Overview

On December 31, 2019, the World Health Organization (WHO) first became aware of an infectious outbreak in China, which, since that time, has become a global pandemic. At the time of this publication, the viral agent, acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resultant disease, coronavirus disease 2019 (COVID-19), has been implicated in more than 4,300,000 cases and more than 149,000 deaths in the US alone (7/27/20). Since there is currently no natural immunity in the population and no established treatments or effective vaccine, cases continue to increase. Currently physicians and researchers are investigating and implementing a number of possible treatments including passive antibody administration using plasma from recovered patients. The product is known as COVID-19 Convalescent Plasma or CCP.

The administration of passive antibody is not a novel idea. The use of convalescent plasma from recovered patients has been in use as a therapeutic modality for the treatment of infectious disease for more than 100 years. Its use in the treatment of various viral infections (eg, hemorrhagic fevers [Ebola], influenza [H1N1], and other coronavirus infections [SARS-CoV-1 and MERS]) have resulted in varying degrees of clinical efficacy. Few studies to date have had a high degree of scientific rigor making it difficult to draw valid conclusions regarding the effectiveness of passive antibody administration; however, some data suggest that administration of passive antibody may result in decreased severity and lower mortality rates.

Originally the US Food and Drug Administration (FDA) approved the use of CCP as an investigational new drug (IND) for the treatment of COVID-19, however; on August 23, 2020, the FDA issued an Emergency Use Authorization (EUA) for the use of CCP in the treatment of hospitalized patients with COVID-19 (FDA EUA 2020).

Use/Indications

Antibodies present in convalescent (immune) plasma may have a therapeutic effect through a number of possible mechanisms including:

- Neutralizing antibodies may bind to the virus or other infective agent directly.
- Antibodies may act indirectly through antibody-mediated pathways such as complement activation, phagocytosis and/or antibody-mediated cellular cytotoxicity.
- Non-neutralizing antibodies may bind to virus particles and may enhance the prophylactic effect and improve recovery (Bloch 2020).

Special Instructions

**CCP donor requirements:**

- Evidence of COVID-19 by laboratory test or positive test for SARS-CoV-2 antibodies
- If antibody titer testing is available, donor must have a demonstrable SARS-CoV-2 neutralizing antibodies (FDA recommended titer >1:160)
- Complete resolution of symptoms at least 14 days prior to donation
- Must meet all other requirements for standard whole blood collection including testing for infectious disease; additional requirements must be met if plasma is collected by apheresis
- Negative for HLA antibodies in order to reduce the risk for transfusion-related acute lung injury (TRALI).

Collection
Donor components are obtained via whole blood collection or apheresis plasma collection in an FDA registered or licensed blood collection facility. Apheresis is generally recommended in order to optimize the CCP yield. Labeling must include the following statement “Caution: New Drug – Limited by Federal law to investigational use (21 CFR 312.6a).” Other requirements for labeling of plasma apply.

Components include:

- **CCP, Fresh Frozen**: This component is frozen at ≤18°C within 8 hours of collection. It expires 1 year from date of collection. OR
- **CCP, Frozen**: This component is frozen within 24 hours of collection. It is stored at 1°C to 6°C for up to 24 hours and frozen at ≤18°C. It expires 1 year from date of collection. OR
- **Liquid Plasma**: This component is stored at 1°C to 6°C. It expires 5 days after expiration of the corresponding Whole Blood unit.

Limitations

- Difficulty identifying and recruiting donors who have developed detectable neutralizing antibodies during convalescence
- Lack of validated SARS-CoV-2 antibody tests

Test Includes

**Recipient** ABO type. Additional compatibility testing is not required.

**Selection of ABO Compatible Plasma**

<table>
<thead>
<tr>
<th>Patient ABO Type (Recipient)</th>
<th>Suitable FFP Types (Donor)</th>
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</thead>
<tbody>
<tr>
<td>Group O</td>
<td>Group O, A, B, or AB</td>
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<tr>
<td>Group A</td>
<td>Group A or AB</td>
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<tr>
<td>Group B</td>
<td>Group B or AB</td>
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<tr>
<td>Group AB</td>
<td>Group AB</td>
</tr>
</tbody>
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**Recipient Requirements**

- Recipient informed consent must be obtained and must include a description of risks and benefits, alternative therapies if available, an opportunity to ask questions, and the right to refuse treatment
- Processes must be in place to verify the identity of the recipient and include a clerical check of physician order and unit identification.
- **Note**: Emergency transfusion may require the use of special identification band systems or other mechanisms to identify the patient. Institutions must have procedures and policies in place for the emergency release of blood and blood components that insure accurate recipient identification and blood type.

**Specimen**

Blood (from recipient for pretransfusion ABO typing)

**Container(s)**

- Recipient specimen: Red top (no additive) tube, lavender top (EDTA) tube, or pink top (EDTA) tube; do not use a serum separator tube.
Volume / Minimum Volume

Tube filled to capacity or 7 mL blood / 3 mL minimum

Collection

Collection of recipient specimen for pretransfusion work-up: Routine venipuncture. As required by AABB Standards for Blood Banks and Transfusion Services all patients must be identified by two independent identifiers. At bedside, patient identity should be confirmed. Specimen(s) should be labeled with the independent identifiers and the date of collection. There must be a process to identify the person who drew the sample. The tube must be labeled before the phlebotomist leaves the room. Use a computer generated label, if available, to avoid transcription errors.

Processing and Storage

- Recipient specimen: Specimen(s) may be collected and transported at room temperature. Processing will be performed by the Transfusion Service. Specimen(s) that cannot be processed and tested immediately should be stored at 2°C to 8°C.

Stability

Recipient specimen: Specimen should be tested within a maximum of 14 days of collection. Institutional policies and procedures should be followed.

Administration

As with all blood components, CCP must be administered through a standard blood component filter (170 to 260 microns). Based on previous experience with the use of convalescent plasma in SARS, current dosage guidelines in planned clinical trials are one unit (200 mL) for post-exposure prophylaxis and one or two units for treatment.

Aftercare

Recipient Post-transfusion: The recipient must be observed for evidence of adverse reactions during transfusion and for a suitable time period thereafter. A process must be in place for the recognition and reporting of suspected adverse events; institutional policies apply.

If direct monitoring is not possible, as in outpatient settings, the patient and/or caregiver must be given a set of written instructions regarding possible adverse reactions and a mechanism to report any suspected reactions.

Potential Adverse Reactions:

- Potential for antibody dependent enhancement (ADE) in which plasma antibodies enhance viral cell entry and replication resulting in disease exacerbation.

- Passive antibody administration may suppress the recipient's immune system resulting in increased susceptibility to reinfection.

- Other risks associated with plasma transfusion including transfusion-related acute lung injury (TRALI), transfusion-associated dyspnea, transfusion-related circulatory overload (TACO), and severe allergic reactions.

Additional Information

On January 31, 2020, HHS declared a public health emergency related to COVID-19. In response to the escalating COVID-19 pandemic, the FDA published guidance documents in April 2020 which contained recommendations for the administration, investigation, and collection of CCP. Because of the grave nature of the pandemic, the guidance was not made available for public comment prior to implementation but it is subject to ongoing comment. Recommendations found in FDA guidance documents are not legally enforceable rather they communicate the FDA’s thinking on the topic. As a result, CCP is considered to be an investigational drug (21CFR Part 312) and the provider must be under an
investigational new drug application (IND). To improve access, two other pathways have been made available: National Expanded Access Protocol and single patient emergency IND (21 CFR Part 312.305).

A recent systematic review of the literature reported that CCP may reduce mortality in seriously ill patients, result in an increase in antibody titers and reduction in viral RNA, and cause a reduction in clinical symptoms. These observations were based on limited data and large multicenter clinical trials were recommended. (Rajendran 2020).

HHS has declared a limited waiver on HIPAA sanctions in order to facilitate the identification and recruitment of donors who have recovered from COVID-19 (HHS 2020).

Index Terms

CCP; COVID-19 Convalescent Plasma

Applies to

Coronavirus Disease; COVID-19; SARS-CoV-2

References


