New Mexico Medical Advisory Team (MAT) Assessment

MAT Workgroup Name: Clinical Care

Date: May 11, 2020

Question or request:
1. What is the role of Convalescent plasma treatment for COVID-19 patients?
2. When might Convalescent Plasma (CCP) treatment become available?
3. How can facilities obtain CCP?
4. Which patients are most likely to benefit from CCP Transfusion?
5. What is the optimal dose of CCP?

Recommendation/s in bullet form:
1. The use of convalescent plasma (CCP) collected from individuals who have recovered from COVID-19 is being implemented at Presbyterian, Lovelace Medical Center and UNMH in select cases as one potential treatment option. To date in Albuquerque, 15 patients have received convalescent plasma.
2. Currently, providers can obtain and transfuse CCP by submitting a single patient Emergency IND to the FDA, by participating in an Expanded Access Program through the Mayo Clinic, and/or by participating in a clinical trial. CCP should be obtained by their hospital blood supplier.
   a. The Mayo Clinic Expanded Access Program may facilitate more rapid availability of these units and enable additional patients to receive CCP (See www.uscovidplasma.org). Both expanded access and clinical trials require Institutional Review Board (IRB) preapproval (21 CFR 56). The expanded access program gives enrolled sites the opportunity to use Mayo’s IRB eliminating the need to seek approval from an independent IRB (UNM and Presbyterian IRBs will still review the package and will cede review to Mayo).
   b. If more than 2 patients are expected to receive CCP, we recommend hospitals enroll in either the Mayo Clinic Expanded Access Program or in a clinical trial. If 2 or less patients are expected to receive CCP, providers may submit an emergency Investigational New Drug (eIND) application to the FDA for each patient.
3. Presbyterian has also obtained eIND approval to transfuse CCP in a single pediatric patient. Treating pediatric patients will require submission of an eIND for each patient or participating in a clinical trial.
4. Currently, it is not known which patients would most benefit from CCP. Whether CCP provides a benefit in severely ill patients, mild/moderately ill patients, or as post-exposure prophylaxis is still unclear. If CCP were to be transfused, recommend transfusing only in patients who meet the eligibility criteria of their IRB-approved clinical trial, of the Mayo Clinic Expanded Access Program, or of the FDA eIND.
5. The optimal dose of CCP (1-unit vs 2-units) is not yet known. Until the local supply of CCP increases, recommend transfusion of 1 unit per patient so more patients have access to the therapy.

Assessment:
The FDA is currently exploring the efficacy of CCP collected from individuals who have recovered from COVID-19, which contains antibodies to SARS-CoV-2, as a possible treatment. Use of convalescent plasma has been studied in outbreaks of other respiratory infections, including the 2009-2010 H1N1 influenza virus pandemic, 2003 SARS-CoV-1 epidemic, and the 2012 MERS-CoV epidemic. It is currently unknown which patients would most benefit from CCP (if it all). Recent small studies from China show a potential benefit of transfusing convalescent plasma to critically ill patients with COVID-19. However, another small case series suggests that CCP may be more beneficial earlier in a patient’s clinical course prior to them becoming critically ill. It is also currently unknown whether 1-unit CCP vs. 2-units CCP is optimal.
The FDA is currently working with the Mayo Clinic to allow for an expanded access protocol to facilitate access to COVID-19 convalescent plasma under an existing IND for acute care facilities (www.uscovidplasma.org).

The FDA has also allowed access to COVID-19 convalescent plasma through an eIND for use in patients with serious or immediately life-threatening COVID-19 infections. In these cases, physicians must request a single dose for their individual patient. If more than 2 patients will be receiving CCP,

Providers wishing to request an eIND should specify the following in the application:

- Laboratory confirmed COVID-19
- Severe or immediately life-threatening COVID-19 evidenced by respiratory failure, septic shock and/or multiple organ dysfunction or failure. Signs of this can include one or more of the following:
  - Dyspnea, respiratory frequency ≥ 30/min, blood oxygen saturation ≤ 93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, and/or lung infiltrates > 50% within 24 to 48 hours
- Informed consent to receive convalescent plasma must be obtained and documented in accordance with 21 CFR 50.

Patients receiving CCP must meet eligibility criteria of the pathway chosen to transfuse (i.e. eligibility criteria of the FDA eIND, Mayo Clinic Expanded Access Program, or of the IRB-approved clinical trial).

New Mexico Convalescent Plasma Treatment

Thus far, Presbyterian, UNMH, Lovelace, San Juan Regional, and Christus St. Vincent have all enrolled in the Mayo Clinic Expanded Access Program. Unknown if other institutions in New Mexico have enrolled. To date in Albuquerque, 15 patients have received CCP. It is still too early to assess outcome data.

Red flags and Concerns:

While treatment with CCP has been successfully used for other outbreaks, it is not without risk. As with other blood transfusions, common risks include allergic transfusion reactions, febrile non-hemolytic transfusion reactions, and volume overload. Very rarely, inadvertent infection with another infectious disease agent and hemolytic transfusion reactions may occur. Many of these risks are mitigated with the modern blood banking techniques used to screen for blood-borne pathogens and match the blood type of donors and recipients, so this risk is considered very low. There is a higher risk, however in treating individuals with pulmonary disease with plasma transfusion, as it can result in transfusion-related acute lung injury (TRALI). Blood centers have worked to mitigate the risk of TRALI as much as possible by only collecting from either female donors without HLA antibodies or male donors. This risk should be considered in the risk-benefit assessment for each patient.

There is also the theoretical risk of causing antibody-dependent enhancement of infection (ADE), which can enhance the disease in the presence of certain antibodies. Since the proposed use of CCP in the COVID-19 epidemic would rely on preparations with high titer of neutralizing antibody against the same virus, this risk is thought to be low. Additionally, there is a risk that antibody administration to those exposed to SARS-CoV-2 may prevent disease by attenuating the immune response, leaving individuals vulnerable to
subsequent reinfection. While additional studies are needed, if this risk proves real, these individuals could
be vaccinated against COVID-19 when a vaccine becomes available.

Given the high mortality of COVID-19, particularly among the elderly and vulnerable individuals, the
potential benefits are thought to outweigh the risks in those who meet eligibility criteria. However, a risk-
benefit assessment should be conducted for all cases where CCP administration is considered. Additionally,
caution and vigilance will be required to identify any evidence of enhanced infection and monitor patients
for signs of reinfection.9, 10, 11 Under the Mayo Clinic expanded access protocol, serious adverse events
judged to be potentially related to the administration of CCP must be reported at www.uscovidplasma.org
and to the institution’s Principal Investigator.

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**Resources/Reference:**
1 U.S. Food and Drug Administration Revised Information for Investigational COVID-19 Convalescent Plasma
Available from: https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-
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