# The Nature of Immune Intelligence: Therapeutic Integration of Lifestyle Medicine Approaches

Deanna Minich, PhD, FACN, CNS American Nutrition Association, Board Member May 2021

### **Faculty Disclosure**

Commercial Interest	Nature of Relevant Financial Relationship	
	What was received	For what role
Metagenics, Inc.	• Fee	Independent     Contractor
Clean/Organic India	• Fee	Independent     Contractor

- This presentation contains educational material only and is not intended to take the place of advice from your own physician(s) or to be a means of diagnosing or treating an illness.
- Deanna Minich is a health educator with a professional platform focused on plant-based eating. She is a consultant to a variety of companies selling nutritional products.

### **Presentation Learning Objectives**

After participating in this presentation, learners should be better able to:

- Define the nature of 'immune intelligence'
- Understand how immunity is a systems web more accurately described as the psychoneuroendocrine immune system
- Identify how aligning with nature, specifically plants, may help with immune intelligence
- Understand the scientific research of a plant-based diet for immune health
- Summarize evidence-based food and lifestyle strategies to support psychoneuroendocrineimmune health

Immune Intelligence

### **DEFINITION OF IMMUNE INTELLIGENCE**

Immune intelligence is the inherent and conscious ability to harmonize the inner milieu with outer environmental factors in an effective homeodynamic manner enabling the organism to equilibrate to optimal function

### CHARACTERISTICS OF IMMUNE INTELLIGENCE

### **Characteristics of immune intelligence:**

- Acts with consciousness
- Exhibits emotional and sentient qualities
- Operates in an algorithmic manner, blending physiology, psychology, inner and outer inputs
- Utilizes multiple sensors, including skin, eyes, gut, fields
- Engages in constant reframing and learning
- · Gathers data over a lifetime
- · Recognizes patterns and acts for the best end goal
- Includes teams and collectives such as microorganisms, viruses, fungi

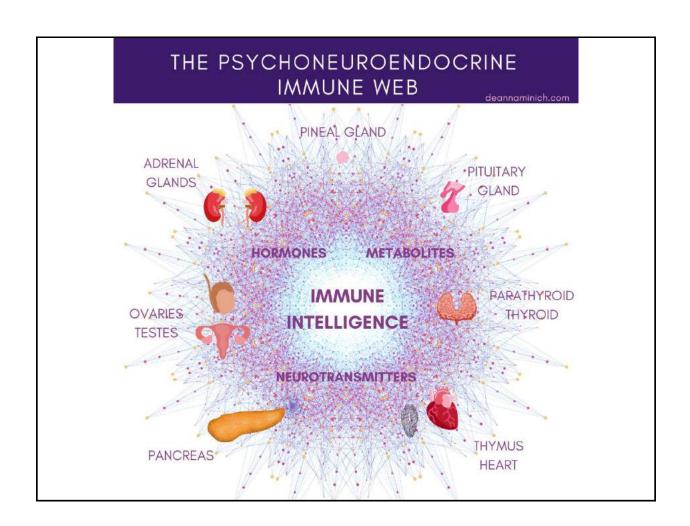
Immune system vs.
Psychoneuroendocrineimmune web

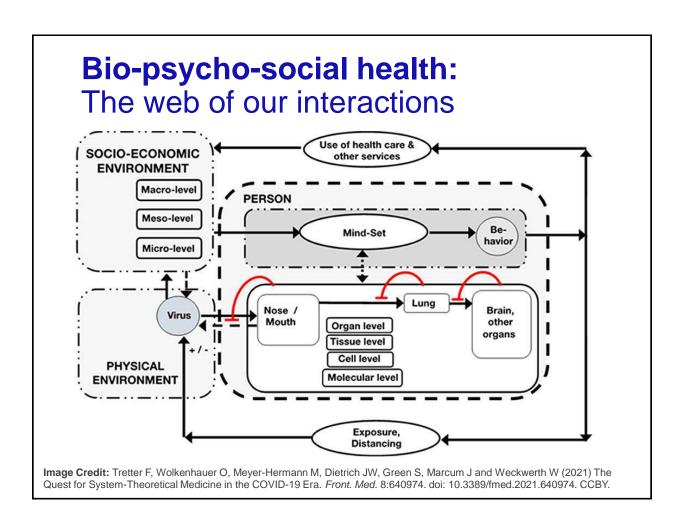
It's not the 'immune system' but the psychoneuroendocrine-immune system

# Adrenal fatigue is an outdated, simplistic term: Go upstream

- HPA axis dysfunction or maladaptation
- Hypocortisolism
- Psychoneuroendocrine immune imbalance

**References**: Guilliams TG. *The role of stress and the HPA axis in chronic disease management*. Point Institute, 2015. Minich DM. Upstream healing: Tips for a healthy hypothalamus. 2017 May 17. https://www.deannaminich.com/upstream-healing-tips-for-a-healthy-hypothalamus/

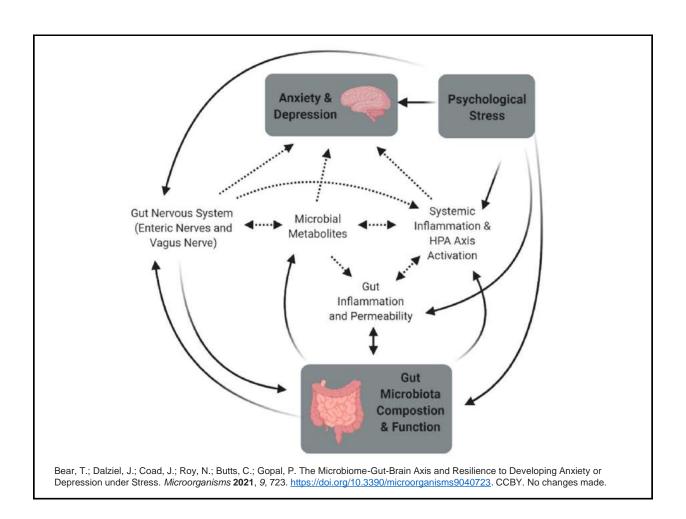




# Stress Results in Shifts in Microbial Populations

- Stress has a 'ripple effect' through the gut, resulting in activation of the vagus nerve and enteric nervous system
- Results in immune changes, inflammation, intestinal damage, and increased GI permeability → all have the potential to influence the gut microbiota

Karl JP, Hatch AM, Arcidiacono SM, et al. Effects of Psychological, Environmental and Physical Stressors on the Gut Microbiota. *Front Microbiol.* 2018;9:2013. Published 2018 Sep 11. doi:10.3389/fmicb.2018.02013

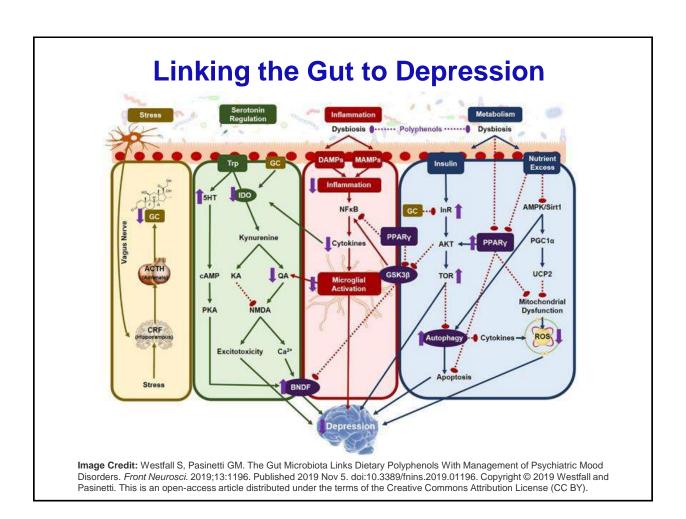


### Stress and the Gut

Effects of stress on the gut include:

- 1) alterations in motility (could be slower or faster);
- 2) visceral sensations ("butterflies in the stomach");
- 3) alterations in secretions (higher or lower);
- 4) increase in intestinal permeability ("leaky gut");
- 5) changes in intestinal cell turnover and blood flow;
- 6) changes to the microbiome

**Reference**: Konturek PC, Brzozowski T, Konturek SJ. Stress and the gut: Pathophysiology, clinical consequences, diagnostic approach and treatment options. *J Physiol Pharmacol*. 2011 Dec;62(6):591-9.



### **Psychobiotics**

Defined as probiotics that have mood-altering or psychological effects such as reducing depression or anxiety

"...patients diagnosed with both IBS and major depression, a twice daily dose of *Bacillus coagulans* MTCC 5856 was administered and treated patients demonstrated reduced depressive phenotypes on multiple scales (Majeed et al., 2018)."

**Reference:** Westfall S, Pasinetti GM. The Gut Microbiota Links Dietary Polyphenols With Management of Psychiatric Mood Disorders. *Front Neurosci.* 2019;13:1196. Published 2019 Nov 5. doi:10.3389/fnins.2019.01196

# Immune dysfunction and disorders from repeat stressors

- Various brief and chronic stressors impact the immune system
  - e.g., public speaking, medical school examinations, unemployment, marital discord, divorce, death of spouse, burnout and job strain, caring for a relative with Alzheimer's disease, and exposure to the harsh climate of Antarctica
- Stressors are associated with weakened immunity
  - Glaser & Kiecolt-Glaser, 2005; Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Segerstrom & Miller, 2004

Reference: https://opentext.wsu.edu/ospsychrevisions/chapter/stress-and-illness/

### **Autoimmune conditions**

- Stress load cannot easily be accommodated
- Role of psychological stress and stress-related hormones in autoimmune disease
- Immune dysregulation and inflammatory cytokine production
- Al disease requires stress management techniques to assist with physiological rebalancing

Reference: Assad S, Khan HH, Ghazanfar H, et al. Role of sex hormone levels and psychological stress in the pathogenesis of autoimmune diseases. *Cureus*. 2017;9(6):e1315. Published 2017 Jun 5. doi:10.7759/cureus.1315

## **Examples of ways people manage** stress

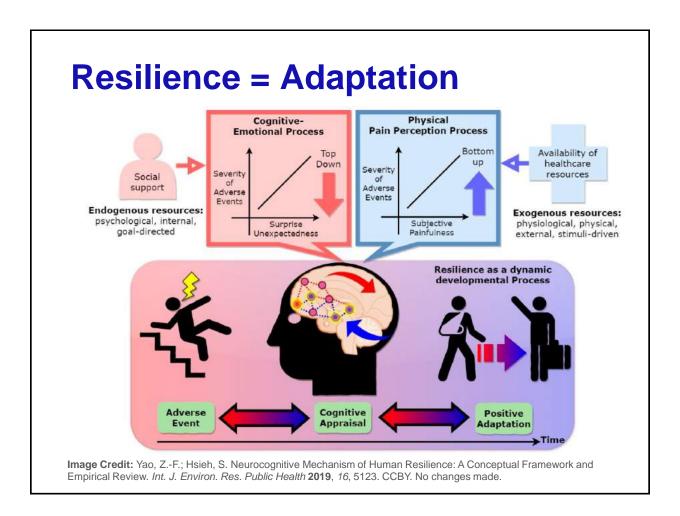
- Stimulants in AM (i.e. coffee)
- Depressants in the PM (i.e. alcohol)
- Highly-processed comfort foods
- High-sugar/chocolate
- Caffeinated beverages throughout the day
- · Over-eating and under-eating
- Over-working
- Over-sleeping
- · Risk-taking behaviors

Reference: Based on presenter's clinical experience

### What about stress genes?

- Redox pathways
- Heat shock proteins
- Immune-related genes
- · Genes associated with inflammation
- Environmental stress and detoxification
- Glucocorticoid receptors

Cornelius C, Perrotta R, Graziano A, Calabrese EJ, Calabrese V. Stress responses, vitagenes and hormesis as critical determinants in aging and longevity: Mitochondria as a "chi". *Immun Ageing*. 2013;10(1):15. Published 2013 Apr 25. doi:10.1186/1742-4933-10-15



# Select laboratory biomarkers of resilience

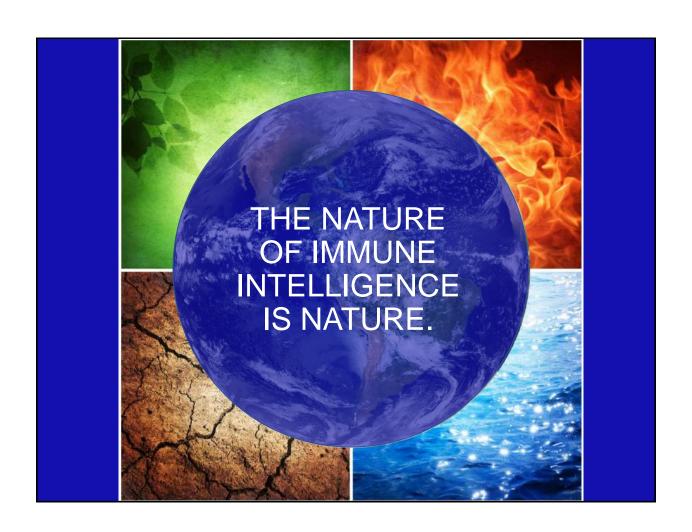
- Inflammaging
  - High hsCRP
  - Low vitamin D
  - High fasting glucose/insulin
  - Low Omega-3 Index
  - Reduced lean body mass
  - High homocysteine (risk factor for chromosome damage, Fenech)
- Elevated oxidative Stress Markers
  - 8-OHdG
  - Urine lipid peroxides
- · Low levels of vitamins and minerals
- Advanced Glycation Endproducts High Hgb A1C
- · Elevated autoantibodies
- Lowered immune function (reduced WBCs)

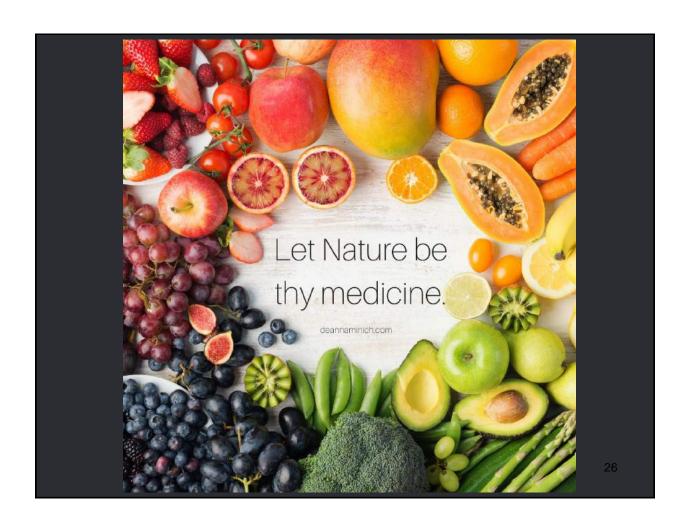
Reference: Based on presenter's clinical experience

The antidote is – NATURE. Outside us, inside us.

"As above, so below, as within, so without, as the universe, so the soul..."

- Hermes Trismegistus





# The immune system is the sum of our relationship with the natural environment

- Are we out of touch with nature?
- How are we connected into our food?
- Are plants the 'divining rod' between nature and the human body to keep us balanced?

Nurminen N, Lin J, Grönroos M, et al. Nature-derived microbiota exposure as a novel immunomodulatory approach. Future Microbiol. 2018;13:737-744. doi:10.2217/fmb-2017-0286



# Harnessing the Four Elements for Mental Health Horticulture Nature exposure Animal therapy Balincotherapy Hydrotherapy Light/sun exposure Light

Sarris J, de Manincor M, Hargraves F and Tsonis J (2019) Harnessing the Four Elements for Mental Health. Front. Psychiatry 10:256. doi: 10.3389/fpsyt.2019.00256. CCBY. No changes made.

### **Nature outside**

- Forest bathing
- Biogenic volatile compounds
- Stress modulating effects

### **Nature-Outer Biomes**

- Forest
- Garden
- Trees/bushes/flowers
- Air
- Ocean

Moelling K, Broecker F. Air Microbiome and Pollution: Composition and Potential Effects on Human Health, Including SARS Coronavirus Infection. *J Environ Public Health*. 2020;2020:1646943. Published 2020 May 28. doi:10.1155/2020/1646943



### The healing green of nature

"Many studies have reported the effect of viewing green plants on physiological relaxation. The findings confirmed that **viewing green plants**, such as foliage plants, in an indoor environment can elicit positive health outcomes with **greater stabilization of prefrontal cortex activity and autonomic nervous activity**."

**Reference**: Jo H, Song C, Miyazaki Y. Physiological Benefits of Viewing Nature: A Systematic Review of Indoor Experiments. *Int J Environ Res Public Health*. 2019 Nov 27;16(23). pii: E4739. doi: 10.3390/ijerph16234739.

### **Nature Therapy: Forest Bathing**

### Concept of nature therapy

Stressed state



Restorative effects of nature (forests, flowers, etc.)



Physiological relaxation Immune function recovery

Individual differences

Evidence-based medicine (EBM)

### **Preventive medical effect**

Hansen MM, Jones R, Tocchini K. Shinrin-Yoku (Forest Bathing) and Nature Therapy: A State-of-the-Art Review. Int J Environ Res Public Health. 2017;14(8):851. Published 2017 Jul 28. doi:10.3390/ijerph14080851

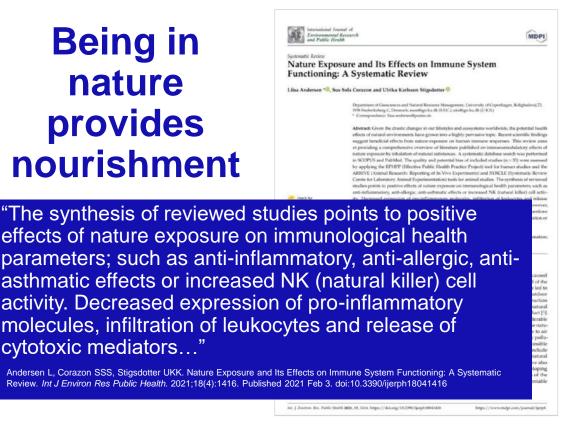
### The Results of Forest Therapy

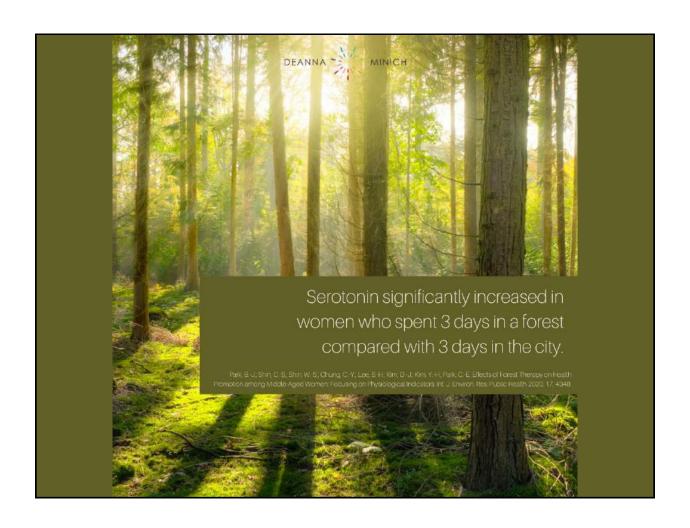
- Enhanced positive mood and reduced negative mood
- Blood pressure and heart rates decreased
- Peripheral oxygen saturation increased
- NK activity increased
- Number of NK cells and perforin-, granulysin-, and granzyme A/B-expressing cells increased
- Corticosterone level in peripheral blood lymphocytes decreased

Lyu B, Zeng C, Xie S, et al. Benefits of A Three-Day Bamboo Forest Therapy Session on the Psychophysiology and Immune System Responses of Male College Students. Int J Environ Res Public Health. 2019;16(24):4991. Published 2019 Dec 8. doi:10.3390/ijerph16244991



cytotoxic mediators..."





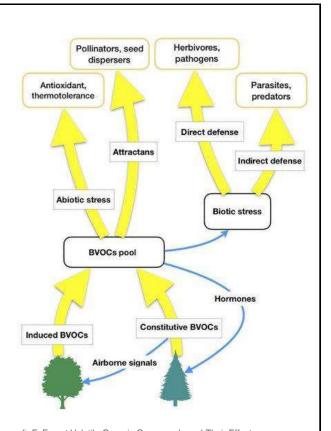
### **Forest Volatile Compounds**

- Trees emit a broad range of up to 200 different biogenic volatile organic compounds (BVOCs) which are primarily terpenes and terpenoids
- While they are for the survival of the tree, they may have benefit for human health.
- Cell and animal studies have shown anti-inflammatory effects upon exposure to these terpenes and terpenoids emitted in the forests

Kim T, Song B, Cho KS, Lee IS. Therapeutic Potential of Volatile Terpenes and Terpenoids from Forests for Inflammatory Diseases. *Int J Mol Sci.* 2020;21(6):2187. Published 2020 Mar 22. doi:10.3390/ijms21062187

### Forest Volatiles and Human Health

"Inhaling forest VOCs like limonene and pinene can result in useful antioxidant and anti-inflammatory effects on the airways, and the pharmacological activity of some terpenes absorbed through inhalation may be also beneficial to promote brain function by decreasing mental fatigue, inducing relaxation, and improving cognitive performance and mood."

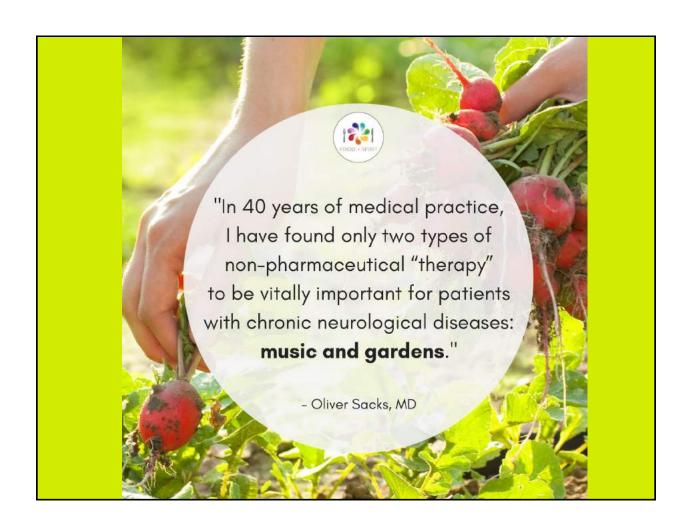


Antonelli, M.; Donelli, D.; Barbieri, G.; Valussi, M.; Maggini, V.; Firenzuoli, F. Forest Volatile Organic Compounds and Their Effects on Human Health: A State-of-the-Art Review. *Int. J. Environ. Res. Public Health* **2020**, *17*, 6506. <a href="https://creativecommons.org/licenses/by/4.0/">https://creativecommons.org/licenses/by/4.0/</a> No changes made.

#### The case for essential oils

Eucalyptus and ginger EOs have the most compelling data to date for beneficial effects on the immune system.

Peterfalvi, A.; Miko, E.; Nagy, T.; Reger, B.; Simon, D.; Miseta, A.; Czéh, B.; Szereday, L. Much More Than a Pleasant Scent: A Review on Essential Oils Supporting the Immune System. *Molecules* **2019**, *24*, 4530.



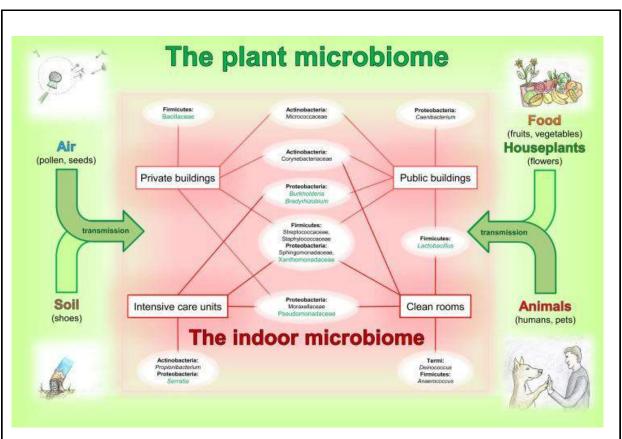


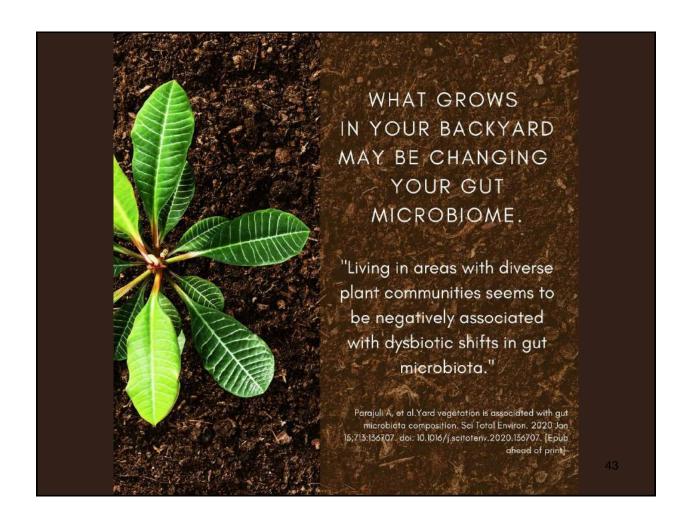
Image Credit: Berg G, Mahnert A, Moissl-Eichinger C. Beneficial effects of plant-associated microbes on indoor microbiomes and human health? Front Microbiol. 2014;5:15. Published 2014 Jan 29. doi:10.3389/fmicb.2014.00015

# Yard vegetation is associated with gut microbiota composition

Shrubs and flowering plants are associated with a healthier gut microbiota composition

The relative abundance of *Faecalibacterium* was high and *Clostridium* was low

Parajuli A, Hui N, Puhakka R, et al. Yard vegetation is associated with gut microbiota composition. Sci Total Environ. 2020;713:136707. doi:10.1016/j.scitotenv.2020.136707



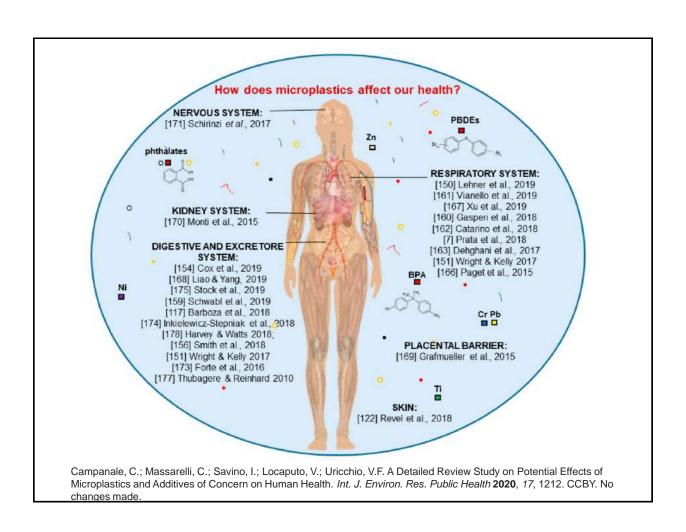
# Nature, Immunity, and Spirituality

Being in nature, such as with 'forest bathing' seems to have an effect on a person's spirituality and sense of well-being.

Hansen MM, Jones R. The Interrelationship of Shinrin-Yoku and Spirituality: A Scoping Review. J Altern Complement Med. 2020 Dec;26(12):1093-1104. doi: 10.1089/acm.2020.0193. Epub 2020 Sep 15. PMID: 32931299.

### "Who knows? Plastic pollution may be the next world pandemic."

Fadare OO, Okoffo ED. Covid-19 face masks: A potential source of microplastic fibers in the environment [published online ahead of print, 2020 Jun 16]. *Sci Total Environ.* 2020;737:140279. doi:10.1016/j.scitotenv.2020.140279





Campanale, C.; Massarelli, C.; Savino, I.; Locaputo, V.; Uricchio, V.F. A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health. *Int. J. Environ. Res. Public Health* **2020**, *17*, 1212. CCBY. No changes made.

### **Nature inside**

- Plant-based eating
- Modulating herbs

The way to get back to nature is to be more like a plant.

Surround yourself with them. Eat them.



### What makes plants protective

- They are 'jack/jill of all trades' they have pleiotropic effects.
- They modulate cellular response.
- They help us adapt to our environment through several mechanisms (e.g., microorganisms).
- The can upregulate endogenous defense systems (Nrf2, MRE, glutathione, etc.).
- They are major dietary sources of:
  - Fibers
  - Micronutrients
  - Phytonutrients

Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. J Nutr Metab. 2015;2015:760689. doi: 10.1155/2015/760689. Epub 2015 Jun 16. PMID: 26167297; PMCID: PMC4488002.

# Plants can heal, plants can be problematic:

# We need to take a personalized approach

Petroski, W.; Minich, D.M. Is There Such a Thing as "Anti-Nutrients"? A Narrative Review of Perceived Problematic Plant Compounds. *Nutrients* **2020**, *12*, 2929.



National 2020, 12: 2029 doi:10.1000/waT2102929

#### What about 'anti-nutrients'?

- Lectins
- Oxalates
- Phytates
- Tannins
- Phytoestrogens
- Goitrogens
- Sulfur?

Antibodies to lectins found in blood of 8-15% of blood samples. These undigested lectins may be problematic in some individuals with autoimmunity.

Vojdani A, Afar D, Vojdani E. Reaction of Lectin-Specific Antibody with Human Tissue: Possible Contributions to Autoimmunity. *J Immunol Res.* 2020;2020:1438957. Published 2020 Feb 11. doi:10.1155/2020/1438957.

Most traditional preparation methods, including cooking, boiling, soaking, fermenting, roasting, milling, and sprouting have been shown to reduce the activities of lectins, oxalates, phytates, tannins, and goitrogens.

### Functional Medicine for Healthy Immunity through Food:

The common denominator is plants

- Eat plenty of fruits and vegetables; 9-13 servings daily
- Consume dietary fiber, 28-35 grams daily
- Eat fermented vegetables or other probioticcontaining foods
- Reduce or avoid immune offenders like sugar, salt



## Overall Therapeutic Intervention: Building a Foundation Based in Plants

- Color
- Creativity
- Variety

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### The Science of the "Rainbow" of Foods



Hindard Journal of Nationan and Metabolism Volume 2018, Article ID 2225076, 19 page https://doi.org/10.1555/2019/22.25878



#### Review Article

A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow"

#### Deanna M. Minich (51.2

Deanna M. Minich 5

Correspondence should be addressed to Dunna M. Mirich, dramaminichithermalicien

Received 27 September 2018, Revised 27 March 2019; Accepted 17 April 2019; Published 2 Sone 2019

Academic Editor: Stat Kabow

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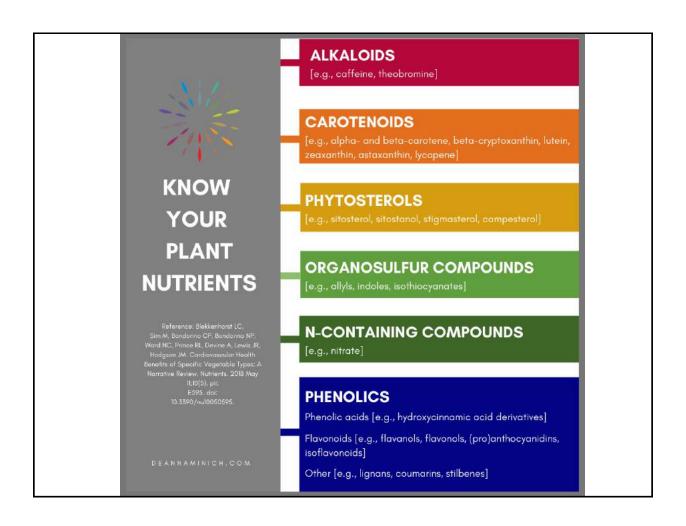
Deanna M. Minich, "A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow"," Journal of Nutrition and Metabolism, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.

# **Colors of Food Associated with Antioxidant Level**

Red, blue, purple foods shown to be highest in total antioxidant capacity

Cömert ED, Mogol BA, Gökmen V. Relationship between color and antioxidant capacity of fruits and vegetables. Curr Res Food Sci. 2019;2:1-10. Published 2019 Nov 21. doi:10.1016/j.crfs.2019.11.001

\*\*we also know that blue-purple foods are most rare and not eaten by most people on a daily basis



### "Color Density Index":

#### Presence of more than one phytonutrient

- Carrots
- Grapefruit
- Mango
- Papaya
- Red cabbage
- Rutabaga
- Tomatoes
- Watermelon

- Lycopene (red)
- Beta-carotene (orange)
- Lutein/zeaxanthin (yellow)
- Folates (green)
- Flavonoids (blue-purple)

Deanna M. Minich, "A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow"," Journal of Nutrition and Metabolism, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.





### Overall Therapeutic Intervention: Building a Foundation Based in Plants

- Color
- Creativity
- Variety

# Enhanced creativity is associated with fruit and vegetable intake.

Conner TS, Brookie KL, Richardson AC, Polak MA. On carrots and curiosity: eating fruit and vegetables is associated with greater flourishing in daily life. Br J Health Psychol. 2015;20(2):413-427. doi:10.1111/bjhp.12113.

# Creative activities are therapeutic for the immune system due to their effects on mental health.

Leckey J. The therapeutic effectiveness of creative activities on mental well-being: a systematic review of the literature. J Psychiatr Ment Health Nurs. 2011;18(6):501-509. doi:10.1111/j.1365-2850.2011.01693.x



### Overall Therapeutic Intervention: Building a Foundation Based in Plants

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#### **Gut microbiome diversity & food:**

A healthy gastrointestinal microbiome is dependent on dietary diversity

"The more diverse the diet, the more diverse the microbiome and the more adaptable it will be to perturbations. Unfortunately, dietary diversity has been lost during the past 50 years and dietary choices that exclude food products from animals or plants will narrow the GI microbiome further."

Heiman ML, Greenway FL. A healthy gastrointestinal microbiome is dependent on dietary diversity. Mol Metab. 2016 Mar 5;5(5):317-320. doi: 10.1016/j.molmet.2016.02.005. eCollection 2016 May.

### **Food Diversity & Immune Resilience:**

Greater diversity, better immune outcomes

- Decreased food allergy
- Maternal diet altering child outcomes for risk of allergic or autoimmune disease

Venter C, Maslin K, Holloway JW, et al. Different Measures of Diet Diversity During Infancy and the Association with Childhood Food Allergy in a UK Birth Cohort Study. J Allergy Clin Immunol Pract. 2020;8(6):2017-2026. doi:10.1016/j.jaip.2020.01.029. Garcia-Larsen V, Ierodiakonou D, Jarrold K, et al. Diet during pregnancy and infancy and risk of allergic or autoimmune disease: A systematic review and meta-analysis. PLoS Med. 2018;15(2):e1002507. Published 2018 Feb 28. doi:10.1371/journal.pmed.1002507

### **Clinical Tool: Variety Tracker**



"Increasing the diversity of brightly-coloured plant foods, even in small amounts, can have a dramatic effect on SCFA production."



Toribio-Mateas M. Harnessing the Power of Microbiome Assessment Tools as Part of Neuroprotective Nutrition and Lifestyle Medicine Interventions. Microorganisms. 2018 Apr 25;6(2):35. doi: 10.3390/microorganisms6020035. PMID: 29693607; PMCID: PMC6027349.

# From Foundation to Specifics: Therapeutic Phytonutrients

### The Science and the Clinical Translation of Immune Mechanisms

#### THE SCIENCE

#### Borders

- Brush border membranes (gut)
- · Gut microbiome
- Mucin layer

#### Inflammation

- · Oxidative stress/cytokine storm
- Antioxidants

#### Immune Dysregulation

- Toxins
- Endocrine disruption
- Chronic stress

#### THE CLINICAL TRANSLATION

- Digestive tract (oral)
- · Respiratory tract
- Skin
- Nasal and ear passages
  - Pain
- Inflammation
- Fatigue
- Autoimmune dysregulation
- Comorbidities

### The Yin and Yang of Immunity

OVERACTIVE	DEPRESSED
<ul> <li>High WBC</li> <li>High inflammatory markers/cytokines</li> <li>May have upregulated sympathetic stress HPA response</li> <li>Active inflammation/inflammaging</li> <li>Metabolic dysfunction (e.g., high cortisol, insulin, glucose)</li> <li>Sleeps poorly; may have sleep apnea</li> </ul>	<ul> <li>Low WBC</li> <li>Unable to mount a response to infection</li> <li>Easily falls ill</li> <li>Immunocompromised due to chronic conditions (e.g., cancer) or medications</li> <li>Sex hormone alterations</li> <li>Low cholesterol</li> <li>High fatigue</li> <li>Increased need for sleep</li> </ul>

# The Borders and Boundaries: Therapeutic Phytonutrients

```
Leaky gut
Leaky brain
Leaky skin
Leaky heart
Leaky membranes
Leaky mitochondria
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We have an epidemic of 'leakiness'.

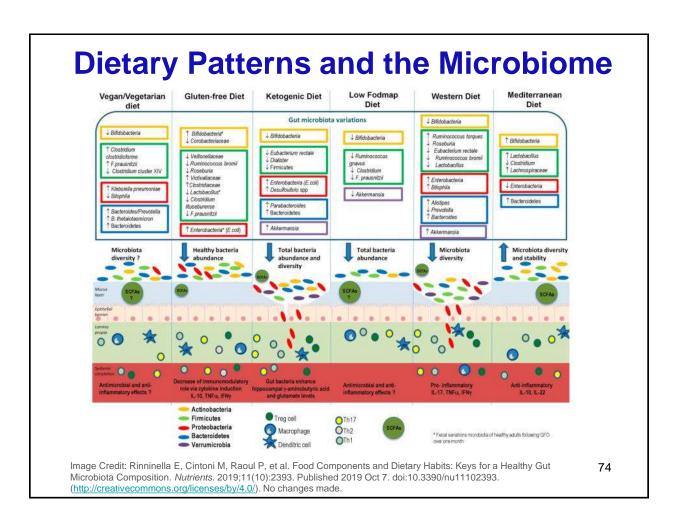


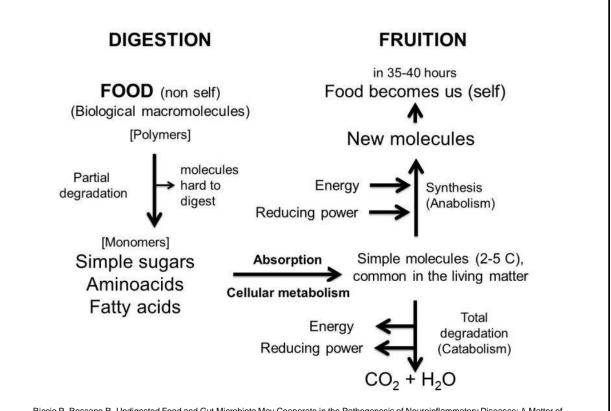
# The Gut Microbiome:

### **Functional Roles in Health**

- · Epithelial cell growth and development
- · Preventing the entry of pathogens:
  - Integrity of the brush border membrane
  - Production of mucin layer (eugenol) and anti-microbial peptides
  - Secretory IgA protects commensal bacteria
- Anti-inflammatory activities and cytokine balance
- Immune system regulation
- Digestion of food
- Mood, memory
- Production of vitamins (B12, K)
- · Biotransformation of heavy metals and other toxicants
- Conversion of primary bile acids into secondary bile acids (helps with shaping the milieu)

Reference: Dupont HL, Jiang ZD, Dupont AW, Utay NS. THE INTESTINAL MICROBIOME IN HUMAN HEALTH AND DISEASE. *Trans Am Clin Climatol Assoc.* 2020;131:178-197. Altveş S, Yildiz HK, Vural HC. Interaction of the microbiota with the human body in health and diseases. *Biosci Microbiota Food Health.* 2020;39(2):23-32. doi:10.12938/bmfth.19-023. Hills RD Jr, Pontefract BA, Mishcon HR, Black CA, Sutton SC, Theberge CR. Gut Microbiome: Profound Implications for Diet and Disease. *Nutrients.* 2019;11(7):1613. Published 2019 Jul 16. doi:10.3390/nu11071613; Wlodarska M, Willing BP, Bravo DM, Finlay 73 BB. Phytonutrient diet supplementation promotes beneficial Clostridia species and intestinal mucus secretion resulting in protection against enteric infection. *Sci Rep.* 2015;5:9253. Published 2015 Mar 19. doi:10.1038/srep09253





Riccio P, Rossano R. Undigested Food and Gut Microbiota May Cooperate in the Pathogenesis of Neuroinflammatory Diseases: A Matter of Barriers and a Proposal on the Origin of Organ Specificity. *Nutrients*. 2019;11(11):2714. Published 2019 Nov 9. doi:10.3390/nu11112714. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/). Full-article link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6893834/

# **Food Allergies**

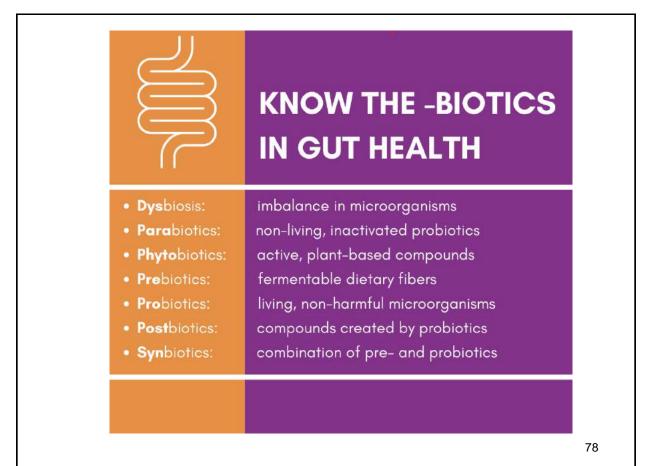
- "Hygiene Hypothesis"\*
- Factors associated with less food allergies:
  - Growing up in a large family
  - Being raised on a farm that practices non-industrialized agricultural methods
  - Earlier introduction of solid foods as an infant\*\*
  - Having pets
  - A healthy microbiome

Nance CL, Deniskin R, Diaz VC, Paul M, Anvari S, Anagnostou A. The Role of the Microbiome in Food Allergy: A Review. Children (Basel). 2020;7(6):50. Published 2020 May 26. doi:10.3390/children7060050; \*Strachan DP. Hay fever, hygiene, and household size. BMJ. 1989;299(6710):1259-1260. doi:10.1136/bmj.299.6710.1259. \*Hicke-Roberts A, Wennergren G, Hesselmar B. Late introduction of solids into infants' diets may increase the risk of food allergy development. BMC Pediatr. 2020;20(1):273. Published 2020 Jun 3. doi:10.1186/s12887-020-02158-x

# Select Nutrients & Intestinal Permeability\*

Increase Permeability	Decrease Permeability
<ul><li>Zinc depletion</li><li>Ethanol</li><li>Acetaldehyde</li></ul>	<ul> <li>Glutamine</li> <li>Tryptophan</li> <li>Vitamin A (retinol)</li> <li>Vitamin D</li> <li>Quercetin</li> <li>Kaempferol</li> <li>Genistein</li> <li>EGCG</li> <li>Curcumin</li> <li>EPA/DHA</li> <li>SCFAs: Acetic and propionic acids</li> </ul>

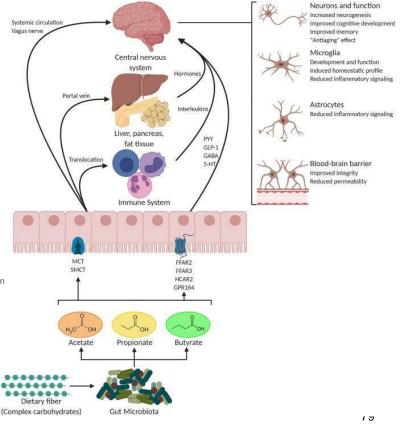
<sup>\*</sup>As tested primarily in cell models; Reference: De Santis S, Cavalcanti E, Mastronardi M, Jirillo E, Chieppa M. Nutritional Keys for Intestinal Barrier Modulation. *Front Immunol.* 2015;6:612. Published 2015 Dec 7. doi:10.3389/fimmu.2015.00612

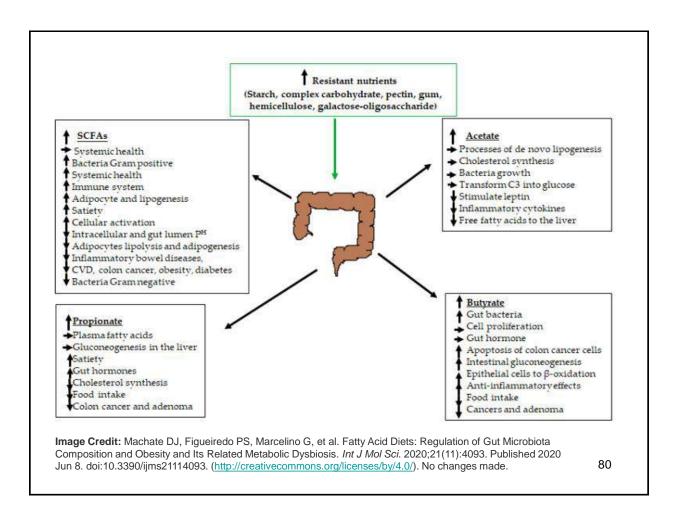




Silva YP, Bernardi A, Frozza RL. The Role of Short-Chain Fatty Acids From Gut Microbiota in Gut-Brain Communication. Front Endocrinol (Lausanne). 2020;11:25. Published 2020 Jan 31. doi:10.3389/fendo.2020.00025.

(http://creativecommons.org/licenses/by/4.0/). No changes made.





### **Elimination Diet**

- Removes top allergens:
  - Common foods and beverages containing corn, soy, wheat/gluten, eggs, sugar, caffeine, alcohol, shellfish, and peanuts, are omitted
  - 10, 21, 28 days
- Some additional modifications include removal of the following:
  - Nightshades, nuts, alcohol, caffeine, pork, citrus, histamines, oxalates, salicylates
- Goal is to remove these foods short-term and then reintroduce them sequentially to observe presence or absence of symptoms
- Reintroduction is to be personalized to the patient.

 $MacIntosh\ A,\ Ball\ K.\ The\ effects\ of\ a\ short\ program\ of\ detoxification\ in\ disease-free\ individuals.\ Altern\ Ther\ Health\ Med.\ 2000\ Jul; 6(4):70-6.$ 

# **Dietary Micro-Rotation**

The pulsing of small amounts of a variety of whole foods in one's daily diet rather than long-term omission of entire food categories for the purpose of building immune resilience

# Inflammation & Antioxidants: Therapeutic Phytonutrients

δS

### The Role of Antioxidants

- Internal network of antioxidants
  - Vitamin E (food sources: wheat germ, seed oils, nuts, seeds, greens)
  - Vitamin C (food sources: citrus fruits, cherries, berries, papaya, broccoli, kiwi)
  - Polyphenols (e.g., teas, fruits such as apples and berries, vegetables)
  - Carotenoids (e.g., sweet potato, bell peppers, yam, carrots, tomatoes)
- Internal system of antioxidant defense enzymes
  - Superoxide dismutase (SOD)
  - Catalase
  - Glutathione peroxidase

### External intake of antioxidants

- Be aware of double-sided nature with high amounts of isolated agents as they can act as pro-oxidants

Iddir M, Brito A, Dingeo G, et al. Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis. *Nutrients*. 2020;12(6):1562. Published 2020 May 27. doi:10.3390/nu12061562; Smith RE. The Effects of Dietary Supplements that Overactivate the Nrf2/ARE System. Curr Med Chem. 2020;27(13):2077-2094. doi: 10.2174/0929867326666190517113533. PMID: 31099320.

# **Anti-inflammatory Nutrients:**

Inflammation, Immunity, Insulin

- Omega-3 fatty acids
- Antioxidant vitamins and minerals
  - Vitamins C & E
  - Selenium, zinc (e.g., nuts, fish, meats, eggs, grains)
- Hormone-like nutrients
  - Vitamin D (e.g., fish, seafood, eggs, mushrooms)
  - Vitamin K (e.g., leafy greens, fermented foods)
- Quercetin (e.g., apples, onions)
- Epigallocatechin gallate (from green tea)
- Turmeric/Curcumin

# Nutrients for the Immune System: Spice it up!

- Based on data from 163 countries, there was a correlation between number of grams of spice consumed and number of COVID cases.
- Lower spice consumption associated with greater COVID cases.
- Examples of some spices to include in one's kitchen:
  - Cloves
  - Turmeric
  - Ginger
  - Oregano
  - Cinnamon

Immunity-Boosting Spices and the Novel Coronavirus. Yehya Elsayed and Naveed Ahmed Khan. ACS Chemical Neuroscience 2020 11 (12), 1696-1698. DOI: 10.1021/acschemneuro.0c00239

# Ayurvedic practices and COVID-19: A long tradition of using plants

- The Indian Government has promoted Ayurvedic practices to its citizens during the COVID-19 pandemic.
- · Suggested Ayurvedic practices:
  - Drinking warm water throughout the day
  - Using spices
  - Doing yoga
  - · Drinking golden milk
  - · Oil pulling therapy
  - Nasal steam inhalation with mint leaves or caraway seeds
  - Using clove powder mixed with honey or sugar for throat irritation or cough

Rajkumar RP. Ayurveda and COVID-19: Where psychoneuroimmunology and the meaning response meet [published online ahead of print, 2020 Apr 22]. Brain Behav Immun. 2020;50889-1591(20)30637-1. doi:10.1016/j.bbi.2020.04.056



# **Nutrients for the Immune System:**

### Spices cool down inflammatory pathways

- Various parts of the plant or flower impart specific activities: root, leaf, bud, seed, bark, berry, stigma of a plant or flower
- Spices add flavor to food, and there may be other health effects connected to taste receptors that we do not fully understand yet.
- Commonly used spices used in cooking with high anti-inflammatory activity: black pepper, cardamom, cinnamon, clove, cumin, fenugreek, fennel, garlic, ginger, onion, rosemary, turmeric
- A combination of spices can address multiple targets:
  - Transcription factors such as NF-κB and STAT3
  - Inflammatory enzymes such as cyclooxygenase-2 (COX-2), matrix metalloproteinase-9 (MMP-9)
  - Inflammatory cytokines such as tumor necrosis factor alpha (TNF- $\alpha$ ), interleukins (IL) such as IL-1, -6, -8

Kunnumakkara AB, Sailo BL, Banik K, et al. Chronic diseases, inflammation, and spices: how are they linked?. *J Transl Med.* 2018;16(1):14. Published 2018 Jan 25. doi:10.1186/s12967-018-1381-2.

# Ways to get more spices into everyday eating

- · Add to smoothies
- Make tea first and add water to smoothies or add spice directly
- Combine finely chopped garlic and basil to extra virgin olive oil and lemon juice for a delicious and nutritious salad dressing
- Add fresh herbs such as cilantro, chives, basil or mint to salads or sandwiches
- Sprinkle spices such as cumin or fennel seeds in soups or salads
- Marinate lean meats in curry powder or curry pastes
- Sprinkle cinnamon and nutmeg over oatmeal or wholegrain toast for breakfast
- Add extra flavor to scrambled eggs with a handful of fresh parsley or chives
- Stew fruits with cinnamon and a vanilla pod
- Substitute tea by steeping lemongrass or mint in hot water
- · Add freshly grated garlic to mayonnaise for an easy aioli
- · Add fresh or dried herbs to your favorite pasta dish
- · Ghees, honeys, oils, salts, sprinkles

# Immune Dysregulation: Therapeutic Phytonutrients

an

# The intelligence of plants informing the intelligence of the immune system

- Certain plants have similar structures to catecholamines.
- These botanical adaptogens work on several stress-related cascades including reducing many stress and inflammatory genes.

Panossian, A.; Brendler, T. The Role of Adaptogens in Prophylaxis and Treatment of Viral Respiratory Infections. *Pharmaceuticals* **2020**, *13*, 236. <a href="https://creativecommons.org/licenses/by/4.0/">https://creativecommons.org/licenses/by/4.0/</a>. No changes made.

Decreased resistance and increased susceptibility to stressors/infections. Sub-optimal function of neuro-endocrine immune system. Low-grade chronic inflammation. Prevention:
Prophylactic
breatment with
Ginseng,
Elautherococcus,
Rhodiola, Schisandra,
Withania, melatonin
adaptogenic and
stress-protective

BASELINE HOMEOSTASIS

Enhanced range of adaptive homeostasis Optimal function of innate immune, antioxidant and xenobiotics detoxitying defensive systems



### Virus-dysregulated immune response

Robust virus replication Detayed IFN responce Innate immunity responce: macrophages, laukocytes and monocytes infiltration Suboptimal T-cell and

### Escalating inflammation

Pro-inflammatory cytokines and chemokins expression unregulated. "Oytokine storm." Severe Oxidative stress: ROS Enhanced epithelial and enotitisital apoptoels increased vascular leakage Impaired virus clearance

#### Pathogenic inflammation

Acute lung injury Acute respiratory distress syndrome Death

# VIRAL EXPOSURE

effect

Adjuvant therapy

Non-specific antiviral actions
on innate and adaptive
immunity

Inhibition of virus life cycle,

Inhibition of virus life cycle, RNA synthesis and replication by Ginseng, Rhodiola, Withenia, Glycyrrhiza.

### Inflammation: Adjuvent therapy

Inhibition of inflammatory cytokines expression by Andrographis, Ginseng, Eleutherococcus, Rhodiola, Schisandra, Withania, Glycymbiza Virus specific antiviral action by Andrographis, Ginseng, Eleutherococcus, Rhodiola,

# Schisandra, Glycyrrhiza. Recovery therapy:

Inhibition of oxidative stress-induced damage Normalized repair and recovery process Andrographis, Ginseng, Eleutherococcus, Rhodiola, Schisandra, Withania, Glycymhiza, melatonin.

#### Protective immune response to infection

Non-Robust virus replication
Early IFN responce
Innate immunity responce:
macrophages, leuknoytes and
monocytes infiltration
Optimal T-cell and
antibody responces

### Regulated inflammation

Pro-inflammatory cytokines and chemokins expression regulated Mild Oxidative stress: ROS Minimal epithelial and endothelial apaptosis Reduced vascular leakage Effective virus clearance

### Recovery

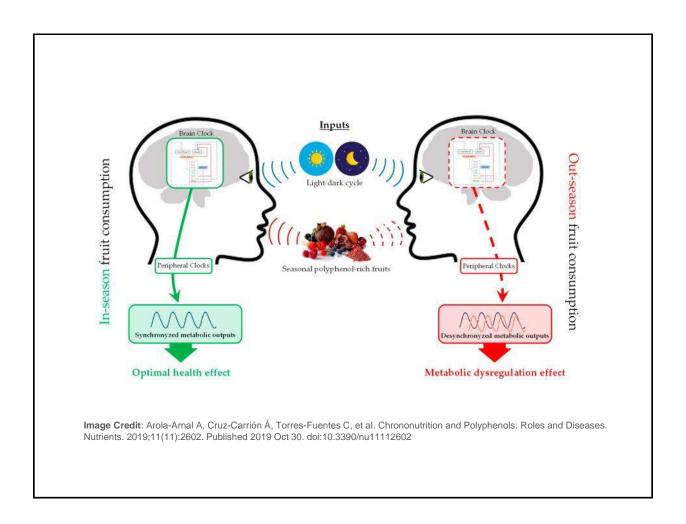
Protective immunity

Host survival

# Orange consumption out of season leads to adipose accumulation

- N=36 rats acclimated for 4 weeks to long-day or short-day photoperiods
- Three groups (n=6) from each period were given orange from the northern or southern hemispheres harvested in the same month or a control vehicle for 10 weeks
- The southern orange promoted a fat accumulation phenotype consumed during the short-day photoperiod.
- Out of ~39 phytochemicals analyzed, the northern and southern oranges statistically differed in 24 phytochemicals

Gibert-Ramos, A., Palacios-Jordan, H., Salvadó, M.J. et al. Consumption of out-of-season orange modulates fat accumulation, morphology and gene expression in the adipose tissue of Fischer 344 rats. Eur J Nutr 59, 621–631 (2020). https://doi.org/10.1007/s00394-019-01930-9



# **Dietary** neurotransmitters

**Table** recreated from: Briguglio M, Dell'Osso B, Panzica G, et al. (2018). Dietary neurotransmitters: A narrative review on current knowledge. *Nutrients*, *10*(5), 591. http://doi.org/10.3390/nu10050591. CC BY 4.0

Dietary Neurotransmitter	Foods and Botanicals
Acetylcholine	Aubergine, bitter orange, common bean, foxglove, mistletoe, mung bean, nettle, species, pea, radish, spinach, squash, wild strawberry.
Glutamate	Caviar, cheese, crackling, chips, dried cod, fermented beans, fish sauces, gravies, instant coffee powder, meats, miso, mushrooms, noodle dishes, oyster sauce, Parmesan cheese, ready-to-eat-meals, salami, savory snacks, seafood, seaweed soups, soy sauces, spinach, stews, tomato, tomato sauce.
GABA	Adzuki bean, barley, broccoli, buckwheat, chestnut, common bean, kale, lupin, maypop, mouse-ear hawkweed, oat, pea, pokeroot, potato, rice, shirtake, soya bean, spinach, St John's wort, sweet potato, tea, tomato, valerian, wheat, wild celery.
Dopamine	Aubergine, avocado, banana, common bean, apple, orange, pea, plantain, spinach, tomato, velvet bean.
Serotonin	Banana, chicory, Chinese cabbage, coffee powders, green coffee bean, green onion, hazelnut kiwi, lettuce, nettle, Griffonia simplicifolia, paprika, passion fruit, pawpaw, pepper, pineapple, plantain, plum, pomegranate, potato, spinach, strawberry, tomato, velvet bean, wild rice.
Histamine	Anchovy, beer, billfish, Champagne and Sherry, dandelion, fermented sausages, ham and other cured dry meat products, herring, ketchup, aged cheese, nettle, red, white and dessert wines, sardine, sauerkraut, Scomberesocidae (for example, sauries), Scombridae (for example, tuna, mackerel, and bonitos) soybean food products (for example, soy, tempeh, soy sauce, soya bean milk, doenjang, doufuru, and nattō), sweet or sour cream. UHT, pasteurized, and fresh milk, yoghurt.

### **Phytonutrients:**

### Goals and Guidelines

- Carotenoids
  - Sweet potato, bell peppers, yam, carrot, greens, tomatoes
- Catechins
  - Green tea, black tea, Oolong tea, berries, cocoa
- Curcumin
  - Turmeric root, turmeric powder
- Quercetin
  - Onions, apples, berries, broccoli, citrus fruits
- Resveratrol
  - Grapes, berries, nuts, peanuts

Reference: Iddir M, Brito A, Dingeo G, et al. Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis. *Nutrients*. 2020;12(6):1562. Published 2020 May 27. doi:10.3390/nu12061562

# **Nutrients for the Immune System:**

### Phytochemicals: Flavonoids

- Includes flavonols, flavones, flavanols, flavanones, anthocyanidins, proanthocyanidins, and isoflavones
- More than 6000 in nature; formed by plant in response to stress
- Commonly found in vegetables, seeds, fruit, and beverages, such as red wine and tea
- Flavonoid intake at 0.2 to 1.2 g/day
- Decreased upper respiratory tract infection incidence by 33% compared with control
- Lack of significant adverse effects
- Sick-day count reduced by 40%; mechanism unclear

Vaughan S Somerville, Andrea J Braakhuis, Will G Hopkins, Effect of Flavonoids on Upper Respiratory Tract Infections and Immune Function: A Systematic Review and Meta-Analysis, Advances in Nutrition, Volume 7, Issue 3, May 2016, Pages 488–497, <a href="https://doi.org/10.3945/an.115.010538">https://doi.org/10.3945/an.115.010538</a>; Russo M, Moccia S, Spagnuolo C, Tedesco I, Russo GL. Roles of flavonoids against coronavirus infection [published online ahead of print, 2020 Jul 28]. Chem Biol Interact. 2020;328:109211. doi:10.1016/j.cbi.2020.109211

# **Nutrients for the Immune System:**

### Quercetin

- · Well-known flavonoid with antiviral properties
- Common food sources: Onions, apples, berries, broccoli, citrus fruits
- May be synergistic with vitamin C, serves as an ionophore for Zn
- Functions:
  - Antioxidant
  - Anti-inflammatory
  - Immunoprotective effects
  - Antiviral through activity in inhibiting polymerases, proteases, reverse transcriptase, and binding viral capsid proteins

Budhwar S, Sethi K, Chakraborty M. A Rapid Advice Guideline for the Prevention of Novel Coronavirus Through Nutritional Intervention [published online ahead of print, 2020 Jun 23]. *Curr Nutr Rep.* 2020;1-10. doi:10.1007/s13668-020-00325-1

# **Nutrients for the Immune System:**Curcumin

- Anti-inflammatory, antioxidant, anti-cancer, and antidiabetic activity (shown in cell/animal studies)
- Can reduce IL-1, IL-6, IL-8, TNF-α
- Beneficial effects for infectious diseases
- Preclinical studies indicate it may be able to inhibit the cytokine storm
- Scavenges ROS
- Reduces injury to lung (e.g., edema as a result of inflammation)

Liu Z, Ying Y. The Inhibitory Effect of Curcumin on Virus-Induced Cytokine Storm and Its Potential Use in the Associated Severe Pneumonia. Front Cell Dev Biol. 2020;8:479. Published 2020 Jun 12. doi:10.3389/fcell.2020.00479

# **Nutrients for the Immune System:**

### Catechins from green tea

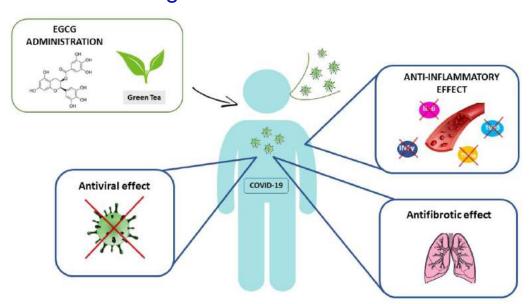
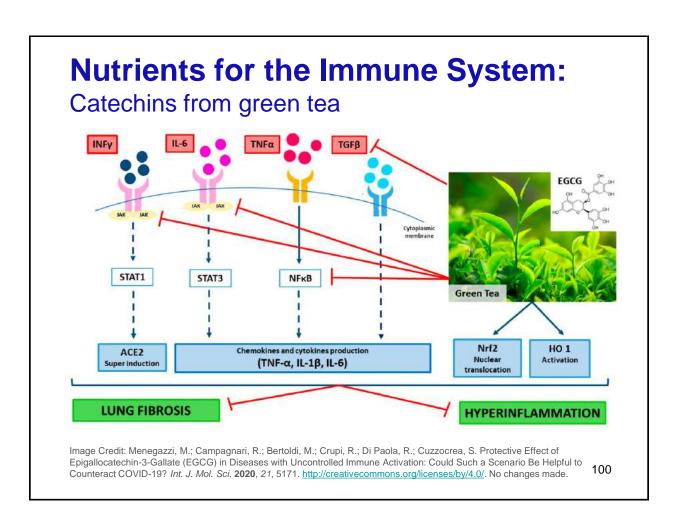


Image Credit: Menegazzi, M.; Campagnari, R.; Bertoldi, M.; Crupi, R.; Di Paola, R.; Cuzzocrea, S. Protective Effect of Epigallocatechin-3-Gallate (EGCG) in Diseases with Uncontrolled Immune Activation: Could Such a Scenario Be Helpful to Counteract COVID-19? Int. J. Mol. Sci. 2020, 21, 5171. http://creativecommons.org/licenses/by/4.0/. No changes made.



# **Summary**The Plant-Person Interface

- We are the sum of our environment.
- All three aspects of the immune system are assisting in the resilience of the individual.
- Food needs to be tailored to all three aspects of the immune system.
- Plants are the 'divining rod' to enable humans to better survive in their environments.
- Clinically, these principles are most important for reestablishing balance:
  - Color → Color and Nutrient Density
  - Creativity → Emotional-Mental Health and Quality of Life
  - Variety → Seasonality, Complexity, Spices, Whole Foods

### **Clinical Actions**

After participating in this presentation, clinicians should be better able to:

- Prescribe nature
- Assess color, nutrient density and variety in a client's daily eating for immune health
- Bring the role of stress, intention, and conscious awareness into therapeutic encounter discussions

### TEM Ś S SY 0 IMMUNE 0 Ĭ. 0 Ш H S ш ΗH ∞ S ш 2 Ы 0 1 O PRIN 0 Z RA V ш ш Z O EN 8 AIN

#### MACRONUTRIENTS FOR THE IMMUNE SYSTEM

#### Protein

- Adequate, quality protein at every meal
- · Foods high in cysteine for glutathione production (meats, fish cheese, yogurt, legumes, seeds, eggs)
- Foods high in glutamine for gut healing (meats, fish, eggs, legumes, a wide variety of vegetables)

### Foods high in lysine to balance arginine (meats, fish, cheese, eggs, legumes) Carbohydrates

- No added sugars or high-glycemic, processed foods (cakes, cookies, candy, refined products)
- · Foods high in fibers (from a variety of plant-based sources)
- · Fermented foods for their prebiotic and probiotic content (krauts, kefirs, miso, sourdough)

#### Fats & Oils

- Less high-heat cooking to damage oils; use water or steaming
- · Foods high in omega-3s (fish, seafood, nuts, seeds, greens)
- Variety of different fats (short-chain, medium-chain, long-chain)

#### VITAMINS FOR THE IMMUNE SYSTEM

#### Fat-Soluble

- Foods high in retinol, or preformed vitamin A (liver, fish, cheese, butter, eggs)
- Foods high in vitamin D (fish, seafood, eggs, mushrooms)
- Foods high in vitamin E (wheat germ, seed oils, nuts, seeds, greens)

### Water-Soluble

- Foods high in 8 vitamins (B1, B2, B3, B6, B9, B12) (whole grains, nuts, seeds, legumes, leafy greens, organ meats)
- · Foods high in vitamin C (citrus fruits, cherries, berries, papaya, broccoli, kiwifruit)

### MINERALS FOR THE IMMUNE SYSTEM

Copper Meats, seafood, seeds, nuts, potatoes, mushrooms, legumes, greens, dark chocolate

Iron Beef, organ meats, legumes, greens, dark chocolate

Magnesium Greens, legumes, nuts, seeds

Selenium Brazil nuts, fish, seafood, meats, eggs, mushrooms, whole grains
Zinc Seafood, beef, lamb, turkey, eggs, nuts, seeds, legumes, yogurt

### PHYTONUTRIENTS FOR THE IMMUNE SYSTEM

Carotenoids Sweet potato, bell peppers, yam, carrot, greens, tomatoes

Catechins Green tea, black tea, Oolong tea, berries, cocoa Curcumin Turmeric root, turmeric powder

Quercetin Onions, apples, berries, broccoli, citrus fruits

Resveratrol Grapes, berries, nuts, peanuts

# **Immune Nutrition in Motion**

Pomegranate arils, sauerkraut, sweet potato with turmeric, Belgian endive, purple daikon radish, wild salmon with garlic, microgreens, blackberries, cauliflower rice





# Calling forth the healer within

"Everyone has a physician inside him or her; we just have to help it in its work. The natural healing force within each one of us is the greatest force in getting well."

- Hippocrates

