

NUTRITION FOR MYELOPROLIFERATIVE NEOPLASM (MPN) PATIENTS

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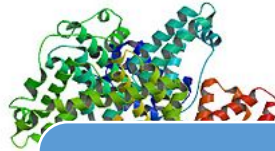
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Saturday April 22, 2017

THREE KEY COMPONENTS OF YOUR NUTRITION



Hydration



Protein

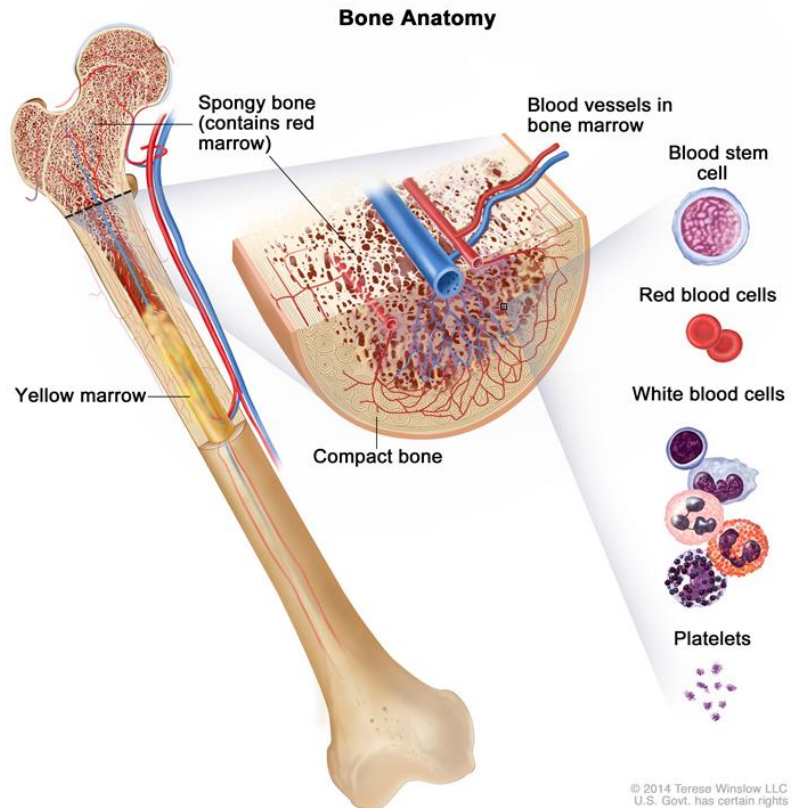


Fuel

- Low Glycemic
- Microbiome

BONE MARROW AND NUTRITION

- Your Bone marrow makes
 - Red cells (RBCs or erythrocytes)
 - Platelets (thrombocytes)
 - White cells (WBCs or leukocytes)
- Nutrients required
 - Protein
 - Essential Fatty Acids
 - Vitamin A
 - Vitamin B Complex
 - Vitamin D
 - Vitamin E
 - Vitamin K
 - Iron
 - Zinc
 - Selenium



MYELOPROLIFERATIVE NEOPLASM (MPN)

- Myelodysplastic/Myeloproliferative neoplasms are a group of diseases in which the bone marrow makes too many white blood cells ¹
- Bone marrow is found in the center of most bones and has many blood vessels. There are two types of bone marrow: red and yellow. Red marrow contains blood stem cells that can become red blood cells, white blood cells, or platelets. Yellow marrow is made mostly of fat ¹
- YAT, or yellow adipose tissue, bears its name due to a moderate number of mitochondria that gives it a yellowish appearance ²
- pRB-1 (Retinoblastoma-1) regulates yellow marrow ³



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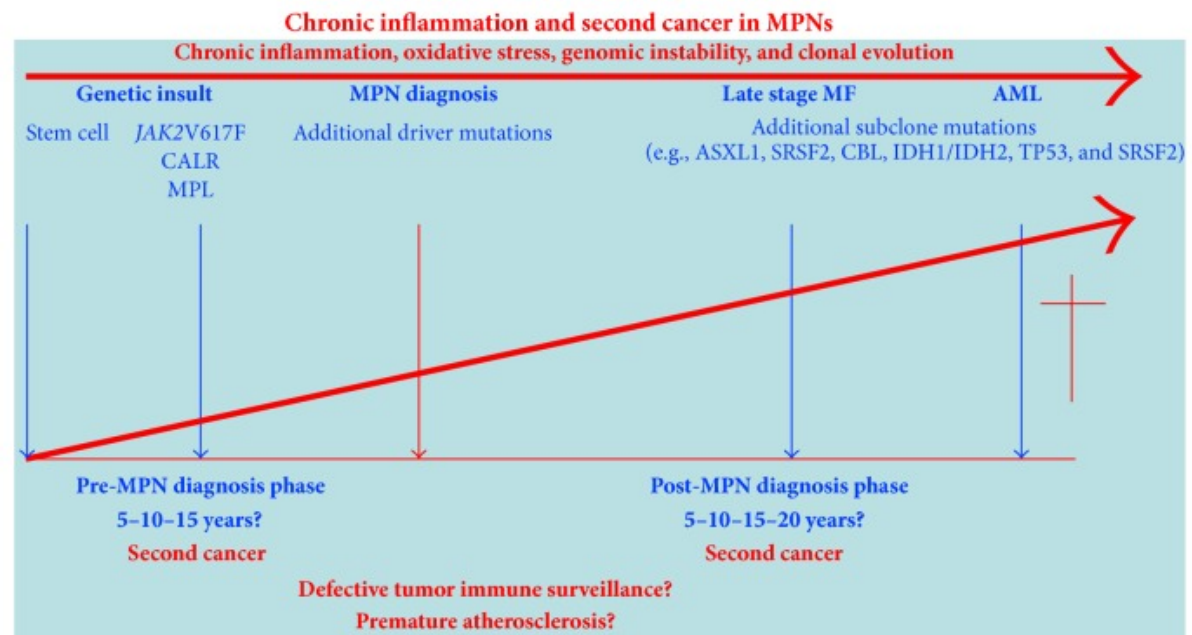
¹ National Cancer Institute, 2017

² Krings, A et al Bone 50:546, 2012

³ Eleizer, C et al Nature 466:1110 2010

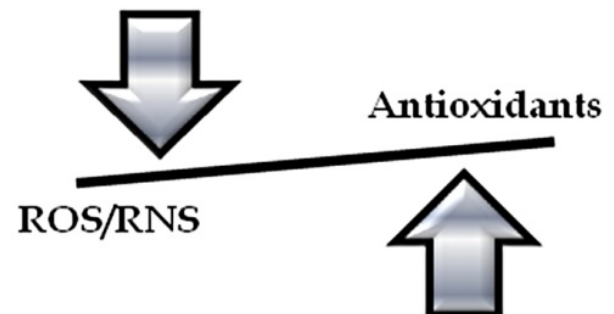
ROLE OF INFLAMMATION IN MPN

- Chronic inflammation may be an important driving force for clonal evolution and disease progression in the Philadelphia-negative **myeloproliferative neoplasms** (MPNs), essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) ¹



CHRONIC INFLAMMATION – IMBALANCE OF ANTIOXIDANTS AND REACTIVE OXYGEN SPECIES

- Energy production occurs in mitochondria (power houses of the cell) using oxygen; Red cells (erythrocytes) do not contain mitochondria but carry oxygen
- **Oxygen is stable in a paired state; unstable in unpaired free radical state (FR) Free Radicals** cause the formation of **Reactive Oxygen Species (ROS)** ROS are involved in apoptosis, necrosis and phagocytosis – ROS are important step in an acute phase immune response. Balance is created between pro-oxidant and antioxidant processes. **Antioxidants** are important in maintaining an equilibrium
- **Oxidative stress** occurs when this is out of balance



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CHRONIC INFLAMMATION

- Oxidative Stress is associated with chronic inflammation
- Chronic inflammation has been suggested to contribute to the development of premature atherosclerosis and may drive the development of other cancers in MPNs, both nonhematologic and hematologic ¹
- Diet plays a role in inflammation – Dietary Inflammatory Index (DII)¹ is a score used to describe the potential of diet to modulate systemic inflammation in the body ²
- Other factors include stress, physical activity and fitness, sleep patterns (night shift work) and central adiposity (visceral adipose tissue or VAT)

¹ Hasselbach, H & Bjørn, M, 2015

² DII developed by Cavicchia et al, 2012 and optimized by Shivappa et al, 2014 PMID2394862

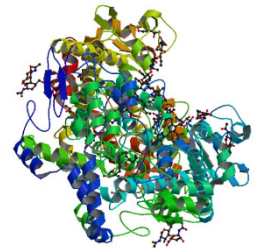


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CYTOKINES AND CELLULAR MEDIATORS

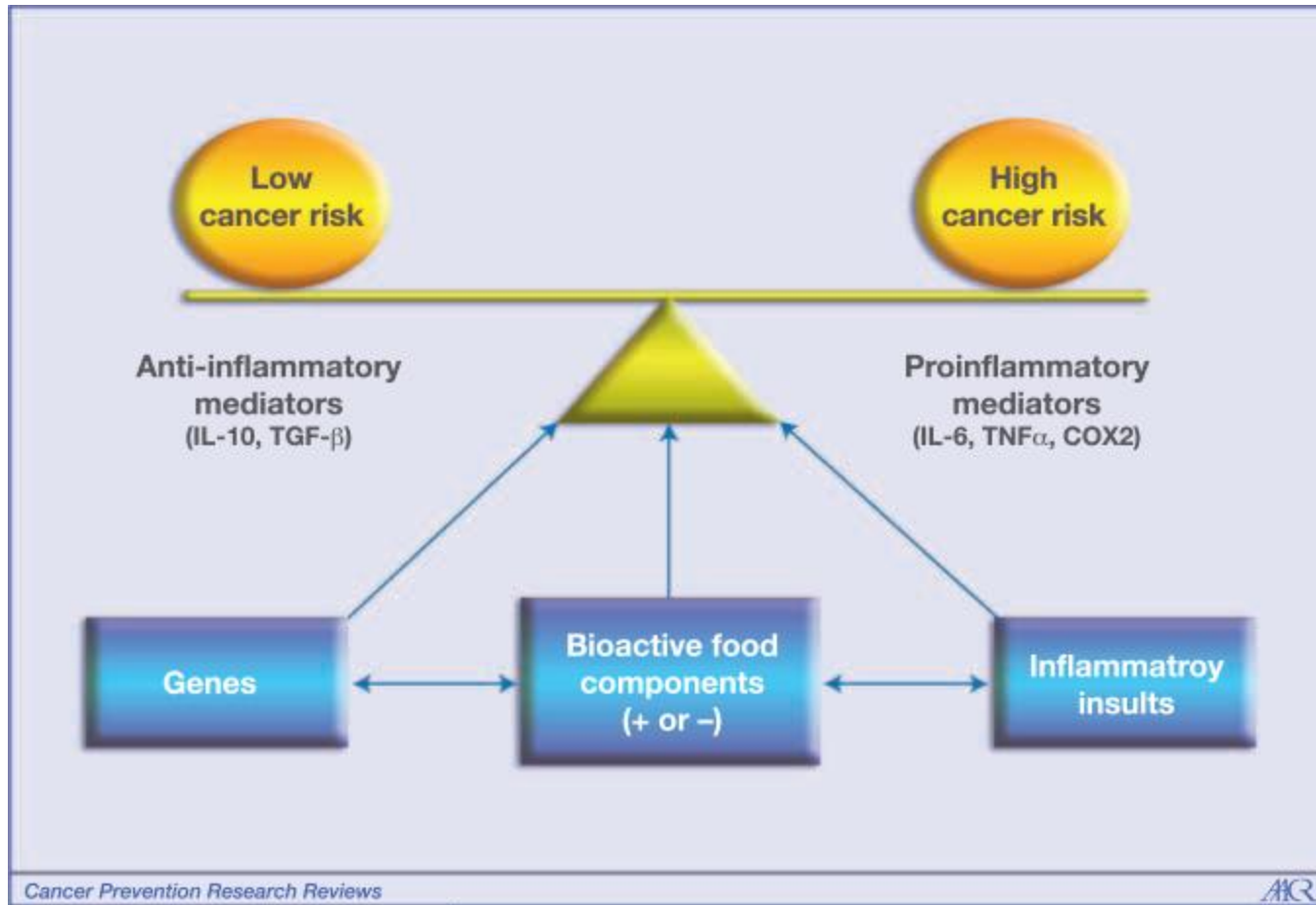
- Cytokines or cellular messengers involved in inflammatory processes include:
 - **NF-kappa B** (nuclear factor *kappa*-light-chain--enhancer of activated B cells)
 - **IL-6** (Interleukin-6)
 - **COX-2** (Cyclooxygenase -2) TNF- α – cytokine in macrophages
 - **IFN- γ** – cytokine in T cells and NK cells
 - **IL-1** – chemokine in macrophages
 - **Eicosanoids** including leukotrienes and prostaglandins

Cyclooxygenase-2 X-ray crystal structure
www.rcsb.org/3MDL



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INFLAMMATION AND CANCER RISK



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DIETARY INFLAMMATORY INDEX (DII)

- Developed as a research tool to characterize an individual's diet and association with inflammatory biomarkers **IL-6**, **hs-CRP** and **TNF α -R2** and **provide a DII score**
- Higher DII scores (pro-inflammatory diet) found to be associated with risk of colorectal cancer in postmenopausal women ¹
- Dietary factors with Anti-inflammatory score
 - Phytochemicals and micronutrients commonly found in vegetables and fruits
 - Whole grains/fiber
 - Certain spices and seasonings
- Dietary factors with a Pro-inflammatory score
 - Saturated fat and trans fat

¹Harmon, BE et al *J Nutr* 147:430, 2017



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FOODS AND SUPPLEMENTS TO SUPPORT HEALTHY REGULATION OF INFLAMMATION – LOW DII

- Chia seeds, hemp seeds, pumpkin seeds and flax seed oils (rich in omega-3 ALA); walnuts
- Oily fish including salmon and sardines (rich in omega-3 fatty acids EPA and DHA)
 - Supplements of DHA from microalgae
 - Purified supplements of fish or krill oil (DHA and EPA) or ethyl esters of omega-3 fatty acids such as salmon oil esters
- Culinary herbs and spices - Oregano, Curcumin and Ginger
- Garlic
- *Discuss all supplements you take with your health care team*



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ANTI-INFLAMMATORY FOODS

Anti-inflammatories prevent elevated rates of cell division which may increase “mistakes” Cells in resting stage have more time to be “corrected” as DNA repair takes place preventing chronic illnesses

- Omega 3 fatty acids (EPA and DHA)
- Flaxseed, borage and blackcurrant seed oils beneficial fatty acids (ALA and GLA)
- Natural salicylates, e.g. turmeric, rosemary, thyme, apricots, broccoli
- Naturally occurring COX-2 inhibitors include many natural plants used for centuries to preserve foods and to enhance flavors
- **Culinary herbs and spices contain natural COX-2 inhibitors**
Examples include basil, garlic, cilantro, chili peppers, rosemary, oregano, thyme, turmeric ¹

¹ Kaefer, CM, Milner, JA. *J Nutr Biochem*, 2008



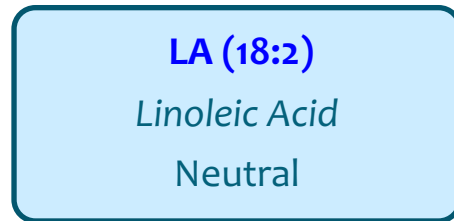
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OMEGA-6 AND OMEGA-3 FATTY ACIDS

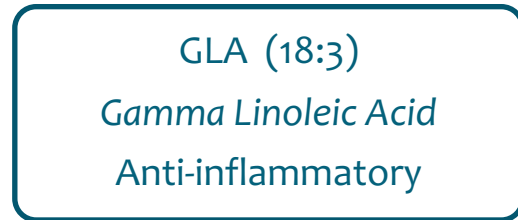
Omega-6

Omega-3

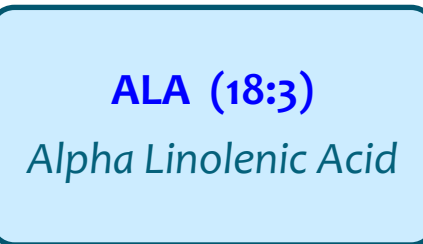
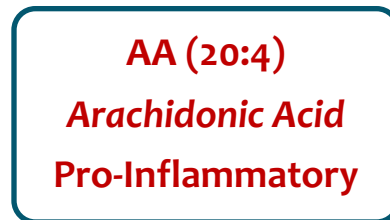
Vegetable oils
nuts and
seeds



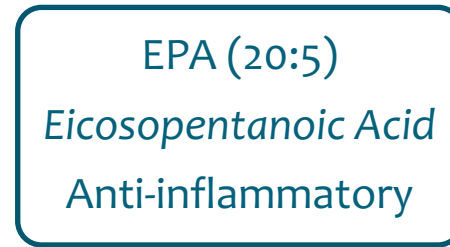
Borage
Evening
Primrose oil



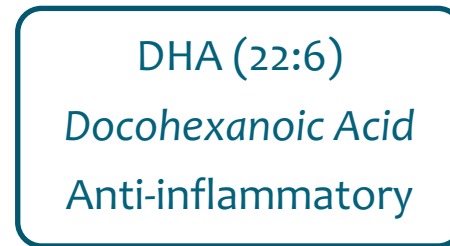
Red Meat
(especially
processed
meats)



Green leafy
vegetables,
flax, walnuts



Fish



Fish and
fortified
milk and
other foods

Table adapted from Simopolous, A. 1998

OTHER FOODS TO HELP PREVENT INFLAMMATION

- Foods rich in Vitamin D ¹
 - Salmon, fortified products including milks (dairy, nut & seeds)
- Low Glycemic Index foods
 - Rich in naturally occurring complex carbohydrates/dietary fiber
 - Low in added sugars
- Foods that support a healthy microbiome
 - High in prebiotics (complex carbohydrates or dietary fiber that support a healthy ecology of microbes – probiotics providing short chain fatty acids and supporting populations of other healthy microbes that are synergistic with each other)
 - Low in simple sugars which encourage growth of yeasts and disturb a healthy microbiome ecology



CHRONIC INFLAMMATION AND FATIGUE PREVENTION

- Eat small, frequent meals with sufficient protein (~60 grams per day for most people)
- Avoid sugar sweetened beverages without having a fiber rich snack (low glycemic load) snack at the same time
- Manage Glycemic load with addition of soluble fiber
- Be physically active to help raise mood and reduce fatigue
 - Yoga, T'ai Chi, Qi' Gong, walking
- Eat dark chocolate or drink organic green tea as healthy sources of stimulants
 - If you are sensitive to caffeine and similar stimulants – avoid after 3 PM
- Have sufficient rest and sleep – ideally 7-8 hours a night



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FOODS TO AVOID TO MINIMIZE FATIGUE AND REDUCE INFLAMMATION

- Foods with a high Glycemic Index
 - Baked goods with white flour, e.g. bagels
 - Pancakes with syrup
 - French fries
 - Candy
 - Breakfast cereals low in fiber with added sugars
- Processed meats (*these may disrupt a healthy microbiome and increase risk for colon cancer*)
 - Hot dogs
 - Salami



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OREGANO

- Oregano *Origanum vulgare* is **a natural COX-2 inhibitor** ¹
- Oregano contains
 - Apigenin
 - Kaepherol
 - Ursolic acid
 - Oleanolic acid
- Oregano is part of a Bouquet Garni (herb combination used in cooking soups, stews and casseroles)
- Oregano is in many soup recipes in The Cancer Nutrition Center Handbook



¹Liang, D et al *Inflammation* 37:1007 s, 2014



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CURCUMIN

- Curcumin is an **active principle found in the culinary spice turmeric** ¹
- Curcumin is both anti-inflammatory and antioxidant
- Traditionally used for pain relief and immune support
- Poorly absorbed for gastrointestinal tract it is best taken as standardized micronized curcumin with essential turmeric oil
- UCLA study on curcumin and Alzheimer's Disease uses Longvida ²
- Curcumin may potentiate some chemotherapies so should be **avoided on days around treatment** ³

¹ Mahashwari, RK et al *Life Sci* 78:2081, 2006

² Cole, GM, Frautschy, SA et al, *J Biol Chem*, 2012

³ Sankar Sen, S et al *J Biol Chem*, 2011



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GINGER

- Ginger *Zingiber officinalis* is a spice with active constituents 6-gingerol, 8-gingerol and 12-gingerol
- Gingerol upon heating becomes zingerone which is less pungent and has a spicy-sweet aroma
- 6-gingerol is a potent inhibitor of NF-kappaB, a signaling protein and mediates COX-2 expression ¹
- Essential oil of ginger is **good for nausea**



¹ Park, M et al, *Phytotherapy Research*, 2008

² Wallace, JM, *Integr Cancer Ther.* 2002



GARLIC

Garlic may be beneficial for MPN patients in several ways:

- Improve cardiovascular health
 - Garlic contains sulfur compounds including allicin
 - Allicin enhances fibrinolytic activity (breaks down clots)
 - Inhibits platelet aggregation in patients with coronary artery disease via a dose-dependent alteration in the production of arachidonic (Omega-6) metabolites
 - Altering physiochemical properties of the platelet membrane
- Improve liver and kidney function
 - Garlic sulfur compounds support healthy detoxification processes



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WHAT ABOUT COCONUT OIL?

- Coconut oil comes from crushing fresh coconut meat; it is rich in MCT (medium chain triglycerides), a type of saturated fat that is digested differently than most other types of fat and is thought to be more healthful
- Virgin “cold pressed” or unrefined coconut oil is healthful and is recommended up to 3 tablespoons daily
- Refined coconut oil (RFD) has been bleached and deodorized and is not recommended
- Much commercial coconut oil is heated and hydrogenated so contains *trans* fat (not recommended)



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COCONUT MILK AND OIL

- Coconut milk is also derived from coconut meat
- It is a rich source of calcium, magnesium and selenium
- Vitamins C,E, B1, B3, B5 and B6
- Coconut milk is also rich in antioxidants (highest in we milled unrefined milk
- Lauric acid is also present which converts in the body to monolaurin. Monolaurin has antibacterial and antiviral properties
- Virgin coconut oil (VCO) may reduce oxidative stress ¹

¹ Arunima, S Food Funct 9:1402, 2013



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HEALTHY BALANCE OF OILS AND FAT

*Recommended Fatty Acid Balance Omega 6:3 of ~4:1
(typical American diet is 15 to one)*

- 1 part Omega-3 (DHA and EPA from oily fish like salmon and sardines, walnuts and pine nuts)
- 3 parts mono unsaturated (olive oil, almonds and avocado)
- 1 part saturated fat (cocoa butter, palm oil or coconut or other plant source)
- Consider a supplement of purified fish oil or DHA from algae



FOODS TO AVOID

- Foods containing *Trans* Fat and PHOs
 - Partially hydrogenated vegetable oils (PHO) and baked goods made from them FDA no longer allows “Generally Recognized As Safe” or GRAS status for PHO’s
 - Deep-fried items such as fish sticks
 - Margarines
 - Shortening – pie crust
 - Refrigerated dough products (biscuits and cinnamon rolls)
 - Frosting
 - Non-dairy creamer
 - Microwave popcorn
 - Animal fat and dairy products



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FOOD SENSITIVITIES AND CHRONIC INFLAMMATION

- Food sensitivities *as separate from food allergy (IgE mediated response)* may be associated with chronic inflammatory responses mediated by IgG ¹
- Some individuals may find benefit from eliminating trigger diet components such as gluten or casein
- Other individuals find benefit in a rotation diet pattern (*3 days without the offending component and then eating a small quantity on the 4th day then repeating the cycle to “teach” the immune system*)
- Digestive enzyme supplements may be helpful for some
- The microbiome is thought to play an important role in food sensitivities. Probiotic supplements may also be helpful

¹ Rafei, A et al *Annals of Allergy* 62:94, 1989



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NUTRIENTS TO AVOID FOR MPN PATIENTS

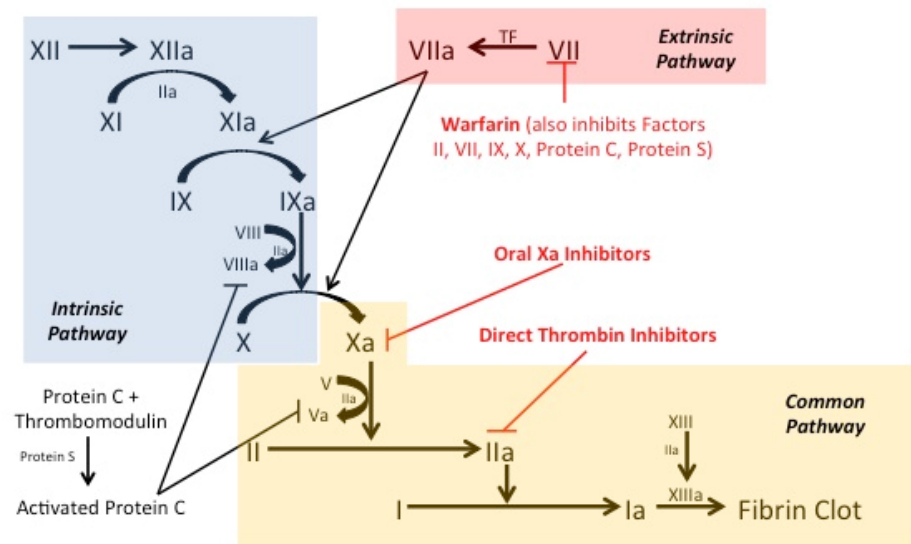
- **Strontium** (*found in some dietary supplements particularly those targeted for bone health and osteoporosis prevention*)
 - Has been associated with thrombosis and clotting
- Vitamin K in large and variable quantities *if taking warfarin (Coumadin®), phenprocoumon, acenocoumarol, or tiocloamarol anticoagulant medications*
 - There is no UL set for Vitamin K in other situations as it has low toxicity; RDA for adults 75 mcg
 - 1 cup of a green leafy vegetable like Kale provides more than 100% RDA of Vitamin K



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ANTI COAGULANTS

- >3200 naturally occurring coumarins in plants¹
- Protein C is coagulation factor XIV
 - Activated form (APC) plays an important role in anticoagulation, inflammation and cell death



I = Fibrinogen
II = Prothrombin, IIa = Thrombin
TF = Tissue Factor

NUTRIENTS WITH POTENTIAL ANTICOAGULANT ACTIVITY – AVOID IF HAVING SURGERY

- Angelica
- Anise
- Borage seed
- Celery
- Chamomile
- Clove
- Danshen
- Fenugreek
- Feverfew
- Garlic
- Ginger
- Ginkgo biloba
- Ginseng
- Horse chestnut
- Licorice root
- Onion
- Papain
- Parsley
- Turmeric
- Willow bark

¹Wang, C-Z et al Commonly Used Dietary Supplements on Coagulation Function during Surgery Medicines (Basel), 2015



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MORE FOODS WITH POTENTIAL BENEFITS FOR MPN PATIENTS -BLACK RASPBERRY AND LEUKEMIA PREVENTION

- Black raspberry *Rubus occidentalis* is native to North America and grows well in MidWest and New England. The cultivar Jewel has been studied for anthocyanin health benefits
- Cyanidin-3-rutinoside induces apoptosis in several leukemia and lymphoma cell lines *in vitro* ¹

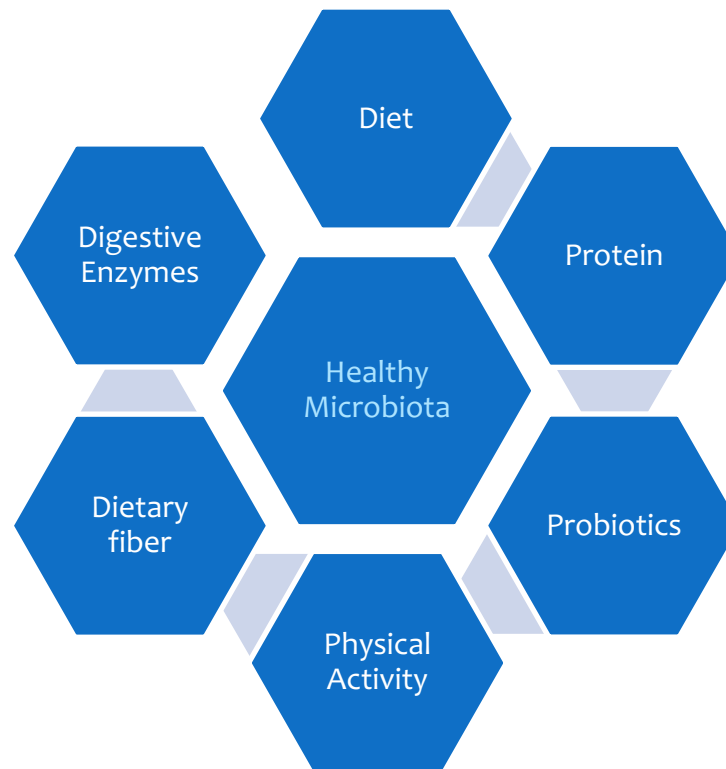


¹Feng, R et al *J Biol Chem* 18:13468, 2007



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WELLNESS CENTERED AROUND THE MICROBIOME

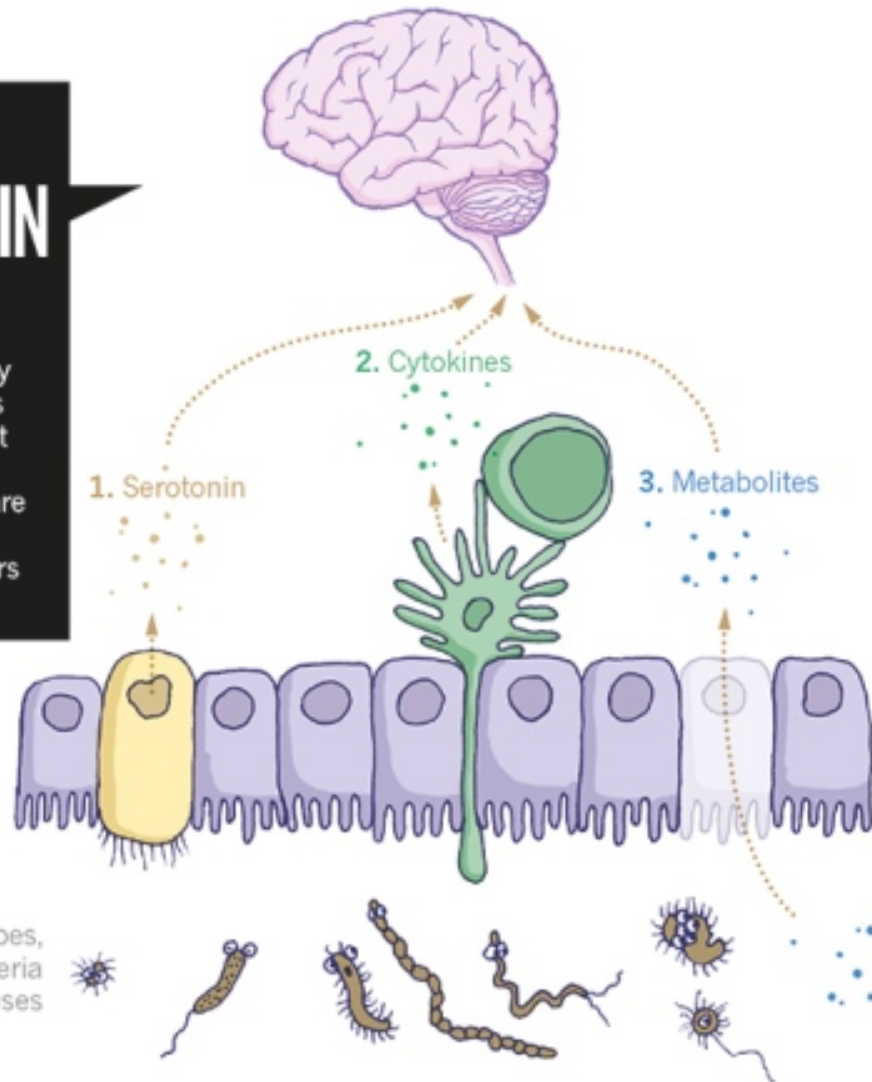


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THE GUT-BRAIN AXIS

The mechanisms by which gut microbes and the brain might communicate are unclear, but there are several tantalizing leads for researchers to follow.

Gut microbes, including bacteria and viruses



1. PERIPHERAL SEROTONIN:

Cells in the gut produce large quantities of the neurotransmitter serotonin, which may have an effect on signalling in the brain.

2. IMMUNE SYSTEM:

The intestinal microbiome can prompt immune cells to produce cytokines that can influence neurophysiology.

3. BACTERIAL MOLECULES:

Microbes produce metabolites such as butyrate, which can alter the activity of cells in the blood-brain barrier.

WHAT ARE PROBIOTICS?

- Probiotics are living microorganisms which, when administered in adequate amounts, confer a health benefit on the host ¹
- Probiotics (Bios is Greek for “Life”) opposite of antibiotics
- Bifidobacterium and Lactobacillus genus ^{2, 3}
- New dietary supplements from new knowledge of the microbiome learned from identification using 16S rRNA include specific strains of Bifidus Spp and/or Lactobacillus Spp, e.g. Activia® yogurt and supplements Align® and Culturelle®
- A good yogurt should contain 20 billion cfu (colony forming units) per 8 fl oz serving ⁴

¹ World Gastroenterology Organization Practice Guidelines, 2008

² International Scientific Assocn for Probiotics and Prebiotics www.isapp.net

³ Woese, CR, 1987

⁴ Hufnagle, G , 2009



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WHAT ARE PREBIOTICS?

- Prebiotics are **non-digestible food ingredients** that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus **improve host health**¹
- Selection of prebiotics should be by 3 criteria
 - Be resistant to degradation by stomach acid, enzymes or hydrolysis
 - Fermented by intestinal microbes
 - Selectively stimulate growth and/or activity of beneficial microorganisms in the gut FOS and GOS are examples
- Examples of prebiotics include inulin and other FODMAPs (Fructo-,Oligo-,Di-,Mono-saccharides And Polysaccharides)

¹ *International Scientific Association for Probiotics and Prebiotics* www.isapp.net



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A TYPICAL MENU PLAN

- *Breakfast* Oatmeal or other whole grain cereal, milk, berries or raisins
- *Snack* Banana or 1 tablespoon apple sauce
- *Lunch* Salad with dark leafy vegetables (lettuces, spinach, etc.) topped with colorful vegetables. Parsley, chives and fresh herbs are good. Sprinkle slices of avocado, a few pine nuts and sunflower seeds for added benefit. Tuna, hard boiled eggs or lean chicken for protein



A TYPICAL MENU PLAN (CONTD.)

- *Snack* 1 tablespoon almond butter on rice cake or whole grain cracker OR small square of dark chocolate
- *Dinner* Salmon or other fish, lean red meat (not more than once a week) or chicken or turkey or tofu or vegetarian protein (Quorn for example), 2 or more steamed vegetables or stir fry in (small quantity) of sesame or olive oil, brown rice, baked potato, corn or whole wheat tortilla, fresh berries for dessert
- *Snack* Warm almond milk with cinnamon
- *Beverages* Iced green tea, water (1.5 – 3 liters a day all fluids)



SOME SNACK IDEAS

○ Nuts

- Lightly salted, roasted almonds or pistachios
- Walnuts (about 14 halves equal 1 ounce)
- Nut butters on apple slices or rice cakes

○ Beans and Dips

- Hummus or Babaganoush ¹ on pita chips

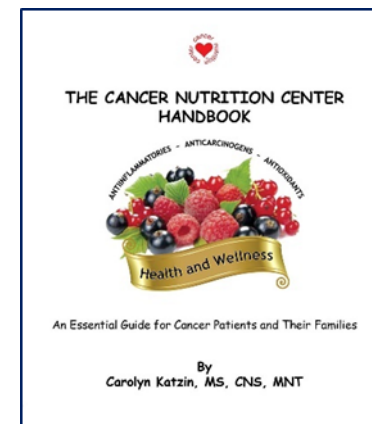
○ Dried fruit

- Prunes and apricots

○ Fresh fruit

- Oranges, kiwi, apples, pears

○ Hard boiled eggs



¹ *The Cancer Nutrition Center Handbook, page 35*
ISBN 978-0-9851736-7-4



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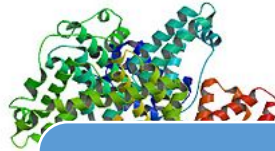
THREE KEY COMPONENTS OF YOUR NUTRITION

Anti-Inflammatory Focus – Omega-3 rich,
Culinary herbs and spices, Vegetables from
Garlic family and Berries



Hydration

- Head & Neck
- Digestive cancers



Protein Focus

- Surgery
- Radiation



Fuel

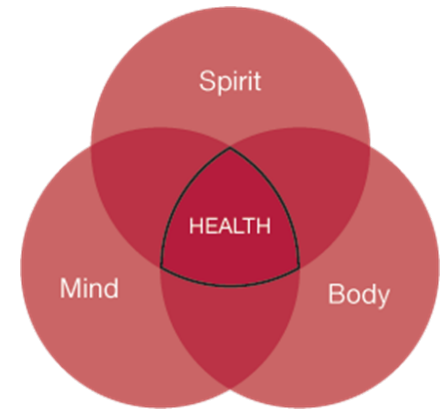
- Low Glycemic
- Microbiome



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INTEGRATIVE ONCOLOGY AND NUTRITION

- Integrative oncology blends conventionally trained and complementary approaches
- Goal of optimizing wellness by balancing
 - MIND
 - BODY
 - SPIRIT
- Symptom management and stress reduction improves quality of life by
 - Reducing side effects during and after treatment
 - Helping to recover and maintain health and wellbeing



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USE INTEGRATIVE TOOLS TO SUPPORT A HEALTHY LIFESTYLE

- Eat small, frequent meals rich in natural colors and aromas
 - Include culinary herbs and spices
 - Include salmon and other oily fish often
 - Include nuts and seeds daily
- Have a regular eating pattern allowing for a small protein snack 2-3 hours before bedtime to support repair processes that occur during the night
- Get restful sleep
- Use breathing techniques to help manage stress



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