# **COVID-19 Conversations**



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### COVID19Conversations.org #COVID19Conversations





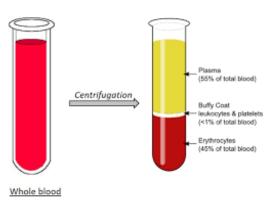
# Convalescent Plasma for Prophylaxis and Treatment of COVID19

Arturo Casadevall MD, PhD Johns Hopkins School of Public Health

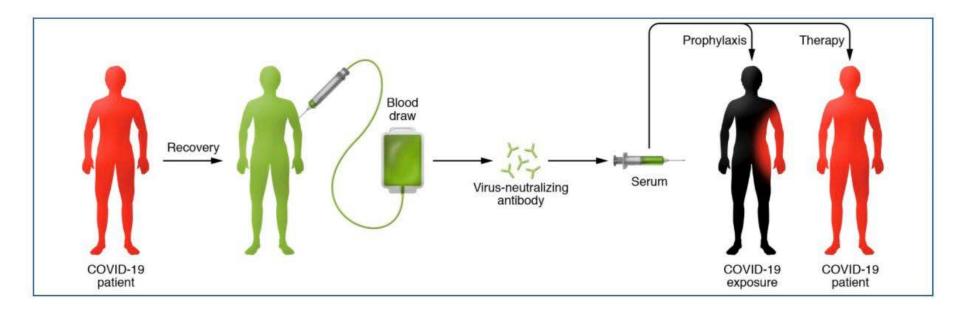
# What is convalescent plasma?

- Plasma is the liquid in the blood that holds the blood cells
- It is obtained by separating the cells from the liquid
- Differs from 'sera' in that it contains clotting factors
- Can be obtained from donors by plasmapheresis
- Obtained by standard transfusion practices





## Principles of Convalescent Plasma Usage



# Convalescent Serum (Plasma) used in past epidemics







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American	Journal of Dis	
Volume 71	JANUARY 19	1946
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## Specific Immunoglobulin (antibody) is the active component in convalescent plasma

- Pathogen (virus) specific immunoglobulin develops during late disease and early convalescent period.
- Immunoglobulin includes both IgM and IgG
- IgG half-life about 20 days
- Complex mixture of antibodies
- Effective immunoglobulins
  - Neutralizing antibody
  - Non-neutralizing antibody mediates antiviral functions through IgG receptor (antibody-dependent cellular cytotoxicity, ADCC; phagocytosis, complement activation)

# Convalescent Plasma for coronavirus disease

### SARS Coronavirus (2003)

Hong-Kong Study: 80 patients with SARS coronavirus infection treated with convalescent sera. A higher discharge rate among those treated with convalescen sera (58.3% vs 15.6%: P<0.001)

Y. Cheng · R. Wong · Y. O. Y. Soo - W. S. Wong · C. K. Lee · M. H. L. Ng · P. Chan · K. C. Wong · C. B. Leung · G. Cheng

### MERS Coronavirus

Anecdotal use – well tolerated but efficacy difficult to assess

### China uses Convalescent Plasma against COVID19

JAMA | Preliminary Communication

Treatment of 5 Critically III Patients With COVI

**JAMA 2020** 

### Effectiveness of convalescent pla COVID-19 patients

PNAS 2020

Journal Pre-proof

**CHEST 2020** 

Treatment with convalescent plasma for critically ill patients v

### Italy Uses Convalescent Plasma against COVID19

Covid, la terapia col plasma funziona. Già dieci i pazienti che sono migliorati, due addirittura dimessi



Di redazione - 2 Aprile 2020



Coronavirus, aumentano i contagi a Mantova. Ma il plasma dai donatori dà i primi risultati



Dopo cinque giorni di calo nuovo rialzo dei contagiati: + 115. La terapia applicata su 12 pazienti: otto sono già migliorati

### Two Publications with Convalescent Plasma Information

### The convalescent sera option for containing COVID-19

#### Arturo Casadevall<sup>1</sup> and Liise-anne Pirofski<sup>2</sup>

First published March 13, 2020 - More info

As of early 2020, humanity is confronting a pandemic in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 causes coronavirus disease, abbreviated as COVID-19. At the time of this writing, SARS-CoV-2 is spreading in multiple countries, threatening a pandemic that will affect billions of people. This virus appears to be a new human pathogen. Currently there are no vaccines, monoclonal antibodies (mAbs), or drugs available for SARS-CoV-2, although many are in rapid development and some may be available in a short time. This Viewpoint argues that human convalescent serum is an option for prevention and treatment of COVID-19 disease that could be rapidly available when there are sufficient numbers of people who have recovered and can donate immunoglobulin-containing serum.

### Deployment of convalescent plasma for the prevention and treatment of COVID-19

Evan M. Bloch,<sup>1</sup> Shmuel Shoham,<sup>2</sup> Arturo Casadevall,<sup>3</sup> Bruce S. Sachais,<sup>4</sup> Beth Shaz,<sup>4</sup> Jeffrey L. Winters,<sup>5</sup> Camille van Buskirk,<sup>5</sup> Brenda J. Grossman,<sup>6</sup> Michael Joyner,<sup>7</sup> Jeffrey P. Henderson,<sup>8</sup> Andrew Pekosz,<sup>3</sup> Bryan Lau,<sup>9</sup> Amy Wesolowski,<sup>9</sup> Louis Katz,<sup>10</sup> Hua Shan,<sup>11</sup> Paul G. Auwaerter,<sup>2</sup> David Thomas,<sup>2</sup> David J. Sullivan,<sup>3</sup> Nigel Paneth,<sup>12</sup> Eric Gehrie,<sup>1</sup> Steven Spitalnik,<sup>13</sup> Eldad Hod,<sup>13</sup> Lewis Pollack,<sup>14</sup> Wayne T. Nicholson,<sup>7</sup> Liise-anne Pirofski,<sup>15</sup> Jeffrey A. Bailey,<sup>16</sup> and Aaron A.R. Tobian<sup>1</sup>

First published April 7, 2020 - More info

### **COVID19 Convalescent Plasma Protocol**

 Suggest completion of donor history questionnaire during pre-donation screening to

avoid unnecessary deferral for reasons that

are unrelated to COVID-19 (e.g. risk of transfusion-transmissible infections)



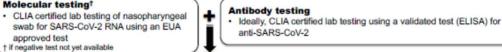
 Diagnosis of SARS-CoV-2 infection/COVID-19 Positive test for SARS-CoV-2 using an EUA approved molecular assay

≥14 days following resolution of symptoms

#### Pre-donation screening: Clinical provider\*

- Clinical assessment that no sign of active infection (i.e. afebrile, no reported symptoms for ≥14 days)
- Negative result for SARS-CoV-2 by nasopharyngeal (NP) swab or molecular testing of blood
- · Serum in red top serum separator tube collection for anti-SARS-CoV-2

#### Molecular testing<sup>†</sup>



#### Negative NP swab for SARS-CoV-2 RNA Seropositive anti-SARS-CoV-2: optimal titer >320

Contact donor and coordinate referral to collections site (e.g. blood center) **Collections: Blood center Criteria for donation** · Satisfies ALL eligibility criteria for community blood donation based on standard donor history questionnaire Collections 450-600mL (if apheresis-collected) plasma (frozen within 24hrs of collection) · Label per IND; quarantine pending results of standard TTI testing

- · Routine donor testing
- Transfusion-transmitted infections
  - HLA antibody screening (female donors)

Negative routine blood donor screening results

#### **Transfusion: ABO compatible**

Needs dedicated recipient consent that explains both general risks of blood products as well as specific --albeit uncertain- risks of convalescent plasma e.g. Transfusion Related Acute Lung Injury (TRALI)

- · Antibody Dependent Enhancement of infection
- Transmission of SARS-CoV-2 (theoretical)



https://www.nbcnews.com/health/health-news/plasma-treatmentbeing-tested-new-york-may-be-coronavirus-gamechanger-n1178436

# FDA Actions (www.fda.gov)

- March 24 Compassionate use of convalescent plasma allowed
- April 3, 2020. Hopkins granted permission of clinical trials of convalescent plasma in high risk individuals
- April 3, 2020. FDA allows Expanded Access to Convalescent Plasma for the Treatment of Patients With COVID-19
- April 8, 2020. Recommendations for Investigational COVID-19 Convalescent Plasma (https://www.fda.gov/vaccines-bloodbiologics/investigational-new-drug-ind-or-device-exemption-ideprocess-cber/recommendations-investigational-covid-19convalescent-plasma)

# Risks

### Known

- Transfusion reaction
- Infectious disease

### Theoretical

• Antibody pro-inflammatory reaction

Risk-Benefit analysis suggests Benefits >> Risk for all age groups. Bloch et al. JCI 2020

# **Current Status**

- Compassionate use being done USA
- Many countries deploying convalescent plasma (UK, France, Italy, Spain, Argentina, Panama...etc)
- Clinical trials in preparation Prophylactic use Early therapeutic use Late therapeutic use Pediatric protocol
- Major problem logistical Plasma is scarce commodity



# **Donation Information**

Red Cross New York Blood Center Specific institutions (Mt Sinai in NYC, Methodist in Houston, Hopkins) ccpp19.org

# **Closing thoughts**

Convalescent plasma history provides strong encouragement for use

Convalescent plasma supported by strong theory of antibody action

Plasma therapy is relatively safe (as safe as transfusion practices)

Efficacy against COVID19 Anecdotal evidence and patient case series encouraging Need randomized control trials to know if, when and how to use

Challenge today: LOGISTICAL, LOGISTICAL, LOGISTICAL...will get easier.