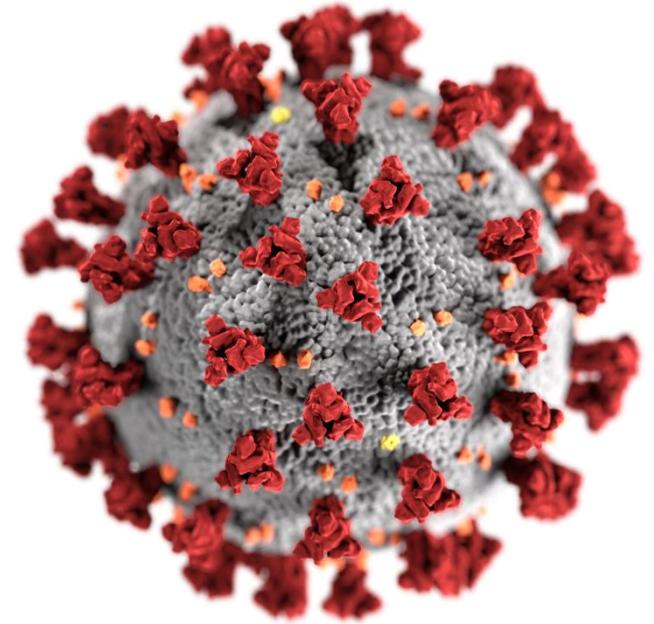
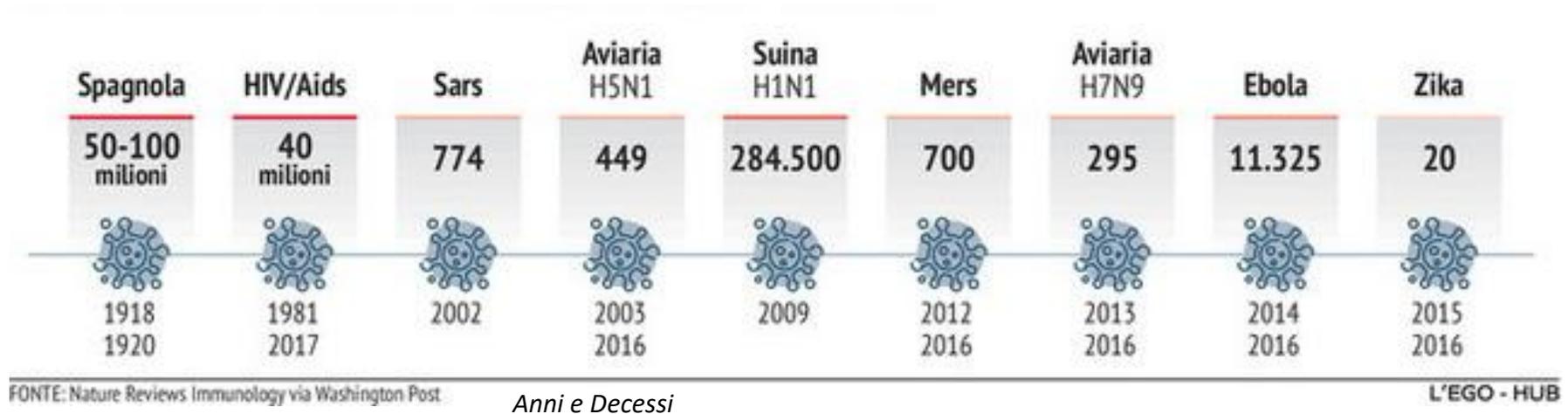


SARS-CoV-2 Virus



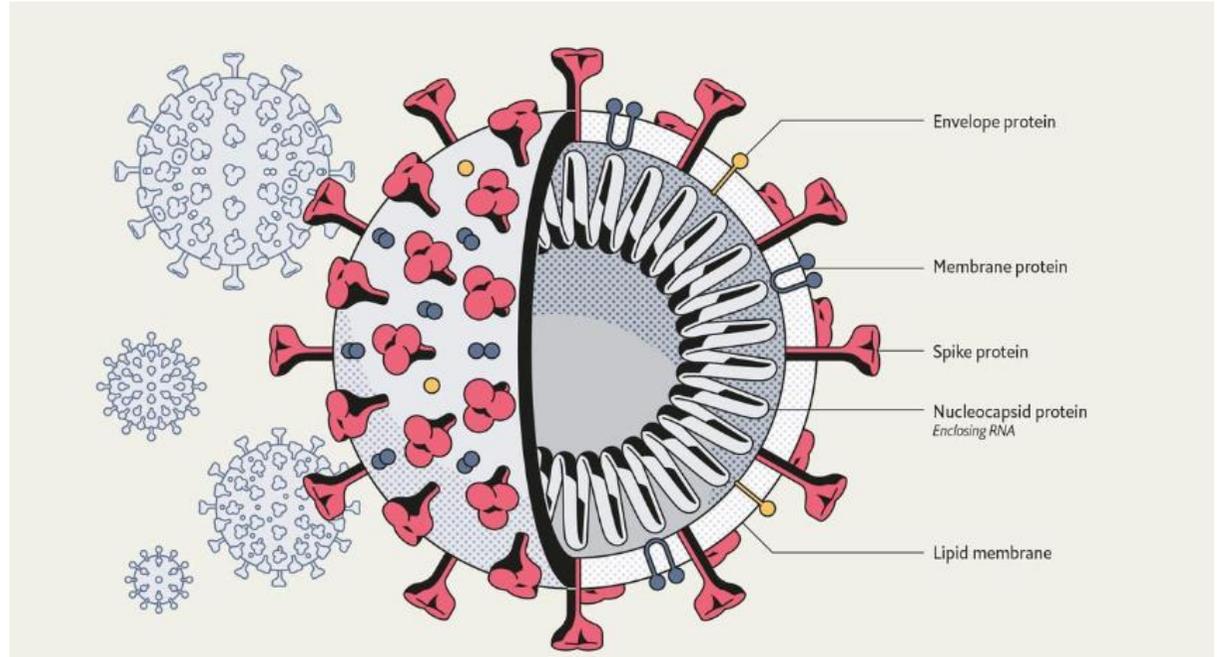
Pandemics in recent history

It is not a new event, as history shows:



SARS-CoV-2 Virus

The SARS-CoV-2 Virus consists of four different proteins and a single stranded RNA.



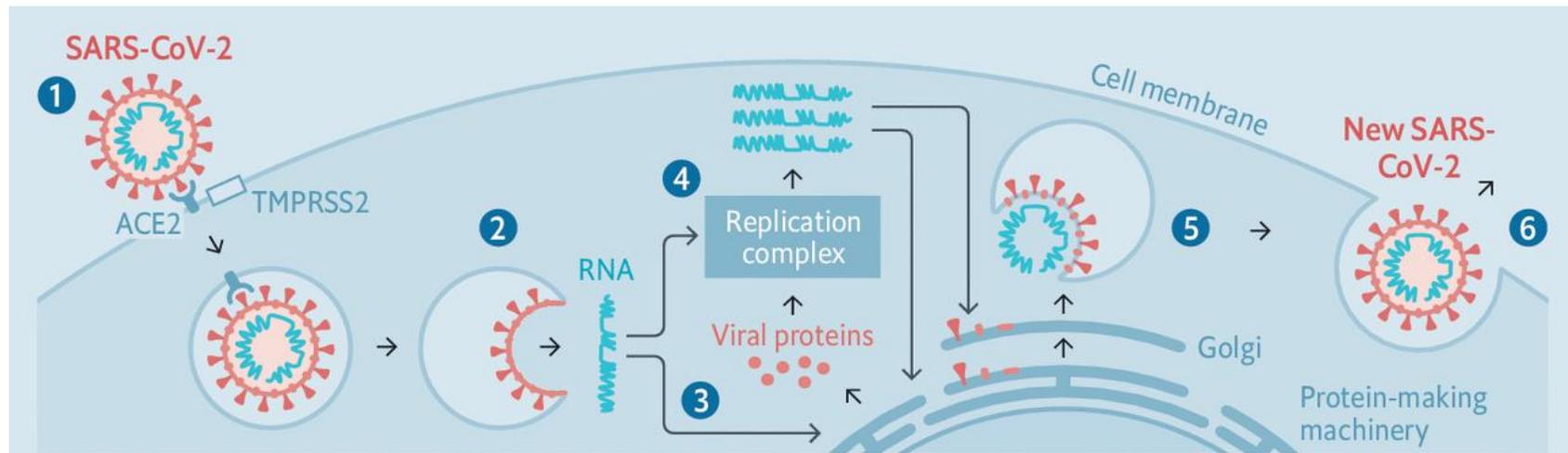
90 nm diameter:

The Virus is a million times smaller than the cells that get infected

How is the virus transmitted and reproduced?

As all viruses, even SARS-CoV-2, containing only strands of RNA and not DNA, cannot reproduce on its own.

To do this, the virus must to penetrate a host cell, use its genetic heritage and win against the guest immune system.



How to fight the virus?

1. «Reducing viraemia»

Environmental disinfections, physical barriers, personal protective equipment,
Antiviral drugs

1. «With antibodies»

Vaccine

Synthetic immunoglobulins?

Convalescent Plasma or Hyperimmune

2. «Fighting the effects»

Anti-inflammatory and anti-cytokines drugs;

Extracorporeal blood purification therapies

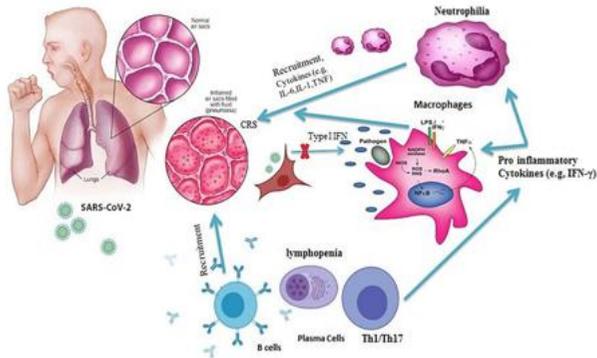
Anti- thrombotic approaches

Our Therapeutic Solutions

Strengthen the immune system

The role of the Immune System

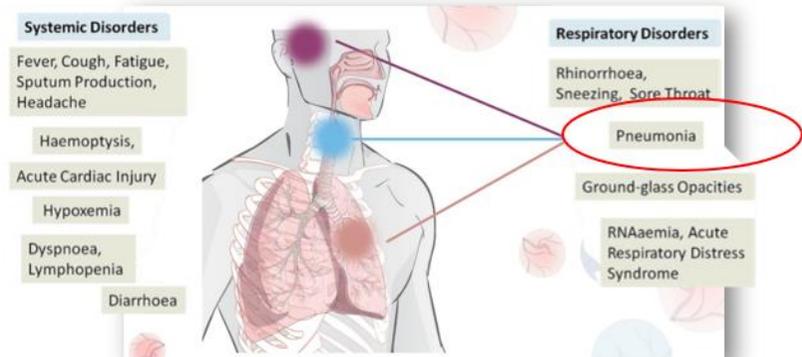
The hyperimmune plasma «concentrated»



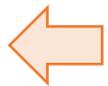
Fighting the effects

The effects of Covid-19

...How to contain the evolution:



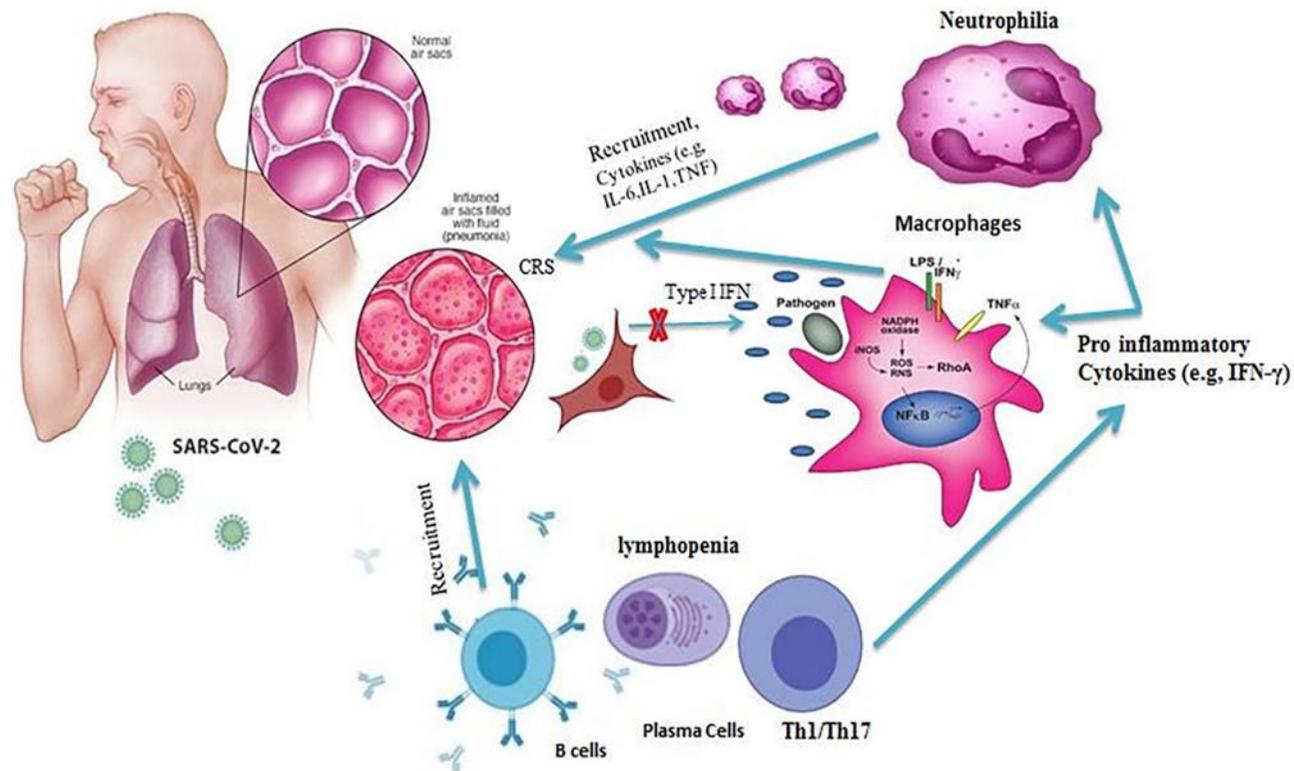
Not only lungs..



Introduction

The role of the Immune System

The hyperimmune plasma «concentrated»



The hyperimmune plasma «concentrated»

Rational:

- Hyperimmune plasma, obtained from «*recovered patients*», it has already been used in previous pandemics;
- Evidence in literature shows that the use of «*convalescent plasma*» or «*hyperimmune plasma*» taken from patients who recovered from Covid-19, can be used to improve the course of critically ill patients with active disease;
- This effect appears to be linked to the development of antibodies, in the blood of such patients, against the Sars-CoV-2 virus capable of suppressing virulence.

Double Filtration Plasmapheresis (DFPP) and Cascade Filtration (CF) allow the automatic filtering and concentration of antibodies from the donor's convalescent plasma with low risk of adverse reactions and loss of «good» components.

Hyperimmune plasma

-Plasma sampling from *convalescent patient* from at least 28 days (virus negative).

-Plasma donation to a compatible patient.

-To date, the technique in use provides the administration (repeatable) of 200 - 600 ml of hyperimmune plasma, with the aim to increase the antibody response of the recipient.

The Hyperimmune Plasma «concentrated»

Double Filtration Plasmapheresis(DFPP) or Cascade Filtration (CF)

Collection of **Concentrated Antibodies**

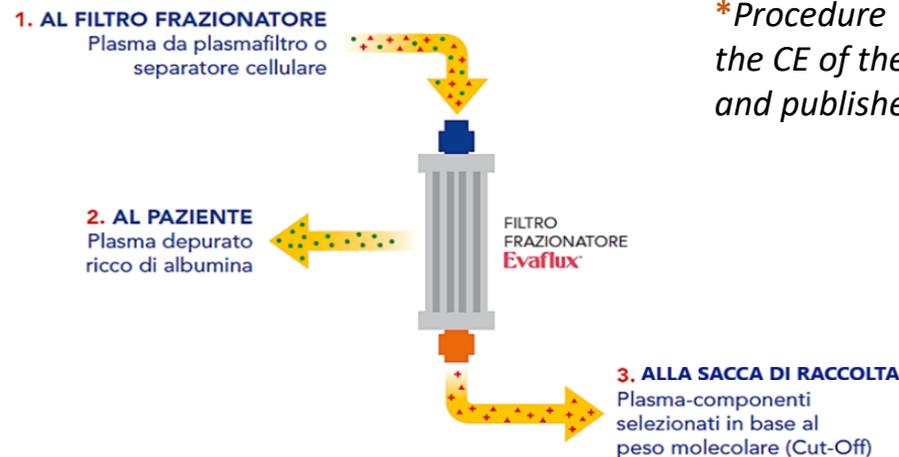
Low risk of **Adverse reactions**

Low loss of **Good components**

The hyperimmune plasma «concentrated»*

The role of the Double Plasmapheresis Filtration (DFPP)/Cascade Filtration (CF)

- Automatic filtering and concentration of antibodies from the donor's "convalescent plasma" in a sterile bag, to be subsequently infused to positive **COVID-19 patients**;
 1. For the donor patient: Reduction of the risk of adverse reactions and loss of 'noble', components, such as albumine, compared to normal Plasmapheresis.
 2. For the recipient patient: this procedure allows to infuse to the patient a more important quantity of antibodies which are 3-5 times more concentrated than a standard «convalescent plasma» donation procedure.

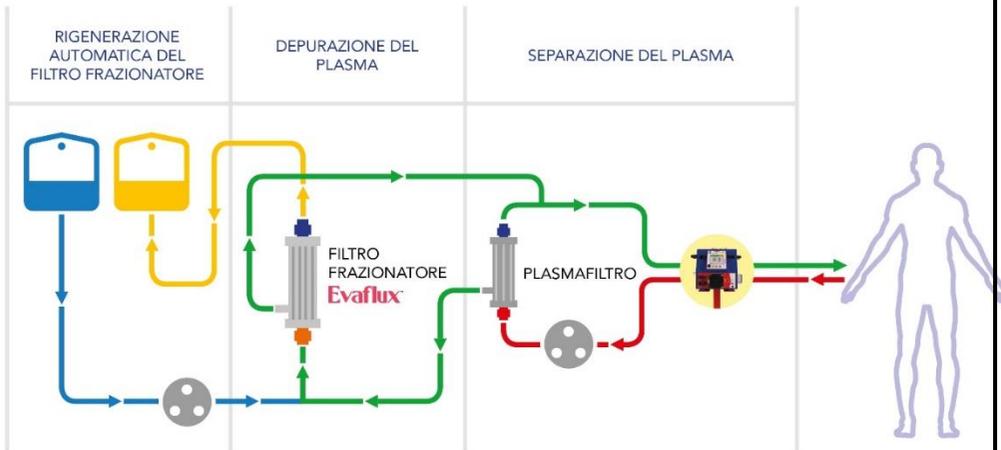


**Procedure approved for Covid-19 patients by the CE of the Giovanni XXIII Hospital (Bergamo) and published on : clinicaltrials.gov*

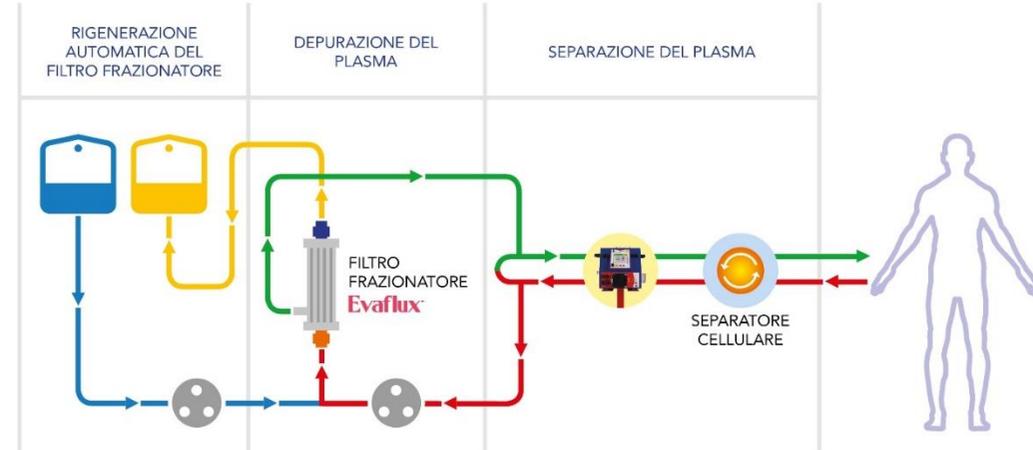
The hyperimmune plasma «concentrated»

Two treatment options:

Double Filtration Plasmapheresis (DFPP) From plasmafilter



Cascade Filtration (CF) From a cell separator

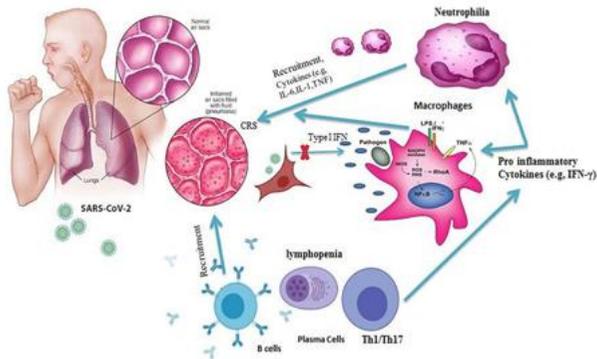


Our Therapeutic Solutions

Strengthen the immune system

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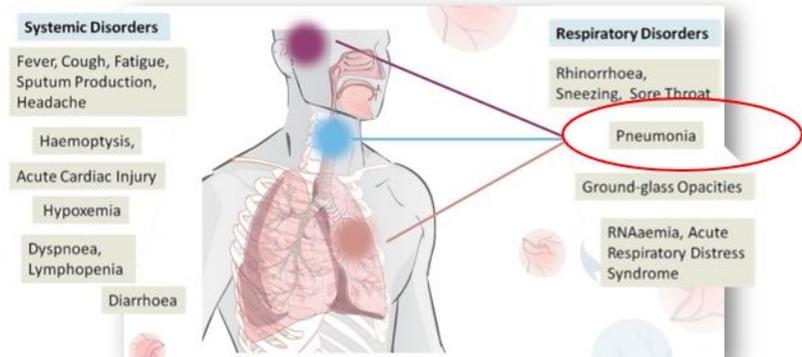
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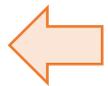
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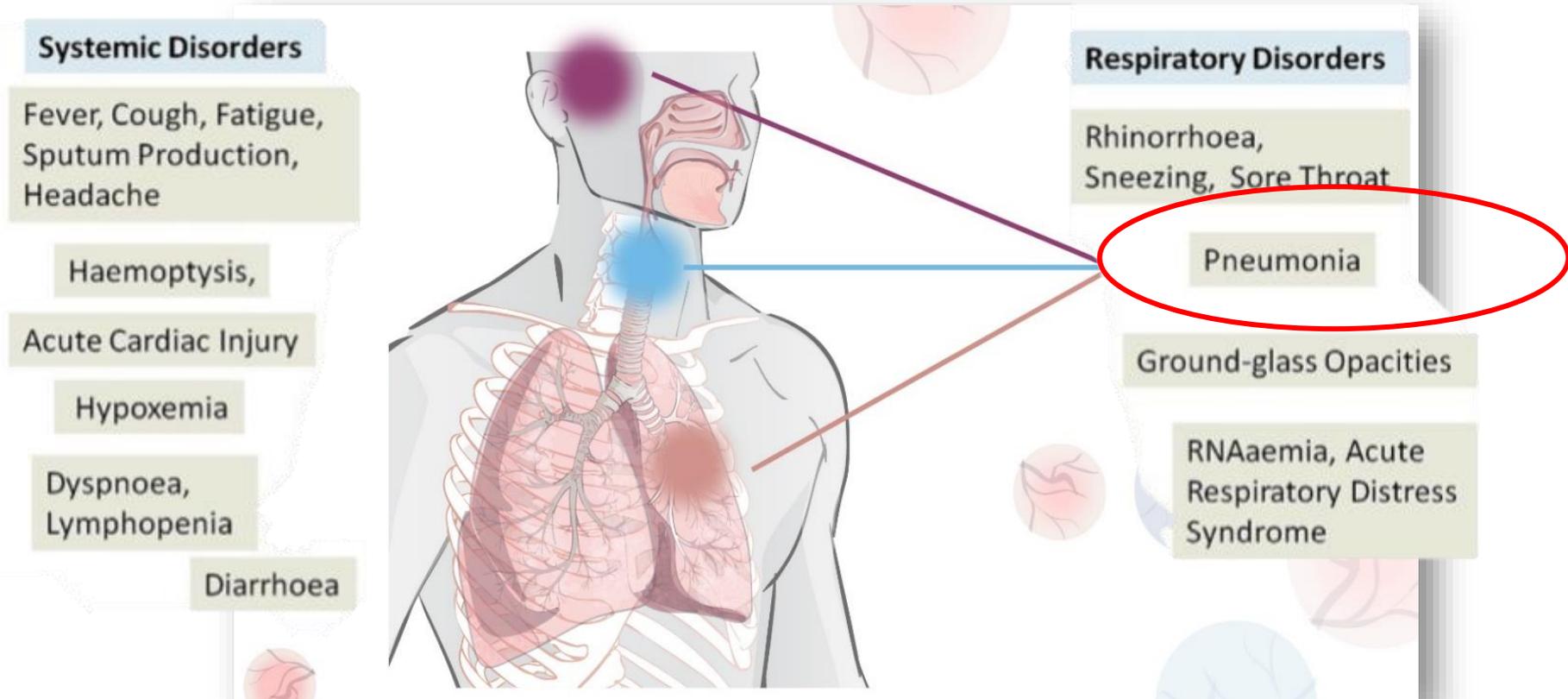
Not only lungs..



Introduction

The effects of Covid-19

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Cytokine storm: The role of inflammation

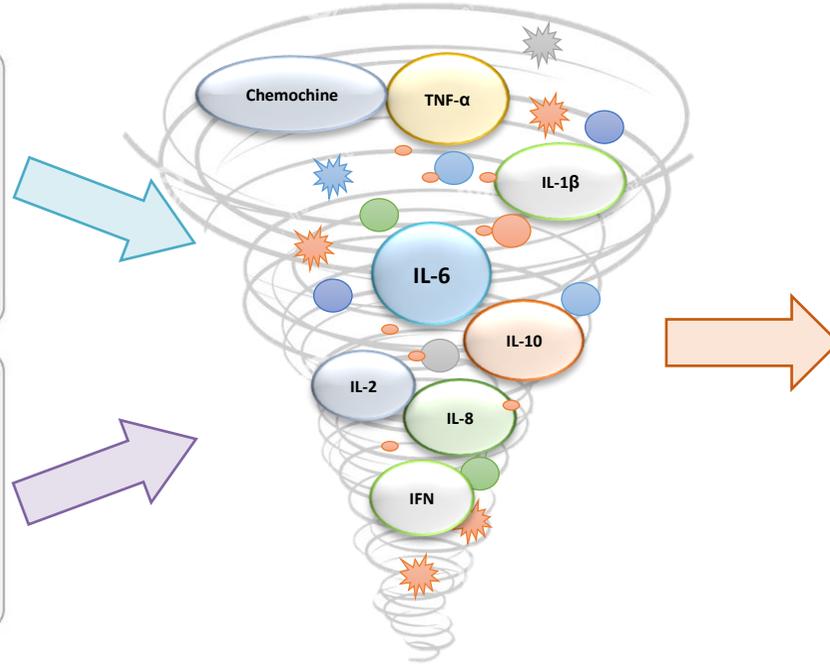
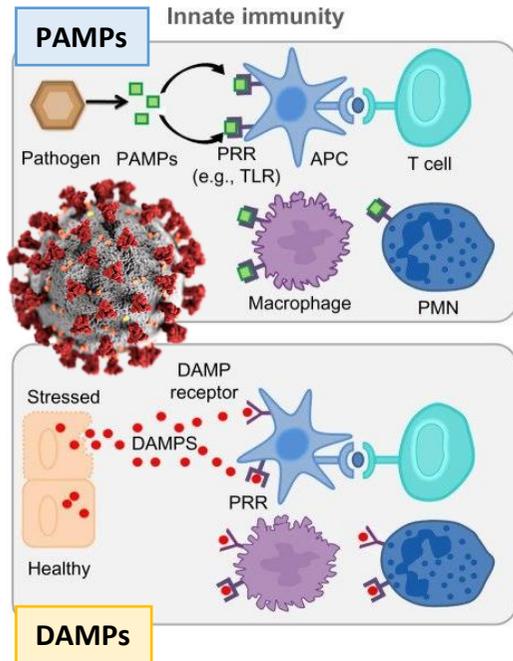
Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Cytokine Storm Syndrome

Cytokine storm syndrome is a hyperinflammatory state that is characterized by fulminant multi-organ failure and elevation of cytokine levels. A recent study from China showed that COVID-19 is associated with a cytokine elevation profile that is reminiscent of secondary hemophagocytic lymphohistiocytosis (HLH) (44).

Cytokine Storm

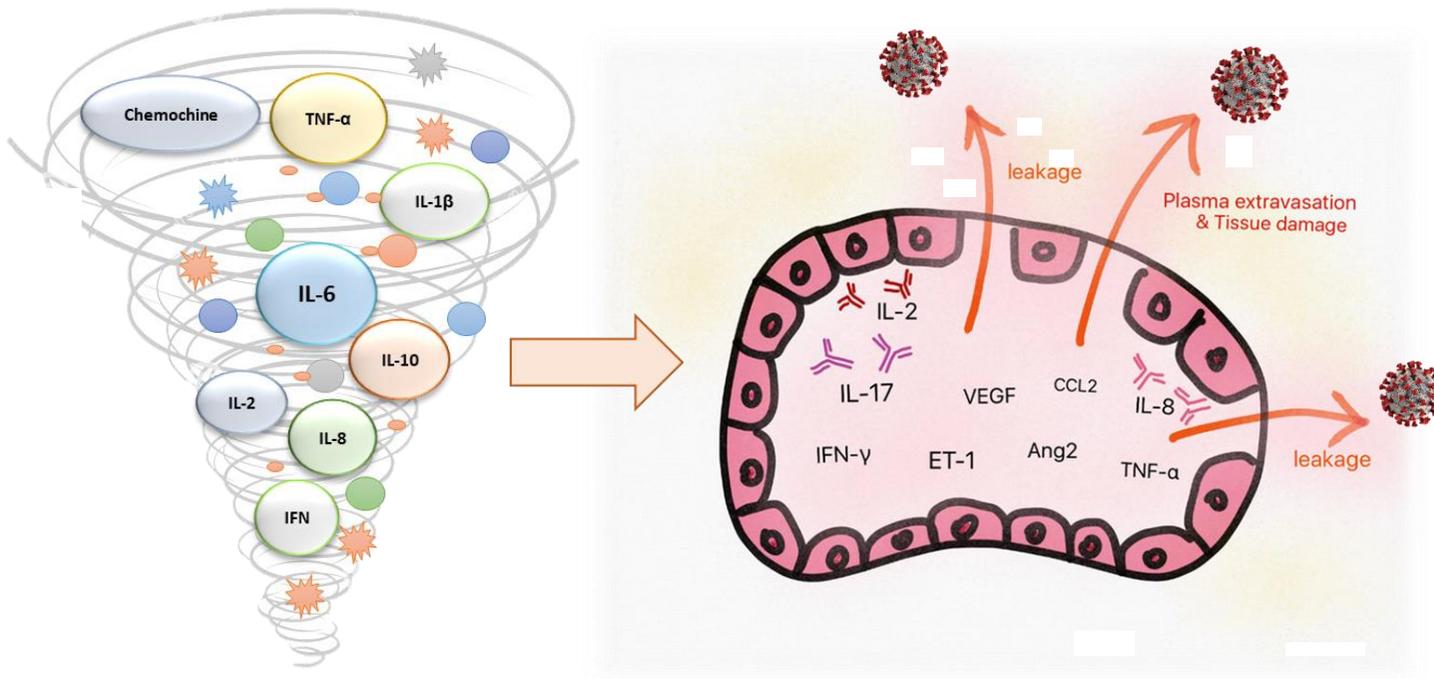
- Activation of an immune response by the body to defend itself from the virus.
 - Release of mediators and inflammation factors, endothelial cells, leukocytes to respond to the insult
- Cytokine Storm** → **'uncontrolled response'** to inflammation that involves all organs.
In Covid-19 the trigger is the SARS Cov-2 virus.



«Capillary Leak Syndrome»

The Cytokine storm causes the loss of capillary selectivity and the consequent passage of liquids in the interstitial space.

Defense mechanism to disperse the «intruder...»



«Capillary Leak Syndrome»



- Extravasation of liquids
- Alveolar damage

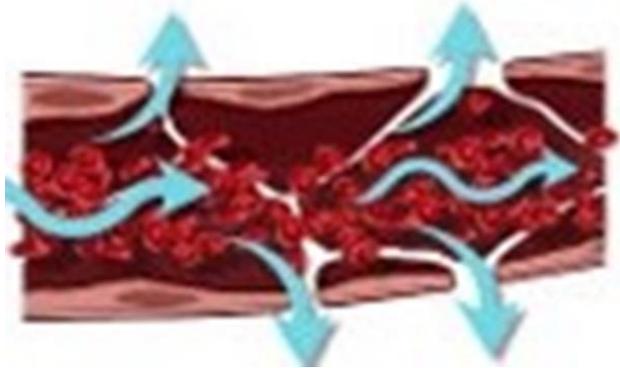
PULMONARY EDEMA



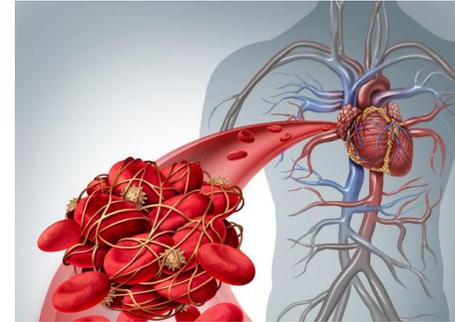
- Edema
- ARDS



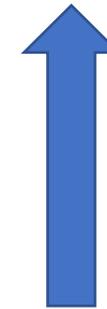
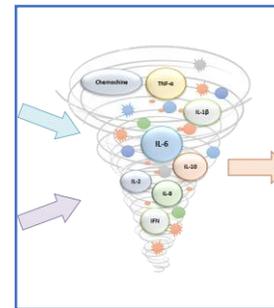
Capillary Leak, hemoconcentration and thromboembolism



The loss of fluids leads to hemoconcentration



Thromboembolism



That with the inflammation



Modulation of «cytokine storm»



The modulation of the «*cytokine storm*» determines a reduction of inflammation, endothelial protection, and, consequently, can lead to a better control of the formation of edema, pulmonary infiltrations and thromboembolic processes

CytoSorb to deal with the effects of Covid-19

Rationale for use

- **Guidelines:**
 - Brescia Renal Covid Task Force.
 - Zhejiang University School of Medicine, Cina
 - **EUA F.D.A. USA**

*Based on bench performance testing and reported clinical experience,
FDA has concluded
that the CytoSorb device may be effective at treating certain patients
with confirmed COVID-19 by removing various pro-inflammatory cytokines from their blood.*

*FDA believes, based on the totality of scientific evidence available,
that the removal of pro-inflammatory cytokines may ameliorate cytokine storm and in turn, provide
clinical benefit...*

*...there is no adequate, approved, and available alternative to the emergency use of the CytoSorb device
for the treatment of these COVID-19 patients....."*

How to use Cytosorb

I.F.U approved by F.D.A.

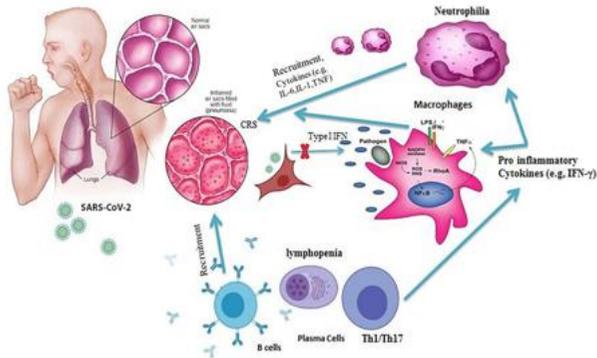
- Day 1: Change Cytosorb every 12 hours;
- Day 2: Change Cytosorb every 24 ore hours;
- Day 3: Change Cytosorb every 24 hours;
- Clinical evalutation after 72 hours of use to determine if the patient is receiving clinical benefits for continue therapy.

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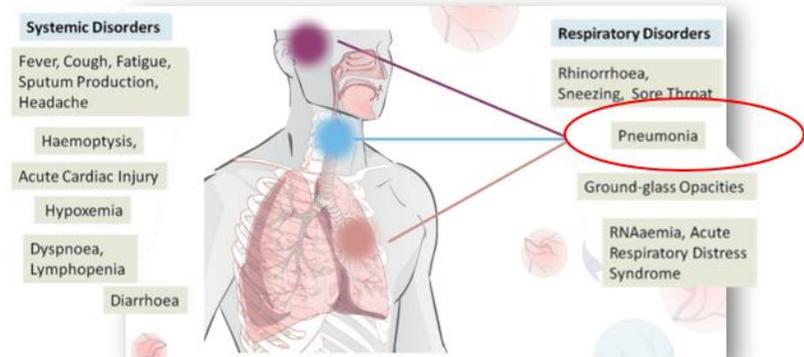
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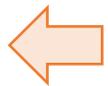
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