment.**

And above all **CREATE TRULLY SAFE ENVIRONMENT FOR THE DONOR AND THE STAFF INVOLVED.**

The use of telephone, sms & mms messages, email and social media, to announce and organise blood donation campaign in such crisis is more valuable now than ever before.

In extreme cases of quarantine of blood and blood components occurring in periods of widespread and sustained transmission of COVID-19, organization of targeted family and friend's donors' pools, the provision of blood cell and tissues from non-or least affected parts of the country may be options or even importing from other countries if feasible in desperate situations

Finally, and very importantly, it is essential during such crises to ensure that mechanisms are in place to mitigate against shortage: A national inventory of blood supplies should be monitored daily so as relevant authorities can move blood across a city, a country or region to where it is most needed.

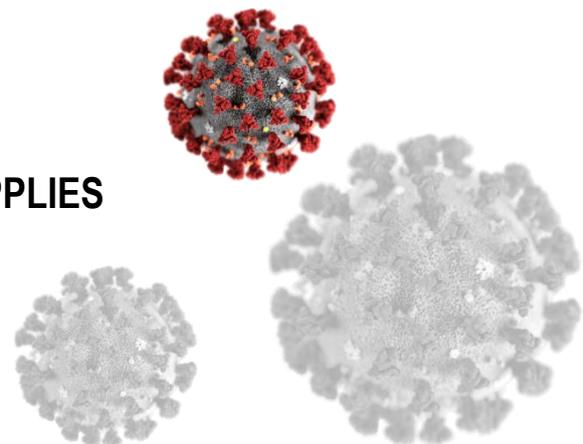
KEY POINTS



NATIONAL INVENTORY OF BLOOD SUPPLIES



POST DONATION QUESTIONNAIRE



Challenges to patients with Haemoglobin Disorders consequent to the COVID-19 pandemic at a glance:

- Blood Shortages;
- Difficulties of patients in traveling to and accessing their treating/transfusion centres particularly where public transportation is necessary (which affects the greatest majority of patients globally);
- Declines/drop of pre transfusion haemoglobin levels (consequent to blood shortage and/or difficulties in reaching specialised centres), to unacceptable values that set patients at great risk of developing new or worsening existing co-morbidities;
- Provision of not appropriately (as per International Guidelines) processed RBCs or even provision of whole blood with all related adverse consequences;
- Diversion from Non-Remunerated Voluntary Blood Donation (NRVBD) practices to replacement or even paid donation (consequent to blood shortages) posing immense risk to public health programmes and the safety/quality of blood/components;
- Loss of trust on the part of blood donors regarding the safety of donation places with consequent damage to the donation programmes;
- Delayed/postponed accessibility of patients to innovative drugs and therapies and to the participation of patients in and progress of ongoing or the initiation of new clinical trials;
- In the absence to date of global collaboration and accumulation of relevant and reliable information, the clinical impact of SARS-CoV-2 to patients with thalassaemia and other haemoglobin disorders remains unknown. The impact however, in suboptimally treated patients who constitute more than 70% of the global patient population is anticipated to be significantly worse than in those who are well managed throughout their lives and during this pandemic ;

- Severe stress and burnout of health care professionals, hospitals and generally national health care systems with jeopardization of the quality of services provided to address emergencies, surgeries, routine patients' needs and in particular those of the chronic ones including haemoglobin disorders is fully anticipated;
- Particularly in countries without a universal coverage health care system (which constitute the majority of our member countries), there is postponement and on many occasions in many countries, cancellation of access of patients to lifesaving chelation drugs due to:
 - i. difficulty to reach pharmacies and/or,
 - ii. drugs not being possible to be imported in the country and/or
 - iii. drugs not been distributed by NGOs which reduce severely or even closed down their activities and/or
 - iv. due to severe financial challenges of patients/family members consequent to losing their job or being 'forced' or 'advised' to stay home or being in quarantine or having been infected with SARS-CoV-2
- Huge economic challenges affect access of patients to health services, appropriate to their disease, in the majority of countries of the developing world devoid of universal covered health care systems with or without COVID-19.

All in all, anxiety, uncertainty, depression, stress on behalf of chronic patients including patients with haemoglobin disorders, are feelings becoming very prevalent amongst them, making their everyday life even more challenging than in periods outside COVID-19.

The world needs to take lessons from the pandemic, each country to revisit and identify its gaps, weaknesses and strengths.

In the meantime, however, standard basic care for patients with haemoglobin disorders should not be INTERRUPTED, as morbidity and mortality rates occurring as a consequence would be higher than those which could result from SARS-CoV-2 infection in these patients.

QUESTIONNAIRE FOR BLOOD DONORS

(provided by AABB)

1. Self-Deferral for Diagnosis/Suspected infection

In the past 28 days, have you been diagnosed with or suspected of having COVID-19?

NO

YES

- Determine date the symptoms resolved after the diagnosis/suspicion of COVID-19
- Refrain from donation for 28 days from the date the symptoms resolved after a diagnosis/suspicion of COVID-19

2. Self-Deferral for 'Close Contact'

In the past 28 days, have you cared for, lived with or otherwise had close contact with an individual(s) diagnosed with or suspected of having COVID-19?

NO

YES

- Determine the last date the donor cared for, lived with or otherwise had close contact with an individual(s) diagnosed with or suspected of having COVID-19 infection
- Refrain from donation for 28 days from the last date the donor cared for, lived with or otherwise had close contact with an individual(s) diagnosed with or suspected of having COVID-19 infection

3. Travel

Have you travelled in the past 28 days?

NO

YES

- Determine the date of departure from the country
- Refrain from donation for 28 days from the date of departure from the date

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