



What Can I Do to Protect Myself, My Family and My Patients During COVID-19?

Role for
Complementary
and Integrative
Health?

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Disclaimer

1. Material presented here is supplemental; does not replace public health guidelines emphasizing hand-washing, masking, social distancing and testing if symptoms present.
2. No CIH measures have been validated in human trials as effective against COVID-19; evidence is from pre-clinical trials or trials related to boosting immunity in general.
3. Opinions expressed here do not reflect those of the Department of Veterans Affairs or the University of California, San Francisco.



Poll Question #1

In addition to public health measures (masking, distancing, handwashing etc.), have you implemented anything new in an attempt to protect you or family members against COVID-19?

YES

NO



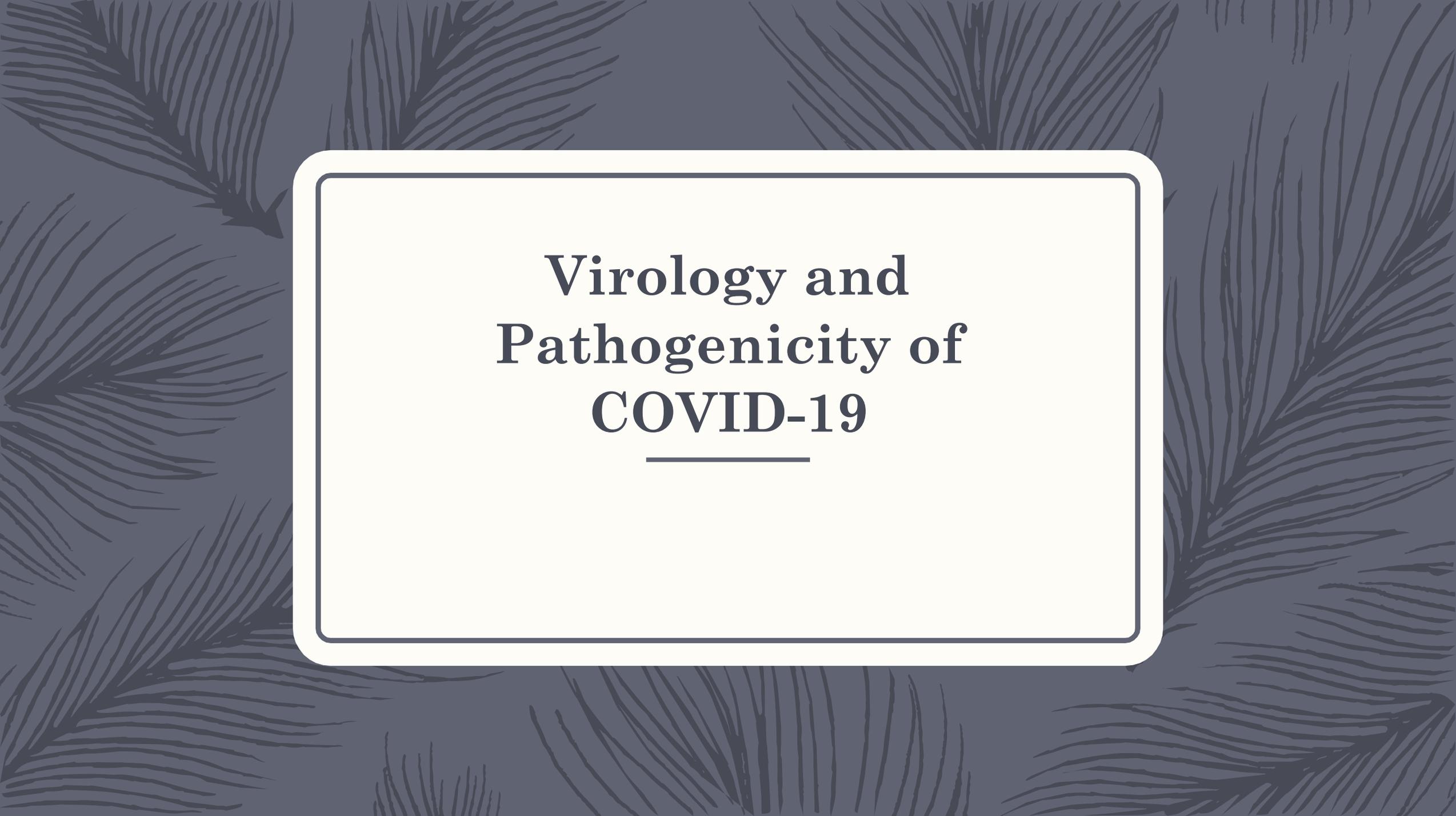
Poll Question # 2

If you have implemented new health measures, in which of the following areas have you made changes? (Indicate all that apply.)

- A. Sleep habits
- B. Diet or dietary supplements (vitamins, minerals, other natural products)
- C. Exercise
- D. Stress Reduction (other than exercise)
- E. None of the above

Overview

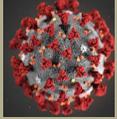
- Virology and pathogenicity of SARS-CoV-2 (Coronavirus disease 2019; COVID-19)
- Strategies to help prevent infection and promote recovery
 - Nutrition
 - Dietary Supplements
 - Sleep
 - Exercise and Stress Reduction
- Summary



**Virology and
Pathogenicity of
COVID-19**



SARS-CoV-2 RNA virus enters human cells through angiotensin-converting-enzyme 2 (ACE2) receptors



SARS-CoV-2 virus penetrates host cell



Virus injects its blueprint



Hijacks cell's "factory" to make new virus proteins



Assembles new SARS-CoV-2 virions



Mature RNA virus released into bloodstream infects other cells

**Main Goal of
Viruses:**

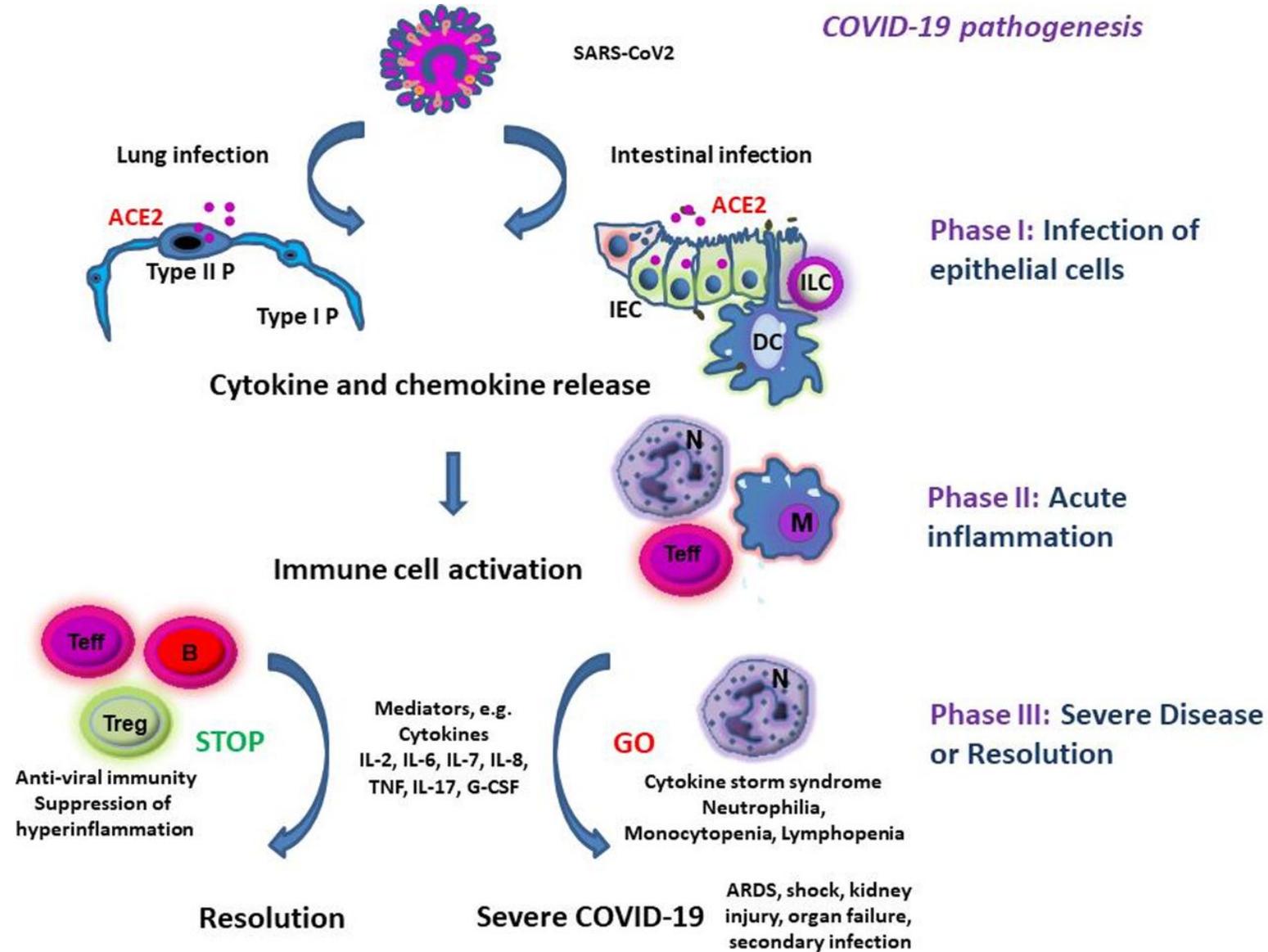
Reproduction



Virology of COVID-19

- Virulence and pathogenicity develops from COVID-19 virus **activating** cytoplasmic NLRP3 inflammasome within immune cells.
- NLRP3 inflammasome signals immune cells to release pro-inflammatory cytokines (e.g., IL1-b, IL-6, IL-8, TNF- α) causing inflammatory response resulting in symptoms of COVID-19.

COVID-19 pathogenesis





Stages of COVID-19 Infection

Transmission:

- SARS-CoV-2 spreads person to person through respiratory droplets.
- ~50% of transmission from asymptomatic spread.

Infection:

- Symptoms include cough, fever, malaise/fatigue, myalgias, GI symptoms, and anosmia
- Cytokine Storm (ARDS, vascular events, organ failure etc.)

Therapy:

- **KEY:** Prevent cytokine storm without inhibiting anti-viral immunity.
- **KEY:** Risk vs. Benefit ratio

Health Status and COVID-19

Table 1. Established and Potential Risk Factors for Severe Covid-19.*

Older age (e.g., >65 years)
Chronic lung disease
Cardiovascular disease
Diabetes mellitus
Obesity
Immunocompromise†
End-stage renal disease
Liver disease

+ smoking

+ heavy alcohol use

Gandhi, RT, *NEJM*, 2020

Healthy people with good health habits who limit their exposures are less likely to contract COVID-19, and if they do, more likely to recover.

Important (unalterable) considerations:

- *Genetics (Nature)*
- *Social determinants (Nurture)*

CIH strategies work in two ways:

- Help prevent infection/promote recovery
- Decrease risk factors for morbidity and mortality related to COVID-19 infection.



Prophylaxis for primary and secondary prevention

#1: Limit exposure (physical distancing, masking and hand-washing)

2 Maintain a healthy immune system

- Good nutrition
- Select dietary supplements
- Better sleep
- Stress reduction

Nutrition and Dietary Supplements



Anti-Inflammatory Diet (aka Mediterranean Diet)

Recommended (organic if possible):

- Fruits (2-3 servings/day), vegetables (5-7 servings)
- Whole grains
- Nuts, olive oil and other fats high in omega-3 fatty acids
- Legumes, lean poultry and fish
- Alcohol in moderation

Avoid :

- Refined carbohydrates and baked goods, sodas and sweets
- Red meat and other processed meats
- Butter and other spreadable fats

- Multiple studies demonstrate anti-inflammatory effects of Mediterranean Diet measured by decreases in serum inflammatory markers.
- Mediterranean diet reduces obesity, HTN, hyperlipidemia, CVD, DM in hundreds of studies.

(Schwingshacki L., *Nutr Metab Cardiovasc Dis*, 2014; Richard C., *Obesity*, 2013; Esposito K, *JAMA* 2004)



"I start every meal with an onion"

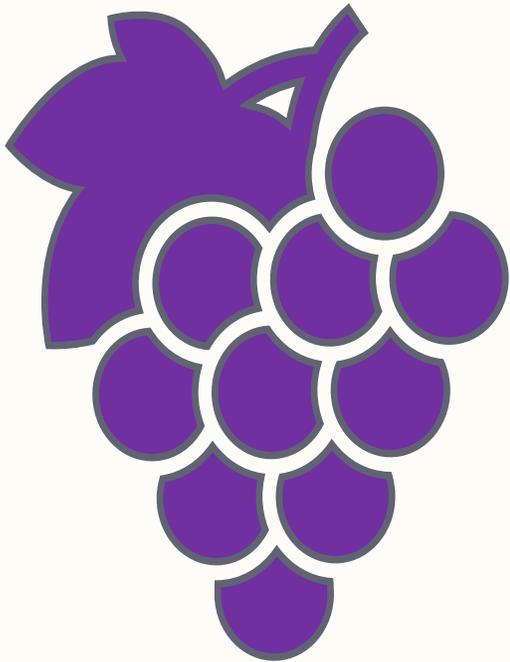
Reid Thaler (husband)

"An apple a day keeps the doctor away"

Joan Seal (mother)

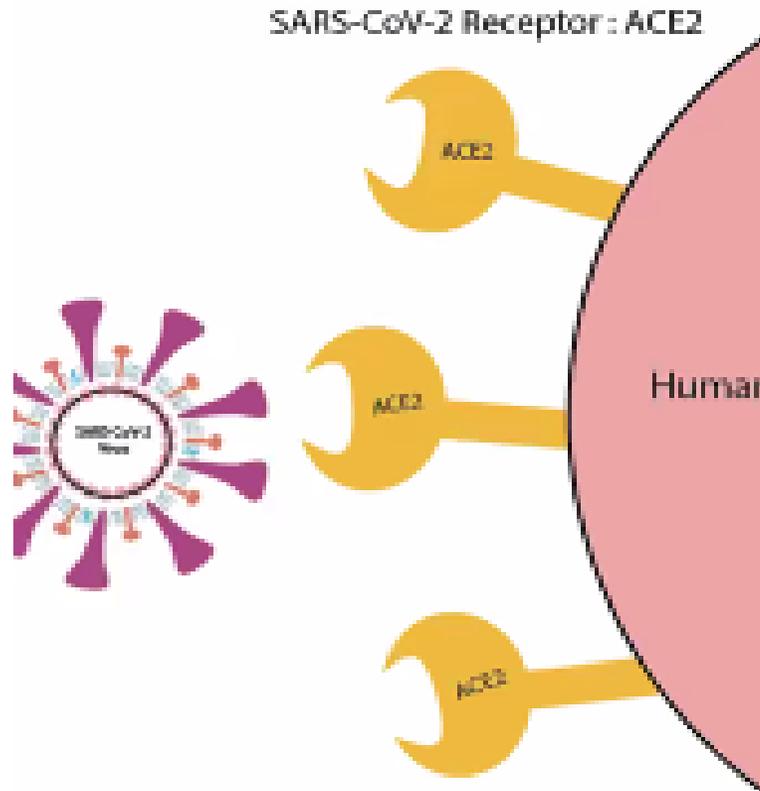
Any "kitchen table" wisdom here?

Colorful Fruits and Vegetables: Flavonoids



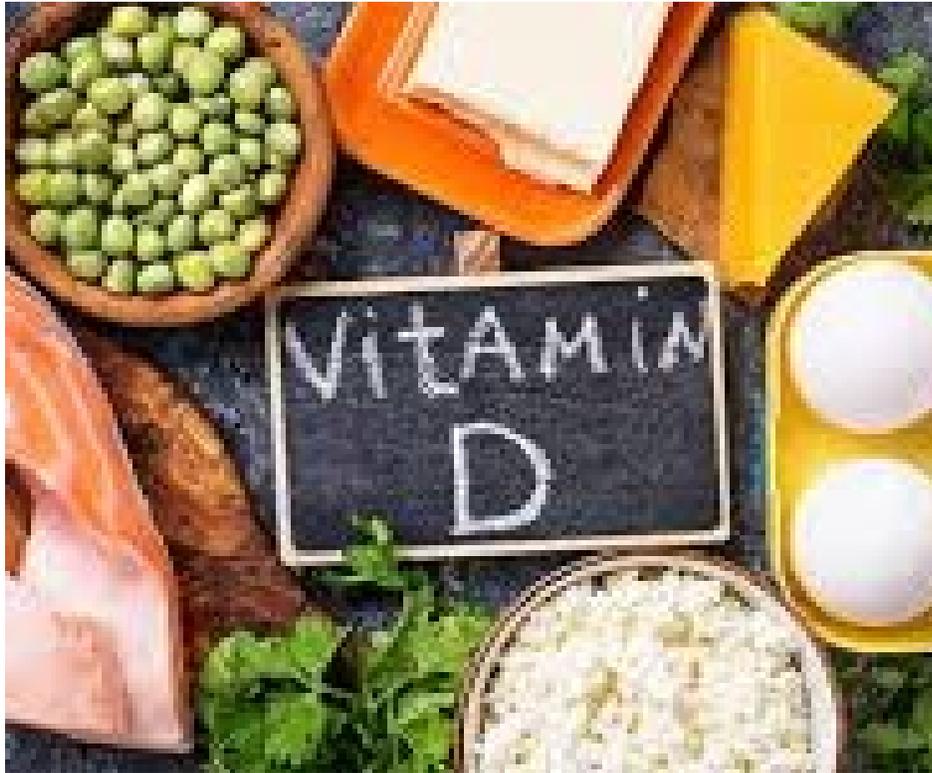
- Many plant flavonoids have been found (in vitro) to suppress inflammatory cytokines (e.g., IL-6, IL-8 and TNF- α) and to boost immunity.
- These include:
 - Quercetin found in **apples** and **onions** (Milcek J., *Molecules*, 2016)
 - Myricetin found in **tomatoes**, **oranges**, **nuts** and **berries** (Chen H, *Toxicol Appl Pharmacol*, 2019)
 - Curcumin found in **turmeric root** (Yin H, *J Immunol*, 2018)
 - Epigallocatechine gallate (EGCG) from **green tea** (Kailhatsu K, *Molecules*, 2018)
 - Garlic (Arreola R, *J Immunol Res*, 2015)

Block SARS-CoV2 Viral Entry



- Quercetin and EGCG Green Tea prevents viral attachment and entry. (Smith M, *ChemRxiv*, 2020; Kailhatsu K, *Molecules*, 2018)
- Astragalus extract (used in Chinese medicine), shown in rats to decrease ACE receptor activity (Wang Q-Y, abstract only; 2015)
- Vitamin D₃ decreases ACE2 receptor activation in vitro (Cui et al., *Redox Biol*, 2019)

Vitamin D₃



- Vitamin D₃ stimulates immune and respiratory epithelial cells to secrete anti-viral peptide (cathelicidin).
- Those with vitamin D₃ levels < 40-50 ng/ml may benefit from vit D₃ supplementation
 - 1000-2000 IUs daily; more if depleted
- **Caution:** Excessive vitamin D can trigger over-exuberant immune response, increasing cytokine secretion; discontinue if COVID-19 infection or (+) test. (Tulk SE, *J Cell Biochem*, 2015)

Zinc



- Zinc has viral inhibitory actions demonstrated in other coronaviruses (Phillips JM, *J Virol*, 2017)
- May help to prevent coronavirus entry into cells and reduce coronavirus virulence (Han Y-S, *Biochemistry*, 2005)
- Dosing of zinc is 15-30 mg/daily; lozenges protective in upper respiratory tract? May cause nausea.
- Zinc found in nuts and seeds.
- Quercetin (onions, apples) & green tea potentiate anti-viral actions of zinc; binds & brings zinc into cells.

Vitamin C



- Since Linus Pauling, half of the 30 clinical trials (12,000 participants) have been positive (2006 & 2013, *Cochrane Reviews*).
- Systematic review: Vitamin C shortens frequency, duration and severity of common cold and incidence of influenza (Hemila H., *Mil Med* 2004)
- Evidence is contradictory; necessary nutrient; few adverse side-effects.
- Dosing of vitamin C ranges from 500 mg to 3,000 mg daily.



Elderberry (*Sambucus Nigra*)

- Preclinical evidence that elderberry inhibits replication and viral attachment of human coronavirus NL63; same family as COVID-19. (Weng, J-R et al., *Virus Res*, 2019)
- Most effective in prevention or early stages of coronavirus infections. (Chen C, *BMC Vet Res*, 2014)
- Dosing of 2:1 elderberry extract is 10-60 ml daily.
- **Caution:** Elderberry increases inflammatory cytokines; discontinue if positive COVID-19 test or symptoms.



Others to Consider; Other Considerations

- **Astragalus:** Medicinal plant in TCM; prevention/ treatment of common cold. Pre-clinical studies: enhanced immunoglobulin production. (McKenna D, *Altern Ther Health Med*, 2002)
 - **Echinacea:** Preventive trials for viral URIs in humans trend in the positive direction. Head to head study echinacea vs. oseltamivir in flu, found echinacea equally effective. (Karsch-Volk, M, *JAMA*, 2015; Raus K, *Current Therapeutic Research*, 2015)
 - **Probiotics:** Live bacteria for gut health. Over a dozen trials suggest probiotics may prevent cold and flu episodes. (King S., *Br J Nutr*, 2014)
- * **Obtain vitamins, minerals, dietary supplements from food sources for greater bioactivity and bioavailability.**



Confused in the “Immunity” Section?

Dietary Supplements:

- Not regulated by the FDA
- FDA published GMPs for purity, strength and potency; noted on label
- Adverse effects often from contaminants; not the product itself.





Summary

Prevention:

- ***Diet:*** Anti-inflammatory (Mediterranean) diet
- ***Flavonoids:*** Found in brightly colored fruits and veggies
- ***Vitamins, Minerals and Botanicals:*** Vitamin D3, Zinc, Vitamin C, Elderberry (look for evidence of GMP)
- ***Other Natural Products:*** Astragalus, Echinacea, probiotics

During COVID infection or positive test:

- *Avoid supplements that could potentiate cytokine storm:* Elderberry, Vitamin D and medicinal mushrooms
- *Likely Safe:* Garlic; Quercetin; Astragalus; Green Tea; Zinc; Vitamin C



Sleep

Importance of a Good Night's Sleep

- Sleep loss associated with disruptions in immune functioning; can increase risk of infection. (Irwin MR, *Arch Intern Med*, 2006)
- < 5 hours/night increased risk of developing rhinovirus by 350% compared to getting 7 hrs./night sleep. (Prather AA, *Sleep*, 2015)
- Sleep deprivation increases NLRP3 inflammasome activation; triggers release of pro-inflammatory cytokines responsible for COVID-19 sx. (Gorbachev AV, *J Immunol*, 2007; Romero JM, *Clin Cancer Res*, 2020)
- Sleep disturbances (from insomnia, OSA etc.) linked to chronic dz (e.g., obesity, HTN, CVD, DM) predict worse outcomes with COVID.





Strategies for Good Sleep

“Sleep Hygiene”

- Avoid PM caffeine; medication side-effects; some health conditions
- Avoid daytime napping; maintain consistent sleep/wake schedule
- Bed is for sleep (and sex); not work; get screens out of bedroom
- Reduce other stimuli- light and noise
- Avoid intense exercise or mental stimulation before bedtime

Meditation/mindfulness; CBT; other stress redux activities

Natural products (mixed evidence): MT, valerian, hops, lemon balm etc.

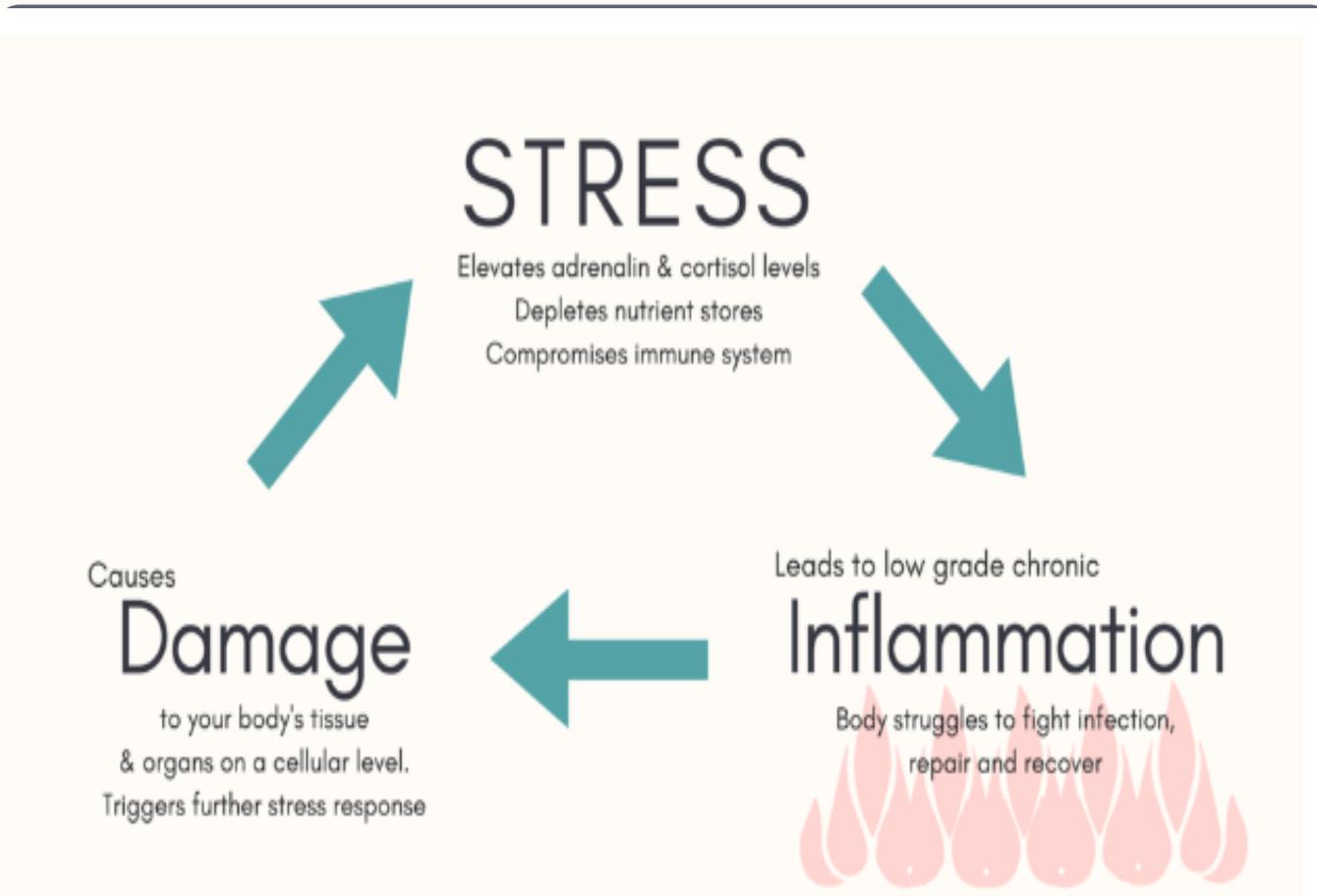
Melatonin: Not just for Sleep?



- Produced by the pineal gland; associated with regulation of sleep-wake cycles
- Role in improving immunity-inhibits NLRP3 inflammasome and NFkB activation; inhibits release of pro-inflammatory cytokines responsible for COVID-19 sx. (Hardeland R, *J Pineal Res.*,2018)
- Less is more. Optimal doses range from 1-3 mg 30 minutes before sleep.

Stress Reduction

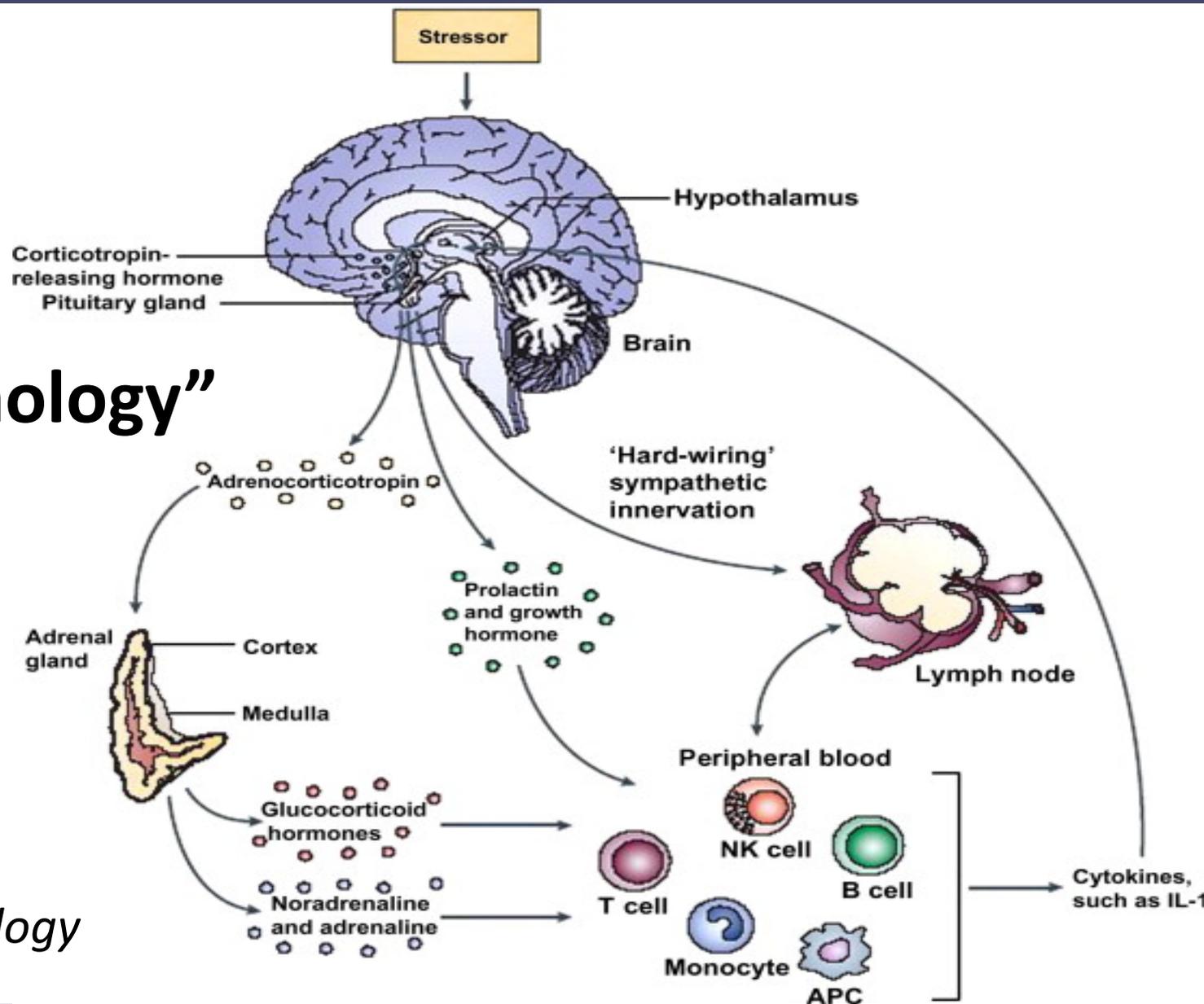
Stress and the Immune System



Psychological stress is associated with increases in pro-inflammatory cytokines (e.g., IL-6). (Godbout, JP, *J Neuroimmune Pharmacol.*, 2006)

Perceived stress predicted whether healthy volunteers would become sick when exposed to rhinovirus (Cohen, S., *NEJM*, 1991)

“Psychoneuroimmunology”



From: Nature Reviews: *Immunology*



Managing Stress with Exercise and Mindfulness: Effects on Immunity

Aerobic exercise and mindfulness techniques (meditation, breathing, guided imagery etc)

- Indirect effects on improving immune function by decreasing stress.
- Direct effects in improved immune function. (Ortega, E., *Scand J Med Sci Sports*, 2012; Black, D., *Ann NY Acad. Sci.*, 2016)
- Improves chronic conditions (i.e., obesity, HTN, DM etc).

Training in MBSR exercises significantly reduced ARI episodes. (Rakel, D., *Fam Pract.*, 2013)

U.S. guidelines recommend a minimum of 150 min of exercise weekly; exercising in nature may have added benefits.

Summary

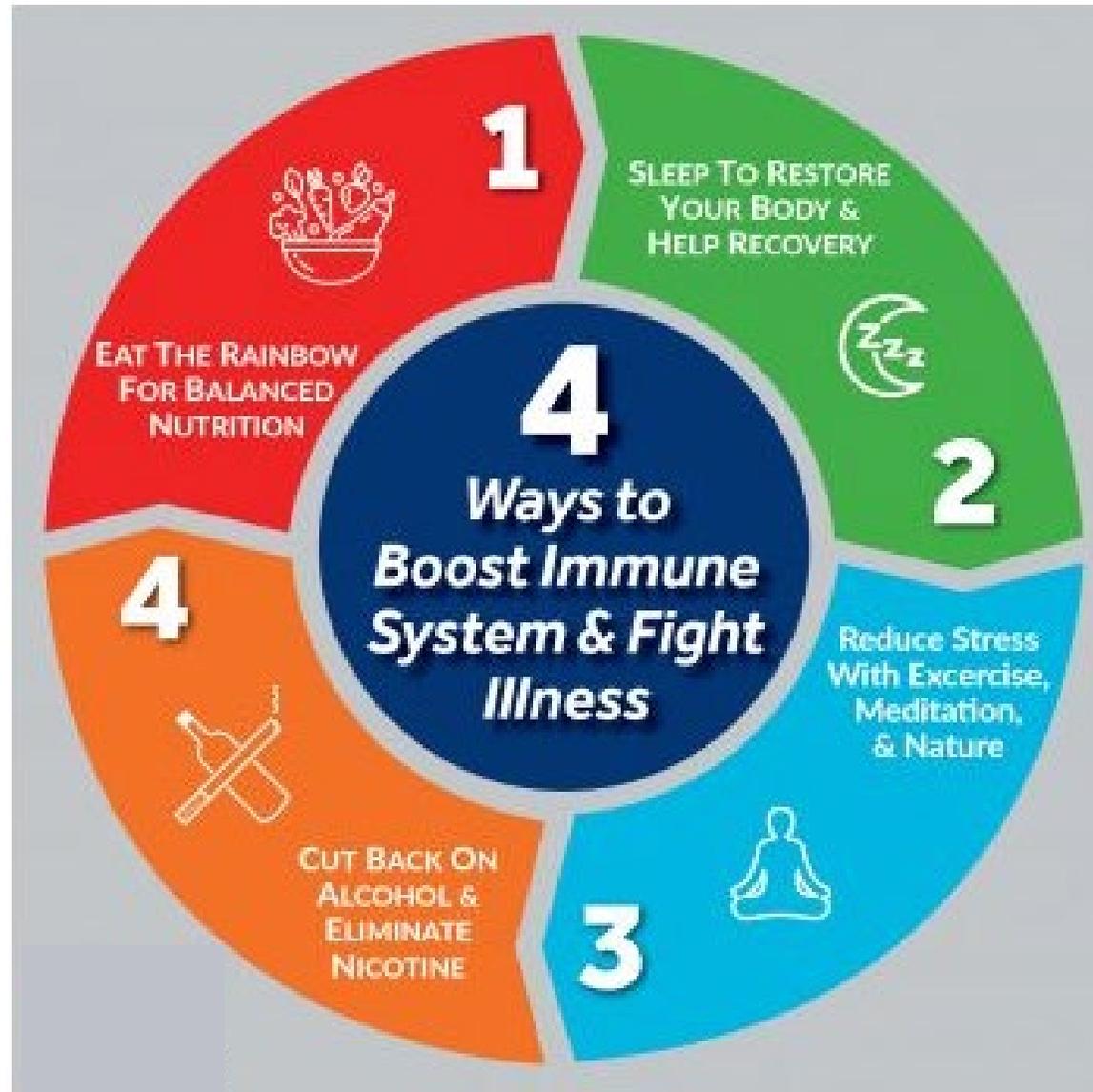


Summary

While integrative measures have not yet been validated in human trials for COVID-19, we have an opportunity to be proactive.

GOAL of Integrative approaches is to complement traditional (biomedical) approaches to help:

- Prevent infection
- Deter virus from replicating and spreading in the body
- Speed recovery
- Prevent risk factors that predict poor clinical outcomes



From: Virginia Spine Institute



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Questions?

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**Thank you and
stay safe!!**