



**EMERGING APPROACHES TO TREATING
SPIKE PROTEIN-INDUCED DISEASES**

April 28-29, 2023 • Fort Worth, Texas

Spike Protein and Amyloid Fibrin Microclots

Pathology of the S1 Subunit of the Spike Protein;

Microclots; and Local Tissue Hypoxia

Hypofibrinolysis and Plasminogen Activator Inhibitor - 1

Presented By:

Jordan F. Vaughn MD



S1 SPIKE PROTEIN ALONE can catalyze fibrin(ogen) formation

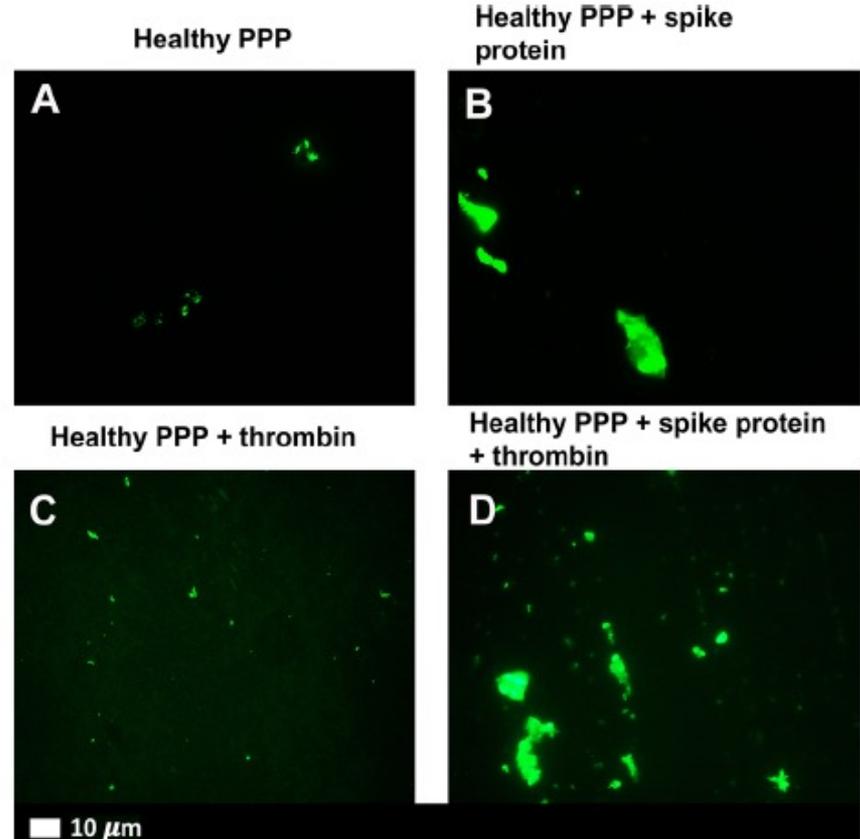
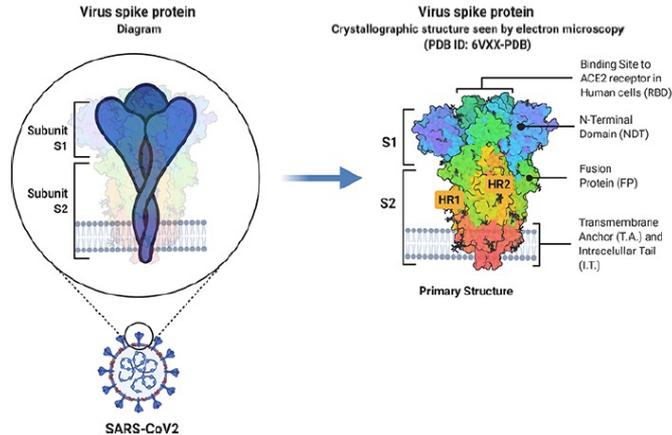
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Research Article

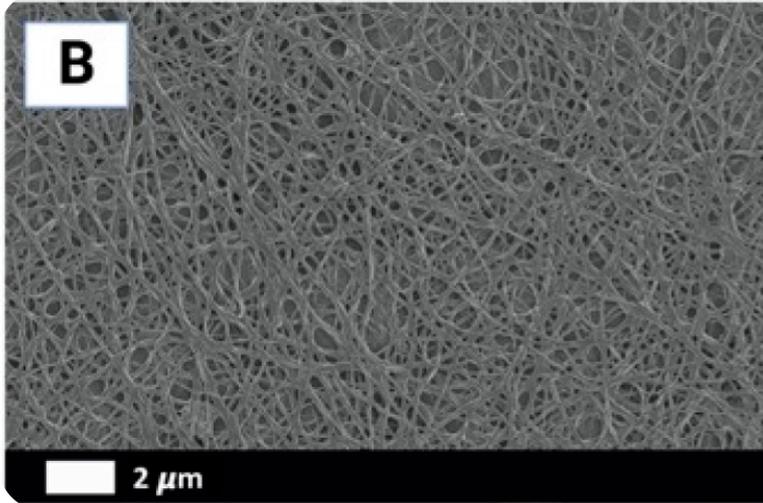
SARS-CoV-2 spike protein S1 induces fibrin(ogen) resistant to fibrinolysis: implications for microclot formation in COVID-19

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 Etheresia Pretorius¹

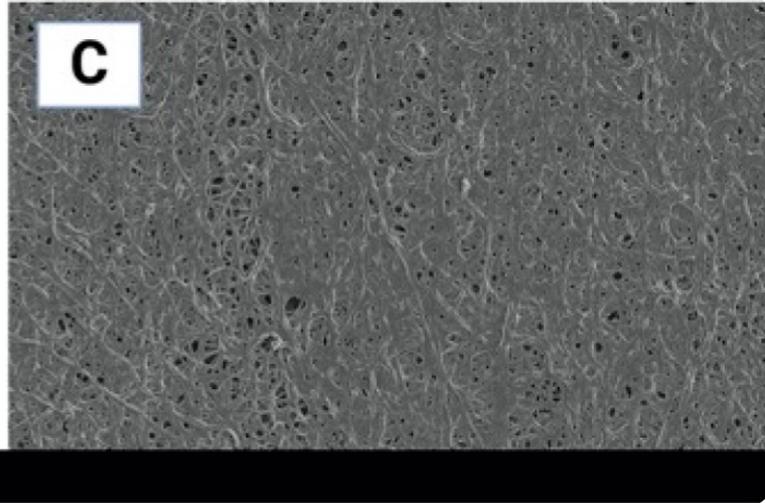


Amyloid Fibrin Structure

Normal Fibrin Structure



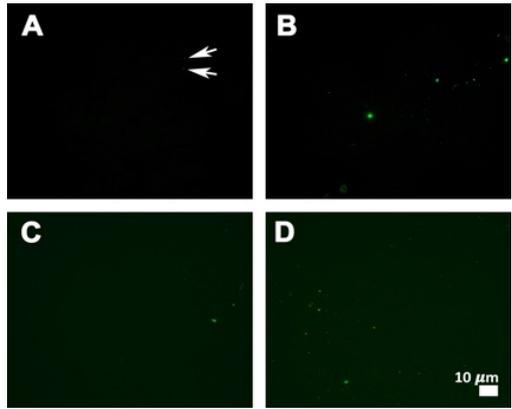
Amyloid Fibrin Structure



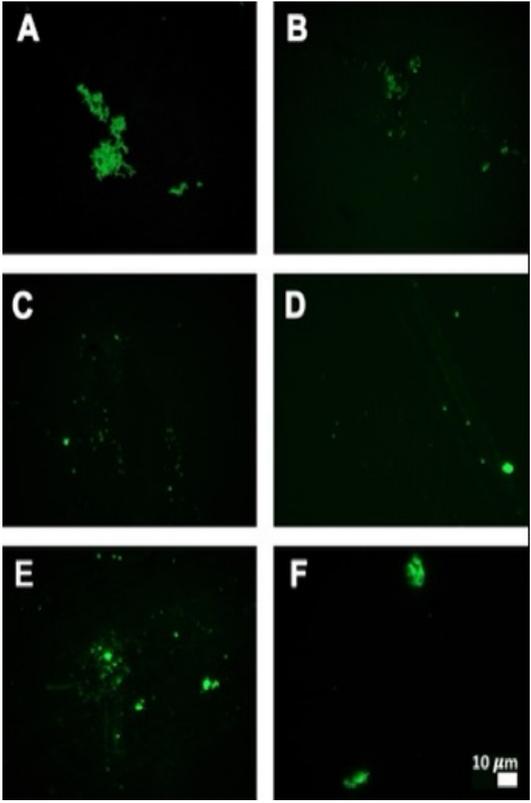
Randeria, S.N.; Thomson, G.J.A.; Nell, T.A.; Roberts, T.; Pretorius, E. Inflammatory cytokines in type 2 diabetes mellitus as facilitators of hypercoagulation and abnormal clot formation. *Cardiovasc. Diabetol.* **2019**, *18*, 72.

Structural Changes in Fibrin(ogen) in **Disease**

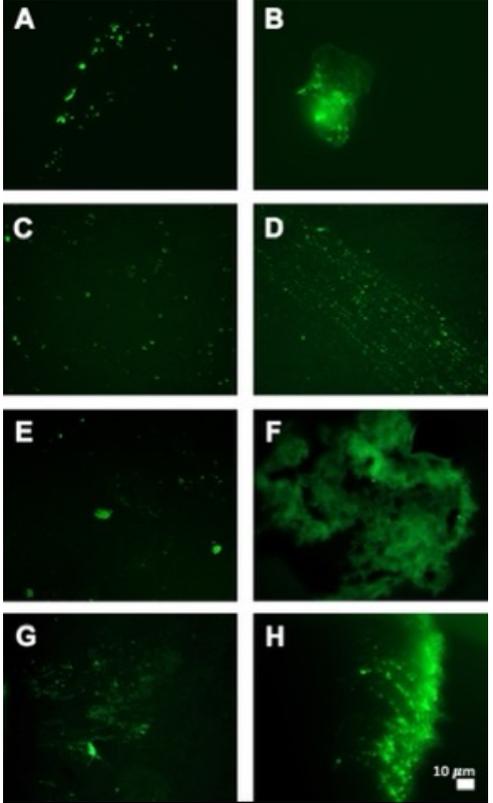
Healthy Plasma



Type 2 DM Plasma

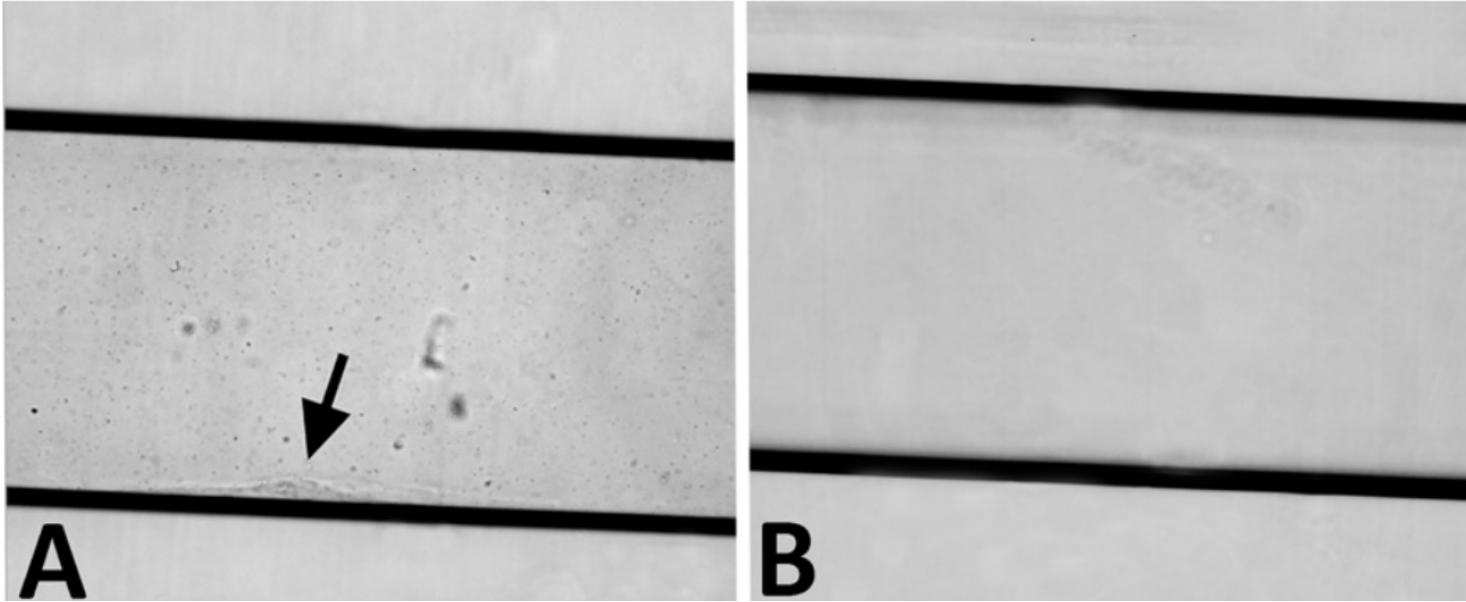


COVID-19 Plasma



Microfluidic Channel and PPP

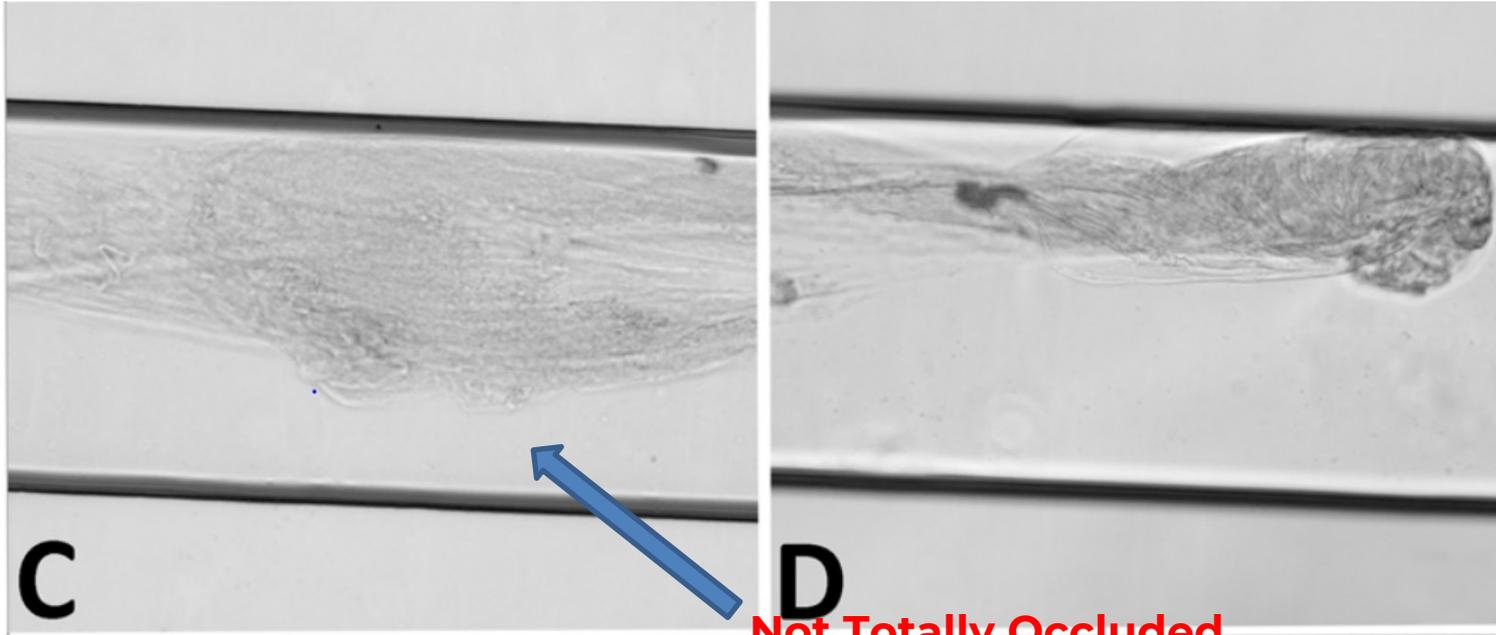
Healthy PPP



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Microfluidic Channel and PPP

COVID-19

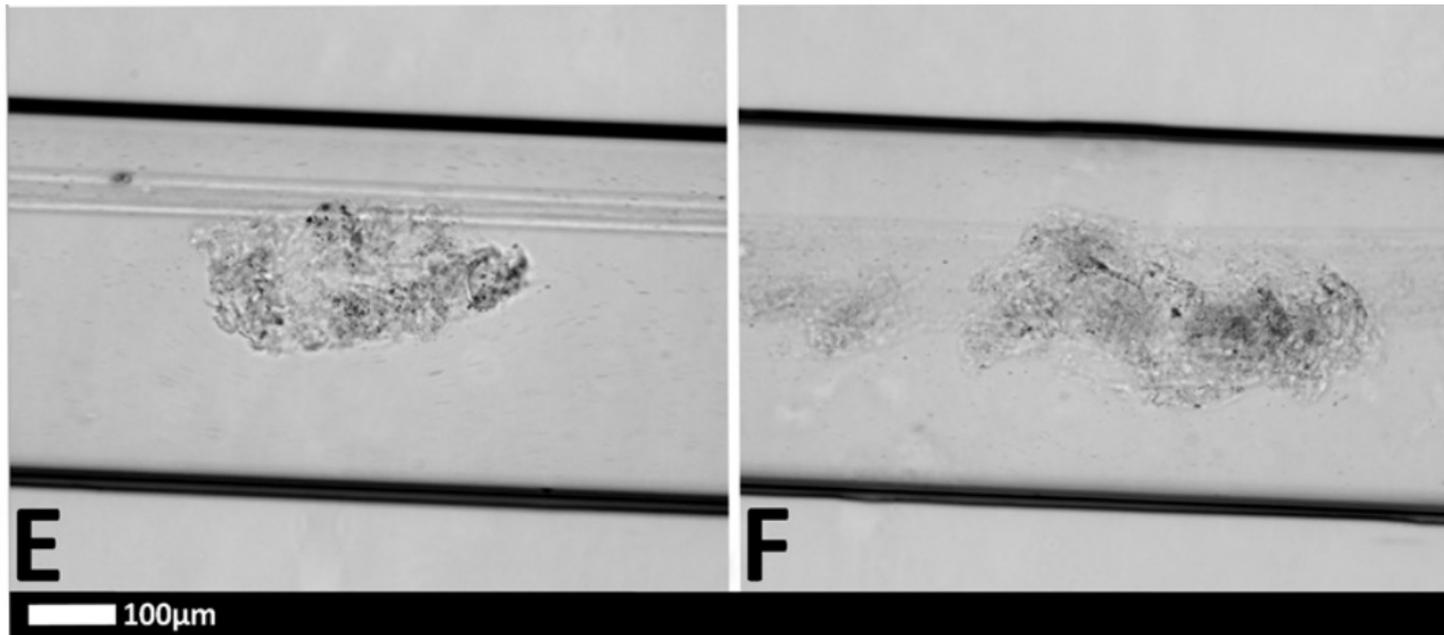


Not Totally Occluded

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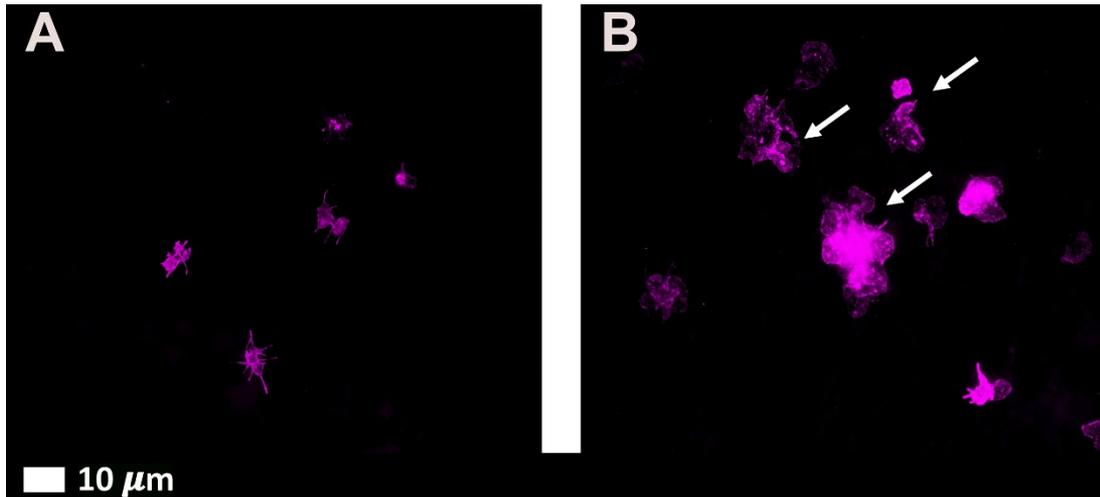
Microfluidic Channel and PPP

Spike Protein



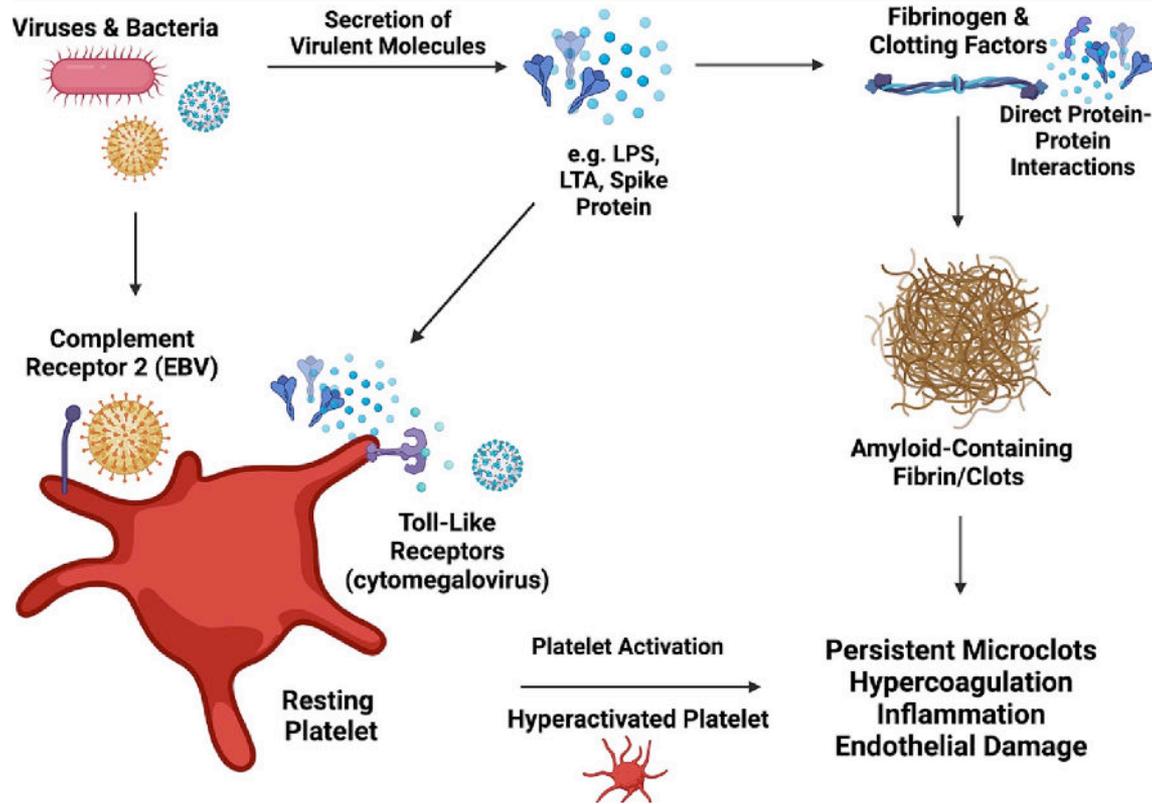
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PLATELETS BEFORE AND AFTER EXPOSURE TO SPIKE PROTEIN

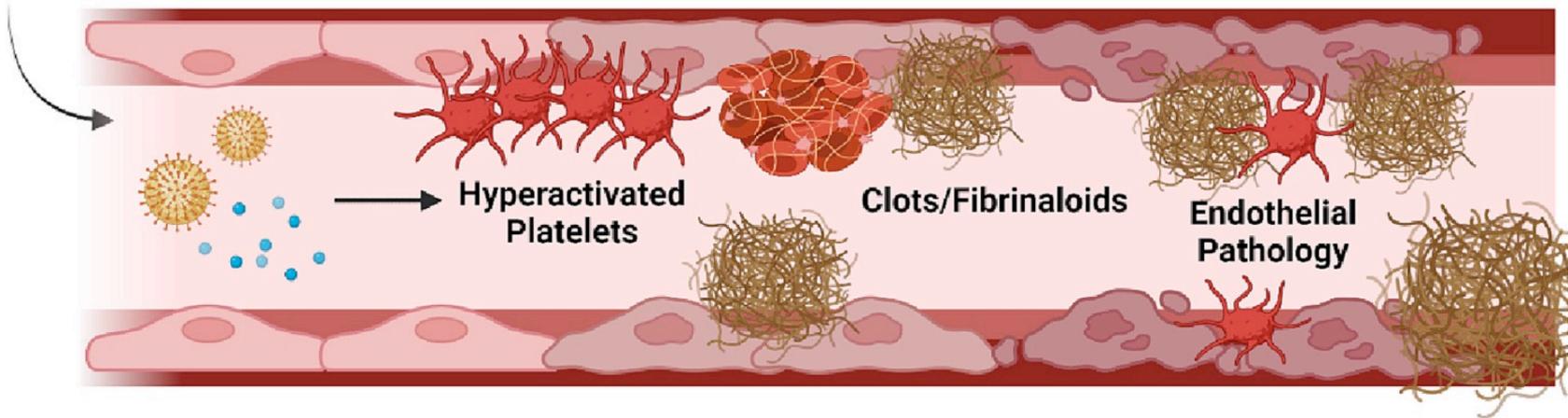


Fluorescence microscopy micrographs of platelets, before and after exposure to spike protein (A) Representative platelets from hematocrit incubated with fluorescent marker, CD62P-PE. (B) Representative micrographs showing activated platelets after exposure to spike protein. The white arrows point to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

A Nasty Sludge of a Mess



Endothelial Pathology leads to Tissue Hypoxia



Anomalous Clotting (Fibrin Amyloid Microdots)

+

Hyperactivated Platelets

+

Endothelial Damage and Dysfunction
From Spike



Vessel Damage/Subtotal Occlusion



Local Tissue Hypoxia and Hypoperfusion



CONSEQUENCES OF **MICROCAPILLARY BLOCKAGE** BY MICROCLOTS

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



Microcapillary blockage by MICROCLOTS:

Areas now use the **Dissolved Oxygen(PP Oxygen)** in Serum not Red Blood Cells.

Partial pressure of oxygen in humans

Table 1. References values of PO_2 measurements using different techniques

PtO ₂ (mmHg)	Organ and Tissue	Reference
108 mmHg	Alveolus	Guyton [4]
30 mmHg	Brain	Meixensberger [51], Hoffman [52], Ortiz-Prado [3]
30 mmHg	Vestibular System (Balance)	
30.6 mmHg	Cornea	Bonanno [64]
28.9 mmHg	Skeletal Muscle fibers	Beerthuizen [58], Carreau [53]
29.6 mmHg	Myocardium	
22 mmHg	The Eye	Bonanno [64]
8 mmHg	Skin epidermis	Wang [35], Carreau [53]
24 mmHg	Dermal papillae	
55 mmHg	Liver	Leary [56]
72 mmHg	Superficial cortex of the kidney	Muller [57], Carreau [53]
90 ± 5 mmHg	Arterial PO ₂	Mah and Cheng [20], Guyton [4]
40 ± 5 mmHg	Venous PO ₂	Mah and Cheng [20], Guyton [4]

Computational Prediction of the Interaction of Ivermectin with Fibrinogen

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Int. J. Mol. Sci. **2023**, *24*(14), 11449; <https://doi.org/10.3390/ijms241411449>



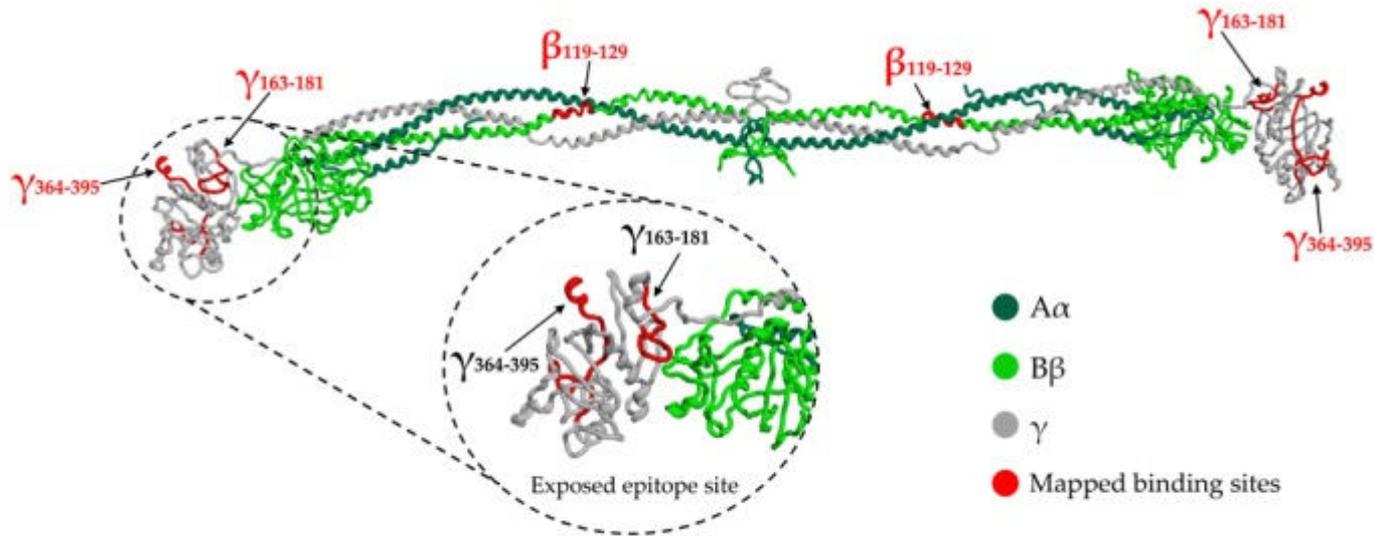


Figure 3. SP binding sites mapped on the fibrinogen structure (PDB entry 3GHG), as identified by Ravi et al., 2021 [2]. Illustration obtained in MOE v2022.02.

Another Phenotype: ILIAC VEIN COMPRESSION

- May-Thurner (Pelvic Venous Disease) Plus MCAS and POTS following Endothelial Injury (Spike Protein) most are Vaccine Injury
- Common in:
 - Hypermobile: EDS or EDS Like
 - Runners/Cyclist/Pelvic Trauma
 - Multiparous Women
 - Men with Left Testicle History including Varicocele, Torsion
- Vaccine Injury and Results in Lower Extremity Symptoms Initially.
 - Most Remember a TIME and DATE when things in their body were DIFFERENT
 - Many had Mild issues prior including Leg going to sleep when sitting for long times etc
- Initially Symptoms are Lower Ext are Heavy or Swollen/Lead Like
- POTS and MCAS symptoms increased.
- Triple Therapy (Antiplatelet and AntiCoags) Help but not Curative
 - Post Thrombotic Syndrome in this Subset explains this



Another Phenotype: ILIAC VEIN COMPRESSION

- Addition Issues Issues:
 - Urinary Urgency or ‘Frequent Urinary Tract Infections’ or Interstitial Cystitis
 - Heavy Menstrual Cycles, Pelvic Pain, all Issues are worse before and during cycle
 - Hemorrhoids and Irritable Bowel Symptoms
 - Lower Sacral Back Pain and Sacral Ileitis Symptoms
 - Men: Boggy Prostate and Nocturia in Younger Men.

Concentration of Inflammatory Markers in Plasma of Varicose Ovarian Veins in Women With Pelvic Venous Disorders: A Pilot Study

Marcin Czezelewski, Eryk Mikos, Sara Moqbil, Maciej Szmygin, Hanna Szmygin, Krzysztof Pyra



PII: S1078-5884(23)00456-2
 DOI: <https://doi.org/10.1016/j.ejvs>
 Reference: YEJVS 8824

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Table 1. Comparison of blood counts and levels of inflammatory markers in samples from the antecubital vein and pelvic varicose vein of 25 patients of reproductive age referred for endovascular treatment of pelvic venous disorder.

Variable	Antecubital vein <i>n</i> = 25	Pelvic varicose vein <i>n</i> = 25	<i>p</i>
Erythrocytes – $10^{12}/L$	4.02 (3.17 – 4.91)	4.23 (3.30 – 4.86)	.002
Leukocytes – $10^9/L$	4.62 (2.98 – 6.52)	5.21 (3.30 – 8.34)	.001
Platelets – $10^9/L$	220.5 (163 – 279)	237 (196 – 302)	.005
Haemoglobin – g/dL	12.00 (9.70 – 15.20)	12.95 (10.80 – 15.40)	.001
D-dimer – pg/mL	9 884 (2 259 – 16 910)	13 330 (3 099 – 114 110)	.081
C-reactive protein – mg/L	0.15 (0.12 – 2.93)	0.24 (0.10 – 3.04)	.038
Fibrinogen – g/L	2.25 (1.7 – 4.50)	2.25 (1.60 – 3.60)	.410
Interleukin-6 – pg/mL	50.88 (36.58 – 87.16)	57.14 (40.03 – 79.38)	.038
von Willebrand – ng/mL	36.28 (21.15 – 168.6)	45.43 (20.68 – 89.00)	.442

Data are presented as median (range).

Another Phenotype: ILIAC VEIN COMPRESSION

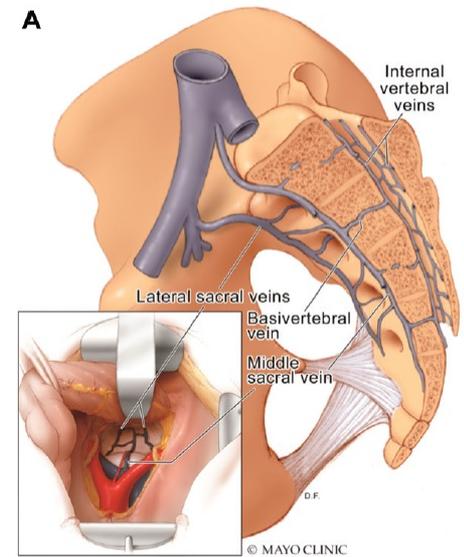
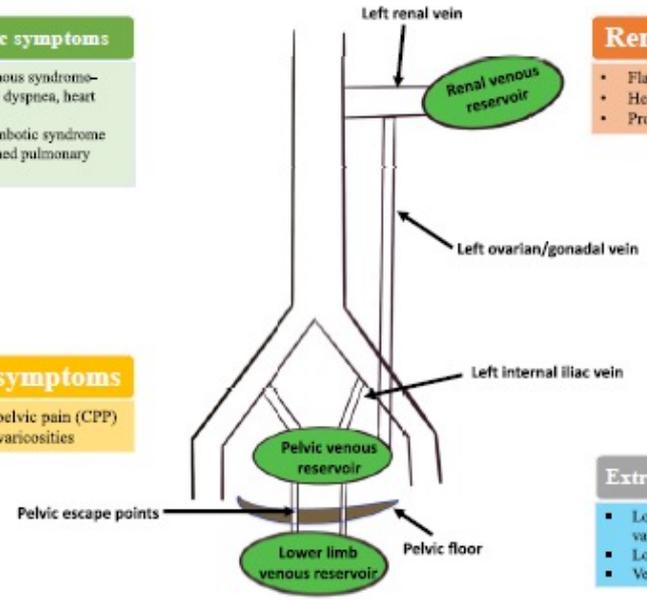
Flank pain, hematuria, proteinuria

- Systemic symptoms**
- Cardiovenous syndrome— exertional dyspnea, heart failure
 - Post-thrombotic syndrome
 - Unexplained pulmonary emboli

- Pelvic symptoms**
- Chronic pelvic pain (CPP)
 - Perineal varicosities

- Renal symptoms**
- Flank pain
 - Hematuria
 - Proteinuria

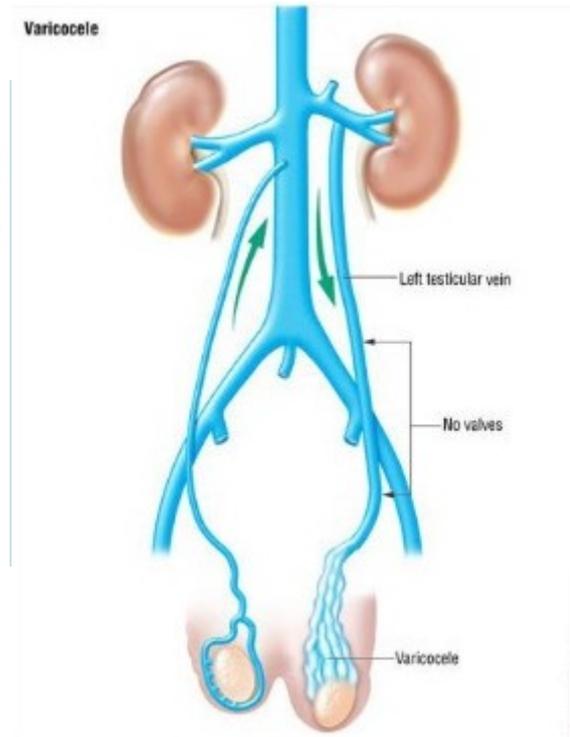
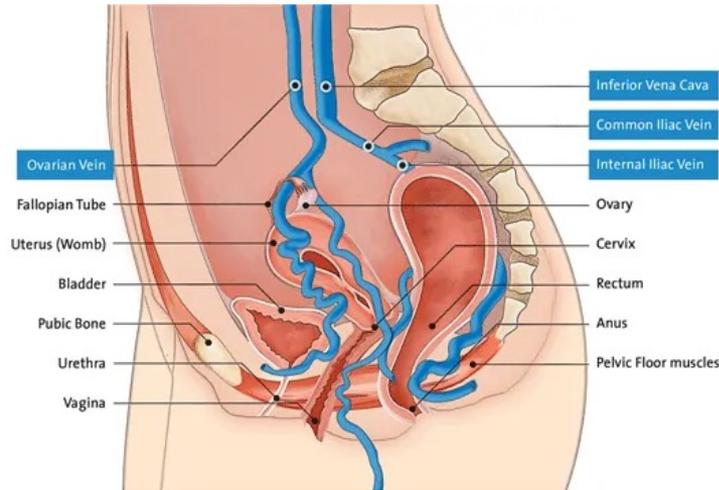
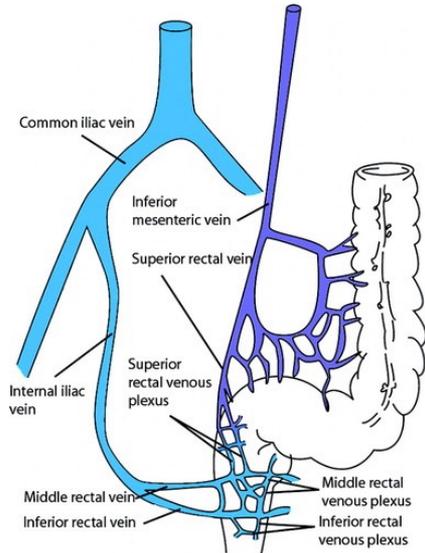
- Extra pelvic symptoms**
- Lower limb, vulvar varicosities
 - Lower limb swelling
 - Venous claudication



Sheikh AB, Fudim M, Garg I, Minhas AMK, Sobotka AA, Patel MR, Eng MH, Sobotka PA. The Clinical Problem of Pelvic Venous Disorders. *Interv Cardiol Clin.* 2022 Jul;11(3):307-324. doi: 10.1016/j.iccl.2022.03.003. PMID: 35710285.

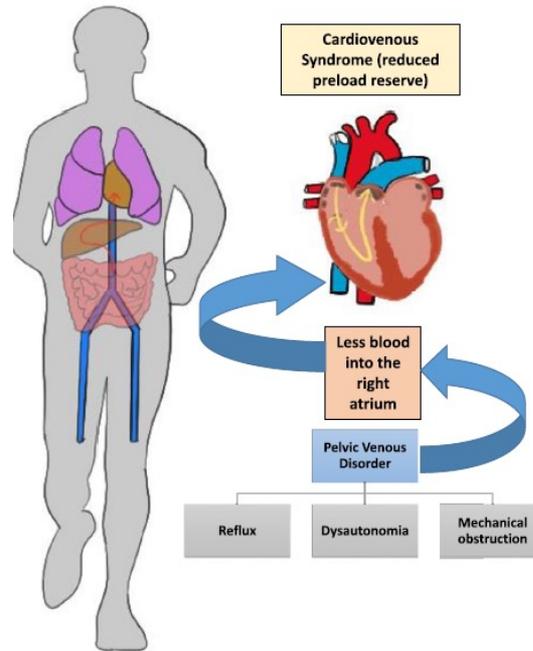


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Mast Cell Activation Syndrome

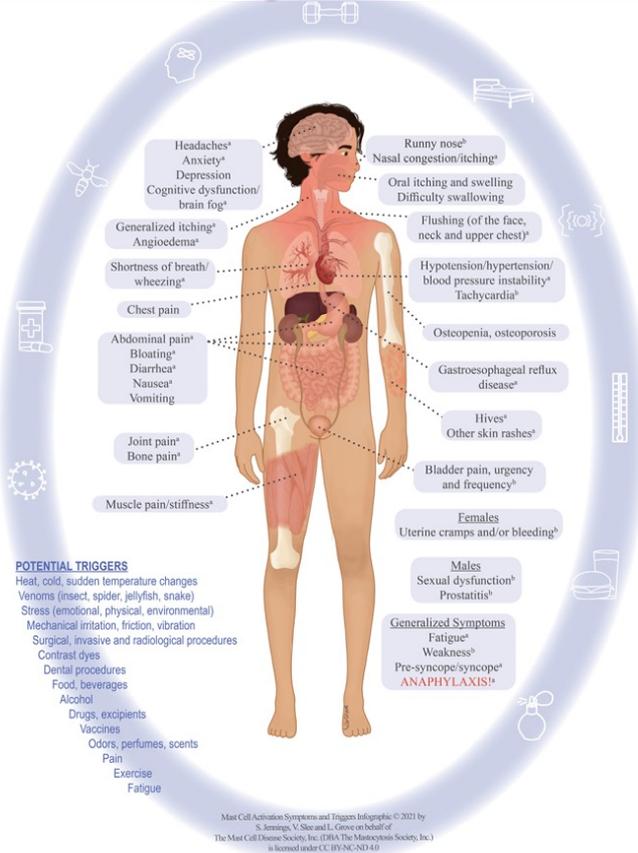


Figure 1. The most common presenting symptoms and potential triggers of mast cell activation.^{1,2,4} Symptoms and triggers are unique to the individual. Specific criteria, as noted in the article text, must be met to fulfill a diagnosis of MCAS. Not all patients react to each of the listed triggers or experience each of the listed symptoms. Mast Cell Activation Symptoms and Triggers Infographic 2021 printed with permission from The Mast Cell Disease Society, Inc. (DBA The Mastocytosis Society, Inc.). The superscript letter "a" indicates symptoms reported by more than 45% of TMS MCAS survey respondents as affecting them either moderately or severely in the course of their illness with MCAS.³ The superscript letter "b" indicates symptoms not queried in the TMS MCAS survey. DBA, doing business as; MCAS, mast cell activation syndrome; TMS, The Mast Cell Disease Society, Inc.

