

An Integrative Approach to Treating Viral Induced Autoimmune Disease

Lindsay Ledwich DO

Rheumatologist

Heidi Weinhold ND

Doctor of Naturopathic Medicine



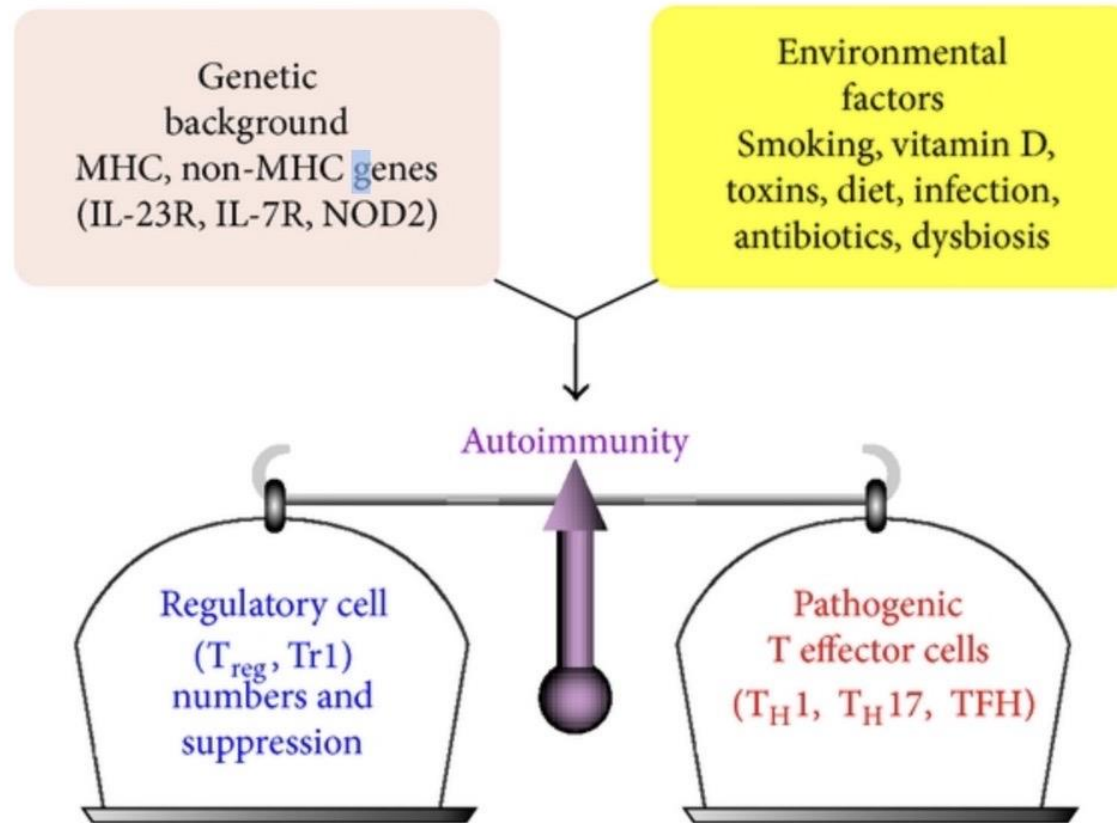
- Introduction: How Viruses Stimulate Immune Responses
- Section 1: How Diet, lifestyle, AND Hormones Affect Health
- Section 2: Botanicals
- Section 3: Homeopathy
- Section 4: Supplements
- Conclusions



1. How Viruses Stimulate Immune Response

- A balanced immune system distinguishes between self and foreign proteins

Nat Rev Immunology, vol 9, pp. 246-228, Antiviral immune responses: triggers of or triggered by autoimmunity?”
“2009. C. Munz, J. D Lunemann, M.T. Getta et al.



Autoimmune Diseases. "A Potential Link between Environmental Triggers and Autoimmunity".
2014. Aristo Vojdani



What Happens when a Virus Invades

- Detection of foreign viral proteins = activation of pro-inflammatory cytokines (ex: IL-1, IL-12, TGF- β , and IL-23)

Nature Medicine. "Dysregulation of immune homeostasis in autoimmune diseases". 2012. V.K. Kuchroo et al.
<https://www.dreamstime.com/royalty-free-stock-photos-alarm-bell-over-white-image20573628>

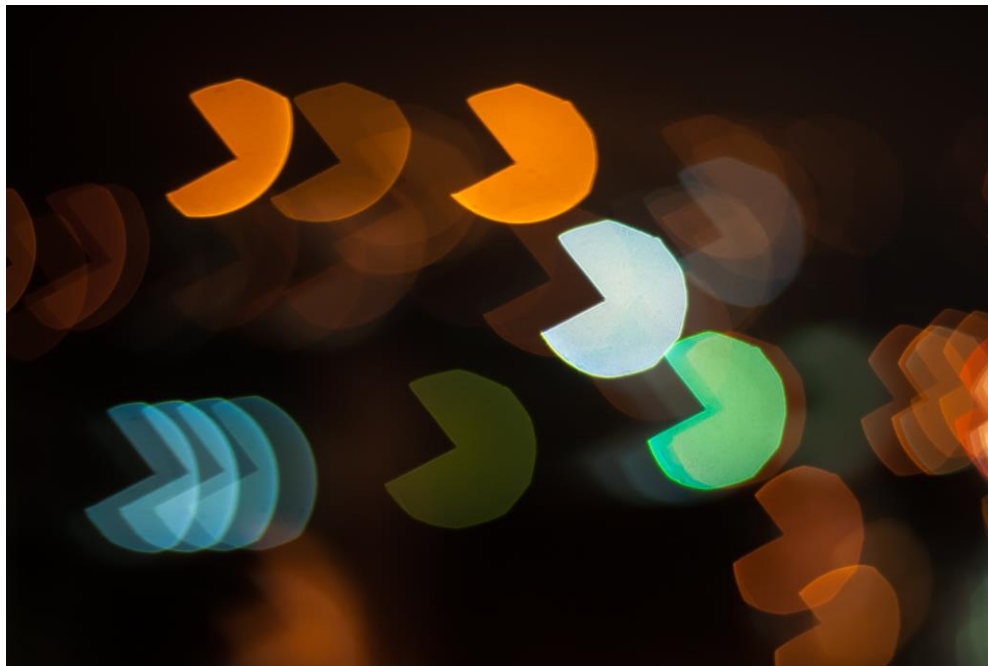
- First line defenders attack: T cells, NK cells.



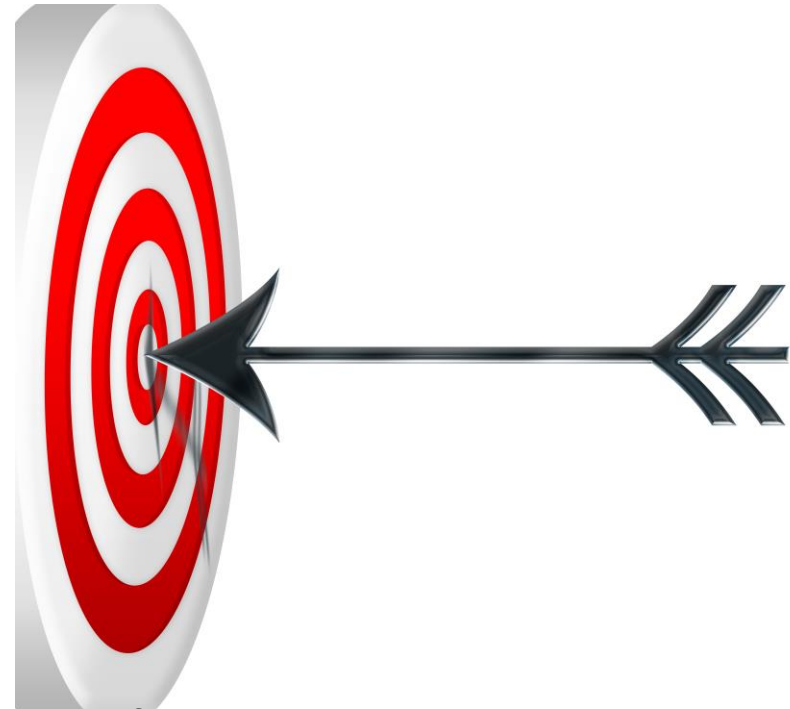
Nature Medicine. “Dysregulation of immune homeostasis in autoimmune diseases”. 2012. V.K. Kuchroo et al.
<https://www.dreamstime.com/stock-photo-brown-army-man-toy-standing-white-background-image50852893>



- Macrophages and dendritic cells engulf and destroy foreign invaders and present to T cells



- Activated T cells migrate to target tissues to promote more focused inflammation



Journal of experimental medicine. "Follicular helper T cells are required for systemic autoimmunity".

2009. Lintermann, M.A, Rigby, R.J., Wong, R. K., et al.

<https://www.dreamstime.com/cool-single-swat-special-ops-cat-weapon-ai-generated-illustration-cool-single-swat-special-ops-cat-weapon-ai-generated-image268781057>

<https://www.dreamstime.com/stock-images-darts-target-image2290294>



- Mast cells and eosinophils with histamine release



Journal of experimental medicine. "Follicular helper T cells are required for systemic autoimmunity". 2009.
Lintermann, M.A, Rigby, R.J., Wong, R. K., et al.
<https://www.dreamstime.com/stock-images-highway-southern-alberta-image10579684>



- Cytokine release that stimulate other cells



Journal of experimental medicine. "Follicular helper T cells are required for systemic autoimmunity". 2009.

Lintermann, M.A, Rigby, R.J., Wong, R. K., et al.

<https://www.dreamstime.com/stock-photography-domino-effect-image1414642>

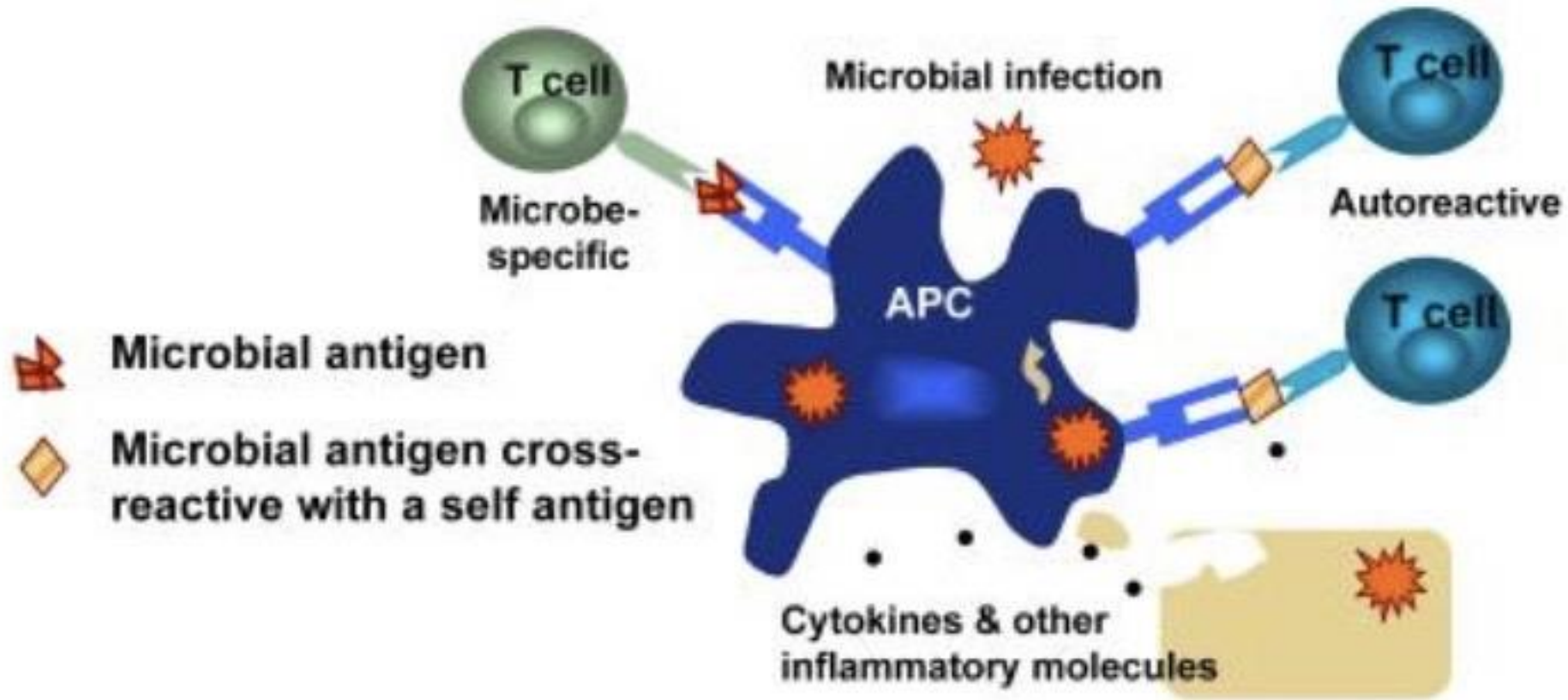


- What could possibly go wrong?

A Few Mechanisms by Which Viruses Cause Autoimmunity

- Molecular mimicry
- Bystander activation
- Epitope spreading
- Proliferation of B cells

A. Molecular mimicry



Nat Rev Immunology. “Antiviral immune responses: triggers of or triggered by autoimmunity?”
“2009. C. Munz, J. D Lunemann, M.T. Getta et al.



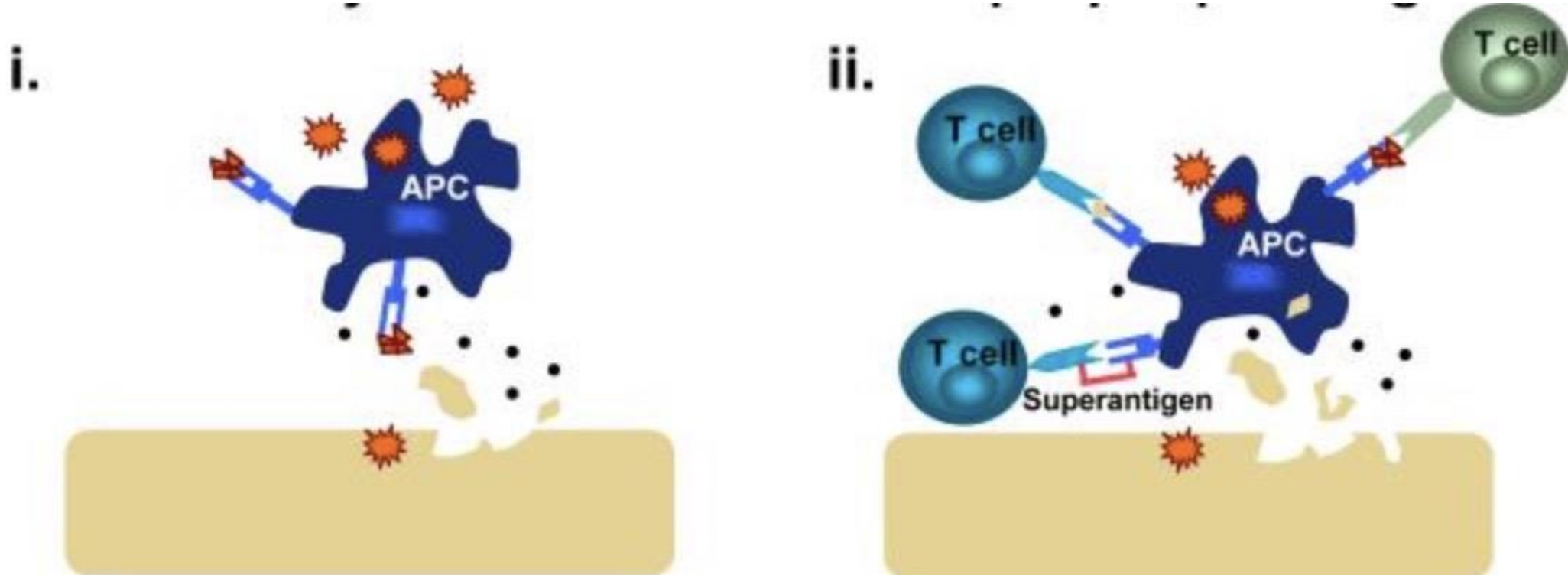
- **Coxsackie virus** can cause myocarditis, may play a role in diabetes
- **HSV** can cause stromal keratitis

Journal of Clinical and Cellular Immunology. "Autoimmune disorders: an overview of molecular and cellular basis in today's perspective." 2012.
FS. Ray, N. Sonthalia, S. Kundu et al

J Virol. Herpes simplex virus-induced keratitis: evaluation of the role of molecular mimicry in lesion pathogenesis. 2001. Deshpande SP, et al.;75:3077–88.

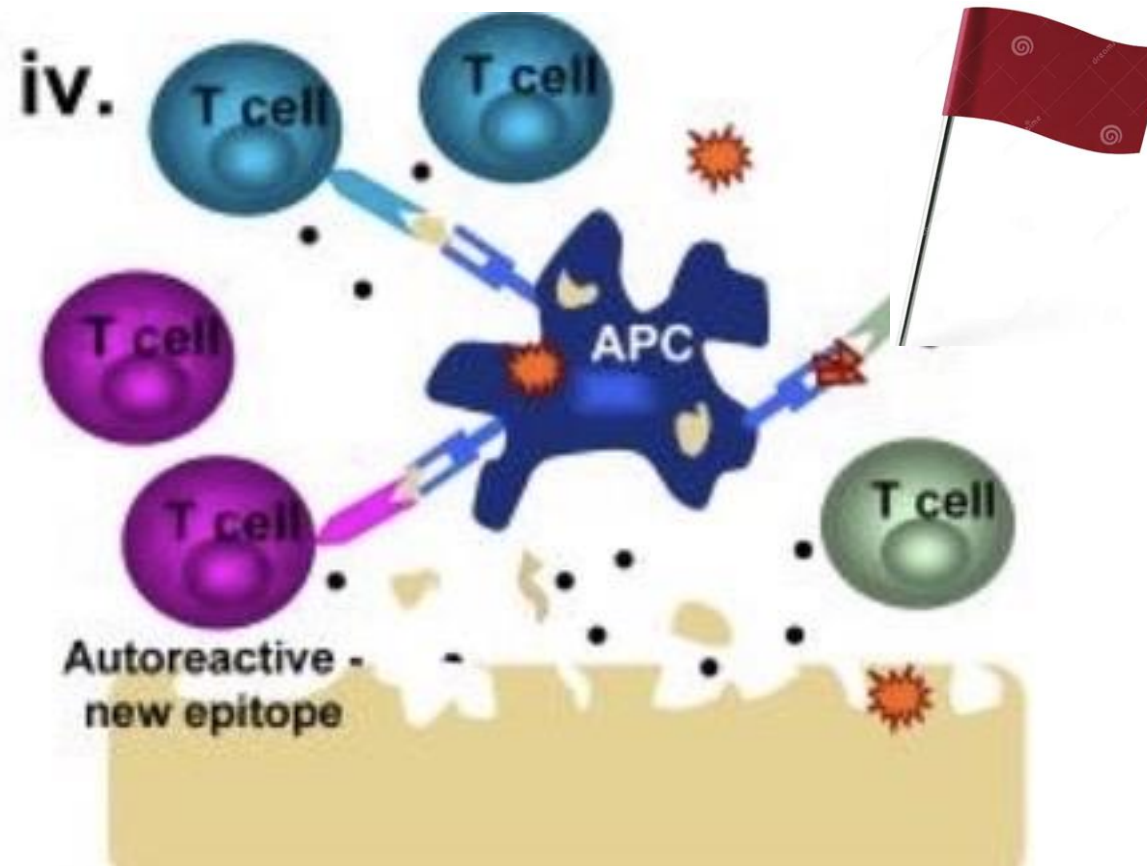
Diabetologia. Coxsackie B virus IgM in children at onset of Type 1 (insulin-dependent) diabetes mellitus: evidence for IgM induction by a recent or current infection. 1992. G. Fri

Bystander activation



Nat Rev Immunology. Antiviral immune responses: triggers of or triggered by autoimmunity?" 2009.
C. Munz, J. D Lunemann, M.T. Getta et al.

Epitope spreading



Nat Rev Immunology. Antiviral immune responses: triggers of or triggered by autoimmunity?" 2009.
C. Munz, J. D Lunemann, M.T. Getta et al.

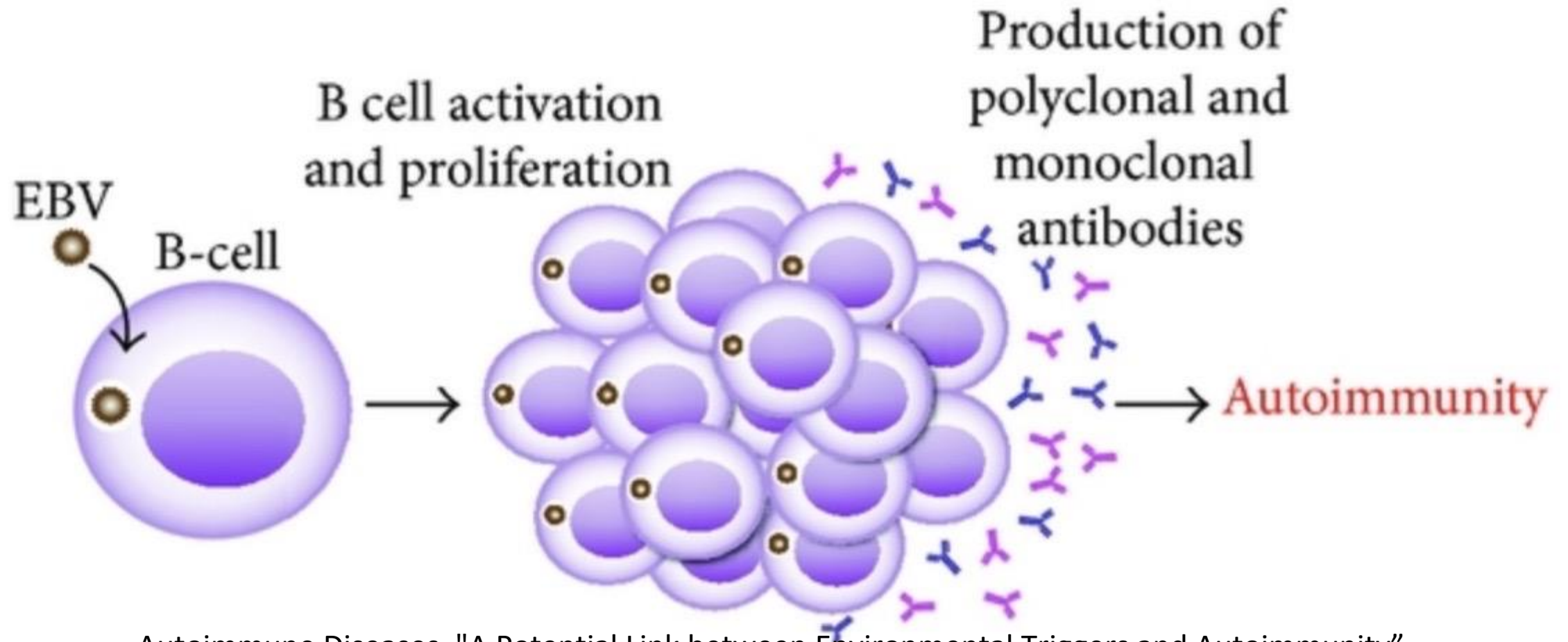




- Over expansion of TH1 can lead to excess antibody production, that triggers diseases, such as lupus

Journal of experimental medicine. “Follicular helper T cells are required for systemic autoimmunity”. 2009.

Lintermann, M.A, Rigby, R.J., Wong, R. K., et al.



Autoimmune Diseases. "A Potential Link between Environmental Triggers and Autoimmunity".
2014. Aristo Vojdani



- **EBV may play a role in multiple sclerosis and rheumatoid arthritis**

J Exp Med. Dysregulated Epstein-Barr virus infection in the multiple sclerosis brain. 2007. Serafini B, et al.

J Exp Med T cell response to Epstein-Barr virus transactivators in chronic rheumatoid arthritis. 1996. Scotet E, et al.



Factors That Increase Baseline Inflammation Can Worsen Viral Complications

Obesity

Vitamin Deficiencies

Hyperglycemia



Obesity and inflammation

- Adipose tissue promotes inflammation
- Adipose tissue can be a reservoir for viruses that can cause dysfunction in multiple organs



J Clin Endocrinol Metab. Adipose tissue as an endocrine organ. 2004. Kershaw EE, Flier JS.

Microbiol. Specific biological features of adipose tissue, and their impact on HIV Persistence. 2019. Bourgeois C, Gorwood J, Barrail-Tran A, Lagathu C, Capeau J, Desjardins D. et al. Sersi

Nat Immunol. Immunological complications of obesity. 2012. Kanneganti TD, Dixit VD.

<https://www.dreamstime.com/doctor-measuring-obese-man-waist-body-fat-obesity-weight-loss-to-loose-image114064583>



Vitamin D Deficiency Can Affect Lungs in Viral Infection

- Low vitamin D associated with increased risk of ICU admission or death from Sars-COV2

Front Public Health, Vitamin D Status and SARS-CoV-2 Infection and COVID-19 Clinical Outcomes. 2021. Chiodini I, Gatti D, Soranna D, Merlotti D, Mingiano C, Fassio A, Adami G, Falchetti A, Eller-Vainicher C, Rossini M, Persani L, Zambon A, Gennari L



High Blood Sugars and Inflammation

- High blood sugars literally change the composition of the lungs, making them more susceptible to damage from viral infection
- High blood sugars can affect viral invasion and body response

Endocr Rev. Pulmonary function and sleep breathing: two new targets for type 2 diabetes care. 2011. Lecube A, Simo R, Pallayova M, Punjabi NM, Lopez-Cano C, Turino C. et al.

J Biol Chem. Adipsin and an endogenous pathway of complement from adipose cells. 1992. Choy LN, Rosen BS, Spiegelman BM.

Intensive Care Med. Factors determining the appearance of glucose in upper and lower respiratory tract secretions. 2003. Philips BJ, Meguer JX, Redman J, Baker EH.

J Med Virol. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. J Med Virol. 2020. Brufsky A.



Viruses Can Trigger Autoimmune Disease

- Parvovirus and Rheumatoid Arthritis

British Journal of Rheumatology. A study of the role of parvovirus B19 in rheumatoid arthritis. 1995
. J. R. Kerr, J. P. Cartron, M. D. Curran, J. E. Moore, J. R. M. Elliott, and R. A. B. Mollan.



Inflammation Can Worsen Autoimmunity

- The inflammasomes are innate immune system receptors that regulate activation of caspase-1 and induce inflammation.
- Respond to infectious microbes and molecules derived from host proteins.
- Implicated in a host of inflammatory disorders.

Guo H, Callaway JB, Ting JP. Inflammasomes: mechanism of action, role in disease, and therapeutics. Nat Med. 2015 Jul;21(7):677-87. doi: 10.1038/nm.3893. Epub 2015 Jun 29. PMID: 26121197; PMCID: PMC4519035.

Everyone's Journey is Different. Observations from Dr. Ledwich and Dr. Weinhold





Dr. Ledwich's Observations

- Clean up the diet
- Get adequate sleep
- Support adrenal health with vitamin C and magnesium
- Support overall immune health with vitamin D
- Support metabolic health with B vitamins
- Support detox pathways with glutathione and/or NAC
- Exercise more
- Adaptogenic herbs, bio-identical hormones
- By the time I get them traditional medications..... they are already subjectively feeling better!



Dr. Weinhold's observations



- **Any disruptor**, such as a cold, flu, & stress, can **change** the way the **body absorbs vitamins & minerals**.
- **Inflammation Progresses Dis-ease**.
- One of the main principles in both Homeopathic & Naturopathic Medicine is to “**Remove Obstacles to Cure**”. Naturopathic supplements, botanicals, and homeopathic medicines are more effective when patients incorporate a **Mediterranean Type Diet**.
- Naturopathic medicine provides many modalities to help **reduce inflammation, modulate the immune system**, increase mobility, & **reduce stress**.

1. How Diet, Lifestyle, and Hormones Affect The Immune System



<https://www.dreamstime.com/photos-images/mediterranean-diet-mediterranean-diet.html>

<https://www.dreamstime.com/stock-photo-businessman-stressed-out-work-casual-office-image84355137>



Diet of Processed Foods Contain Substances That Promote Inflammation

- Salt
- Sugar
- High Fructose Corn Syrup



<https://www.dreamstime.com/royalty-free-stock-photography-obesity-you-what-you-eat-image14470637>



Salt

- Adversely affects macrophages (the pacmen)
- Causes CD4 T cells to differentiate into TH17 cells (associated with abnormal inflammation)

Cell Res. High salt primes a specific activation state of macrophages. 2015. Zhang WC, Zheng XJ, Du LJ, et al.

Nature. Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells.. 2013. Kleinewietfeld M, Manzel A, Titze J, et al.

Nature. Induction of pathogenic TH17 cells by inducible salt-sensing kinase SGK1. 2013. Wu C, Yosef N, Thalhamer T, et al
<https://www.dreamstime.com/stock-photo-salt-shaker-old-wooden-table-close-up-shot-selective-focus-image69610312>



Sugar and high fructose corn syrup

- Remember, hyperglycemia enhances viral attack and impedes the body's response to infection
- High fructose corn syrup is linked to hyperglycemia...which worsens viral infection

Intensive Care Med. Factors determining the appearance of glucose in upper and lower respiratory tract secretions. 2003. Philips BJ, Meguer JX, Redman J, Baker EH.

J Med Virol. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. 2020. Brufsky A

Circulation. Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. 2010. Malik VS, Popkin BM, Bray GA et al.

Diabetes Care. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. 2010. Malik VS, Popkin BM, Bray GA et al

<https://www.dreamstime.com/stock-photo-sweet-sugary-donuts-rustic-table-filled-chocolate-cream-wooden-kitchen-tasty-bakery-doughnuts-selective-focus-shallow-image59333>



Sugar

- Small study revealed that by eating 100 grams (24tsp) of carbohydrates from glucose, sucrose, honey, or orange juice, the capacity of neutrophils to engulf bacteria was significantly decreased; the neutrophils became “paralyzed”.

Sanchez A, Reeser JL, Lau HS, Yahiku PY, Willard RE, McMillan PJ, Cho SY, Magie AR, Register UD. Role of sugars in human neutrophilic phagocytosis. Am J Clin Nutr. 1973 Nov;26(11):1180-4. doi: 10.1093/ajcn/26.11.1180. PMID: 4748178.



Mediterranean Diet

- Increase vegetables & healthy fats.
- Limiting dairy, fatty meats, and processed carbs
- Oleic acid in olive oil is similar in structure to salicylic acid in aspirin
- Increase of n-3 PUFAS rather than n-6 PUFAS enhance anti-inflammatory response



Mazzocchi A, Leone L, Agostoni C, Pali-Schöll I. The Secrets of the Mediterranean Diet. Does [Only] Olive Oil Matter? *Nutrients*. 2019 Dec 3;11(12):2941. doi: 10.3390/nu11122941. PMID: 31817038; PMCID: PMC6949890.

Tosti V, Bertozzi B, Fontana L. Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. *J Gerontol A Biol Sci Med Sci*. 2018 Mar 2;73(3):318-326. doi: 10.1093/gerona/glx227. PMID: 29244059; PMCID: PMC7190876.
<https://www.dreamstime.com/stock-photo-branch-olives-bottle-olive-oil-image14720600>



Mediterranean Diet

- Significant improvement in pain in RA patients on the Mediterranean Diet vs Standard American Diet.
- Mediterranean diets tended to have a greater effect on pain than vegetarian or vegan diets.
- **Caution patients: Gluten sensitivity** is more common in patients with rheumatic diseases than general population.

Schönenberger K.A., Schüpfer A.-C., Gloy V.L., Hasler P., Stanga Z., Kaegi-Braun N., Reber E. Effect of anti-inflammatory diets on pain in rheumatoid arthritis: A systematic review and meta-analysis. *Nutrients*. 2021;13:4221. doi: 10.3390/nu13124221



Sleep Deprivation

- Increases production of pro-inflammatory cytokines like IL 6, IL-1B, and TNF-a

Journal of Clinical Endocrinology & Metabolism. Acute effects of recombinant human interleukin-6 on endocrine and central nervous sleep functions in healthy men. 1998. Spath-Schwalbe E, Hansen K, Schmidt F, Schrezenmeier H, Marshall L, Burger K, Fehm HL, Born J.

Advances in Neuroimmunology. Sleep deprivation and human immune function. 1995. Dinges DF, Douglas SD, Hamarman S, Zaugg L, Kapoor S.

Sleep. Elevated inflammatory markers in response to prolonged sleep restriction are associated with increased pain experience in healthy volunteers. 2007. Haack M, Sanchez E, Mullington JM.

<https://www.dreamstime.com/woman-working-late-night-grim-reaper-standing-over-her-shoulder-eps-vector-illustration-danger-sleep-deprivation-image109574847>





Exercise

- Improves blood and lymphatic flow, enhances activity of macrophages, and stimulates cellular immunity



J Sport Health Sci. The compelling link between physical activity and the body's defense system. 2019. Nieman DC, Wentz LM.

<https://www.dreamstime.com/young-happy-sexy-sweaty-asian-woman-sport-clothes-lying-plank-position-gym-doj-flo-flo-hard-training-fitness-image100735937>



Stress hurts the immune system

- Decreased natural killer (NK) cells
- Lower antibody titers to the influenza vaccine
- Decreased lymphocyte proliferation.

Association of Family Stress With Natural Killer Cell Activity and the Frequency of Illnesses in Children. *Arch Pediatr Adolesc Med*. 2007. Wyman PA, Moynihan J, Eberly S, et al

Psychosocial modifiers of immunocompetence in medical students. *Psychosom Med*. 1984. Kiecolt-Glaser JK, Garner W, Speicher C, Penn GM, Holliday J, Glaser R.



<https://www.dreamstime.com/hormonal-imbalance-concept-wooden-blocks-crossword-puzzle-flat-lay-blue-background-conceptual-hormonal-imbalance-concept-wooden-image253782142>



- Estrogen dominance exacerbates autoimmunity
- Pan-hypopituitarism increases frequency of infections
- Low levels of progesterone can be associated with pro inflammatory IL1

Science Signaling. E strogen receptor α contributes to T cell-mediated autoimmune inflammation by promoting T cell activation and proliferation. 2018. Mohammad I, Starskaia I, Nagy T, Guo J, Yarkin E, Väänänen K, Watford WT, Chen Z.

Clin Infect Dis. High frequency of serious infections in patients with panhypopituitarism: a case-control study. 2001. Sharma MD, Sagar B, Wang S, White AC Jr, Balasubramanyam A.

Curr Drug Targets Inflamm Allergy. Interactions of sex steroids with mechanisms of inflammation. 2004. Obendorf M, Patchev VK.

Autoimmun Rev. Immunology and the menstrual cycle. 2012. Oertelt-Prigione S.



2. Botanical Medicine

Immune modulators, Anti-inflammatory Herbs, Adaptogens



Lamiaceae family of plants have been shown to contain both calming & anti-viral properties

- Thyme
- Mint
- Oregano
- Basil
- Sage
- Savory
- Rosemary
- Lemon Balm
- Hyssop
- Self-heal

Bekut M, Brkić S, Kladar N, Dragović G, Gavarić N, Božin B. Potential of selected Lamiaceae plants in anti(retro)viral therapy. Pharmacol Res. 2018 Jul;133:301-314. doi: 10.1016/j.phrs.2017.12.016. Epub 2017 Dec 16. PMID: 29258916; PMCID: PMC7129285.

Stress is a Trigger of Autoimmune Disease

- Studies found that up to **80%** of patients reported uncommon **emotional stress before disease onset**.
- Stress causes disease, but disease itself causes significant stress in patients, creating a vicious cycle

Stojanovich L, Marisavljevich D. Stress as a trigger of autoimmune disease. Autoimmun Rev. 2008 Jan;7(3):209-13. doi: 10.1016/j.autrev.2007.11.007. Epub 2007 Nov 29. PMID: 18190880.

Melissa officinalis (Lemon Balm)



- Traditionally used to relieve cold sores aggravated by stress. Reduce inflammasomes (IL-1 & IL-6)
- Research shows Melissa has anti-viral properties against (SARS-CoV-2), Virus (HSV), and (HIV) through various mechanisms.
- Inhibits HSV-1 from binding to host cell
- Inhibiting HSV-1 replication during the post-adsorption or inhibiting main protease and spike protein of SARS-CoV-2.
- More randomized controlled trials should be done in humans

Behzadi A, Imani S, Deravi N, Mohammad Taheri Z, Mohammadian F, Moraveji Z, Shavysi S, Mostafaloo M, Soleimani Hadidi F, Nanbakhsh S, Olangian-Tehrani S, Marabi MH, Behshood P, Poudineh M, Kheirandish A, Keylani K, Behfarnia P. Antiviral Potential of Melissa officinalis L.: A Literature Review. Nutr Metab Insights. 2023 Jan 12;16:11786388221146683. doi: 10.1177/11786388221146683. PMID: 36655201; PMCID: PMC9841880

Scutellaria lateriflora (American Skullcap)



- In the Mint Family
- Part Used: Aerial herb in bud
- Dose: Liquid Extract 40 drops, 1-4 x day
- Calms and Relieves Stress & Anxiety.
- Antispasmodic action helps with Muscle tension, spasms, tremors.
- Dull headaches, insomnia, & nervous exhaustion
- No known contraindications

Chevallier, Andrew. (1996), The Encyclopedia of Medicinal Plants. London. Dorling Kindersley Limited.

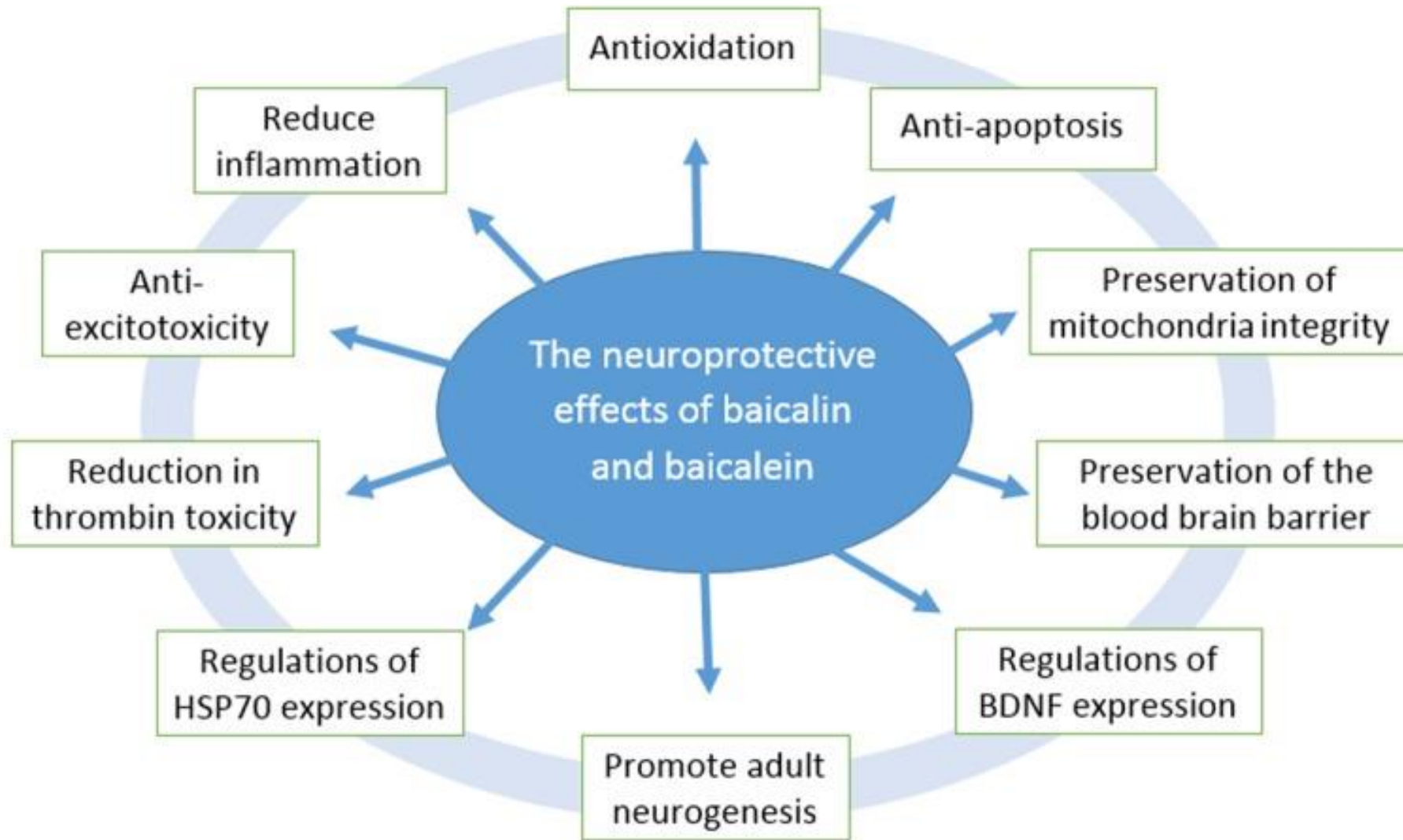
<https://www.dreamstime.com/scutellaria-lateriflora-known-commonly-as-blue-skullcap-mad-dog-skullcap-american-skullcap-scutellaria-lateriflora-close-up-image216490037>



Scutellaria baicalensis (Chinese Skullcap, *Huang Qin*)

- **Baicalin** is a flavonoid isolated from the root
- Traditionally used for dysentery, now suggested for **Inflammatory Bowel Disease**
- Pharmacological actions: antibacterial, **antiviral, anti-inflammatory, antioxidant, liver and nerve protection, maintenance of intestinal barrier**, maintain intestinal flora balance

Wang X, Xie L, Long J, Liu K, Lu J, Liang Y, Cao Y, Dai X, Li X. Therapeutic effect of baicalin on inflammatory bowel disease: A review. J Ethnopharmacol. 2022 Jan 30;283:114749. doi: 10.1016/j.jep.2021.114749. Epub 2021 Oct 16. PMID: 34666140.



Wei Liang, Xiaobo Huang, Wenqiang Chen. "The Effects of Baicalin and Baicalein on Cerebral Ischemia: A Review." **Aging & Disease**. 2017, Dec. 8(6)850-867. www.aginganddisease.org/EN/10.14336/AD.2017.0829



Role of Herbs & Spices in Rheumatic Disease

- Curcumin interferes with arachidonic acid metabolism, by binding to proteins such as cyclooxygenase (COX)-2 and lipoxygenase.
- Mechanism of action similar to the mechanism of non-steroidal anti-inflammatory drugs (NSAIDS)
- 31 Randomized Controlled Trials demonstrated that curcumin decreased activity in RA (CRP).
- Effect on gut microbiota.

Charneka S, Hernando A, Costa-Reis P, Guerreiro CS. Beyond Seasoning-The Role of Herbs and Spices in Rheumatic Diseases. *Nutrients*. 2023 Jun 20;15(12):2812. doi: 10.3390/nu15122812. PMID: 37375716; PMCID: PMC10300823.



Curcuma longa Curcumin



- Inhibits microglial activation
- Mitigates neuroinflammation
- Increases BDNF
(Brain Derived Neurotrophin Factor)

Jiawei Zhang, Yaling Zheng, Yan Luo, Yu Du, Xiaojie Zhang, Jianliang Fu. Curcumin inhibits LPS-induced neuroinflammation by promoting microglial M2 polarization via TREM2/ TLR4/ NF- κ B pathways in BV2 cells. *Molecular Immunology*. 2019. Dec.116: 29-37. ISSN 0161-5890, doi.org/10.1016/j.molimm.2019.09.020.



Curcumin may have therapeutic potential in multiple sclerosis

Numerous properties of curcumin have been identified recently, some of which **can be effective** in the treatment of **MS, particularly the anti-inflammatory properties via inhibition of secretion of proinflammatory cytokines.**

Ghanaatian N, Lashgari NA, Abdolghaffari AH, Rajaei SM, Panahi Y, Barreto GE, Butler AE, Sahebkar A. Curcumin as a therapeutic candidate for multiple sclerosis: Molecular mechanisms and targets. J Cell Physiol. 2019 Aug;234(8):12237-12248. doi: 10.1002/jcp.27965. Epub 2018 Dec 10. PMID: 30536381.



The Role of Adaptogenic Herbs in Prophylaxis and Treatment of Viral Respiratory Infections

- *Andrographis paniculata*, *Eleutherococcus senticosus*, *Glycyrrhiza* spp., *Panax* spp., *Rhodiola rosea*, *Schisandra chinensis*, *Withania somnifera*



Panossian A, Brendler T. The Role of Adaptogens in Prophylaxis and Treatment of Viral Respiratory Infections. *Pharmaceuticals (Basel)*. 2020 Sep 8;13(9):236. doi: 10.3390/ph13090236. PMID: 32911682; PMCID: PMC7558817

<https://www.dreamstime.com/stock-photo-licorice-root-sticks-image37616820>



Adaptogenic Herbs can be useful in Prophylaxis & Treatment of all stages of Viral Respiratory Infections

- Modulate innate and adaptive immunity
- Anti-inflammatory activity
- Direct anti-viral effects of inhibiting viral docking or replication
- Detoxification & repair of oxidative stress-induced damage in compromised cells.
- Improving quality of life during convalescence

Panossian A, Brendler T. The Role of Adaptogens in Prophylaxis and Treatment of Viral Respiratory Infections. Pharmaceuticals (Basel). 2020 Sep 8;13(9):236. doi: 10.3390/ph13090236. PMID: 32911682; PMCID: PMC7558817.



Andrographis paniculata

- Statistically significant effect in **improving overall symptoms of acute respiratory tract infections** when compared to placebo, usual care, and other herbal therapies.
- Evidence suggests AP **shortened the duration of cough, sore throat, and sick/leave time to resolution** when compared to versus usual care.

Hu, X.-Y.; Wu, R.-H.; Logue, M.; Blondel, C.; Lai, L.Y.W.; Stuart, B.; Flower, A.; Fei, Y.-T.; Moore, M.; Shepherd, J.; et al. *Andrographis paniculata* (Chúān Xīn Lián) for symptomatic relief of acute respiratory tract infections in adults and children: A systematic review and meta-analysis. PLoS ONE 2017, 12, e0181780.



Korean Red Ginseng-

Study on Maintaining Antibodies after COVID-19 Vaccine

- The antibody formation rate of the KRG group was sustained higher than that of the control group for 12 weeks after the second dose
- This trend was prominently observed in those above 50 years old.
- Study found that Korean Red Ginseng can **help to increase and maintain vaccine response**, highlighting that KRG could potentially be used as an **immunomodulator** with COVID-19 vaccines.

Yoon J, Park B, Kim H, Choi S, Jung D. Korean Red Ginseng Potentially Improves Maintaining Antibodies after COVID-19 Vaccination: A 24-Week Longitudinal Study. *Nutrients*. 2023 Mar 24;15(7):1584. doi: 10.3390/nu15071584. PMID: 37049424; PMCID: PMC10097014.



Eleutherococcus senticosus Siberian Ginseng

- Epidemiological studies in the Soviet Union
- Reduce mortality rates during influenza epidemics
- Reduce complications of influenza infection (pneumonia, bronchitis, & otitis)



Panossian A, Brendler T. The Role of Adaptogens in Prophylaxis and Treatment of Viral Respiratory Infections. Pharmaceuticals (Basel). 2020 Sep 8;13(9):236. doi: 10.3390/ph13090236. PMID: 32911682; PMCID: PMC7558817.

<https://www.dreamstime.com/dried-root-siberian-ginseng-dark-background-medicine-alternative-image136378729>

3. Homeopathic Medicine

“Similia similibus curentur”
‘Law of Similars’



‘Law of Similars’

- The theory ‘**like treats like**’ is the same basic principle behind today’s modern vaccination. A patient is given something very similar that the patient is sensitive to in order to create an immune response to bring the body back into balance. It’s not unlike sublingual immunotherapy. Whatever most closely matches the person’s symptoms is what needs to be used
 - Concept of the Minimum Dose or Microdose to help Modulate the Immune System
-
- Hjelvik M, Mørenskog E. Homøopatens prinsipper [The principles of homeopathy]. Tidsskr Nor Lægeforen. 1997 Jun 30;117(17):2497-501. Norwegian. PMID: 9265314.
 - Ullman D, Frass M. A review of homeopathic research in the treatment of respiratory allergies. Altern Med Rev. 2010 Apr;15(1):48-58. PMID: 20359268.



Evaluation of Homeopathic Therapy in Rheumatoid Arthritis: Double Blind Clinical Trial

- 23 patients with Rheumatoid Arthritis received conventional first line anti-inflammatory treatment plus homeopathy, and the second group of 23 patients with RA received the same first line treatment plus a placebo.

Gibson, R., Gibson, S., MacNeill, A. and Buchanan, W. (1980), Homoeopathic therapy in rheumatoid arthritis: evaluation by double- blind clinical therapeutic trial.. British Journal of Clinical Pharmacology, 9: 453-459. <https://doi.org/10.1111/j.1365-2125.1980.tb05840.x>



Homeopathic Medicines most commonly used in the trial

- Arnica
- Pulsatilla
- Rhus toxicodendron
- Ruta
- Sepia
- Sulphur
- *Remedies of wide action in RA used more often
- Bryonia
- Calcarea carbonica
- Causticum
- Arsenicum album
- Natrum muriaticum
- Nux Vomica
- Thuja

Gibson, R., Gibson, S., MacNeill, A. and Buchanan, W. (1980), Homoeopathic therapy in rheumatoid arthritis: evaluation by double- blind clinical therapeutic trial.. British Journal of Clinical Pharmacology, 9: 453-459. <https://doi.org/10.1111/j.1365-2125.1980.tb05840.x>

Results: Homeopathic Therapy in RA

- Significant **Improvement in subjective pain, Articular index, stiffness, and grip strength** in those patients receiving homeopathic medicines.
- No significant change in the group who received a placebo
- **No side effects** with homeopathic medicine
- Effective in alleviating symptoms of Rheumatoid arthritis



Gibson, R., Gibson, S., MacNeill, A. and Buchanan, W. (1980), Homoeopathic therapy in rheumatoid arthritis: evaluation by double- blind clinical therapeutic trial.. British Journal of Clinical Pharmacology, 9: 453-459. <https://doi.org/10.1111/j.1365-2125.1980.tb05840.x>

<https://www.dreamstime.com/young-woman-having-rheumatoid-arthritis-takes-rest-sitting-bench-yard-hospital-hands-legs-deformed-sitting-image152451785>



Individualized Classical Homeopathy Improves Symptoms of Fibromyalgia

- study demonstrated that individualized homeopathy is significantly better than placebo in:
 - **lessening tender point pain**
 - improving the quality of life
 - Improving global health and a trend toward **less depression**



Bell IR, Lewis DA 2nd, Brooks AJ, Schwartz GE, Lewis SE, Walsh BT, Baldwin CM. Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. *Rheumatology (Oxford)*. 2004 May;43(5):577-82. doi: 10.1093/rheumatology/keh111. Epub 2004 Jan 20. PMID: 14734789



4. Vitamins & Nutraceuticals



Vitamin D

- Deficiency associated with lupus, psoriatic arthritis, and multiple sclerosis
- Supplementation can improve viral infection outcomes

J Rheumatol. The effect of vitamin D supplementation on inflammatory and hemostatic markers and disease activity in patients with systemic lupus erythematosus: a randomized placebo-controlled trial. 2013. Abou-Raya A, Abou-Raya S, Helmii M, Gamonal SBL, Gamonal ACC, Marques NCV, Brandão MAF, Raposo

Sao Paulo Med J. Is vitamin D status relevant to psoriasis and psoriatic arthritis? A retrospective cross-sectional study. 2022. Gamonal SBL, Gamonal ACC, Marques NCV, Brandão MAF, Raposo NRB.

Br J Pharmacol. Immunoregulatory effects and therapeutic potential of vitamin D in multiple sclerosis. 2020. Yeh WZ, Gresle M, Jokubaitis V, Stankovich J, van der Walt A, Butzkueven H.

Nutrients. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. 2020. Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL. et al.

Health Technol Assess. Vitamin D supplementation to prevent acute respiratory infections: individual participant data meta-analysis. 2019. Martineau AR, et al.



N-Acetylcysteine (NAC)

- Natural precursor to glutathione, ability to modulate glutamate levels, improve depression, and promote neurogenesis
- May be beneficial for lupus nephritis

J Clin Psychiatry. The efficacy of adjunctive N-acetylcysteine in major depressive disorder: a double-blind, randomized, placebo-controlled trial. .2014. Berk M, Dean OM, Cotton SM, et al.

Arthritis Rheum. Attention deficit and hyperactivity disorder scores are elevated and respond do N-acetylcysteine treatment in patients with systemic lupus erythematosus. 2014. Garcia RJ, Francis L, Dawood M, et al

Cells. Dipyridamole, N-Acetylcysteine and Statins as Adjunctive Therapy for Systemic Lupus Erythematosus. 2019. Tan MKX, Heng TYJ, Mak A.



Glutathione

- Liver is a major organ of detoxification, potential for improving liver health with glutathione
- Has anti-inflammatory effects
- Levels can be depleted in SLE patients with active disease

BMC Gastroenterol. Efficacy of glutathione for the treatment of nonalcoholic fatty liver disease: an open-label, single-arm, multicenter, pilot study. 2017. Honda y, et al.

J Am Heart Assoc. Glutathione Infusion Before and 3 Days After Primary Angioplasty Blunts Ongoing NOX2-Mediated Inflammatory Response. 2021. Tanzilli G, et al.

Nat Rev Rheumatol. Oxidative stress in the pathology and treatment of systemic lupus erythematosus. 2013. Perl A.



Cysteine and Glutathione

- **Increasing Glutathione and Cysteine can increase Vitamin D levels in the blood even without vitamin D supplementation or sunlight.**
- Cysteine and Glutathione help to decrease inflammation
- Impaired GSH metabolism may be why some people don't respond to vitamin D supplementation.

Jain SK, Parsanathan R, Achari AE, Kanikarla-Marie P, Bocchini JA Jr. Glutathione Stimulates Vitamin D Regulatory and Glucose-Metabolism Genes, Lowers Oxidative Stress and Inflammation, and Increases 25-Hydroxy-Vitamin D Levels in Blood: A Novel Approach to Treat 25-Hydroxyvitamin D Deficiency. *Antioxid Redox Signal*. 2018 Dec 10;29(17):1792-1807. doi: 10.1089/ars.2017.7462. Epub 2018 Oct 9. PMID: 30160165; PMCID: PMC6208166.



SLE

- Depleted glutathione levels in T cells may increase autoimmunity in Lupus patients.

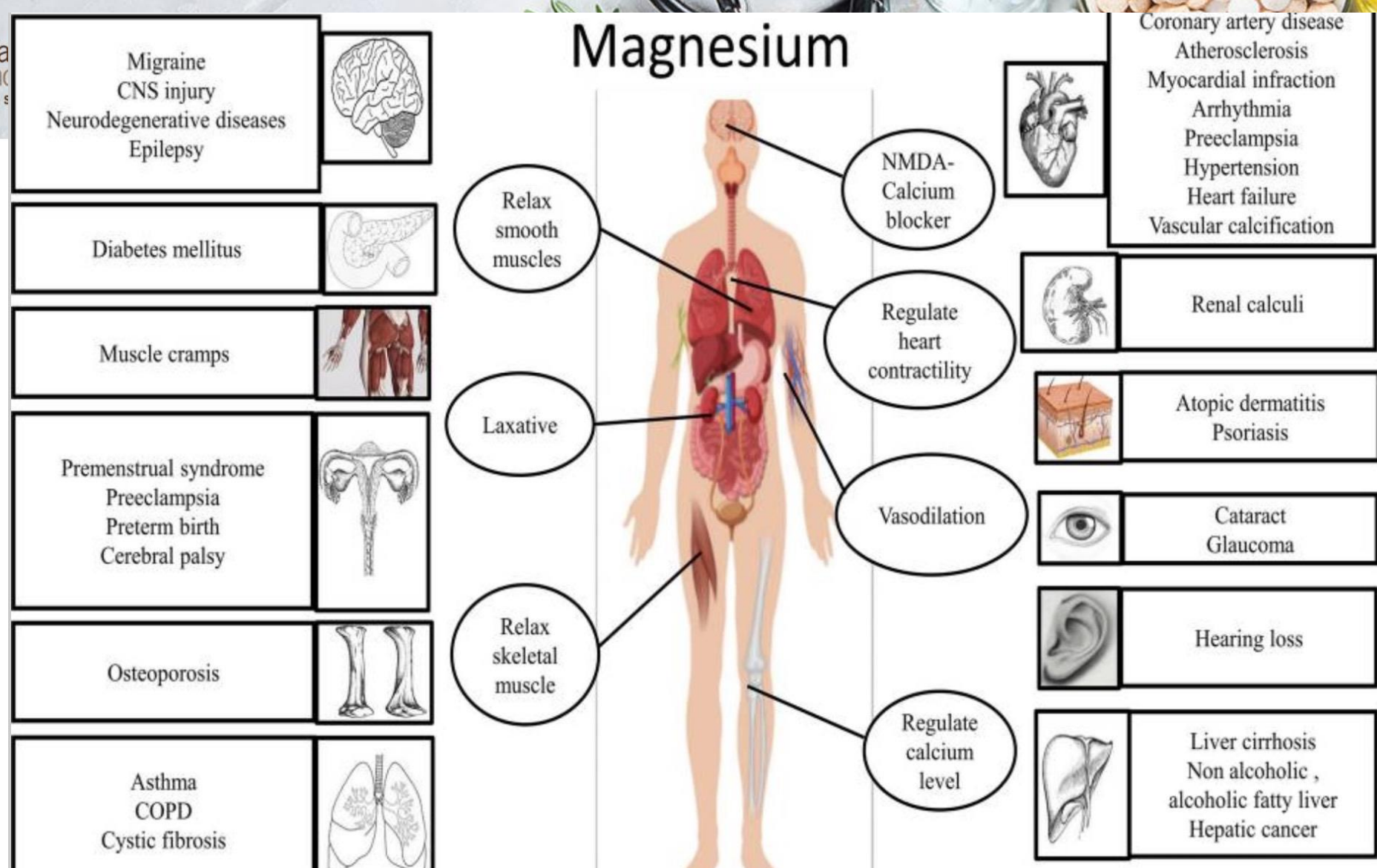
Perl A. Oxidative stress in the pathology and treatment of systemic lupus erythematosus. *Nat Rev Rheumatol*.2013;9(11):674-686.



Human Trial 36 SLE patients & NAC

- Study found that 2.4g of NAC was well tolerated, while 4.8g caused nausea in 33% of subjects.
- Both dosages were found to significantly **improve disease activity scores, improve T-cell mitochondrial membrane potential, enhance apoptosis, and block mTOR activation.**

Lai ZW, Hanczko R, Bonilla E, et al. N-acetylcysteine reduces disease activity by blocking mTOR in T cells of systemic lupus erythematosus patients: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2012;64(9):2937-2946.



Biometals. Magnesium-the master cation-as a drug-possibilities and evidences. 2021.Mathew AA, Panonnummal R



Magnesium

- Can be a supportive treatment in covid infections

Eur J Pharmacol. Possibility of magnesium supplementation for supportive treatment in patients with COVID-19. 2020. Tang CF, Ding H, Jiao RQ, Wu XX, Kong LD



Zinc

- Can decrease levels of IFN
- Deficiency can be associated with autoimmunity, gatekeeper of immune function

Nat Commun. Zinc is a potent and specific inhibitor of IFN- λ 3 signalling. 2017. Read SA, O'Connor KS, Suppiah V, Ahlenstiel CLE, Obeid S, Cook KM, Cunningham A, Douglas MW, Hogg PJ, Booth D, George J, Ahlenstiel G.

Autoimmun Rev. Zinc and its role in immunity and inflammation. 2015. Bonaventura P., Benedetti G., Albareda F., Miossec P.

Nutrients. Zinc as a Gatekeeper of Immune Function. 2017. Wessels I, Maywald M, Rink L.



Vitamin C

Can improve cardiovascular outcomes, decrease glucose levels, decrease bronchoconstriction in viral infections, and can shorten duration of viral infections

Nutrients. Vitamin C Can Shorten the Length of Stay in the ICU: A Meta-Analysis. 2019. Hemilä H, Chalker E.



B vitamins

- Deficiencies usually associated with metabolic issues but can be associated with decreased immune health

Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. 1998.



Folate (B9)

- Deficiency = impaired cell division, accumulation of toxic metabolites, and decreased gene expression

Med Clin North Am. Megaloblastic Anemias: Nutritional and Other Causes. 2016. Green R, Datta Mitra A.



MTHFR mutation

- Associated with psychiatric disease, cancers, and CV disease
- In patients with RA, may have higher CV risk with mutation
- Can supplement with methylated folate

Transl Psychiatry. Methylenetetrahydrofolate reductase and psychiatric diseases. 2018. Wan L, Li Y, Zhang Z, Sun Z, He Y, Li R
Genes (Basel). THFR C677T and A1298C Polymorphisms in Breast Cancer, Gliomas and Gastric Cancer: A Review. 2021. Petrone I, Bernardo PS, Dos Santos EC, Abdelhay E.
Nutrients. Methylenetetrahydrofolate (MTHFR), the One-Carbon Cycle, and Cardiovascular Risks. 2021. Raghubeer S, Matsha TE
Sci Rep. Osteoprotegerin and MTHFR gene variations in rheumatoid arthritis: association with disease susceptibility and markers of subclinical atherosclerosis. 2022. Arida A, Nezos A, Papadaki I, Sfrikakis PP, Mavragani CP.
J Clin Med. Folate Insufficiency Due to MTHFR Deficiency Is Bypassed by 5-Methyltetrahydrofolate. 2020. Vidmar Golja M, Šmid A, Karas Kuželički N, Trontelj J, Geršak K, Mlinarič-Raščan I.



Cannabinoids

- Numerous studies report that cannabinoids may function as **immune modulators** limiting the adverse effects of inflammatory disease
- Endocannabinoids are produced in the respiratory system and cannabinoids **induced bronchial dilation** suggests a significant therapeutic potential for cannabinoids
- **cannabidiol, CBD**, a phytocannabinoid produced by the cannabis plant, **can block IL-6** in several models of inflammatory diseases.

Khodadadi H, Salles ÉL, Jarrahi A, Chibane F, Costigliola V, Yu JC, Vaibhav K, Hess DC, Dhandapani KM, Baban B. Cannabidiol Modulates Cytokine Storm in Acute Respiratory Distress Syndrome Induced by Simulated Viral Infection Using Synthetic RNA. Cannabis Cannabinoid Res. 2020 Sep 2;5(3):197-201. doi: 10.1089/can.2020.0043. PMID: 32923657; PMCID: PMC7480719.



Cannabinoids Conclusion

- Administration of CBD **downregulated the level of proinflammatory cytokines** and ameliorated symptoms of Poly I:C-induced ARDS
- **Modulates Cytokine Storm** in ARDS and mitigates effects of exaggerated inflammation
- Potential of cannabinoids as a therapeutic agent in the treatment of various inflammatory conditions and virus-induced ARDS

Khodadadi H, Salles ÉL, Jarrahi A, Chibane F, Costigliola V, Yu JC, Vaibhav K, Hess DC, Dhandapani KM, Baban B. Cannabidiol Modulates Cytokine Storm in Acute Respiratory Distress Syndrome Induced by Simulated Viral Infection Using Synthetic RNA. Cannabis Cannabinoid Res. 2020 Sep 2;5(3):197-201. doi: 10.1089/can.2020.0043. PMID: 32923657; PMCID: PMC7480719.



Iron

- Iron is part of hemoglobin, a protein which carries oxygen from our lungs throughout our bodies.
- It helps our muscles store and use oxygen
- Shown to influence activation of Nf-Kb, required for transcription of a number of genes involved immunity

Natural Medicines Comprehensive Database Consumer Version (Internet). Stockton (CA): Therapeutic Research Faculty: c1995-2018. Iron; (updated 2015 April 2. Available from: <https://medlineplus.gov/iron/html>

Annu Rev Immunol. Regulation and function of NF- κ B transcription factors in the immune system. 2009. Vallabhapurapu S, Karin M.



“Anemia of Inflammation” Iron Deficiency Anemia

- Observational Study, 206 patients with COVID-19 at the time of hospitalization in Internal Medicine Unit.
- Prevalence of Anemia was 61% in COVID-19 group
- Anemia does not directly influence mortality, it affects elderly, frail, and impact quality of life.

Bergamaschi G, Borrelli de Andreis F, Aronico N, Lenti MV, Barteselli C, Merli S, Pellegrino I, Coppola L, Cremonte EM, Croce G, Mordà F, Lapia F, Ferrari S, Ballesio A, Parodi A, Calabretta F, Ferrari MG, Fumoso F, Gentile A, Melazzini F, Di Sabatino A; Internal Medicine Covid-19 Collaborators. Anemia in patients with Covid-19: pathogenesis and clinical significance. Clin Exp Med. 2021 May;21(2):239-246. doi: 10.1007/s10238-020-00679-4. Epub 2021 Jan 8. Erratum in: Clin Exp Med. 2021 Mar 17;; PMID: 33417082; PMCID: PMC7790728.



“Anemia of Inflammation” Iron Deficiency Anemia

- Patients with rheumatoid arthritis have impaired Iron uptake, diversion of iron into macrophages
- **Anemia of chronic disease in rheumatoid arthritis is associated with increased apoptosis of bone marrow erythroid cells**

Vreugdenhil G, Kroos MJ, van Eijk HG, Lowenberg B, Swaak AJG. Impaired iron uptake and transferrin binding in erythroid cells in the anemia of rheumatoid arthritis. *Blood* 1990; 75: 335-9.

[Helen A. Papadaki](#), [Heraklis D. Kritikos](#), [Vasilis Valatas](#), [Dimitrios T. Boumpas](#), [George D. Eliopoulos](#), *Blood* (2002) 100 (2): 474–482.



Conclusion

- Viruses stimulate the immune system. If you are nutritionally deprived, toxin overloaded, and stressed (physically, mentally, and emotionally) these effects are amplified and may trigger autoimmunity.
- Botanical Medicine, Homeopathy, and Nutraceuticals can play a role in reducing abnormal inflammation triggered by viruses.

Contact Information

Lindsay Ledwich DO

- E-mail: Lindsayjledwich@gmail.com
@DrLindsay
www.make rheum4u

Heidi Weinhold ND

- E-mail: Doctorheidis@gmail.com
@Drheidiproducts
www.Doctorheidi.net



Saturday 10:00am – 11:00am

An Integrative Approach to Treating Viral Induced Autoimmune Disease

Please scan this QR code on you mobile
or tablet device to access the session feedback survey



An Integrative Approach to Treating Vir
al Induced Autoimmune Disease