



### **Is there criteria of age or immunity for a critically ill patient to be a recipient of convalescent plasma treatment? Thank you.**

The expanded access program is applicable only to folks 18 years or older; eIND and clinical trials may be able to better examine its use / efficacy in younger individuals. Otherwise, we are not using any age or immunity status cut off for enrollment.

### **Am I correct in that blood being donated at a plasma center would never be used as convalescent plasma, but instead, only potentially for manufacturing?**

That is correct. A paid donation would not be used in our hospital setting as convalescent plasma.

### **Any information as to optimal efficacy relative to shelf life, i.e., the freshest is the best?**

Standards for plasma for medical use and shelf life are best practices.

### **Any specific tests to determine the level of LPS ( septesemia) in the convelescent plasma?**

I'm not aware of any testing to look at LPS in plasma; as a primarily bacterially-derived toxin, not sure this would have much value.

### **Are asymptomatic COVID people who recovered eligible to donate their plasma?**

Yes, after a positive test and 14 days symptom free, patients may donate convalescent plasma.

### **Are COVID-specific antibody titers being performed on donors so that we can get an idea of the titer levels and isotypes that are effective? If so, what testing methodology is being utilized? I read that there are about 150 antibody tests out there, but most are not very specific and/or sensitive.**

As this pandemic is evolving, this type of data is being collected in order to have data for best practices as we move forward.

### **Are donors being tested for Covid before they can donate?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible.

### **Are platelets depleted in these patients due to pathological clotting?**

Thus far, we have not seen significant platelet depletion in the vast majority of our COVID patients despite their thromboses.

### **Are the recovered patients for Covid 19 allowed to donate blood for transfusion?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.

### **Are there many people who have recovered from Covid donating their plasma, and do we know what the numbers look like?**

I can only speak to the Red Cross process. I know that over 80,000 have registered on line for consideration to serve as donors. They are calling all those who have registered to see if they are actually qualified to donate before making a donation appointment.

### **Are there other coagulation tests that should be monitored besides PT and D-dimer for Covid-19 patients?**

There are some recommendations for routine monitoring of fibrinogen and FVIII, although results may not necessarily be directly actionable. Anti-Xa assays may also be useful if patients are receiving LMWH therapies to ensure that they are therapeutic. Otherwise, no other routine coagulation tests are currently advised. There have also been some specific guidelines issued to avoid specific testing for things like antiphospholipid antibodies in all COVID pts.

### **Are they putting the patients on UFH when they are put on a ventilator, and are sites monitoring the UFH 0.4-0.7 IU/mL?**

We are using primarily LMWH at my facility due to a perceived increased bleeding risk (locally) that we have seen with UFH. And, yes, we are monitoring anti-Xa assays for such patients to ensure that they are therapeutic.

### **Are we limiting plasma therapy within the same race?**

We are not and there would not appear to be any scientific basis to do so.

### **Are you billing for the product? Blood product or drug?**

Yes, we are billing patients for this as a blood product, although all of the patients receiving the plasma are inpatients. So, they fall under a DRG.

### **At what point in time or at what point of convalescence can a Covid-positive patient be able to donate?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.



### **At what stage in the disease is the administration of CCP most effective?**

Early stage is clearly most effective, with some preliminary data suggesting if given more than 14-21 days after viral detection, then it may not be nearly as effective.

### **Can an individual donate if he/she has a reinfection? Will it have antibodies produced, even if reinfected?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.

### **Convalescent plasma are just given to critical patients?**

Currently, when used via the expanded access program, criteria for enrollment requires being an inpatient with "serious" disease per clinical criteria. However, individual eINDs as well as clinical trials are underway examining conv plasma use for patients across the spectrum of disease severity

### **COVID patients needing convalescent plasma are already severely ill. So in addition to the current list of symptoms to determine transfusion reaction, are there additional symptoms to determine if the patient is experiencing a transfusion reaction?**

Pulmonary reactions would be very hard to assess in someone with severe pulmonary symptoms. One would need to use clinical judgment in those cases. Otherwise, reactions that are allergic and/or hemolytic in nature should be able to be differentiated from COVID by clinical appearance and/or laboratory testing.

### **Do you extend the life of the plasma to 5 days? If so, what ISBT code are you using?**

At my institution, we are thawing the plasma and converting it to thawed plasma, which is good for 5 days. The ISBT code is E9752.

### **Does an apheresis collection-only center need a BLA to give convalescent plasma to local hospitals or is being registered with FDA enough?**

If you are already licensed to collect and manufacture plasma for donors, then you should be able to collect convalescent plasma. You would need to meet the appropriate labeling requirement for this product, which can be found via the FDA. At our institution, we are only registered to administer blood products and not collect; we would have to submit a BLA if we wanted to collect our own convalescent plasma for our patients.

### **Does anyone know whether patients who have been transfused convalescent plasma have improved their condition? What volume? Compatibility?**

Those studies are under way as part of this pandemic and evolving as we move forward with more patients being treated. Dr. Sanford also discussed dosing and compatibility in her other response.

### **Does thawing the plasma affect the antibody's efficiency? Must the FFP be transfused within half an hour to ensure the best response of the antibody in the body or it can be transfused within the normal 5 day expiration date?**

At this point, when we receive the plasma, we check with the bedside physicians before thawing it to make sure once we thaw it they are ready to transfuse it. Antibodies are relatively stable for days in plasma, although there have been no studies verifying the titer changes over 5 days that the product is thawed.

### **Does the titer of the convalescent plasma affected by the presence of other viral antibodies in the plasma, eg Hep abs**

No, convalescent plasma is not being titered at this time.

### **Dr. Tormey mentioned giving low molecular wt heparin 3 days post convalescent plasma. Are others doing the same?**

Thus far, the majority of our patients who've received a dose have gotten somewhat better (or not particularly worse).

### **For Dr. Tormey: After using LMWH, do you not see arterial thrombosis in patients after receiving convalescent plasma?**

In our cases, thrombotic events occurred within 48 hours of a convalescent plasma dose. Thrombotic complications can also be seen at baseline in COVID patients and are often seen as a mid-to-later stage manifestation of the disease, particularly in those with moderate-to-severe illness. So it can be tough parsing out the causes of thrombosis.

### **Given the fact that we are still learning about the coronavirus, are you concerned that the process could be transferring fragments of antigens that are not totally removed from the body that may be a different strain and could introduce the disease?**

Plasma is given to patients from subjects who have recovered from infection and no longer have the active virus in their blood. Although they may have free antigen, the main substance present are antibodies against the collective protein signature of the virus. Thus, convalescent plasma provides an immune boost to a patient, but should not present additional virus or particles that would create a new viral infection.



### **Has plasmapheresis been used successfully to ameliorate or lessen effects of “cytokine storm”?**

I'm aware of only a single case report of plasmapheresis being used for COVID; we are treating such requests as “research use only” at my facility given lack of efficacy and safety data.

### **Have there been reports of patients acquiring COVID-19 due to blood transfusion?**

At this point, there is no evidence that COVID-19 is transfusion transmitted.

### **Have you run into any Factor 5 patients, or patients that were tested with Factor 5 in the Covid patients? What if they are already on Coumadin?**

We have not encountered any FV deficient patients, nor patients on warfarin due to FV Leiden. If already on Coumadin and required convalescent plasma, this would result in only a transient reversal of their warfarin.

### **How about the Thalassemic patients? How can they be treated if infected with Covid-19?**

Great question! So far we haven't had a patient with a hemoglobinopathy to present with COVID-19, but when we do we will make sure that a benign hematologist is involved in their care to help support. Some patients have experienced marrow suppression, and this vulnerable population may require more transfusion support than normal.

### **How close are we to having an anti-SARS-CoV-19 neutralization test? The plasma is being collected against a transfusable product standard for donor qualification in order to assure the safety of the product is that of FFP/PF24. However, we don't have a good way to assess the activity of the purported active antibody in the product.**

Agree. More data is needed to understand neutralizing antibody activity and titers to further improve the use of convalescent plasma in treating patients..

### **How do you assure donors that they are safe from getting Covid-19 in the donor center? Is blood tested for Covid-19?**

Precautions using masks, social distancing, and other recommended procedures are used during any medical interactions including blood donation.

### **How do we know if the plasma is actually working if it isn't being titered and/or given to patients at a mild state vs. a very critical state?**

Those studies are under way as part of this pandemic and evolving as we move forward with more patients being treated.

### **How do we know that antibodies are neutralizing? Are there any convalescent plasma studies that will assess if any antibodies are neutralizing?**

We do not know yet that antibodies are neutralizing, but these studies are being performed.

### **How infective are blood products from Covid-19 patients? I am a researcher working toward a possible retrospective study. I will be handling the products. Any extra precautions that I should be taking? Thank you!**

To date, there are NO reported cases of transmission of the novel coronavirus via transfusion; therefore, concerns are minimal-to-zero for passing the virus via convalescent plasma. Convalescent plasma units are also tested using FDA licensed assays for a number of viral (e.g., HIV, HCV) and bacterial (e.g., syphilis) pathogens. However, no testing is perfect and risks for non-COVID transmission remain. Therefore, if working with plasma for research purposes, we strongly recommend following appropriate precautions.

### **How is the supply of convalescent plasma? If you have a limited supply, how do you determine which patients receive it?**

Supplies remain very limited and we are evolving a flow sheet to make difficult decisions if multiple patients qualify, but only 1-2 units are immediately available.

### **How long does it take from collection to bedside use?**

Plasma is collected through routine donor process for regular blood.

### **How many times can a convalescent plasma donor donate? What is the timeline?**

Individuals can donate on the same cycle as for routine blood product donation.

### **How often can someone donate their convalescent plasma ? Or is it only on time case?**

Once patients are cleared to donate, they can donate as often as allowed by standards for any other plasma donation.



### **How often can an individual donate ?**

As often as one can donate for any routine blood donation, plus criteria Dr. Sanford is discussing now.

### **What is considered one dose of convalescent plasma? Is it one unit of plasma, a certain # of mL?**

The answer was one unit of convalescent plasma.

### **I have read and heard that some COVID patients develop coagulopathies. Has this impacted anyone and increased the need for cryo and/or FFP, platelets?**

The coagulopathies are largely prothrombotic in nature; therefore, we have not seen increased use of plasma, cryo or plts in these patients

### **I work at a hospital in Maine that is receiving convalescent plasma from Bloodworks in Washington state. Do we know whether there are different strains of the virus in the country, and whether that would affect choice of source for plasma for a lab?**

At this point, we are working under the assumption of limited strains and , given a presumed polyclonal immune response, are not selecting plasma products based on region of donation.

### **If a potential donor tests positive for IgG at an independent lab, is that enough to qualify them as a convalescent donor?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.

### **In resource-limited countries where blood supplies are scarce, what should be an alternative ?**

In these countries where blood supplies are scarce, the patients would have to rely on supportive medical management instead of convalescent plasma transfusions.

### **Is a particular blood type more susceptible to more severe disease and/or morbidity?**

We have seen COVID impact folks across the ABO spectrum in about the percentages seen with typical blood group distribution. But, I'm not aware that this has been formally studied.

### **Is anyone using Viscoelastic testing at their facility to both monitor for hypercoagulation or for determining specific transfusion needs? Can we see this being important as surgeries come back?**

We have piloted TEG testing in a subset of COVID patients and have seen some markers of hypercoagulation, primarily related to MA and alpha angle (with little-to-no evidence of abnormalities suggesting bleeding). We are not using for assessing transfusion needs, although as mentioned it could be potentially used for guiding therapy in subsequent surgery or trauma.

### **Is convalescent plasma being used from females donors who have had children? I know there is a concern with TRALI, but in some areas it is more difficult to get convalescent plasma.**

Typical FDA/blood donor criteria apply. Therefore, given a local center's preference, plasma may not be collected from women who have had children, or such donors may be tested for the presence of leukocyte antibodies that could potentially mediate TRALI.

### **Is every unit received from a donor tested for Covid and the plasma pulled off that unit, or is the lab contacting individuals who have tested positive and asking them to come in to donate plasma?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.

### **Is it possible to give the antibody like we do rhogam once the right dose is figured out?**

Certainly possible and may be the future of COVID antibody therapy, particularly as hyperimmune globulin formulations are made.

### **Is purifying IgG from convalescent plasma, or removing pro-thrombotic factors from it, in the pipeline to avoid thrombotic adverse events?**

Yes, several commercial entities are looking at making "hyperimmune" globulin, essentially COVID ab concentrates. These are estimated to be available in the next 6 months.

### **Is the plasma being tested to see if there is any fragments of the antigen present?**

Testing for the presence of virus antigen is not part of the current preparation of convalescent plasma.



### **Is the convalescent plasma being titered?**

No, convalescent plasma is not being titered at this time.

### **Is the convalescent plasma done via plasmapheresis or is it donated and given to the patient?**

It can be collected either way using standard protocols.

### **Is the plasma issued on a first-come, first-served basis, or does it depend on the severity of the patient's condition?**

We are currently evolving a work flow to triage based on severity rather than first-come, first-served.

### **Is there a criteria (age or immunity) for a patient to be determined as a candidate for convalescent plasma?**

Donors must meet standard criteria for donating blood as well as a documented recovery from a COVID infection.

### **Is there a specific D-dimer reference from Covid patients ?**

I'm not aware of a specific d-dimer reference range for COVID patients.

### **Is there an ability to quantitate the antibody levels in donated plasma?**

No, convalescent plasma is not being titered at this time.

### **Is there an antibody assay out for people who may have had Covid previously (unknowingly) that may have developed antibodies if so, and they do have antibodies? Can they donate their plasma?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.

### **Is there any indication that receiving convalescent plasma would affect patients' own immune response/antibody production (such as the way Rhogam prevents anti-D formation)?**

Great question that we don't know the answer to, as yet!

### **Might there be a considerable difference in effectiveness/stability using plasma within 24 hrs or 5 days of thawing?**

There would have to be a study looking at the difference in antibody stability in 24 hour vs 5 day thawed product, but usually antibodies remain stable for days. So, I anticipate the antibody titers would be close to the same.

### **My blood bank saw an increase in red cell usage for Covid patients. Have other hospitals seen this? We also saw an increase in DAT testing.**

We have not seen increased RBC usage, although we have seen (and have also read anecdotal reports) about higher rates of autoantibodies in COVID patients, which may explain the increased DAT assessment.

### **Should patients be tested for the presence of IgG or IgM before receiving convalescent plasma?**

Ideally, yes, but this may not be practical if sites do not have antibody testing available.

### **Some individuals have tested positive for coronavirus antibodies without documentation of prior disease. Will these people be eventually able to donate for convalescent plasma?**

Criteria for donation of plasma after Coronavirus infection include a negative RT-PCR test and 14 days free of symptoms. At that point, a recovered patient can donate.

### **Has anyone linked DIC (disseminated intravascular coagulation) with COVID-19 patients w/hypercoagulopathy?**

What we are seeing is not traditional DIC. While d dimers are markedly elevated, virtually all other parameters typically seen as abnormal in DIC (PTT, plts, schistocytes, fibrinogen) are normal in COVID or show elevations (e.g., fibrinogen, plt count). Therefore, the coagulopathy has been largely interpreted as pre-disposing to a thrombotic state, rather than a bleeding state (as can be seen in end-stage or late DIC). We don't fully understand what is driving this coagulopathy at this stage.

### **There are cases of recurring infection of Covid on recovered patients. Won't there be a risk of giving the latent virus through the plasma transfusion?**

To date, there are NO reported cases of transmission of the novel coronavirus via transfusion; therefore, concerns are minimal-to-zero for passing the virus via convalescent plasma.

### **Use of immunoglobulin tests other than to evaluate convalescent plasma, is it practical in the hospital setting? Is it being considered for convalescent plasma evaluation in the near future? I'm unaware of FDA (not EUA) available immunoglobulin tests.**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed. No other testing is performed.



### **We are seeing more ferritin and vit D testing.**

It's unclear why vit D testing is increasing! Ferritin is an acute phase reactant and can be measured as an assessment of the acute phase. We have seen many ferritins being ordered as well.

### **What about immunogenicity to these humanized antibodies from plasma? Are there any reported data about them? Would this be a potential issue or not at all?**

Yes, since we initiated our LMWH protocol for convalescent plasma recipients, we have not observed abnormal thromboses in the immediate days following dosing.

### **What about Thromboelastography to monitor or diagnose hypercoagulability?**

We have piloted TEG testing in a subset of COVID patients and have seen some markers of hypercoagulation, primarily related to MA and alpha angle (with little-to-no evidence of abnormalities suggesting bleeding).

### **What are the percentages of success in this study?**

Data are still being analyzed for US studies; for international (admittedly) small case series published, high percentages of patients have recovered after convalescent plasma, but these are uncontrolled studies, not trials, and trial data / strong evidence is lacking.

### **What are the primary dangers of such preliminary clinical application of convalescent plasma transfusion for COVID patients?**

Transfusion reactions and unanticipated side effects of plasma are our main worries, e.g., thrombotic complications.

### **What are the tests performed on a convalescent plasma before being transfused into the patient's body?**

The standard tests for production of plasma for medical use are performed.

### **What expiration date are the panel giving to the thawed plasmas?**

Expiration dates are per routine standards for other plasma blood products.

### **What if one breaks with thawing, or a patient let's say passes and the product can not be used when allocated for that patient? How do we handle the convalescent plasma?**

We have experienced both occurrences at our institution. For the broken plasma, we contacted our blood supplier and they sent us a replacement unit for the patient. For the patient who passed before receiving the plasma, we contacted the blood supplier and had the unit reassigned through the EAP to another patient.

### **What if the convalescent plasma comes from a Covid survivor and then reinfection occurs days after? What is the protocol?**

To date, there are NO reported cases of transmission of the novel coronavirus via transfusion; therefore, concerns are minimal-to-zero for passing the virus via convalescent plasma.

### **What is better 1 collection eplasma donation from patient recovered from sever covid 19 or few symptoms?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible. Routine testing for any blood products are also performed.

### **What is considered a therapeutic dose of convalescent plasma? Volume of plasma?**

Experts are using one unit of plasma from a donor. Titers are not known.

### **What is the neutralizing antibody titer minimum required to infuse a unit of convalescent plasma?**

Not known as this time as titers and the confirmation of neutralizing titers are not routinely available. As data evolves, we will be able to move towards this level of usage.

### **What is your opinion on the current antibody tests that the U.S. is using to determine if an individual has contracted the coronavirus before? How accurate do you think these antibody tests are? Can it really identify the stage of one's immune system toward COVID-19?**

Very hard to know; there was an excellent AJCP editorial on this subject by my colleagues at Yale (Torres and Rinder) that delves into these concerns; would recommend reading that for details!

### **What method of testing are they using to screen donors?**

Donors must be symptom free for 14 days after a confirmatory test for infection to be eligible.



### **What do we need to watch out for when using ilama antisera to Sars-CoV2?**

I'm a little unsure of the question -- not sure what ilama antisera is!

### **What percentage of patients recovered following administration? Did any of your patients get worse or die?**

Those studies are under way as part of this pandemic and evolving as we move forward with more patients being treated.

### **What specific volume of convalescence plasma will provide artificial immunity to a patient?**

Experts are using one unit of plasma from a donor. Titers are not known.

### **What's the standard dose amount?**

There is no standard dose amount, but the experience of the speakers is using a single dose (unit) of plasma.

### **What's the timeline (roughly) for a thrombic event? When to give the dose and when is too late?**

I'm aware of a few other centers that are providing more aggressive anticoagulation to COVID pts, particularly those receiving convalescent plasma.

### **Would it be possible to routinely test healthy blood donors/donations for COVID-19 neutralizing antibody? Would this be a practical way to identify antibody-positive individuals to donate convalescent plasma?**

Donors can be tested for positive serology using currently available kits, but there is no indicated that the antibodies detected are neutralizing antibodies or not. Further work is needed.

### **Would titer of antibodies play a role in plasma dosage?**

If available and with future evidence, they may change management but, for not, they do not play a role.

### **Would you consider convalescent plasma as a first choice of treatment for critical cases infected with Covid-19? Compared to the other treatment protocols provided to patients in critical condition, how do you evaluate convalescent plasma as a choice of treatment?**

We do this in close collaboration with our clinical partners in Infectious Disease and Critical Care Medicine, who are typically making the determination of whether convalescent plasma or another therapy may be useful.

### **You mentioned dosing. Is there a preference for getting plasma rich in IgM specific COVID-19 antibody over IgG specific antibody? Or, do you take what you can get from the donor?**

Based on the current protocol for treating patients with convalescent plasma, the plasma is collected several weeks after a confirmed case has recovered; therefore, the bulk of the intended effect is from IgG and not IgM.