

## Q & A: Convalescent Plasma Therapy

*Interview with Edward Cachay, MD*

By Scott LaFee | November 19, 2020

**M**ost media and public attention during the pandemic has focused upon efforts to develop an effective vaccine to prevent COVID-19, which is caused by the novel coronavirus SARS-CoV-2. Some attention has been paid to investigational therapeutics for treating infected patients, such as the antiviral drug remdesivir or the corticosteroid dexamethasone, both of which may reduce severity of illness and mortality.

Less noticed are trials exploring the novel utility of a therapy that has been around for more than 100 years. Convalescent plasma (CP) is a strategy of passive immunization for preventing infections (like vaccines) and treating infections (like therapeutics). Researchers at University of California San Diego School of Medicine and UC San Diego Health are part of a [nationwide clinical trial](#) to assess the efficacy of CP to prevent COVID-19 after a known exposure to the virus.



Blood plasma. Photo credit: Getty Images

We asked [Edward Cachay, MD](#), an infectious disease specialist at UC San Diego Health

professor of medicine at UC San Diego School of Medicine and one of the trial's principal investigators, to elaborate on CP therapy and its role in ending the pandemic's terrible toll.

### **How does this convalescent therapy trial differ from other pandemic efforts, most notably the vaccine development trials?**

This is the only study focusing on post-exposure prophylaxis available in our county. In other words, after a person has had a high-risk exposure to someone with confirmed COVID-19, and the exposed person has not tested positive yet, this is an option to prevent the exposed person from becoming infected or seriously ill with coronavirus infection.

A person who receives a vaccine does so in the hope that he or she has future protection against COVID-19. The vaccinated person needs to wait for 4 to 6 weeks to develop protecting antibodies. A person who has a high risk of exposure to someone infected with COVID-19 needs protection immediately to avoid becoming infected and ill. Convalescent plasma therapy is intended to provide immediate protection to the exposed person through the passive infusion of neutralizing antibodies.

### **How does CP therapy work?**

Plasma is the yellow liquid portion of blood that contains proteins and antibodies produced by the body's immune system to fend off invasive pathogens. Most people who recover from COVID-19 develop antibodies (proteins that the immune system creates in response to infection) to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Plasma is collected from donors who have recovered from COVID-19 through a process called apheresis, which uses a special machine to separate the blood into different components. The plasma is removed and the remaining blood components (red blood cells, white blood cells, platelets) are returned to the donor's body.

Convalescent plasma is given through an infusion to persons who have had a high-risk exposure. The transfused convalescent plasma provides the SARS-CoV-2 antibodies that bind to the targeted coronavirus, stopping it from latching onto new cells and producing more viral particles. In short, it is a dose of antibodies coming from a person who has already recovered from COVID-19 to prevent an exposed individual from developing the infection or becoming ill.

### **What is considered a high-risk exposure to COVID-19?**

A high-risk exposure is when someone has had close contact with a person already diagnosed with COVID-19. For example, someone living in the same household, riding the same car, caring for someone, being at a party or not practicing appropriate precautions, such as wearing a mask and maintaining social distancing (six feet apart).

**CP therapy has been around for a long time, more than 100 years, but results have been mixed. It was used to some effect during the 1918 flu pandemic, but tests in**

## **2009 for the H1N1 flu produced no measurable benefit. What lessons have been learned? Are there any indicators that CP could be more effective in preventing SARS-CoV-2?**

We still need to accrue data to answer this question. Most studies have focused on the treatment of hospitalized patients with COVID-19 with different levels of disease severity. So far, the data are inconclusive due to underpowered studies and the lack of well-designed randomized placebo-controlled clinical trials. In other words, trials where neither the participant nor treating physician knows who is being infused with CP. This is the gold standard for clinical studies seeking to show efficacy.

We have learned three essential concepts so far from the Mayo Clinic study that transfused 35,000 hospitalized people with COVID-19. First, convalescent plasma is safe. Second, the time of transfusion matters. The Mayo clinic study observed the one-week mortality transfusion within three days of being diagnosed with COVID-19 rate was lower (8.7 percent) than for patients transfused with the therapy four days after diagnosis (11.9 percent). The earlier the treatment for the disease, the better. This is the rationale for the current post-exposure prophylaxis clinical trial.

Finally, third, the amount or concentration of neutralizing antibodies matters. The Mayo Clinic study also noted a 35 percent decrease in the risk of mortality (from 13.7 percent to 8.9 percent) when convalescent plasma containing high neutralizing antibody concentration was used compared with low concentrations. In this clinical trial for post-exposure prophylaxis, we use a high concentration of neutralizing antibodies.

### **If CP ultimately proves to provide significant preventive or therapeutic benefit, how do you imagine that treatment will look like in the future?**

If convalescent plasma proves to be effective to stem and prevent COVID-19, I can foresee that a person who has been exposed to COVID-19 can go to an urgent care or minute clinic to get a quick plasma transfusion to prevent COVID-19. The thinking is similar to taking medication when one feels like a migraine might be coming on. It's all about prevention or reducing ill effects.

This trial seeks to answer questions that have existed for more than a century. We depend upon community support — people who have been exposed — to participate and help us find answers, not just for this pandemic but to help us better prepare for the next.

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