Multiple Sclerosis Disease Intervention Program

DISCUSSION ON DIET, SUPPLEMENTS AND HEALTHY EATING PRACTICES

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Objectives;

- Discuss Quality of Life
- Discuss key terms
- Discuss modifiable risk factors
- Discuss the role of inflammation
- Discuss proinflammatory conditions
- Review popular diets
- Discuss intermittent fasting
- Review supplements
- Review behavioral changes

MS Disease Intervention program

12-week adherence to suggested lifestyle changes

Whole foods diet, reduced processed foods, reduced added sugar, antioxidants, Vitamin D, low in saturated fats

Intermittent fasting 12:12 daily

Exercise 30 minutes 3-5 times per week , yoga, tai chi, stretching, walking

Sleep- Consistent sleep/wake cycle, sleep routine, 8 hours per night

Mindfulness- daily practice for stress mitigation, mood adjustment

Quality of Life

- What is Quality of Life (QOL)?
- Defined by the World Health Organization as an individuals perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns
- Defined by Britannica as the degree to which an individual is healthy, comfortable and able to participate in or enjoy life events
- Defined by CDC as an individual's or a group's perceived physical and mental health over time. (HRQOL)

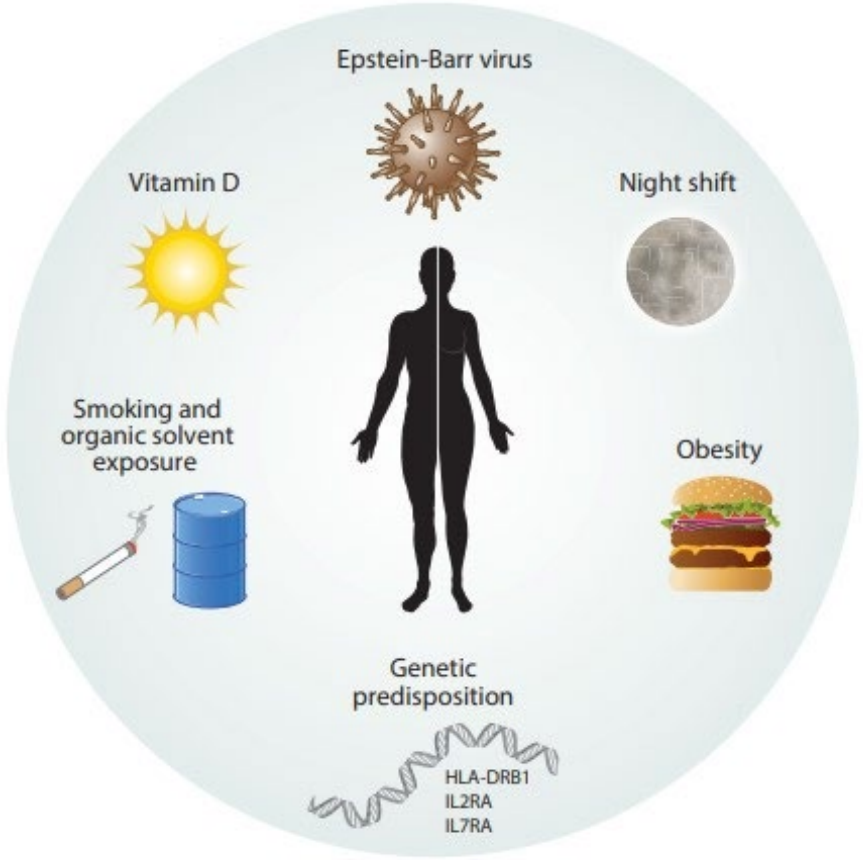
Domains of Quality of Life

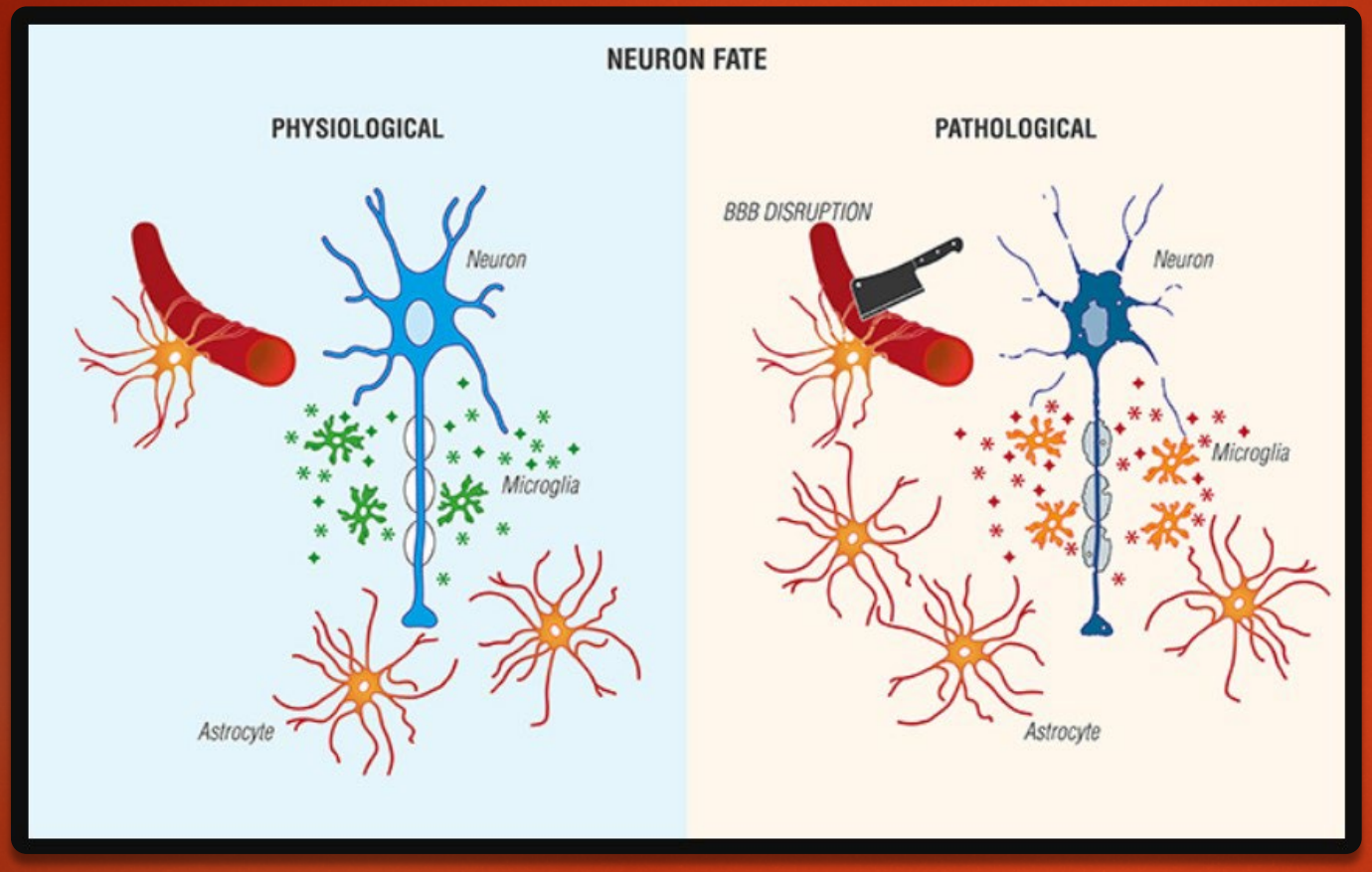
Key Terms

- **Inflammation**- body's normal response to injury or infection, chronic inflammation damages tissues
- **Oxidative Stress**-imbalance between accumulation of oxygen reactive species (ROS) and the cell's ability to eliminate/detoxify
- **Antioxidants**-compounds in foods that scavenge and neutralize free radicals
- **Mitochondrial support**-utilize nutrients that facilitate cellular ATP production and reduce oxidative stress
- **Gut-brain axis**-bidirectional network connecting enteric and central nervous system
- **Gut microbiome**-microbes that are helpful and potentially harmful breakdown foods, synthesize vitamins and amino acids, stimulate the immune system maintain symbiosis
- **Intermittent fasting**-periodic gut rest allowing gut bacteria to repopulate, maintain tight junctions
- **Circadian rhythm**-24 hour cycle known as biological clock driven by light dark

Known MS Risk Factors

1) First degree family member 2-4% risk over general population
2) Low vitamin D levels
3) Latitude-risk increases with distance from equator
4) Smoking, obesity, circadian disruption
5) Infection such as EBV
6) Women 3x more likely than men
7) Over 1 million affected in US, 2.8 million globally





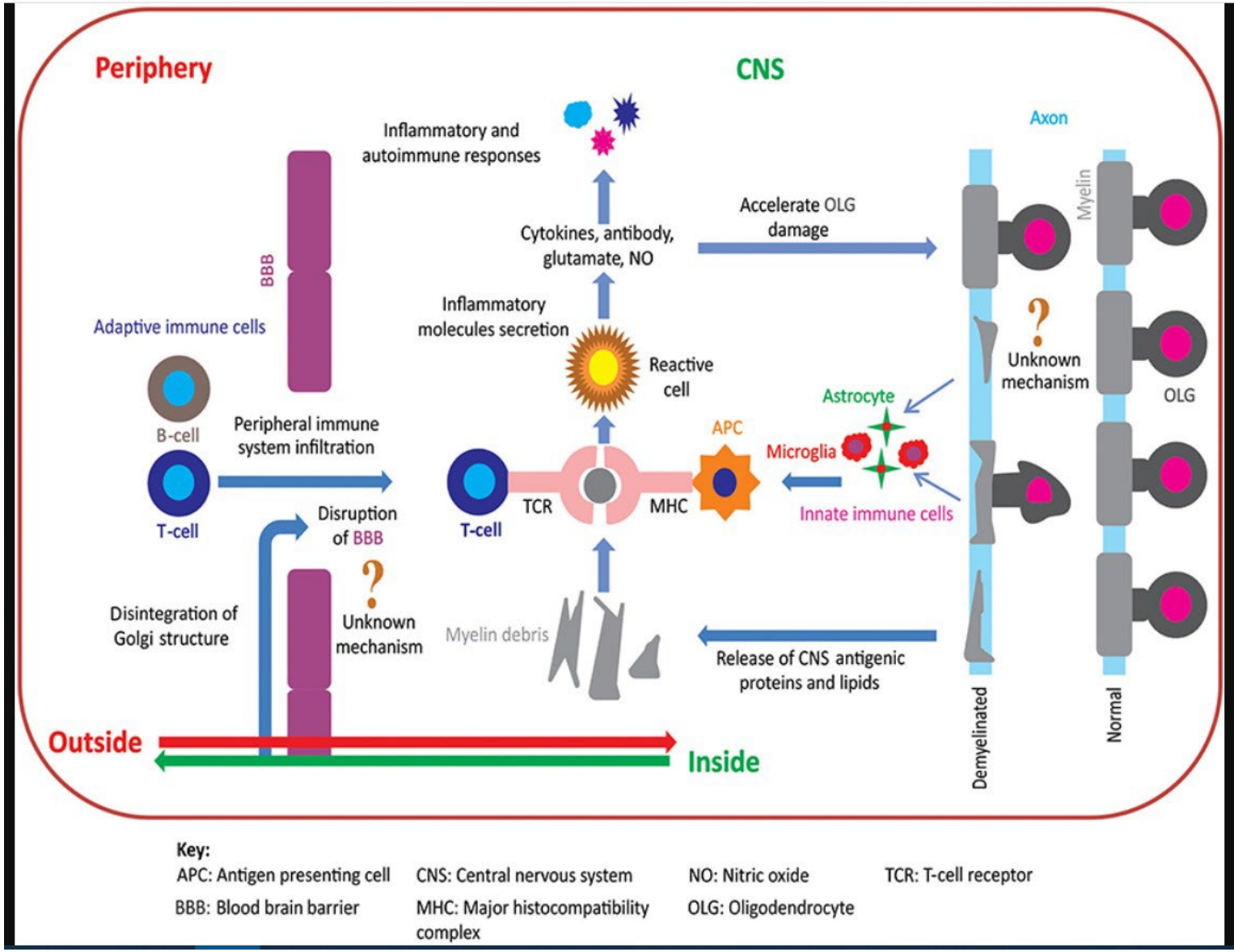
The role of immune cells in inflammation

The autoimmune component of the disease (through genetic predisposition or by possible environmental triggers) is initiated by myelin-reactive T cells, then amplified by an inflammatory response that involves myeloid cells, including microglia and infiltrating macrophages (Peferoen et al., 2015; Sospedra and Martin, 2016). | https://doi.org/10.3389/fncel.2018.00072

Demyelination in MS

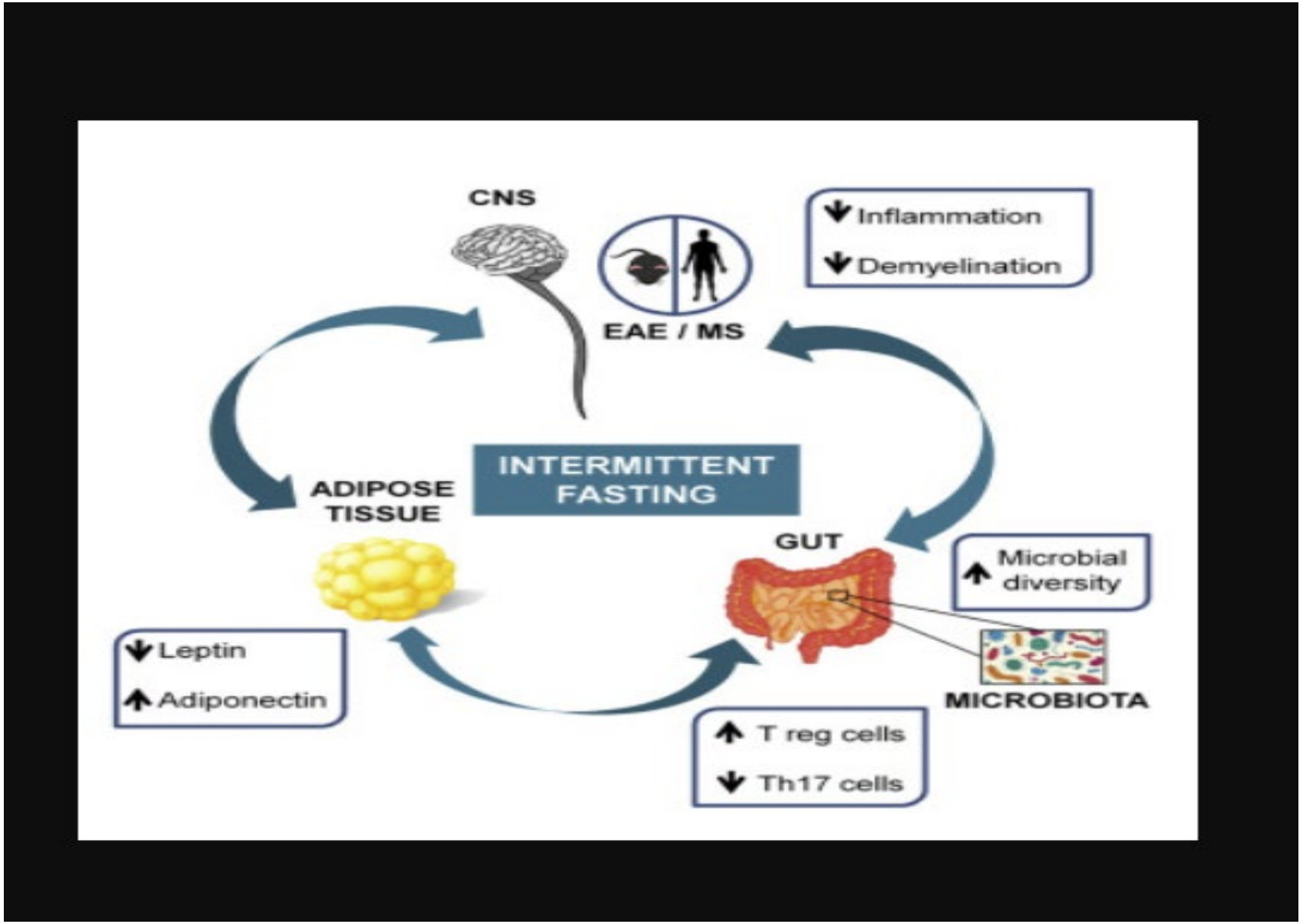
Demyelination causes signal loss and axonal damage that leads to loss of function
Gray matter and white matter damage
Specific antibodies identified in other CNS demyelinating diseases
MOGAD/ MOG, NMOSD/AQP4

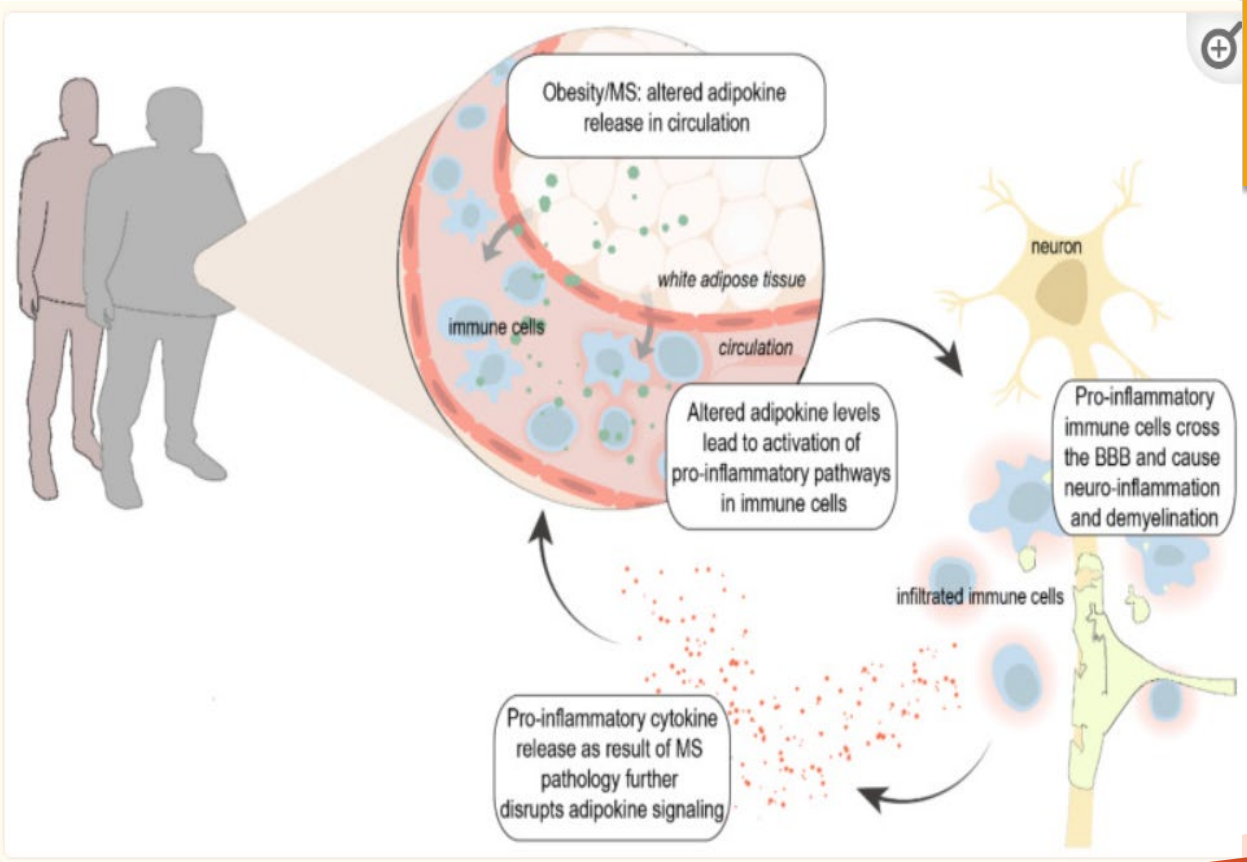
- January 2020, Journal of Neuroinflammation 17(1):21,DOI:10.1186/s12974-019-1667-1
- https://doi.org/10.3389/fimmu.2020.572186



Intermittent Fasting and Gut Microbiome

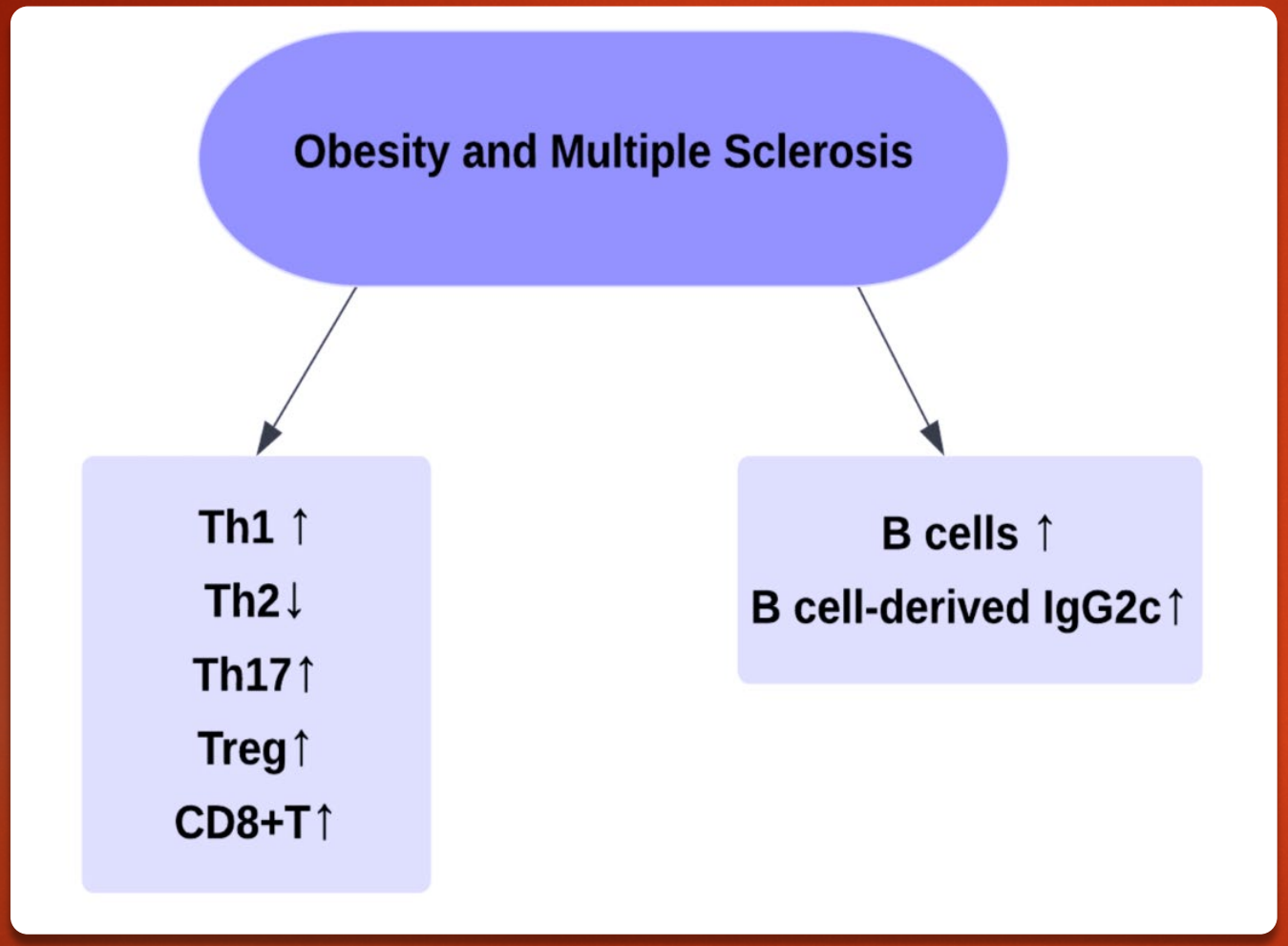
Reported at Actrims 2021 'Weight,Obesity and Adipokines" Laura Piccio MD PhD





Obesity and pro-inflammatory signaling

doi: 10.3390/ijms221910845

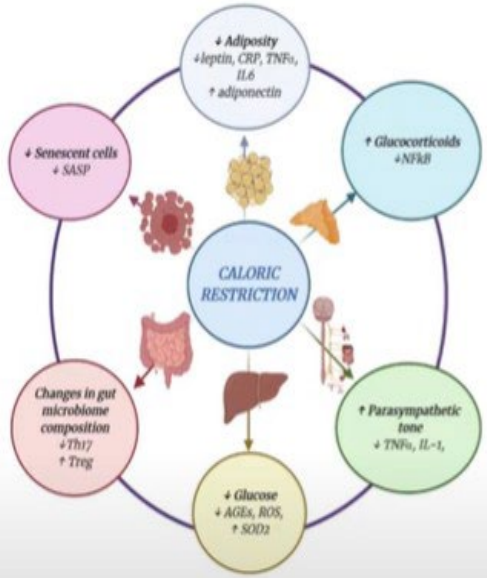


Obesity proinflammatory effects DOI: 10.7759/cureus.28975

ACTRIMS 2023 Calorie Restriction

- At the 2023 Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum, held February 23-25, in San Diego, California, research looked at the effects of intermittent calorie restriction (iCR) on adipokines levels, metabolic and immune/inflammatory biomarkers, clinical and brain MRI features in those with relapsing remitting MS.
- Led by Laura Piccio, MD, PhD, the study identified significant reductions in anthropometric and body adiposity measures in those on iCR over a 12-week period compared with those on an unrestricted diet. Other findings showed increases in adiponectin over the 6 and 12 weeks of dieting, as well as decreases in Th1 levels. Above all, patients on iCR showed significant improvement compared with an unrestricted diet in cognitive scores, assessed through the Symbol Digit Modalities Test.
- Ghezzi L, Tosti V, Cantoni C, et al. Randomized clinical trial of intermittent calorie restriction in people with multiple sclerosis: effects on immunometabolic and cognitive measures. Presented at: 2023 ACTRIMS Forum; February 23-25; San Diego, CA. Cutting Edge Developments.

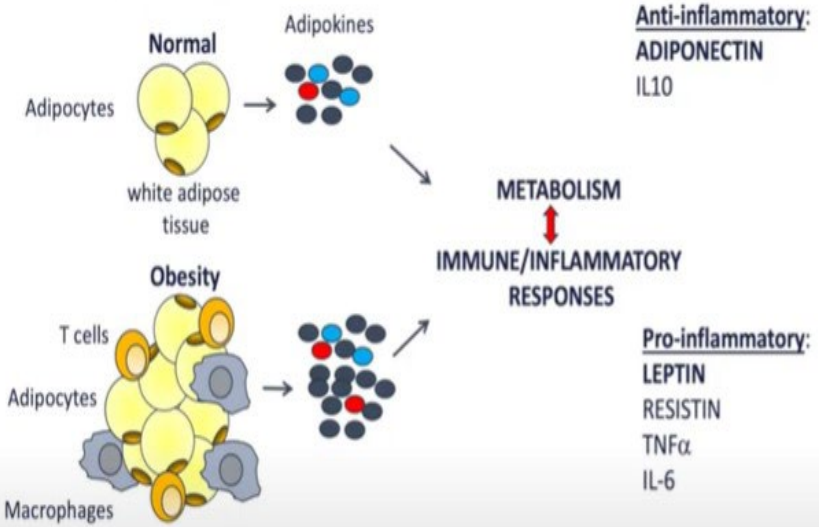
ANTI-INFLAMMATORY EFFECTS OF CALORIE RESTRICTION



- DR has an overall anti-inflammatory effect through different mechanisms.
- All main adaptations induced by CR on metabolic, hormonal, gut microbiota pathways lead to a reduction of systemic inflammation.

THE ADIPOSE TISSUE VIEWED AS AN ENDOCRINE ORGAN

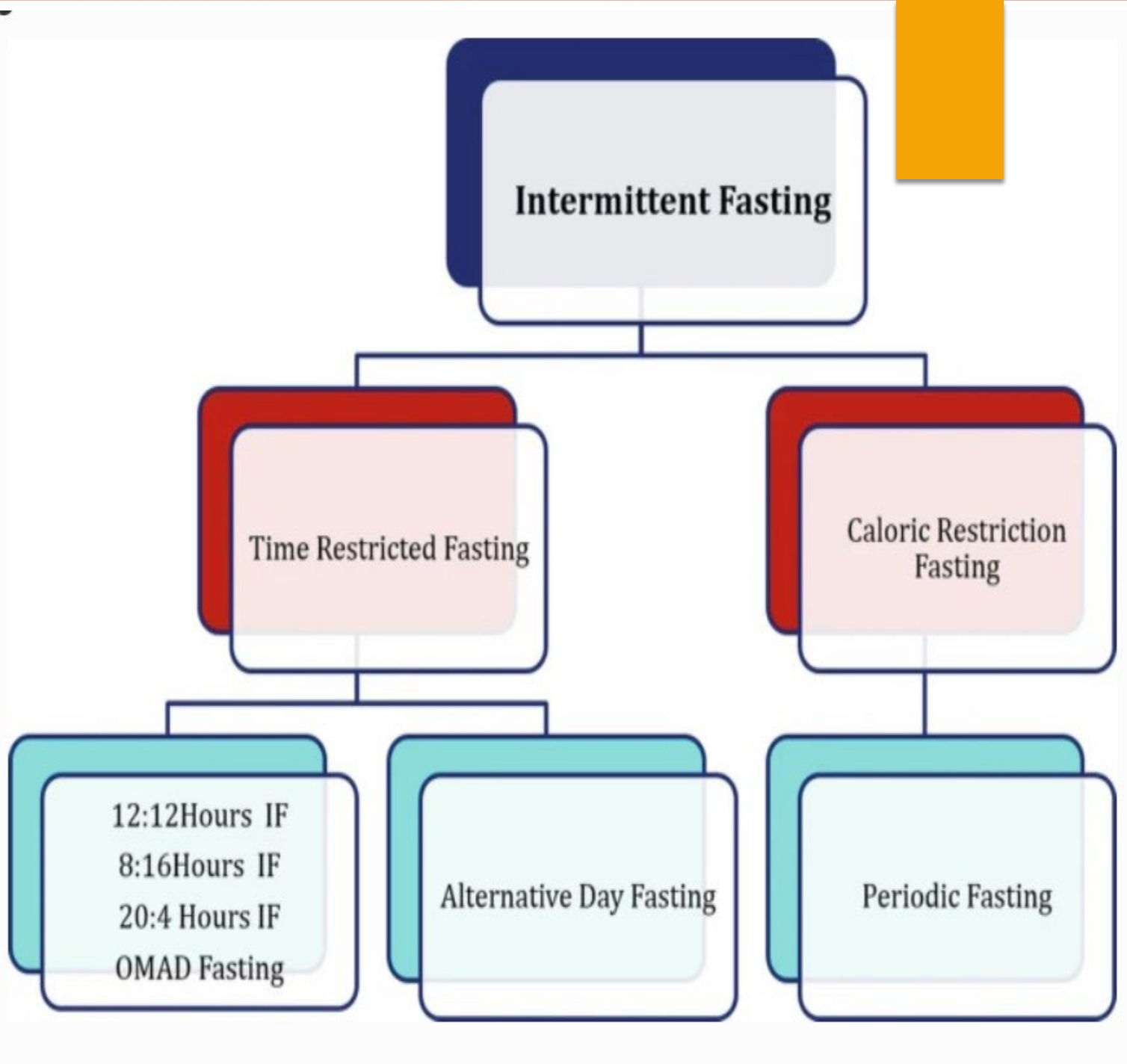
The white adipose tissue (WAT) functions is an endocrine organ secreting hormones, peptides and cytokines which are collectively referred as **ADIPOKINES**



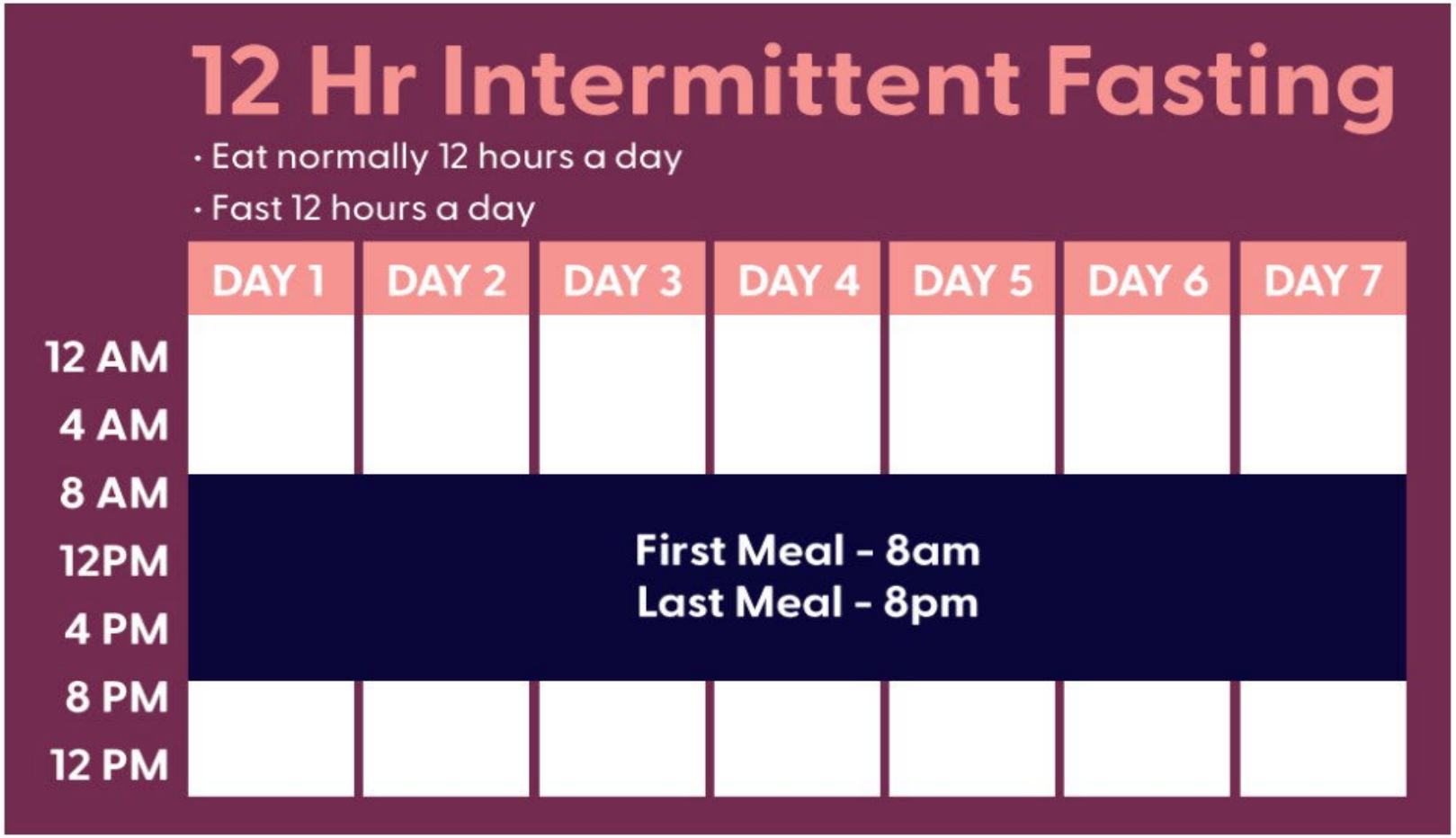
Calorie restriction in MS *Dr Laura Piccio ACTRIMS 2023

Types of intermittent fasting

- https://doi.org/10.1007/978-3-030-45923-9_26



Basic 12:12 Fasting Schedule



The Antioxidant Effect

▶During an MS flare, microglia become activated and release large amounts of free radicals (ROS). The brain is vulnerable to oxidative stress as a result of high metabolic activity. Evidence suggests that the antioxidant neutralizing mechanisms in MS patients are impaired leading to dysregulation and an inability to detoxify the tissue-damaging effects created by the inflammatory process.

▶Recent studies indicate that DMT's work in part by activating antioxidant mechanisms. Dimethyl fumarate has been shown to boost Nrf2 levels and increase the release of scavengers to reduce ROS in the brain. Other DMT such as Natalizumab Fingolimod, and cladribine have all demonstrated reduction in oxidative damage and increase in antioxidant effects by regulating the impaired free radical neutralizing mechanisms.

▶The use of diet and other interventions to reduce oxidative stress and increase antioxidant activity can be used as adjunct to traditional DMT to reduce the inflammation caused by dysregulation.

Can Diet Effect MS?

Diet can positively affect the overall health of an individual living with chronic disease. Reducing comorbidities can reduce the risk of disease progression. (CombiRx Trial)

Poor diet, obesity, low vitamin D and smoking can increase the risk of developing MS due to the pro-inflammatory effects of this type of lifestyle. Once the abnormal immune response has started however, ***there is no evidence to suggest that any diet can reverse this process*.**

Making changes such as eliminating food allergens, eating a healthy balanced diet, smoking cessation, belly fat reduction and vitamin D supplementation can have very significant effects on reducing inflammation by reducing oxidative stress.

Questions to ask before starting a Diet or Supplement;

Is it Harmful?

Is it cost prohibitive?

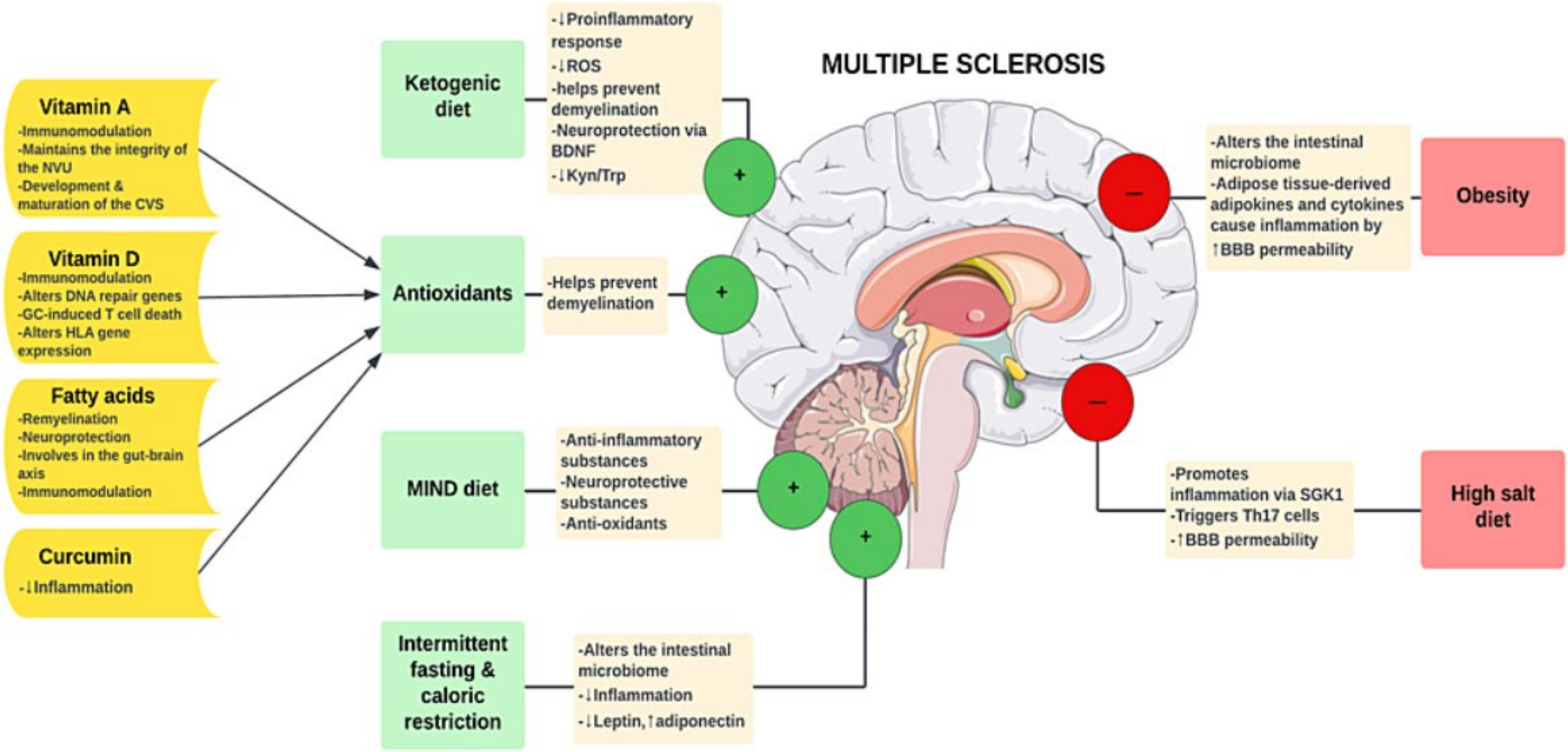
Is there evidence to support its use?

What is the best diet? Investigating popular trends

- **Ketogenic-** high fat, low carb diet mimics fasting. Small study presented AAN 2022, improved QOL metrics
- **Mediterranean Diet-** vegetables, fruits, whole grains, beans, nuts and seeds and olive oil. No refined foods, added sugars or processed meats
- **Anti-inflammatory Diets-** omega 3 fatty acids, long chain fatty acids
- **Protocol Diets-** Dr. Terry Wahls. Physician with SPMS U of Iowa. Increase cellular function and ATP production. Swank Protocol, MIND DIET
- **Intermittent Fasting/ Calorie Reduction**-. Intermittent fasting has recently received a lot of attention as a tool to reduce inflammation. There are some good results in MS trials regarding reduction of inflammatory markers and reduction of adiposity (body fat) which is pro-inflammatory. There are many ways to achieve intermittent fasting results with modified plans, strict 72- hour fasting is not the only method to achieve results

Effect of Diet Review

DOI: 10.7759/cureus.28975



Mitochondria

FUNCTIONS OF MITOCHONDRIA

- production of ATP (energy)
- regulation of immunity
- calcium balance
- cell death and renewal (autophagy)
- stem cell regulation

Mitochondria Functions

Figure 5 - Summary illustration that describes the solid impact of each diet upon five aspects of mitochondrial physiology. HFD, high-fat diet; CR, caloric restriction; Keto, ketogenic; MedD, Mediterranean diet.

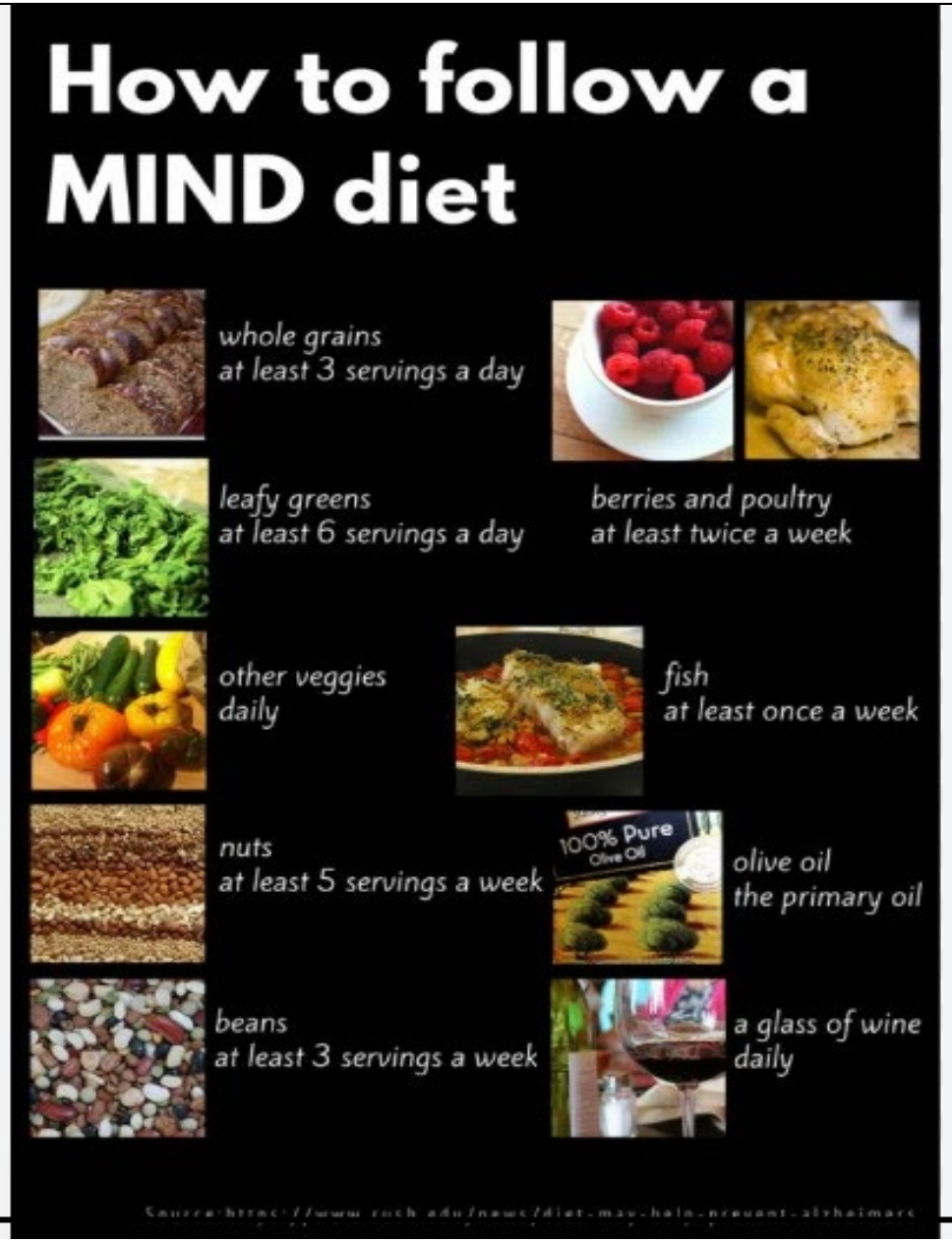
Mitochondrial Support

Mitochondria are known as the 'powerhouses' of cells, generating the essential energy in the form of adenosine triphosphate that is needed for energy demands. Their function easily adapts to the energy demands and the availability of chemical substrates. This allows cells to buffer sudden changes and reassure cellular metabolism, growth or survival. Humans have different dietary habits, that provide several stimuli to the cell. According to the energy substrate availability due to the diet quality and diet temporality, mitochondrial physiology is greatly affected.

https://doi.org/10.3892/ijmm.2022.5191

Whole foods diet

- **Whole plant foods**, which provide antioxidants to prevent or reduce inflammation in your body:
  - Vegetables
  - Fruit
  - Whole grains
  - Beans and lentils
  - Nuts and seeds
  - Herbs and spices
  - Extra virgin olive oil
  - Tea, ideally green tea
  - Coffee
- **Mushrooms (cooked)**, such as white button, crimini, shiitake, enoki, maitake, and oyster mushrooms.
- **Foods high in omega-3 fats:**
  - Walnuts
  - Ground flax seeds
  - Salmon
  - Mackerel
  - Anchovies
  - Sardines
  - Herring



MIND diet- Mediterranean-DASH Intervention for Neurodegenerative Delay developed by Dr Martha Clare Morris nutritional epidemiologist at Rush Chicago

doi:10.1016/j.jalz.2015.04.011.

Individualized Diet

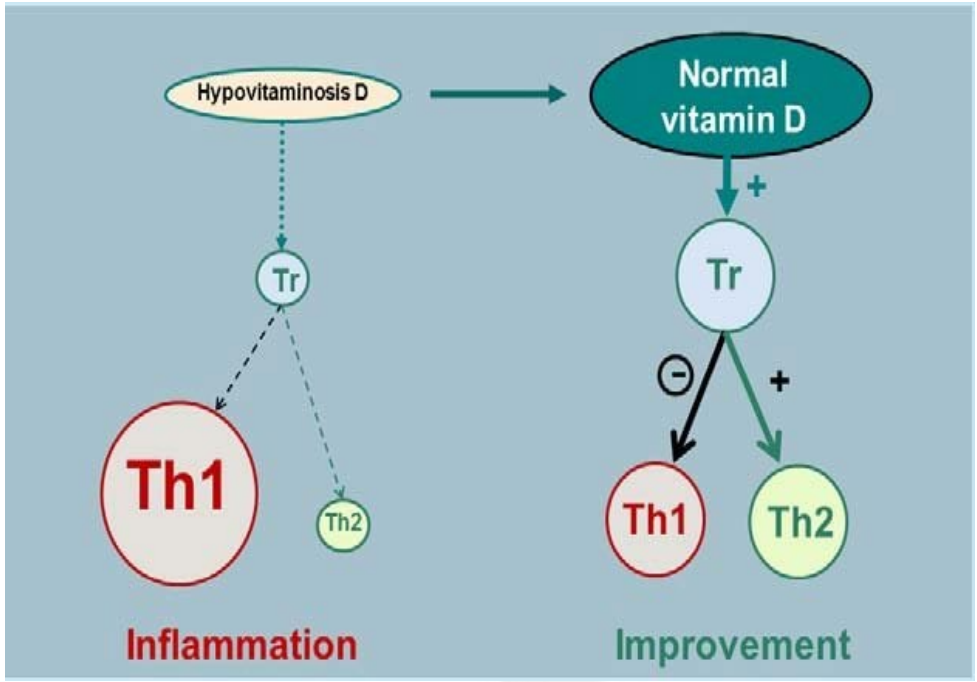
- Balanced diet with RDA of calories from protein, carbohydrates and fat. Reduce/avoid processed food, added sugar, saturated fats and processed meats. Heart healthy diet.
- Food Sensitivity Testing- Blood test, skin test
- Elimination Diets
- Food Journaling
- Gut Microbiome- Pre and Probiotics. Increase anti-inflammatory cytokines and T-regs. Keep tight gut junctions. 8-12 week adherence
- Consulting GI, Dietician when needed
- Interpreting results and formulating diet plan based on allergies, BMI and caloric RDA

Supplements frequently asked about in MS Clinic

- **Vitamin D**- Downregulates inflammation in CNS. Check serum levels and prescribe appropriately. Ample evidence in numerous trials.
- **Alpha Lipoic Acid-** some evidence in reduction of atrophy in progressive MS patients
- **Biotin**- Recent studies do not support any change in disability. MS SPI, SPI 2 trials
- **Turmeric Curcumin-** studies show curcumin exhibits neuroprotective effects in MS through anti-oxidant, anti-inflammatory, anti-proliferative and anti-differentiation mechanisms. Psoriasis trials. More MS trials are needed.
- **Antioxidants**- Reduce cellular oxidative stress. Examples ; Vitamin C, Vitamin E, Carotenoids
- **Pre and Probiotics –** Evidence suggests probiotic consumption via gut microbiome changes can have beneficial effects on improving immune/inflammatory response in MS.

Vitamin D

- Hypovitaminosis D is linked to higher disease activity
- Risk factor for development of MS
- Innate immune response is promoted, and adaptive response muted resulting in reduced cytokine production mediated by Type 1 T helper cells
- Provider will determine recommended daily dosage
- Monitor Serum levels regularly, avoid toxicity



Behavioral Changes

Energy Conservation

Exercise

Circadian Rhythm adherence

Yoga

Aqua therapy

Mindfulness

Fit Bit/Tracker

Counseling/Talk Therapy

Cognitive behavioral therapy

Summary

- MS has known risk factors some of which are modifiable
- Reducing risk can impact onset, and potential for progression of disease
- Chronic inflammation has negative impact on chronic disease
- Comorbid conditions can impact risk of disease progression
- Lifestyle interventions have been shown to positively impact chronic symptom severity
- Lifestyle modifications need to be evidence-based and practical to increase compliance
- The health care team is an integral part of implementing lifestyle changes by providing evidence-based recommendations and referrals to appropriate resources

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