



**UNDERSTANDING & TREATING
SPIKE PROTEIN-INDUCED DISEASES**

October 14-16, 2022 • Orlando, Florida

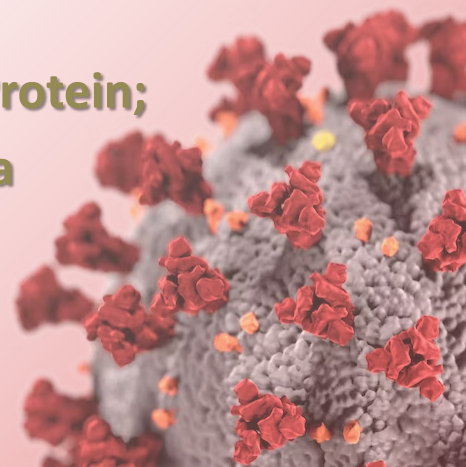
COVID-19:

An Endothelial and Vascular Disease

**Covid Associated Coagulopathy
Pathology of the S1 Subunit of the Spike Protein;
Microclots; and Local Tissue Hypoxia**

Presented By:

Jordan F. Vaughn MD



Figured it out in Spring of 2020



Dr Jaco Laubscher

Specialities
Physician (Internal Medicine)

MEDICLINIC



Stellenbosch, South Africa



Core competencies

Cardiology, Intensive Care



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Posted to You Tube: June 8, 2020

Standing of the Shoulder of and Special Thanks to:

Prof. Etheresia Pretorius
Department of Physiological Sciences
Stellenbosch University



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Standing of the Shoulder of and Special Thanks to



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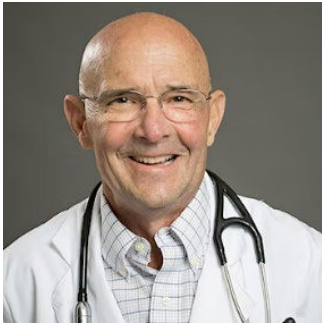
<http://dbkgroup.org/publications/>



Simple Metaphor for Patients

It is kind of like:

My Father= **SARS-CoV2**



Play with

My 4yo and 6yo Boy =
Immune System



@

My House =
My Body/Organ Systems Etc



Simple Metaphor for Patients

What Really Happens:

My 4yo and 6yo Boys act
like themselves
= Immune System Over
Activation

My Father Plays with the boys
= SARS-CoV2 Replication



My House is a mess=
Organ System dysfunction at
every level inside and out.

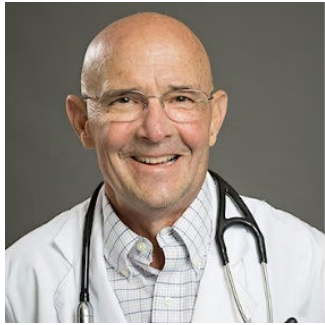


Simple Metaphor for Patients

To Fix it:

Father Leaves to go
home to eat with
mom =

SARS-CoV2 Clearance



Put the 4yo and 6yo Boy
to bed = **Immune System
Down Regulation**



*Used Stock Photo from Web Given I have never
actually seen my kids do this.*

Clean up the Mess in My House =
**Clearance of Microvascular
Sludge, Inflammatory Cytokines,
Auto antibodies, etc**



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Overview

COVID-19 as an Endothelial and Vascular Disease

Spike Protein Injury: From Vaccines to PASC/Long COVID

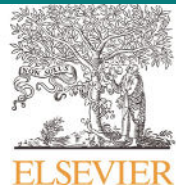
PASC/Long COVID/Vaccine Induced Spike Injury or Persistent Spike Symptoms

Consequences in blocking capillaries

What can we do about it?

Initial Vascular Hypothesis is result of Respiratory Anomalies

- Severely hypoxic patients despite relatively normal lung compliance and minimal auscultatory findings on exam
- Increased reports of thrombotic complications
- Poor Outcome of Patients that Progress to Full ARDS Despite Optimal ARDS Treatment.
- Consistent Autopsy Findings of thrombi in the microcirculation of the lung.



Trends in Cardiovascular Medicine

journal homepage: www.elsevier.com/locate/tcm



COVID-19 – A vascular disease

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ARTICLE INFO

Keywords:

Endothelium
Coagulation
Thrombosis
Inflammation
Microvessels

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leads to multi-system dysfunction with emerging evidence suggesting that SARS-CoV-2-mediated endothelial injury is an important effector of the virus. Potential therapies that address vascular system dysfunction and its sequelae may have an important role in treating SARS-CoV-2 infection and its long-lasting effects.

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[Trends Cardiovasc Med.](#) 2021 Jan; 31(1): 1–5.

Published online 2020 Oct 14. doi: [10.1016/j.tcm.2020.10.005](https://doi.org/10.1016/j.tcm.2020.10.005)

Vascular Hypothesis: Treatment Implications

- Management of the Hypercoagulable State in COVID-19 is Imperative to Good Outcomes
- Therapeutic blocking of the enzymatic pathway of coagulation needed.
- Therapeutic blockade of platelets with antiplatelet therapy.
- Addressing V/Q Mismatch with Pulmonary Vasodilators etc?

Overview

COVID-19 as an Endothelial and Vascular Disease

Spike Protein Injury: From Vaccines to PASC/Long COVID

PASC/Long COVID or Persistent COVID Symptoms

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What can we do about it?

S1 SPIKE PROTEIN ALONE can catalyse fibrinaloid formation

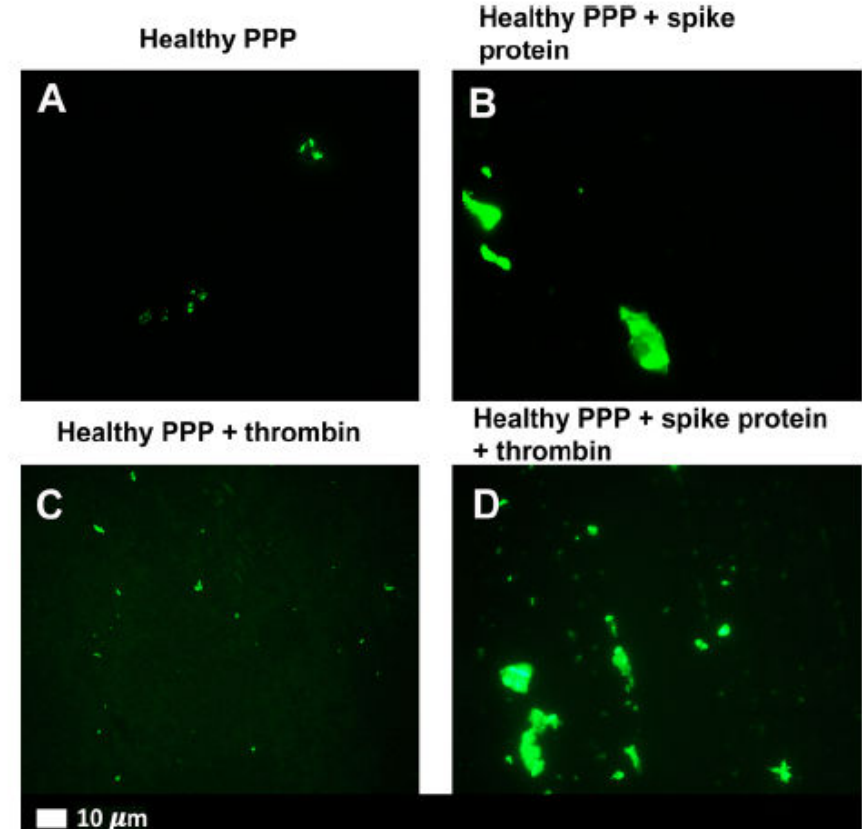
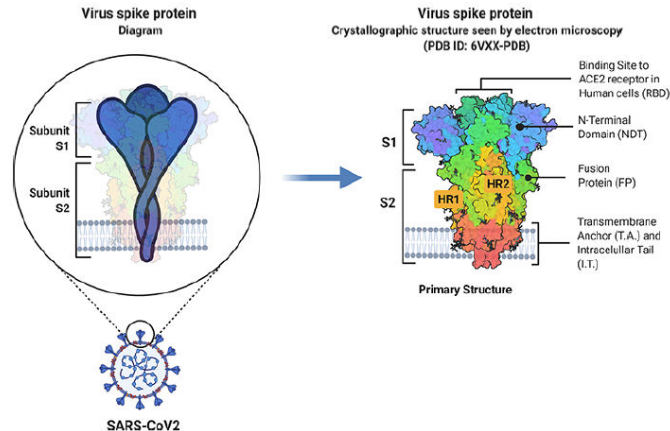
Bioscience Reports (2021) 41 BSR20210611
<https://doi.org/10.1042/BSR20210611>



Research Article

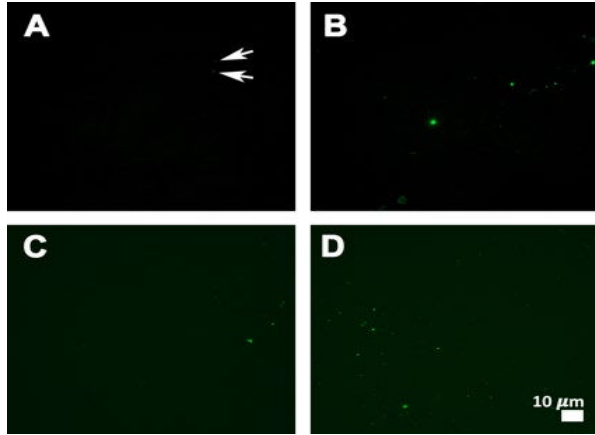
SARS-CoV-2 spike protein S1 induces fibrin(ogen) resistant to fibrinolysis: implications for microclot formation in COVID-19

Lize M. Grobbelaar¹, Chantelle Venter¹, Mare Vlok², Malebogo Ngoepe^{3,4}, Gert Jacobus Laubscher⁵, Petrus Johannes Lourens⁵, Janami Steenkamp^{1,6}, Douglas B. Kell^{1,7,8} and Ethersia Pretorius¹

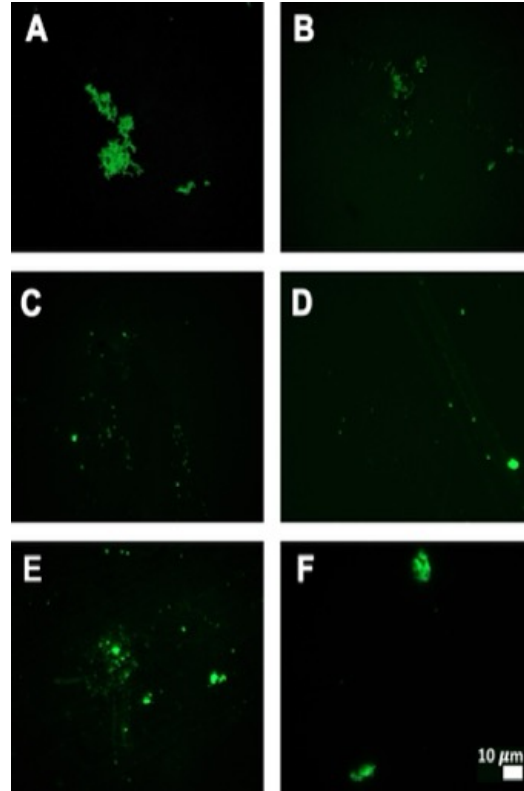


Structural Changes in Fibrin(ogen)

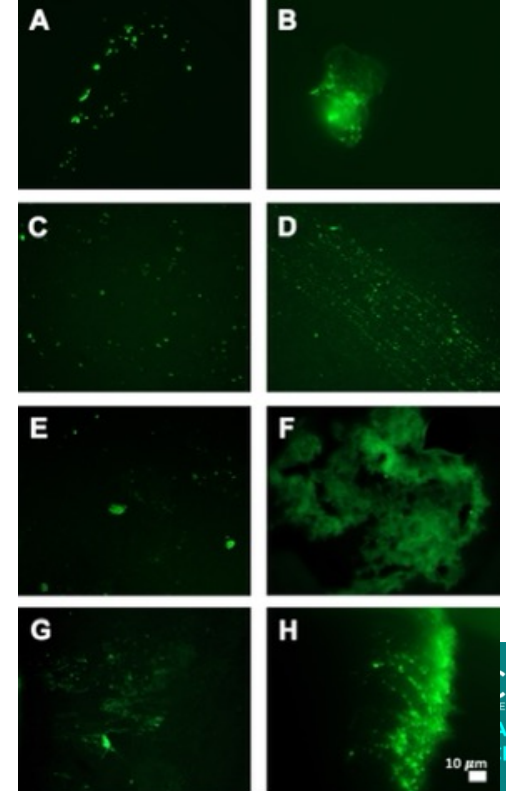
- **Healthy Plasma**



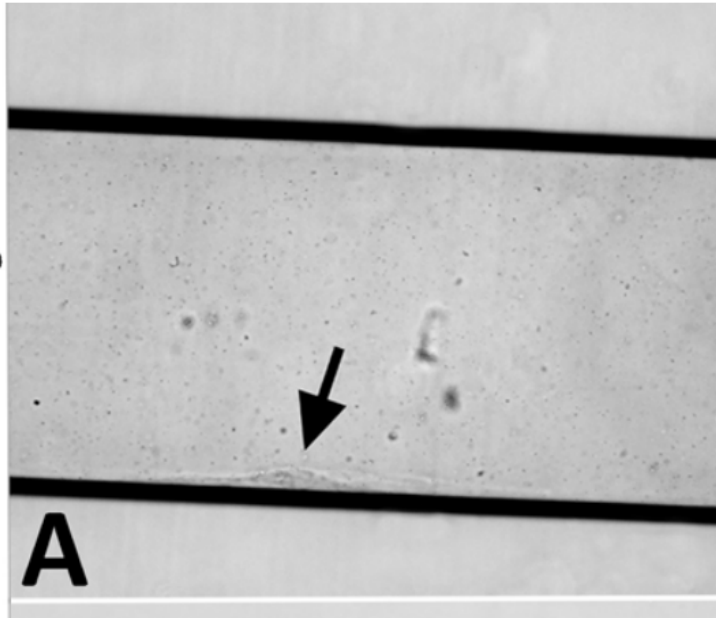
Type 2 Diabetes Plasma



COVID-19 Plasma

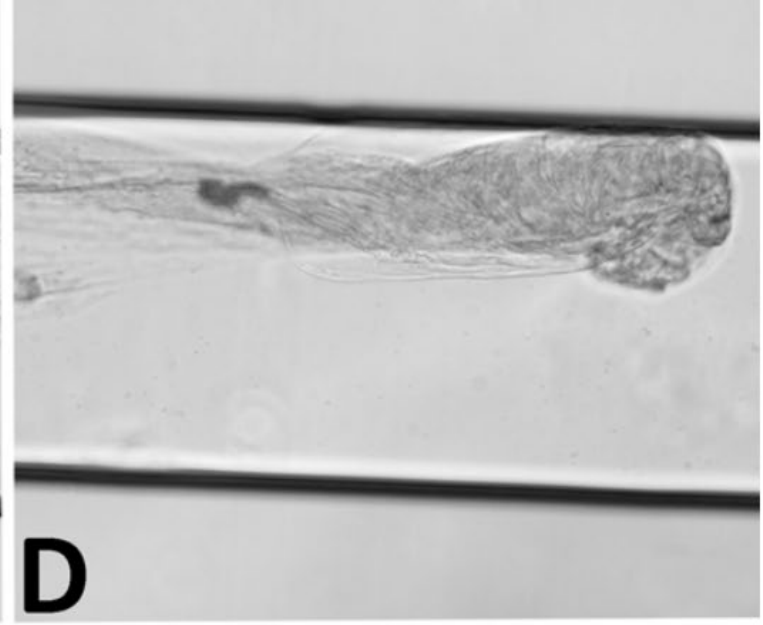
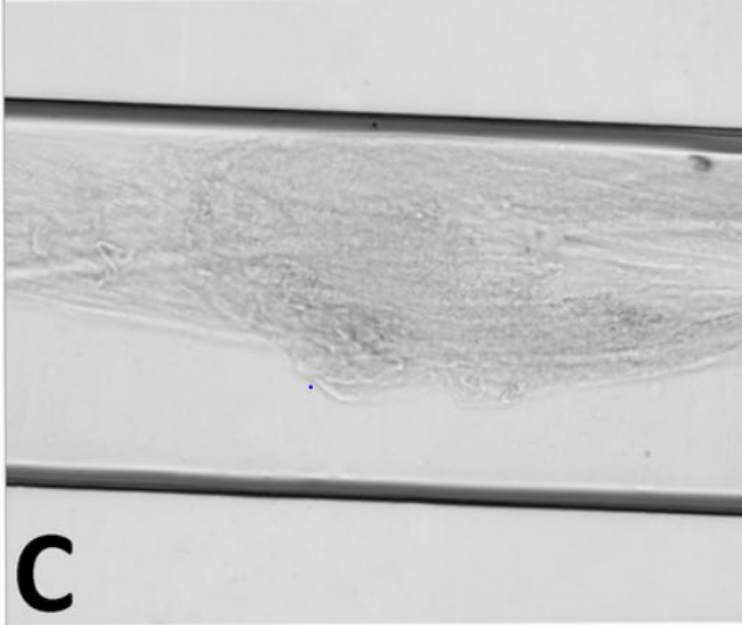


Healthy PPP



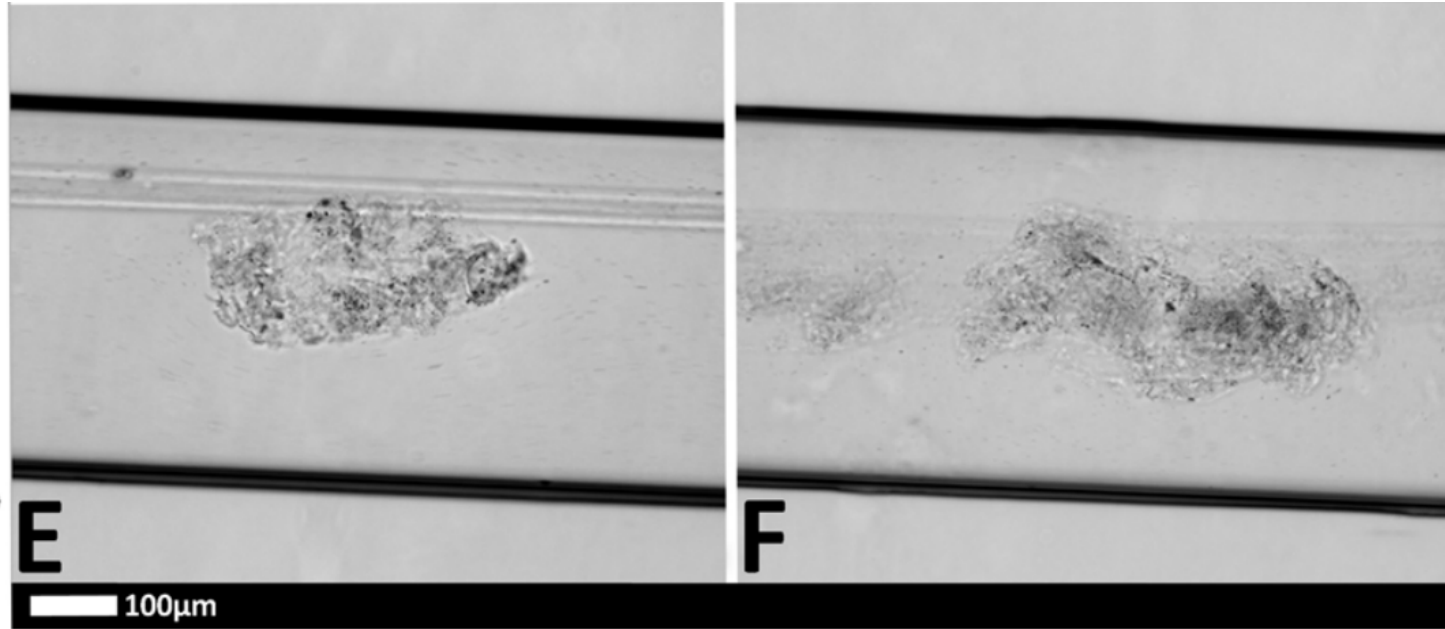
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COVID-19



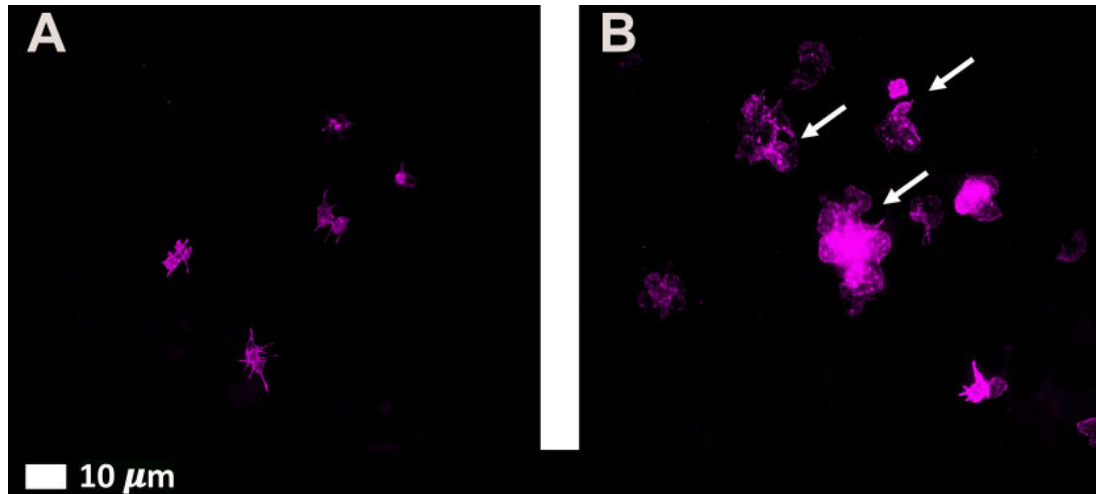
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Spike Protein



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<https://doi.org/10.1042/BSR20210611>

FLUORESCENCE MICROSCOPY MICROGRAPHS OF PLATELETS, BEFORE AND AFTER EXPOSURE TO SPIKE PROTEIN



Fluorescence microscopy micrographs of platelets, before and after exposure to spike protein (A) Representative platelets from hematocrit incubated with fluorescent marker, CD62P-PE. (B) Representative micrographs showing activated platelets after exposure to spike protein. The white arrows point to hyperactivated activated platelets. White arrows show hyperactivated platelets clumping together.

Overview

COVID-19 as an Endothelial and Vascular Disease

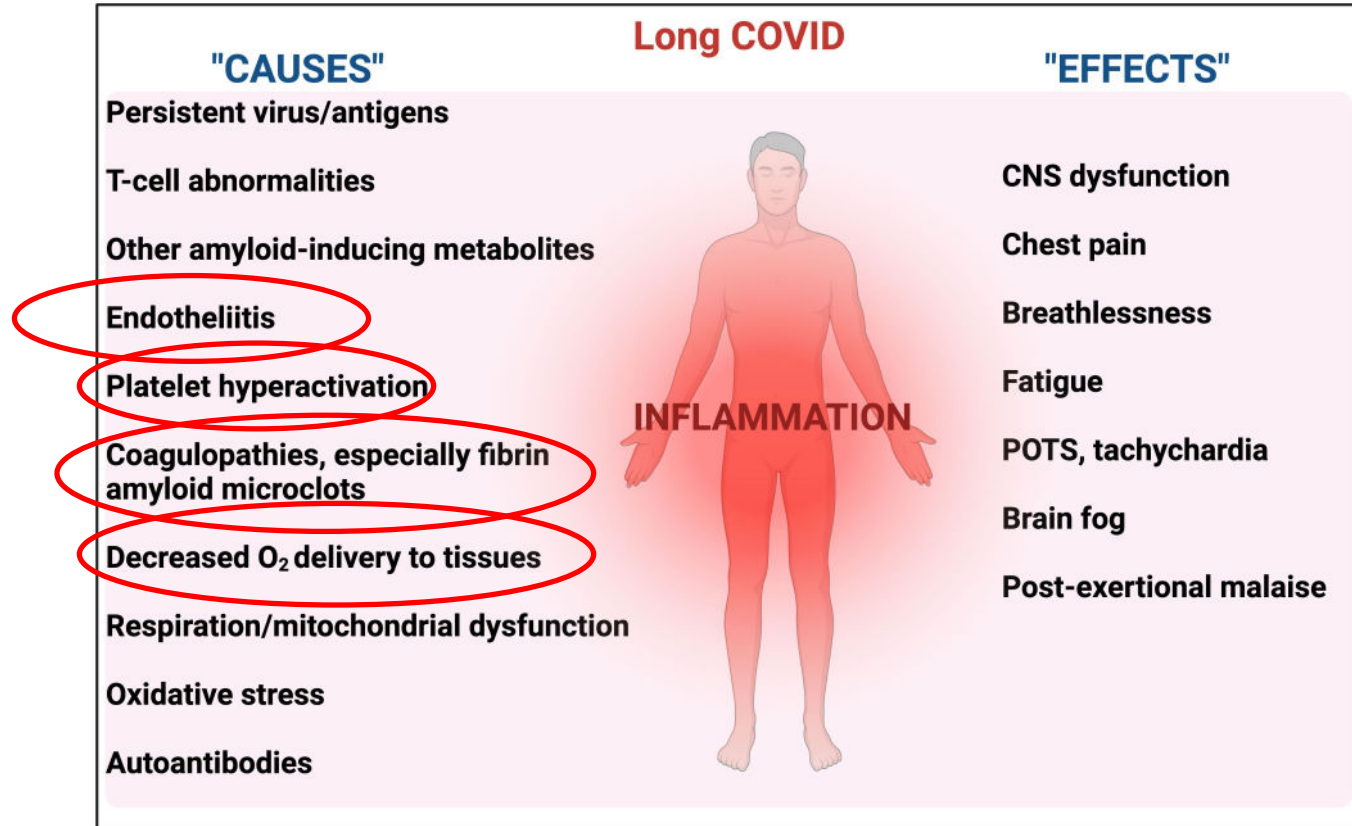
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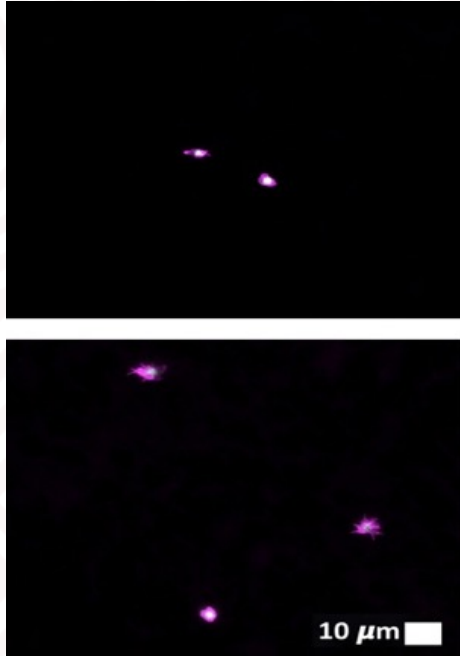
What can we do about it?

Persistent Spike Protein manifestations

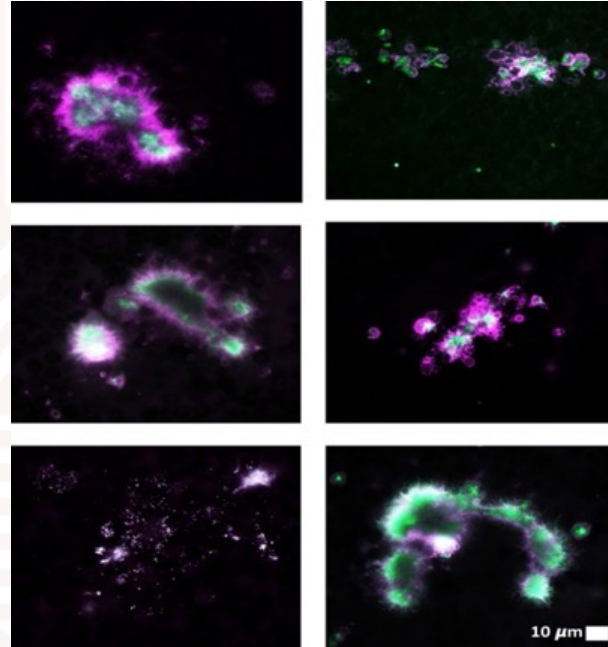


Platelet ultrastructure

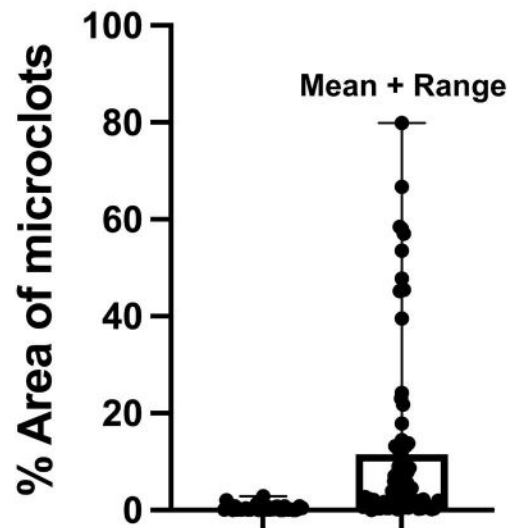
Platelets from Healthy
Individuals



Platelets from Individuals
with Long COVID



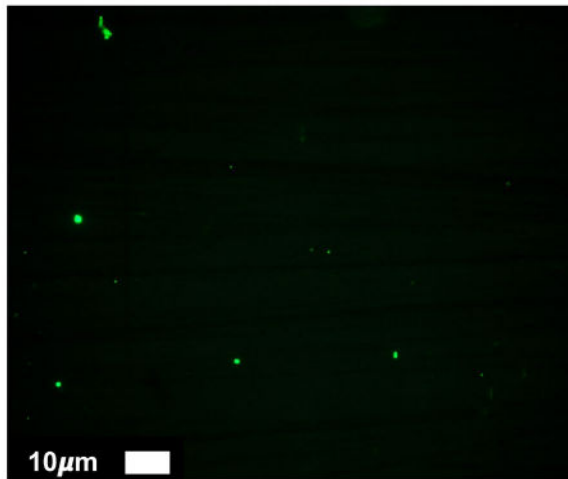
% Microclot area per analysed micrograph



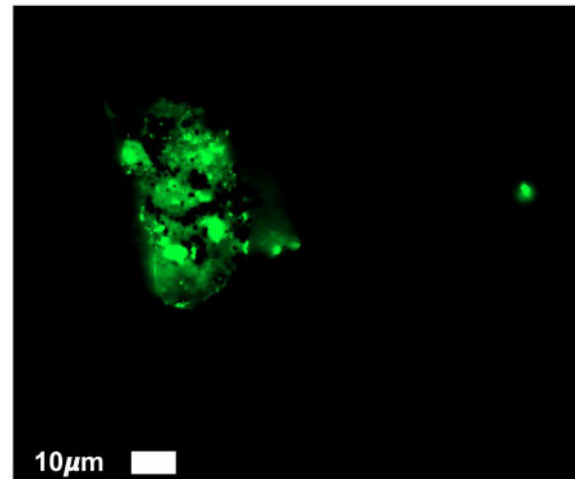
Healthy participants
COVID-19 participants

**Microclots
typically
2-200 μm**

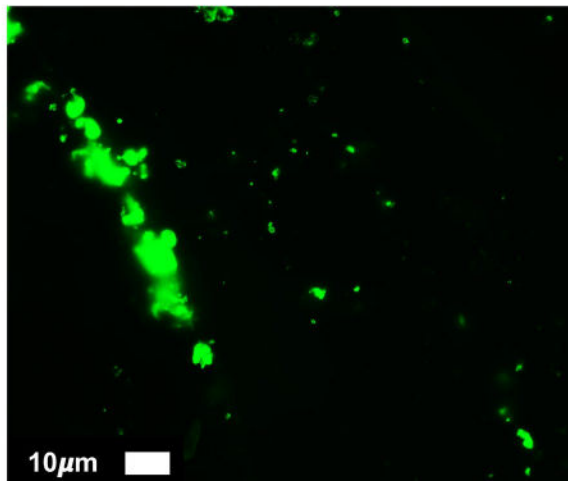
Microclots in a healthy participant



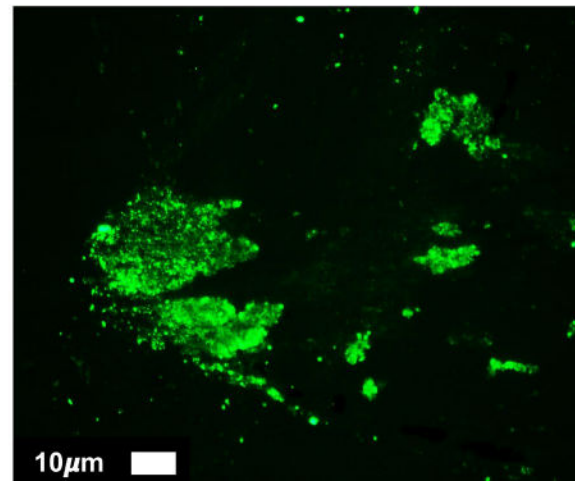
Microclots in acute COVID-19



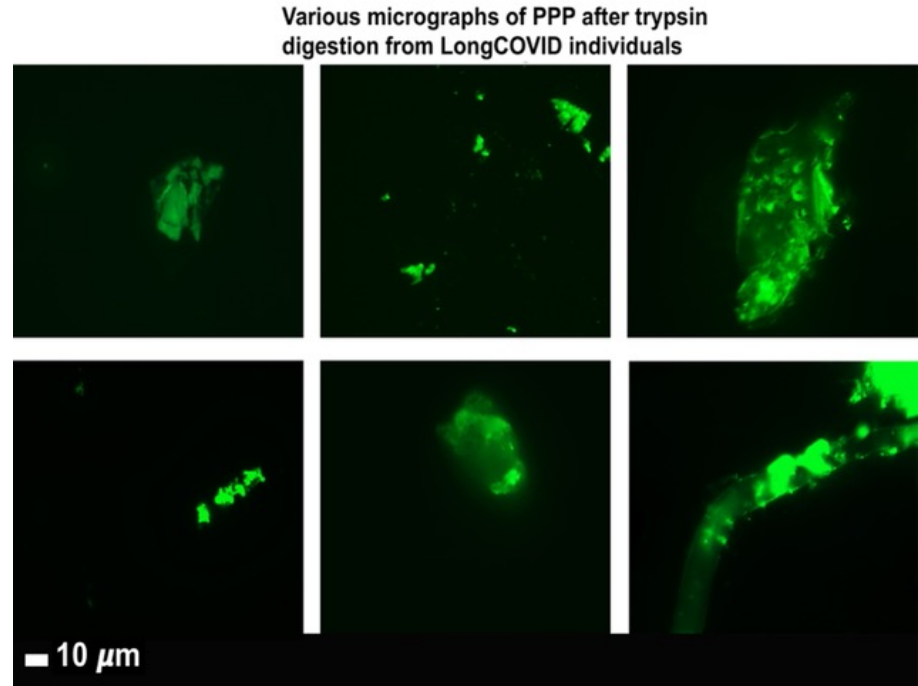
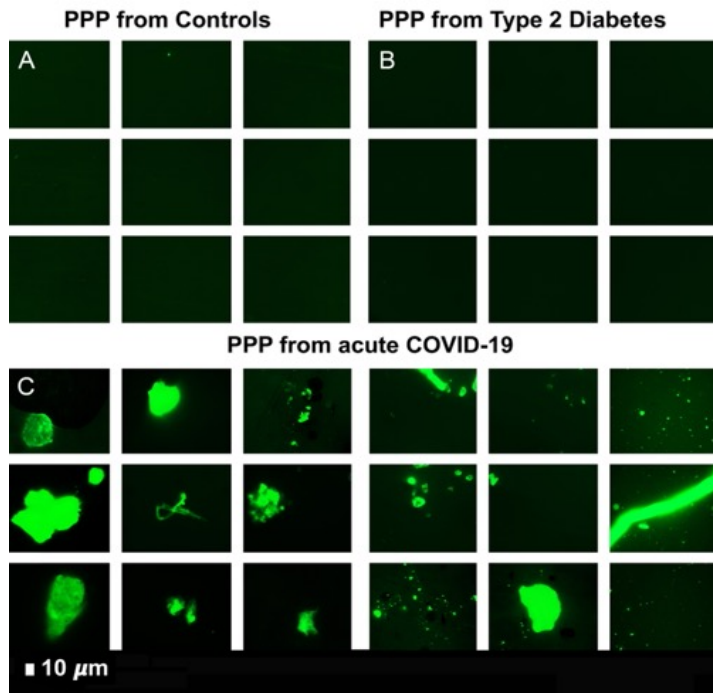
Microclots in acute COVID-19



Microclots in Long COVID



Microclots remaining in Acute COVID-19 and Long COVID after 1st digestion step



Pretorius E, Vlok M, Venter C, et al. 2021 Persistent clotting protein pathology in Long COVID/ Post-Acute Sequelae of COVID-19 (PASC) is accompanied by increased levels of antiplasmin. *Cardiovascular Diabetology*

Microclot Proteomics Analysis

Kruger A, Vlok M, Turner S, Venter C, Laubscher GJ, Kell DB, Pretorius E. Cardiovasc Diabetol. 2022 Sep 21;21(1):190. doi: 10.1186/s12933-022-01623-4. PMID: 36131342; PMCID: PMC9491257.

Digested pellet deposits (microclots) from acute COVID-19 samples vs digested plasma from Control samples

These proteins are present in both sample types; and a fold change value more than 1 = the protein that more prevalent inside the digested pellet deposits from COVID-19 samples. These proteins were concentrated inside the digested pellet deposits.

Protein name	Fold change	P-value
→ von Willebrand Factor	4.5	0.02
Complement component C4b	4.1	0.05
C-reactive protein	18.7	0.003

Digested pellet deposits from Long COVID/PASC microclots samples vs digested plasma from Control samples

These proteins are present in both sample types; and a fold change value more than 1 = the protein that more prevalent inside the digested pellet deposits from Long COVID/PASC samples. These proteins were concentrated inside the digested pellet deposits.

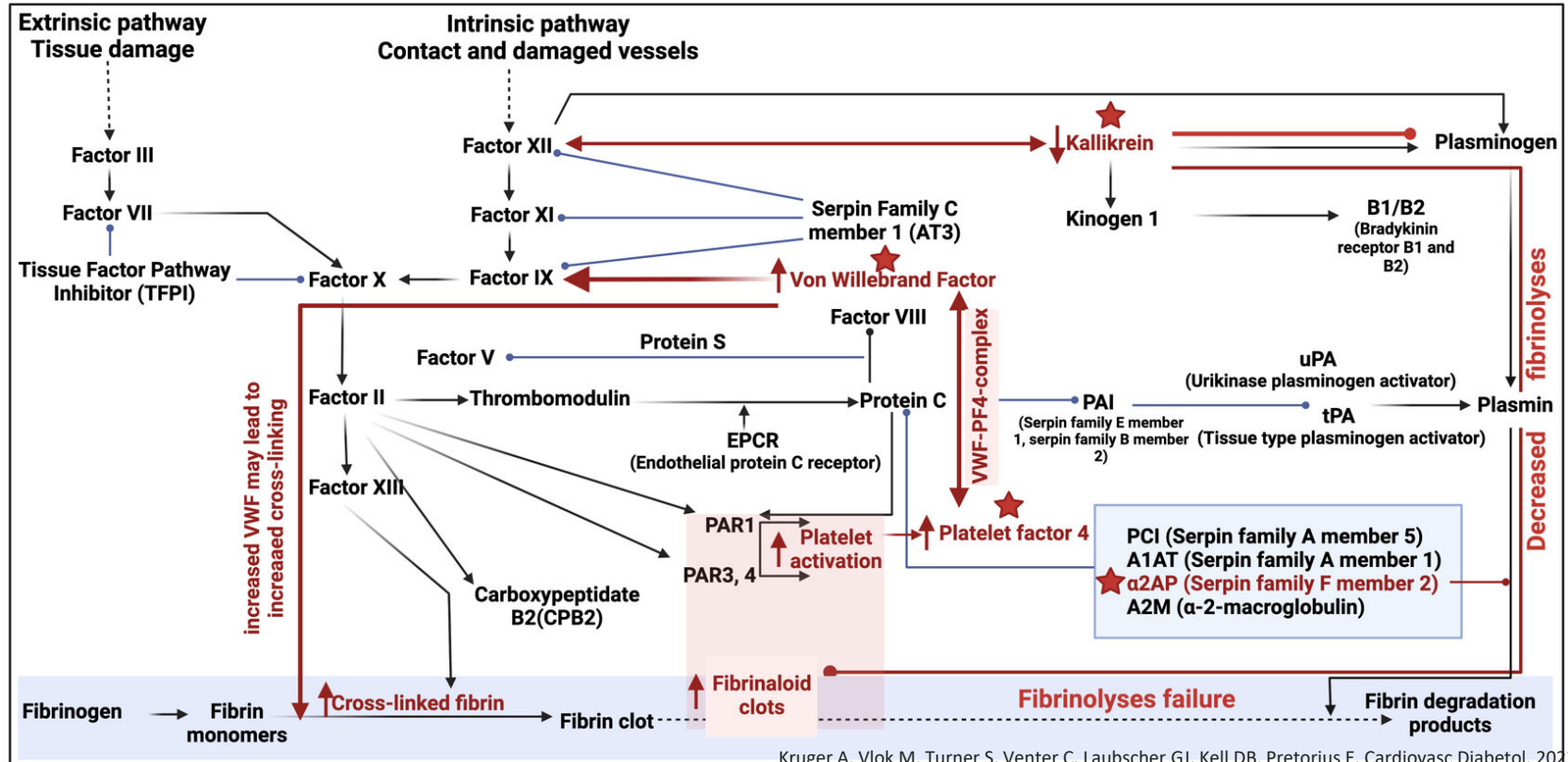
→ Coagulation factor XIII A chain	6.9	0.001
→ Plasminogen	3	0.001
→ Fibrinogen alpha chain	4.1	0.0001
→ α2 antiplasmin (α2AP)	7.9	0.0002
→ von Willebrand Factor	10.2	0.001
→ C-reactive protein	11.2	0.007
→ Serum Amyloid A (SAA4)	17.5	0.01
→ Complement component C7	20	0.0002

Digested pellet deposits from Long COVID/PASC microclots samples vs digested pellet deposits (microclots) from acute COVID-19 samples

These proteins are present in both sample types; and a fold change value more than 1 = the protein that more prevalent inside the digested pellet deposits from Long COVID/PASC samples. These proteins were concentrated inside the digested pellet deposits.



→ Plasminogen	2.3	0.0007
→ Fibrinogen B chain	2.8	0.007
→ Coagulation factor XIII B	2.7	0.01
→ Fibrinogen α chain	3.1	0.0002
→ Complement component C6	7.5	0.01
→ α2 antiplasmin (α2AP)	9.2	0.0003
→ Complement factor 1	25	0.0009

2022 Proteomics Analysis





Increased levels of inflammatory molecules in blood of Long COVID patients point to thrombotic endotheliitis

Simone Turner, Caitlin Naidoo, Thomas Usher, Arneaux Kruger, Chantelle Venter, Gert J Laubscher, M Asad Khan,
 Douglas B Kell,  Ethersia Pretorius

doi: <https://doi.org/10.1101/2022.10.13.22281055>

This article is a preprint and has not been certified by peer review [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

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Posted October 13, 2022.

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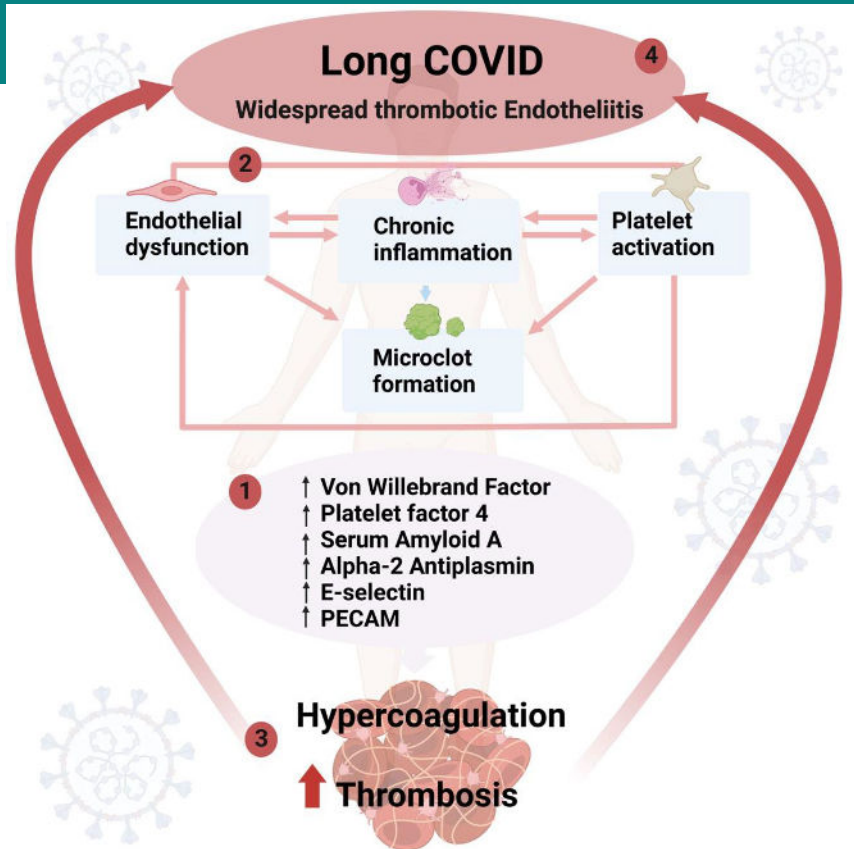
 [Data/Code](#)

Table 2: Inflammatory molecule concentration [or % antigen in the case of Von Willebrand Factor (VWF)] data of 15 controls and 25 Long COVID patients. Parametric data is expressed as Mean (SD), and non-parametric data as Median(Q1-Q3). **Abbreviations:** SD: standard deviation.

Inflammatory molecule	Reference range	Controls (n=15): Mean (SD) OR Median (Q1-Q3)	Long COVID(n=25): Mean (SD) OR Median (Q1-Q3)	Unit	P-value
SAA	0-10	5.3(1.9-8.0)	6.9(4.8-17.25)	mg.L ⁻¹	*p<0.05
α-2AP	60-80	71.73(±18.48)	90.28(±11.31)	mg.L ⁻¹	**p<0.01
PF4	197-1390	484.2(412.8-526.8)	572.4(430.6-779.9)	ng.ml ⁻¹	*p<0.05
VWF	55.9 - 161.6	76.6(±28.03)	104.8(±60.1)	%	*p<0.05
E-selectin	8.5-26	10.26(±3.07)	13.86(±5.4)	ng.ml ⁻¹	**p<0.01
PECAM-1	5.3-15	8.19(7.06-10.08)	10.27(8.32-11.45)	ng.ml ⁻¹	*p<0.05

Increased levels of inflammatory molecules in blood of Long COVID patients point to thrombotic endotheliitis.

Simone Turner, Caitlin Naidoo, Thomas Usher, Arneaux Kruger, Chantelle Venter, Gert J Laubscher, M Asad Khan, Douglas B Kell, Etheresia Pretorius medRxiv 2022.10.13.22281055; doi: <https://doi.org/10.1101/2022.10.13.22281055>



Increased levels of inflammatory molecules in blood of Long COVID patients point to thrombotic endotheliitis. Simone Turner, Caitlin Naidoo, Thomas Usher, Arneaux Kruger, Chantelle Venter, Gert J Laubscher, M Asad Khan, Douglas B Kell, Etheresia PretoriusmedRxiv 2022.10.13.22281055; doi: <https://doi.org/10.1101/2022.10.13.22281055>

Overview

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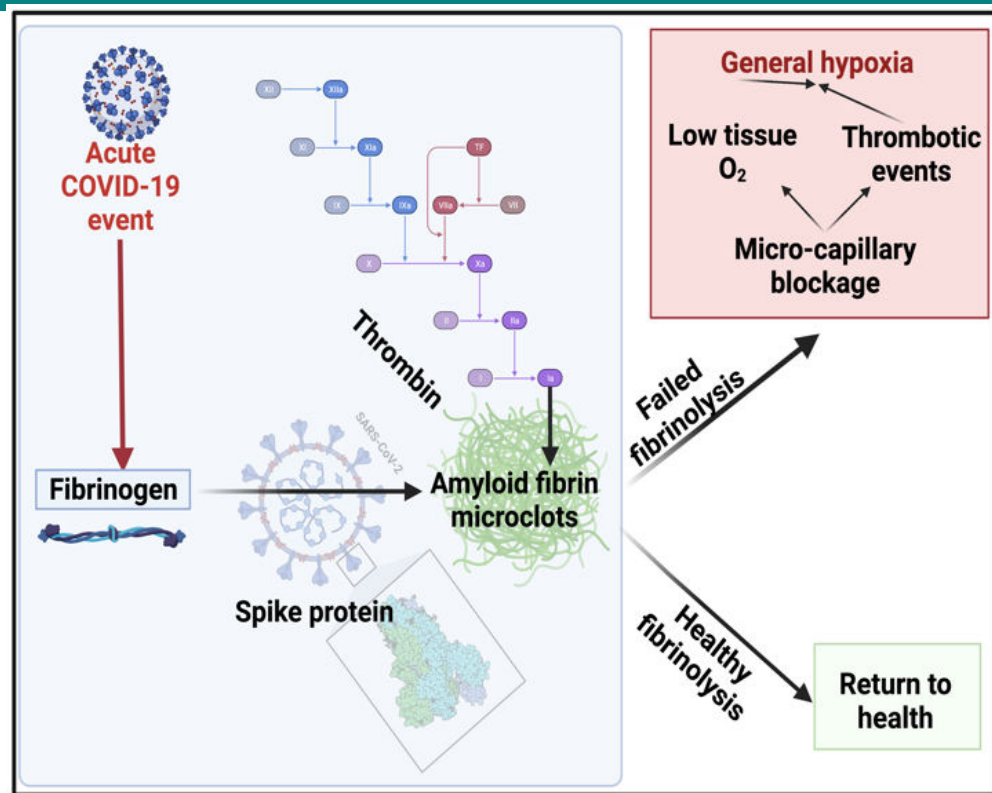
Consequences in blocking capillaries

What can we do about it?

Consequences of microcapillary blockage by microclots

- RBC cannot penetrate to tissues
- Ischemia
- Hypoxia
- Fatigue
- Damage to any tissue undergoing hypoxia
- → Ischemia-reperfusion injury

Simplified diagram of microclot formation



Microclot resolved via the usual **fibrinolytic processes** after acute COVID-19 or, in Long COVID patients, result in a failed fibrinolytic process

Microclots and Symptoms of Long COVID

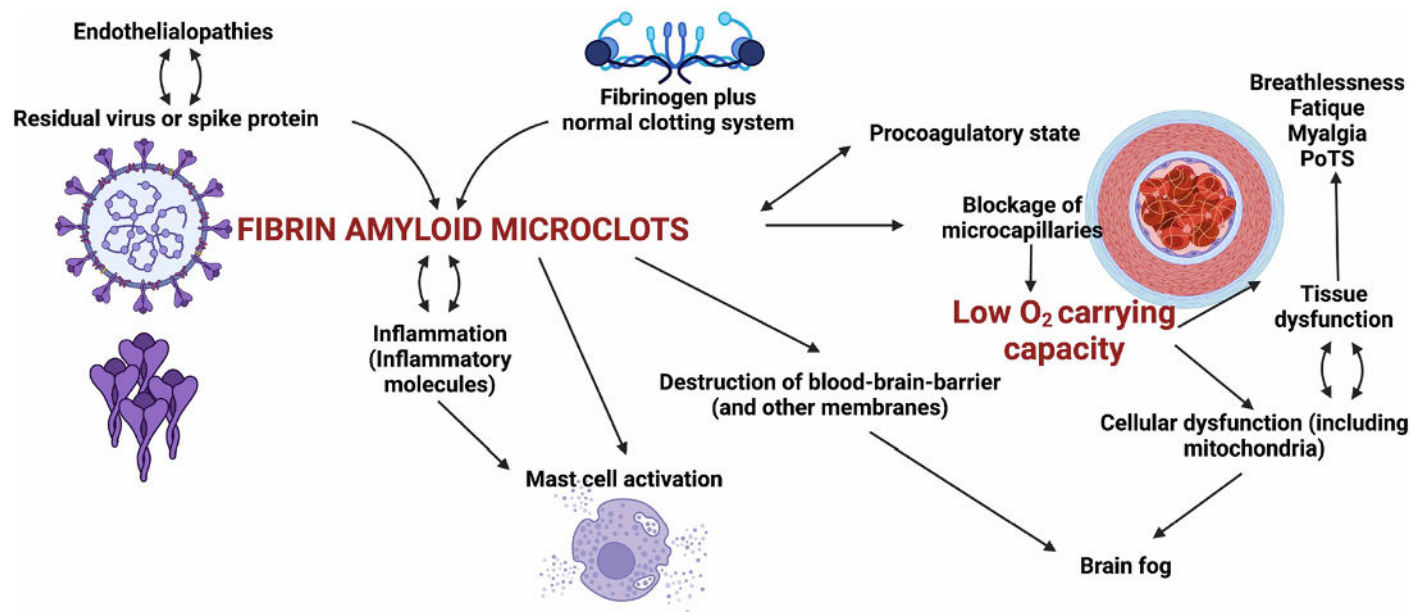
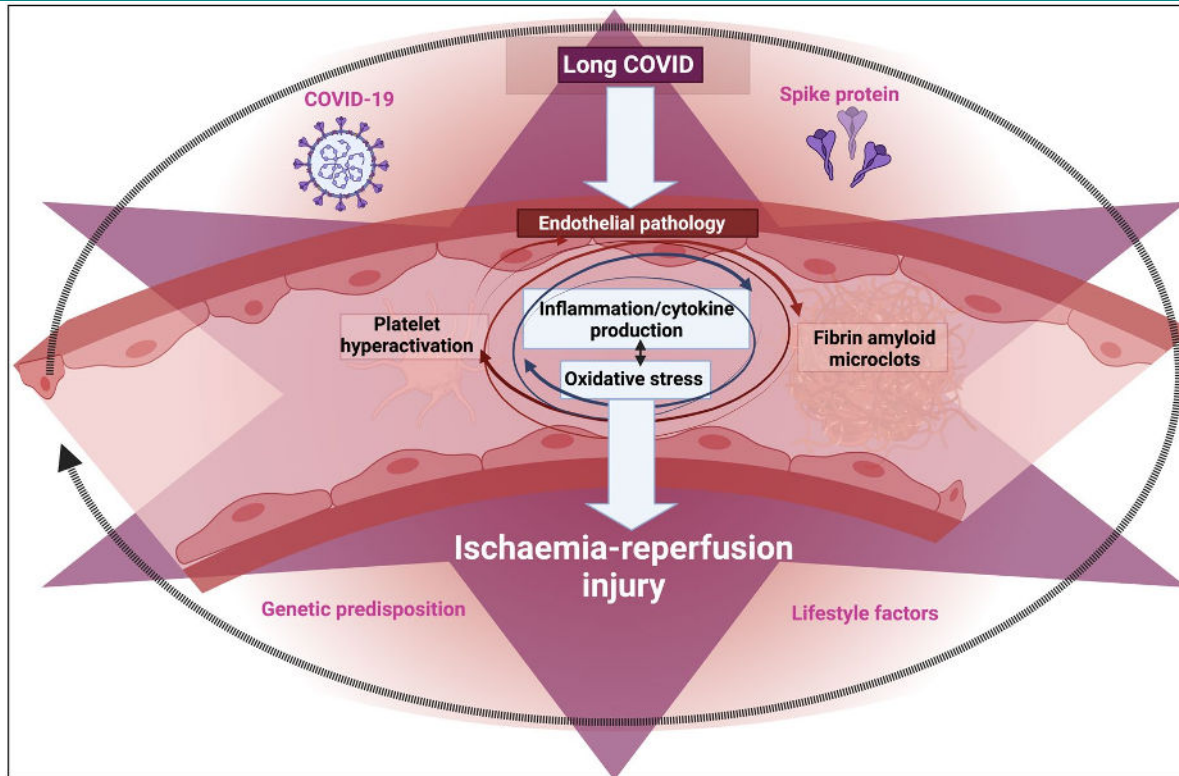


Figure 10. Some of the sequelae of fibrin amyloid microclot formation in the symptomology of Long COVID.

Many others, such as a role for auto-antibodies, are not shown.

Douglas B. Kell, Ethersia Pretorius; The potential role of ischaemia–reperfusion injury in chronic, relapsing diseases such as rheumatoid arthritis, Long COVID, and ME/CFS: evidence, mechanisms, and therapeutic implications. *Biochem J* 31 August 2022; 479 (16): 1653–1708. doi: <https://doi.org/10.1042/BCJ20220154>



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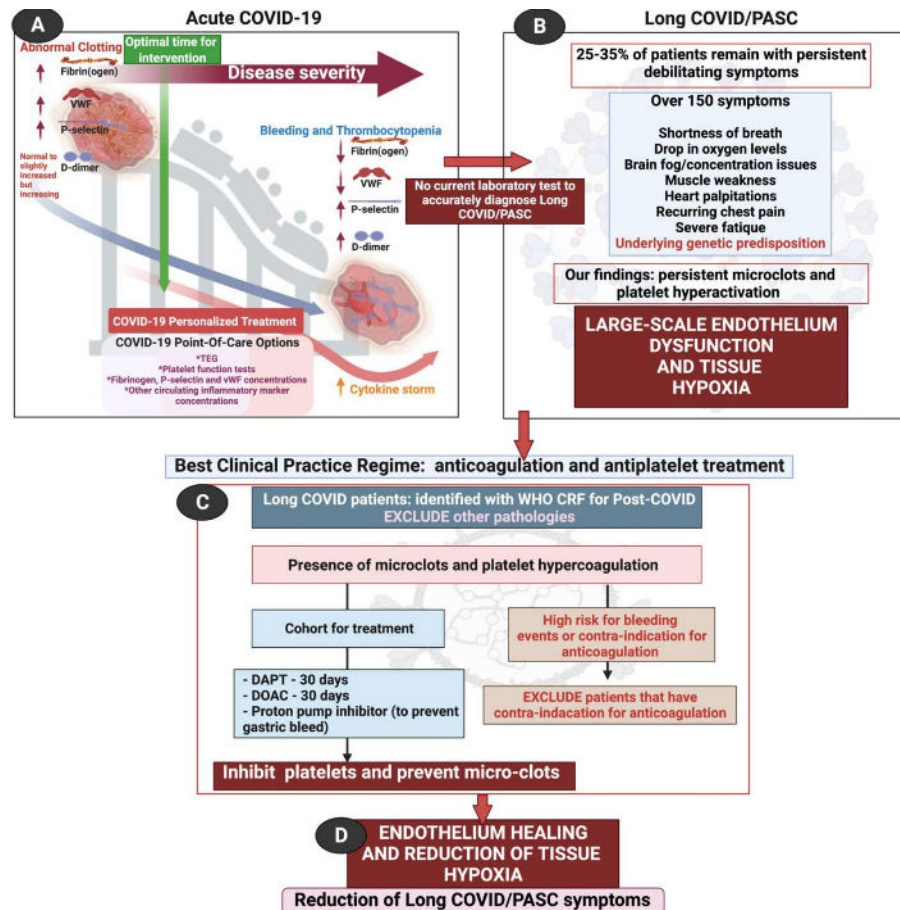
Consequences in blocking capillaries

What can we do about it?

Combined triple treatment of fibrin amyloid microclots and platelet pathology in individuals with Long COVID/ Post-Acute Sequelae of COVID-19 (PASC) can resolve their persistent symptoms

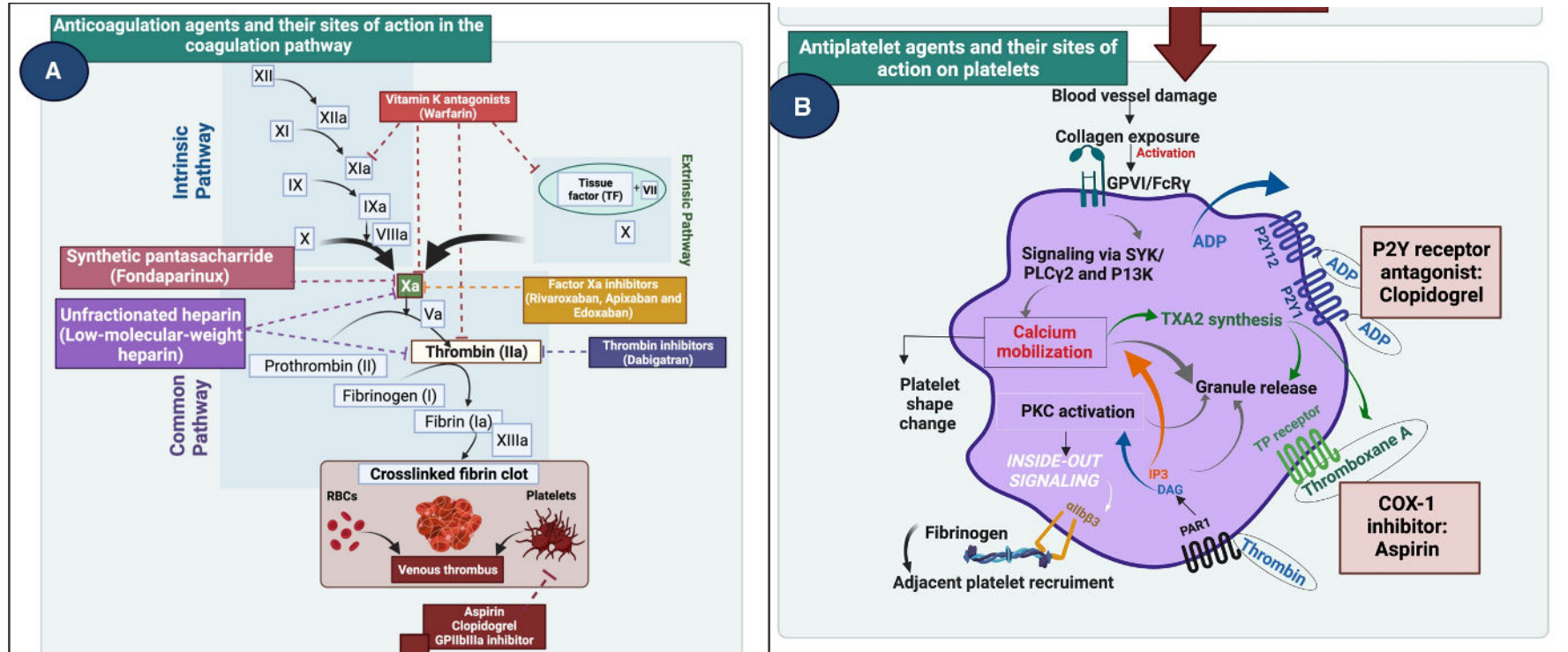
Etheresia Pretorius (✉ resiap@sun.ac.za)

Stellenbosch University <https://orcid.org/0000-0002-9108-2384>



Douglas B. Kell, Etheresia Pretorius; The potential role of ischaemia–reperfusion injury in chronic, relapsing diseases such as rheumatoid arthritis, Long COVID, and ME/CFS: evidence, mechanisms, and therapeutic implications. *Biochem J* 31 August 2022; 479 (16): 1653–1708.
doi: <https://doi.org/10.1042/BCJ20220154>

Why Triple Therapy instead of single agent?



Why Triple Therapy?

Remember they are Resistant **NOT** Impervious

- Aspirin stops Platelets from Sticking to Each Other
- Plavix Stops Platelets from Sticking to Endothelium
- Direct oral Anticoagulant (DOAC) Stops Precipitation of Fibrin from Fibrinogen out of Plasma to Serve as Mortar in Microclot Complex
- Famotidine for Stomach Protection.

Assessing for Patients:

- Obviously, Using Dual Antiplatelet and DOAC in combination has risk beyond other Treatments in the very safe FLCCC Protocol.
- Despite these risk, in the patients that have microclots in vasculature treatment is life altering.
- A good history of Spike protein related interactions and resultant symptoms is important.
- Younger, otherwise healthy prior to COVID or Vaccination are easiest.
 - Unvaccinated High Functioning Young people including some college athletes were my first few patients to utilize the triple therapy.
 - Easy Objective History of Decline with spike exposure and no chronic disease states.
 - Easy to avoid skydiving, ATV usage, gutter cleaning, (in men anything wife would say is stupid).
 - Women of Menstruating Age require close monitoring around Cycle.
- Older and Patients with Multiple Chronic Conditions More Difficult to Parse Spike Disease.
 - Older is age is Heterogenous thank goodness! A 1yo is a 1yo but a 65yo is not a 65yo.
 - More extensive history is needed and closer following on therapy.
 - I usually see them weekly or even closer.

Assessing for Patients:

Preprint

PDF Available

TEST FOR THE DIAGNOSIS OF SYMPTOMS OF HYPOPERFUSION, HYPERCOAGULABILITY AND MICROCLOTS - HHM TEST.

August 2022

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Authors:



Gustavo Aguirre Chang

National University of San Marcos



Aurora Natividad Trujillo Figueredo

SIGESA

Test for hypoperfusion, Hypercoagulability and Microclots Syndrome (HHMS)

1. SIGNS OF HYPOPERFUSION AND HYPERCOAGULABILITY IN THE HANDS AND FEET.

In the last 6 months, have you presented any of the following signs in your hands or feet:

- Cyanotic, bluish or purplish skin, sometimes greenish, or mottled skin
- Dark reddish in the most distant areas of the fingers
- Excessive cold in the hands and feet, accompanied by paleness or whitish areas

Mark with an X as appropriate:

- No, I have not presented any of the 3 signs mentioned. ☐ 0
- Yes, but I have only had it once or twice, and it lasted a few days. ☐ 1
- Yes, I present them frequently, almost every day. ☐ 3
- Yes, every day I present one of the 3 signs described. ☐ 4

2. SYMPTOMS OF STASIS OR STAGNATION OF BLOOD FLOW, WHICH INCREASES WITH IMMOBILITY DURING SLEEP.

In the last 6 months, have you had any of the following symptoms, especially when you wake up and get out of bed in the morning:

- Stiffness, lack of flexibility, numbness or difficulty moving the fingers of the hands
- Tingling, numbness or feeling that one of both hands have fallen asleep, "pins or needles sensation to hands of fingers"
- Sensation of heaviness in the legs and feet and swelling in the calves

Mark with an X as appropriate:

- No, I have not presented any of the 3 symptoms mentioned. ☐ 0
- Yes, but I have only had it once or twice, and it lasted a few hours. ☐ 1
- Yes, I present them frequently, but not every day. ☐ 3
- Yes, every day I present one of the 3 symptoms described. ☐ 4

3. OTHER SYMPTOMS OF HYPOPERFUSION, HYPERCOAGULABILITY AND MICROCLOTS (SYMPTOMS OF HHM), AND ENDOTHELITIS AND BLOOD STASIS.

Since becoming ill, has had (mark with an X as appropriate):

- Non-Restorative Sleep, wake up tired and not rested ☐ 2
- Dilated/bulging/protruding veins in arms or legs (not previously varicose) ☐ 2

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Underlying Principles to this Treatment:

- Be a Physician: Listen and CARE!!!!
 - Two C's of Medicine:
 - CARE about your Patient!
 - Be CURIOUS about them specifically and the disease they are suffering from!
- Informed Consent is Fundamental
- Start on Core Therapy Initially!
 - Avoid Too many Supplements or adjuvants it will just confuse you both.
 - Time for these is at least a month after core Triple Therapy
- Find a Pharmacy that understands what you are doing!.

Treatment Expectations:

- Response: If selected right patient results are incredibly for patient.
- Learned from Treating 300+ people:
 - First 1-2 weeks on Therapy Old Symptoms come back or new ones appear.
 - Symptoms appearing from Antiplatelet and DOAC therapy are discomforting but in my clinical experience a sign that:
 - Picked the correct patient.
 - Discussing this ahead of time is a way to help stave off worries and confirm to the patient that 'something' positive is happening. (Avoids Anxiety to Patient and Calls for Physician)

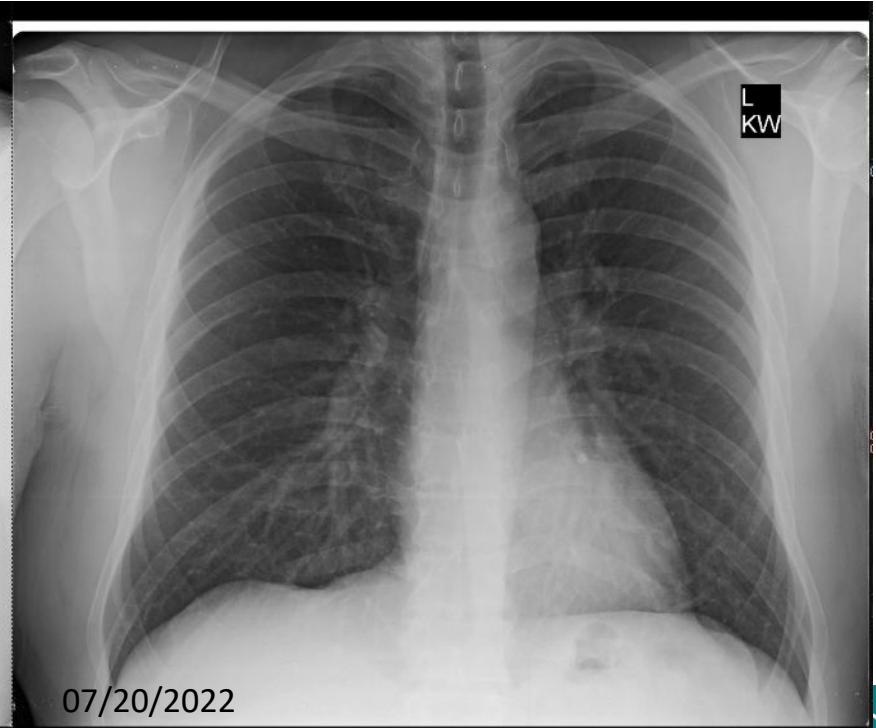
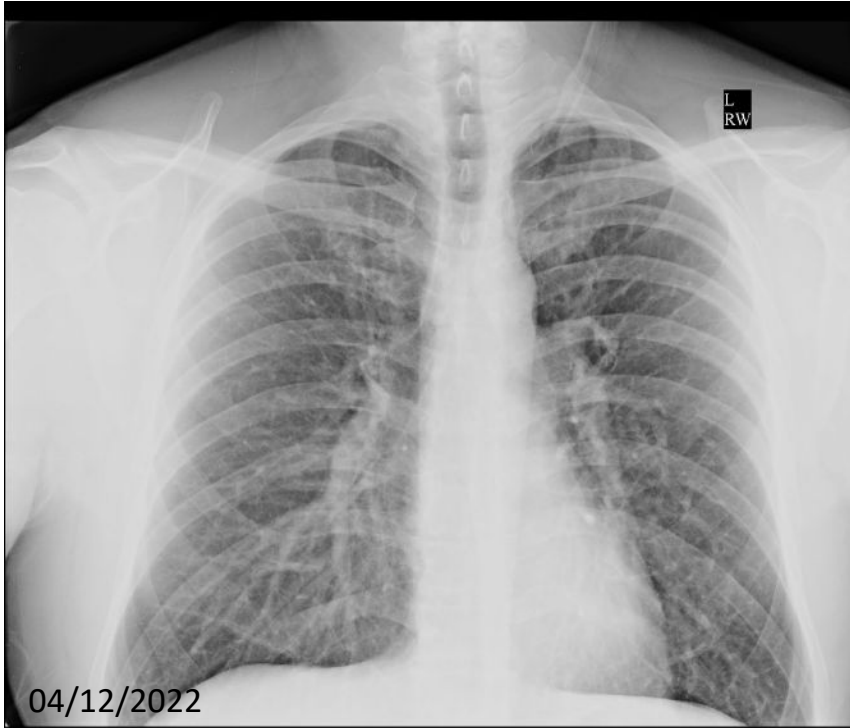
Treatment Length? I DON'T KNOW:

- Seems to depend on how long since infection or vaccine and the Immune Systems Status:
- Basically , whether the 'boys' are still up and when and how much damage they did playing with dad, or even Dad comes back over after dinner with MOM to play?!!!:
- Easiest and Shortest: (4-6 weeks)
 - Young, previously healthy, unvaccinated, Long COVID
- Hardest and Longest: (3 months to -----?)
 - Older, chronic disease (esp autoimmune), multiple jabs and boosters, post covid.
- Need Studies for Signs of Objective Resolution.

Current Surrogate 'Objective' Measures I use:

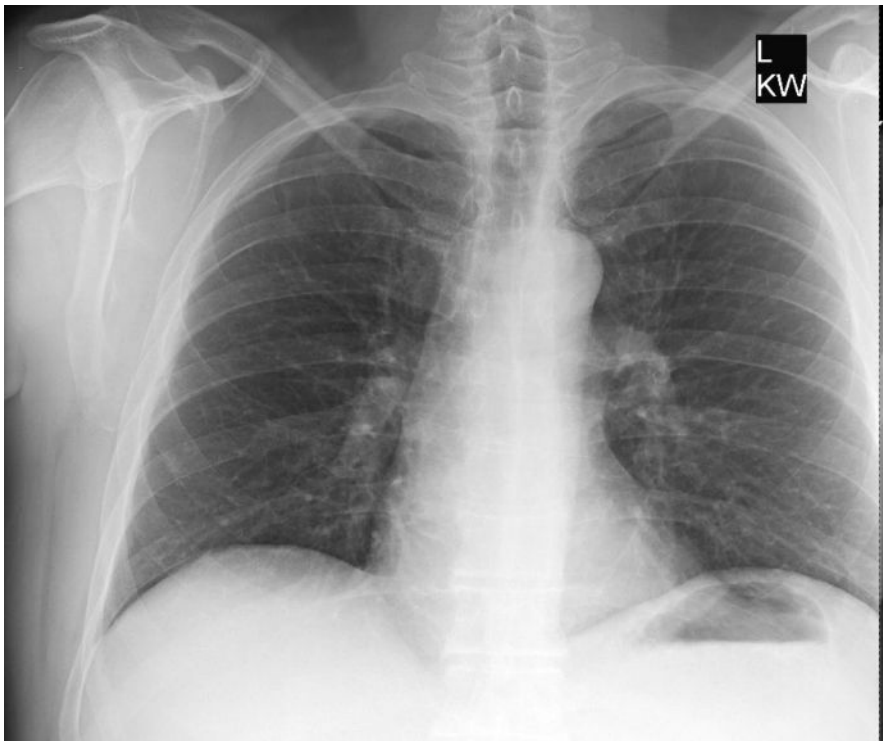
- In acute or subacute covid, D-dimer reduction is easy.
 - Problem is in Post Acute Spike Disease will likely be normal from start to finish
- CXR Changes:
 - You tube: Oro-Systemic Health Symposium 2022 – Part 3: Graham Lloyd-Jones – The anatomy of COVID-19
 - Primary Pulmonary Vasculopathy Resolution?
- Serum Inflammatory Marker Resolution? TBD
- DLCO Before and After?
- PLEASE HELP Develop some validated methods!

Clinical Surrogates of Blood Test?





2/8/2022



6/20/2022



THANK YOU

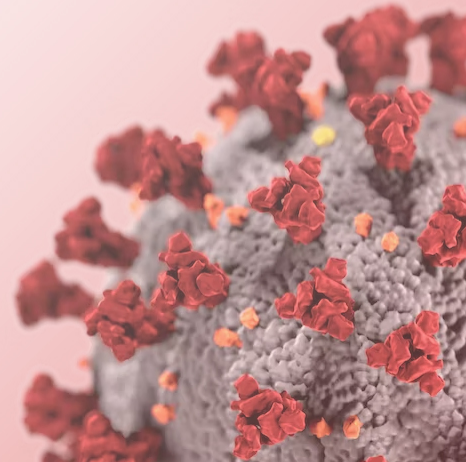


Figure 11: Representative fluorescence micrographs of platelet pathology before and after treatment. Moderate platelet spreading and mild platelet clumping (white arrows) was seen in the naïve patient's samples (Fig. A, C, E, G, I) that improved after treatment, with mild platelet spreading and no clumps (Fig. B, D, F, H, J).

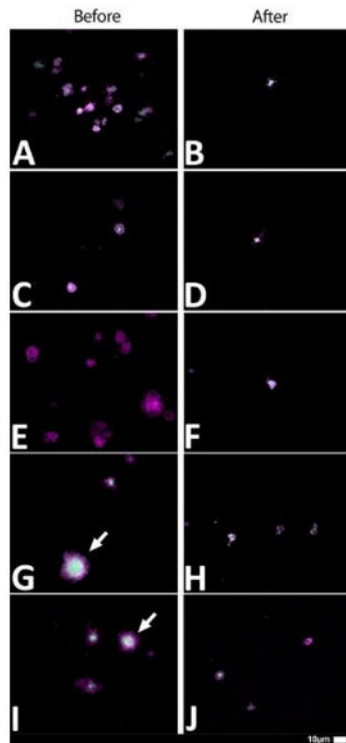
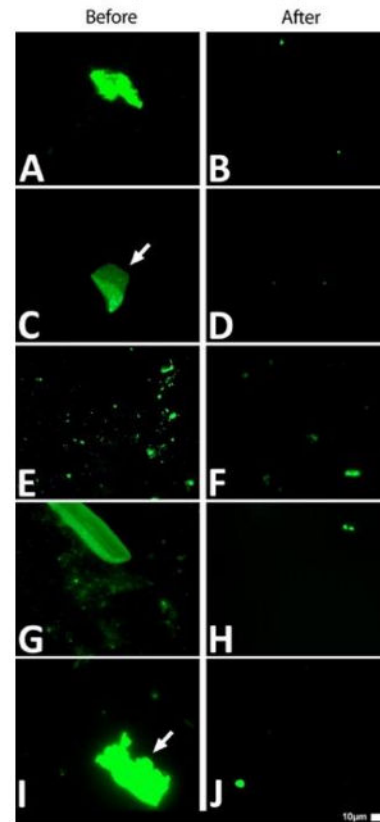
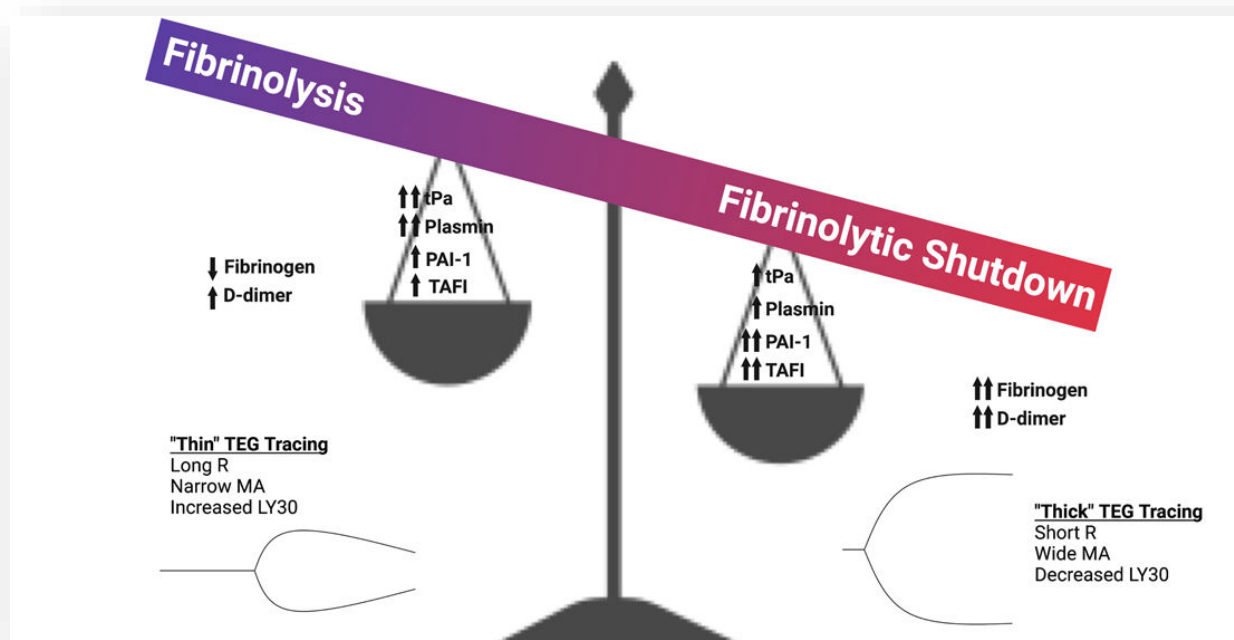


Figure 12: Representative PPP fluorescence micrographs with moderate areas of plasma protein misfolding forming microclots (some larger than $15\mu\text{m}$; white arrows) before treatment (Fig. A, C, E, G, I), with a few microclots visible in the samples after treatment (Fig. B, D, F, H, J).

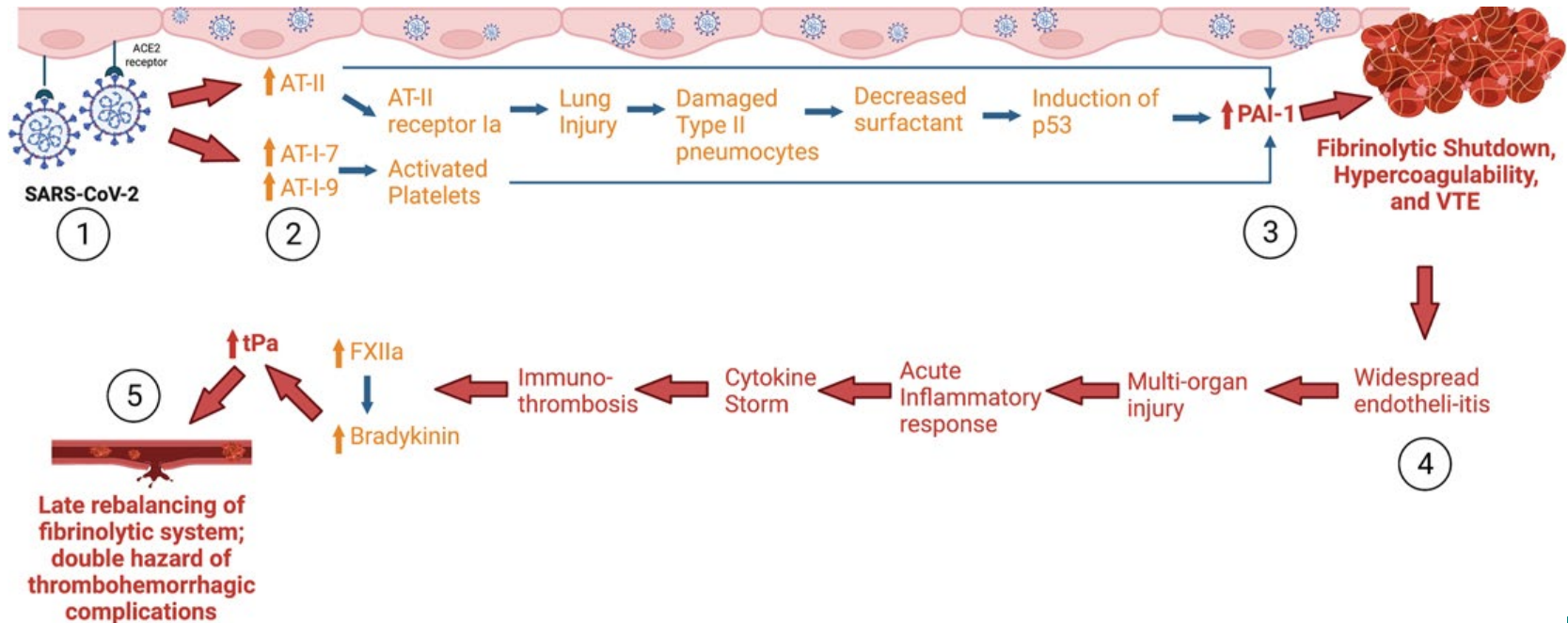


COVID 19 COAGULOPATHY



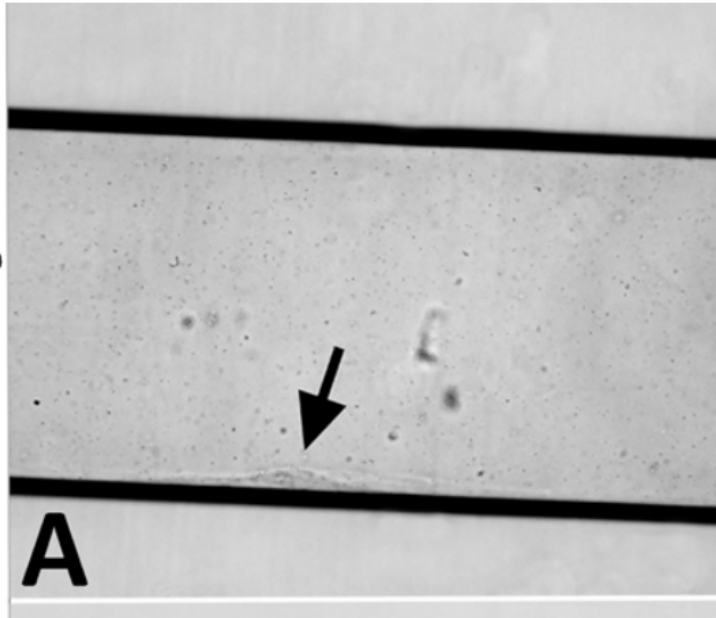
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SARS-CoV-2-Induced Endotheliitis



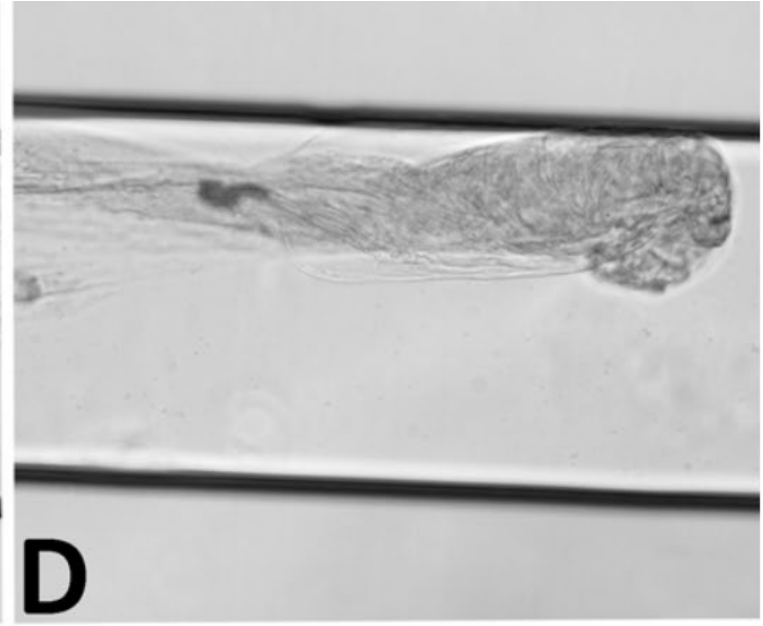
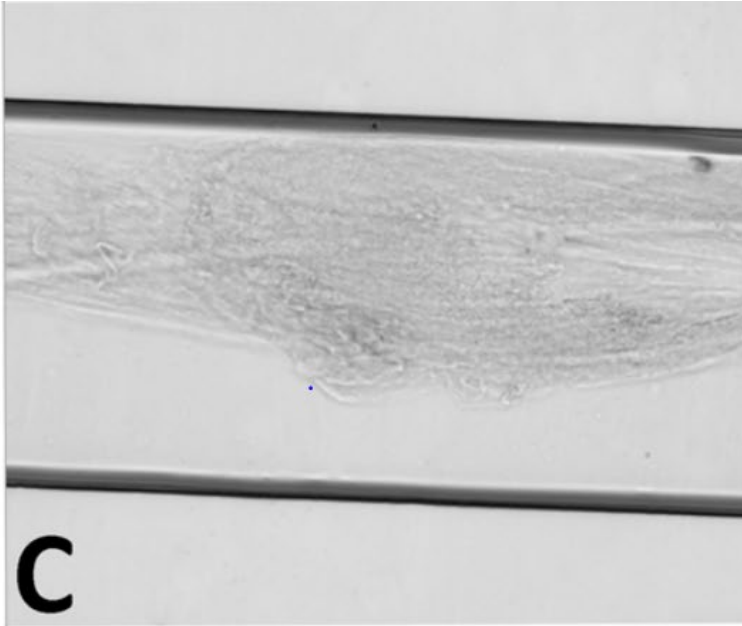
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Healthy PPP



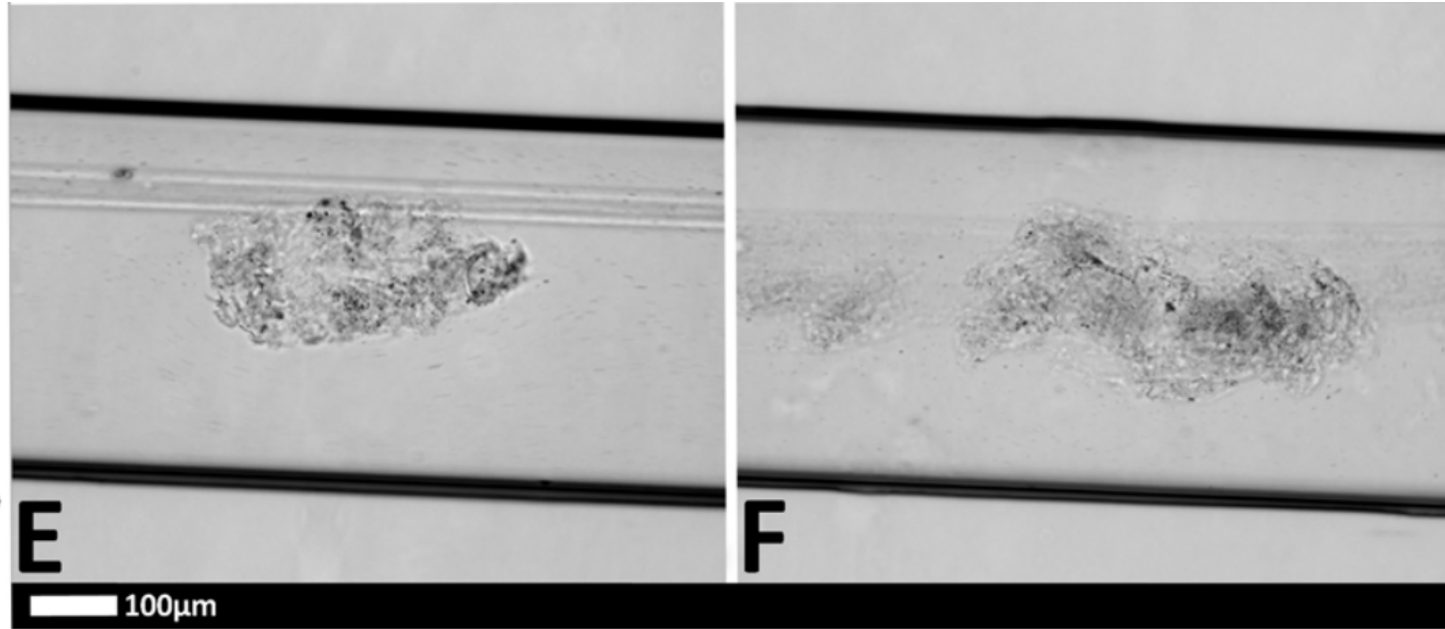
Bioscience Reports (2021) 41 BSR20210611
<https://doi.org/10.1042/BSR20210611>

COVID-19

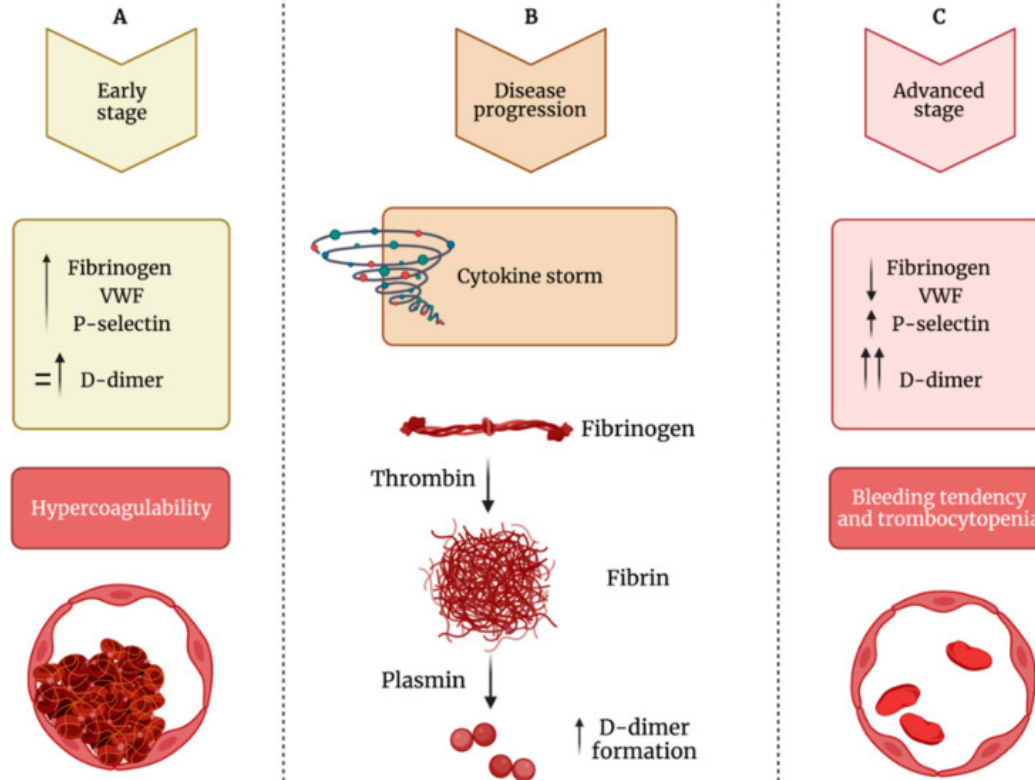


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<https://doi.org/10.1042/BSR20210611>

Spike Protein

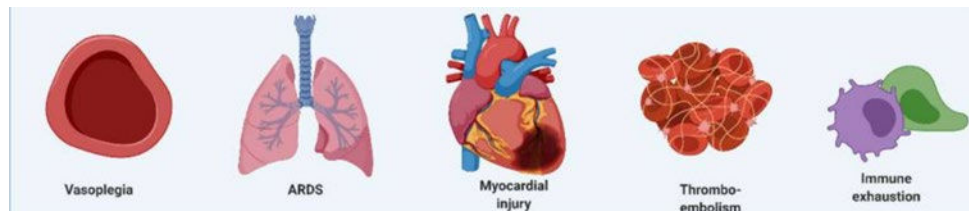
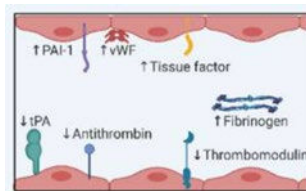
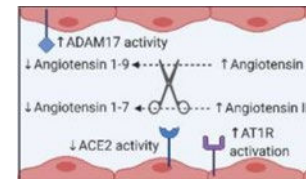
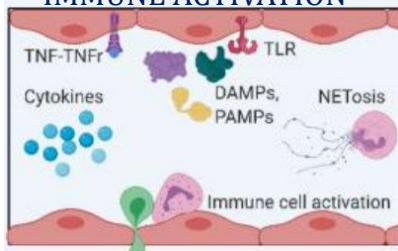


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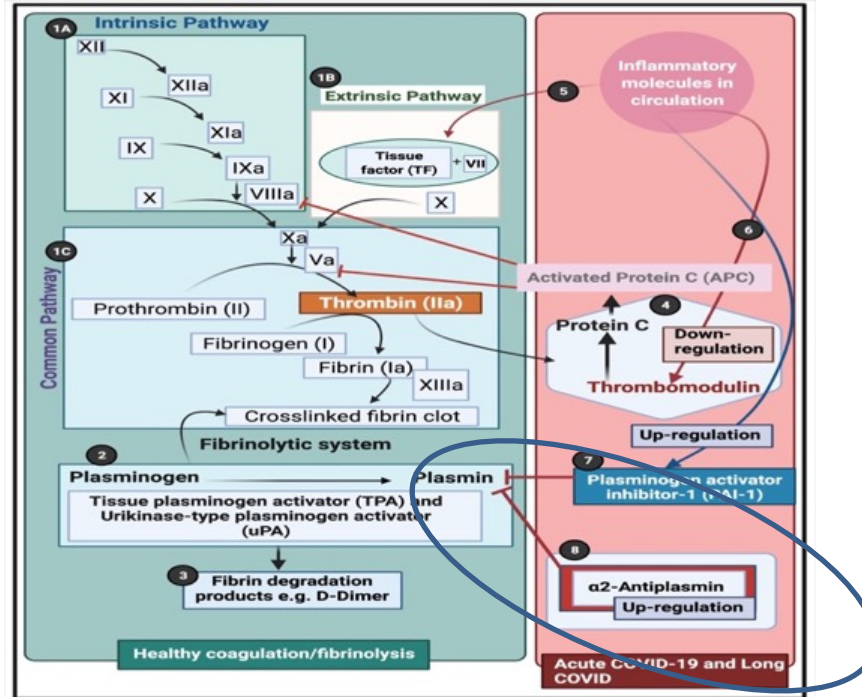


Endothelial injury, involving immune activation, pro-thrombotic milieu, and RAAS dysregulation.

IMMUNE ACTIVATION

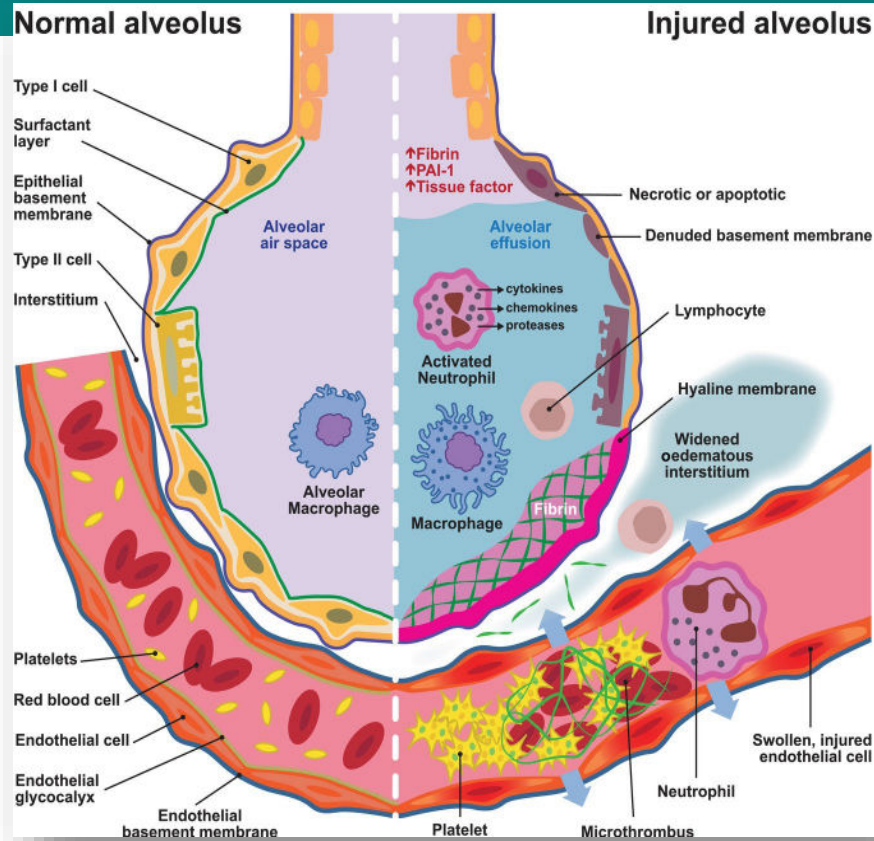


Long COVID and trapped inflammatory molecules



α 2-antiplasmin (α 2AP) inhibit plasmin and ultimately will prevent sufficient fibrinolysis to happen

COVID 19 COAGULOPATHY



Acute COVID-19: a Vascular Disease

- Cardiovascular complications are rapidly emerging as a key threat in coronavirus disease 2019 (COVID-19) in addition to respiratory disease (Varga et al 2020: The Lancet)
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