# Thrombosis and COVID-19: Pathophysiology

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MEET THE HEMOSTASIS EXPERTS IV

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## RM, \*22.11.1961 M

- 24.3.20 Emergency USB, upper respiratory tract infection
- 24h later COVID-positiv
- 29.3.20 self referral with cough, dyspnea
- ∘ O<sub>2</sub> saturation 85% at 10L O<sub>2</sub>
- ICU



## RM, \*22.11.1961 M

Hämostase Routineanalytik										
Abteilung Probenentnahme Laboreingang Auftragsnummer	Einheit	Referenz- bereich			4602 29.03.20 21:45 29.03.20 22:27 42211881		4602 29.03.20 20:36 29.03.20 20:45 42211824		4800 29.03.20 17:30 29.03.20 17:43 42211766	
Hämostase Routine										
Quick	%	70 - 120	64	$\mathbf{\downarrow}$			68	<b>V</b>	66	4
Quick INR		<1.3	1.3				1.2		1.2	
aPTT	S	25-34	29				30			
Thrombinzeit 1	S	13-18	19	<b>1</b>			17			
Fibrinogen	g/l	1.7-4.0	6.2	<b>1</b>			6.8	<b>1</b>		
Faktor II	%	70 - 120	68	$\downarrow$			73			
Faktor V	%	70 - 120	114				>120	<b>1</b>		
Faktor VII	%	70 - 120	57	$\mathbf{\downarrow}$			53	<b>4</b>		
D-Dimere	μg/ml	0.19 - 0.5	5.65	<b>1</b>	7.28	<b>↑</b>	10.41	<u> </u>		

## DIC-Score according to ISTH

#### Platelet count

>100 Giga/L =0; <100 Giga/L = 1; <50 Giga/L = 2</p>

#### **D-dimers**

- Fibrinmonomers or d-dimers
- normal = 0; high= 2; very high= 3

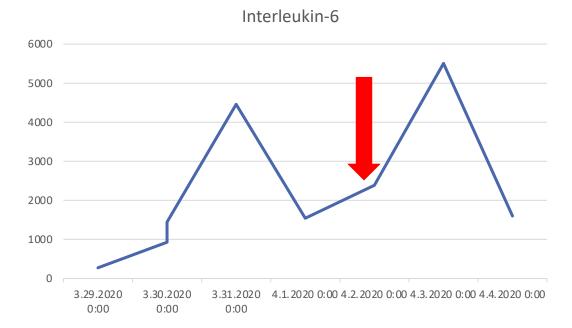
#### Prolonged PT/INR

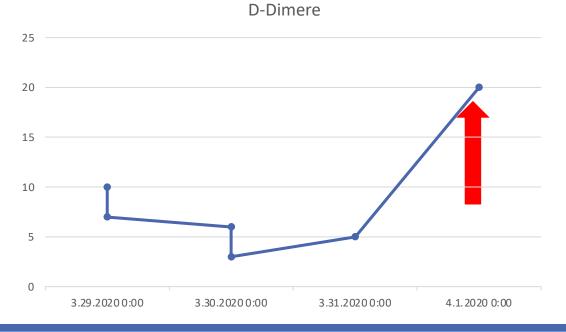
- <3 Sec. = 0; 3-6 Sec. = 1; >6 Sec. = 2
- INR <1.3 = 0, INR 1.3-1.6 = 1, INR >1.6 = 2

#### Fibrinogen

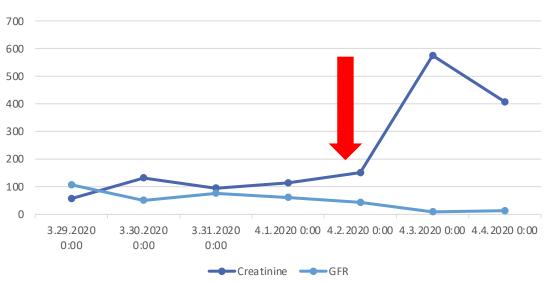
 $\circ$  >1.0 g/l = 0, <1.0 g/l = 1)

Score ≥ 5 : overt DIC

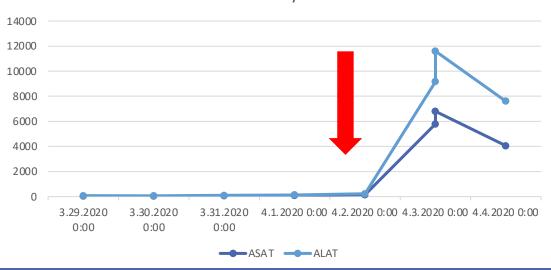




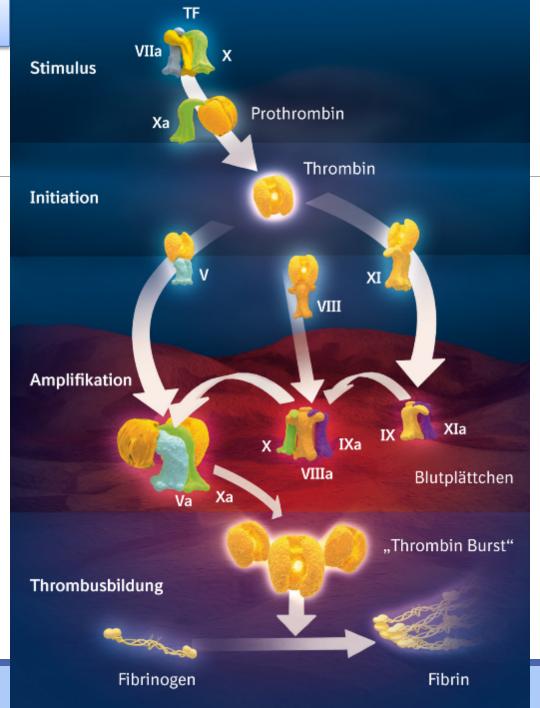




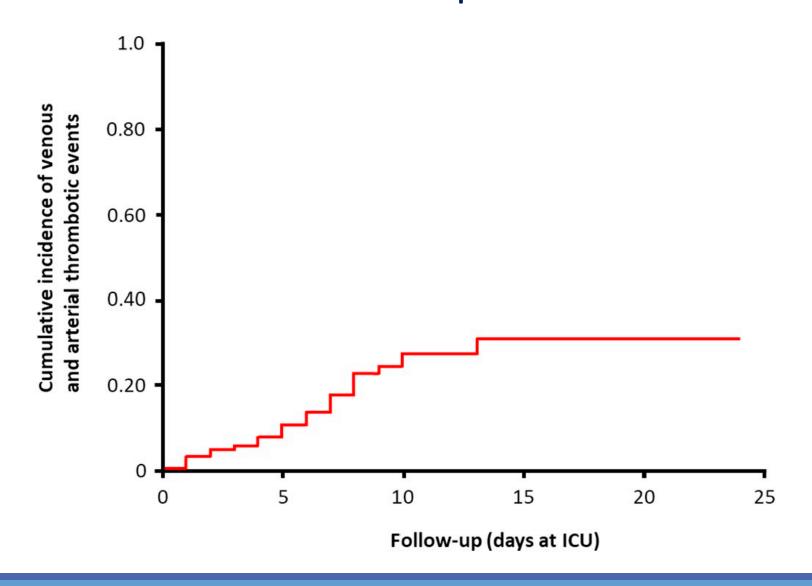
#### Liver enzymes



#### Cell based Hemostasis



## Thrombosis is frequent in COVID-19



# Pathophysiological changes in COVID-19 cause small- and large-vessel thrombosis

#### Local inflammation

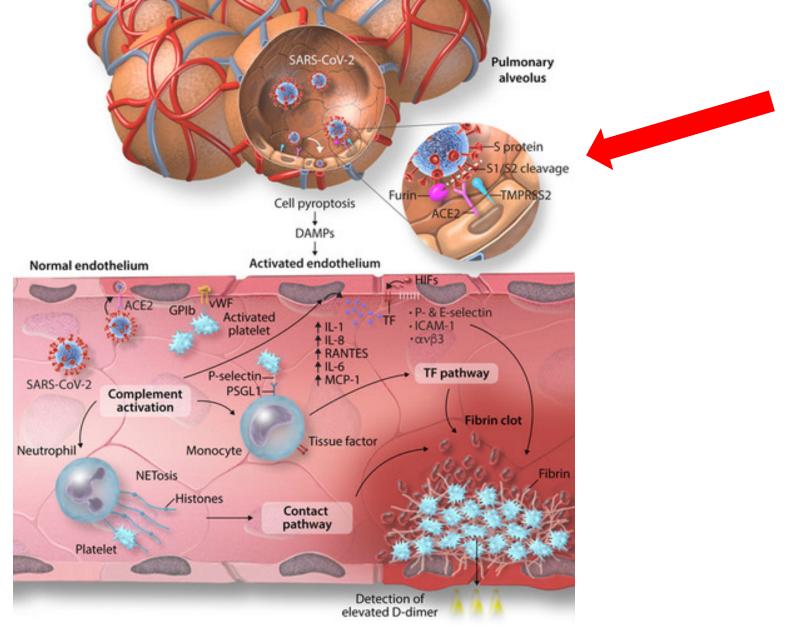
Local viral damage

#### Systemic inflammation

- Cytokines
- Viremia

#### Endotheliopathy

- Local
- Remote



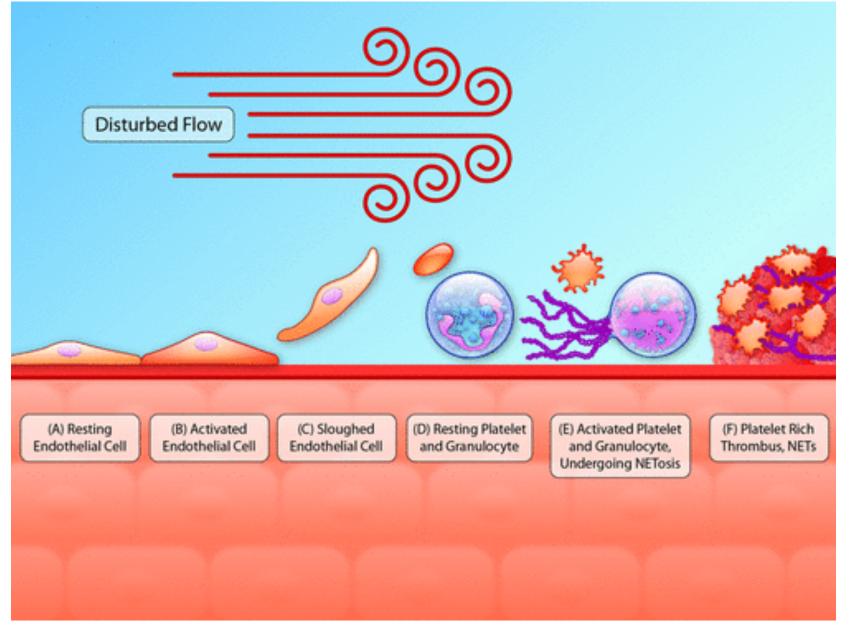


James D. McFadyen. Circulation Research. The Emerging Threat of (Micro)Thrombosis in COVID-19 and Its Therapeutic Implications, Volume: 127, Issue: 4, Pages: 571-587, DOI: (10.1161/CIRCRESAHA.120.317447)

## Pathophysiological changes in COVID-19

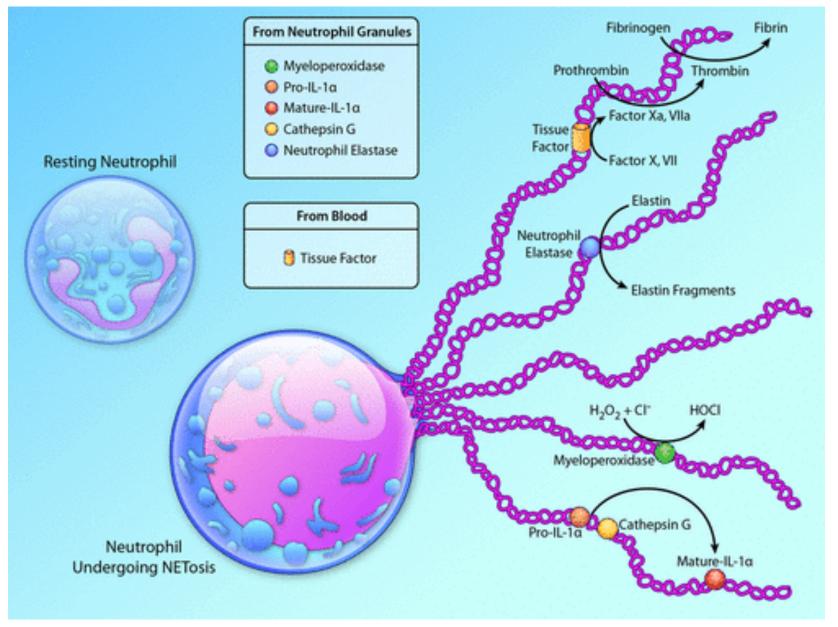
#### Local inflammation

- Pyroptosis of lung epithelium
  - Local damage
  - ARDS
- Alveolar fibrin depositions
  - High d-dimers without evident thrombosis
- Endothelial stimulation
  - High fibrinolytic capacity
  - High d-dimers without evident thrombosis
  - High procoagulant fibrinogen, VWF, other





Peter Libby. Circulation Research. Reassessing the Mechanisms of Acute Coronary Syndromes, Volume: 124, Issue: 1, Pages: 150-160, DOI: (10.1161/CIRCRESAHA.118.311098)





## Pathophysiological changes in COVID-19

#### Systemic inflammation

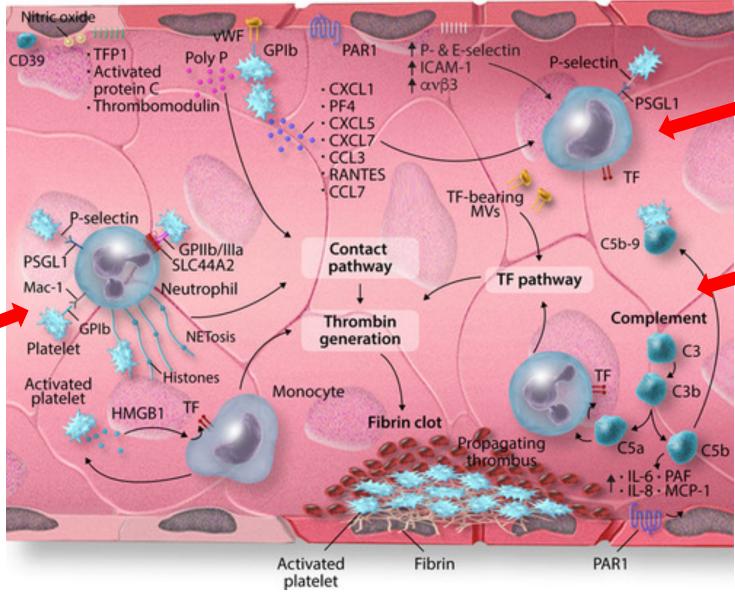
- Viremia
- Macrophage activation
- Ferritin, Cytokine storm, IL-6

## Pathophysiological changes in COVID-19

#### Endotheliopathy

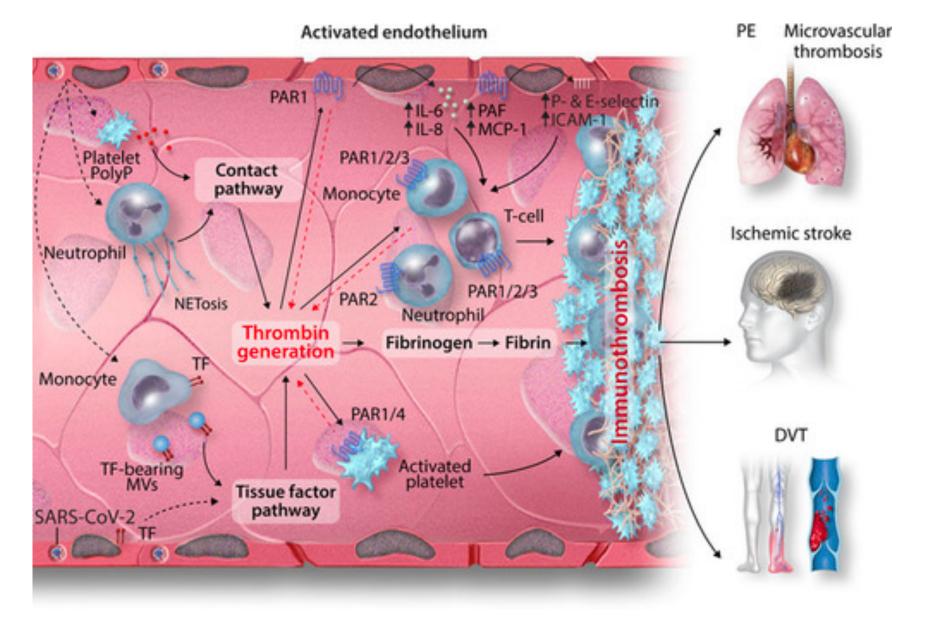
- Viral inclusions
- Macrophage and neutrophil infiltration
  - Tissue factor release
  - NETs
  - Complement activation
- Endothelial cell apoptosis
  - Microvascular thrombosis
  - Large vessel thrombosis

#### Normal endothelium Activated endothelium





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#### FORUM



### jth

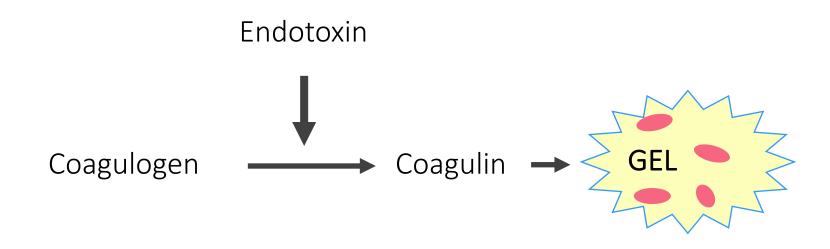
## The protective rather than prothrombotic fibrinogen in COVID-19 and other inflammatory states

Jecko Thachil

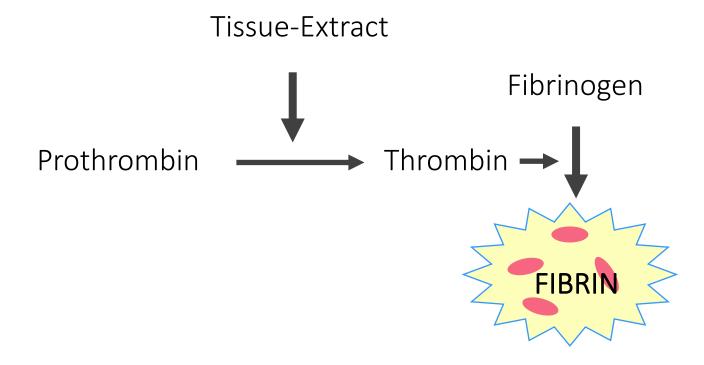
## Limulus polyphemus

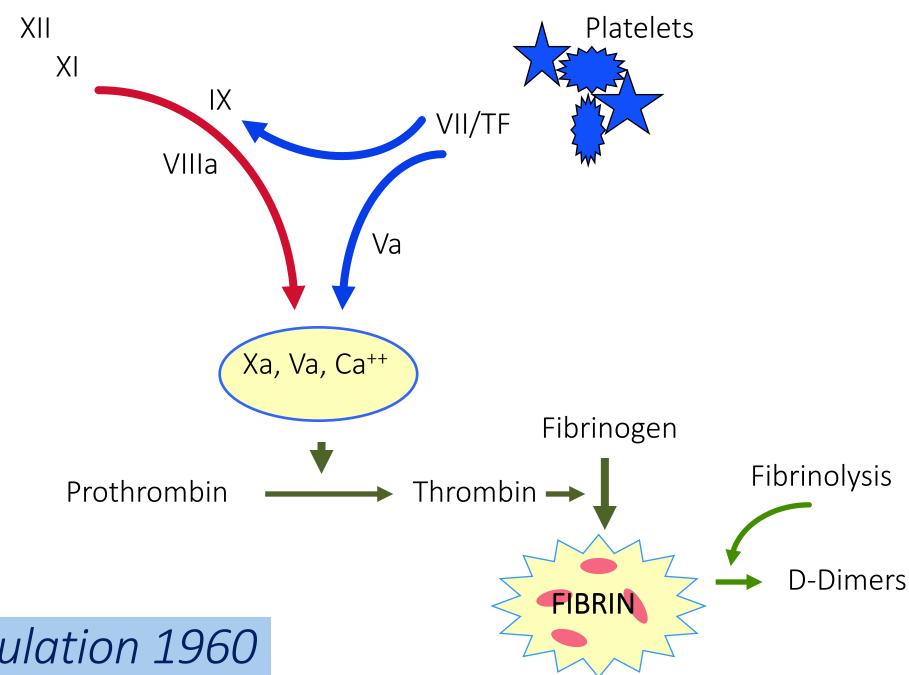


### Limulus test 1964



## Human coagulation theory 1904





Human coagulation 1960

# Pathophysiological changes in COVID-19 cause small- and large-vessel thrombosis

#### Local inflammation

Local viral damage

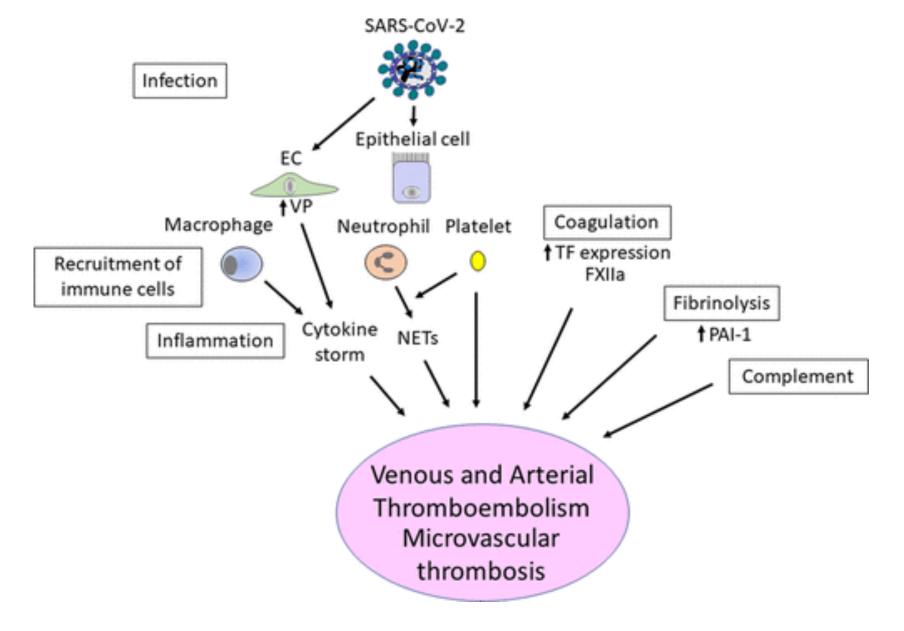
#### Systemic inflammation

- Cytokines
- Viremia
- High procoagulant proteins

#### Endotheliopathy

- Local
- Remote

## Thank you!





Nigel Mackman. Arteriosclerosis, Thrombosis, and Vascular Biology. Coagulation Abnormalities and Thrombosis in Patients Infected With SARS-CoV-2 and Other Pandemic Viruses, Volume: 40, Issue: 9, Pages: 2033-2044, DOI: (10.1161/ATVBAHA.120.314514)