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REVIEW

TRANSFUSION MEDICINE WILEY

Beyond COVID-19 and lessons learned in the United States

Richard Gammon[1] | Louis M. Katz[2] | Donna Strauss[3] | Kathleen Rowe[4] | Jay Menitove[5] | Richard J. Benjamin[4] | Ruchika Goel[2] | Dayand Borge[6] | Stefan Reichenberg[7] | Roxane Smith[8]

[1]OneBlood, Orlando, Florida, USA

[2]ImpactLife Blood Services, Davenport, Iowa, USA

[3]New York Blood Center, New York, New York State, USA

[4]Cerus Corporation, Concord, California, USA

[5]Kansas University Medical Center, Kansas City, Kansas, USA

[6]Memorial Sloan Kettering Cancer Center, Center for Laboratory Medicine, New York, New York State, USA

[7]Maco Pharma International GmbH, Langen, Germany

[8]Macopharma USA, Duluth, Georgia, USA

Correspondence
Richard Gammon, OneBlood, Inc., 8669 Commodity Circle, Orlando, FL 32819, USA.
Email: richard.gammon@oneblood.org

Abstract

The COVID-19 pandemic severely tested the resilience of the US blood supply with wild fluctuations in blood donation and utilisation rates as community donation opportunities ebbed and hospitals post-poned elective surgery. Key stakeholders in transfusion services, blood centres, supply chains and manufacturers reviewed their experiences during the SARS-CoV-2 pandemic as well as available literature to describe successes, opportunities for improvement and lessons learned. The blood community found itself in uncharted territory responding to restriction of its access to donors (approximately 20% decrease) and some supplies; environmental adjustments to address staff and donor concerns about coronavirus transmission; and the development of a new product (COVID-19 convalescent plasma [CCP]). In assuring that the needs of the patients were paramount, the donation process was safe, that clinicians had access to CCP, and vendor relationships aligned, the blood banking community relearned its primary focus: improving patient outcomes.

1 | INTRODUCTION

The COVID-19 pandemic tested the resilience of the US blood supply as it experienced wild fluctuations in blood donations following closure of community donation venues and post-ponement of hospital elective admissions. Shortages of supplies, reagents and personal protective equipment impacted blood centres at a time when they were initiating production of an unproven, novel therapeutic, COVID-19 convalescent plasma (CCP). These problems were unparalleled but not unforeseen: most hospitals and blood centres had decades old pandemic plans designed for influenza.[1] In this light, the COVID-19 pandemic offers an opportunity to consolidate lessons learned and plan for future disasters.

The US blood supply is dependent on a complex supply chain that converges on blood centres as the ultimate suppliers of blood components.[2] Donor recruitment, phlebotomy, testing, manufacturing and distribution must operate synchronously to ensure that the right blood is available for the right patient at the right time. Disruptions impact all stages of the process. Agencies such as the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism, arising out of the 9/11/2001 terrorist attacks, coordinate local and federal responses following environmental disasters and massive trauma situations that overwhelm local and regional resources. Pandemic influenza plans made a decade ago inadequately address the epidemiology of COVID-19 pandemic, but provided an indispensable blueprint.[3]

While large scale disruptions of the blood supply in the United States occur infrequently, the 9/11 disaster, Hurricane Katrina, West Nile virus, severe acute respiratory syndrome (SARS), the 2009 flu pandemic, Ebola and Zika epidemics serve as a prologue to COVID-19. Assuming the occurrence of another pandemic, we seek prescient lessons from the current episode to inform preparations for the next.

2 | BLOOD DONATION- ESSENTIAL SERVICES AND APPOINTMENTS

Several routes exist for engaging donors and raising awareness of the need for blood donations. During disasters, governmental officials and professional societies offer assistance. From the blood center

perspective, coordinated media and public relations campaigns including an integrated social media appeal provide the broadest visibility. Sustained messaging that aligns with anticipated needs serves as the key element so that all render the same script obviating confusion or conflicting information.

In this regard, the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism virtually assembles all stakeholders, untangles conflicting communications and disseminates information about all aspects of emergent needs and regulatory compliance issues.[3,4]

Messaging to the public is challenging at the best of times, but during the pandemic, when prospective donors faced multiple social contact and lockdown concerns and safety messages evolve, reducing noise and motivating individuals to action required unprecedented diligence. In March 2020, as the new virus' airborne transmission threat virus became clear, six US blood centres constituting 67.9% of whole blood collections noted blood drive cancellations.[5] Understanding the growing deficit and risk to health system security, Dr. Jerome Adams, the incumbent US Surgeon General, used the daily coronavirus press briefing platform to urge young donors to donate. As with many of his communications, Dr. Adams highlighted the need hospitals have for an adequate blood supply while reassuring the public that measures were in place to make the donation process safe for everyone.[6]

This created a surge of donations (at least in some geographic areas) for approximately 2 weeks (personal communications A. Hess [ImpactLIFE Blood Services], March 2, 2021, and D. Borge [American Red Cross], March 15, 2021), but not necessarily from the targeted audience. Decreases in donors under age 30 were seen from March to June 2020 compared to 2019.[7–9] This resulted, at least to some degree, from high schools and universities closures where the majority of blood donations from younger donors occurred.

Incentives relevant to the current situation such as antibody testing for SARS-CoV-2 significantly increased donations at some centres. In May 2020 the mean daily donations rose from 2759 to 3476 before and after offering the test ($p = 0.001$) (Figure 1).[7]

Appeals and incentives induced lapsed donors (established donors absent for ≥2 years) to present for donation. In general, blood centres now focus efforts on keeping these donors engaged and returning more regularly via digital marketing strategies and "personalised" messaging. As such, illustrating the need for a greater understanding about motivations, particularly those of the disaster donor and the younger generation to assure daily blood supplies and embedded resilience against unforeseen hazards.[10]

3 | DATA AND ANALYSIS

The dramatic decrease in blood use combined with substantial reductions in blood donation associated with the COVID-19 pandemic required new data analytical approaches for aligning transfusion demand with the donated blood supply.[11] One survey quantified the impact of COVID-19 on blood utilisation and discards among 72 hospitals. RBC and platelet utilisation declined, _9.9% ($p < 0.001$) and 13.6% ($p = 0.014$), respectively. Discards increased for RBCs (30.2%, $p = 0.047$) and platelets (60.4%, $p = 0.002$). The study concluded that because the pandemic led to delaying of elective surgical procedures, blood utilisation declined substantially while blood discards increased, resulting in substantial wastage of blood products.[12]

Previously acceptable data lags between hospital and blood center inventory levels lost utility as the blood supply exceeded demand for several months only to be replaced with blood shortages following resumption of routine hospital practices in late Spring 2020. Blood

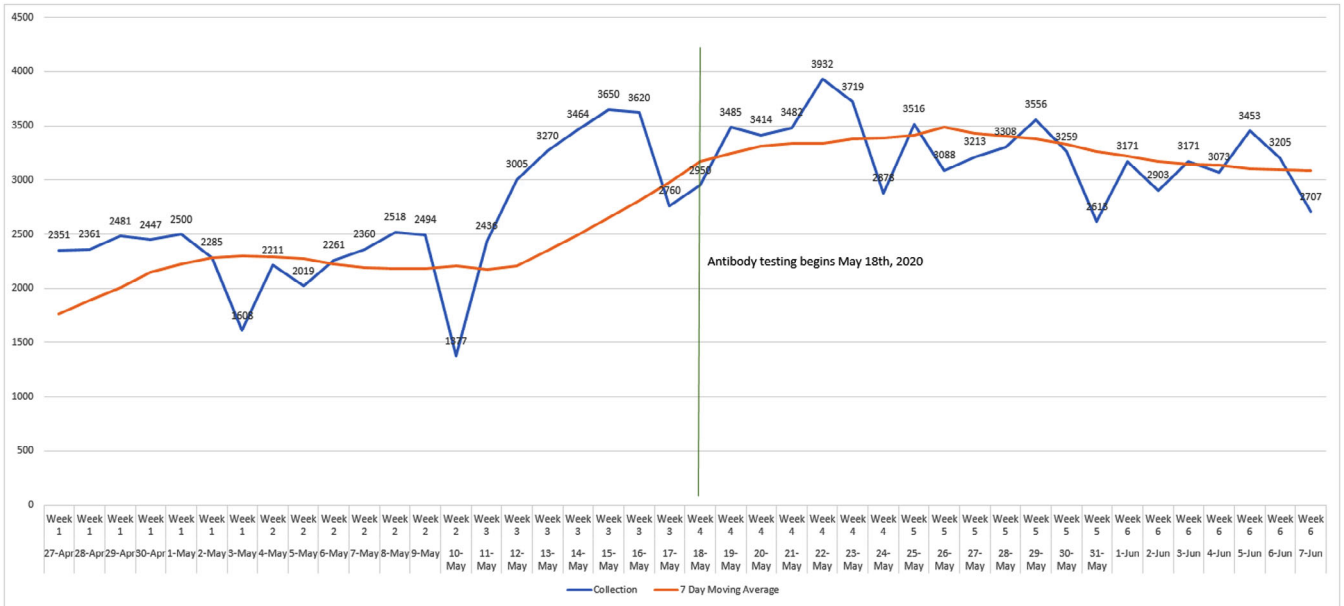

FIGURE 1 Mean daily donations were significantly increased from 2759 daily prior to implementation of anti-SARS-CoV-2 testing for all donors to 3476 post-implementation ($p = 0.001$). (Provided by Kelly Counts-OneBlood).

centres explored new business and computational analyses to mesh legacy utilisation data with current hospital demand to predict blood use and donation rates in real time.[11]

Previous heuristics proved useful during routine times but were inadequate for the agile responses required during the pandemic. For example, one center found, 30% of hospitals utilised 70% of blood collections. Through real-time communication with these hospitals, the blood center's IT department calculated three-day moving averages of blood utilisation. As blood donation venues changed from 80% off-site or mobile collections to less than 20%, it linked these data in designing algorithms for aligning blood demand and supply. This approach optimised product use and minimised wastage. In addition, blood centres revised approaches for obtaining antigen-negative units previously donated by demographically diverse donors who had historically given blood at mobile blood drives away from fixed sites.[11]

Change detection is a statistical method of identifying when current data points have diverged from the normal distribution with high levels of sensitivity. When COVID emerged and altered hospital demand, a blood center used this method to understand increasing and decreasing demand trends. A change comparison with pre-COVID demand was calculated by comparing the same day demand to the previous four same day pre-COVID averages. A leading demand indicator was calculated by comparing current demand to the four previous same day demand averages. The combination of these two metrics allowed for sensitive understanding of the shifts in demand relative to the demand decrease caused by COVID. If the leading indicator decreased, the demand relative to COVID will decrease. When the leading demand indicator increased, the demand relative to COVID would increase. It is important to note that the leading indicator precedes the COVID change in most instances; therefore, the change in demand relative to COVID will lag behind the leading indicator with general trends (Figure 2).[11]

Likewise, CCP collections and distribution demanded development of new relationships and associated data management involving hospital or healthcare provider-identified patients who were recovering from COVID-19 and soliciting plasma donations from them to maintain adequate and changing CCP utilisation patterns. Subsequently, the data fields were expanded to include changing anti-SARS CoV-2 antibody titers. Thus, real-time data availability and agile data management highlight tools and approaches needed for current and future pandemic preparedness responses (Figure 3).

4 | CONVALESCENT PLASMA

4.1 | Plasma collections

CCP donor recruitment challenges were mainly attributable to the blood centres' lack of access to patients who qualified as CCP donors early in the pandemic. This resulted from regulations intended to protect patient privacy (i.e., US Health Insurance Portability and Accountability Act- HIPPA) having the unintended consequence of inhibiting the hospitals as well as state and county health departments from

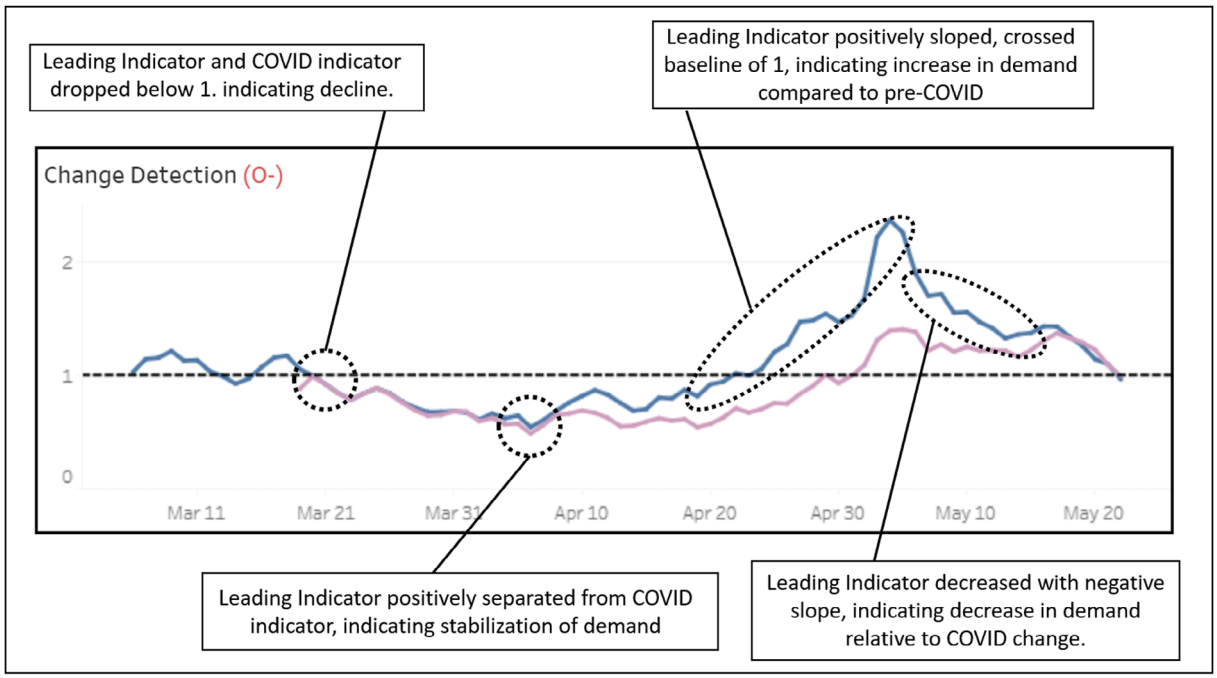

FIGURE 2 The change comparison of demand to pre-COVID demand was calculated by comparing the same day demand to the previous four same day pre-COVID averages (purple line). The leading demand indictor was calculated by comparing the current demand to the four previous same day demand averages (blue line). The combination of these two metrics is beneficial because it allows for sensitive understanding of the sifts in demand relative to the demand decrease caused by COVID. (Provided by Kelly Counts-OneBlood).

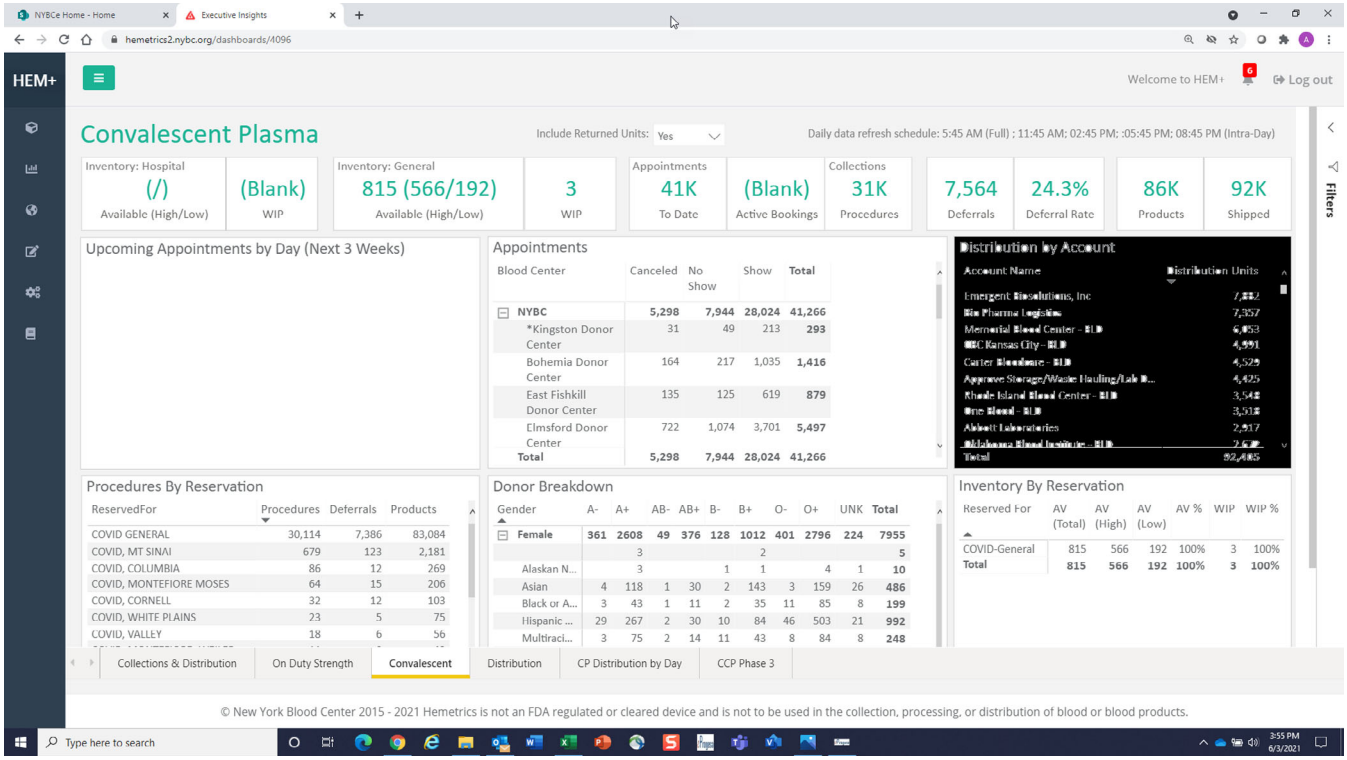

FIGURE 3 An example of real time data availability and agile data management highlight tools and approaches needed for robust pandemic and disaster preparedness responses. (Provided by author D. S.).

sharing needed information about COVID recovered patients.[13] Cooperation by blood centres with their hospitals overcame this barrier.[10]

For example, a blood center's communications team gathered testimonials from early CCP donors, posted them on social and traditional news media, and created behind-the-scenes videos to show the efforts taking place to collect, test, and distribute CCP. Public service announcements aired on local television stations and cable outlets that brought additional awareness to the need for more CCP donors.[13]

A strong pre-existing support structure for implementation f new initiatives such as a project management office, in-house information technology (IT) and business intelligence (BI) units and a business continuity team greatly enhanced blood center responsiveness to CCP collection challenges critical to disaster management at the pandemic onset. The IT/BI team was instrumental in streamlining and automating process intake and distribution. The BI team tracked and transformed complex data into highly functional dashboards and reports that allowed real-time assessment and strategy development (Figure 4).[13]

The continuity team performed daily horizon scanning on a global level keeping leadership apprised of the progression of the pandemic and additional threats. They gathered the CCP implementation team together daily for updates to facilitate and maintain communication in an extremely fluid environment, including frequent changes in food and drug administration (FDA) requirements.[13]

4.2 | COVID-19 convalescent plasma

Passive immunotherapy for infectious diseases has a long history in modern medicine. Early, uncontrolled reports from China suggested therapeutic benefit from CCP as early as February 2020.[14,15]FDA issued the first guidance for industry on collection and use of investigational CCP issued by FDA in March 2020[16] with multiple updates since, revising donor eligibility and later on requiring exclusive distribution of "high-titre" plasma. On August 23, 2020, a major shift in the transfusion of CCP occurred with issuance of the emergency use authorisation (EUA) lowering the barrier for transfusion, based on the "totality of the evidence" that suggested benefits would outweigh risk.[17,18]

4.3 | Hospitals and clinicians

Though unproven, the promise of the safety and effectiveness of CCP in the absence of other therapeutic modalities for COVID-19 resulted in high demand despite uncertainty about optimal use of the product. This necessitated ongoing communication between clinicians and blood center physicians.[13]

A relatively user-friendly expanded access protocol (EAP) under a single eIND facilitated access to CCP by hospitals, clinicians and patients who were unfamiliar with complex clinical research imperatives. Early issues of coordination and preparation at the blood center

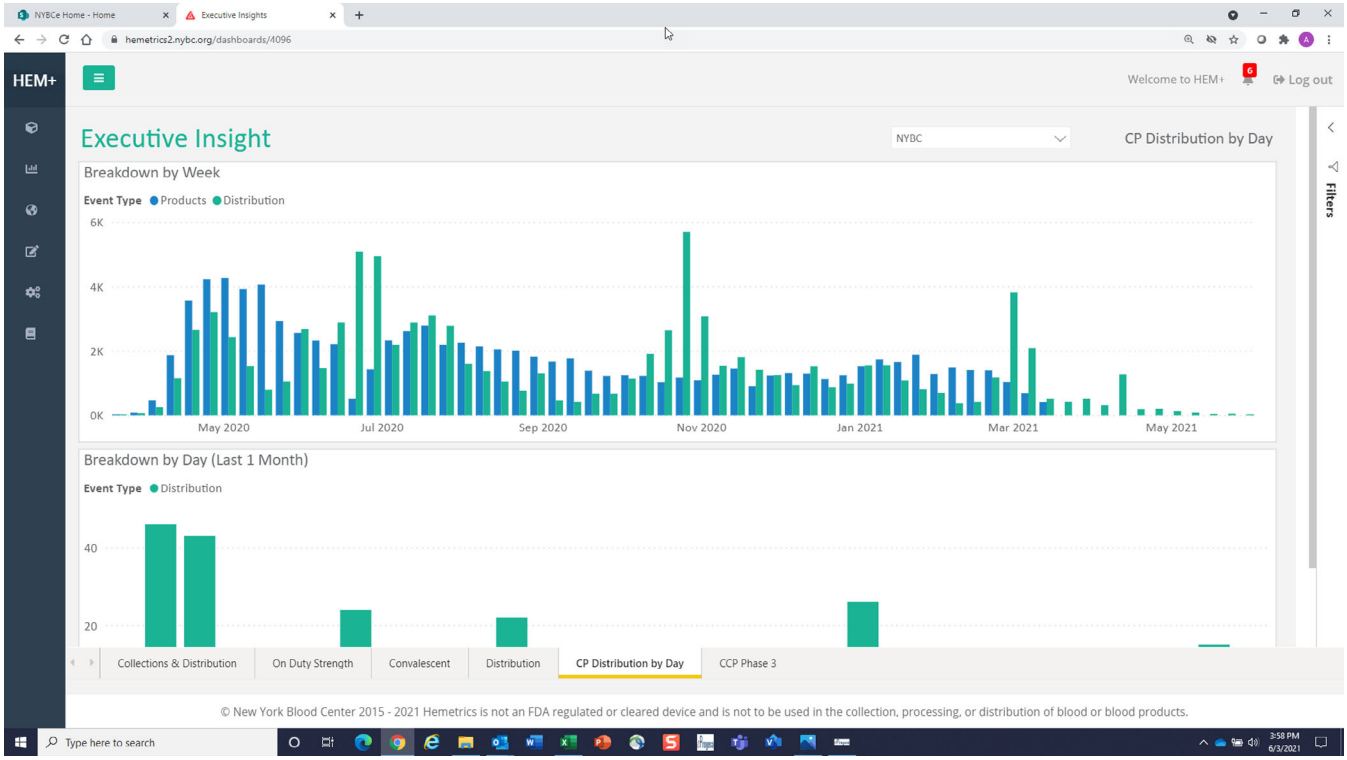

FIGURE 4 Example of a dashboard provided by BI. It displays blood products available in inventory and those distributed. The top half is a breakdown by week and the bottom is by month. (Provided by author D. S.).

and hospital levels for the national programs (eIND and EAP) and the need for use of manual systems caused delays and frustration and led to public relations issues when CCP was not immediately available. Ordering physicians required education on the use of plasma generally and ABO discordant products specifically, highlighting the generic need for improved transfusion medicine education.[13]

4.4 | Randomised controlled trials

The RCT designs for CCP have varied significantly; some were double blind trials in which CCP was compared to a control (placebo or standard plasma) and some were open label trials with the comparison arm being an evolving standard of care. The patients ranged from outpatients with post-exposure prophylaxis and outpatients/emergency room patients with clinically mild COVID, to inpatients with moderate, severe, or life-threatening illness with ranges of oxygen requirements including critically-ill patients on extracorporeal membrane oxygenation. The Randomised, Embedded, Multifactorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) showed that among critically ill adults with confirmed COVID-19, treatment with two units of high-titre, ABO-compatible convalescent plasma (CP) had a low likelihood of providing improvement in the number of organ support–free days.[19]

While some open label, uncontrolled and/or case-retrospective control studies showed a reduction in disease progression or mortality in patients treated[20]they were clearly insufficient to establish the role of CCP in clinical practice. Available data from non-randomised clinical studies to date preclude the development of clinical guidelines based on disease duration, severity or risk status. Some trials have been terminated pre-maturely due to futility, either related to lack of an efficacy signal at an interim analysis or because ebbing of a local infection surge precluded meeting enrollment targets prior to meeting clinical endpoints.[21,22] These represent ongoing issues for current and future trials.

In addition, several meta-analyses of these studies were performed.[23–27]One, compiling 10 studies concluded with a low to moderate certainty that CCP compared with placebo or standard of care was not significantly associated with a decrease in all-cause mortality or with benefit for clinical outcomes including length of hospital stay, clinical improvement, clinical deterioration, mechanical ventilation use, and serious adverse events.[28]However, it is important to recognise that some sample sizes in the included studies were quite small, the characteristics of the study CCP were heterogeneous, the serostatus of recipients was not well characterised, and the timing of infusion relative to disease onset was highly variable and often quite long.[29] Overall, an outpatient trial using well-characterised plasma very early after symptom onset is convincing evidence that CCP may have a role in the armamentarium, and is consistent with data that resulted in the EUA for monoclonal antibodies in the United States, an analogous form of passive immunotherapy.[19] A large randomised controlled trial conducted in outpatients with COVID-19, most of whom were unvaccinated, demonstrated that the administration of CCP within 9 days after the onset of symptoms reduced the risk of disease progression

leading to hospitalisation.[30] A review of 30 available RCTs demonstrated that signals of efficacy (including reductions in mortality) were more likely if the CCP neutralising titre was >160 and the time to randomization was less than 9 days.[31]It is important to interpret the results of clinical trials conducted amid a pandemic with caution.[32]

In retrospect, several issues are obvious. The impetus to deploy CCP for severely ill patients without other treatment options rapidly and early on during the pandemic was completely understandable. It entailed uncertainty regarding the optimal timing of use and characteristics of CCP for clinical use. In a majority of studies, the CCP SARS-CoV-2 antibody titers in donor plasma were not determined prior to clinical use or were introduced while the study was ongoing. Some studies administered CCP with completely unknown titre while in others the analysis of neutralising antibody titers was performed post-hoc. Likewise, where this information is available, the diverse assays used make direct comparison of studies difficult, especially in the absence of consensus correlates of protection.

Another variable that data from RCTs can address with greater rigour is the effect of concurrent therapies patients with COVID-19 receive. These therapies varied by center and evolved over time as treatment protocols were implemented and often changed by the week, particularly at the onset of the pandemic. Without randomization, factors such as age, severity of illness, the role of recipient antibodies prior to transfusion, and concurrent therapies cannot be adequately controlled. In summary, at present, the effectiveness of CCP in reducing severity of COVID-19 illness and mortality in different patient groups, for example general populations versus those with compromised humoral immunity or unable to respond to immunisation, is uncertain, particularly in those with longer durations of illness.[33,34]

4.5 | Role of Emerging Variants and new questions for evaluation by RCT's

SARS-CoV-2 variants were reported as early as late spring and summer during 2020 and have replaced "wild type" virus due to increased transmissibility. It can be hypothesised that CCP obtained from donors infected with earlier strains may be less efficacious for neutralisation against newer SARS-CoV-2 variants. This important question will need to be addressed in a timely fashion in upcoming trials. Early data suggests that boosting serologic responses of recovered COVID-19 patients using authorised mRNA vaccines may be able to provide cross-neutralisation of these variants of concern which may be useful to determine selection of CCP donors in the future.[35,36]

4.6 | Data harmonisation

The recruitment challenges as well as the range of study designs led to the design and launch of a study, "Continuous Monitoring of Pooled International Trials of Convalescent Plasma for COVID-19 Hospitalised Patients (COMPILE)" to pool deidentified patient level data from ongoing and discontinued RCTs with a goal to reach a consolidated answer on CCP efficacy. COMPILE will analyse data from 100s of patients in the United States and internationally using novel statistical methods to determine the effect of CCP on clinical status as the primary outcome and the effect of covariates, including CCP titre and concomitant medications in secondary analyses.[37] The COMPILE effort aimed at pooling individual results may provide a platform to meaningfully merge data from some of the national and international clinical trials.

5 | THE IMPORTANCE OF THE SUPPLY CHAIN

5.1 | United States

Prior to the pandemic, collection facilities rarely used masks, but, disposable or cloth ear loop mask, face shields, visors and various ancillary items quickly became critical items essential for daily operations. This lack of prior purchasing from suppliers presented a challenge since many suppliers could only commit available product to their "existing customers" and would not take on new business.

Routine supplies frequently purchased by blood centres such as exam gloves, surface disinfectants, hand sanitiser and disposable apparel (e.g., lab jackets, gowns) suddenly became increasingly difficult to source as global demand for these items reached unprecedented levels. As manufacturing production capability fell further; many had to close for a period of time due to COVID outbreaks in their facilities; these difficulties were compounded by raw material shortages. Products produced outside of the United States became difficult to obtain as their home countries prioritised supplies of critical equipment for their population or as borders closed and international shipping was delayed or came to a halt.

To overcome these challenges, the group purchasing organisations worked with suppliers and regulators to lobby for the critical importance of the US blood supply, including CCP, in maintaining a functional healthcare system, thus, convincing suppliers and regulators to prioritise shipments of available supplies to collection facilities. Other successful strategies included working with the manufacturers to develop a monthly allocation of products, and allowing group purchasing organisations to leverage blood centres' combined volume against extended purchasing commitments. This greatly helped to alleviate shortages of critical supplies (Table 1).

5.2 | Outside of the United States

An international survey from 42 countries, including 24 low- and middle income countries, was analysed and found similar challenges to those faced in the United States. Decreases in blood donations occurred in 70.6% of collecting facilities. Despite safety measures and recruitment strategies, donor fear and refusal of institutions to host blood drives were major contributing factors. Almost half of

TABLE 1 Critical PPE items.

Mask (disposable and reusable ear loop mask)
N95 respirator style mask
Face shields/visors
Exam gloves
Surface disinfectants/wipes
Hand sanitizer
No touch or "touch less" thermometers
Disposable apparel (lab jackets, GOWNS)

Abbreviations: PPE, personal protective equipment.

TABLE 2 Some new collection/donor advocacy groups and funding partners of blood centres.

Survivor corps
Refuah health/orthodox Jewish community-chaim lebovits
Archdiocese
Big 10 network
Microsoft (The fight is in United States)
Department of defence
Operations warp speed
BARDA

Abbreviation: BARDA, biomedical advanced research and development authority.

respondents working at transfusion medicine services were from large hospitals with over 10 000 red cell transfusions per year, and 76.8% of those hospitals.

experienced blood shortages. Practices varied in accepting donors for blood or CCP donations after a history of COVID-19 infection, CCP transfusion, or vaccination. Operational challenges included loss of staff, increased workloads and delays in reagent supplies.[38]

6 | NEW PARTNERSHIPS

COVID-19 created opportunities to strengthen current blood center relationships and create new ones. The pandemic and supplying CCP as a first-line therapy forced many blood centres to engage regulators in a new, more collaborative way. Officials in many jurisdictions, with little prior understanding of the blood system, were engaged to support the needs of blood centres and CCP programs.

Another positive benefit was that blood centres in the United States had to work more closely, sharing capacity with one another where this had not been done before. Centres that had CCP would send to those who did not, as with red blood cells (RBC) and other components. Centres became more familiar with hospital customers by not only dealing with their transfusion services but with their administration, treating physicians and public relations personnel. Many worked with plasma fractionators to provide plasma for the development of hyperimmune globulin to treat and prevent COVID-19. Researchers who had not previously worked with blood organisations now had opportunities to collaborate on providing access to sample tubes and components from large and fairly representative populations.

New opportunities for public health collaboration arose including testing, seroprevalence studies and finally some providing SARS-CoV-2 vaccinations to blood center employees. New collection/donor advocacy groups and funding partners formed with which many blood centres collaborating with Blood Centres of America and America's Blood Centres (Table 2).

7 | THE CHANGING NATURE OF REGULATORY COMPLIANCE

Early in the pandemic, the FDA communicated the critical need for a continuous blood supply and moved quickly to augment inventories by liberalising recommendations that previously made some donor populations ineligible.

Although issued for immediate implementation, the public was unaware of the complexities of executing such changes in the highly-regulated blood center environment that requires updates to blood establishment computer systems, revisions to procedures, staff training, and proper notification to the donating public.[39,40]The associated weeks-to-months lag between FDA rule changes and blood center implementation caused frustration among donors and the media. Some stories about failed attempts to donate received national attention, especially when the involved persons were otherwise eligible to give the much-coveted CCP.[41]Understanding and addressing this disconnect is a necessary component for positive donor and community engagement.

As it is likely that there will be future outbreaks of viruses that may require treatment with CP or other novel blood products, the interpandemic period provides an opportunity for developing protocol templates and rigourously evaluating them (e.g., RCTs) to minimise the time required to move from theory to clear guidance on their clinical value and optimal use. In the event of a pandemic caused by an agent that is transfusion transmissible, regulatory options include mandating pathogen reduction of the entire blood supply is required. Current platforms are insufficient to accomplish this. Decision making parameters and funding for this capacity must be a top priority of governmental policy makers.[13]

8 | PREPARATION FOR FUTURE PANDEMICS AND OTHER WIDESPREAD DISASTERS

The US Department of Health and Human Services (HHS) released a report to Congress on the adequacy of the US national blood supply calling out several vulnerabilities including the ageing of the donor base, the centralisation of laboratories, and the deteriorating profitability of centres that has limited innovation.[42] While these issues are managed daily, a disaster or pandemic could overwhelm and debilitate the system similar to a storm surge that breaches an inadequate levee. Given the unknown nature of emerging pathogens, there is no "one

size fits all" plan for preparedness. However, while we cannot predict exactly when or in what form the next threat to our health system will appear, we need to be broad and creative in setting up systems that will promote rapid response resiliency or face the consequences of inadequate supply or inability to utilise available blood.

Elements of preparedness include horizon scanning and formal surveillance for early detection, identifying vulnerabilities among staff and donors to facilitate necessary protections, defining and recognising pandemic phases and staged responses, risk management principles and resource allocation. These elements intersect and complement each other. Depending on the given circumstances, certain activities will take precedence at certain times, but all of them require forethought and a structure (i.e., policies and personnel) on which to perform when needed.[43]

Planning is not a process with a beginning and an end. Just as the blood community has embraced continuous quality improvement, so should it view preparedness as continuous and iterative. COVID-19 has given us a clearer understanding of what is essential in many areas of life and work. Coordination with hospital partners, public health and disaster response organisations will prove invaluable, especially to avoid well intentioned public messaging that can threaten the blood supply. Good communication underpins good relationships. These need to be cultivated to permit rapid decisions makings and access to resources as a catastrophe evolves; just knowing who to call for help in a crisis can save valuable time. In the meantime, securing "essential worker" status for employees and ensuring blood center inclusion with public health planning venues could be a lynchpin for healthcare continuity.

9 | DISCUSSION

There are important lessons in the COVID-19 experience that should inform a blueprint for the inevitable next pandemic. In regard to CCP, this is not a critique of the truly impressive on-the-fly implementation of CCP collection programs, compliant with current good manufacturing practices in the midst of a pandemic that stressed the blood supply in many ways. Rather, it is an important "after action" responsibility in the context of disaster preparedness.

The EAP effort in the United States was biassed toward treatment of severe illness. The long history of passive immunotherapy suggests that, for acute pathogens, very early use (even pre-exposure) was likely to be more effective. For the next pathogen we need to address the issue of early versus later treatment explicitly and in advance of being called upon to design both expanded access and high-quality clinical investigations.[44]

There is a need for a prospective plan for systematically banking, locally and nationally, an appropriate range of donation specimens, anticipating the early scarcity of effective assays, both for diagnosis and characterisation of convalescent therapeutics, even if that characterisation will occur after the fact.

Another consideration is at a minimum, a realistically accessible set of objective recipient demographics and clinical outcomes to be collected from the very beginning. Examples might include elevation of the level of care, mortality, length of stay among others. Details requiring expert adjudication should be avoided. These must be suited to the assessment of what can be provided from the blood community, but also other aspects of care such as additional therapeutics, risk stratification and assessment. This may require federal action and funding to maximise the ability to collect and share the data, for example harmonisation of minimum regulatory requirements of electronic medical records. Facilitated data sharing that respects privacy interests must be included.

Many questions remain unanswered. What are the elements of the process required to decide which donors are safe sources of a convalescent product and when? Does uncertainty about the transfusion transmissibility of a future pathogen impose an affirmative responsibility for blood and plasma collectors to be able to apply available pathogen reduction to a convalescent product, even if that is not the standard-of-care for routine collections? Do we need to consider emergency authority from the regulatory authorities (e.g., FDA) to pool products from multiple recovered donors to increase the probability that a convalescent product will, in fact, contain reasonable levels of the antibodies we think may be clinically useful? If the answer is "yes" that sets a task for the regulator now, and then for the blood community to design and validate processes and have the capacity to implement them, either before or on short notice when they are needed.

While blood centres have become efficient at controlling costs and inventory under normal circumstances, there are lessons to be learnt to consider moving forward beyond the COVID-19 pandemic. (Table 3).

TABLE 3 Lessons learnt

Consider dual and multi-sourcing directly with manufacturers and distributors.
Develop product prioritisation approvals with each supplier in preparation of the next disaster.
Develop a broader contract portfolio of domestic-based suppliers to provide more control of access to critical products when international supplies may not be reliable.
Re-evaluate just-in time inventory management levels. Increase the critical items' supply-on-hand in the event of a disaster for both suppliers and blood center.
Address resistance at the local blood center level to funding the expense of maintaining inventories of supplies in excess of immediate need.
Establish a strategic stockpile of PPE and other supplies designated as critical that is prepositioned and managed by an appropriate entity and supported by HHS or other governmental agencies to accelerate capability.
Create and access the national stockpile of PPE products as needed such as with the EU model[45,46]
Consider the potential value of pathogen reduction of blood products as technologies become available. Future emerging infections may be transfusion transmitted and, even if this is not the case, pathogen reduction technologies would provide assurance during the inevitable delay between the onset of the threat and definitive discernment of the transfusion risk.

Abbreviations: EU, emergency use; HHS, health and human services; PPE, personal protective equipment.

New partnerships as a result of the COVID-19 pandemic assisted the industry during this event and are expected to provide similar assistance in future disasters. Maintaining and enhancing such partnerships facilitates new treatment development involving blood products and blood derivatives for example, encouraging investigators to envision blood centres and transfusion services as research material sources This requires in place donor/patient consents that meet contemporaneous requirements and allow immediate use of available materials and subsequent follow- up consent from donors/patients that obviates the current frustrating process and loss of potentially willing, eligible study participants.

10 | CONCLUSIONS

Our traditional assertion that blood donations "save lives" is our organising principle for selecting our lessons learned. By assuring the needs of the patients were paramount, that the donation process was safe to sustain inventory adequacy, that new products (CCP) might improve outcomes, and that vendor relationships align with these principles, the blood community "relearned" their mission focuses on improving patient outcomes.

At the time of submission of this manuscript, the pandemic is not over, nor is the involvement of the blood community in the response. The list above will grow as we have more time to reflect on what was done and what could have been improved, leaving us better prepared for both the next wave and the next pathogen.

Ultimately, we will not know if our work toward resilience was successful until the crisis has come and gone. When we ever find ourselves saying, "we should have done more" it is impossible to go back in time and make corrections, but we should aim to do better the next time.

AUTHOR CONTRIBUTIONS

Richard Benjamin, employee and shareholder of Cerus Corporation.
Kathleen Rowe employee and shareholder, Cerus Corporation.
Stefan Reichenberg, employee Maco Pharma International GmbH, Langen, Germany.
Roxane Smith, employee Macopharma USA, Duluth GA.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ORCID

Richard Gammon https://orcid.org/0000-0002-1175-9579

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