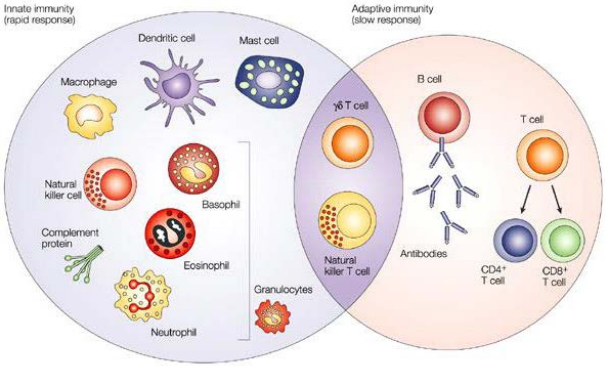
Experience Rochester

UNDERSTANDING THE IMMUNE RESPONSE AND COVID-19

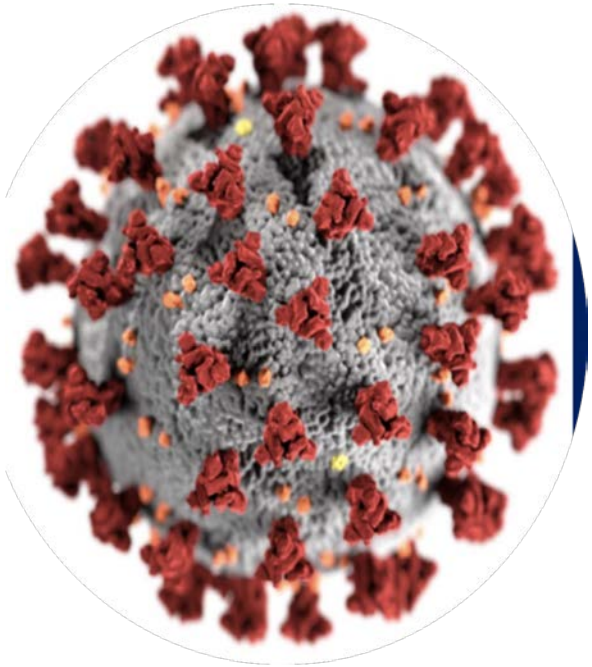
November 19, 2020



UNDERSTANDING COVID-19

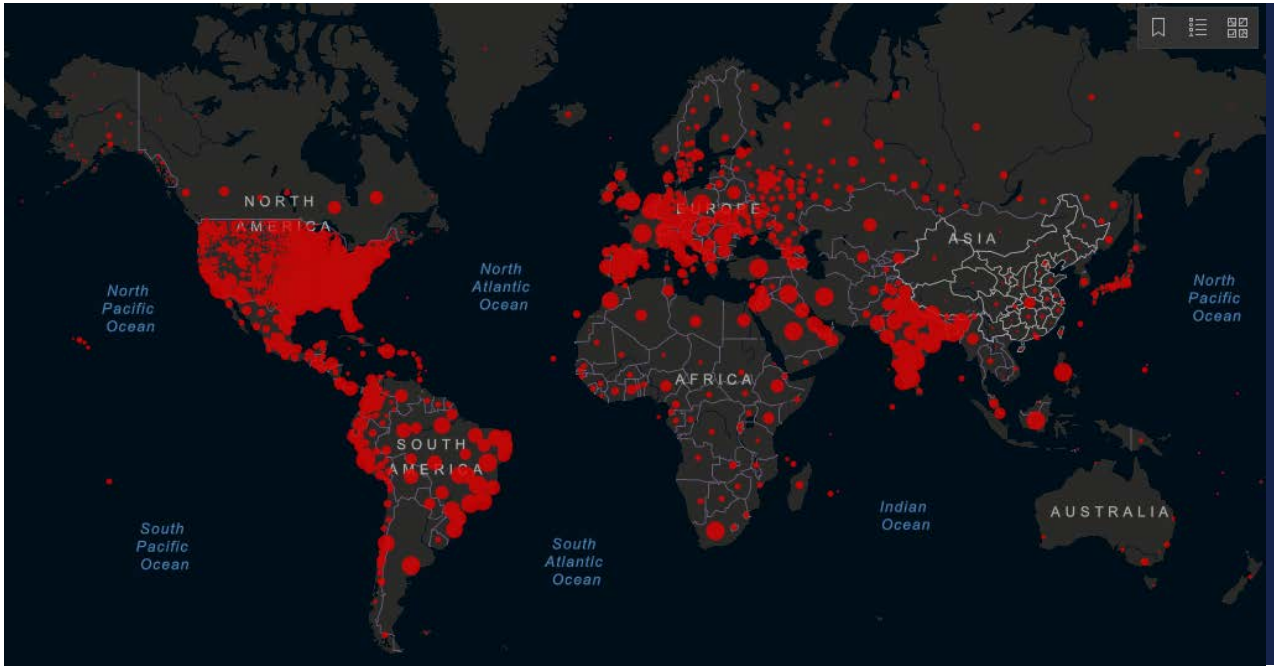
Benjamin Korman
Assistant Professor
Department of Allergy, Immunology, and Rheumatology

SARS-CoV2 (COVID-19): BASIC FACTS



- Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2 virus)
- Causes COVID-19 (Corona virus disease 2019 illness)
- Single Stranded RNA Virus
- Binds cells and enters through ACE2 receptor
- Closely related to SARS-CoV1 (2002 SARS outbreak)
- First identified in Wuhan, China in late 2019

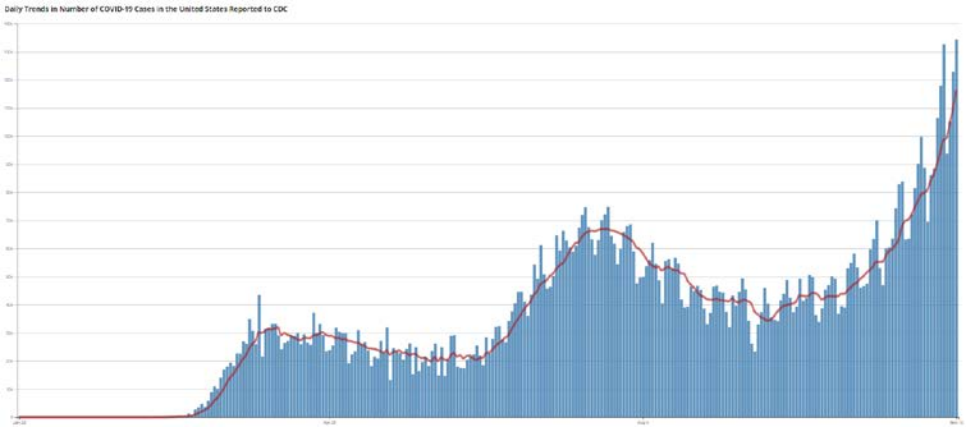
COVID-19: PANDEMIC SPREAD

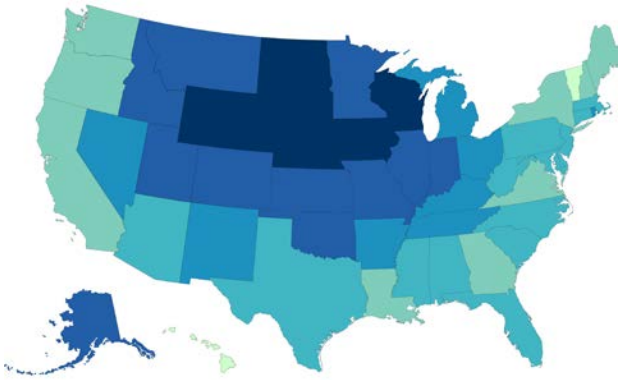


52 Million Cases
1.2 Million Deaths

Johns Hopkins Coronavirus Resource Center | 11/11/2020

COVID-19: PANDEMIC SPREAD





Cases/100,000

- 0-1,109
- 1,326-2,095
- 2,160-2,640
- 2,700-3,202
- 3,267-3,934
- 4,008-6,355

10.1 Million Cases

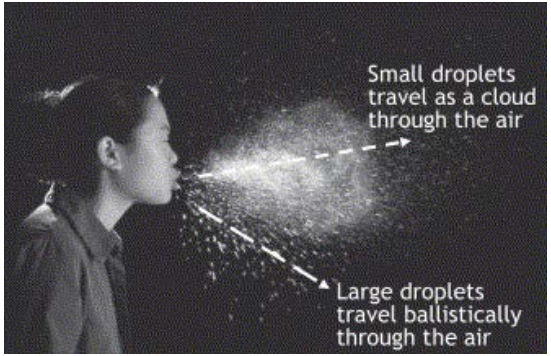
240,000 Deaths

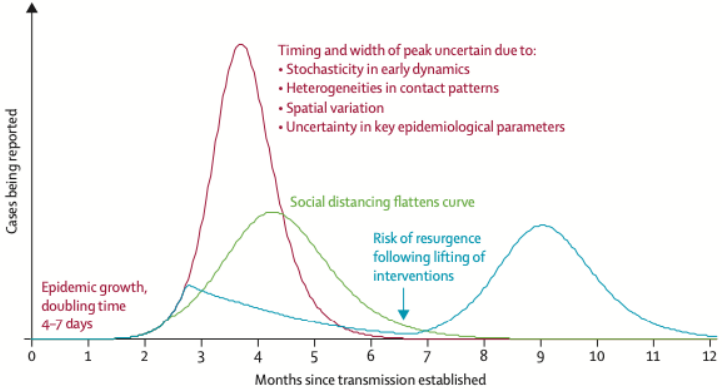
US CDC | 11/11/20

COVID-19: TRANSMISSION + PREVENTION

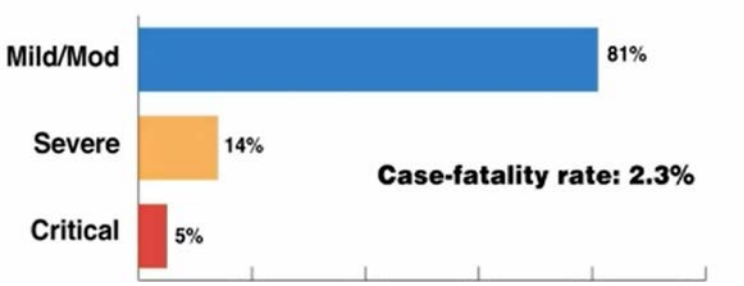
Fundamentals to Prevent Acquisition/Transmission of SARS-CoV2:

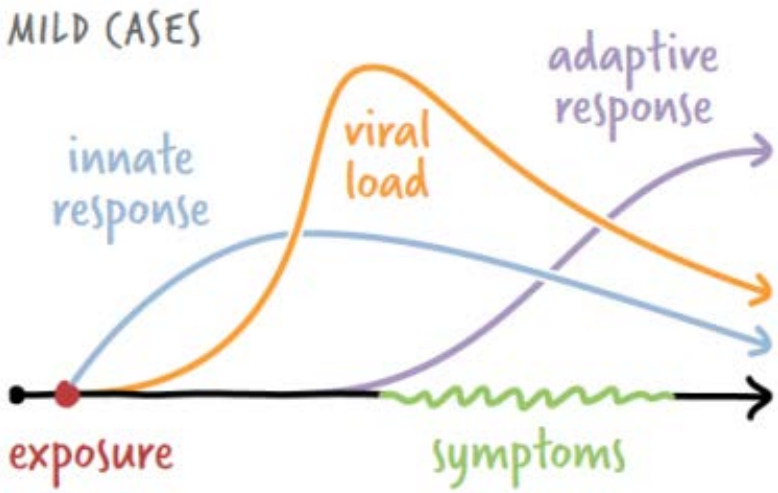
- Universal wearing of masks/face coverings.
- Maintain physical distance—at least 6 feet.
- Avoid crowds and congregated settings.
- Frequent washing of hands.
- Outdoors are better than indoors.





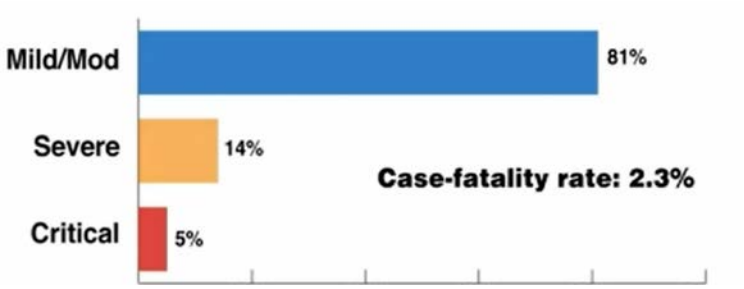
SPECTRUM OF COVID-19 DISEASE

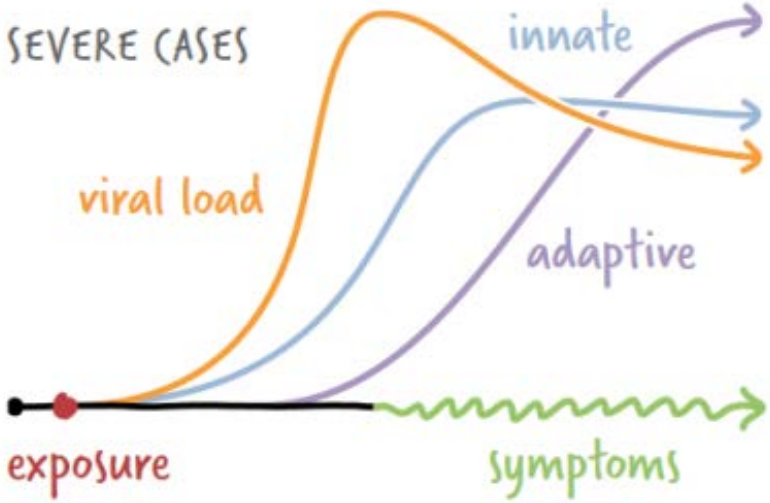




Fever	Sore Throat
Cough	Nasal congestion
Fatigue	Headache
Loss of Appetite	Diarrhea
Shortness of Breath	Nausea
Muscle pain	Loss of Smell

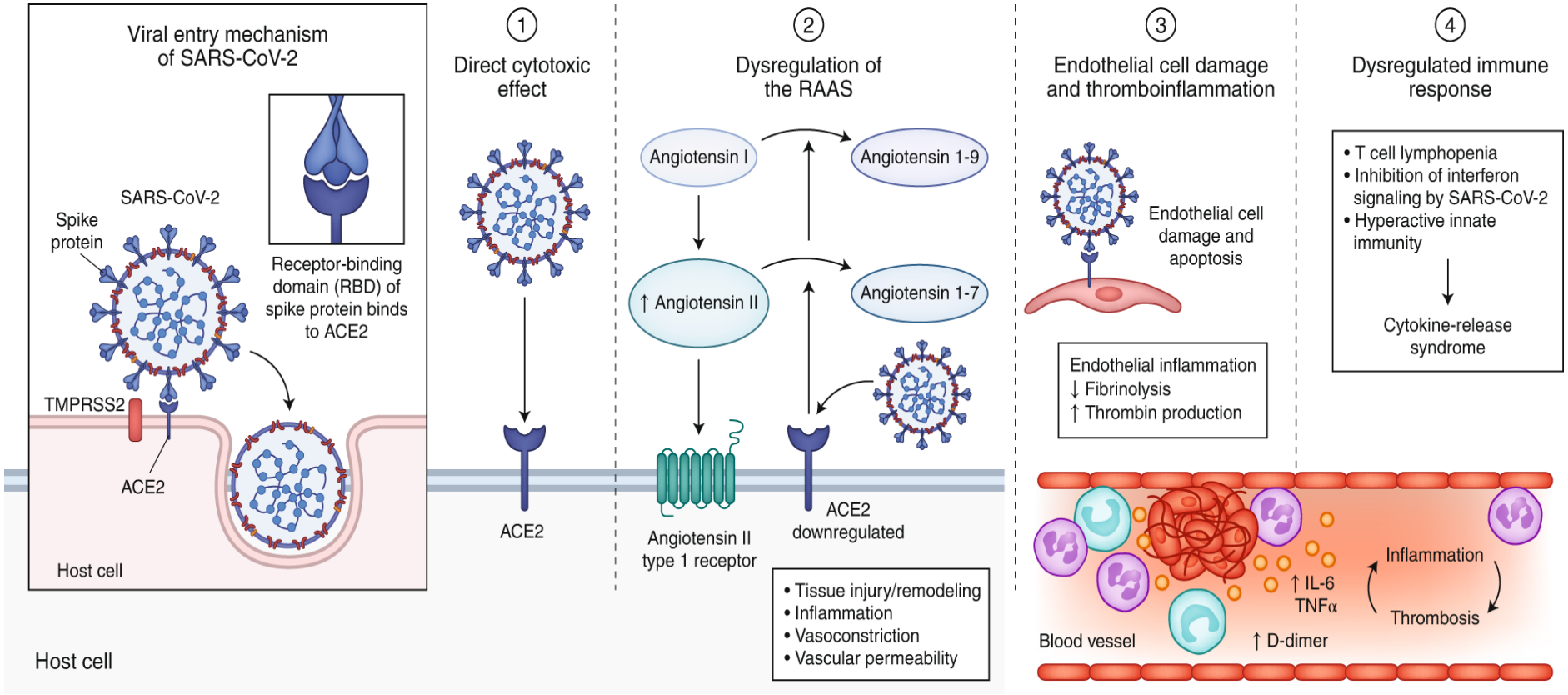
SPECTRUM OF COVID-19 DISEASE



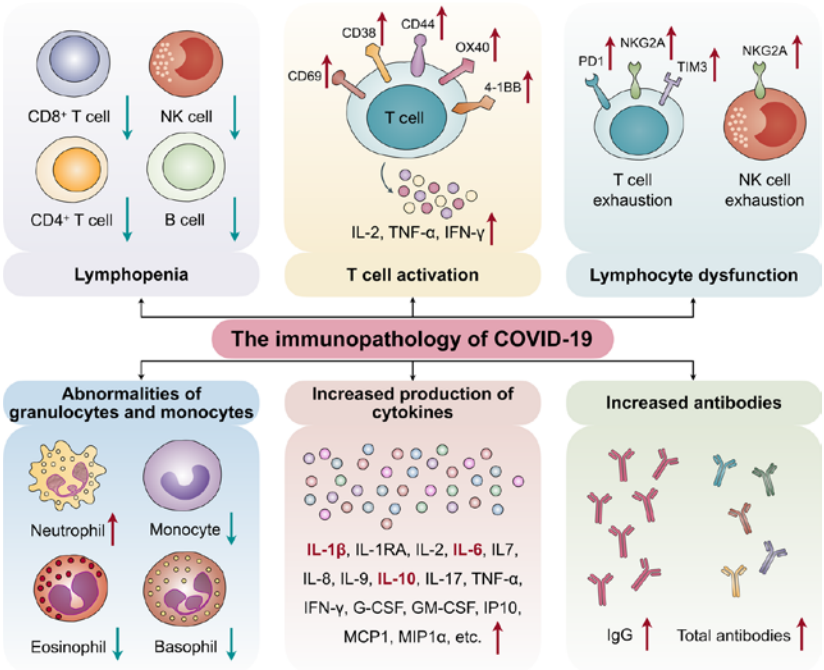


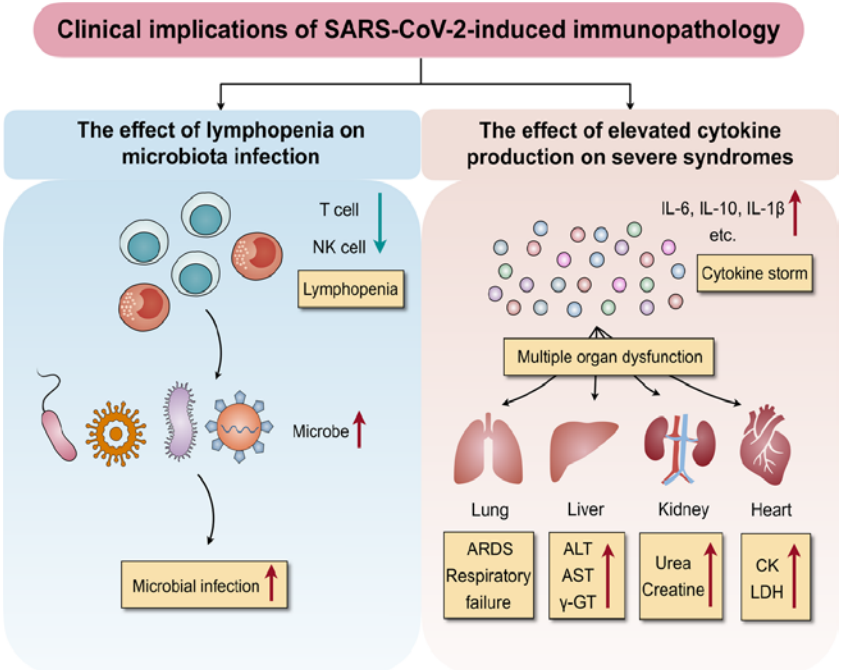
Acute Respiratory Distress Syndrome (ARDS)
Hyperinflammation
Heart dysfunction
Kidney injury
Neurologic disease
Hypercoagulability

PATHOGENESIS OF COVID-19 DISEASE



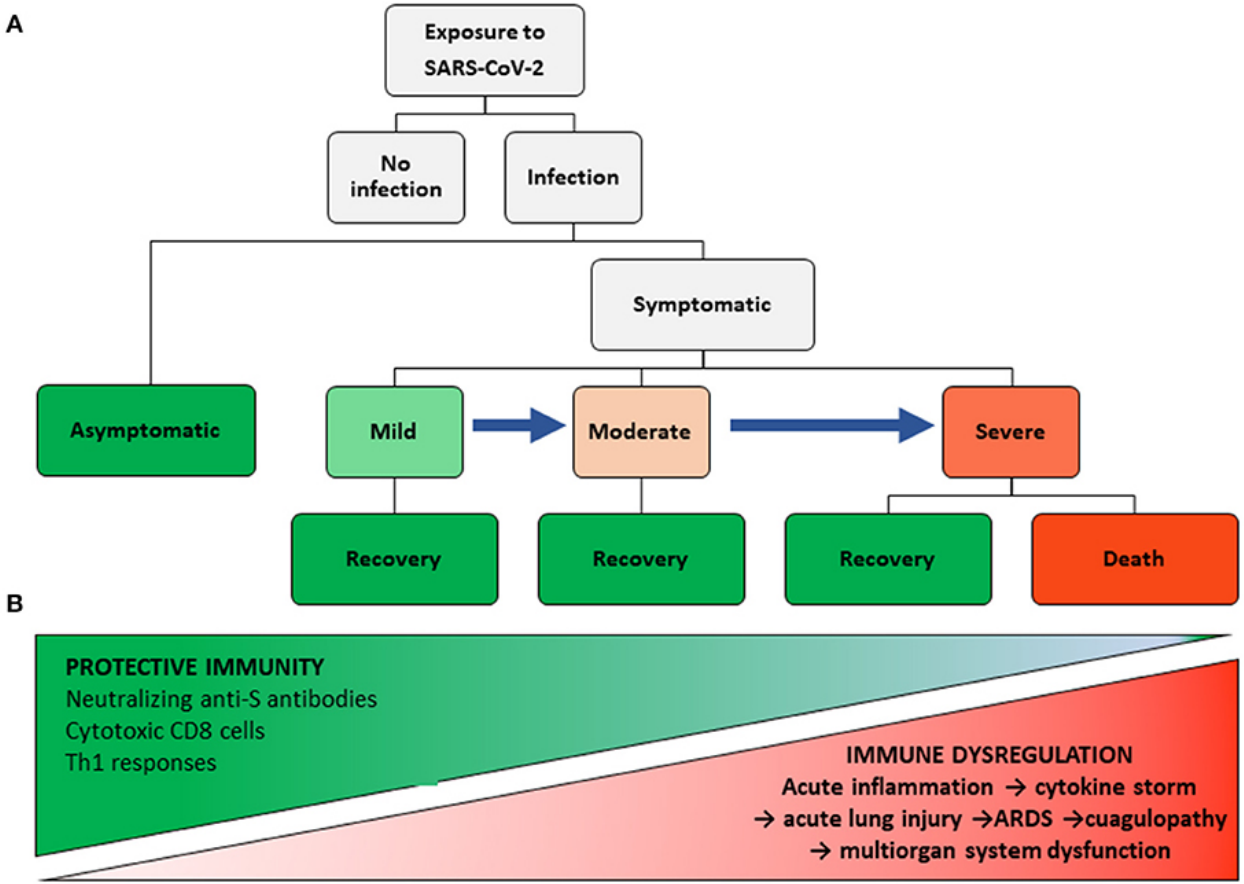
ALTERED IMMUNE RESPONSE IN COVID-19





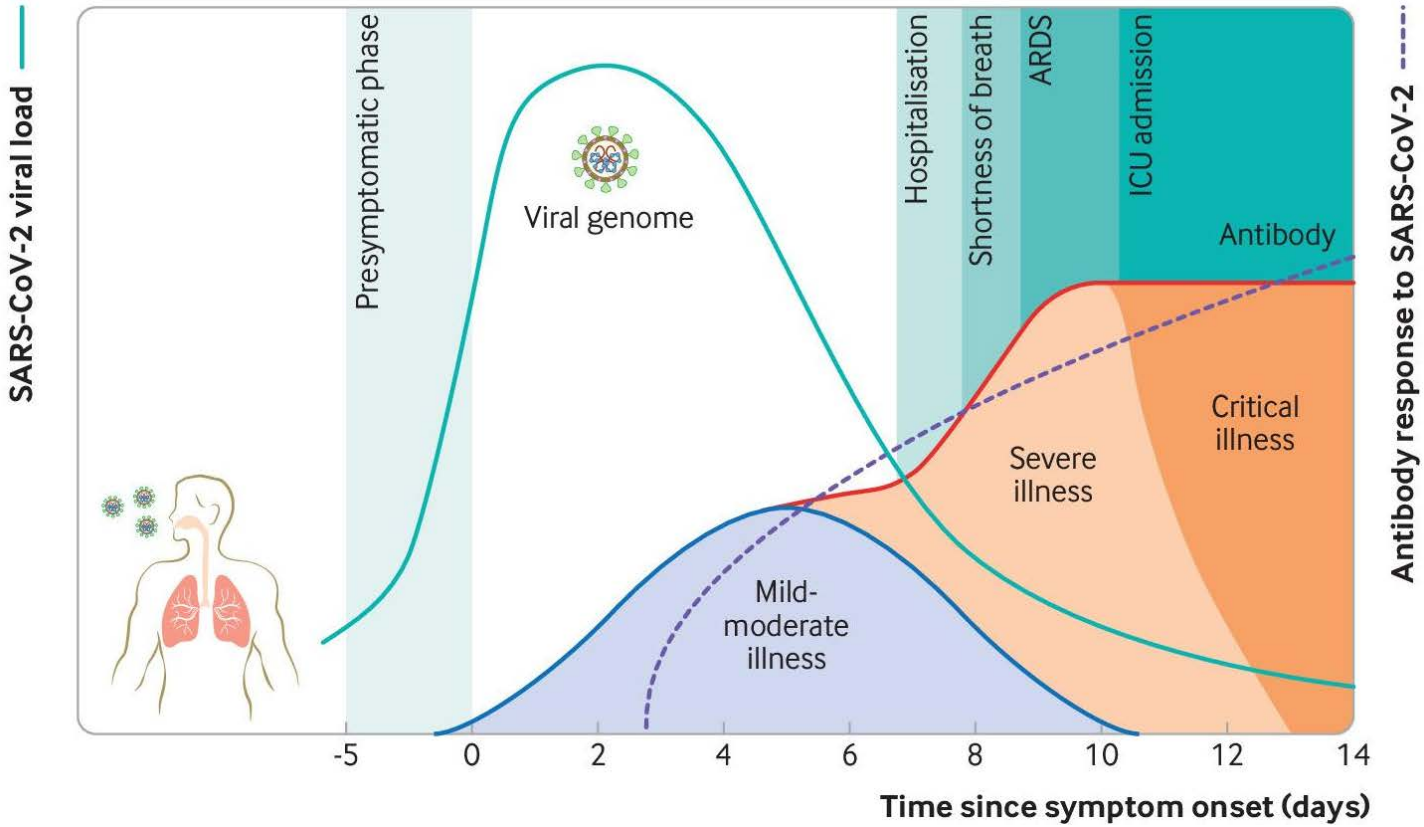
Nature Signal Transduction and Targeted Therapy

COVID-19 COURSE: RESOLUTION OR DETERIORATION



Frontiers in Immunology
British Medical Journal

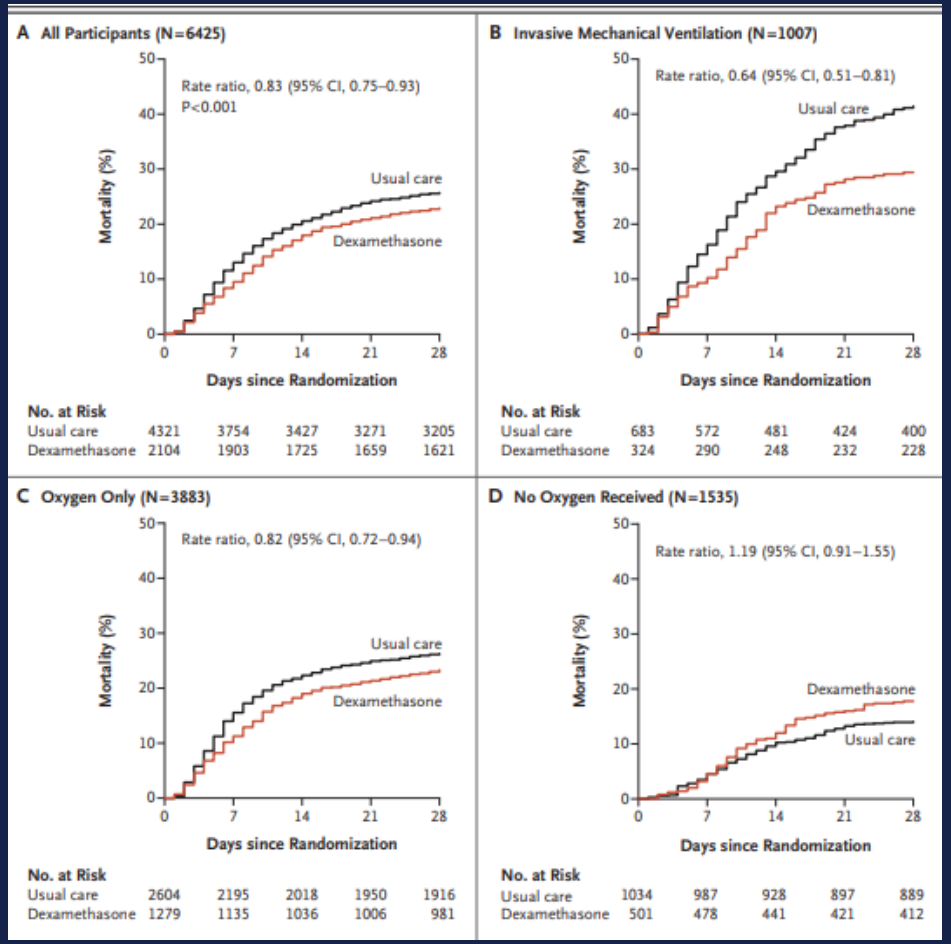
COVID-19 COURSE: RESOLUTION OR DETERIORATION



COVID-19 THERAPIES

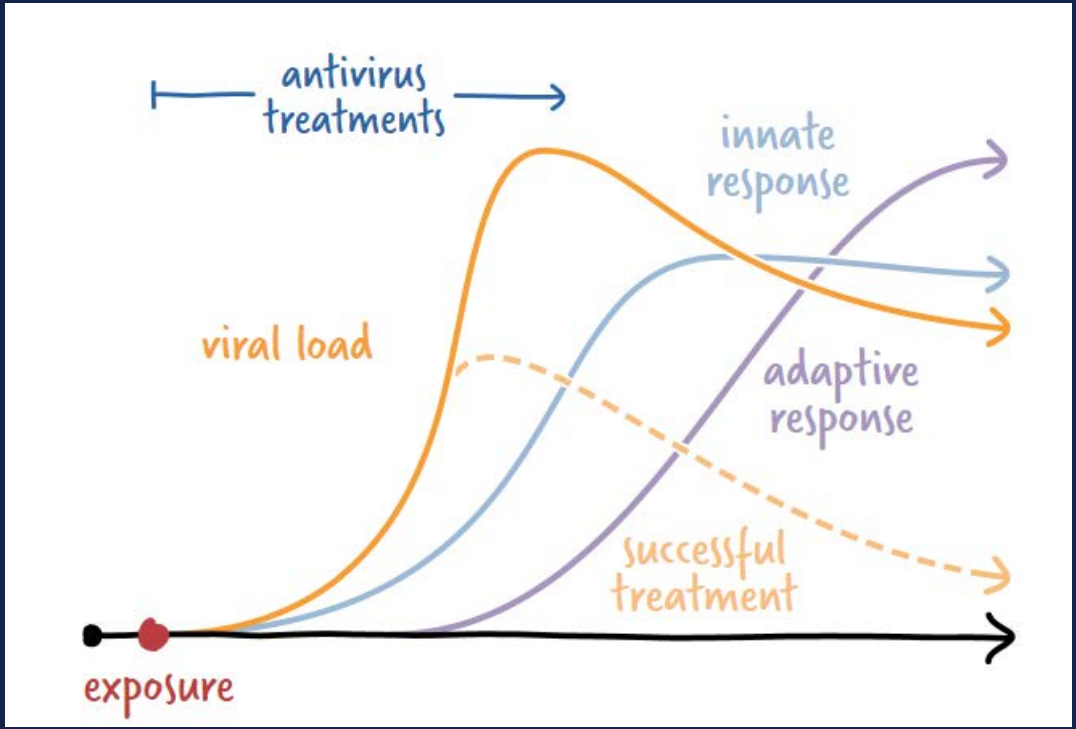
Christopher Ritchlin ’76, ’08M (MPH)
Chair,
Department of Allergy, Immunology, and Rheumatology

DEXAMETHASONE

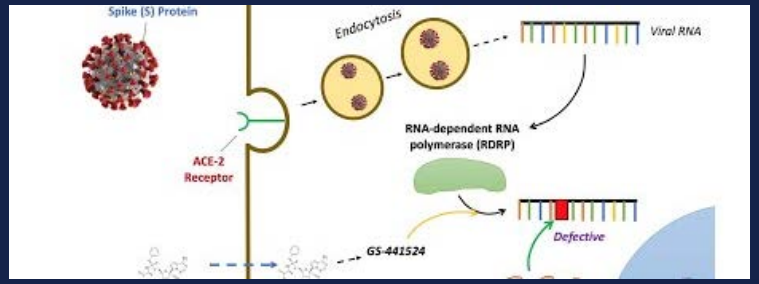


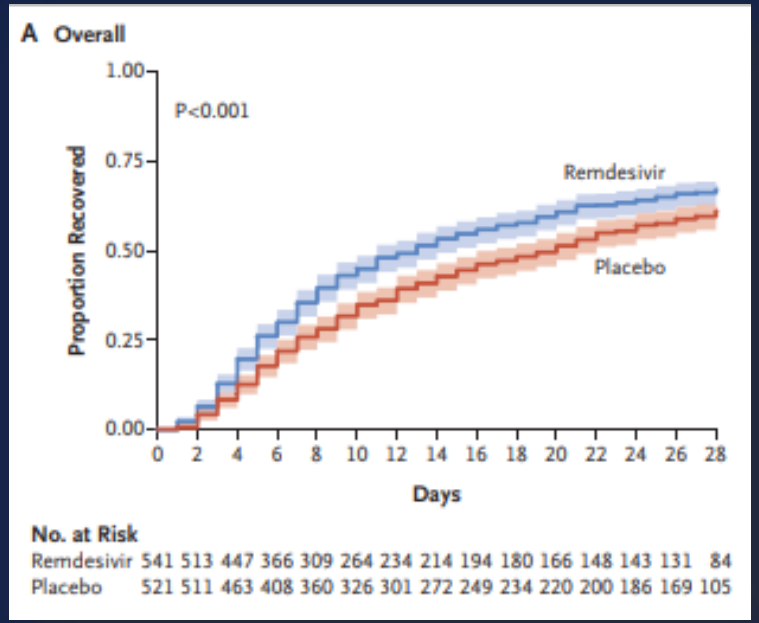
Recovery Collab Group, NEJM July 2020

ANTIVIRAL TREATMENTS



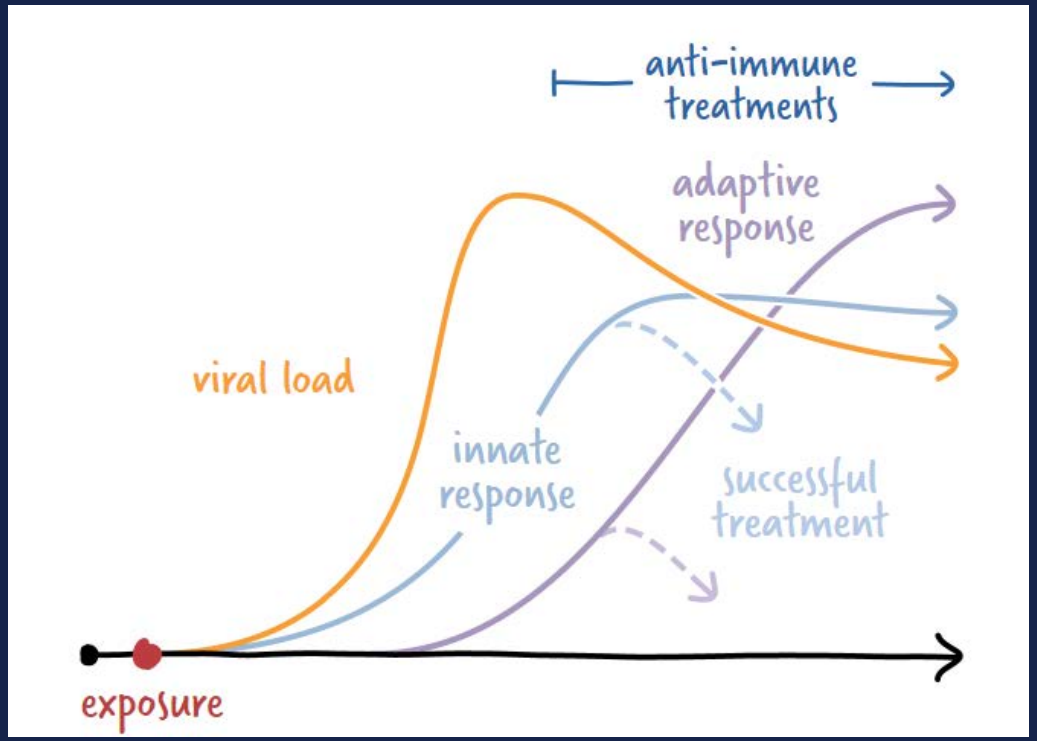
REMDESIVIR
Act-1 Trial





Biegel, JH NEJM | Oct 2020

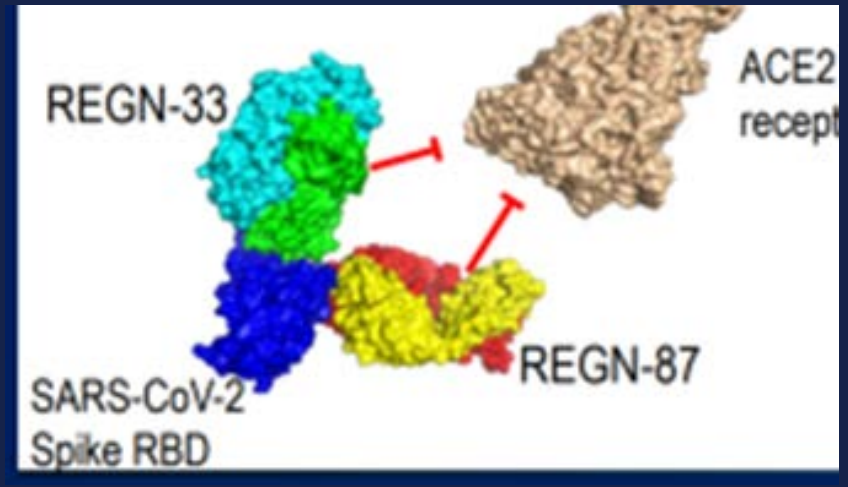
ANTI-IMMUNE TREATMENTS



ANTIBODY COCKTAILS

- **Lilly** - Neutralizing antibodies in the COVID-19 outpatient setting—September 16, 2020

- **Regeneron** - Antibody cocktail reduced viral levels and improved symptoms in non-hospitalized COVID-19 patients—September 29, 2020



CONVALESCENT PLASMA

FDA issues emergency use authorization for convalescent plasma as potential promising COVID–19 treatment.

Impact of convalescent plasma therapy in COVID-19 management:

- Clinical improvement
- Decrease in mortality
- Increase in viral clearance

Sarkar S., Medical Virology August 2020

Vaccine Platform Refresher

DNA-based vaccines work by inserting synthetic DNA of viral gene(s) into small DNA molecules (called plasmids). Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognized by the immune system, and prepare it to respond to disease exposure

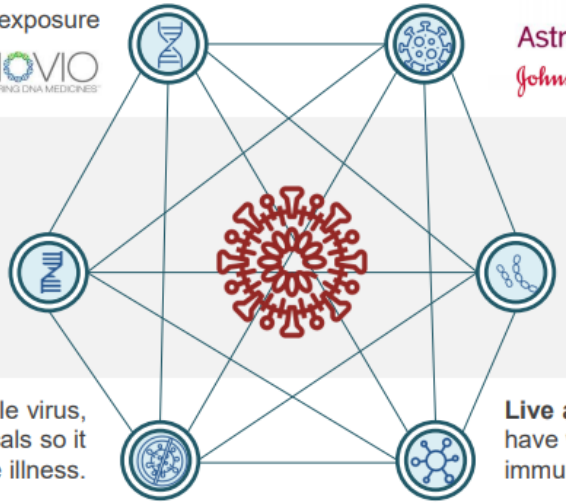
SANOFI INOVIO POWERING DNA MEDICINES

Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating), which delivers the viral protein to the vaccine recipient, triggering an immune response.

AstraZeneca Johnson & Johnson MERCK CanSinoBIO МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РОССИЙСКОЙ ФЕДЕРАЦИИ

RNA vaccines introduce an mRNA sequence coded for a disease-specific antigen. Once this antigen is reproduced within the body, it is recognized and triggers an immune response

Pfizer moderna CUREVAC the RNA people



Subunit vaccines introduce a fragment of the virus into the body. This fragment is enough to be recognized by the immune response and stimulate immunity.

NOVAVAX Creating Tomorrow's Vaccines Today Clover Biopharmaceuticals

Inactivated vaccines consist of the whole virus, which has been killed with heat or chemicals so it can't cause illness.

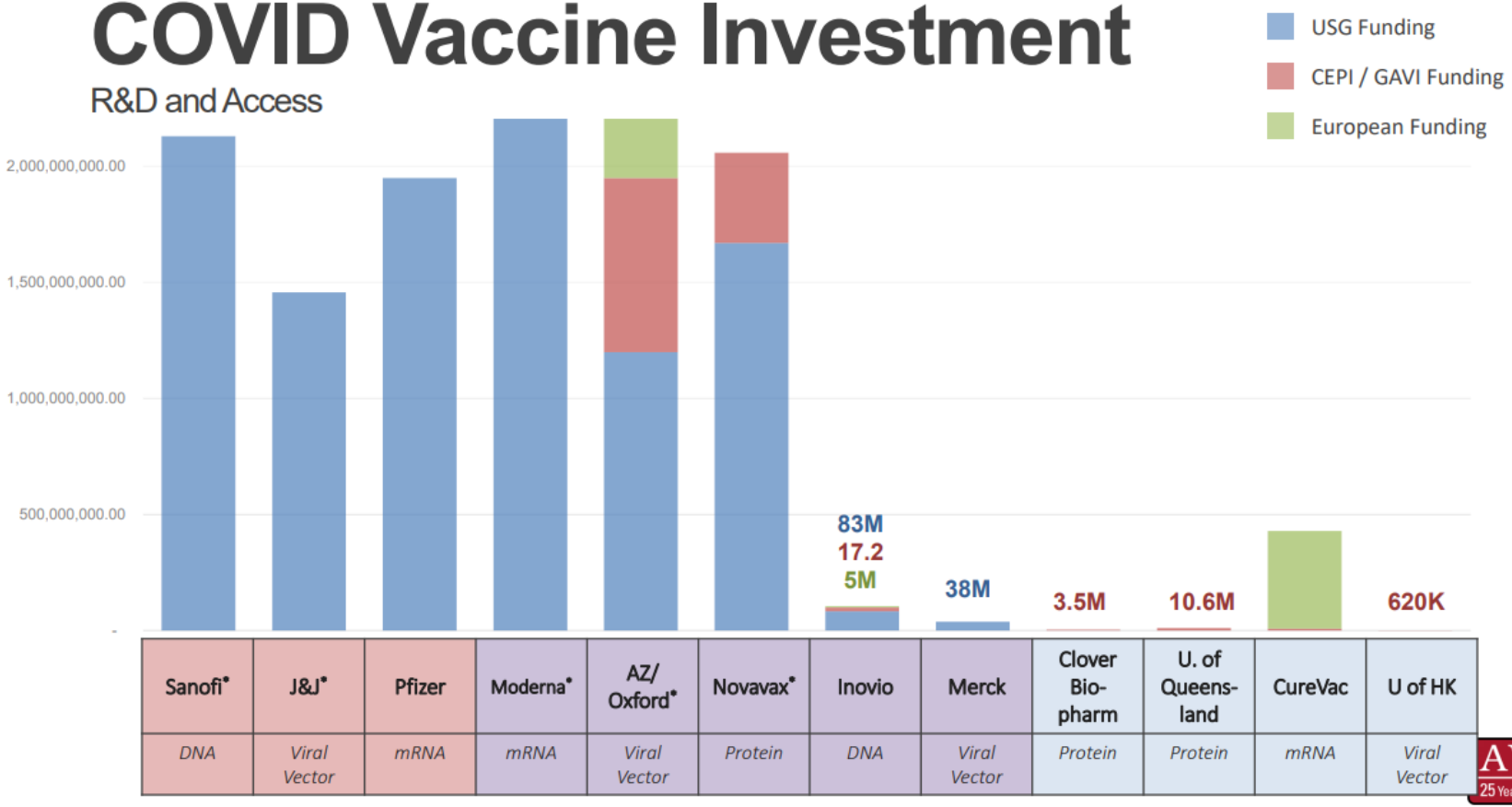
武汉生物制品研究所有限责任公司 WUHAN INSTITUTE OF BIOLOGICAL PRODUCTS CO.,LTD. SINOPHARM sinovac

Live attenuated vaccines are made up of whole viruses that have weakened in a lab. They tend to elicit a stronger immune response than inactivated vaccines.

AVAC 25 Years and Counting

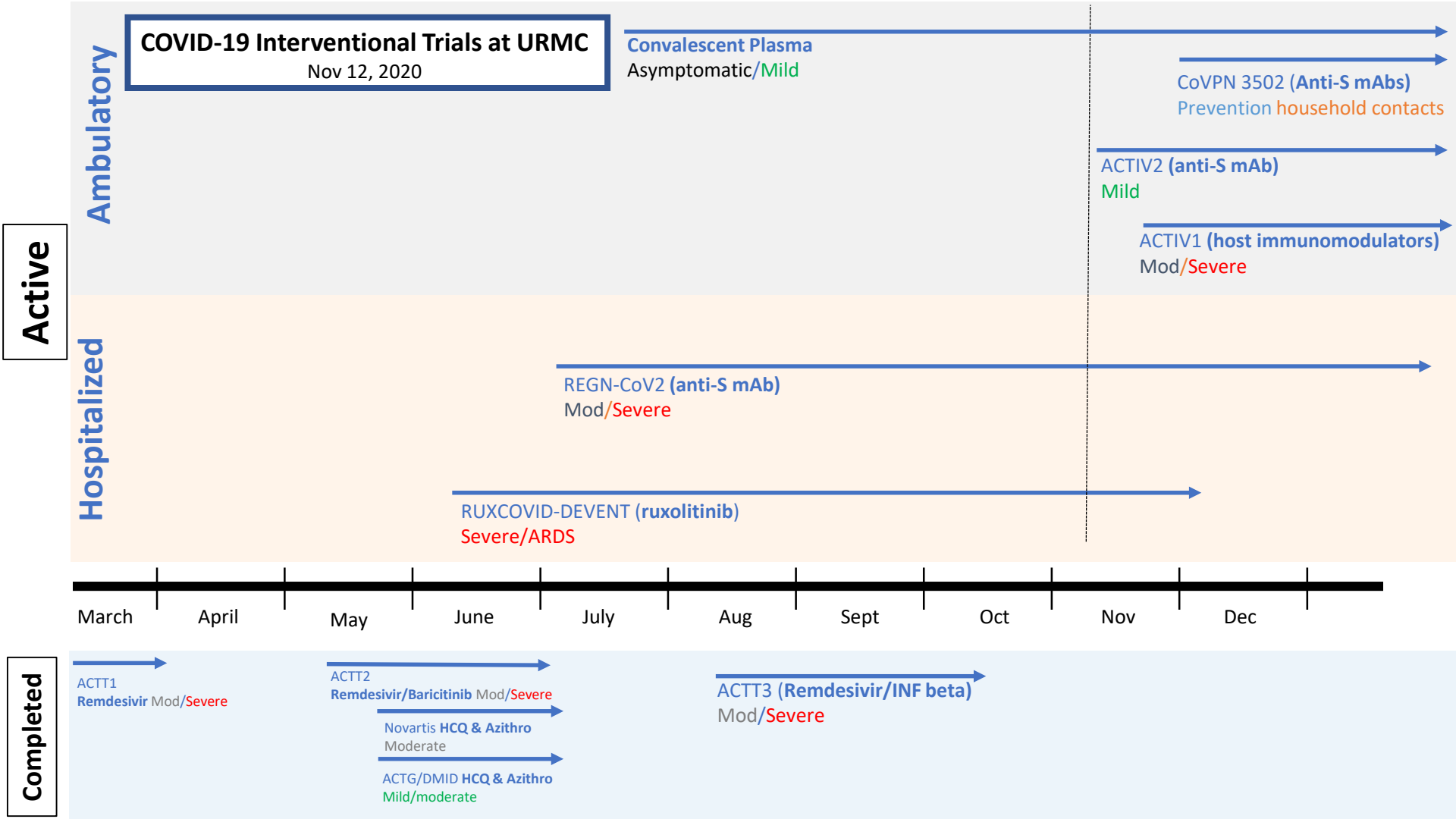
COVID Vaccine Investment

R&D and Access



MAJOR COVID-19 TREATMENT TRIALS AT URMC

Christopher Palma ’11M (MD)
Assistant Professor,
Department of Allergy, Immunology, and Rheumatology


COVID-19 Interventional Trials at URMC
Nov 12, 2020
Active
Ambulatory
Convalescent Plasma
Asymptomatic/Mild
CoVPN 3502 (Anti-S mAbs)
Prevention household contacts
ACTIV2 (anti-S mAb)
Mild
ACTIV1 (host immunomodulators)
Mod/Severe
Hospitalized
REGN-CoV2 (anti-S mAb)
Mod/Severe
RUXCOVID-DEVENT (ruxolitinib)
Severe/ARDS
March
April
May
June
July
Aug
Sept
Oct
Nov
Dec
Completed
ACTT1
Remdesivir Mod/Severe
ACTT2
Remdesivir/Baricitinib Mod/Severe
Novartis HCQ & Azithro
Moderate
ACTG/DMID HCQ & Azithro
Mild/moderate
ACTT3 (Remdesivir/INF beta)
Mod/Severe

COVID-19 Interventional Trials at URMC

Nov 12, 2020

Fight The Virus

Active

Ambulatory

Convalescent Plasma
Asymptomatic/Mild

CoVPN 3502 (**Anti-S mAbs**)
Prevention household contacts

ACTIV2 (**anti-S mAb**)
Mild

ACTIV1 (**host immunomodulators**)
Mod/Severe

Hospitalized

REGN-CoV2 (**anti-S mAb**)
Mod/Severe

RUXCOVID-DEVENT (**ruxolitinib**)
Severe/ARDS

March | April | May | June | July | Aug | Sept | Oct | Nov | Dec

Completed

ACTT1
Remdesivir Mod/Severe

ACTT2
Remdesivir/Baricitinib Mod/Severe

Novartis **HCQ & Azithro**
Moderate

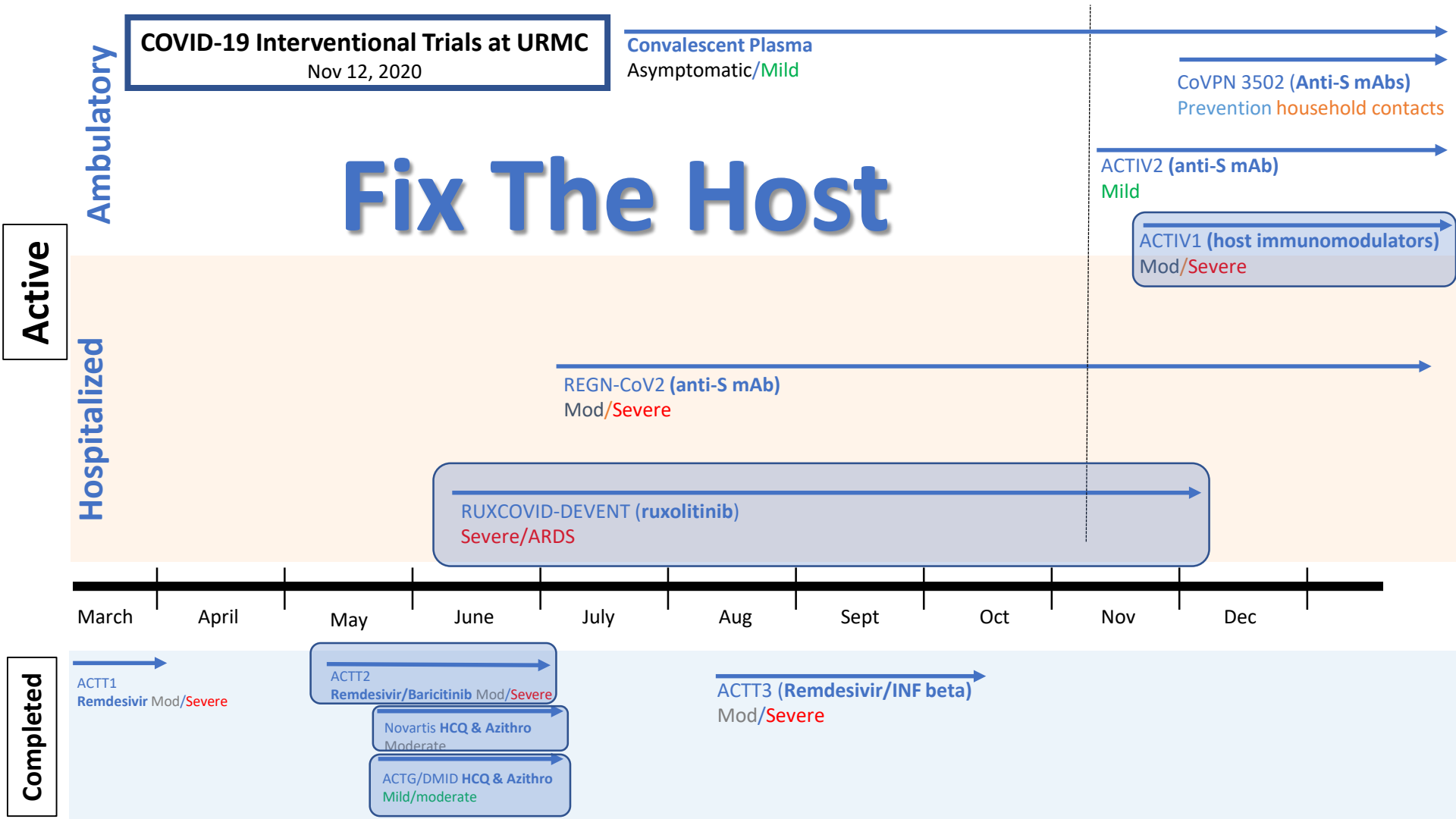
ACTG/DMID **HCQ & Azithro**
Mild/moderate

ACTT3 (**Remdesivir/INF beta**)
Mod/Severe

PRELIMINARY DATA ON COVID-19 TREATMENTS

Antiviral Antibodies (Regeneron/Lilly):

- Few risks/side effects
- Reduces viral load – much more effective in patients who present with high viral load and no antibodies –> 99% reduction
- Improves symptoms
- Reduces need for further medical visits/hospitalizations
- No clear benefit for patients hospitalized with severe disease – too late to be effective likely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Fix The Host
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Novartis HCQ & Azithro
Moderate
ACTG/DMID HCQ & Azithro
Mild/moderate
ACTT3 (Remdesivir/INF beta)
Mod/Severe

PRELIMINARY DATA ON COVID-19 TREATMENTS

Baricitinib (anti-inflammatory)

- Improved time to recovery by 1 day (7 days instead of 8)
- Less people died – 5.1% vs 7.8% - but not clearly statistically significant
- Larger studies still ongoing to refine extent of benefit