The Ecology and Biology of COVID-19: SARS-CoV-2 viral structure and replication

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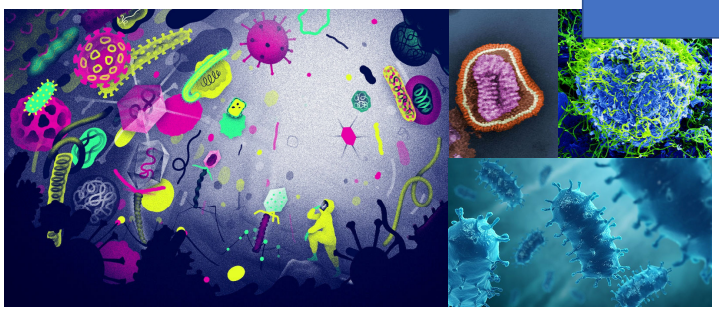
Image Source: https://commons.wikimedia.org/wiki/File:Novel_Coronavirus_SARS-CoV-2.jpg

Viral Abundance: 1 in a Trillion…



- Virus: "Obligate intracellular parasites." → Require hosts.
- 10^{31} viruses on Earth: 10,000,000,000,000,000,000,000,000,000,000
- >10 million times more viruses than there are stars in the universe.
- Trillions of different species of virus.
- Only about 250 viral species infect humans.

Source: https://nyti.ms/39FTKiz; https://commons.wikimedia.org/; https://www.nationalgeographic.com/science/phenomena/2013/02/20/an-infinity-of-viruses/

SARS-CoV-2 Coronavirus = Causative agent of COVID-19 disease

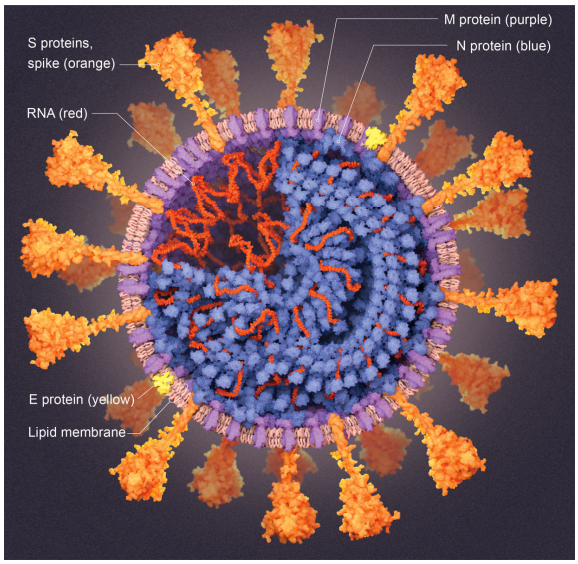
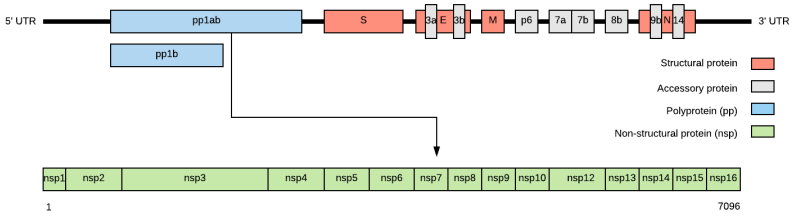


Image Source: Veronica Falconieri Hays; Lorenzo Casalino, Zied Gaieb and Rommie Amaro, U.C. San Diego (*spike model with glycosylations*) https://www.scientificamerican.com/article/a-visual-guide-to-the-sars-cov-2-coronavirus/

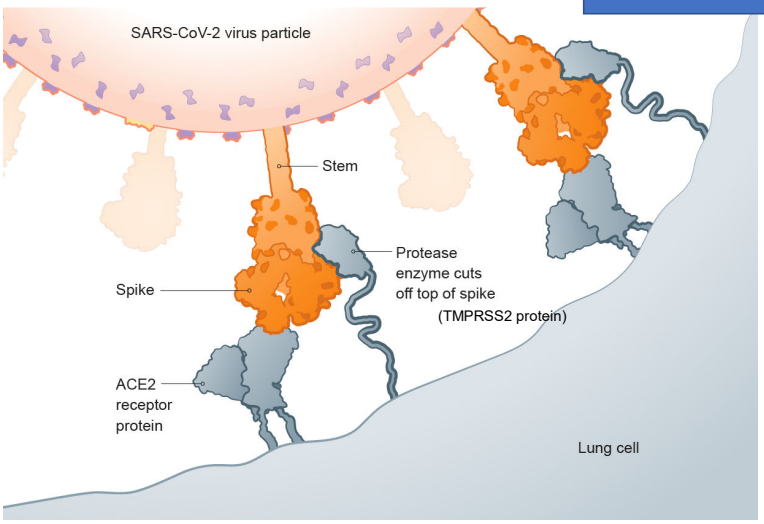
SARS-CoV-2 Genome



Viral proteins include:
-Protease (chop up long protein chains)
-RNA polymerase (copy the genome)
-Proofreading exonuclease (correct mistakes during genome replication)
-Structural components of the virus (spike protein, nucleocapsid, membrane proteins)

Image Source: https://commons.wikimedia.org/wiki/File:SARS-CoV-2_Genome.png

SARS-CoV-2 Infection: Attach to host cell



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SARS-CoV-2 Infection: Entry into host cell

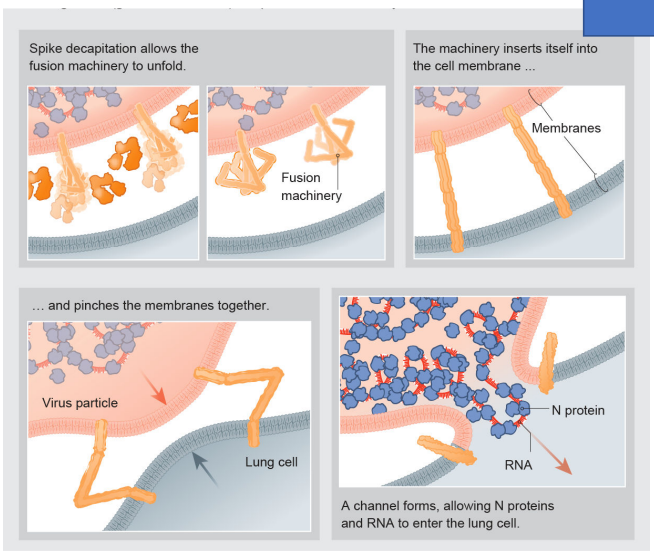
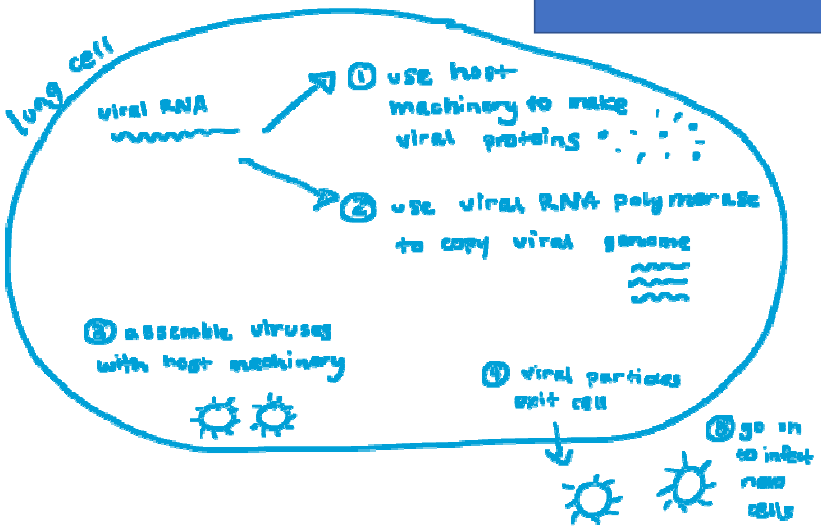


Image Source: Veronica Falconieri Hays. https://www.scientificamerican.com/article/a-visual-guide-to-the-sars-cov-2-coronavirus/

SARS-CoV-2 Infection: Replication and Assembly



SARS-CoV-2 Infection: Cell Death and Immune Response

- Infection and release of viral particles damages host cells.
- The host cell then releases chemicals that trigger the immune system.
- Sometimes, infection causes an aggressive inflammatory response that ultimately can cause even more cellular damage.

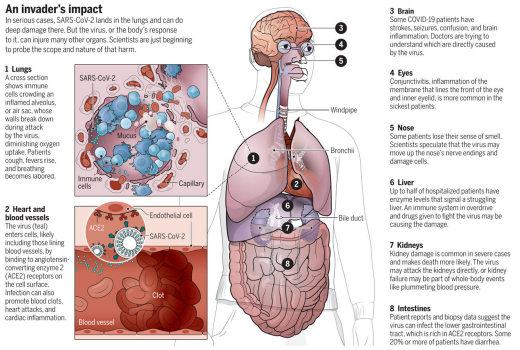


Image Source: https://science.sciencemag.org/content/368/6489/356?_ga=2.22462462.417260829.1589271178-2041434061.1572985313

SARS-CoV-2: Viral Load for Infection

- If someone gets sick with the flu, every infected cell produces ~10,000 new viruses → 100 trillion flu viruses within a few days (Zimmer, 2013).
- In order to get infected, you need to get exposed to ~1000 viruses.

- Viruses released from an infected person:

Cough/sneeze: contains ~200,000,000 viruses [pretty easy to inhale 1000 viruses]

Breathing: ~33 viruses are released per minute (based on flu data) [< 1 hr to inhale 1000 viruses]

Speaking: ~200 viruses released per minute [~5 minutes to inhale 1000 viruses]

Source: https://www.erinbromage.com/post/the-risks-know-them-avoid-them; https://www.nationalgeographic.com/science/phenomena/2013/02/20/an-infinity-of-viruses/ Image source: https://commons.wikimedia.org/wiki/File:Sneeze.jpg

SARS-CoV-2: Impact of Soap and Disinfectant

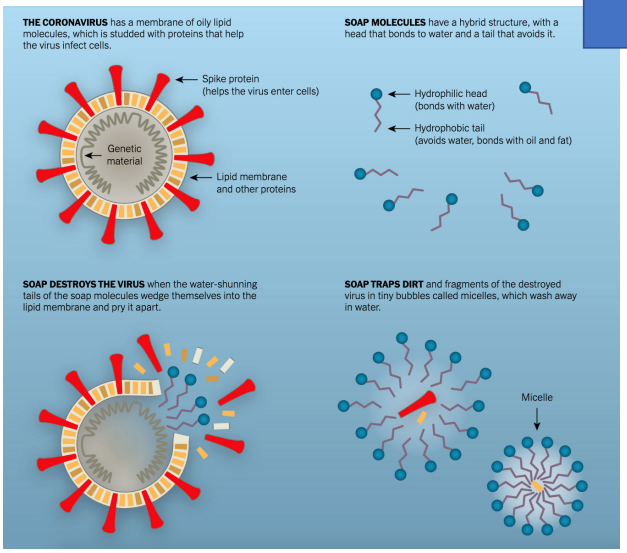


Image Source: https://www.nytimes.com/2020/03/13/health/soap-coronavirus-handwashing-germs.html

SARS-CoV-2: Impact of Masks

- SARS-CoV-2 viral size: 100 nm
- N95 masks effectively filter particles >100-300 nm
- Surgical and cotton masks less effective for small particles, but do block droplets

Image Source: https://commons.wikimedia.org/wiki/File:Coronavirus_SARS-CoV-2.jpg; https://commons.wikimedia.org/wiki/File:Unfolded_Face_Mask.jpg

SARS-CoV-2 Structure and Function

- Viral genome, structure and replication → Informs science and policy:
  - Testing and serology
  - Targets for drug therapies
  - Vaccine development
  - Epidemiology
  - Viral origin
  - Viral mutations

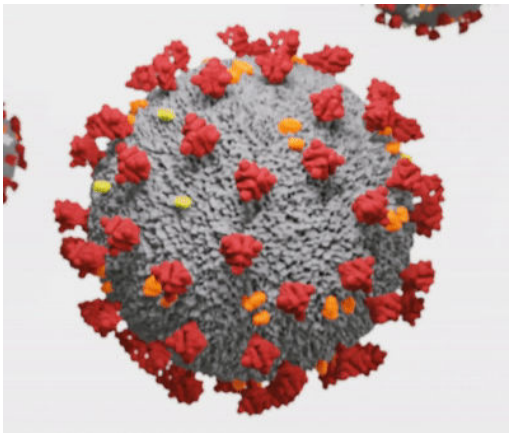
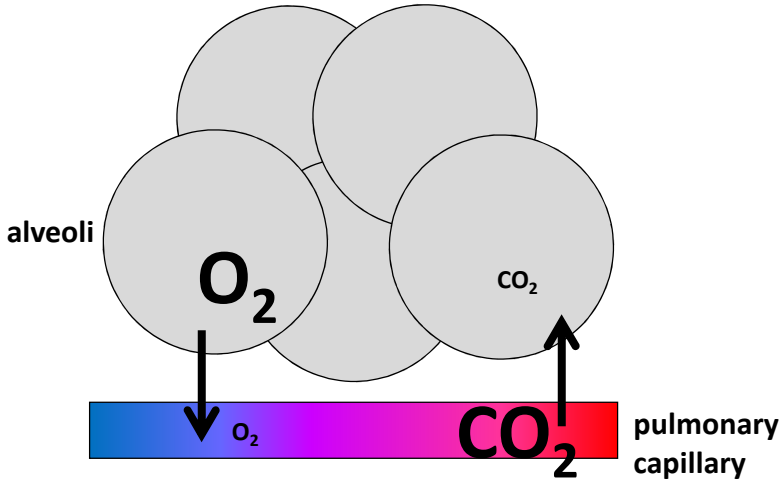


Image Source: https://upload.wikimedia.org/wikipedia/commons/2/21/SARS-CoV-2_virion_animation.gif

physiological and immune responses in COVID:
impacts of SARS-CoV-2 on respiratory distress
and the immune system.

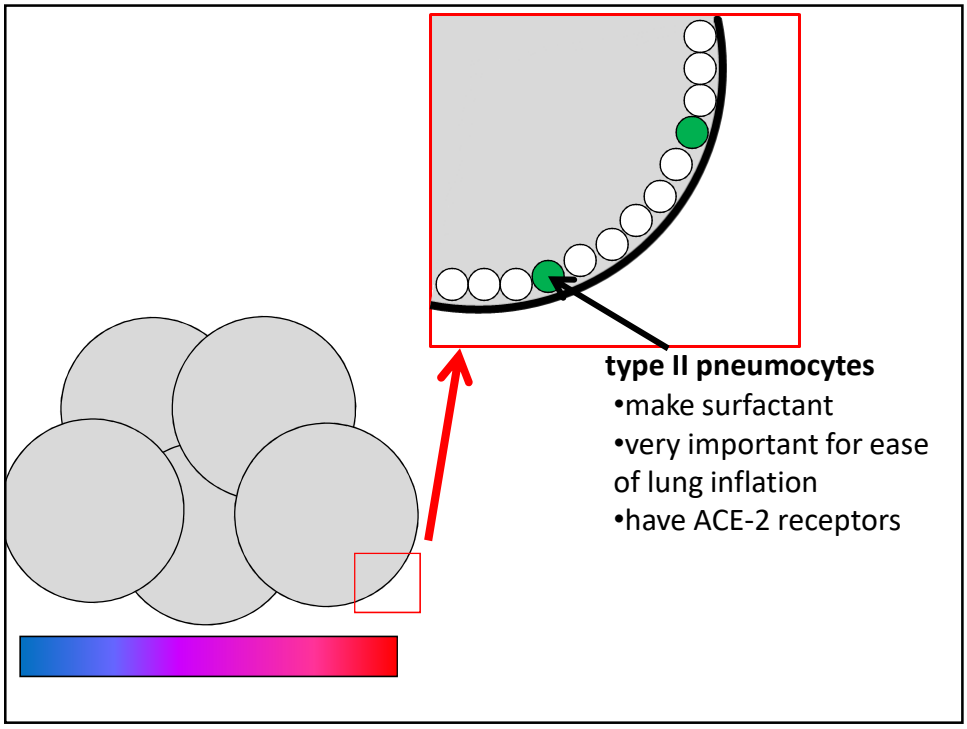
Laurel A. Beck, PhD

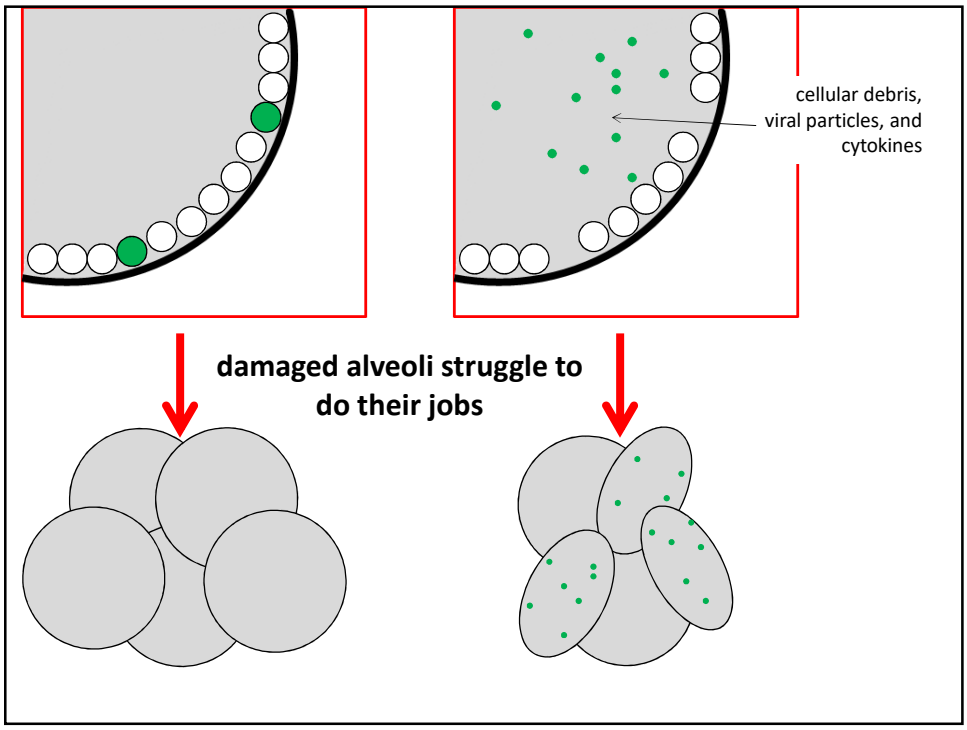


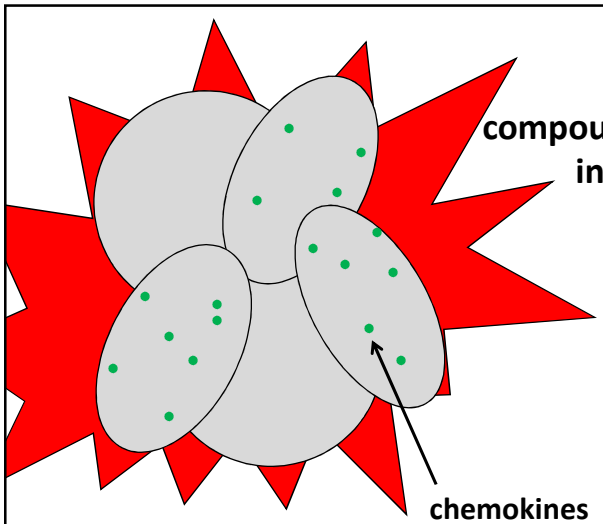
two ways in which SARS-CoV-2 disrupts this process

directly: uses alveolar cells as hosts, damaging them

indirectly: induces a large immune response which could get out of control


type II pneumocytes
•make surfactant
•very important for ease of lung inflation
•have ACE-2 receptors


cellular debris, viral particles, and cytokines
damaged alveoli struggle to do their jobs

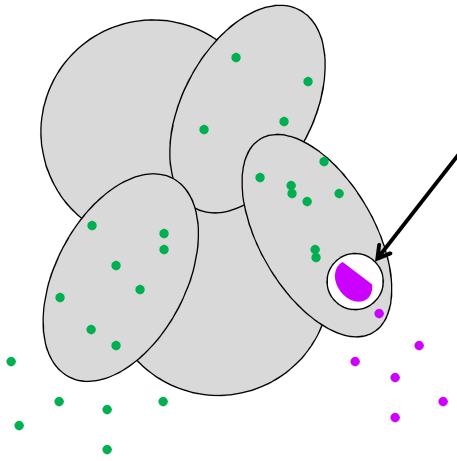


cytokines

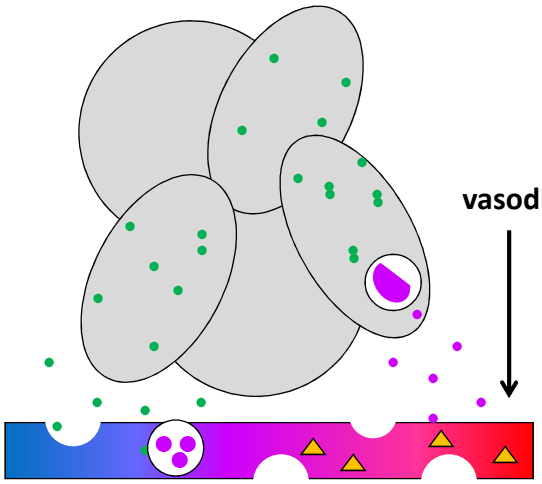
compounds that promote inflammation

goals of inflammation:
- destroy foreign proteins
- protect against immediate re-infection

chemokines
- released from damaged cells
- get attention from immune cells, help initiate immune response



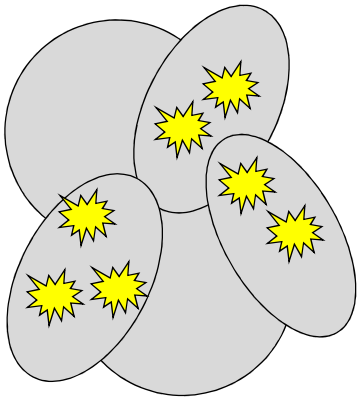
macrophages
- type of immune cell
- live in tissues with greater exposure to the outside world
- clean up cellular debris
- secrete lots of different kinds of cytokines
  - IL-6 is of particular interest



vasodilation

complement proteins
- get activated and initiate cascades following infection
- promote cell destruction

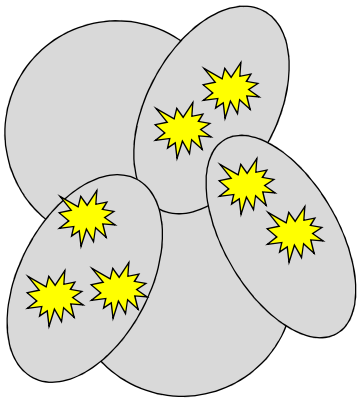
neutrophils
- type of leukocyte or white blood cell
- secrete cytokines and other chemicals, some of which can be toxic
- clear debris



ARDS

the cytokine storm
- cytokines can help recruit leukocytes to the site of injury
- leukocytes continue to release cytokines

effects of the cytokine storm
- fluid leaves plasma and enters the alveoli
- toxic chemicals from those leukocytes can damage healthy cells as well as infected cells
- activation of complement system, which can lead to cellular destruction



hypoxic conditions

↓

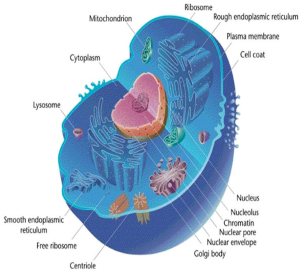
organ failure

How are cures for COVID19 being developed and when will we have one or more of them??

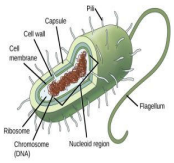
Dr. Amanda Charlesworth, Ph.D.
Integrative Biology

Cures exploit differences

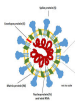
HUMAN CELL



BACTERIA



VIRUS



ANTIBIOTICS

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https://doi.org/10.1016/j.immuni.2020.03.007

https://openoregon.pressbooks.pub/mhccmajorsbio/chapter/comparing-prokaryotic-and-eukaryotic-cells/

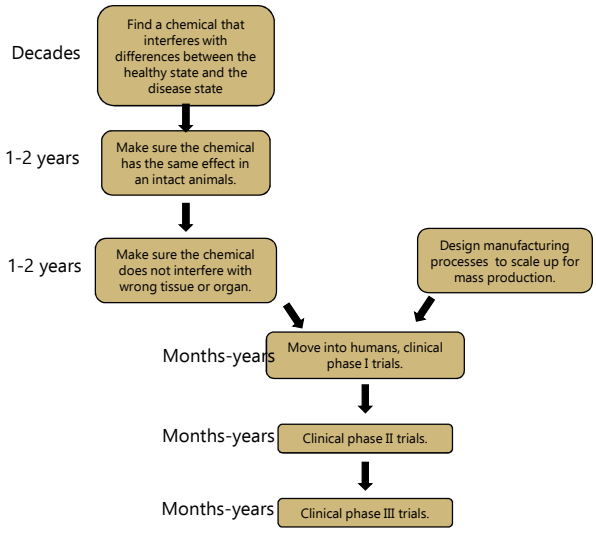
Common strategies for infectious diseases

Bacterial diseases	Viral diseases
Chlamydia	
Cholera	
Gonorrhea	Hepatitis A, B
Salmonella	HPV
Staph	Measles
Strep	Polio
Syphilis	Smallpox
Antibiotics	Vaccination
	Hepatitis C
	HIV
	Influenza
	Antiviral

Three strategies to treat viral infection.

- Strategy 1:
  Slow SARS-CoV-2 replication cycle.
- Strategy 2:
  Modulate the immune system.
- Strategy 3:
  Prevent infection with vaccines.

Developing a new drug – 20 years

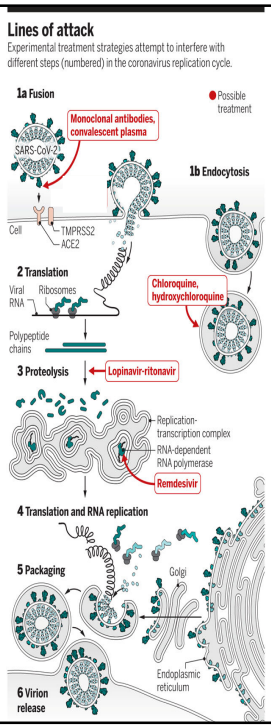


- "Rather than taking years to develop and test compounds from scratch, WHO and others want to repurpose drugs that are already approved for other diseases and have acceptable safety profiles."

- (Science 367 (6485), 1412-1413. DOI: 10.1126/science.367.6485.1412)

Strategy 1: Slow SARS-CoV-2 replication cycle.

- Remdesivir (Ebola)
- Hydroxychloroquine (Malaria, lupus, rheumatism)
- Lopinavir and ritonavir (HIV)
- Convalescent plasma

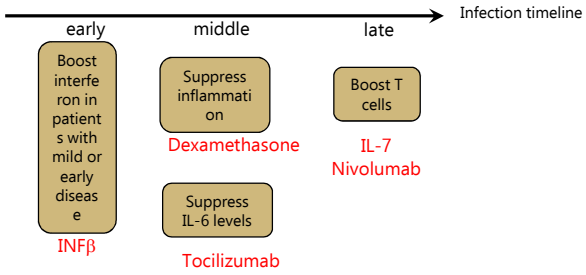


https://science.sciencemag.org/content/sci/367/6485/1412/F1.large.jpg

Strategy 2: Modulate the immune system.

Suppress or boost?

- INFβ (multiple sclerosis)
- Dexamethasone (general anti-inflammatory)
- Tocilizumab (Autoimmune disorders)
- IL-7 (sepsis)
- Nivolumab (cancer therapy)



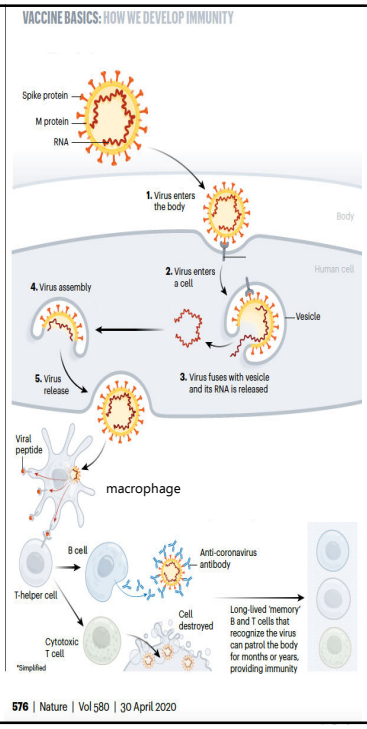
Derived from: *doi: 10.1038/d41573-020-00110-3*

Strategy 3: Prevent infection with vaccines.

Immunity is creation of memory B and T cells.
- You don't get sick.
- You don't spread the disease.

Vaccines provoke an immune response, without using a deadly virus.

How long will this take?
- 100 candidates
- Astra Zeneca is in phase III
- CSU has an animal model (hamster)



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Ecology of Infectious Disease AND What is the deal with the bats?

Dr. Laurel Hartley
Associate Professor
Department of Integrative Biology

COVID-19 is a newly emerged zoonotic disease that has spilled over from bats.

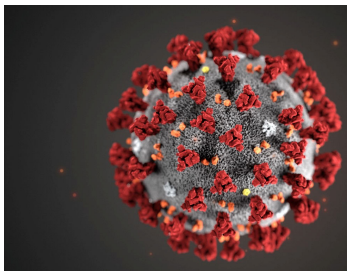
Some diseases have been in humans for a very long time.

Some diseases are emerging

An emerging disease is one that has recently:

- been newly discovered or evolved;
- increased markedly in incidence;
- increased in geographic range;
- moved into a new species or host population.

SARS-CoV-2



35

Zoonotic Disease: A disease that normally exists in other animals, but that can be transmitted to humans

Wildlife

Domestic animals

Wildlife

Humans

At least 70% of the **emerging diseases** that humans presently face **are zoonotic** in origin

36

Spillover

- A disease moves from its original host species to a new host species
- Happens all the time
- But if it happens all the time, why don't we see more epidemics?

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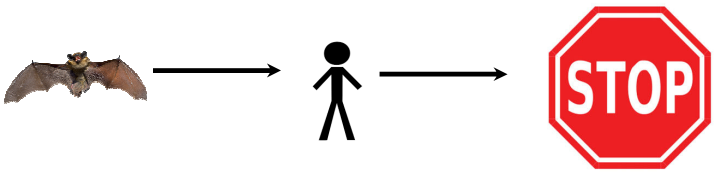

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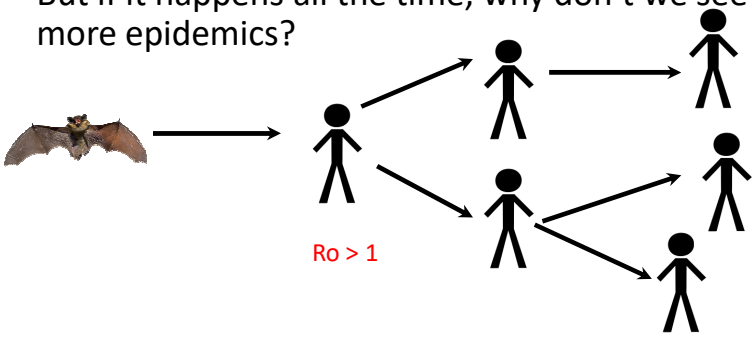
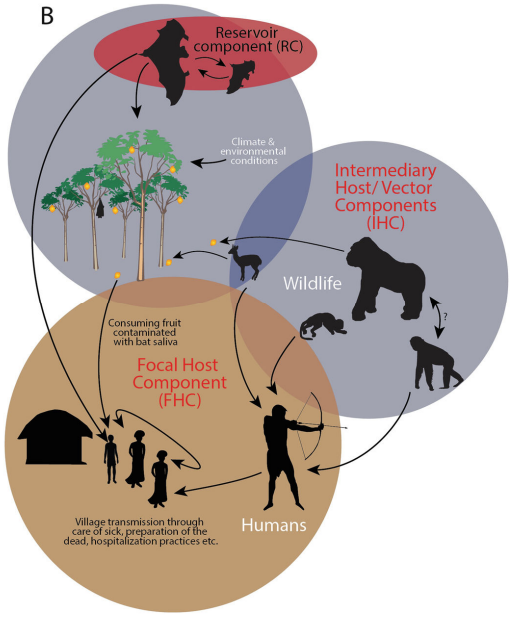


Conditions for Spillover

- Ecological niche overlap between original hosts, the pathogen and humans

NPR.org

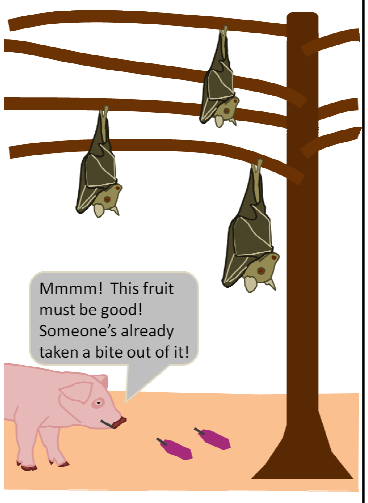
Spillover may be a single event with two species or much more complex.



Alexander K.A. et al. (2018) The Ecology of Pathogen Spillover and Disease Emergence at the Human-Wildlife-Environment Interface.

Spillover leading to zoonotic outbreaks more likely because

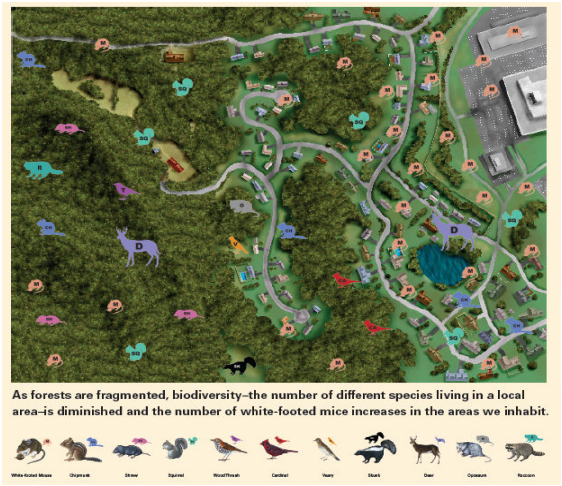
- Agricultural practices



parasiteecology.wordpress.com

Spillover leading to zoonotic outbreaks more likely because

- Habitat fragmentation and loss



As forests are fragmented, biodiversity–the number of different species living in a local area–is diminished and the number of white-footed mice increases in the areas we inhabit.

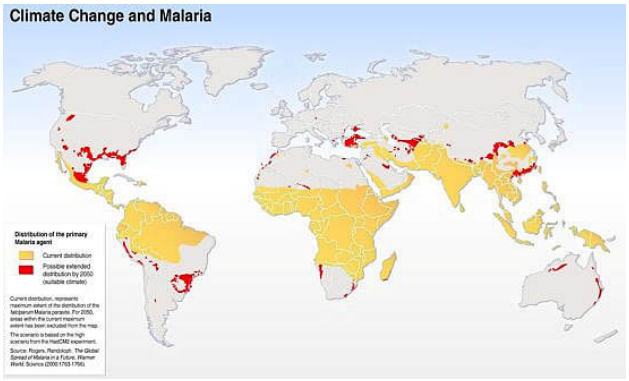
Cary Institute of Ecosystem Studies

Spillover leading to zoonotic outbreaks more likely because

- Globalization

Spillover leading to zoonotic outbreaks more likely because

- Climate Change



UCAR Center for Science Education

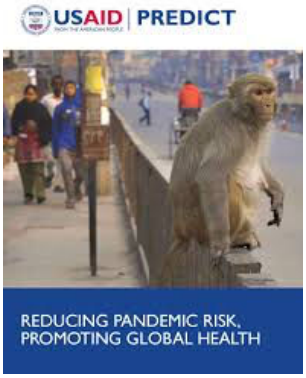
Back to the bats

"Viruses that originate in bats may be the most notorious emerging zoonoses that spill over from wildlife into domestic animals and humans." Plowright RK, Eby P, Hudson PJ, et al. (2015) Ecological dynamics of emerging bat virus spillover. *Proc Biol Sci*.

Nipah
Hendra
Marburg
Ebola
Coronaviruses (e.g., SARS, MERS, SARS-CoV-2)

How do we know?

- Trap, sample, isolate pathogens, sequence and compare pathogen genomes



Why bats?

Ecological Reasons

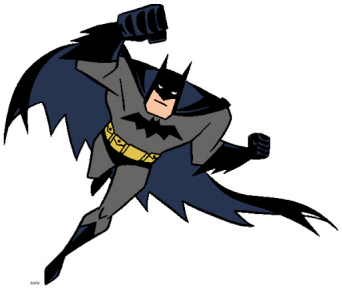
- Bats, potential reservoir hosts, and humans overlap in habitat
- Some bat species share roosts

Biological and Immunological Reasons

- Bats and humans are related
- Bats may have a peculiar immune system

Disclaimer

- Bats aren't villains.
- Bats provide important ecosystem services like pollination and eating mosquitos.



Mexican Long-Tongued Bat (*Choeronycteris mexicana*). Photo by Steve Buchmann.

We exist in environments and so do other species and diseases. Understanding ecology of disease is important.