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Article type : International Forum

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Vox Sanguinis International Forum on Hospital Transfusion Services' Response to COVID-19

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Introduction

The novel coronavirus (SARS-Cov-2) that was first reported in Wuhan, China and provokes the COVID-19 disease has developed into a pandemic with hundreds of thousands of people infected. Many

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/vox.12943
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governments have enforced social isolation protocols on their citizens, which has led to the closure of many large public gatherings in order to limit the spread of the virus. These closures could reasonably be expected to affect blood collections, thereby presaging shortages of blood for transfusion. On the other hand, steps such as the postponement of elective surgeries and other non-urgent transfusions could mitigate against potential shortfalls in the blood supply.[1]

The transfusion community has faced epidemics and pandemics before,[2-9] but little has been published about the preparations made by hospital-based transfusion services for handling samples and performing pretransfusion testing on patients who are affected by the disease. A study of the policies and procedures vis-à-vis pre-transfusion testing and the provision of blood products at three Japanese hospitals during the recent Ebola epidemic revealed different approaches to performing pre-transfusion testing on potential recipients and how the blood products were issued.[10] Given the urgent need to develop best practices for conducting pre-transfusion testing and issuing blood products not just during the current novel coronavirus pandemic but also for future pandemics, the time is now propitious to understand how transfusion services in cities with different burdens of this disease are approaching these issues and for the dissemination of different policies and procedures that facilitate the timely provision of blood products to our patients while maintaining a high level of safety for transfusion service staff.

Summary of Responses

Question 1: *Demographics of respondents*

Responses were received from a total of 12 centers from around the world including Australia, Brazil, Canada, Denmark, Iran, Israel, Italy, Japan, Korea, Spain, UK, and USA. **Table 1** demonstrates the demographics of the respondents and the cities in which their institutions were located. All respondents worked in large academic medical centers, although the Brazilian respondent worked at a hospital that only treated hematology oncology patients and the Iranian respondent worked in a private specialty hospital. At the time of survey completion, the absolute number of confirmed coronavirus cases ranged

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from a low of 4,831 (Israel) to a high of 386,817 (USA), but accounting for the population of each country, the rate of confirmed cases ranged from 0.01% (Brazil and Japan) to 0.30% (Italy). The rate of coronavirus infections was felt to be increasing in Israel, USA, Canada, Japan, and Brazil, stable in the UK, and Korea, and decreasing in Spain, Denmark, Australia, and Italy. However, the survey responses were received between 31 March, 2020 and 24 April, 2020, so the number of confirmed cases and the respondent's opinion as to the extent of the spread of coronavirus throughout their country reflected the state of the disease at the time the survey was completed; this number and opinion might have changed in the time between survey completion and the publication of this International Forum.

Table 2 presents a short summary of each respondent's answer to each question.

Question 2: *Did your hospital blood bank/transfusion service accept samples for pre-transfusion testing (including DAT) from patients who were confirmed or suspected to be infected with novel coronavirus?* All of the respondents indicated that their transfusion services accepted samples from patients with confirmed or suspected coronavirus infections. The American, Australian, Iranian, and Japanese respondents indicated that they did not make any changes to the processes of sample procurement and labeling, accepting the sample in the transfusion service, testing, storing, or discarding the sample. For the centers that did institute new policy changes for handling these samples, the Israeli and Korean respondents indicated that the sample label had the word COVID written on it to alert the technologists to implement the enhanced safety measures for handling and testing these samples, and the samples were transported to the transfusion service in clear plastic bags. The Italian respondent indicated that the labeling was performed outside of the patient's room in a designated safe area.

The Spanish respondent indicated all samples that were received at the transfusion service for pre-transfusion testing were assumed to be potentially contaminated with coronavirus and so they were all cleaned with hypochlorite before being processed, and they were also UV irradiated for 30 minutes. Similarly, the Danish respondent indicated that samples from coronavirus patients were cleaned by the phlebotomist before they arrived at the transfusion service. Interestingly, the Italian respondent indicated

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that paper requisitions were sealed in plastic bags for 5 days to sanitize them before being archived. At the Brazilian and Canadian respondents' sites, all samples regardless of the presence of coronavirus were opened behind a plastic shield, while in a similar vein, at the UK respondent's site, the sample tubes were left for a while to settle after centrifugation so as to reduce the probability of aerosolizing the contents. Also, at the Canadian site, all laboratory staff wore face masks as maintaining appropriate physical distancing is not always possible.

All of the respondents indicated that the samples were tested in the usual location in the transfusion service except for the Israeli respondent who indicated that pre-transfusion testing was performed in a biosafety cabinet and the Korean respondent who indicated that the samples were tested in a fume hood.

In terms of the personal protective equipment (PPE) that was worn by the transfusion service technologists, the Spanish, American, Brazilian, Danish, Australian, and British respondents indicated that the standard laboratory PPE was worn when testing these samples. The Israeli respondent indicated that double gloves, goggles, an N95 respirator, and a gown was worn when testing samples from known or suspected coronavirus patients, while the Italian respondent indicated that a mask was added to the standard PPE when testing such a sample. At the Korean respondent's transfusion service, gloves, goggles, and a surgical mask were worn when testing these samples.

Once the pre-transfusion testing had been completed, most of the respondents stored these samples in their routine manner, expect at the Israeli respondent's laboratory where the samples were stored in a separate shelf in a sealed container, and at the Italian respondent's laboratory where the samples from known or suspected coronavirus patients were kept in a dedicated rack in the same refrigerator as the other samples. The Korean respondent indicated that the samples were returned to the plastic bag into which they were received for storage, and when it was time to dispose of the samples they were sent to their department of microbiology for disinfection and disposal. All of the other respondents indicated that the samples were discarded following their routine protocol.

Lastly, as stated above, all of the respondents indicated that their transfusion services accepted samples from known or suspected coronavirus patients. However, the Israeli respondent indicated that

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prior to receiving the biosafety cabinet, samples from these patients were not accepted for pre-transfusion testing. Instead, group O RBCs and group AB plasma would have been issued to these patients. All of the patient's available transfusion and immunohematological history was reviewed prior to issuing blood products, and antigen negative RBCs would have been issued to an alloimmunized recipient. Uncrossmatched RBCs were rarely required in this setting as the biosafety cabinet was available quickly after the need for it arose.

Question 3: *If a cooler (i.e., a temperature controlled device used for storing blood products outside of the blood bank) of blood products was issued on such a patient how did the transfusion service handle the cooler?*

The American respondent indicated that blood products were loaded into the cooler in the routine manner for patients with known or suspected coronavirus, while the Australian respondent indicated that RBCs were individually put into bags and then loaded into the cooler. These coolers always remained outside of the patient's room, thus the cooler did not need to be decontaminated upon its return to the transfusion service. RBCs that were taken into a patient with known or suspected coronavirus' room but not transfused were discarded if they were returned to the blood bank. The Canadian respondent also issued RBCs in individual plastic bags that had been sealed to indicate if the bag had been opened; at this center, coolers were decontaminated upon return to the transfusion service, which had been the routine practice before this pandemic, and any RBCs that were returned in unopened plastic bags were returned to the inventory; RBCs that were returned in opened bags were discarded. The Australian and Canadian policy of issuing RBCs in individual plastic bags in a cooler were new policies that were implemented during this pandemic. The American and Italian respondents indicated that RBCs that were returned in a cooler were wiped down and restocked. The Canadian, American, and Brazilian respondents indicated that the coolers were also disinfected, with the latter indicating that this was a new policy that had been implemented during this pandemic and that it would become permanently adopted.

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The Spanish and British respondents indicated that they did not make any changes to their cooler issuing policy, while the Israeli, Danish, Italian, and Korean respondents indicated that they do not routinely issue coolers to any patient.

Question 4: *Does your facility have an existing plan to deal with samples from patients with novel pathogens?*

Many of the respondents indicated that they had a pre-existing plan for handling samples from patients with novel pathogens. For example, the Israeli plan was derived from their experience with the 2003 SARS outbreak, the Korean respondent's plan was based on their experience with the MERS outbreak, and the Canadian respondent's plan was based on the Ebola virus outbreak. The Spanish respondent indicated that the hospital had a plan but that it had been dormant before it was reactivated for this pandemic, while the Danish respondent indicated that their pre-existing plan was designed for patients who were contaminated with radiation, chemical or biological agents. Both the American and Italian respondents indicated that they did not have a specific plan for dealing with novel pathogens because standard universal precautions were always being used for all samples. Both the Brazilian and the British respondents indicated that their hospitals did not have a pre-existing plan.

Question 5: *Was any additional training provided to the staff about the nature of this virus and its infectivity?*

All of the respondents indicated that some form of training was provided to their transfusion service technologists and/or hospital house staff. The training generally involved education about the proper use of PPE and the application of universal precautions, as well as reminders about the importance of handwashing and frequent surface disinfection. The Israeli and British respondents provided specific education about how to use the biosafety cabinet and about the new policy of not immediately opening the centrifuged samples, respectively. See the individual responses for more details about the specific nature of the training that each respondent provided.

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Question 6: *How has the utilization of red blood cells, platelets and plasma in your hospital changed since the start of the pandemic?*

Only the Australian and Korean respondents indicated that the use of RBCs, plasma, and platelets were unchanged from pre-pandemic levels. The other respondents indicated that they had either quantitatively or qualitatively noticed reductions in transfusions at their centers of around 30% for RBCs, 20-47% for platelets, and about 40% for plasma. Not surprisingly, the Brazilian respondent whose hospital exclusively treats hematology oncology patients reported no change in platelet transfusions thus far in the pandemic.

Question 7: *Does the respondent anticipate blood product shortages as a result of this pandemic?*

The Israeli, Spanish, Danish, British, and Korean respondents did not expect a blood shortage as a result of this pandemic. Others, such as the Brazilian, Italian and Iranian respondents, expected shortages in the short, medium, and long terms, while the American, Australian, Canadian, and Japanese respondents expected medium term shortages. The Canadian respondent also expects a shortage of plasma fractionation products such as IvIg in the long term.

In terms of shortage mitigation strategies, many respondents such as the Israeli, Australian, and Italian respondents indicated that their hospitals had cancelled elective surgeries thereby helping to preserve their blood product inventories. Others, such as the respondents from USA, Brazil, Australia, and Canada held information campaigns to remind clinicians about appropriate transfusion thresholds and transfusing a single RBC unit at a time. The Canadian respondent also indicated that they reminded their clinicians about the appropriate use of pharmaceuticals such as prothrombin complex concentrates, tranexamic acid, and intravenous iron. The British respondent indicated that they reduced their hospital's blood inventory level by about 30% to reduce wastage.

Question 8: *Other lessons learned from this pandemic*

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See the individual responses for more details. In general, the advice from the respondents was to plan ahead of time for how the transfusion service should respond when these events happen. The Spanish and Canadian respondents mentioned their lack of advance preparedness for implementing a convalescent plasma program, while the Brazilian respondents advised having a plan for employee travel to and from the hospital when public transport is unavailable and for dealing with reduced staffing due to illness. The Italian respondent was concerned about having too many people donate blood early in the pandemic when the need for products was low thereby potentially creating waste and making donors ineligible to donate as the pandemic wanes and demand returns to normal. The British respondent suggested keeping the workflow as routine as possible to avoid confusion and errors.

Question 9: *Will your center offer convalescent plasma (CP)?*

The Spanish, Canadian, and British respondents indicated that CP will be available in the context of a clinical trial; the multicenter Spanish trial will randomize 278 patients into either the standard of care or standard of care plus CP arms, and primarily use clinical outcomes such as if the patient needs hospitalization and if any supplemental oxygen is required. Patients in the CP arm will receive one unit that will be between 250-300 ml collected by any approved apheresis machine, and the plasma will undergo pathogen inactivation using any approved method. Details of the Canadian and British trials are provided in the response section. The American respondent also plans to offer CP in the context of a clinical trial an also for compassionate use without pathogen inactivation. The Israeli and Brazilian respondents indicated that the Intercept (Cerus) technology will be used for their CP, while the respondents in Denmark, USA, and the UK indicated that the CP will not undergo pathogen inactivation. At the time of survey completion, CP was not available in Australia, Korea, and Japan.

Summary

Among countries with different levels of people affected by the SAR-Cov 2 pandemic, the hospital blood banks/transfusion departments have reacted differently to the pandemic. A third of the respondents did

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not change their policies/procedures for samples received from known or suspected patients while the remainder changed their practice in some way to minimize the exposure to potential contaminated specimens. Interestingly 75% of the respondents reported a decrease in overall blood components utilization due to the changes introduced at the hospitals to treat the COVID-19 patients. Convalescent plasma is also being considered or used in 75% of the responding centers to treat COVID-19 patients.

Table legends

Table 1. Demographics of the respondents to this International Forum.

Table 2. Summary of replies to the questions posed in this International Forum. PPE: Personal protection equipment. BSC: Biosafety cabinet.

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TABLE 1						
1a. Country/City	**1b. Type of Hospital**	**1c. Number of Beds**	**1.d Approximate number of RBCs Transfused/Year**	**1e. Confirmed Novel Coronavirus Cases at the time of survey completion (Deaths)**	**1f. Country Population in Millions**	**1g. Were novel Coranavirus Cases Increasing, Decreasing or Stable at the time of survey completion ?**
Melbourne, Australia	Academic medical center	1639	22190	6553 (67)	25.65	Decreasing
Rio de Janeiro, Brazil	Academic medical center	100	12604	23830 (1355)	209.50	Increasing
Toronto, Canada	Academic medical center	1355	10500	42110 (2149)	37.6	Increasing
Odense, Denmark	Tertiary hospital	1000	41000	6876 (309)	5.82	Decreasing
Oxford, England	Academic medical center	1185	17000	129044 (17337)	66.50	Stable
Tehran, Iran	Private specialty hospital	200	4200	89328 (5650)	83.00	Stable
Be'er Yaakov, Israel	Academic medical center	956	9000	4831 (17)	9.14	Decreasing
Udine, Italy	Academic medical center	980	16580	181228 (24214)	60.00	Decreasing
Tokyo, Japan	Academic medical center	749	10000	12429 (328)	125.96	Increasing
Seoul, Korea	Academic medical center	1989	59838	10674 (236)	51.78	Stable
Madrid, Spain	Tertiary hospital	869	13167	117710 (10935)	46.45	Decreasing
Stanford, United States	Academic medical center	969	41000	386817 (10686)	332.64	Increasing

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TABLE 2

Country/City	2. Did your hospital blood bank/transfusion service accept samples from patients confirmed or suspected to be infected with novel coronavirus?	2h. Were changes made in testing policies/procedures for samples from known or suspected patients?	2i. If yes, what changes?	2j. Changes made for all samples or only for known or suspected cases?	3. Were blood products dispensed in coolers?	3i-o. Changes made for products dispensed/returned in coolers	4. Did your facility have an existing plan to deal with samples from patients with novel pathogen?	5. Was any additional training provided to the staff about the nature of this virus and its infectivity?	6. Overall blood product use since the start of pandemic increasing, decreasing or stable?	7. Do you anticipate blood shortages at your hospital?	8. Describe specific measures to avert or minimize these shortages	9. Are you planning to use/using convalescent plasma from COVID-19 patients to treat severe forms of the disease?
Melbourne, Australia	Yes	No	NA	NA	Yes	Cooler remains outside patient room. Products discarded if taken into patient room and not transfused.	Yes	Yes, use of PPE and laboratory disinfection protocols	Stable	Yes	Cancellation of elective surgeries, enforcement of single unit transfusions in non-bleeding patients	Yes
Rio de Janeiro, Brazil	Yes	Yes	Plastic film used to open tubes	All	No	NA	No	Yes, unspecified training session for staff	Decreasing	No	NA	Yes
Toronto, Canada	Yes	Yes	Addition of splash guard for decapping samples	All	Yes	Units placed in individual plastic bags and sealed with a sticker to indicate integrity, coolers disinfected upon return	Yes, created in response to Ebola	Yes, town hall on risk to lab staff from handling COVID samples	Decreasing	Yes	Maximize use of iv iron, TXA, epo, PCCs and strict adhesion to strict transfusion triggers	Yes
Odense, Denmark	Yes	Yes	Samples from infected or potentially infected patients were externally cleaned before arriving at transfusion service	Only COVID patients	No	NA	No	Yes, e-learning program concerning hand hygiene and infection prevention	Decreasing	No	NA	Yes
Tehran, Iran	Yes	No	NA	NA	Yes	NA	Not specified	Yes, nature of training not specified	Decreasing	Yes	Cancellation of elective surgeries, adopting more restrictive transfusion thresholds	Yes, but not at respondent's hospital
Be'er Yaakov, Israel	Yes	Yes	Labeled as COVID suspected, received in biohazard packages, no tubing of specimens, sample tested in BSC, additional PPE used by staff, samples stored on designated shelf	Only COVID patients	No	NA	Yes, created in response to SARS in 2003	Yes. Use of new PPE and BSC	Stable	No	NA	Yes
Udine, Italy	Yes	Yes	Surgical mask added to PPE and samples placed in segregated storage	Only COVID patients	No	NA	No	Yes, unspecified online courses	Decreasing	Yes	Decrease of non-urgent surgeries and admissions, use of restrictive transfusion triggers	No
Tokyo, Japan	Yes	No	NA	NA	Yes	No	Yes, samples are sent to the National Institute of Infectious Diseases	Yes, general hospital wide education	Decreasing	Yes	No current plan	No
Seoul, Korea	Yes	Yes	Sample bags labeled as possible COVID patient , samples tested in fume hood, stored in labeled bag and sent to micro for disinfection and disposal	Only COVID patients	No	NA	Yes, created in response to MERS in 2015	Yes, unspecified hospital wide training	Stable	No	NA	No
Madrid, Spain	Yes	Yes	Sample tubes underwent hypochlorite wiping and UV light treatment for 30 minutes.	All	Not specified	NA	Yes, but it had been inactive	Yes, workers trained according to their risk assessment.	Decreasing	No	NA	Yes
Oxford, UK	Yes	Yes	Testing delayed after centrifugation to minimize aerosol droplets	Only COVID patients	Yes	Not specified	Yes	Yes, education on testing procedure changes	Decreasing	No	NA	Yes
Stanford, United States	Yes	No	NA	NA	Yes	No	No	Yes, assigned lesson and corresponding quizzes for lab guidelines	Decreasing	Yes	Reinforce good transfusion practices	Yes

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