

PHYSICS 1444-002

COVID-19

Transmission, prevention, treatment

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Monday, April 27, 2020

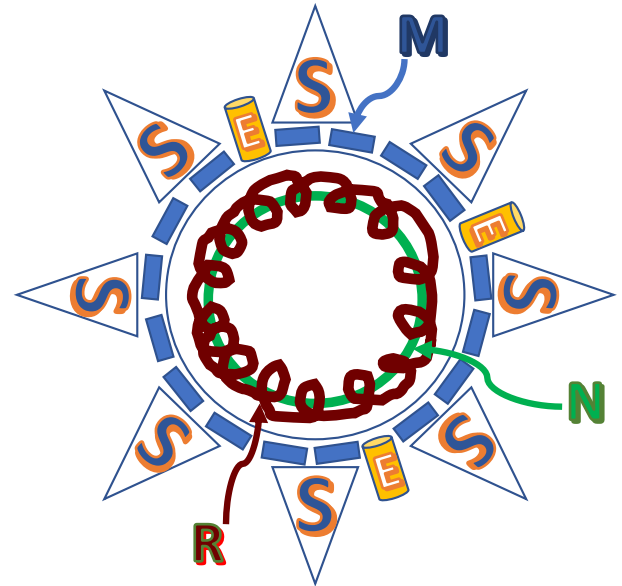
(Department of Dermatology, Medical College of Wisconsin)

DISCLAIMERS

- I have no financial conflict of interest

OBJECTIVES

- Infection transmission
- Coronaviruses
- Infection detection
- Infection prevention
- COVID-19 treatment



WHAT IS COVID-19?

- Coronav**irus** **D**isease of 20**19**
- Infectious disease
- Fever, cough, loss of energy, overall feeling unwell
- Shortness of breath, nausea, loss of smell, sore throat, other aches, pains, skin lesions



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**



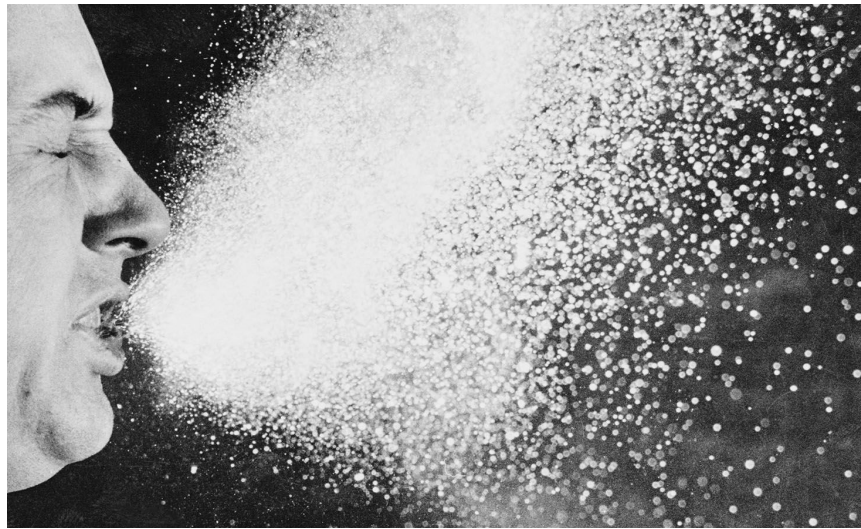
HUMAN DISEASE

- REPORTING databases for new/unusual diseases
- Review and look for patterns
- Search for cause: Toxin? Infection? Medication? Other?
- Koch's postulates suggest INFECTION
- Isolate infectious agent
- More pattern recognition

HOW MIGHT WE BECOME INFECTED?

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

INFECTION TRANSMISSION: “DROPLET”



Respiratory droplet ($\sim 5\mu\text{m}$) carries infectious agent to recipient

INFECTION TRANSMISSION: “AEROSOL”



Aerosol droplet (<5 μ m) suspends agent in air for inhalation

INFECTION TRANSMISSION: “CONTACT”



Contact with person/object directly inoculates recipient

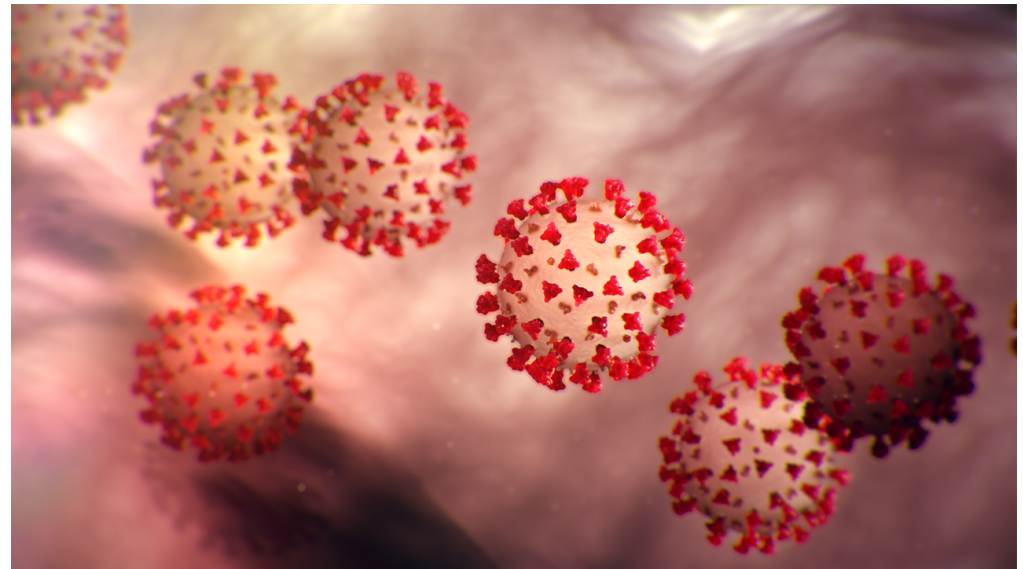
INFECTION TRANSMISSION “BLOODBORNE”



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

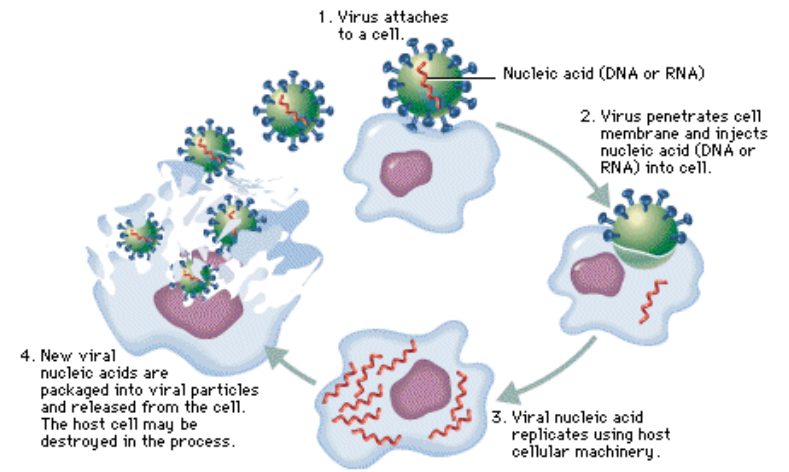
WHAT CAUSES COVID-19?

- A virus
- A coronavirus
- A coronavirus called SARS-CoV2



VIROLOGY (1)

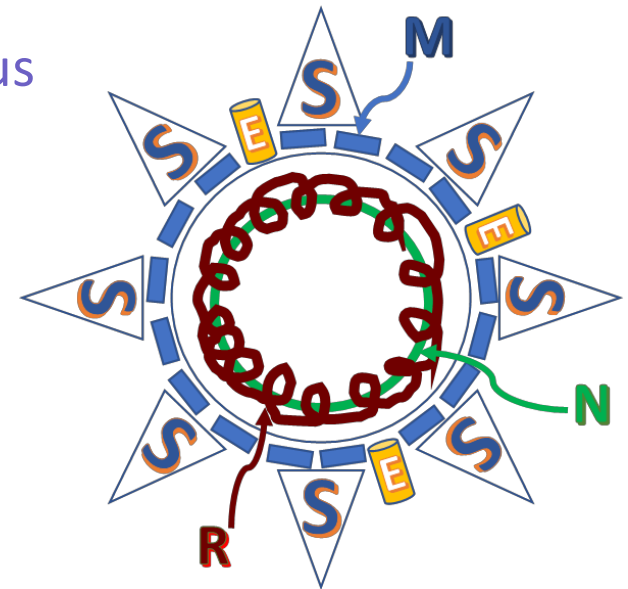
- Virus, from Latin, means “**poison**”
- Has a protein **shell**
- Genome (**RNA** or DNA) encodes proteins
- Requires a “**HOST CELL**” to multiply



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

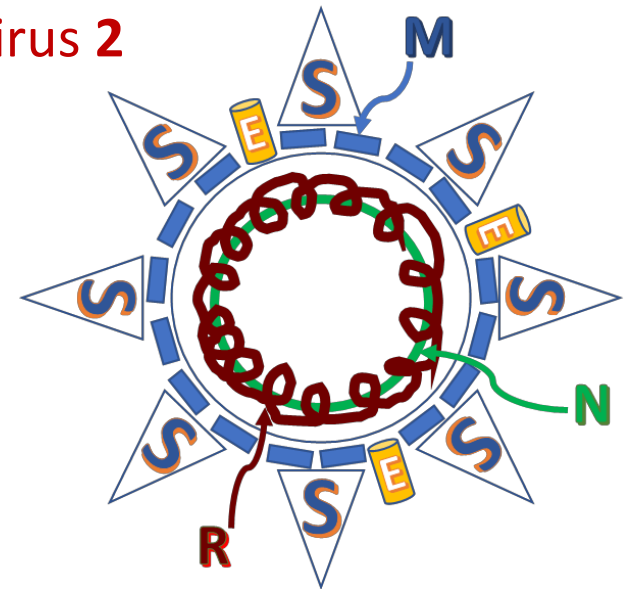
VIROLOGY (2): Coronaviruses

- Named from the Latin for “crown” or “wreath”
- **Envelope** with “**spikes**”
- **LARGE** (30,000 base) single-stranded **RNA** virus
- HUMAN Coronaviruses (HCoV):
 - HCoVNL63 (c.1320)
 - HCoV229E (c.1800)
 - HCoVOC43 (c.1900)
 - HCoVHKU1 (c.1950)
 - SARS-CoV (c.2002)
 - MERS-CoV (c.2006)
 - **SARS-CoV2** (c.2019)

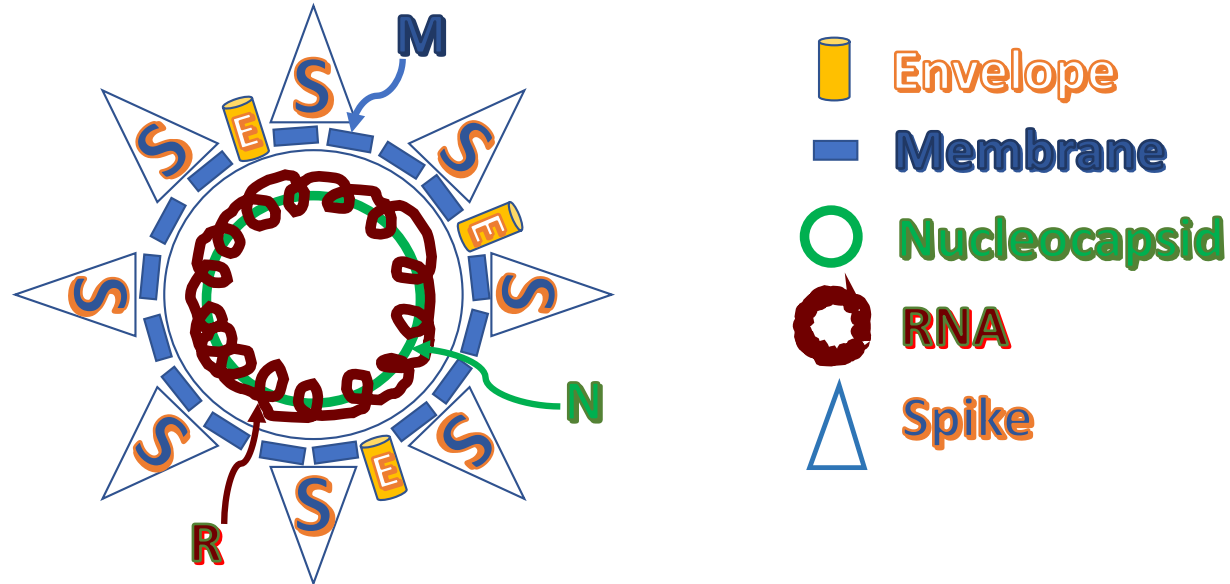


VIROLOGY (3): SARS-CoV2

- **S**evere **A**cute **R**espiratory **S**yndrome **C**orona **V**irus **2**
- Viral particle is $\sim 0.12 \mu\text{m}$ diameter
- Proteins encoded:
 - Non-structural (nsp)
 - Structural proteins
 - Accessory proteins



How SARS-CoV2 Causes COVID-19

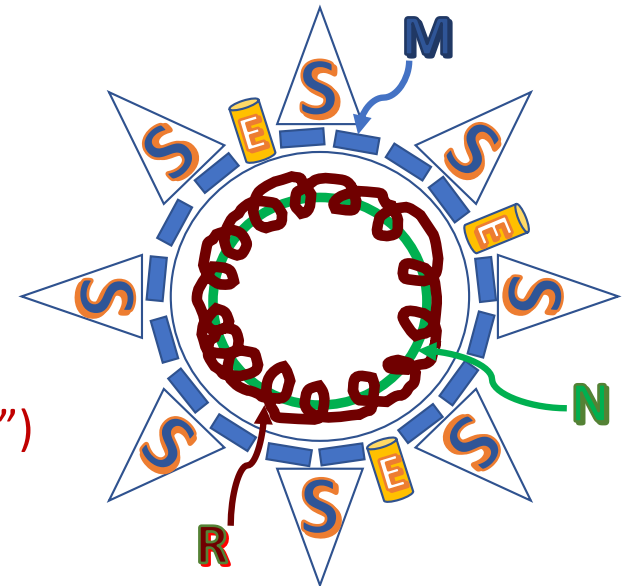


SARS-CoV2 Uses SPIKE Protein to ENTER Human Cells



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 MANIPULATES the IMMUNE System

Envelope

E PROTEIN

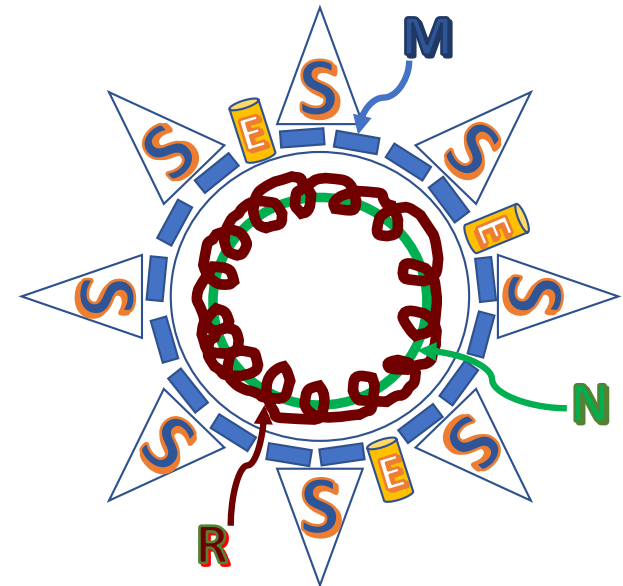
- Viroporin
- Ion CHANNEL
- Causes fluid shifts in lung tissue
- Causes unbridled release of cytokines: “STORM?”

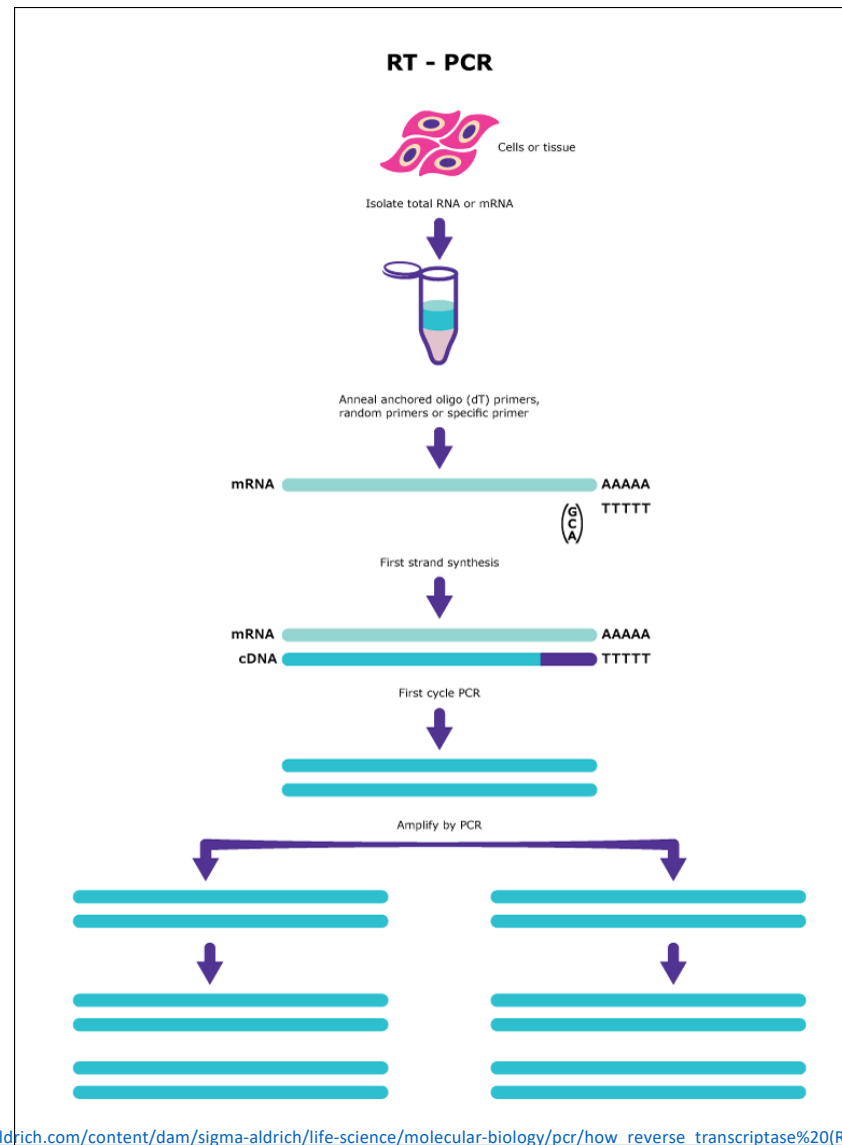
Membrane

Nucleocapsid

M, N, and nsp PROTEINS

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





Cells from upper respiratory tract
How collected??

Carefully destroy cells and purify
RNA (viral AND cellular)

Add "oligo dT primer" to RNA

Extend* primer to create cDNA

MELT strands, add SPECIFIC* primer

Extend primer SPECIFIC for target

MELT strands and repeat

QUEST DIAGNOSTICS SARS-CoV2 RT-PCR

- RT-PCR
- SARS-CoV2 nucleocapsid gene N1, N3
- Sample collection
- Sample transport
- Contamination
- Mutation

Now you have a number

- People
- Who have an illness (COVID-19)
- Caused by infection with a virus (SARS-CoV2)
- But WHAT is a NUMBER??

WHAT IS A NUMBER?

- Nineteen
- An adjective
- A quantity
- A symbol representing a finite arithmetic value

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

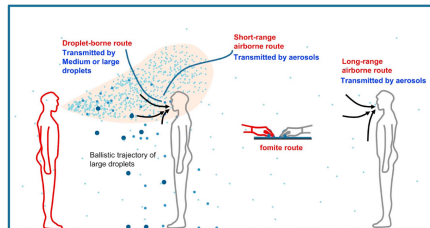
The numbers we have for COVID-19 (April 25, 2020)

- NUMBER of PEOPLE with COVID-19: 2,917,994
- NUMBER of DEATHS by COVID-19: 203,138
- SEVERITY of illness: 3%
- LONG-TERM health problems: unknown
- We have NO proven TREATMENT
- We have NO proven specific PREVENTION

HOW MIGHT WE BECOME INFECTED?

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

Maintain **distance: 3-10 feet**



- Large droplets ($>100\ \mu\text{m}$): Fast deposition due to the domination of gravitational force
 - Medium droplets between 5 and $100\ \mu\text{m}$
 - Small droplets or droplet nuclei, or aerosols ($<5\ \mu\text{m}$): 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/blocking-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.cascadehealthcare.com/resolutions.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/farmemirai/item/021106/>

Goggles



<https://www.burkhardental.com/event/oshai-infection-control-hiqa-compliance-january-16-2020/>

Gloves



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

Gown



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

Eye Shield



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

R95 mask



<https://www.geosonco.com/product/1940-r95-particulate-respirator/#prettyPhoto>

P100 mask



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

Sanitize INANIMATE Objects



<https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2>
<https://images.app.goo.gl/UCUJfHPqghz7hG9>

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
- Medication prophylaxis (Post-Exposure Prophylaxis, or “PEP”)?
- Immunoglobulins?
- Vaccination (typically 3-12 yrs from concept to market)

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”

SOME POTENTIAL PITFALLS

- BIOLOGY
 - Coronavirus mutation rate
 - Accurate animal models
- PATIENT CARE
 - Limited equipment
 - Limited medications
 - Limited human resources
 - Limited on-the-spot analytical skills
- EPIDEMIOLOGY/PUBLIC HEALTH
 - HIPAA: Data collection, contact tracing
 - Defining cause of death
 - True random/blinded testing for incidence of COVID-19
 - Determining risk factors for severe illness/death from COVID-19
 - Best messaging practices

WISH -- WANT -- WALK

- WISH
 - Curative Treatment
 - Specific and Sensitive Testing
 - Effective Prevention
 - No or Low Cost
 - “Remuneration”
 - Obedience
- WANT
 - Reasonable Management of COVID-19
 - Adequate Human and Material Resources
 - Society Understands and Agrees with Protective Measures
- WALK
 - Inequitable Protection
 - Society Disagrees with Protective Measures
 - Greed Drives Decision-Making

SELECTED REFERENCES

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- Channappanavar, R. and S. Perlman (2017) Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Sem Immunopath* (39)529-539.
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- Enjuanes, L. et al (2016) Molecular basis of coronavirus virulence and vaccination development. *Adv in Virus Res* (96)245-286.
- Forni, D. et al (2017) Molecular evolution of human coronavirus genomes. *Trends in Microbiol* (25)1:35-48.