COVID-19: KEEPING UP WITH A MOVING TARGET MAY 6, 2020 UPDATE

Paul Auwaerter, MD, MBA, FIDSA
Clinical Director, Division of Infectious Diseases
Sherrilyn and Ken Fisher Professor of Medicine
Fisher Center for Environmental Infectious Diseases
Johns Hopkins University School of Medicine
Baltimore, Maryland

COVID-19: Keeping Up With A Moving Target

Twice Every Week @ COVID19.DKBmed.com

Every Wednesday Evening and Friday Morning

CME Information

Jointly provided by Postgraduate Institute for Medicine, DKBmed, and the Institute for Johns Hopkins Nursing.

Disclosure of Conflicts of Interest

Postgraduate Institute for Medicine (PIM) requires instructors, planners, managers, and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest (COI) they may have as related to the content of this activity. All identified COI are thoroughly vetted and resolved according to PIM policy. PIM is committed to providing its learners with high quality activities and related materials that promote improvements or quality in healthcare and not a specific proprietary business interest of a commercial interest.

The faculty reported the following financial relationships or relationships they or their spouse/life partner have with commercial interests related to the content of this continuing education activity:

Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials. These include hydroxychloroquine/chloroquine, hydroxychloroquine/chloroquine in combination with azithromycin, lopinavir plus ritonavir, tocilizumab, corticosteroids, and COVID-19 convalescent plasma. All activity, content, and materials have been developed solely by the activity directors, planning committee members, and faculty presenters, and are free of influence from a commercial entity.

CME Information

To attest for CME/CE credit, please visit

COVID19.DKBmed.com

Learning Objectives

- Describe testing priorities for COVID-19 illness
- Review remdesivir data and what is known from randomized controlled trials
- Discuss tissue injury mechanisms in COVID-19

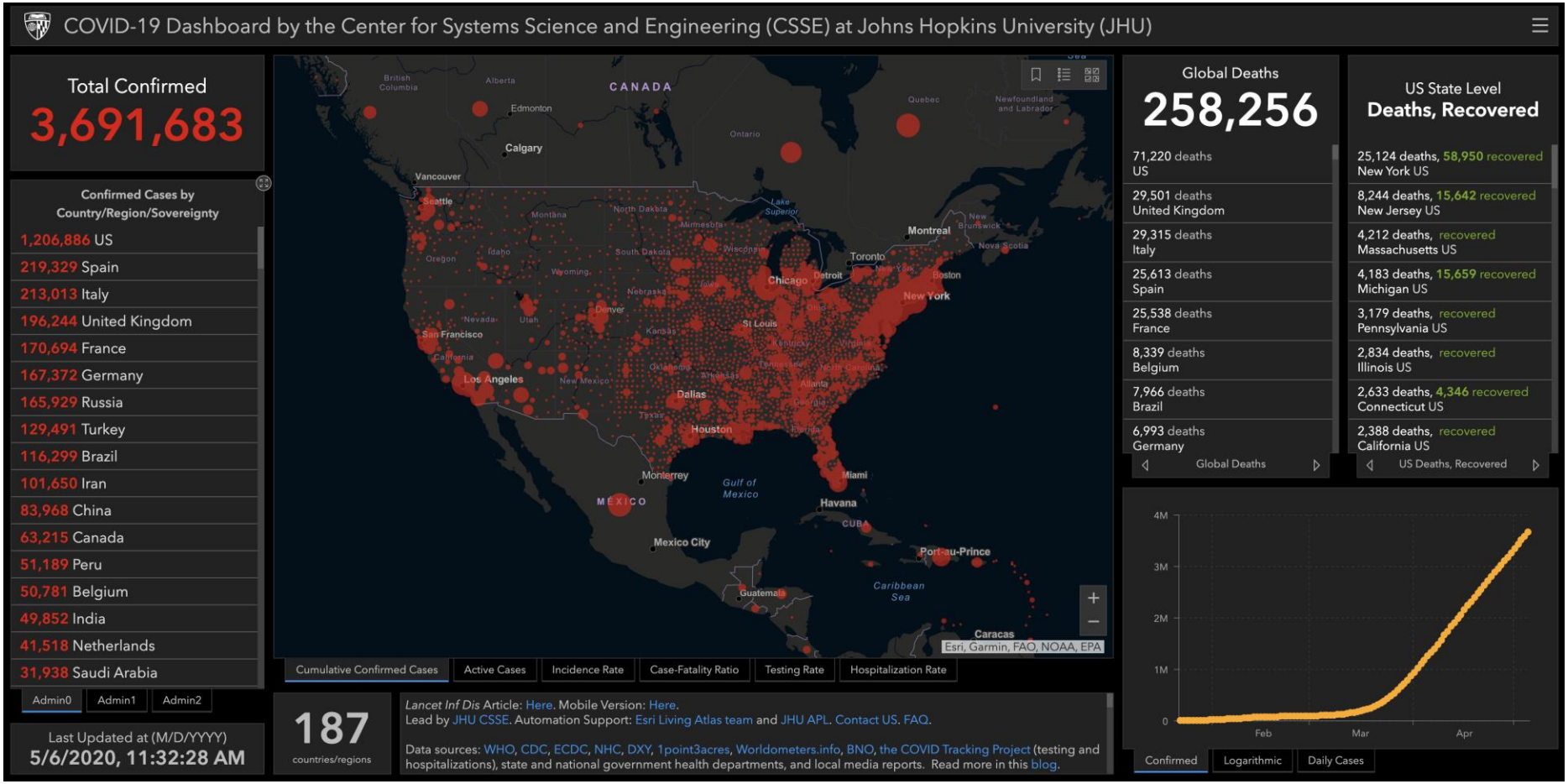
Paul Auwaerter, MD, MBA, FIDSA
Clinical Director, Division of Infectious Diseases
Sherrilyn and Ken Fisher Professor of Medicine
Fisher Center for Environmental Infectious Diseases
Johns Hopkins University School of Medicine
Baltimore, Maryland

Thank You

This program is brought to you through the generous support of DKBmed, Postgraduate Institute for Medicine, and the Institute for Johns Hopkins Nursing.

Please see **COVID19.DKBmed.com** for additional resources and educational activities

Total Cases: N. America (5/6/20)



coronavirus.jhu.edu/map.html

Updated CDC COVID-19 Testing Recommendations

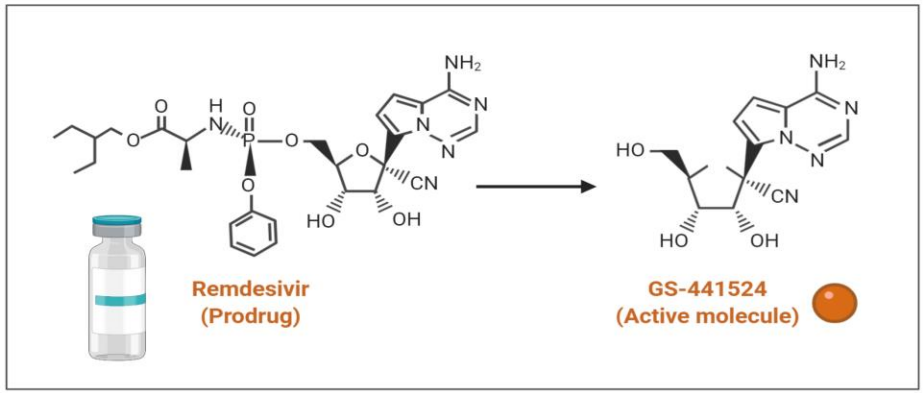
Priorities for Testing Patients with Suspected COVID-19 Infection (CDC)†¶

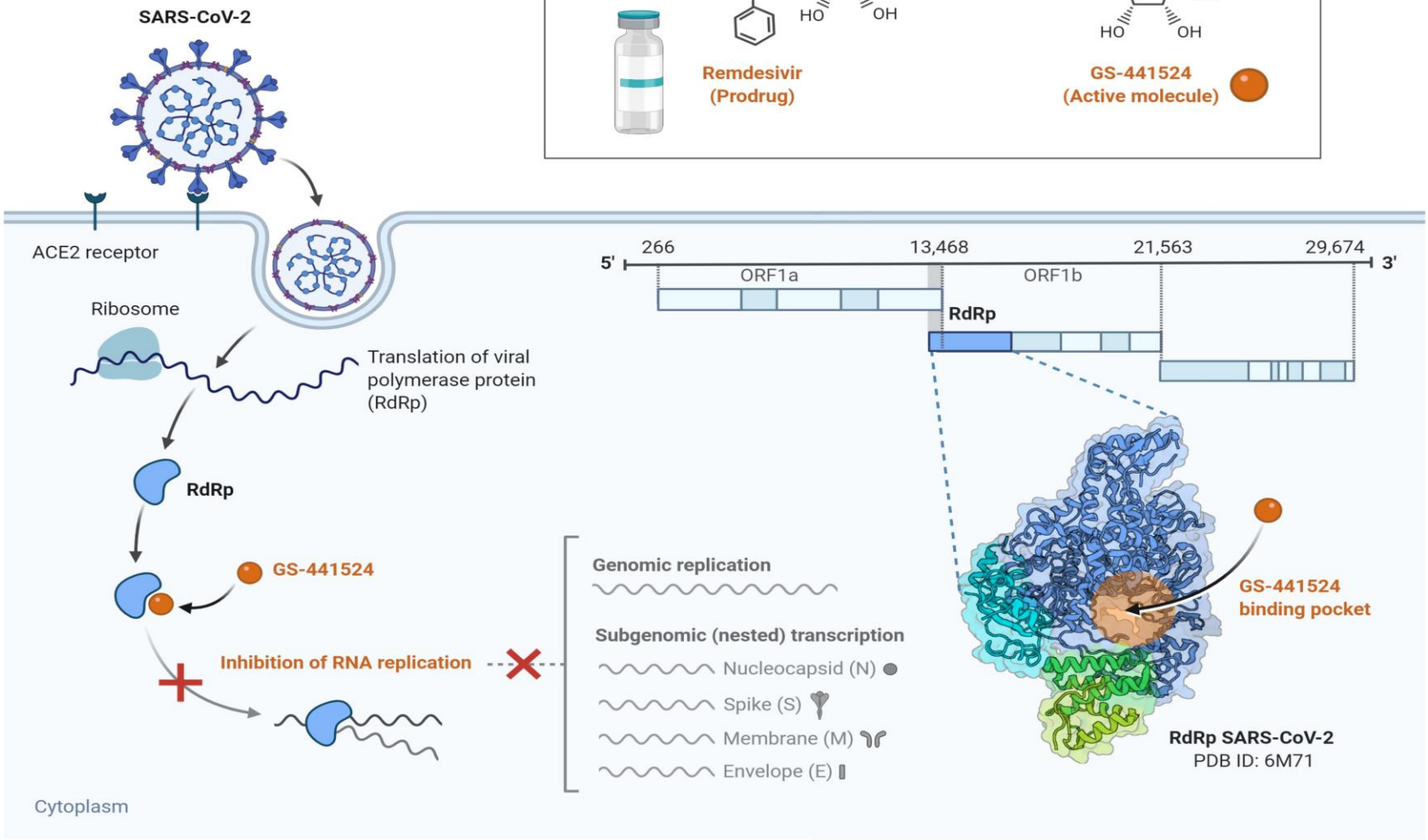
High Priority (Nucleic acid or antigen testing)¶
• Hospitalized patients
• Healthcare facility workers, others in congregate living settings, first responders with symptoms
• High priority patients:
  ◦ With COVID0-19 symptoms
  ◦ Asymptomatic people IF from a racial or ethnic minority group disproportionately affected by adverse COVID-19 outcomes
  ▪ African-Americans, Hispanics and Latinos, some American Indian tribes (e.g., Navajo).
  ◦ Asymptomatic people who are prioritized by clinicians or public health departments
  ▪ Public health monitoring
  ▪ Sentinel surveillance,
  ▪ Co-morbidities or disability
  ▪ Residence in congregate housing, homeless shelter or long-term care facility
• **Recommendations for Antibody testing**
  ◦ CDC has no recommendations for diagnostic purposes

†*Source*: U.S. Centers for Disease Control and Prevention. Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19) Revised May 3, 2020.¶

Remdesivir

Potential repurposed drug for COVID-19





Remdesivir Trials

Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial

Yeming Wang, Dingyu Zhang*, Guanhua Du*, Ronghui Du*, Jianping Zhao*, Yang Jin*, Shouzhi Fu*, Ling Gao*, Zhenshun Cheng*, Qiaofa Lu*, Yi Hu*, Guangwei Luo*, Ke Wang, Yang Lu, Huadong Li, Shuzhen Wang, Shunan Ruan, Chengqing Yang, Chunlin Mei, Yi Wang, Dan Ding, Feng Wu, Xin Tang, Xianzhi Ye, Yingchun Ye, Bing Liu, Jie Yang, Wen Yin, Aili Wang, Guohui Fan, Fei Zhou, Zhibo Liu, Xiaoying Gu, Jiuyang Xu, Lianhan Shang, Yi Zhang, Lianjun Cao, Tingting Guo, Yan Wan, Hong Qin, Yushen Jiang, Thomas Jaki, Frederick G Hayden, Peter W Horby, Bin Cao, Chen Wang*

N = 237 patients, halted
Confirmed infection, 12d or fewer of symptoms, lung involvement
Remdesivir 200 mg d 1 then 100 mg IV daily vs. placebo

Findings:

1. No clinical improvement (subgroup < 10d with trend)
2. No difference in mortality (subgroup < 10d with trend)
3. No effect on viral load in upper or lower respiratory tracts

Lancet 4/29/20

NIH Press Release (4/29/20)

- RCT (data not released) in patients with lung involvement
  - 200 mg day 1, then 100 mg q 24 IV x 10d (max)
  - 1063 pts (68 sites: 47 US, 21 Europe & Asia)
  - LOS reduction 31% (11d v 15d, $P < 0.001$)
    - Mean duration of symptoms not provided
  - Mortality trend suggested (8% v 11.6%, but not statistically significant, $P = 0.059$).
- Data safety monitoring board did not suggest halting the study due to a clear and convincing benefit of treatment.
- **Primary endpoint changed during trial (in April)**
  - Original: 8-point severity scale (death, mechanical ventilation, hospitalized with oxygen to discharged without limits on activity)
  - Revised: time to recovery

https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19

Remdesivir dosing (Adults)

FDA EUA for Use of Remdesivir to Treat Hospitalized Patients with COVID-19		
Patient Status	**Treatment Duration**	**Dosing and Administration**
Receiving mechanical ventilation or extracorporeal membrane oxygenation (ECMO)	10 days	• Day 1 (loading dose): Remdesivir 200 mg IV • Days 2 through 9: Remdesivir 100 mg IV daily
SaO2 ≤94% on room air or supplemental oxygen required	5 days; if no improvement after 5 days, continue for an additional 5 days	• Day 1, loading dose: Remdesivir 200 mg IV • Days 2 through 5: Remdesivir 100 mg IV daily

https://www.fda.gov/media/137566/download (accessed 5/4/20)

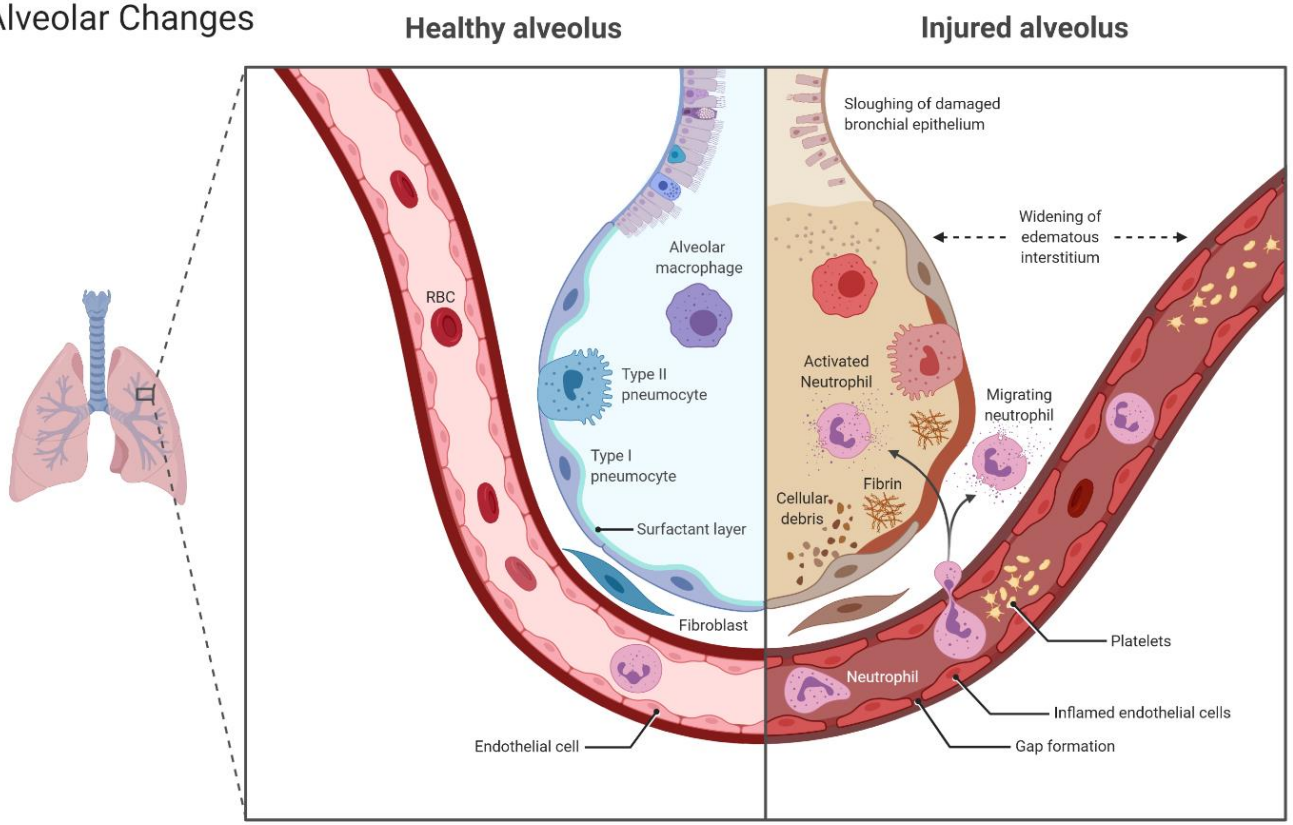
Direct viral or cytokine storm, tissue injury

- ARDS
- Renal failure
  - Common in severe, correlates with mortality
- MI
- PE/DVT
- LFT
  - Abnormal ~50%
- CNS
  - Stroke, seizure, encephalitis
- GI
  - ~ 20% with diarrhea
- Smell loss
- Ocular
  - Conjunctivitis, described more in sicker patients

Acute Respiratory Distress Syndrome

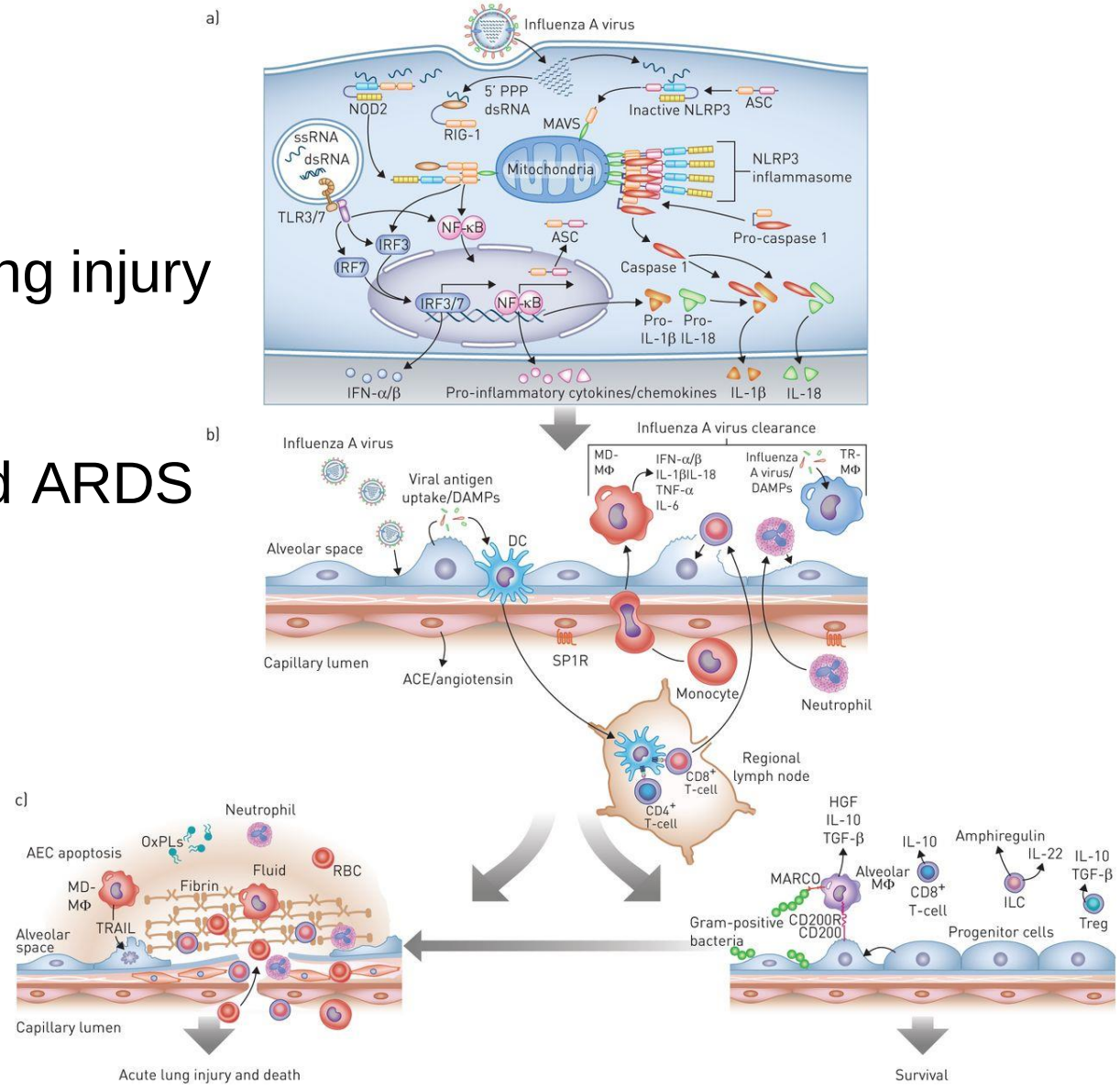
Typical Acute Respiratory Distress Syndrome (ARDS, bacterial sepsis or pneumonia)

Alveolar Changes



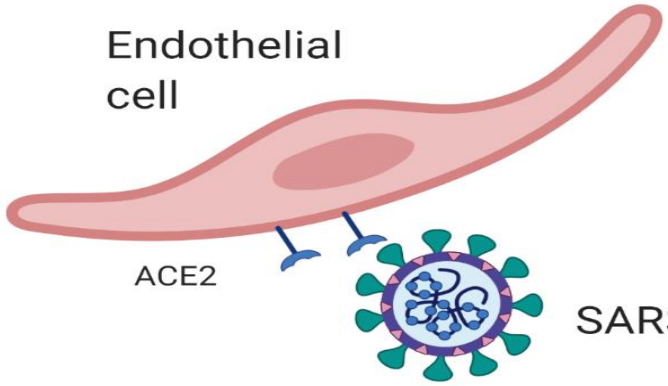
SARS-CoV-2 lung injury

Likely similar to influenza-related ARDS



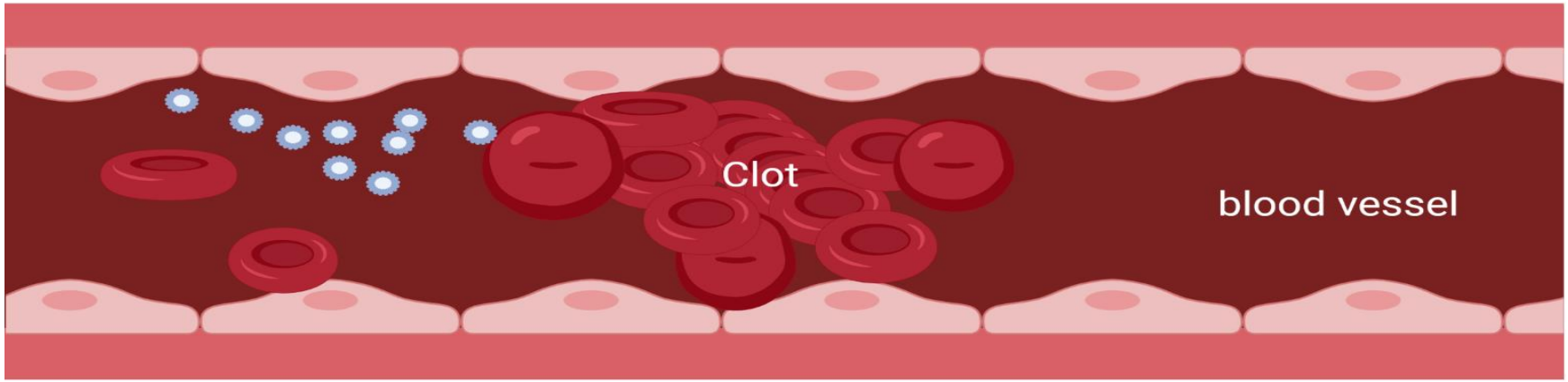
Herold, et al. Eur J Resp Dis 2015, 45: 1463-1478;

COVID-19 and Thrombotic Events



Blood vessels

ACE2 receptors and virus appear to promote clots, MIs, troponin leaks



and/or vasoconstriction?

To receive CME/CE credit:

- Complete the evaluation on at COVID19.DKBmed.com
- Upon registering and successfully completing the activity evaluation, you will have immediate access to your certificate.

To access more resources related to COVID-19:

- Access our resource hub at COVID19.DKBmed.com

To ask your own question:

- Email QA@dkbmed.com

Clots, clots and more clots (selected papers)

- Italy, 388 pts, 68% men, 16% ICU
  - Prophylaxis 100% ICU, 75% on ward.
    - Thrombosis 21% (27.6% ICU, 6.6% ward).
    - 50% diagnosed in first 24h
    - Overt DIC in 8 (2.2%) [Lodigiani, Thromb Res 2020; 191:9-14]
- France, high incidence in fully anticoagulated patients

  ICU (n=26) 100% vs. 56% p=0.03 [Llitjos JF J Thromb Haemost 2020]
- Netherlands, high incidence thrombosis in ICU
  - N = 184, 31% incidence thrombotic complications [Klok, Thromb Res 2020, Apr 10]
- China, hospitalized patients
  - 19.7% of 416 pts, cardiac injury [Shi, JAMA Cardiology, 2020]

Debate: who to anticoagulate, prophylactically? High – intensity? Multiple guidelines.