

SARS-CoV-2/COVID-19 pandemic: first wave, impact, response and lessons learnt in a fully integrated Regional Blood and Tissue Bank. A narrative report

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Background - The COVID-19 pandemic is placing blood and tissue establishments under unprecedented stress, putting its capacity to provide the adequate care needed at risk. Here we reflect on how our integrated organisational model has faced the first impact of the pandemic and describe what challenges, opportunities and lessons have emerged.

Materials and methods - The organisational model of the Catalan Blood and Tissue Bank (*Banc de Sang i Teixits*, BST) is described. The new scenario was managed by following international recommendations and considering the pandemic in a context of volatility, uncertainty, complexity, and ambiguity (VUCA), allowing rapid measures to be taken. These aimed to: ensure donor safety, promote proper responses to patients' needs, ensure the health and well-being of personnel, and prepare for future scenarios.

Results - The BST has adapted its activities to the changes in demand. No shortage of any product or service occurred. Donor acceptance, safety and wellbeing were maintained except for tissue donation, which almost completely stopped. To support the health system, several activities have been promoted: large-scale convalescent plasma (CP) production, clinical trials with CP and mesenchymal stromal cells, massive COVID-19 diagnoses, and participation in co-operative research and publications. Haemovigilance is running smoothly and no adverse effects have been detected among donors or patients.

Discussion - Several elements have proven to be critical when addressing the pandemic scenario: a) the early creation of a crisis committee in combination with technical recommendations and the recognition of a VUCA scenario; b) identification of the strategies described; c) the integrated donor-to-patient organisational model; d) active Research and Development (R&D); and e) the flexibility of the staff. It is essential to underline the importance of the need for centralised management, effective contingency strategies, and early collaboration with peers.

Keywords: COVID-19, pandemic, blood and tissue bank.

INTRODUCTION

On March 11th, the World Health Organization (WHO) declared the outbreak of SARS-CoV-2/COVID-19 a pandemic¹. Since then, more than 17 million people have been infected and more than 670,000 have died from the disease². The Spanish Government declared a state of alarm on March 14th³.

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The Spanish National Health Service is a decentralised system where each region has its own Blood Transfusion and Tissue Bank Service, which aims to meet the same medical and technical requirements⁴.

In Catalonia (7.5 million inhabitants), the Blood and Tissue Bank (*Banc de Sang i Teixits*, BST) is the public institution responsible for the supply and proper use of human blood, cells and tissues and, by extension, any substance of human origin (SoHO), and other related services, such as immunology and congenital coagulopathies. The BST, with a central management and production facility (CMP) in Barcelona, has developed an organisational model covering the complete value chain of all activities regarding the donation, procurement, processing, distribution and administration of SoHO, as well as haemovigilance and biovigilance.

The CMP, where all blood component products are received and manufactured, co-ordinates a first radial network of BST units located in 11 reference hospitals, responding to the local needs and acting as hubs that support BST units located in less specialised hospitals (secondary network) (Figure 1). Thanks to this model and advanced logistics, the BST provides products and services to more than 100 health care providers.

The product stock is stored in the CMP, and covers the requirements for approximately ten days and the volume of each hub's stock is established to respond to emergencies in their assigned areas.

In addition to donations in mobile units, every BST hub and the BST services in the secondary network are also responsible for obtaining donations. This structure also optimises haemovigilance and biovigilance.

During the SARS-CoV-2/COVID-19 outbreak, Catalonia has been the second most affected region in Spain with more than 77,000 persons infected and more than 5,700 deaths (data available 28/10/2020)⁵. In this context, the BST has had to face an unprecedented challenge to cope with this new situation, with the risk of a decrease in donations, and the subsequent shortage of transfusion and transplant products⁶⁻¹².

The purpose of this report is to evaluate how our fully integrated organisational model has dealt with the impact of the pandemic, and to describe the challenges and opportunities that have emerged. Finally, we will reflect on the lessons learnt in order to be better prepared to face new waves of this pandemic or other global health crises.

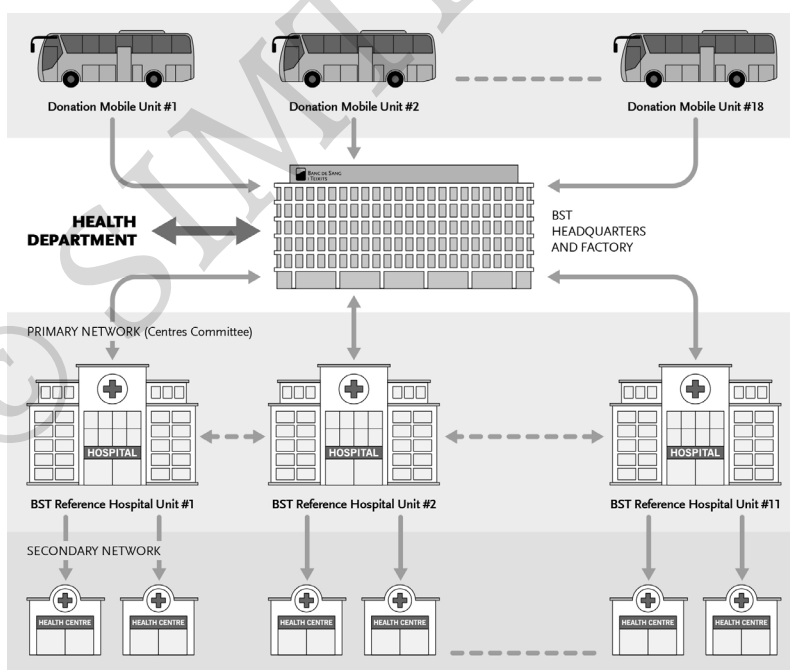


Figure 1 - The organizational structure of the Catalan Blood and Tissue Bank (*Banc de Sang i Teixits*, BST) showing how the entire value chain is integrated from donor to patient

This comprehensive network allows real-time internal communication, and the simultaneous implementation of improvement and corrective measures between all the centres and services that cover the entire territory.

METHODOLOGY AND OUTCOMES

On March 14th, a Crisis Committee (CC) including top BST management representatives was established to manage the impact of the pandemic on BST activities and internal and external communication agencies. It included the Chief Executive Officer (CEO), the Deputy Director and all directors of operational and support processes, i.e., blood bank, tissue bank, hospital services, information technologies, operations, and human resources and communication. The CEO was responsible for the management and monitoring of the action plan as well as for communication with the Board of Directors and health authorities. The CC met during the alert phase on an almost daily basis and its continuity was assured by dividing the team into two groups that alternated between face-to-face and video conference meetings.

The pandemic was internally defined as a VUCA situation^{13,14} (volatility, uncertainty, complexity and ambiguity) and decisions were made accordingly. The Spanish Royal Decree released in March³, and the Contingency Plan of the Department of the Presidency of the Generalitat of Catalonia¹⁵, as well as those from the World Health Organization (WHO)^{16,17} and the European Centre for Disease Prevention and Control (ECDC)¹⁸, were taken as a reference for actions that were implemented both at a global level and in every operational, support and strategic process. The most relevant actions were focused on four major objectives.

ENSURING DONOR SAFETY

Donation campaigns were reorganised and conducted in public and private buildings adapted for blood donation and, in order to satisfy social distancing requirements, blood donation buses were discontinued. An appointment system was implemented to avoid gatherings of an inappropriate number of people and queues, and weekly donation goals for every donation campaign were set.

Safe spaces in all donation rooms were created by adopting preventive measures, such as controlling the access to a limited number of people at a time, body temperature screening, satisfying social distancing requirements, and providing masks to all donors and skin protective film for the puncture area.

The criteria for accepting donors were modified with respect to those travelling from areas with

community-acquired SARS-CoV-2 transmission and in relation to having a fever or a history of possible contact with individuals with COVID-19.

To reduce volunteer donor attendance at hospitals of the Spanish Registry of Bone Marrow Donors (REDMO), a telephone health questionnaire was carried out. Additionally, all patients were polymerase chain reaction (PCR)-tested for SARS-CoV-2. Unexpectedly, from February to June, there was a high number of voluntary progenitor donations; 13 products were collected from these donors. During the same period, 24 apheresis aimed at CAR-T production were performed and shipped, and 18 CAR-T products were received. Some deliveries were compromised by problems with flights, but they did eventually take place according to schedule.

To date, the well-being of donors has not been affected and no additional adverse effects have been found. Post-donation information protocols, lookback and trace backs have been established and no post-transfusion SARS-CoV-2 infection has been reported to the Catalan Haemovigilance Programme, which is a reliable system that has been successfully operating since 2005 with a very high notification rate (10.5% in 2019). Professionals in charge of hospital blood transfusion and patients' haemovigilance are also members of the BST, critically contributing to the proper functioning of the programme. All patients transfused during the pandemic with products from donors who, after donation, had symptoms that were compatible with the infection or a positive PCR have been evaluated and followed. As expected, transmission of the infection through the blood was not observed in any of the patients.

PROMOTING PROPER RESPONSE TO PATIENTS' NEEDS

Blood transfusion and immunohaematology

Blood component stocks were adapted to meet patient needs by checking the requirements of each and every hospital on a daily basis and a strict follow-up on use of supplies. To avoid any disruption in the availability and supply of blood components due to personnel shortage, volunteer BST employees were specifically trained as a back-up; however, they were only needed on a few occasions.

To ensure the adequate supply of platelets, a pathogen reduction system was introduced to extend their shelf life from five to seven days. One-third of the platelets produced were treated with the Mirasol Pathogen Reduction Technology (Mirasol PRT; Caridian BCT, Lakewood, CO, USA), which uses riboflavin and ultra violet light to introduce irreparable lesions into nucleic acids. Successive changes in donor eligibility criteria were introduced according to the evolution of the pandemic and health authorities' recommendations. Nevertheless, all samples were treated as potentially SARS-CoV-2-positive. This policy was extended to immunohaematology and transfusion laboratories.

Health authorities allowed blood donation during the nationwide lockdown. Blood donation appointments were also encouraged, thus reinforcing the message that blood donation is safe.

Procedures were urgently adapted to allow for blood transfusion outside hospitals, such as at home and in hotels, ensuring the same level of safety as in a hospital setting.

Hospitalised COVID-19 patients in Catalonia had low usage. Ten percent of hospitalised COVID-19 patients required transfusions. Hospitalised COVID-19 ward patients had significantly lower transfusion rates of red blood cells (RBCs), platelets and plasma transfusion than hospitalised patients without COVID-19 hospitalised at the same time. The COVID-19 intensive care units (ICUs)

had higher rates of RBCs and plasma transfusion than COVID-19 ward patients who were not in ICUs, but the overall blood usage in both groups remained low.

To cover the supply needs from either clinical trials or observational studies, a COVID-19 convalescent plasma programme was launched. To date, 1,200 apheresis have been treated with the two plasma pathogen reduction systems usually used in the BST: methylene blue inactivation (Theraflex MB-Plasma system; MacoPharma, Tourcoing, France) and the Springe method (Grifols; Parets del Vallés, Spain). Currently, a stock of 2,400 inactivated hyperimmune plasma units is available for clinical use. Additionally, samples of plasma from convalescent COVID-19 donors have been made available in our biobank.

According to established internal protocols, blood component stock was constantly adapted to hospitals' demands. Shortage was avoided (**Figure 2**), and supply and services were constantly maintained during the maximum peak of contagions and during the different phases of de-confining. Consequently, no elective surgeries or non-urgent clinical interventions were deferred.

There was a modest decrease in global immunohematology activity during the pandemic, reaching a nadir in April (**Figure 3**). Nevertheless, the manufacture of erythrocyte reagents that are critical for transfusion compatibility testing was maintained. In fact, the number of reagent units delivered increased by 30%. The availability of

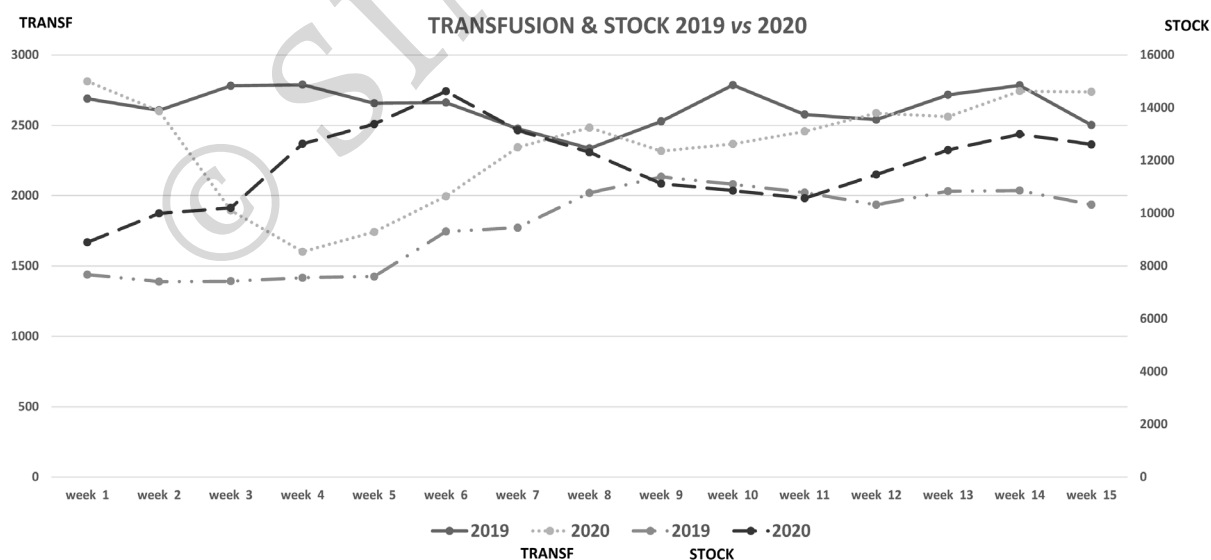


Figure 2 - Transfusion and stock of blood concentrates activity during the state of alarm compared with the same period in 2019

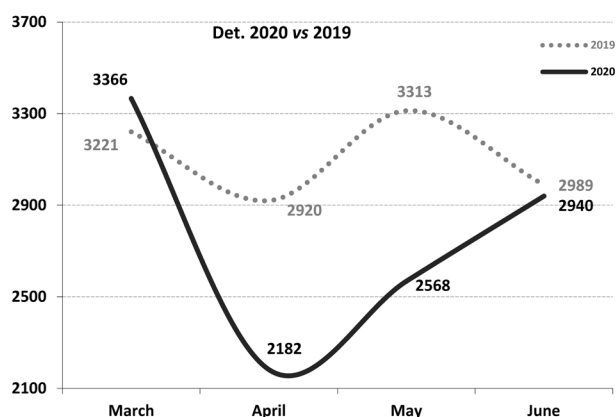


Figure 3 - Immunohaematology tests performed during the state of alarm compared with the same period in 2019

anti-HNA and anti-HPA antibody techniques made it possible to specifically screen donors to exclude hidden carriers such as those from blood and convalescent plasma donors. Furthermore, these techniques allowed the diagnosis of suspected transfusion-related acute lung injury (TRALI) in patients receiving convalescent plasma. To date, more than 50 patients have been transfused with convalescent plasma. Only plasma from non-transfused donors was used for this purpose. TRALI was suspected in three patients transfused with male convalescent plasma. Anti-HLA and HNA antibodies investigation in the plasma donors was negative. Similarly, no anti-leukocyte antibodies were detected in the three patients.

Cell therapy services

The Spanish National Transplant Organisation (*Organización Nacional de Trasplante*, ONT) recommended

against the use of bone marrow as a source of stem cell transplantation due to logistical complications and the potential risk for donors, and recommended not initiating conditioning regimens until product receipt and donor eligibility were confirmed. In addition, given the need for a 14-day quarantine in the absence of PCR tests, there has been an increase in cryopreserved and transplanted allogeneic products, and a corresponding decrease in freshly infused products (**Figure 4**). Remarkably, during the peak of the pandemic, cell processing and distribution procedures maintained their activity in supporting the haematopoietic stem cell transplantation programme and were able to provide all Catalan hospitals with the products and services needed. The co-ordinated network and centralised stem cell therapy laboratory were essential for adopting changes and facilitating the activity.

This was also the case with the international exchange of haematopoietic progenitor cell grafts. A contingency plan was developed together with the REDMO and the Catalan Transplants Organization (*Organización Catalana de Trasplantes*, OCATT), and a hub for product exchange was created at Barcelona airport to prevent couriers from crossing the border. It is relevant to point out the collaboration with the World Marrow Donor Association (WMDA) and the contribution to an article highlighting the importance of adapting volunteer donor programmes to the pandemic⁹.

Cord blood collection and banking was deemed non-essential and was stopped. Nevertheless, five maternity units continued their cord blood collection to maintain platelet rich plasma (PRP) eye drop production.

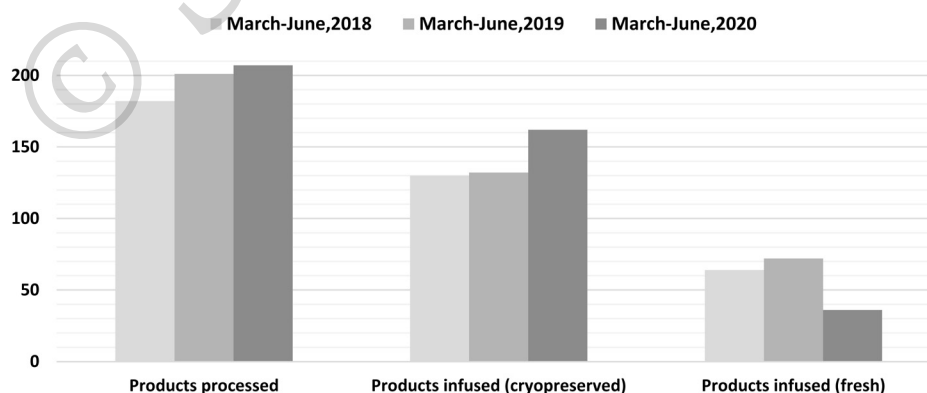


Figure 4 - Fresh and cryopreserved cell therapy products supplied during the state of alarm compared with the same period in 2019 and 2018

Thanks to the 20,000 units available, the number of supplies has been maintained and during the pandemic 12 cord blood units were released for transplantation. In addition, because of the reduction in these activities, the histocompatibility laboratory experienced a 45% reduction in tests performed in April and May.

Tissue bank

Cadaveric donation activities ceased completely during the first four weeks of the health emergency, although there was a slow recovery after the end of April. This decrease was directly related to the structure of the donation model, based on the detection of potential donors in the ICUs and other critical care services. There was a sudden lack of professionals to identify and select donors and of procurement facilities within hospitals. Additionally, personal protection equipment (PPE) and real-time-PCR testing kits required for deceased donation procedures were redirected to feed the resources against the pandemic, causing a serious shortage, which compromised tissue donation activities.

No major changes were implemented in processing procedures, since these are performed in 'clean' rooms with adequate protective equipment after confirmation of negative PCR tests for SARS-CoV-2 and all transmissible diseases according to the European and national legislation and Good Tissue Practices¹⁹. Processing activities focussed mainly on musculoskeletal (MSK) tissues stored before the outbreak. These procedures were continued as a strategy aimed at preparing tissue stocks to be supplied once surgeries were resumed.

Tissue distribution for transplantation experienced a

decrease of around 58% compared to the same period in 2019, due to the cancellation of elective and non-urgent surgical procedures. For example, **Figure 5** shows the evolution of cornea and musculoskeletal tissue donations and the slow recovery of donations coinciding with the reduction in pressure on care in hospitals. To date, the pre-pandemic donation levels have not yet been reached.

However, the disruption in the distribution of tissues from autologous and living donors, such as serum eye drops (SED) and amniotic membrane (AM) was not as significant. The AM extract increased its distribution, since it was used to replace autologous SED therapy of older patients who, due to confinement, could no longer perform their autologous donations.

Currently, tissue bank activities are focussed on the management of the risk associated with tissues stored between December and March, since donors were not tested for SARS-CoV-2 during this period. In collaboration with national and European experts, this has been proven to be essential for adopting preventive measures when managing future stocks of tissues during a potential new outbreak.

Clinical research

One of the most pressing needs is that of identifying therapeutic interventions with a favourable benefit : risk balance for COVID-19 patients, which means that both cell- and plasma-based therapies are strategies that are being tested in clinical trials.

Mesenchymal stromal cells (MSC) have immunomodulatory and tissue-regenerative properties and are widely used in cellular therapy²⁰. They are safe and effective in acute respiratory failure and acute respiratory distress syndrome (ARDS) of multiple causes and show promising

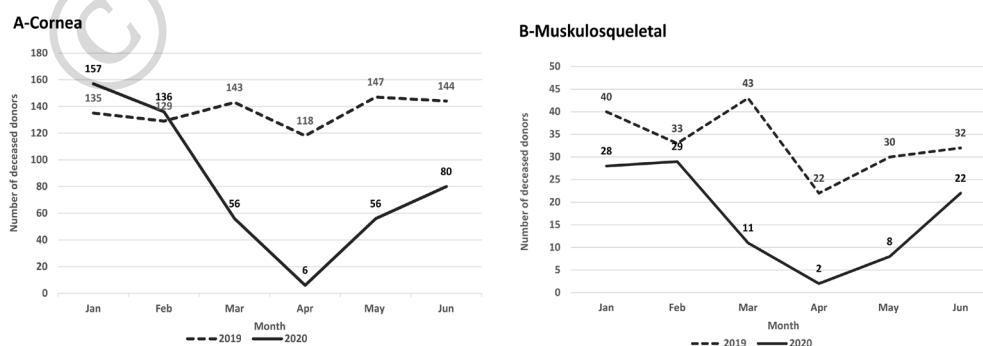


Figure 5 - Cornea (A) and musculoskeletal (B) tissue donation during the state of alarm compared with the same period in 2019

preliminary evidence in ARDS in COVID-19 patients²¹⁻²⁵. We have designed and completed all administrative and regulatory procedures needed to initiate a phase I/II clinical trial (COVIDMES; *clinicaltrials.gov identifier: NCT04390139*) to assess the efficacy and safety of Wharton's jelly MSC in patients with COVID-19 ARDS with the participation of five Catalan hospitals²⁶. We will begin to prepare production of new batches of such cells should this trial prove effective²⁷.

The use of plasma from patients who have recovered from COVID-19 has the potential benefit of providing disease-specific neutralising antibodies before targeted therapies can be developed. The BST COVID-19 convalescent plasma programme has been able to meet the clinical research needs for both internal and external collaborative clinical research studies. As sponsor, the BST is conducting a prospective observational study to assess the clinical impact of convalescent plasma transfusion on COVID-19 patients treated in the Catalan hospital network. The BST is also supplying convalescent plasma to four different clinical trials sponsored by Spanish public hospitals and the country's pharmaceutical industry²⁸⁻³¹.

ENSURING THE PREVENTION OF INFECTION AND WELL-BEING OF BST PERSONNEL

All operational activities were classified after assessing their critical status. Non-critical activities were cancelled or postponed, and the minimum number of professionals needed to perform the priority tasks was defined. Working schedules were modified. Staff and work teams were split into physically separated groups on a rota system to ensure continuity of the workflow, and vulnerable personnel were exempted from performing activities with risk of exposure to SARS-CoV-2.

Social distancing and protection measures were mandatory when conducting face-to-face activities and, when possible, process directors and key staff adopted a variety of remote working strategies. To meet social distancing requirements and avoid internal transmission, additional space was provided for the staff dining area. As the situation started to improve slightly, face-to-face interaction was gradually re-introduced.

The ongoing experimental work on research projects was also postponed if this did not hamper eventual experimental results.

The acquisition, warehousing and supply of PPE to all territorial centres was centralised at the BST headquarters. When needed, upgraded protection masks were added to critical activities such as GMP tissue processing. Their daily distribution and supply, co-ordinated by the Risk Prevention Service, has so far been successful in preventing any shortage.

ANTICIPATION AND PREPAREDNESS FOR FUTURE SCENARIOS

Increasing technical capabilities

A new laboratory with four automatic analysers (Procleix Panther system) has been set up for the detection of SARS-CoV-2 by transcription-mediated amplification (TMA) and made available to the health system to help in the diagnostics of COVID-19. It relies on the BST's strengths such as expertise in TMA, strong logistics and existing interfaces with the information systems of the Health Department. This laboratory has the potential to perform up to 4,000 tests per day. The first tests were carried out on May 7th, 2020, and the laboratory is being adapted to meet increasing demand. More than 20,000 tests from 37 health centres have already been performed with a turnaround time of less than 24 hours. To support this, the Genomics Core Laboratory has implemented SARS-CoV-2 detection by rt-PCR technology and amplicon-based SARS-CoV-2 genome sequencing.

Epidemiological and genomics research

To assess the anti-SARS-CoV-2 seroprevalence in an asymptomatic healthy population in Catalonia (blood donors) at the end of the containment phase and at the end of the confinement phase, an epidemiological study has been designed and initiated. A complementary study is analysing the distribution of exposure, immunity, and susceptibility according to the demographic and geographical characteristics of donors, as well as the persistence over time of anti-SARS-CoV-2 antibodies in a healthy adult population.

Fostering immunohaematology

The immunohaematology laboratory has been deeply involved in the study of the influence of the ABO group on the susceptibility and severity of SARS-CoV-2 infection. Furthermore, a study involving hospitals with COVID-19 patients and transfused persons and a study on convalescent plasma donors who are regular blood

donors is being conducted to assess if the ABO group is also associated with the susceptibility and severity of SARS-CoV-2 infection.

Two publications have resulted from this, one in the *New England Journal of Medicine*³², to which we contributed with our knowledge and experience of the distribution of ABO blood groups among our first-time donors. The other is an editorial for *Vox Sanguinis*³³, which we co-authored in collaboration with Professor Fumichiro Yamamoto, expressing our opinion and summarising current data regarding the relationship between the ABO group and COVID-19.

Virus-specific T-cell bank

In collaboration with the ACT4COVID international consortium³⁴, the BST virus-specific T-cell bank is being expanded by storing SARS-CoV-2 front-end memory cells from convalescent plasma donors³⁵. Additionally, it will make it possible to study cellular immunity against SARS-CoV-2 infection and, eventually, assess their efficacy in future clinical trials.

Genomics research

In collaboration with the Group of Genomics of Complex Diseases of the Sant Pau Hospital Research Institute and the Haemostasis Unit of the same hospital, a project on the study of genetic factors affecting the development of thrombotic complications in patients with COVID-19 has been started. At the same time, a multidisciplinary data analysis project entitled "MINING4COVID: Machine Learning, Internet Keyword Trends and Genetics to Model COVID-19" has been launched. We are seeking funding for their development.

DISCUSSION

The COVID-19 pandemic is putting blood and tissue establishments at an unprecedented level of stress worldwide, placing at risk their capability to provide the adequate care needed to protect the health and well-being of the whole population⁶. Over time, blood services have adopted several organisational models, the most frequent one being based on the "vein-to-vein" approach³⁶⁻³⁸. In this regard, the BST has implemented several additional steps by building a complex but robust structure, integrating the central management of the complete value chain of products offered (practically all SoHO) with services organised as independent operative processes.

This structure is complemented by a network of

11 territorially functional units integrated into all reference hospitals acting as actual hospital Blood and Tissue Service Units. This model can be described as a "donor-to-patient" model.

Although the BST have risk analyses and contingency plans that cover predictable eventualities identified so far, given the magnitude of the pandemic, it has also followed WHO recommendations on contingency plans to guarantee the blood supply, as well as the ECDC publications on the supply of substances of human origin during the COVID-19 outbreak.

Several publications have focussed on how COVID 19 has affected the transfusion chain such as: impact on donor recruitment and eligibility, blood and plasma inventory management, how personnel and donors must be protected, and how to guarantee product safety^{6,12, 39,40}. In this regard, Stanworth *et al.*⁶ have comprehensively shown several relevant studies regarding the transfusion chain under the pandemic and how blood establishments could respond to a shortage. The organisational models included in this article share to a certain extent the characteristics and recommendations we have discussed above.

It is worth pointing out that the BST, a mixture of blood establishment and hospital-based transfusion services with blood donation activity, has been able to implement them in real time in the entire organisation thanks to its integrated "donor-to-patient" model. Furthermore, the independence from external blood suppliers has much facilitated the management of the inventory of blood components.

The creation of a multidisciplinary Crisis Committee gathering national and international recommendations with an early recognition of a VUCA scenario became critical in the effective response and has allowed the organisation to propose actions such as the identification of the four above-described strategical targets.

The organisational model allowed the collection of information, the adoption of rapid decisions, and the immediate and simultaneous implementation of corrective measures, research projects, clinical trials and scientific collaborations. Staff flexibility made it possible to quickly adapt to unforeseen situations. Teleworking has been an opportunity to gain more focus, and is a tool that might result, not only in giving greater value to responsible self-organisation and conciliation, but also in higher overall efficiency.

Lessons learnt

It is essential to reformulate risk analyses and plans with a broader view and perspective. Moreover, collaboration with peers and exchange of knowledge are critical for the assessment of risks associated with outbreaks and the implementation of measures in a timely manner.

Public organisations that manage SoHO rely on the solidarity and altruism of healthy donors; consequently, the pandemic has seriously jeopardised the donation of blood and tissues. Blood and tissue establishments, in collaboration with health services, should define alternative circuits to ensure minimum levels of donation and stocks of blood components and grafts for sustaining medical activity in future crises.

Some of the measures adopted will remain after the pandemic, such as the blood donation prior appointment system, the telephone health questionnaire and consent procedures for progenitor donors, and the contingency plan with REDMO and OCATT. Other measures, such as tissue viral inactivation techniques, are likely to be adopted with the aim of improving safety without compromising the quality of the products⁴⁰.

As of today, as we are writing, the BST has fully entered the second phase of the pandemic. Objectively it is better prepared and, in a few hours, the new contingency plan will be executed. The new activities incorporated are operating at a good pace: more than 6,000 TMAs per day are being carried out (taking the total to more than 180,000), more than 1,800 plasmapheresis on COVID-19 patients have been performed, and about 3,000 units of convalescent plasma (CP) are available and more than 130 patients have been transfused. Clinical trials as well as epidemiological and observational studies are progressing well.

CONCLUSIONS

Organisations around the world have been subjected to unprecedented stress during the COVID-19 health crisis. However, the BST has skilfully sailed in these troubled waters by combining an effective decisions process, an adherence to valuable recommendations of national and international organisations, and the characteristics of its “donor-to-patient” organisational model. The combined processes, shared knowledge, versatility and, above all, the territorial structure bringing the BST closer to local needs have made it possible to quickly adapt to new situations. Valuable lessons must be learned and called upon by the

SoHO establishments and health systems when dealing with similar situations in the future.

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AUTHORSHIP CONTRIBUTIONS

JGL conceived the idea and wrote the manuscript. JGL, JD and EM developed the concepts and structure of the draft. All Authors, contributed to the writing, critically reviewed the draft and approved the final version of the manuscript.

The Authors declare no conflict of interests.

REFERENCES

1. World Health Organization. Coronavirus disease (COVID-19) pandemic. 2020. Available at: <https://coronavirus.jhu.edu/map.html>. Accessed on 28/10/2020.
2. Johns Hopkins University. COVID 19 dashboard by the Center for Systems Science and Engineering (CSSE) Johns Hopkins University. Available at: <https://coronavirus.jhu.edu/map.html>. Accessed on 28/10/2020.
3. Agencia Estatal Boletín Oficial del Estado. [Royal Decree 463/2020, of March 14, which declares the state of alarm for the management of the health crisis situation caused by COVID-19.] Available at: https://www.boe.es/diario_boe/txt.php?id=BOE-A-2020-3692. Accessed on 28/10/2020. [In Spanish.]
4. Agencia Estatal Boletín Oficial del Estado. [Royal Decree 1088/2005, of September 16, which establishes the technical requirements and minimal conditions for hemodonation and transfusion centres and services. Available at: <https://www.boe.es/eli/es/rd/2005/09/16/1088>. Accessed on 28/10/2020. [In Spanish]]
5. Generalitat de Catalunya. Open data and COVID-19. 2020. Available at: http://governobert.gencat.cat/en/dades_obertes/dades-obertes-covid-19/index.html. Accessed on 28/10/2020.
6. Stanworth SJ, New HV, Apolseth TO, et al. Effects of the COVID-19 pandemic on supply and use of blood for transfusion. *Lancet Haematol* 2020; **7**: e756-64.
7. Wang Y, Han W, Pan L, et al. Impact of COVID-19 on blood centres in Zhejiang province China. *Vox Sang* 2020; **115**: 502-6.
8. Baron DM, Franchini M, Goobie SM, et al. Patient blood management during the COVID-19 pandemic: a narrative review. *Anaesthesia*. 2020; **75**: 1105-13.
9. Szer J, Weisdorf D, Querol S, et al. The impact of COVID-19 on the provision of donor hematopoietic stem cell products worldwide: collateral damage. *Bone Marrow Transplant*. 2020; **55**: 2043-4.
10. Pagano MB, Hess JR, Tsang HC, et al. Prepare to adapt: blood supply and transfusion support during the first 2 weeks of the 2019 novel coronavirus (COVID-19) pandemic affecting Washington State. *Transfusion* 2020; **60**: 908-91.

11. Shander A, Goobie SM, Warner MA, et al. Essential role of patient blood management in a pandemic: a call for action. *Anesth Analg* 2020; **131**: 74-85.
12. Grandone E, Mastroianno M, Caroli A, Ostuni A. Blood supply and transfusion support in southern Italy: findings during the first four weeks of the SARS-CoV-2 pandemic. *Blood Transfus* 2020; **18**: 230-2.
13. Wolf D. *Prepared and resolved: the strategic agenda for growth, performance and change*. Tallahassee, FL, USA: Dsb Pub; 2007.
14. VUCA: Soportar la incertidumbre. *New Medical Economics: Health Economics S.L.*; 2019.
15. Generalitat de Catalunya. [Pla de contingència davant la pandèmia de coronavirus SARS-CoV2.] Vol 20202020. [in Catalan.] Available at: <http://educacio.gencat.cat/ca/departament/pla-contingencia-covid19/>. Accessed on 28/10/2020.
16. World Health Organization. Maintaining a safe and adequate blood supply during the pandemic outbreak of coronavirus disease (COVID-19). 2020. Available at: [https://www.who.int/publications/i/item/maintaining-a-safe-and-adequate-blood-supply-during-the-pandemic-outbreak-of-coronavirus-disease-\(covid-19\)](https://www.who.int/publications/i/item/maintaining-a-safe-and-adequate-blood-supply-during-the-pandemic-outbreak-of-coronavirus-disease-(covid-19)). Accessed on 28/10/2020.
17. World Health Organization. Protecting the blood supply during infectious disease outbreaks: guidance for national blood services. 2019. Available at: <https://www.who.int/publications/i/item/protecting-the-blood-supply-during-infectious-disease-outbreaks-guidance-for-national-blood-services>. Accessed on 28/10/2020.
18. European Centre for Disease Prevention and Control. Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA - First update. 2020. Available at: <https://www.ecdc.europa.eu/en/publications-data/coronavirus-disease-2019-covid-19-and-supply-substances-human-origin>. Accessed on 28/10/2020.
19. European directorate for the quality of medicines & healthcare. New guide to the quality and safety of tissues and cells for human application. 2019. Available at: <https://www.ecdc.europa.eu/en/publications-data/coronavirus-disease-2019-covid-19-and-supply-substances-human-origin>. Accessed on 28/10/2020.
20. Vives J, Mirabel C. Multipotent mesenchymal stromal cells from bone marrow for current and potential clinical applications. In: Reis RL, ed. *Encyclopedia of Tissue Engineering and Regenerative Medicine*. Oxford: Academic Press; 2019: 503-512.
21. Sánchez-Guijo F, García-Arranz M, López-Parra M, et al. Adipose-derived mesenchymal stromal cells for the treatment of patients with severe SARS-CoV-2 pneumonia requiring mechanical ventilation. A proof of concept study. *EClinicalMedicine* 2020; **25**: 100454.
22. Leng Z, Zhu R, Hou W, et al. Transplantation of ACE2. Mesenchymal Stem Cells Improves the Outcome of Patients with COVID-19 Pneumonia. *Aging Dis* 2020; **11**: 216-28.
23. Chen J, Hu C, Chen L, et al. Clinical study of mesenchymal stem cell treating acute respiratory distress syndrome induced by epidemic Influenza A (H7N9) infection, a hint for COVID-19 treatment. *Engineering (Beijing)* 2020; **6**: 1153-61.
24. Golchin A, Seyedjafari E, Ardeshiryajimi A. Mesenchymal stem cell therapy for COVID-19: present or future. *Stem Cell Rev Rep* 2020; **16**: 427-33.
25. Atluri S, Manchikanti L, Hirsch JA. Expanded umbilical cord mesenchymal stem cells (UC-MSCs) as a therapeutic strategy in managing critically ill COVID-19 patients: the case for compassionate use. *Pain Physician* 2020; **23**: E71-83.
26. ClinicalTrials.gov. NCT04390139. Efficacy and safety evaluation of mesenchymal stem cells for the treatment of patients with respiratory distress due to COVID-19 (COVIDMES). 2020. Available at: <https://clinicaltrials.gov/ct2/show/NCT04390139>. Accessed on 28/10/2020.
27. Oliver-Vila I, Coca M, Grau-Vorster M, et al. Evaluation of a cell-banking strategy for the production of clinical grade mesenchymal stromal cells from Wharton's jelly. *Cytotherapy* 2016; **18**: 25-35.
28. EudraCT 2020-001953-36. A multicenter, randomized, open-label, parallel group pilot study to evaluate the safety and efficacy of Prolastin® plus standard medical treatment (SMT) versus SMT alone in hospitalized subjects with COVID-19. 2020. Available at: <https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001953-36/ES>. Accessed on 28/10/2020.
29. Avendano-Sola C, Ramos-Martinez A, Munez-Rubio E, et al. Convalescent plasma for COVID-19: a multicenter, randomized clinical trial. *medRxiv*. 2020: 2020.2008.2026.20182444.
30. ClinicalTrials.gov. NCT04547127. A study to evaluate safety and efficacy of convalescent methylene blue treated (MBT) plasma from donors recovered from coronavirus disease 2019 (COVID-19). 2020. Available at: <https://clinicaltrials.gov/ct2/show/NCT04547127>. Accessed on 28/10/2020.
31. ClinicalTrials.gov. NCT04432324. Study to evaluate the safety and efficacy of high dose ivig in hospitalized participants with Coronavirus disease (COVID-19). 2020. Available at: <https://clinicaltrials.gov/ct2/show/NCT04432324>. Accessed on 28/10/2020.
32. Ellinghaus D, Degenhardt F, Bujanda L, et al. Genomewide association study of severe Covid-19 with respiratory failure. *N Engl J Med* 2020; **383**: 1522-34.
33. Yamamoto F, Yamamoto M, Muñoz-Díaz E. Blood group ABO polymorphism inhibits SARS-CoV-2 infection and affects COVID-19 progression. *Vox Sang* 2021; **116**: 15-7.
34. Hospital Clinic de Barcelona. A consortium of European hospitals led by Clínic IDIBAPS is launching a cellular immunotherapy project to tackle COVID-19 with the support of Cellnex Telecom. 2020. Available at: <https://www.clinicbarcelona.org/en/news/a-consortium-of-european-hospitals-led-by-clinic-idibaps-is-launching-a-cellular-immunotherapy-project-to-tackle-covid-19-with-the-support-of-cellnex-telecom>. Accessed on 28/10/2020.
35. Maeng J-J, Sabharwal K, Ülkü MA. Vein to vein: exploring blood supply chains in Canada. *JOSCM* 2018; **11**: 13.
36. The New Zealand Blood Service—a 'vein-to-vein' supply chain. *FTD MAGAZINE*. 2014. Available at: <https://www.nzblood.co.nz/assets/News/A-vein-to-vein-supply-chain-article.pdf>. Accessed on 28/10/2020.
37. Finnish Red Cross Blood Service. Vein to vein-project. 2020. Available at: <https://www.bloodservice.fi/blood-donation/services-for-blood-donors/vein-to-vein-information-system>. Accessed on 28/10/2020.
38. Ngo A, Masel D, Cahill C, et al. Blood banking and transfusion medicine challenges during the COVID-19 pandemic. *Clin Lab Med* 2020; **40**: 587-601.
39. Gniadek TJ, Mallek J, Wright G, et al. Expansion of hospital-based blood collections in the face of COVID-19 associated national blood shortage. *Transfusion* 2020; **60**: 1470-5.
40. Singh R, Singh D, Singh A. Radiation sterilization of tissue allografts: a review. *World J Radiol* 2016; **8**: 355-69.