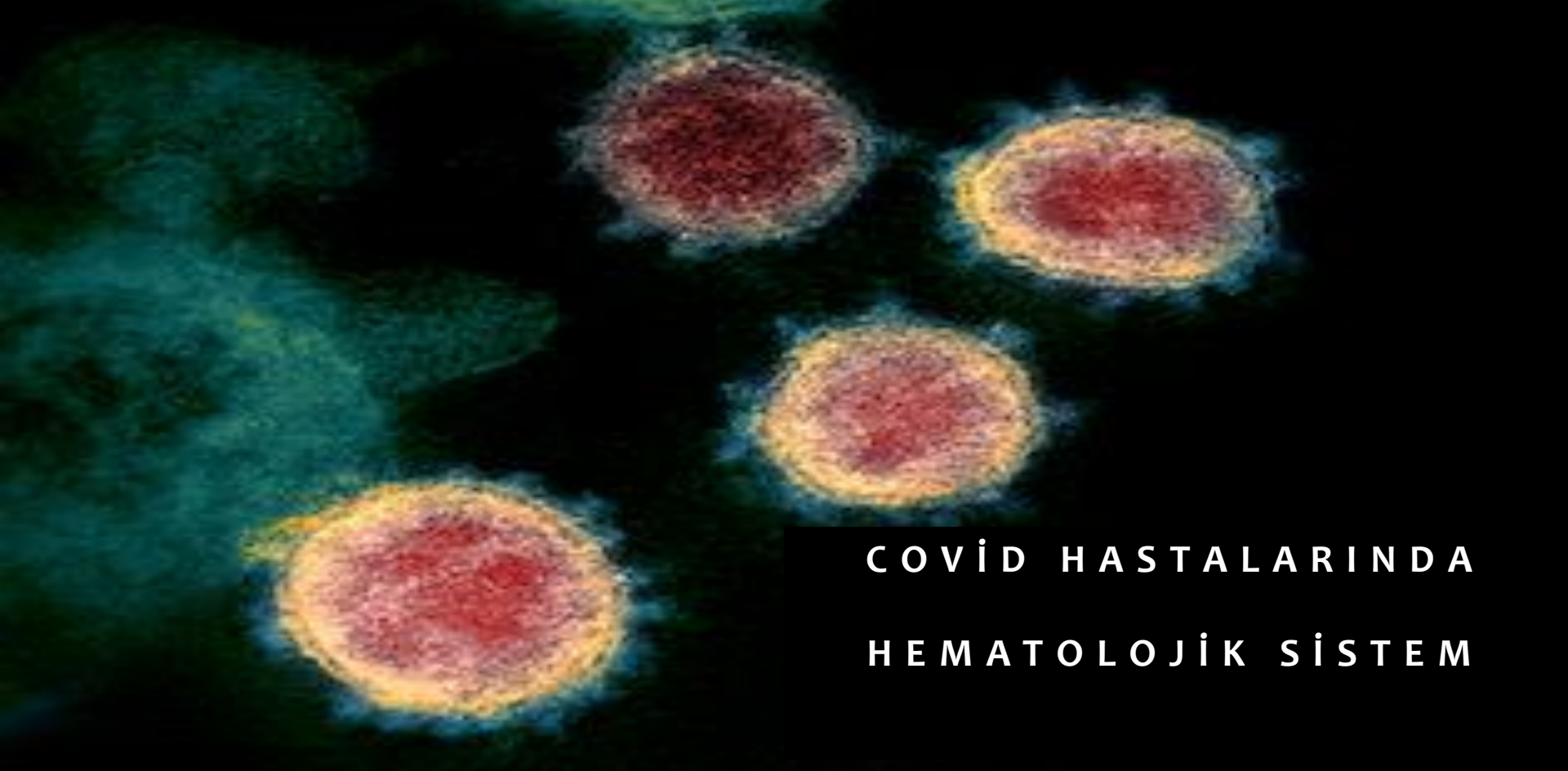
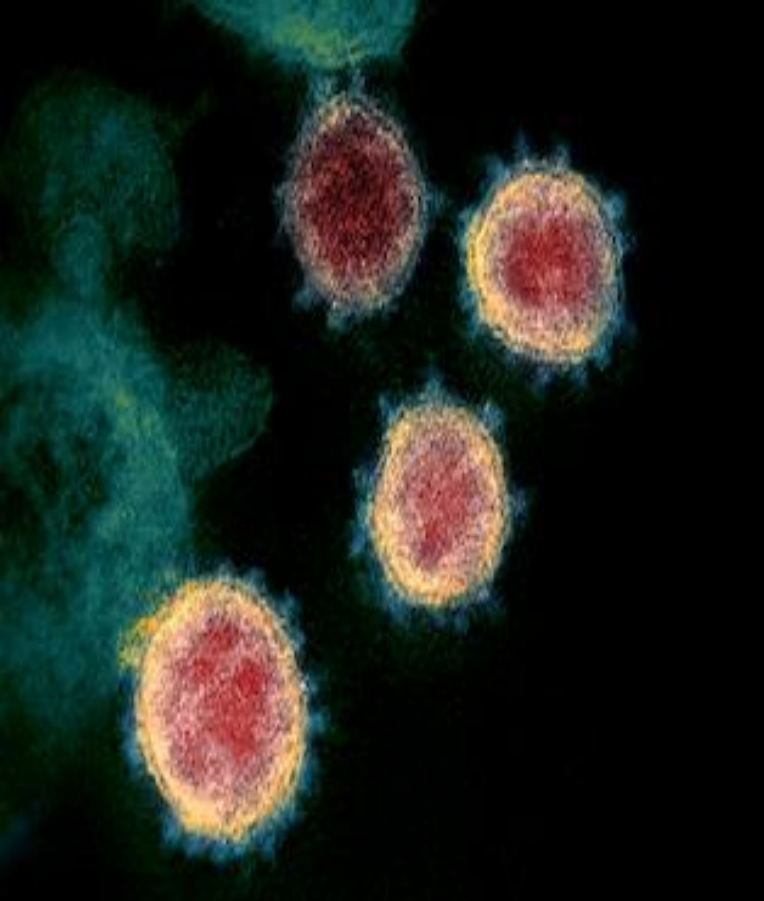




COVID HASTALARINDA HEMATOLOJİK SİSTEM

Dr. Öğretim Görevlisi
Vahide Aslihan DURAK
Bursa Uludağ Üniversitesi Tıp Fakültesi
Acil Tıp Anabilim Dalı



- 31 Aralık 2019 – Wuhan
- 7 Ocak 2020 – Etken
2019-nCoV
- International Virus
Taksonomy Committee –
SARS-CoV-2
- 30 Ocak 2020- Yeni
epidemik başlangıcı
Uluslararası Boyutta Halk Sağlığı
Acil Durumu
- 11 Şubat 2020- COVID 19
- 11 Mart 2020- Pandemi
ilan edilmesi

SARS-CoV-2

Order: Nidovirales

Family: Arteriviridae

Family: Roniviridae

Family: Mesoniviridae

Family: Coronaviridae

Subfamily: Torovirinae

Subfamily: Coronavirinae

Genus: Alphacoronavirus

Alphacoronavirus 1

HCoV-229E

HCoV-NL63

Murine coronavirus

HCoV-OC43

HCoV-HKU1

Lineage A

Lineage B

SARS-CoV

Lineage C

MERS-CoV

BtCoV-HKU4

BtCoV-HKU5

Lineage D

BtCoV-HKU9

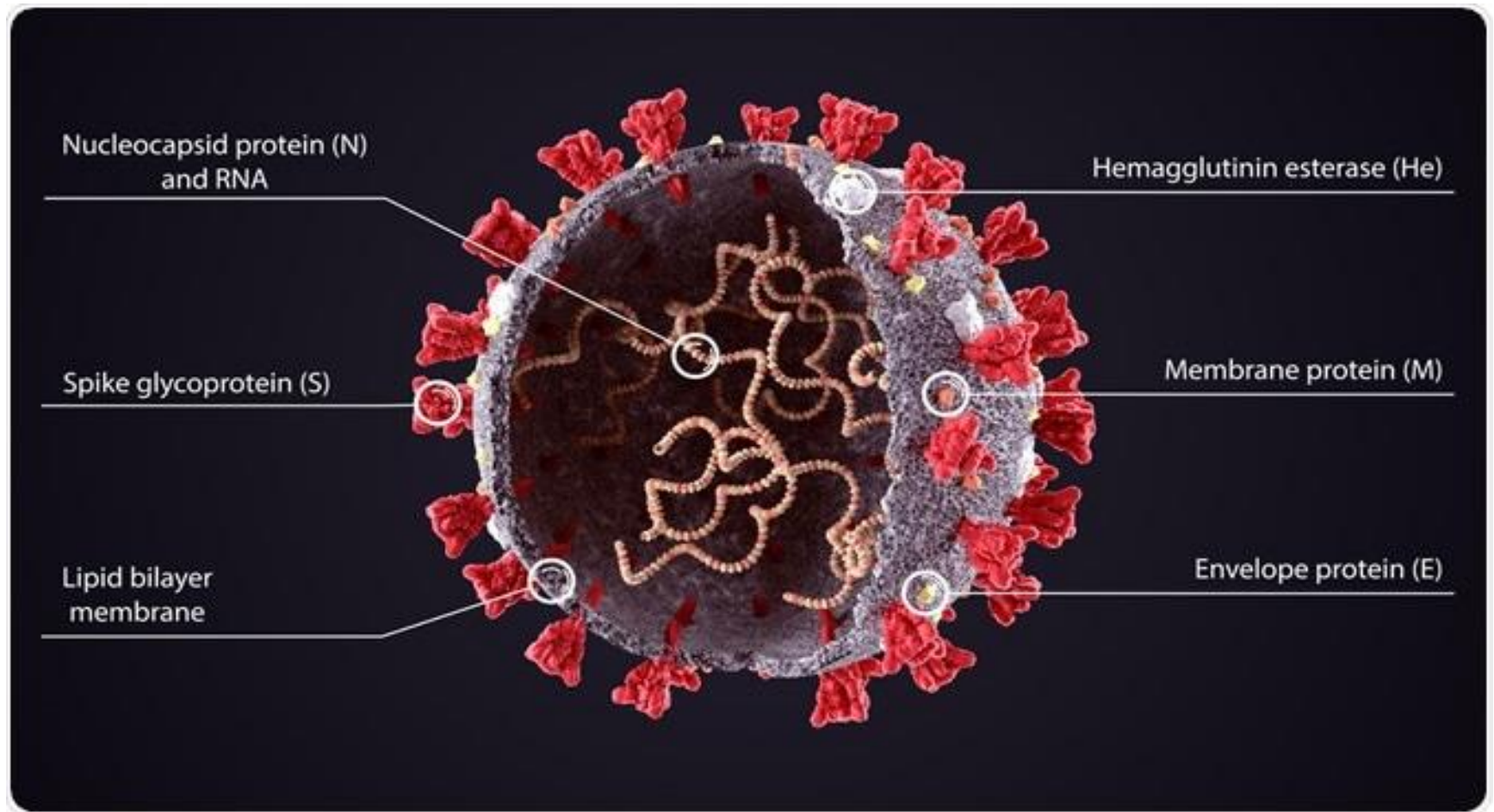
Genus: Gammacoronavirus

Avian coronavirus

Genus: Deltacoronavirus

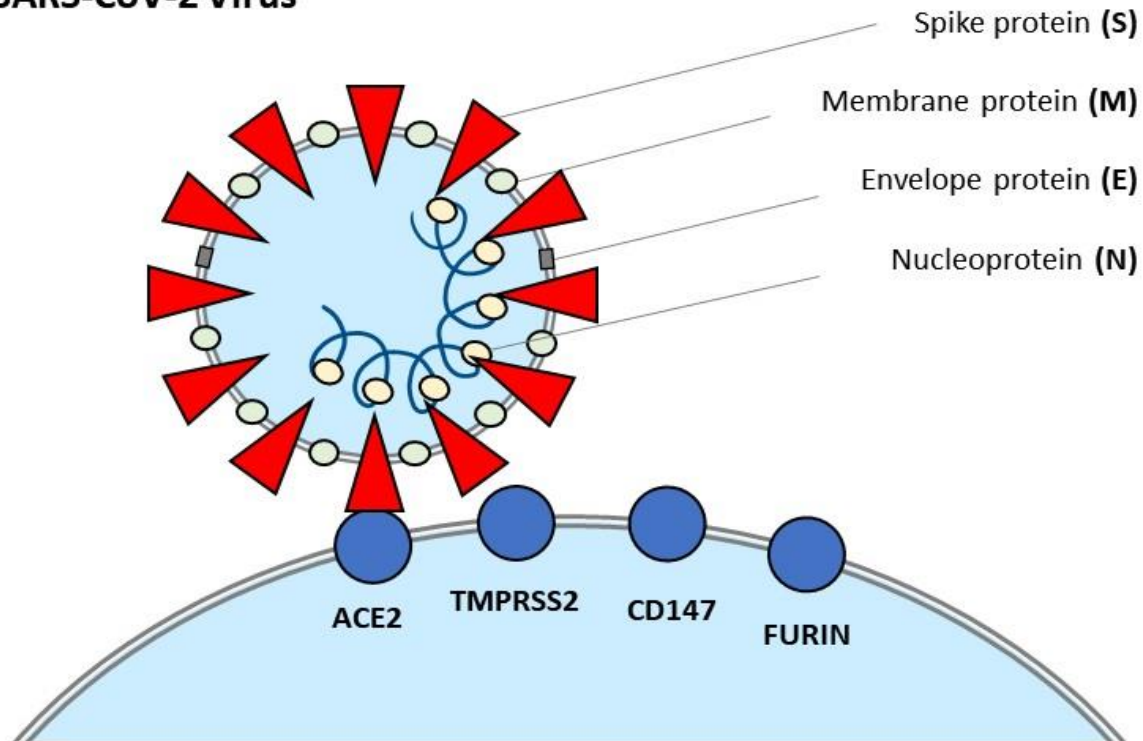
BuCoV-HKU11

SARS-CoV-2



Patogenez

The SARS-CoV-2 Virus



*Debuc B, Smadja DM. Is COVID-19 a New Hematologic Disease? Stem Cell Rev Rep. 2020 May 12:1–5. doi: 10.1007/s12015-020-09987-4.

**YENİ BİR HEMATOLOJİK
HASTALIK MI??**



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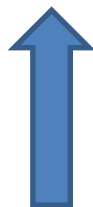
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Hematolojik Sistem

- Lenfopeni (%35-83)*
 - Nötrofili *
 - Eozinopeni *
 - Trombositopeni* (daha az sıklıkla trombositoz)
 - Lökosit **
 - Meta analizlerde***
 - Lökositoz
 - Lenfopeni
 - Trombositopeni
- } Mortalite ile ilişkili

*Letícia de Oliveira Toledo S, Sousa Nogueira L, das Graças Carvalho M, Romana Alves Rios D, de Barros Pinheiro M. COVID-19: Review and hematologic impact..ClíChim Acta. 2020 Nov;510:170-

176•

**Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069.

***Henry, B., de Oliveira, M., Benoit, S., Plebani, M., & Lippi, G. (2020). Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis, *Clinical Chemistry and Laboratory Medicine (CCLM)*, 58(7), 1021-1028.

Prognoz ilişkisi

- YBU ve SARS ilişkisi
- **Hastalık erken dönemi**
 - Lökosit sayısı normal / azalmış
 - Lenfosit sayısı normal / azalmış
- **7. ve 14. günler arası**
 - Organ tutulumu görülmesi
 - Sitokin artışı
 - İnflamatuvar medyatörlerin artışı
 - Lenfosit sayısında belirgin azalma

Lenfopeni Patofizyolojisi*

- Lenfositlerde direk lizis (ACE2 reseptörlerine bağlı olarak)
- Aşırı miktarda sitokin üretimine bağlı lenfosit apoptozisi
- Lenfoid organlarda atrofi
- Laktik asidozun lenfosit proliferasyonunu inhibe etmesi(Kanser hastaları)

* E. Terpos, I. Ntanasis-Stathopoulos, I. Elalamy, E. Kastiris, T.N. Sergentanis, M. Politou, T. Psaltopoulou, G. Gerotziafas, M.A. Dimopoulos, Hematological findings and complications of COVID-19, Am. J. Hematol. (2020).

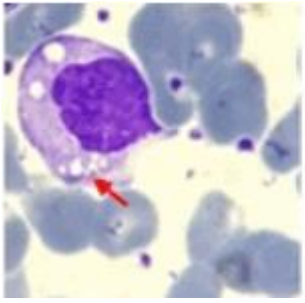
Prognoz ilişkisi

- **Lenfopeni**
 - Mortalite ile ilişkisi en yüksek*
- **Lenfosit/ Lökosit oranı azalması****
 - Ağır klinik tablo
- **Nötrofil/ Lenfosit oranı artışı,
Nötrofil/Platelet oranı artışı*****
 - Myokardiyal hasar ve Mortalite artışı

* Letícia de Oliveira Toledo S, Sousa Nogueira L, das Graças Carvalho M, Romana Alves Rios D, de Barros Pinheiro M. COVID-19: Review and hematologic impact..Clim Acta. 2020 Nov;510:170-176.

* * C. Qin, L. Zhou, Z. Hu, S. Zhang, S. Yang, Y. Tao, C. Xie, K. Ma, K. Shang, W. Wang, D.S. Tian, Dysregulation of immune response in patients with COVID-19 in Wuhan, China, Clin. Infect. Dis. (2020).

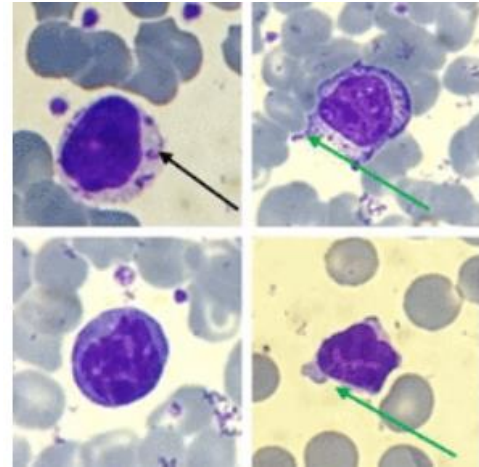
***T. Guo, Y. Fan, M. Chen, X. Wu, L. Zhang, T. He, H. Wang, J. Wan, X. Wang, Z. Lu, Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19), JAMA Cardiol., 2020.



Morfolojik Özellikler*

- Reaktif ve plazmositoid lenfositler
- Nötrofillerde toksik granülasyon benzeri koyu renkli granülasyonlar
- Çekirdekte kromatin kümelenmesi
- Apoptotik nötrofiller
- İmmatür ve displastik granülositler
- Dev plateletler (hiperkromatik, psöpod ve vakuol içeren)

* G. Zini, S. Bellesi, F. Ramundo, G. d'Onofrio, Morphological anomalies of circulating blood cells in COVID-19, Am. J. Hematol. (2020).



Hemostaz Testleri*

- PT ve aPTT uzaması
- D-dimer artışı (Kötü prognoz)
- Fibrin yıkım ürünleri/ Fibrinojen artışı



MORTALİTE İLİŞKİLİ

* N. Tang, D. Li, X. Wang, Z. Sun, Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia, J. Thromb.Haemost. 18 (4) (2020) 844–847.

COVID-19 ilişkili Koagülopati

- Pulmoner Emboli
 - DVT
 - İskemik strok
- 
- YBU yatış (%30)*

*Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, Kaptein FHJ, van Paassen J, Stals MAM, Huisman MV, Endeman H. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020 Jul;191:145-147.

- a PTT uzaması olan hastalarda
 - VWF, F8 ve Antifosfolipid antikor artışı **

** Escher R, Breakey N, Lämmle B. Severe COVID-19 infection associated with endothelial activation. Thromb Res. 2020 Jun;190:62.

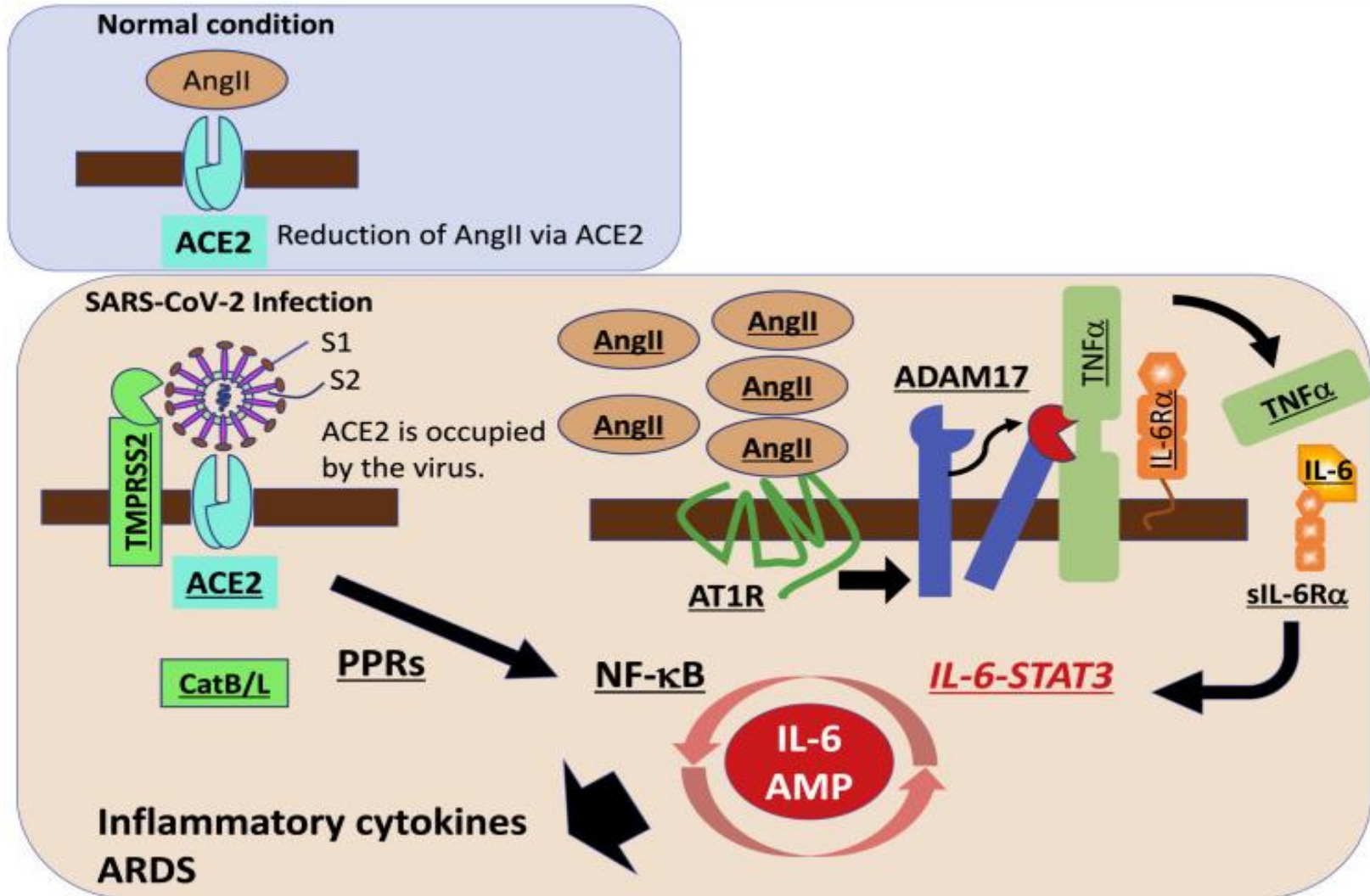
COVID-19 ilişkili Koagülopati*

- **Tedavi**

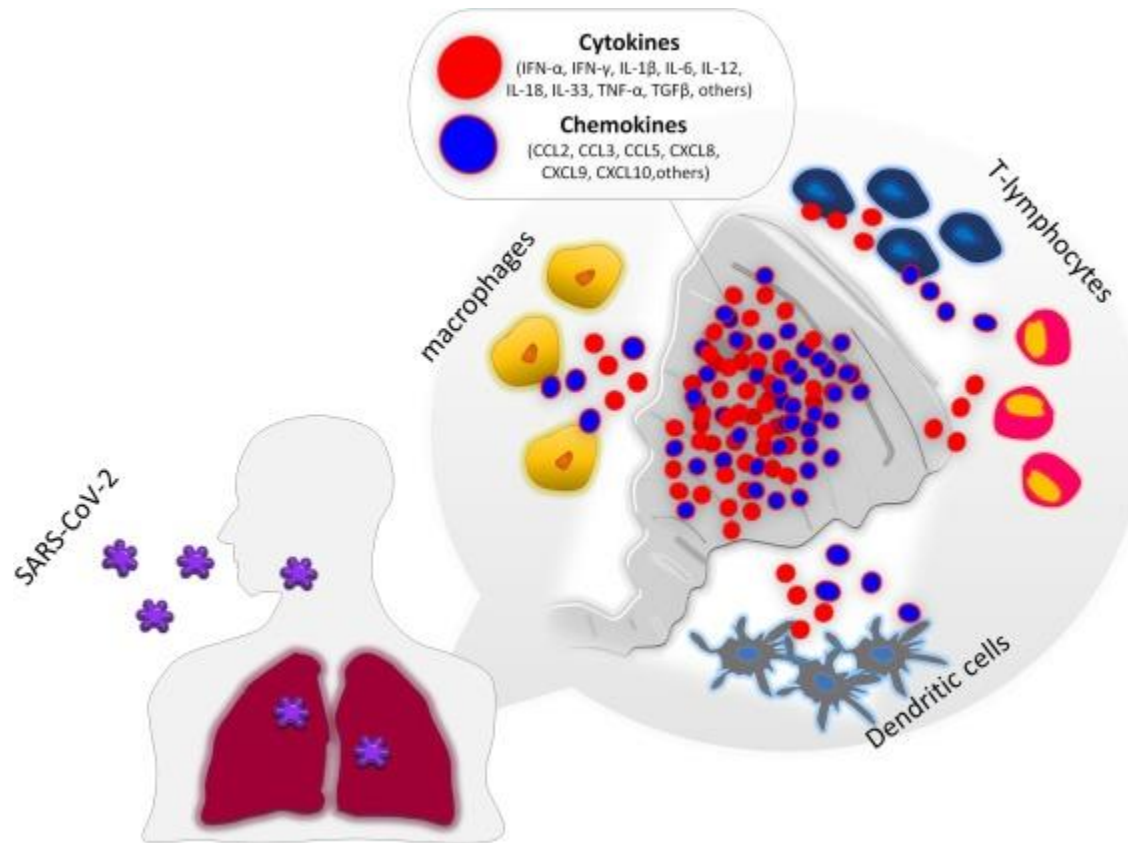
- Proflaktik heparin (DMAH) verilmesi
- Anfraksiyone heparin
- Fibrinolitik tedaviler (TPA) deneysel aşamada

*Agboduwe C, Basu S. Haematological manifestations of COVID-19: From cytopenia to coagulopathy. Eur J Haematol. 2020 Jul 14;10.1111/ejh.13491.

COVID-19 Sitokin Fırtınası



COVID-19 Sitokin Fırtınası



COVID-19 Sitokin Fırtınası

- **Tedavi Hedefleri**

- Immunmodülatör terapiler

- Deksametazon,

- **Tocilizumab(IL-6 reseptör antagonisti)***

- *De Luna G, Habibi A, Deux JF, Colard M, Pham Hung d'Alexandry d'Orengiani AL, Schlemmer F, Joher N, Kassasseya C, Pawlotsky JM, Ourghanlian C, Michel M, Mekontso-Dessap A, Bartolucci P. Rapid and severe Covid-19 pneumonia with severe acute chest syndrome in a sickle cell patient successfully treated with tocilizumab. Am J Hematol. 2020 Jul;95(7):876-878.

- *Guaraldi G, Meschiari M, Cozzi-Lepri A, Milic J, Tonelli R, Menozzi M, Franceschini E, Cuomo G, Orlando G, Borghi V, Santoro A, Di Gaetano M, Puzzolante C, Carli F, Bedini A, Corradi L, Fantini R, Castaniere I, Tabbi L, Girardis M, Tedeschi S, Giannella M, Bartoletti M, Pascale R, Dolci G, Brugioni L, Pietrangelo A, Cossarizza A, Pea F, Clini E, Salvarani C, Massari M, Viale PL, Mussini C. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. Lancet Rheumatol. 2020 Aug;2(8):e474-e484.

- Anakinra(IL-1 reseptör antagonisti)

- Mezenkimal kök hücre verilmesi

Diğer Belirteçler*

- Sedimentasyon artışı
- LDH artışı
- CRP artışı
- Troponin artışı
- Total bilirubin artışı
- AST ve ALT artışı
- Prokalsitonin artışı
- Kreatinin artışı
- Ferritin artışı
- Albumin azalması

*Letícia de Oliveira Toledo S, Sousa Nogueira L, das Graças Carvalho M, Romana Alves Rios D, de Barros Pinheiro M. COVID-19: Review and hematologic impact..CliChim Acta. 2020



TEŞEKKÜRLER