

**Clarifying the Emergency Use Authorization Framework for  
COVID-19 Convalescent Plasma: Considerations for Clinicians**  
**Prepared jointly by the Infectious Diseases Society of America and AABB**

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**KEY POINTS**

- COVID-19 convalescent plasma (CCP) is available through the Emergency Use Authorization (EUA) from the FDA and via clinical trials.
  - CCP given through the EUA is available only for hospitalized adult and pediatric patients.
  - The safety and effectiveness of CCP in the pediatric patient population have not been evaluated.
  - The data to guide clinicians on the use of CCP for nonhospitalized patients remains unclear.
- The Infectious Diseases Society of America (IDSA) recommends that COVID-19 convalescent plasma should be used only in the context of a clinical trial (IDSA guidelines available at: <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>).
- Evidence suggests that CCP confers similar risk to that of standard plasma (eg, risk of allergic reaction, transfusion-associated circulatory overload [TACO], transfusion-related acute lung injury [TRALI]).
- In patients who received CCP available evidence indicates that the best outcomes are likely to occur in those who receive a high-titer unit of CCP within 3 days of COVID-19 diagnosis or admission to the hospital.
- Patients who are critically ill and in the intensive care unit are unlikely to benefit from CCP.
- For the EUA the Food and Drug Administration (FDA) recommends starting with one CCP unit and providing additional units based on the patient's response to CCP and underlying medical conditions.
- It is uncertain how many high-titer vs low-titer units are needed to confer a comparable clinical outcome.
- In the absence of the availability of group B or AB plasma, there are data to support the use of group A or O plasma with low-titer anti-A for transfusion to group B and AB patients who require CCP.

## **INTRODUCTION**

Convalescent plasma has been used as passive immunotherapy for prevention and treatment of infectious diseases for more than 100 years.<sup>1,2</sup> The proposed protective mechanism is antibody-mediated pathogen neutralization, although antibody-dependent cellular cytotoxicity and phagocytosis may also play a role. Data from some published and preprinted studies suggest that high-titer units of Coronavirus Disease 2019 (COVID-19) convalescent plasma (CCP), administered soon after hospital admission, provide some benefit to patients with COVID-19.<sup>3-5</sup> Although the quality of the available evidence, which is mostly from uncontrolled, nonrandomized studies, is low to moderate, the FDA determined that the level of safety and efficacy of CCP was sufficiently high to allow its use through the Emergency Use Authorization (EUA) pathway. Although IDSA recommends that CCP should be used only in the context of a clinical trial, it is anticipated that the CCP available via the EUA will be widely used.

This document is designed to provide information to clinicians on the risks and benefits of CCP, the use of CCP under the EUA regulatory framework, how to engage patients in CCP donation, and how to contribute to ongoing research efforts.

### **CCP Available through the Emergency Use Authorization**

The FDA issued an EUA on August 23, 2020 to permit treatment of hospitalized adult patients with COVID-19 using CCP. Because CCP for the treatment of COVID-19 has not yet been approved for use by FDA, it is regulated as an investigational product. As such, administration of CCP must be under the EUA or an IND, as described in the November 16, 2020 FDA Guidance. In the clinical memorandum,<sup>6</sup> as well as in the EUA Fact Sheet for Health Care Providers (HCPs),<sup>7</sup> FDA noted that CCP met the “may be effective criterion” based on “four lines of evidence,” which are:

1. History of convalescent plasma use for respiratory coronaviruses.
2. Evidence of preclinical safety and efficacy in animal models.
3. Published studies of the safety and efficacy of CCP.
4. Data on safety and efficacy from the National Expanded Access Treatment Protocol (EAP) sponsored by the Mayo Clinic.

Under the EUA, health-care providers in the United States can request CCP from their hospital blood banks for their patients based on their assessment of the risks and benefits of this investigational CCP for treatment of COVID-19. Subsequently, administration of CCP by the health-care provider is governed by institutional policies, procedures, and practices for blood transfusions.

Before obtaining patient consent and transfusing CCP available through the EUA, health-care teams must provide patients with the “Fact Sheet for Patients/Caregivers,”<sup>8</sup> available at: <https://www.fda.gov/media/141479/download>. (Please note: For CCP labeled as an “investigational product”—ie, not tested and appropriately labeled for the EUA—please see “CCP as an Investigational Product Prior to Full Implementation of the EUA,” concerning investigational products and limitations for the use of the EUA provision of the Fact Sheet during the patient consent process.)

Also, clinicians are required to communicate the following information to the CCP recipient<sup>7</sup>:

1. The FDA has authorized emergency use of CCP, which is not an FDA-approved biological product.
2. The patient or caregiver has the option to accept or refuse administration of CCP.
3. Information on the significant known and potential risks and benefits of CCP and the extent to which such risks and benefits are unknown.
4. The information that is available for alternative treatments and their risks and benefits.

The EUA requires health-care providers to monitor the patient, conduct a thorough investigation of adverse reactions to CCP, maintain records on the transfusion of CCP, and report to FDA any fatalities due to CCP, in accordance with the Fact Sheet for HCPs. The EUA Fact Sheet for HCPs states that because the clinical evidence supporting this EUA was not obtained from prospective, well-controlled randomized clinical trials (RCTs), additional RCTs are needed, and CCP should not be considered a new standard of care for the treatment of patients with COVID-19. Moreover, providers are encouraged to enroll patients in ongoing clinical trials. Information regarding ongoing clinical trials is available at: <https://clinicaltrials.gov>.

The EUA Fact Sheet for HCPs also notes that the use, risks, and benefits of CCP in special populations such as pediatric, geriatric, and pregnant patients, as well as nursing mothers either have not been evaluated or are not fully known (more information on CCP use in pediatric patients, below). These

special groups and nonhospitalized patients suffering from COVID-19 also could be candidates for clinical trials (see below).

### **CCP as an Investigational Product Prior to Full Implementation of the EUA**

As detailed below (Blood Banking and Transfusion Medicine Issues), only one assay has currently been approved to qualify CCP for labeling as high-titer or low-titer under the EUA. As a result, most of the units currently available have been tested with other test systems and as such are considered by the FDA as “investigational CCP.” The updated recommendations in FDA’s November 2020 Guidance provide a period of temporary enforcement discretion to permit the use of investigational CCP through February 28, 2021, that is not under the EUA or IND regulatory framework. They require specific patient consent to transfuse an investigational product, and the FDA has stated that the “Fact Sheet for Patients” intended for use with EUA CCP should not be provided to patients during the consent process when investigational CCP products are used. Nonetheless, the core tenets contained within the fact sheet still apply for these “non-EUA” units and the information may be used to counsel patients about the use of investigational CCP during this interim period. After February 28, 2021, the CCP used for treatment of COVID-19 must meet the requirements of the EUA to be qualified utilizing an “approved” test and labeled according to the November 2020 FDA Guidance.

## **DATA ON SAFETY, EFFICACY, TIMING, AND DOSAGE**

### **What Is the Safety of CCP?**

Potential risks of CCP can be categorized broadly as being general (ie, risks inherent to transfusion of any blood product) or specific (ie, related to CCP).<sup>9</sup>

**General Risks:** There are both infectious and noninfectious risks of plasma transfusion.<sup>10,11</sup> Infectious risk from the major transfusion-transmissible infections (eg, human immunodeficiency virus, hepatitis B, and hepatitis C) is low in the United States and other high-income countries given robust donor selection coupled with laboratory infectious screening of blood donors.<sup>12,13</sup> Of note, CCP donors must satisfy all eligibility criteria for community blood donation. Nonetheless, many CCP donors have donated for the first time. First-time donor status is a well-established risk factor for transfusion-transmissible infections, raising concerns about an increase in associated infectious risk.

Noninfectious risks of plasma transfusion include febrile nonhemolytic transfusion reactions and allergic transfusion reactions.<sup>10</sup> Although these are relatively common (approximately 2% of transfusions with plasma), they are rarely serious.<sup>10</sup> More severe reactions include TACO and TRALI. All donors are screened for HLA antibodies to mitigate the risk of TRALI. However, hospitalized patients with severe or life-threatening COVID-19 may be at higher risk of TACO, given the shared comorbid risk factors (eg, advanced age, cardiorespiratory disease) of severe COVID-19 with the individual conditions.

**Specific Risks:** Several specific risks of CCP should be noted. One theoretical risk is antibody-dependent enhancement (ADE), a phenomenon whereby antibody development following infection with a given pathogen potentiates the severity of illness during subsequent infection with a similar—albeit different—pathogen. ADE is described with dengue, but not with SARS-CoV-2 or other coronavirus infections (eg, severe acute respiratory syndrome and Middle East respiratory syndrome). Second, transmission of SARS-CoV-2 via CCP is deemed unlikely. Respiratory viruses have not been shown to be transfusion transmissible and SARS-CoV-2 RNAemia is rare, even in symptomatic patients. Further, there is a minimum required interval of 14 days following resolution of symptoms before donation of CCP is permitted. Therefore, the risk of viable virus was projected to be very low. Third, blunting of the natural immune response has been considered, particularly when administered for the indication of postexposure prophylaxis. This remains theoretical with no evidence that this occurs. Finally, COVID-19 has been associated with thromboembolic phenomena, raising concerns as to whether CCP could compound that risk by rendering a transfusion recipient hypercoagulable. This has not been shown to be the case.

Despite these concerns, prevailing evidence suggests that CCP confers similar risk to that of standard plasma. Reports from China suggested that CCP was well tolerated with few adverse effects that were similar in scope to those seen with standard plasma transfusion (eg, mild allergic transfusion reactions).<sup>14,15</sup> This has been the experience in a wide range of observational studies and clinical trials.<sup>16-19</sup> In the United States, more than 100,000 patients have been transfused with CCP. Two publications from a national EAP reported on the safety outcomes of CCP transfusion recipients.<sup>20,21</sup> The incidence of transfusion reactions and thromboembolic events was less than 1%. Further, the vast majority of serious adverse events were deemed to be unrelated to transfusion. Of reported deaths, none were deemed to be definitely ascribed to transfusion.

## What Is the Evidence for Efficacy?

CCP transfusion failed to show, or to exclude, a beneficial or detrimental effect on mortality based on the body of evidence from RCTs (relative risk [RR]: 0.60; 95% confidence interval [CI]: 0.33, 1.10; very low class of evidence [CoE]). However, nonrandomized studies suggest a decrease in mortality at 7 and 30 days (RR: 0.75; 95% CI: 0.61, 0.93; moderate CoE and RR: 0.65; 95% CI: 0.46, 0.92; moderate CoE, respectively).<sup>22</sup> Similarly, receipt of CCP may reduce the odds of worsening oxygenation (adjusted odds ratio [OR]: 0.86; 95% CI: 0.75, 0.98; very low CoE); however, the evidence is uncertain because of concerns with risk of bias. (For a full discussion of data from RCTs please see below).<sup>22</sup>

### **When in the Course of Illness Has CCP Been Shown to Be Most Effective?**

There are ongoing RCTs to identify which patients might benefit the most from CCP. The best available data suggest that if CCP is to be effective, it should be of sufficiently high antibody titer and given early in the course of disease. If it is to be used within the framework of the EUA, the best outcomes are likely to be seen in those receiving CCP within 3 days of COVID-19 diagnosis or admission to the hospital.<sup>3</sup> Patients who are critically ill and in the intensive care unit are unlikely to benefit from CCP.<sup>18</sup>

### **What Dosage Has Been Shown to Be Most Effective?**

The CCP available through the EUA will be labeled as either high or low titer, based on the signal to cut-off (S/C) ratio from the Ortho Clinical Diagnostics VITROS assay, which is a semi-quantitative measure of IgG specific for the SARS-CoV-2 spike protein (for more information see Blood Banking and Transfusion Medicine Issues, below). FDA guidance states CCP with high antibody titer may be effective in reducing mortality in hospitalized patients with COVID-19; however, low-titer units are also authorized for use. Based on the limited evidence available, use of a single high-titer unit within 3 days of admission to the hospital appears to be most effective.<sup>4,23</sup> However, if only a low-titer unit is available, the question of how many units of low-titer CCP are equivalent to a single high-titer unit remains. Because the VITROS assay is semi-quantitative, the actual dose of antibody within each CCP unit is not known; therefore, it is not possible to know how many low-titer units are needed to equal a single high-titer unit. Delivering a neutralizing antibody (nAb) load equivalent to that of a high-titer unit may be possible only by transfusing 2 or 3 low-titer units. The FDA provides no additional guidance regarding low-dose units.

The FDA recommends that clinicians administer CCP according to standard hospital procedures and institutional medical and nursing practices. The agency suggests starting with one CCP unit and providing

additional units based on the patient’s response to CCP and underlying medical conditions. Patients with impaired cardiac function and heart failure may require a smaller volume or more prolonged transfusion times. Consideration should be given to the patient’s cardiac status and the risk of TACO when additional units are transfused.

## **CCP USE OUTSIDE THE EUA**

### **Nonhospitalized Patients**

There is compelling evidence that early timing of transfusion of convalescent plasma relative to symptom onset and/or diagnosis is associated with more favorable outcomes.<sup>3,9,24</sup> However, most observational and clinical trial data pertain to transfusion of CCP in hospitalized patients, particularly those with advanced (ie, severe and life-threatening) disease.<sup>16-18</sup> By contrast, studies of CCP in the context of postexposure prophylaxis or early treatment of nonhospitalized patients are few. One trial led by investigators at Johns Hopkins University is under way to evaluate CCP transfusion as prophylaxis in those individuals who have an exposure risk yet are neither positive by polymerase chain reaction nor symptomatic. The outcome of this blinded RCT is evidence of infection at day 28 after enrollment. The control arm employs a placebo of standard plasma that has been collected in the United States in 2019 before the emergence of COVID-19 or has been shown to be seronegative for antibodies against SARS-CoV-2 if the units have been collected in 2020.

At least two trials are evaluating early treatment of nonhospitalized patients following a laboratory diagnosis of SARS-CoV-2 infection. The first, titled “Convalescent Plasma to Limit SARS-CoV-2 Associated Complications (CSSC-004)” is a multicenter, double-blinded RCT that is using 28-day hospitalization or death as its primary outcome measure. The second, the “Convalescent Plasma in Outpatients With COVID-19 (C3PO)” trial, supported by the National Heart, Lung, and Blood Institute, is a multicenter randomized, single-blind, two-arm, placebo-controlled Phase III trial that has a primary outcome measure of death, hospital admission, or seeking emergency or urgent care within 15 days of randomization. Saline with multivitamin is being employed as placebo. Both trials have a range of secondary clinical and laboratory outcome measures that will be evaluated over time.

Trials of CCP in nonhospitalized patients are challenging, particularly given the uncertain infectious risk of participants. This introduces logistical challenges pertaining to how to maintain safety for research personnel in an outpatient setting.

## Pediatric Patients

The overall infection rate of COVID-19 in pediatric patients is low.<sup>25</sup> The vast majority of pediatric patients diagnosed with COVID-19 are asymptomatic or have mild disease, with only a minority developing severe disease.<sup>26</sup> Patients with coexisting conditions are at higher risk of developing severe disease.<sup>27</sup> Although the overall incidence is low, COVID-19 infection is a major cause of multisystem inflammatory syndrome in children.<sup>28,29</sup>

Thus far, the limited data evaluating the safety and efficacy of CCP in pediatric patients originate mainly from case series and case reports.<sup>30-32</sup> Although there are clinical studies that include pediatric patients, only a small number of patients with moderate or severe disease qualify to receive CCP.

At the present time, six RCTs are evaluating the use of CCP in pediatric patients (less than 18 years old, or 16 years and older). One of these studies, titled “Efficacy of Human Coronavirus-Immune Convalescent Plasma for the Treatment of COVID-19 Disease in Hospitalized Children (CONCOR-KIDS, NCT04377568),” exclusively includes hospitalized children age 0 to 18, with early onset (<12 days) of COVID-19 symptoms and who are randomly assigned to standard-of-care plus CCP treatment or standard-of-care treatment alone. Another is “Safety and Pharmacokinetics of Anti-SARS-CoV-2 Human Convalescent Plasma in High-risk Children (NCT04377672),” which is intended to evaluate the safety and pharmacokinetics of high-titer anti-SARS-CoV-2 in children. This trial is currently enrolling patients.

Without published RCT data, the evidence needed to guide clinicians on the use of CCP for pediatric patients remains unclear. Therefore, CCP in pediatric patients remains an individualized decision.

## Randomized Controlled Trials

CCP is a promising investigational therapy, but its efficacy remains unknown. In response to the emerging pandemic, multiple RCTs assessing the efficacy and/or safety of investigational CCP were launched in the United States and internationally. To date, three peer-reviewed studies have been published<sup>18,19,24</sup> and results from several others (not yet peer-reviewed) are available online. It is important to interpret the results of clinical trials conducted amid a pandemic with caution.<sup>33</sup> RCT study designs vary significantly; some are double-blind RCTs in which investigational CCP is compared to a control (placebo or standard plasma) and some are randomized open-label trials in which the comparator is standard of care. The target populations of patients in ongoing RCTs are diverse, ranging from postexposure prophylaxis in outpatients to inpatients with mild, moderate, severe, or life-threatening illness with varied oxygen requirements. The results of these RCTs have the potential to establish safety and efficacy across the vast spectrum of COVID-19 disease, which is critically important to inform the development of clinical guidelines for CCP use.

Available data suggest that CCP effectiveness may vary as a function of disease severity as the results of several open-label uncontrolled and/or case-retrospective control studies show a reduction in mortality in patients treated within 72 hours of hospital admission. Unanswered questions from these studies include CCP efficacy in older/elderly patients and those with more advanced disease. Randomization based on risk, a feature of several ongoing RCTs, may answer this question. Another important question that RCTs may answer concerns the quality and quantity of CCP that may mediate a beneficial effect. It is critically important to define a minimum CCP SARS-CoV-2 titer for clinical use.

In studies made public so far, nAb titers were determined by post-hoc analysis in some, whereas in others, titers of the investigational CCP were known before administration. Presence of SARS-CoV-2 antibody and nAb titers in administered investigational CCP may be highly variable. This is underscored by the results of one study that did not show a benefit of CCP in hospitalized patients, but only ~71% of the patients received CCP with any detectable SARS-CoV-2 nAb and only ~29% receiving investigational CCP with a nAb titer  $\geq 1:80$ .<sup>19</sup> Uncertainty regarding the optimal characteristics of CCP for clinical use is expected given that the ability to deploy CCP rapidly antedated the practice of vetting CCP SARS-CoV-2 antibody titers before clinical use. It is worth noting that FDA guidance for CCP IgG and/or nAb titer suitable for therapy emerged from open-label studies demonstrating a dose-response in hospitalized patients. It is anticipated that data from ongoing RCTs in which investigational CCP antibody titer is a covariate can harmonize with data from open-label studies. Another variable that data from RCTs can address with rigor is the effect of concurrent therapies that patients with COVID-19 receive. These therapies vary by center, as well as by time because 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, and concurrent therapies cannot be adequately controlled.

The efficacy of CCP in hospitalized patients may be difficult to establish even with ongoing RCTs. This is because the incidence of COVID-19 can rise and fall quickly in any given area, making it difficult for the RCTs to meet their enrollment targets. To date, two RCTs were stopped before meeting their targeted enrollment due to a lack of patients to enroll.<sup>17,18</sup> Given shifting locations of the pandemic, this is likely to be a recurrent problem, leaving individual RCTs underpowered for their primary and secondary outcomes or for adequate, meaningful subgroup analyses.

The above challenges led to the design and launch of a study, “Continuous Monitoring of Pooled International Trials of Convalescent Plasma for COVID-19 Hospitalized Patients (COMPILE)” to pool deidentified patient-level data from ongoing and discontinued RCTs to reach an answer on CCP efficacy faster. COMPILE will analyze data from hundreds 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 titer and concomitant medications, in secondary analyses.<sup>34</sup>

An additional challenge includes enrolling appropriately diverse trial participants. Although COVID-19 has disproportionately affected African Americans, Latinx, and Native Americans, as well as those in vulnerable and underserved communities, efforts to include these populations have not been robust.

Moreover, these groups are often ambivalent about participating in RCTs due to multiple factors including mistrust of the health-care system stemming from historical events.<sup>35,36</sup>

Clinical trial designs should prioritize enrollment in high-risk populations and aim to increase the representation of these populations in CCP RCTs. Efforts should be made to facilitate community outreach and increase clinical trial literacy through translation services, educational webinars, workshop series, and/or town halls.

In sum, at present, the effectiveness of CCP in reducing severity of COVID-19 illness and mortality remains uncertain, particularly in high-risk and elderly patients, patients of racial and ethnic backgrounds disproportionately affected by COVID-19, and those hospitalized for more than 72 hours. At this time, available data from nonrandomized clinical studies preclude the development of clinical guidelines based on disease severity or risk status.

## **BLOOD BANK AND TRANSFUSION MEDICINE ISSUES**

### **Antibody Testing for Qualification and Labeling of CCP**

The FDA guidance from November 16, 2020 indicates that only the Ortho VITROS SARS-CoV-2 IgG assay can be used at this time to determine the presence of antibodies within the CCP. The FDA has indicated that units must have S/C ratios of 12 or greater in order to be considered “high titer.” Units of CCP that are positive but with S/C ratios less than this are considered “low titer.” The Ortho VITROS SARS-CoV-2 IgG assay is a high throughput, automated chemiluminescence assay that detects antibodies reacting with a recombinant SARS-CoV-2 spike antigen. Correlation of the results of this assay with nAb has not been published, but the FDA has indicated that the selection of the S/C ratio of greater than or equal to 12 was determined by comparison of the assay with the Broad Institute PRNT nAb assay. The exact titer on this assay that correlates with the S/C ratio of  $\geq 12$  has not been included in information released by the FDA. High throughput automated assays that specifically identify nAb are not available.

The FDA has indicated that additional high throughput automated assays would be considered for qualifying CCP. In the September 2, 2020 guidance, they indicated that blood collection establishments could contact the FDA to determine the acceptability of other assays. This would require the requesting blood collector to provide data correlating the proposed assay with the Broad Institute PRNT neutralizing assay or possibly the Ortho VITROS SARS-CoV-2 IgG assay. At the time that this statement was written, blood collectors are in communication with the FDA to provide additional data to expand the testing that could be utilized.

### **Factors Influencing the Availability of CCP for a Given Patient**

As described above, only one assay has currently been approved to qualify CCP under the EUA. As a result, most of the units currently available have been tested with other systems and as such are considered by the FDA as “investigational products.” Based on the temporary enforcement discretion described in the November 2020 FDA guidance, these products can be transfused as investigational CCP through February 28, 2021, not under the EUA or IND framework. After February 28, 2021, the EUA requires CCP units will be qualified utilizing an “approved” test and labeled according to the FDA guidance. As blood collection centers attempt to implement this assay or obtain FDA approval for other assays, this could limit the availability of CCP for a period of time.

Additional factors that will influence availability of CCP include donor qualification. Donors of CCP must fulfill all of the usual allogeneic blood donation criteria including those related to risk factors for relevant communicable diseases. To be considered for donation, donors must have either symptomatic COVID-19 and a positive test result on an FDA-approved and -cleared test or in the case of asymptomatic individuals with no prior diagnostic testing, reactive or positive results on two different FDA-approved assays for SARS-CoV-2 antibodies. Individuals who were symptomatic must have had resolution of symptoms for 14 days and donors must either test negative for HLA antibodies or have no risk factors for such antibodies.

As indicated, individuals must fulfill usual blood donation criteria for relevant communicable disease that could be transmitted by transfusion. The FDA has indicated that patients with COVID-19 who receive CCP are not eligible to donate CCP for 3 months as required following any blood transfusion. Because of the uncertainty of the persistence of antibodies to SARS-CoV-2, this may likely preclude such individuals from becoming donors as blood centers are focusing collection efforts on recently recovered patients in order to maximize SARS-CoV-2 antibody levels. The FDA has also noted that individuals whose antibodies have resulted from vaccination with potential SARS-CoV-2 vaccine candidates are also not eligible to donate CCP.<sup>37</sup> Once an FDA-licensed vaccine becomes available, additional guidance from the FDA will be needed.

A final factor that will influence the availability of CCP for a given patient is the patient's ABO group. Traditionally, blood products have been transfused so that ABO-identical or ABO-compatible plasma products are provided. This has been done out of concern over the possibility that anti-A and anti-B present in the plasma could produce hemolysis of the recipient's red cells. The frequency of ABO group in the Caucasian blood donor population is 45% group O, 40% group A, 11% group B, and 4% group AB. The frequency will vary in other populations as determined by ethnicity and region. For patients with less frequent ABO groups, namely blood groups B and AB, ABO-identical or -compatible CCP may not be available. Because of the limited inventories of group B and AB plasma, institutions have implemented special practices in the trauma setting. In these patients, group A plasma or, less commonly, group O plasma with low-titer anti-A, can be safely transfused to blood group B patients, blood group AB patients, or patients whose ABO group is not known.

Published literature and clinical experience have found it to be safe and within the standard of care to use group A or O plasma with low-titer anti-A in the absence of group B or AB plasma.<sup>38</sup>

## HOW CAN CLINICIANS HELP?

The limited availability of donors and as a result, CCP, can be addressed by health-care providers. Physicians who specialize in treating infectious diseases and other clinicians can play a critical role in recruiting donors by encouraging recovered COVID-19 patients to contact a local blood collection center about donating convalescent plasma. This information should be a standard component of discharge instructions provided to patients who have recovered from COVID-19.

For those who wish to donate CCP, the AABB provides information on donation requirements and locations of collection centers at <http://www.aabb.org/giveblood>.

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