

COVID-19 and Haemovigilance

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The SHOT Steering Group and Working Expert Group would like to extend their heartfelt gratitude to all our reporters and indeed everyone in the transfusion community and the wider NHS for their contributions during the pandemic. During these times of crisis, everyone has come through by supporting each other and working together. Staff have been working tirelessly to ensure patient care is not compromised. Haemovigilance reporting continued. The period of the pandemic was also a period of accelerated transformation across services – this was only possible through the dedication of all our colleagues in the transfusion community. From the introduction of a new blood component (COVID-19 convalescent plasma, CCP), new CCP trials run during the pandemic, continuing education and training of staff, introduction of electronic systems and digital acceleration, this was a period of transformation. Our ability to adapt, innovate and grow during these unprecedented circumstances has been extraordinary. When faced with the very worst, we have seen the transfusion community come together, helping, and supporting each other. It is the kindness and support that we give to each other that will help us get through these unprecedented times. For this and everything, we extend our sincere appreciation and gratitude.

Key SHOT message

- Experiences during the pandemic have stressed the importance of collaboration, communication, and co-operation to help reduce risks and improve safety

Abbreviations used in this chapter

ADE	Antibody-dependent enhancement	NHS	National Health Service
CAS	Central alerting system	RCA	Root cause analysis
ССР	COVID-19 convalescent plasma	RCT	Randomised controlled trial
ECMO	Extracorporeal membrane oxygenation	RECOVERY	Randomised Evaluation of COVID-19 therapy
HCWLN	Health & Care Women Leaders Network	REMAP-CAP	Randomised, embedded, multi-factorial, adaptive platform trial for community-acquired pneumonia
нтт	Hospital transfusion team	SAE	Serious adverse event
ICU	Intensive care unit	SAR	Serious adverse reaction
lgG	Immunoglobulin G	SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
JPAC	Joint UKBTS Professional Advisory Committee	TACO	Transfusion-associated circulatory overload
MHRA	Medicines and Healthcare products Regulatory Agency	TAD	Transfusion-associated dyspnoea
NBTC	National Blood Transfusion Committee	UK	United Kingdom



Recommendation

• All National Health Service (NHS) organisations should ensure that learning from the pandemic experiences is captured and used to improve patient safety

Action: All NHS organisations

COVID-19 pandemic and impact on transfusions

The COVID-19 pandemic has massively disrupted and exacerbated the shortcomings in healthcare but has also served as a catalyst for much needed transformation, which occurred at an accelerated pace. The challenge now is to harness all the learning from experiences and build on the momentum from efforts during the pandemic to improve systems further. This new chapter will specifically cover the influence of the pandemic on haemovigilance.

The COVID-19 pandemic has had major implications for blood transfusions. This period has been marked by uncertain demand patterns. Elective and non-COVID-19 related care largely stopping during the pandemic. The demand for blood reduced during the first peak but was as predicted during the second wave with continuation of most services in the NHS. The NBTC Emergency Planning Working Group produced the Emergency Preparedness, Resilience and Response guidance for hospital transfusion teams in 2020 and an emergency preparedness gap analysis tool both of which can be accessed from the JPAC website (link provided in references). The NBTC also produced guidance for appropriate specification for emergency red cells and a platelet shortage plan in October and November 2020.

The four UK Blood Services worked collaboratively to ensure a continuing safe supply of blood during the pandemic. COVID-19 challenged donor selection practices, balancing the need to supply whilst ensuring donor safety. Donor haemovigilance was particularly important given donors were recovering from an emerging illness (see Chapter 7, Donor Haemovigilance). Donor selection guidelines were regularly reviewed and updated in line with international guidance. Revised collection guidelines ensured donor, donation, and staff safety.

To date, there has not been any evidence of transmission of SARS-CoV-2 via transfusion of blood components, and this risk is therefore currently theoretical and considered highly unlikely. The pandemic has had an impact on blood supplies through reduced blood donation and reduced availability of appropriate collection facilities. It is the responsibility of Blood Services to take steps to assess, plan, and respond to the challenges appropriately and proportionately after undertaking a data-driven risk assessment (WHO 2021).

Nightingale hospitals

New pop-up COVID-19 hospitals were set up as temporary hospitals in the UK as part of the response to the COVID-19 pandemic. This reflected wider NHS re-structuring to prepare for the pandemic and anticipated strain on NHS services. They principally include the eight NHS England Nightingale Hospitals (London, Birmingham, Bristol, Cumbria, Exeter, Harrogate, Manchester, and Sunderland), NHS Scotland's Louisa Jordan hospital, NHS Wales' Dragon's Heart Hospital, and the Northern Irish Health and Social Care site at Belfast City Hospital. The field hospitals were intended to be used to treat critical care patients who were regarded as being less severely ill, while the most severely ill patients were treated in mainstream NHS hospitals. Transfusion needs were predicted to be low at these sites, nevertheless a transfusion service needed to be established within a tight time frame ensuring full traceability with staff trained and competent in transfusion-related procedures including recognition, management and reporting of transfusion reactions. Transfusion staff from local hospitals supported by the UK Blood Services. SHOT is planning a survey to capture learning from establishing these transfusion services at the pop-up sites later this year and results will be shared widely.

Blood use in COVID-19 patients

Transfusion requirements in COVID-19 patients is low even in those who are critically ill (Barriteau et al. 2020). Sanz et al. (2020) showed that bleeding, mostly related to the use of anticoagulants, was the main indication for red blood cell transfusion in patients with COVID-19. A single centre experience showed that red cell concentrates were the most frequently transfused component in COVID-19 infected patients with higher use during veno-venous ECMO (Doyle et al. 2020). This study from the international Extracorporeal Life Support Organisation Registry provides data on 1035 ECMO-supported patients with COVID-19 who received care in 36 countries and showed that in patients with COVID-19 who received ECMO, both estimated mortality 90 days after ECMO and mortality in those with a final disposition of death or discharge were less than 40%. This supports the use of ECMO in refractory COVID-19-related respiratory failure.

Impact on staff

Undoubtedly, staff working in the NHS are its greatest asset and are key to delivering high-quality care. Poor workforce planning, weak policies and funding shortages which are longstanding and worsened during the pandemic have resulted in a workforce crisis. These staffing challenges across the NHS invariably impact transfusion practices as blood transfusions occur in various medical, surgical, and obstetric settings and across adult and paediatric patients. These challenges are not only in the clinical but also in the transfusion laboratory setting. Serial UKTLC surveys have highlighted staffing concerns both with numbers and skill mixes (Bolton-Maggs et al. 2019; UKTLC, 2019). Many reports submitted to SHOT have highlighted the challenges with reduced staffing due to any reason (redeployment, sickness, etc) during the pandemic with staff unfamiliar with transfusion practices needing to undertake these roles with little or no training/supervision reflective of the challenging circumstances. One of the greatest challenges lies in nursing, with nearly 38,000 vacancies (one in ten posts). Unfilled vacancies increase the pressure on staff, leading to high levels of stress, absenteeism, and turnover (Kings Fund 2021). This has been compounded by the COVID-19 pandemic which has exacerbated long term issues such as chronic excessive workload, burnout and inequalities experienced by ethnic minority staff.

The NHS Confederation (2021) and HCWLN have recently undertaken a survey to gather information about the impact COVID-19 has had on all health and care workers, the survey closed on 5th March 2021 and results are awaited. In June 2020, the HCWLN commissioned a survey to better understand the impact the pandemic has had on women working across health and care services. Over 1,300 women responded, and the report describes the struggles, pains and fears women working in health and care services have faced during the pandemic. The physical and emotional impact due to caring responsibilities both in and outside of work are significant. It also draws out some of the positive experiences, such as opportunities for learning and the strength of support many have received from their managers and provides valuable recommendations. With NHS staff being predominantly female (77%), this is very pertinent and the recommendations in this report along with the NHS People Plan for 2020/21 and People Promise (links provided in the reference list) will help improve staff well-being with several measures being identified that organisations need to be equipped with.

Digital acceleration

Healthcare has undergone a rapid digital progression in 2020. This has been a period of great innovation and use of digital technology for both patients and staff, while supporting enhanced quality of care and increased efficiency. From telephone/video consultations for patients, electronic patient records, electronic decision-making systems, electronic prescribing to virtual staff inductions, virtual training for healthcare professionals, team meetings and collaborations using platforms such as Zoom, Microsoft Teams or Skype, this has truly been a period of digital transformation in the NHS.

However, there needs to be a huge cultural change before a fully digital NHS can become a reality. Lack of digital awareness, reluctance to fund digital solutions, insufficient resources, and lack of universal solutions results in each institution trying to find optimal solutions that fit in with their outdated legacy systems. Barriers to interoperability have been highlighted which need to be addressed urgently. Any solution for a clinical setting should be designed with patients and users in mind. Clinicians are rarely

consulted about digital solutions, and this is critical to have meaningful transformation and uptake. It is important to ensure that digital inclusion tools and effective broadband are available to all so that health inequalities are not further exacerbated, and every effort must be made to improve digital literacy of patients.

COVID-19 convalescent plasma (CCP)

CCP, donated by persons who have recently recovered from COVID-19, is the acellular component of blood that contains antibodies, including those that specifically recognise the SARS-CoV-2 virus. These antibodies, when transfused into patients infected with SARS-CoV-2, are thought to exert an antiviral effect, suppressing virus replication before patients have mounted their own humoral immune responses. Safety and efficacy of CCP were tested as part of two large randomised controlled trials in the UK. Early in the pandemic, the Chief Medical Officers of England, Wales, Scotland and Northern Ireland, and the NHS Medical Director, wrote to all doctors in the UK strongly encouraging participation in the national randomised trials in COVID-19, CCP was included as part of RECOVERY and REMAP-CAP trials (CAS Alert April 2020 and links to trial websites provided in the references section).

REMAP-CAP included CCP as a treatment randomisation option (CCP versus standard care +/other randomised treatments) in adults admitted to ICU within the preceding 48 hours with confirmed COVID-19 and patients received up to two ABO-compatible CCP on study day 1 and day 2. Early findings from REMAP-CAP established that treatment with CCP provided no benefit for the general critically ill population with COVID-19. There was no evidence of harm associated with CCP and enrolment of severely ill COVID-19 patients to this arm of REMAP-CAP study was stopped early January 2021.

The RECOVERY trial was an investigator-initiated, individually randomised, controlled, open-label, adaptive platform trial to evaluate the effects of potential treatments in patients hospitalised with COVID-19. Hospitalised patients of any age were eligible for the trial if they had clinically suspected or laboratory-confirmed SARS-CoV-2 infection and no medical history that might, in the opinion of the attending clinician, put them at significant risk if they were to participate in the trial. Between 28 May 2020 and 15 January 2021, 5795 patients were randomly allocated to receive CCP and 5763 to usual care alone. Data from RECOVERY has shown that among patients hospitalised with COVID-19, high-titre CCP did not improve survival or other pre-specified clinical outcomes (The RECOVERY Collaborative Group 2021).

Following these results from REMAP-CAP and RECOVERY, the Chief Medical Officers of England, Wales, Scotland and Northern Ireland, and the NHS Medical Director, wrote to all doctors in UK in March 2021 recommending that CCP must NOT be used in the management of hospitalised patients with confirmed or suspected SARS-CoV-2 infection (CAS Alert March 2021).

CCP is a blood component and as such all SAE and SAR related to CCP are reportable to the MHRA and SHOT in the UK as part of the national haemovigilance scheme. Data from SHOT helped inform safety data regarding CCP and provided a unique opportunity to collaborate and have direct input into clinical trials from a haemovigilance perspective. Just over 13,000 units of CCP were transfused under the two trials with only 14 confirmed SAR (from RECOVERY and REMAP-CAP) equating to a risk of SAR of 1 in 958 units of CCP, over the trial period. The most common reactions seen in CCP recipients were febrile, allergic, or hypotensive reactions and pulmonary reactions (TACO/TAD). No reactions have been noted to be definitely related to CCP. Cases which were submitted during 2020 are counted in the figures for this Annual SHOT Report and are covered in more detail in the respective chapters. Of note, there were no reports of ADE related to CCP administration. ADE refers to a form of immune enhancement, a poorly understood group of phenomena occurring when components of the immune system that usually protect against viral infections somehow end up being counterproductive. Antibodies created during a first-time infection could, under very specific circumstances, end up enhancing the disease rather than protecting against subsequent infections. While there is a theoretical risk that antibodies in CCP could enhance disease via ADE, literature available shows that CCP therapy is safe (Lee et al. 2020). This has been corroborated by the UK trials. Errors were reported relating to CCP use, and these have been covered in respective chapters and reflect challenges faced by staff during the pandemic along with the dynamic situations when managing seriously ill patients deteriorating rapidly.

The two large RCT from UK have helped establish the evidence that CCP does not improve survival or other clinical outcomes in patients hospitalised with COVID-19. A systematic review and meta-analysis published in February 2021 confirmed that treatment with CCP compared with placebo or standard of care was not significantly associated with a decrease in all-cause mortality or with any benefit for other clinical outcomes. The certainty of the evidence was low to moderate for all-cause mortality and low for other outcomes (Janiaud et al. 2021). However, a recent small scale (160 patients) randomised, double-blind, placebo-controlled trial of CCP with high IgG titres against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild COVID-19 symptoms showed that early administration of high-titre CCP to mildly ill infected older adults reduced the progression of COVID-19 (Libster et al. 2021). While this is encouraging, further large-scale trials are needed in this subset of patients.

The CCP trials also helped increase transfusion awareness in frontline staff. At the time of closure, there were 226 hospitals in the UK open to CCP in the RECOVERY trial and 122 sites recruited to REMAP-CAP (staff received training before opening). The need for the administration checklist and TACO checklist prior to CCP and transfusion safety messages were cascaded to staff at these sites and helped raise awareness of transfusion and haemovigilance issues.

Haemovigilance reporting during the pandemic



Just over 2 million blood components were issued in 2020 from the 4 UK Blood Services. A total of 4063 reports were received by SHOT in 2020 equating to 19.6 reports per 10,000 components issued which continues a steady upward trend from the preceding years despite all the challenges.

The variation in the number of reports submitted at different periods in the year has been described further in Chapter 2, Participation in United Kingdom (UK) Haemovigilance. The distribution of the reports across the reporting categories is similar to preceding years apart from a large increase in febrile, allergic and hypotensive reactions. Errors continue to account for majority of the reports and whilst pressures relating to the pandemic have been identified as contributory to some of these, there does not seem to be any steep increase in the proportion of errors. RCA summaries submitted have highlighted the staffing challenges including staff shortages, staff unfamiliar with transfusions, hyperdynamic situations with critically ill patients, and challenges with carrying out tasks with full personal protective equipment in COVID-19. These have been alluded to in the respective chapters.

It is encouraging to see haemovigilance activities continue despite challenges faced by frontline staff because patient safety is a priority. The 2019 SHOT recommendations survey showed that 98.9% of

Figure 5.1 Trend in reports per 10,000 components issued in the UK respondents continued with haemovigilance reporting, however, 67% noted difficulties in obtaining information due to restricted access to clinical areas, staff redeployment and staffing levels. Investigating incidents was also reported to be challenging due to these factors (SHOT Recommendations survey 2019 https://www.shotuk.org/wp-content/uploads/myimages/2019-Recommendations-Survey.pdf).

Several factors emerge as being key to haemovigilance reporting during the pandemic:

- The importance of electronic reporting: the pandemic underlines how electronic or paperless reporting is the most effective and reliable reporting method. Reporting to SHOT has been paperless since 2005
- Established communication channels with haemovigilance staff: proactive communications help understand challenges and requirements, helps to engage with key stakeholders and resolve issues in a timely manner
- Importance of a robust, reliable, and responsive team of haemovigilance experts: Haemovigilance plays a fundamental role in enhancing transfusion safety by learning from reports submitted and then putting in place system changes to prevent them in future. Haemovigilance reporting is useless if it does not result in quality improvement. Learning from intelligence gathered from haemovigilance reporting is vital and this is only possible with access to subject matter experts who will be able to review submitted reports and recognise trends and actions that need to be taken
- An established reporting culture: Cultivating an atmosphere where people have the confidence to report safety concerns without fear or blame and trust that the information, they submit will be acted upon is vital for any reporting system including haemovigilance. When there is an established reporting culture, staff are themselves motivated to continue reporting in the interest of patient safety even in challenging times
- Robust business continuity and contingency plans in healthcare organisations help teams identify, prioritise actions and allocate resources proportionately when faced with staffing challenges and unprecedented demands on care provision as seen during the pandemic. Minimum staff needed for governance activities must be identified. Whilst safety reporting is important, and should continue especially during these challenging periods to help identify emerging risks, patient care takes precedence
- Relevant meaningful outputs from the haemovigilance system and feedback loops: supporting
 educational materials and safety alerts as appropriate from haemovigilance schemes, digital learning
 resources to support staff learning are important to optimise patient safety. Feedback loops help
 understand challenges, prompt behaviour change and establishes an adaptive haemovigilance
 system
- Collaboration with international haemovigilance experts and sharing resources and experiences: When faced with these unprecedented challenges, sharing experiences, issues faced, and solutions applied helped teams and organisations to learn from each other. This helped ensure appropriate measures could be instituted in a timely manner. The pandemic is borderless so should patient safety learning be

It is important to look back and acknowledge progress with respect to transfusion safety. Although the COVID-19 pandemic has forced major changes and challenges for the NHS, we have seen staff and systems rise to meet these. New ways of working, improved cooperation, collaboration and communication have been amply demonstrated, all contributing to patient safety despite the ongoing challenges.

Highlights of lessons learnt through the COVID pandemic

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The National Transfusion Laboratory Managers and Practitioner groups in England worked together to produce a summary of the lessons learnt through the pandemic.

The highlights of this included:

- Stock management is key to ensuring adequate supplies of blood components whilst not limiting wastage. Reviewing stock levels frequently is important to react to changing situations quickly
- Maintaining traceability remained a legal responsibility and changes were needed for clinical areas treating infectious patients. This included quarantining tags. Overall Trusts using electronic systems found the impact less
- The use of satellite refrigerators caused issues in lots of hospitals. Management were keen to purchase new refrigerators or re-site existing refrigerators. The logistics of this were often complex and the impact on the HTT was not considered. Maintenance of refrigerators was more complex especially in COVID-19 'hot' areas
- Training of clinical staff was difficult, but the need also increased as staff were redeployed. The use
 of e-learning was well used and most adapted sessions to make the most of electronic remote
 meeting capacity

Overall, the HTT worked hard at maintaining standards and found taking a safe but adaptable approach was the best way forward.

Conclusion

While we may feel the urge to bury the past year for obvious reasons, we must harness a growth mindset and learn from experiences, grow stronger and build safer systems, being wiser from the challenges we have faced together. There is much to take away from our pandemic experiences, the most important being that despite personal and professional challenges, the transfusion community and indeed the whole NHS came together, worked, and supported each other and all those who needed our help. It was resilience in action that helped navigate the uncertain and challenging times. It is also important to recognise and acknowledge that it is people who matter. Ensuring staff safety and wellbeing with adequate resources and a good safety culture will automatically translate to improved staff engagement, safer systems, and better patient outcomes. Sharing experiences and developing expert consensus based on emerging evidence has certainly helped transfusion services during the pandemic (Stanworth et al. 2020).

As we tentatively look towards a recovery from the pandemic, it is an opportunity to collectively reflect, grieve, learn, and develop as a global community.



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