The Immune Response: Therapeutic Application of Micronutrients and Phytonutrients

PATHOGEN



Physical/chemical barriers

[i.e. skin, mucous membranes, gastrointestinal (GI) tract]

Therapeutic goals:

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Support healthy mucous membranes, encourage microbiome diversity, support membrane integrity

Inflammatory response

- Inflammatory mediators (i.e. bradykinins, prostaglandins) trigger cardinal signs: swelling, heat, redness, pain
- Response supports neutrophil chemotaxis, fever, & upregulation of costimulatory molecules that encourage activation of adaptive response

Therapeutic goals:

Modulate NLRP3 inflammasome activation and support resolution

Cellular response

- Pathogens are identified, killed, and digested by phagocytes (via toll-like receptors)
- Natural killer (NK) cells are cytotoxic to pathogens
- Process produces reactive oxygen species (ROS) and nitric oxide (NO) in the oxidative (respiratory) burst

Therapeutic goals:

Contain/modulat oxidative burst and support innate immune-cell proliferation and function

Biochemical response

- \bullet $\;$ Complementary system is activated and generates enzyme C3 convertase
- Contributes primarily to bacterial immunity

Antigen presentation

- Dendritic cells present antigens to naïve T helper (Th) cells via MHC-II complexes
- Th cells then differentiate into Th1 or Th2 subtypes

Therapeutic goals:

Support innate and adaptive immune system functions

Humoral immunity

 Th2 cells activate B cells via MHC II, which then mature into plasma cells and make antibodies

Therapeutic goals:

Support the production and function of antibodies

Cell-mediated immunity

ADAPTIVE IMMUNE RESPONSE

NNATE IMMUNE RESPONSE

- Th1 cells activate antigen-presenting cells (APCs) and cytotoxic T cell response via MHC I
- After infection has cleared, activated cytotoxic T cells remain as dormant memory T cells

Therapeutic goals:

Support immunologic functions of Th1 cells

Gombart AF et al. A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. *Nutrients*. 2020;12(1):236.

NLRP3 = NLR Family Pyrin Domain Containing 3

MHC I = major histocompatibility class I

MHC II = major histocompatibility class II





Therapeutic Goal	Suggested Nutritional Bioactive ¹⁻⁹
Prevention/maintenance Support pillars of health (nutrition, stress management, sleep, movement) with lifestyle strategies and essential nutrients to promote immune health.	Essential bioactives to support immune health in the prevention and management of acute infections include: • Vitamins A, C, D Note: Therapeutic doses of vitamins A, C, and D as well as minerals, selenium and zinc, may be achieved from a good-quality multivitamin.
Support membrane integrity Membranes (i.e. skin, mucous membranes, GI tract) of the external and internal surfaces of the body are the immune system's first lines of defense. Providing essential and targeted nutrients may help optimize barrier structure and function.	 N-acetyl cysteine (NAC) Quercetin Vitamins A, C, D Zinc
Promote microbiome health A diverse microbiome may enhance and support a balanced immune response.	FiberProbiotics
Modulate inflammatory response An exaggerated inflammatory response may contribute to a dysregulated immune response. Targeted nutrients may help modulate the NLRP3 inflammasome activation, enhance repair mechanisms, and support resolution.	 Curcumin Epigallocatechin gallate (EGCG) Melatonin NAC Omega-3 fatty acids Palmitoylethanolamide (PEA) Quercetin Specialized pro-resolving mediators (SPMs) Vitamin D
Reduce oxidative stress Nutrients may support antioxidant capacity, contributing to a reduced oxidative burst and support for innate immune-cell proliferation and function.	 EGCG Medicinal mushrooms NAC PEA Vitamins A, C
Support innate immune cells Provide supportive nutrients for the proliferation and function of innate immune cells (i.e. NK cells, macrophages, neutrophils).	 Andrographis paniculata Vitamins A, C, D Medicinal mushrooms
Support humoral immunity Consider nutrients that support the production and function of antibodies.	Vitamins A, C, DZinc
Support cell-mediated immunity Enhance the immunologic functions of Th1 cells and provide antimicrobial action with targeted nutrients.	 Berberine Echinacea purpurea Perilla frutescens Selenium Thymus vulgaris Vitamins A, C, D Zinc

- Gombart AF et al. A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients. 2020;12(1):236.
 Yanuck SF et al. Evidence supporting a phased immuno-physiological approach to COVID-19 from prevention through recovery. Integ Med J.
- 3. Tozsér J et al. Natural compounds as regulators of NLRP3 inflammasome-mediated IL-1B production. *Mediators Inflamm.* 2016;2016:5460302.

 4. Haghighatdoost F et al. The effect of green tea on inflammatory mediators: A systematic review and meta-analysis of randomized clinical trials. Phytother Res. 2019;33(9):2274-2287.
- 5. Anand David AV et al. Overviews of biological importance of quercetin: a bioactive flavonoid. Pharmacogn Rev. 2016;10:84-89.

- 6. Guo H et al. Inflammasomes: mechanism of action, role in disease, and therapeutics. Nat Med. 2015;21:677-687.
- $7. \quad Lopategi\ A\ et\ al.\ Frontline\ science: Specialized\ proresolving\ lipid\ mediators\ inhibit\ the\ priming\ and\ activation\ of\ the\ macrophage\ NLRP3$ inflammasome. J Leukoc Biol. 2019;105(1):25-36.
- 8. Serhan CN et al. Resolvins in inflammation: emergence of the pro-resolving superfamily of mediators. *J Clin Investigation*. 2018;128(7):2657-2669.
 9. Keppel Hesselink JM et al. Palmitoylethanolamide: A natural body-own anti-inflammatory agent, effective and safe against influenza and common