PHYSICS 1444-001

COVID-19

Transmission, prevention, treatment

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DISCLAIMERS

- I have no financial conflict of interest

WHY ARE WE INTERESTED IN COVID-19?

- May cause a lot of suffering
- May cause a lot of deaths
- Definitely causing a lot of anxiety
- Provides AMAZING OPPORTUNITIES FOR IMPROVEMENT

https://www.washingtonpost.com/health/2020/03/07/how-doctors-treat-sickest-coronavirus-patients/

THE DATA WE HAVE FOR COVID-19 (*July 6, 2020*)

- ***"Coronavirus cases": 11,598,155 (cumulative)***
- ***"Deaths": 537,616 (cumulative)***
- ***"Currently infected patients": 4,497,984***
- ***"Serious or critical": 58,735 (~1%)***
- ***LONG-TERM health problems: unknown***
- ***"USA TOTAL": 2,985,897 cases; 132,601 deaths***
- ***"USA NEW": 2,969 cases; 41 deaths***

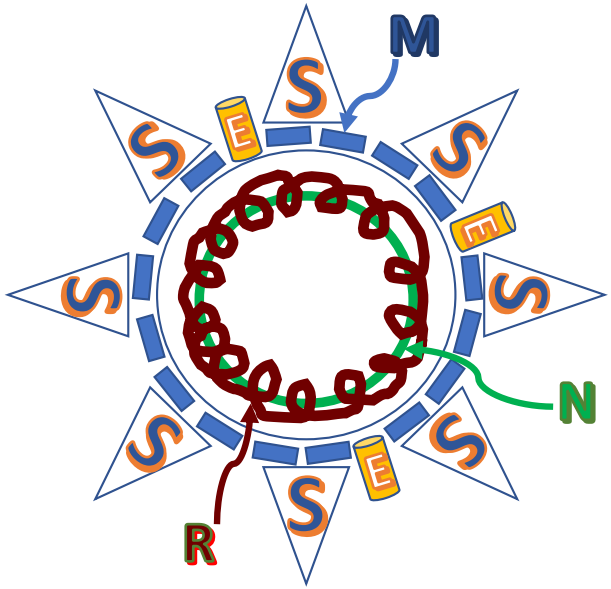
https://www.worldometers.info/coronavirus/?utm_campaign=homeAdUOA?Si

IS COVID-19 a SERIOUS PROBLEM?

- NUMBER of PEOPLE who do or could get sick or die
- SEVERITY of illness
- LONG-TERM health problems
- IF it can be TREATED
- IF it can be PREVENTED
- HOW MUCH it COSTS to TREAT/PREVENT
- ***We have NO proven TREATMENT***
- ***We have NO proven specific PREVENTION***

OBJECTIVES

- Define SARS-CoV2 and COVID-19
- Explain how SARS-CoV2 causes disease
- Explain how people get COVID-19
- Explain how COVID-19 might be prevented
- Explain how COVID-19 can be treated
- Outlook



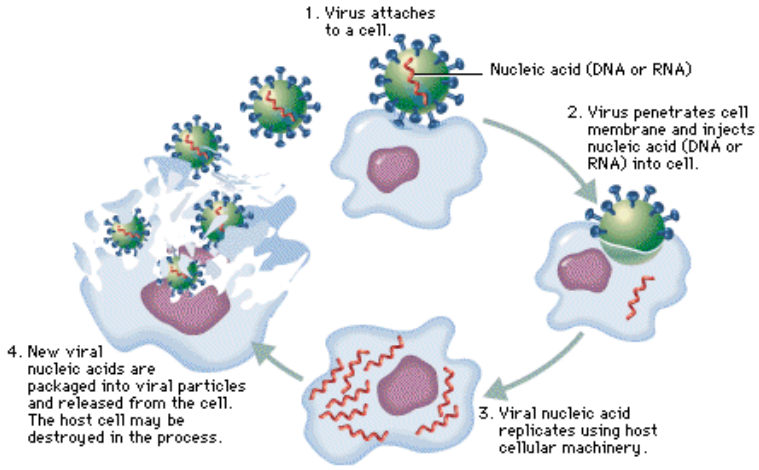
WHAT ARE SARS-CoV2 and COVID-19?

- **S**evere **A**cute **R**espiratory distress **S**yndrome-causing **C**orona**v**irus type **2**
  - Is the virus that causes COVID-19
- **Co**rona**vi**rus **D**isease of 20**19**
  - Is an infectious disease
  - Most patients have
    - fever
    - cough
    - loss of energy
    - overall feel unwell
  - Some patients also have
    - Shortness of breath
    - Nausea
    - Loss of smell/taste
    - Sore throat
    - Aches/pains
    - Skin lesions

https://www.nbcnews.com/news/us-news/tests-doctors-hazmat-suits-lots-gatorade-report-inside-coronavirus-quarantine-n1150601

HOW SARS-CoV2 CAUSES DISEASE

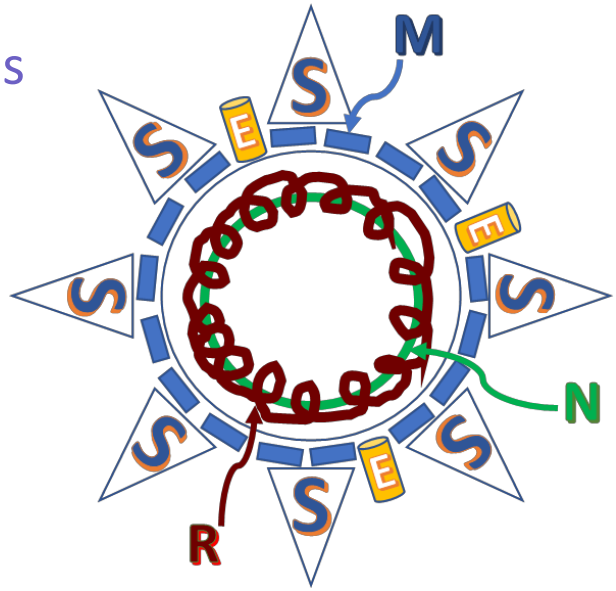
- Virus, from Latin, means "poison"
- Every virus…
  - …has a protein shell
  - …has a genome of RNA or DNA
  - …has a genome that encodes proteins
  - …requires a "HOST CELL" to multiply



https://joycehtchan.files.wordpress.com/2013/10/viralreplication.gif

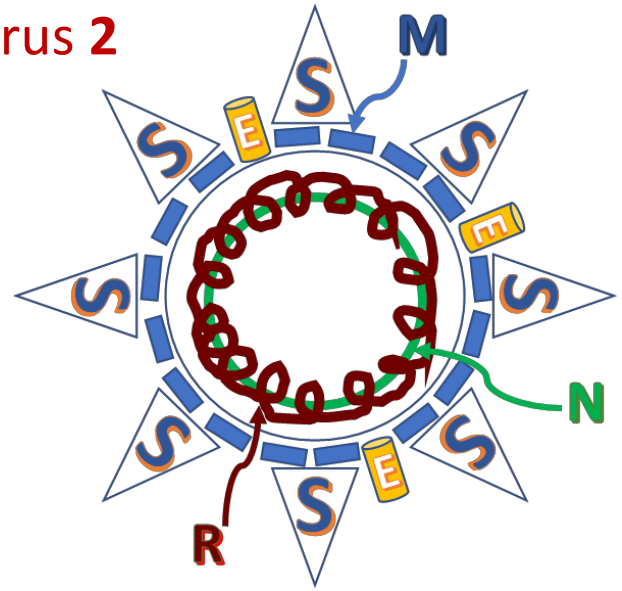
SARS-CoV 2 IS A CORONAVIRUS

- Named from the Latin for “crown” or “wreath”
- **Envelope** with “**spikes**”
- **LARGE** (30,000 base) single-stranded **RNA** virus
- Emergence of other Human Coronaviruses
  - HCovNL63 (c.1320)
  - HCoV229E (c.1800)
  - HCoVOC43 (c.1900)
  - HCoVHKU1 (c.1950)
  - SARS-CoV (c.2002)
  - MERS-CoV (c.2006)
  - **SARS-CoV2** (c.2019)

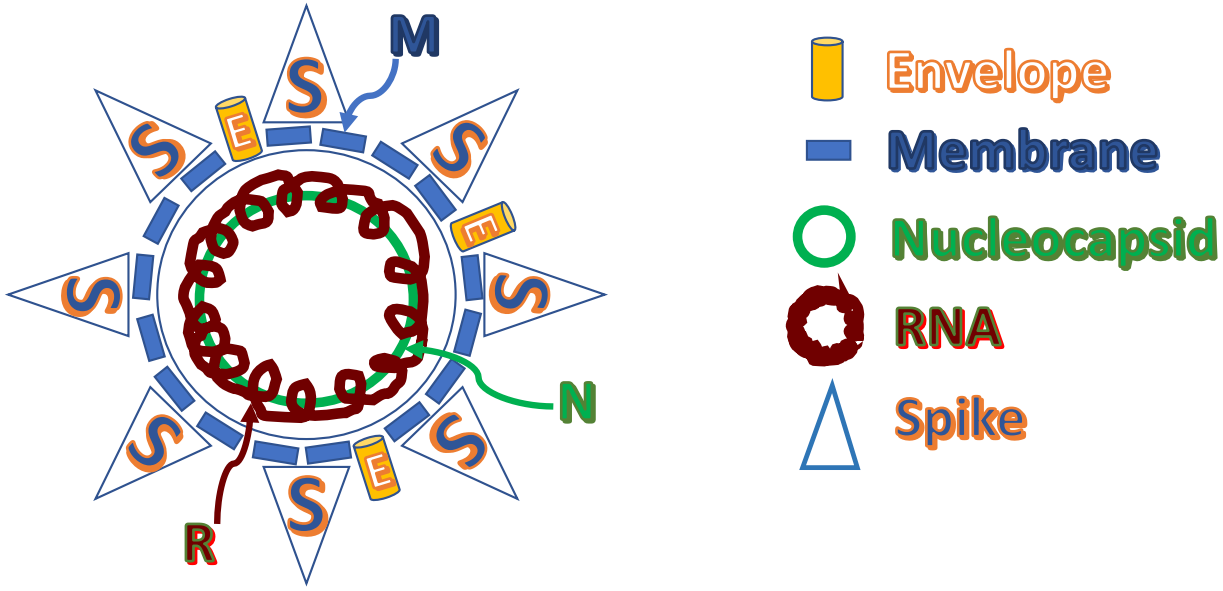


STRUCTURE OF SARS-CoV2

- **S**evere **A**cute **R**espiratory **S**yndrome **Co**rona **V**irus **2**
- Viral particle is ~ 0.12 μm diameter
- Proteins encoded:
  - Non-structural (nsp)
  - Structural proteins
  - Accessory proteins



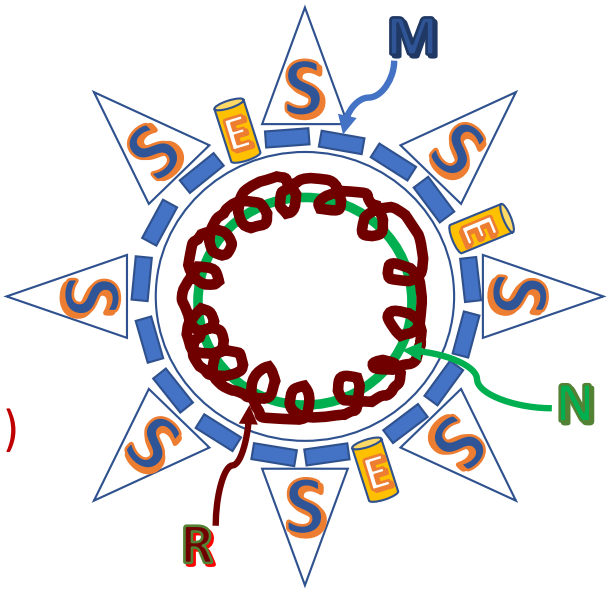
STRUCTURAL PROTEINS OF SARS-CoV2



SARS-CoV2 USES SPIKE TO ENTER HUMAN CELLS

S PROTEIN

- RESEMBLES human antibody (**Fc**)
- Binds host cell MEMBRANE
- Binds Angiotensin Converting Enzyme 2 ("**ACE2**")
- Enters cells in the lung
- Human cells that express ACE2:
  - Lung, Blood vessels, Heart, Kidney, Intestines, Testes



SARS-CoV2 SPIKE VARIANT

S Spike

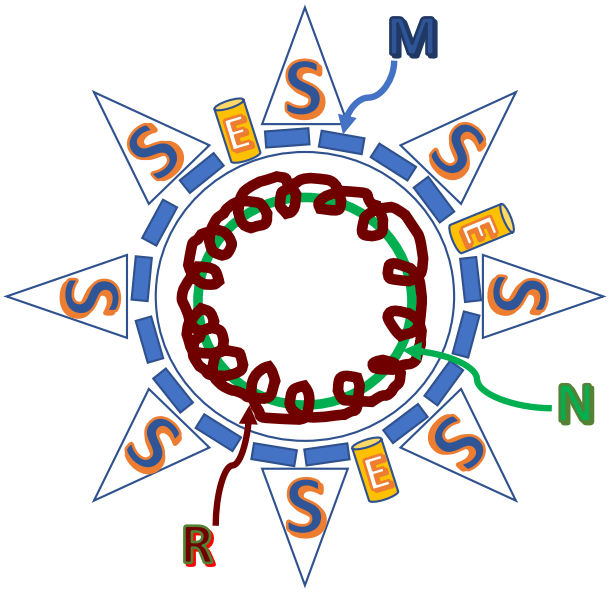
D614G Variant

Over time, G614 seems to dominate

Independent of initial viral distribution

Eastern USA, Western USA, Eastern Europe, Western Europe, Asia

PREPRINT INFORMATION

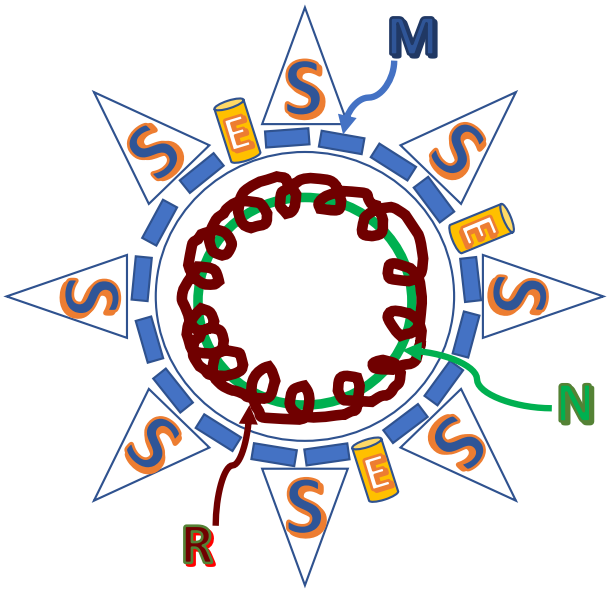


SARS-CoV2 MANIPULATES the IMMUNE System

Envelope

E PROTEIN

- Viroporin
- Ion CHANNEL
- Causes fluid shifts in lung tissue
- Causes unbridled release of cytokines: "**STORM**?"



Membrane

Nucleocapsid

M, N, and nsp PROTEINS

- Inhibit INTERFERON (host's anti-viral defense)
- Cause cytokine "storm?"

HOW MIGHT WE BECOME INFECTED?

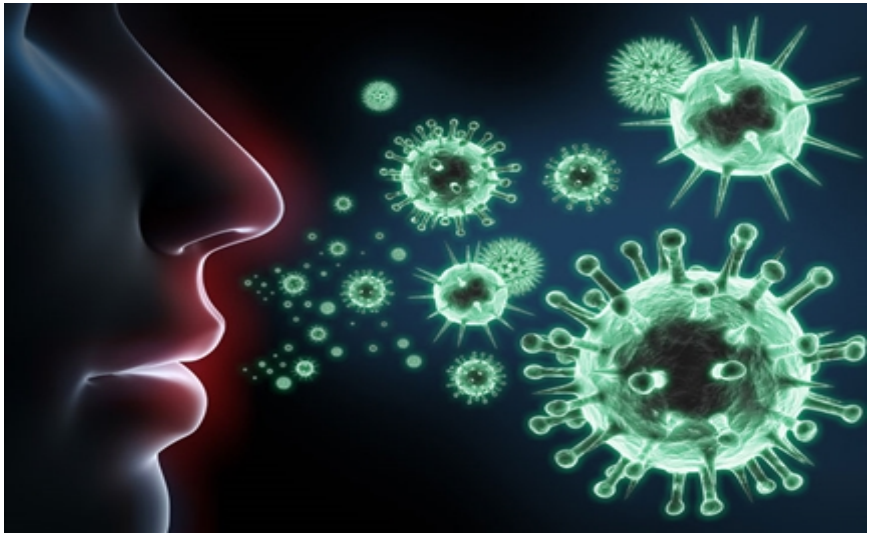
- Respiratory droplet
- Aerosol droplet
- Contact
- Blood-borne

INFECTION TRANSMISSION: “DROPLET”

Respiratory droplet (~5μm) carries infectious agent to recipient

https://www.esquire.com/lifestyle/health/a15172105/holding-back-sneeze-throat-damage/

INFECTION TRANSMISSION: “AEROSOL”



Aerosol droplet (<5μm) suspends agent in air

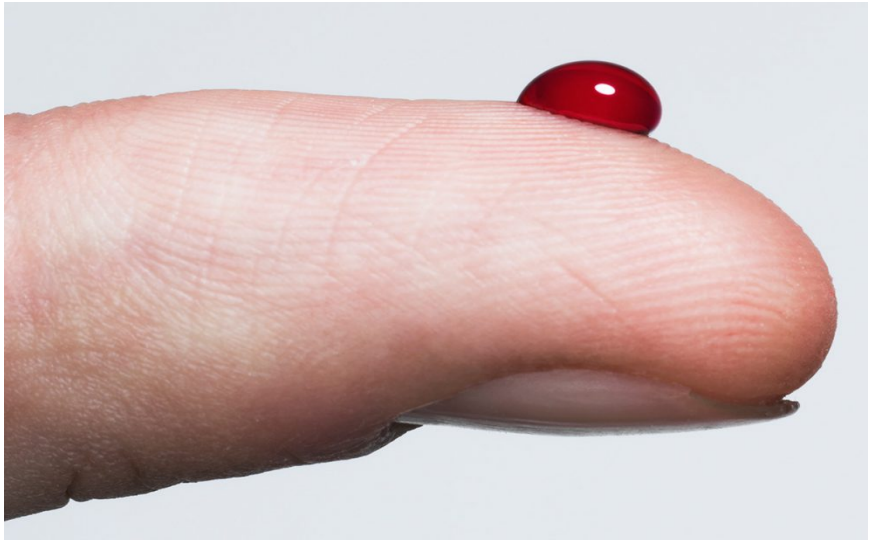
https://seguridadbiologica.blogspot.com/2019/10/recognition-of-aerosol-transmission-of.html

INFECTION TRANSMISSION: “CONTACT”

Contact with person/object directly inoculates recipient

https://www.internationalairportreview.com/article/33571/tackling-spread-pathogens-airports/

INFECTION TRANSMISSION “BLOODBORNE”



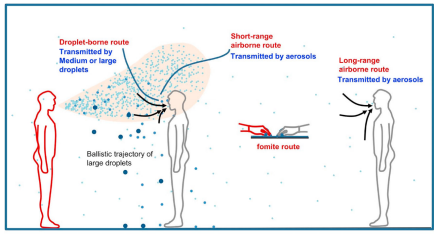
Puncture of skin or mucosa inoculates recipient’s **blood**

https://corplus.co/2018/09/26/bloodborne-pathogens/

PRINCIPLES OF INFECTION PREVENTION

- **As Low As Reasonably Achievable (ALARA)**
- MEASURES INDIVIDUALS CAN TAKE
  - Stay away from people/places where infection risk is high
  - Limit TIME and DISTANCE exposed to potential sources of infection
  - Responsibly use barriers to infection
  - Report possible exposures
  - Allow transparency
- MEASURES PUBLIC HEALTH OFFICIALS CAN TAKE
  - Offer responsible testing (broad, appropriate, inexpensive)
  - Identify potentially infected people (broad, quick, private)
  - Offer administration of protective medications (broad, quick, inexpensive)
  - Offer responsible vaccination programs (broad, inexpensive, safe, effective)

Maintain **distance: 3-10 feet**



- Large droplets (>100 µm) : Fast deposition due to the domination of gravitational force
- Medium droplets between 5 and 100 µm
- Small droplets or droplet nuclei, or aerosols (< 5 µm): Responsible for airborne transmission

Wei, J and Y. Li (2016) Airborne spread of infectious agents in the indoor environment. Am. J Infection Cont. (44) S102-S108.

Protect **mucosae**: eyes, nose, mouth

https://prohousekeepers.com/blog/killing-the-coronavirus-with-cleaning-how-to-clean-sanitize-and-disinfect-your-workplace-and-home/

https://www.vogue.com/article/cant-stop-touching-my-face

Personal **P**rotective **E**quipment ("PPE")

Isolation mask

https://www.cascadehealthcaresolutions.com/isolation-face-masks-with-earloops-p/non27122z.htm

Surgical mask

https://www.fishersci.com/shop/products/kimberly-clark-soft-touch-ii-surgical-mask-surgical-mask-blue/189994819

N95 mask

https://global.rakuten.com/en/store/anzen-mirai/item/021106/

R95 mask

https://www.gersonco.com/product/1940-r95-particulate-respirator/#prettyPhoto

P100 mask

https://safetyworks.com/products/respiratory-protection/half-mask-respirator/toxic-dust-respirator/

Goggles

https://www.burkhartdental.com/event/osha-infection-control-hipaa-compliance-january-16-2020/

Gloves

https://www.dhs.wisconsin.gov/ic/ppe.htm

Eye Shield

https://www.dhs.wisconsin.gov/ic/ppe.htm

Gown

https://www.dhs.wisconsin.gov/ic/ppe.htm

Sanitize INANIMATE Objects

https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2
https://images.app.goo.gl/UCUJjfHPqqshz7hG9

INFECTION PREVENTION

- Contact tracing
  - Controversial in the United States
  - Has shown promise in other countries
  - Can identify infected patients prior to the onset of symptoms
- Vaccination (typically 3-12 yrs from concept to market)
- Medication prophylaxis (Post-Exposure Prophylaxis, or “PEP”)?
- Immunoglobulins from convalescent serum?

CONTACT TRACING

- Controversial in the United States
- Extremely effective in other countries
- Can identify infected patients PRIOR to onset of symptoms
- Therefore PREVENTS spread of infection
- ESPECIALLY important with infections that have a “silent” period
  - **Syphilis**
  - **Tuberculosis**
  - **Human Immunodeficiency Virus**
  - **Ebola Virus**

VACCINATION

- Typical time-line is 3-12 years from concept to market
- Vaccine design
  - Based on hypothesis regarding viral behavior
  - Based on antibodies present in convalescent sera
- Avoiding Antibody Dependent Enhancement (“ADE”)
- Ensuring efficacy
  - Avoiding “false sense of security”
- Ensuring safety

VACCINATION AGAINST SARS-CoV 2

- SPIKE protein
- Nucleocapsid protein
- Hemagglutinin
- M2 Matrix ion channel
- Neuraminidase
- SARS (CoV-1)?

GOALS OF TREATING PATIENTS WITH COVID-19

- Treat mild to moderate symptoms
- Decrease infection efficiency
- Decrease viral replication
- Supplement neutralizing antibodies
- Decrease cellular destruction
- Address “cytokine storm”

MEDICATIONS USED TO TREAT COVID-19

- Azithromycin: Immune mediator, viral uptake inhibitor
- Chloroquine: Immune mediator, ACE inhibitor, membrane fusion inhibitor
- Hydroxychloroquine: Same probable mechanism/s as chloroquine
- Interferon: Immune mediator
- Lopinavir/ritonavir: Protease inhibitor combination
- Methylprednisolone: Steroid immunosuppressant
- Remdesivir: Adenosine analog prodrug, prevents RNA polymerase from making RNA
- Ribavirin: Guanosine analog, prevents RNA polymerase from making RNA
- Tocilizumab: Interleukin-6 (IL-6) receptor blocker
- Antibodies (Laboratory/convalescent serum): Virus “neutralizer”

SELECTED REFERENCES

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