Nutrition in Cancer?

Nature Immunology volume 18, pages 843–850 (2017)
Diets
Effective in Other Diseases

Blood Clots

- South Beach Diet?
- Ketogenic diet?
- Mediterranean diet?
- Anti-Inflammatory Diet?

Mortality

- Vegan Diet?
- Intermittent Fasting?
- Paleo diet?
- Juice Cleanses?
- Atkins Diet?

Inflammation

Chronic Myeloid Blood Cancers are not the Typical “Cancer”

Hematopoietic Stem Cells → Driver Mutation Arises → Hematopoietic Clone Develops → Hematologic Cancer Develops

MPNs are not Alone…

![Graph showing the percent of participants with various types of clonal hematopoiesis across different age groups.](N Engl J Med 2014; 371:2477-2487)
What are Important Nutrients for Blood?: B12

B12 Deficiency

- Low Blood Counts
- Hypothyroidism
- Fatigue
- Depression
- Neuropathy (Numbness, tingling)
- Memory/Cognitive Issue
What are Important Nutrients for Blood?: B12

Key:
B12 can become elevated in inflammation: Methylmalonic Acid can help better identify B12 issues
What are Important Nutrients for Blood?: Folate

Folate Deficiency

- Low Blood Counts
- Mouth Sores
- Fatigue
What are Important Nutrients for Blood?: Folate

**Key:** Sometimes other than testing for folate, I will test for Homocysteine
What are Important Nutrients for Blood?: Iron

Iron Deficiency

- Low Blood Counts
- Fatigue
- Restless Leg Syndrome
- Memory/Cognitive Issue
Ferritin can be elevated in inflammation, I also check Iron Studies

**Keys to taking oral iron:**
- Only once per day needed
- Phosphates inhibit absorption
  - No sodas, teas, coffee around the time of taking iron
- Vitamin C (ascorbic acid)
  - Take iron with a glass of orange juice

**Iron Rich Foods:**
- Chicken
- Liver
- Beef
- Pork
- Egg Yolk
- Shrimp
- Broccoli
- Dried Beans/Green Peas
- Potatoes with Skin
- Spinach
- Iron Fortified Cereals
- Raisins
- Dried Apricot
- Watermelon
Glucose... Good or Bad?

Monosaccharides (glucose)
Disaccharides (sucrose)
Polysaccharides (amylose starch)

Carbohydrates

Simple
Monosaccharides
- Glucose
- Fructose
- Galactose

Disaccharides
- Maltose
- Lactose
- Sucrose

Complex
Polysaccharides
- Starches
- Fibers
- Glycogen

Fibers = Indigestible sugars (Good)
Excess Nutrient Consumption
Obesity, PCOS, Diabetes
Metabolic Syndrome

HSC

Oxidative Stress
Increased

Excess Glycosylation

Carbohydrates

Amino Acids

MTOR

RAS
RAF
MEK
ERK

Inflammation
IL-6, TNF-α

IGF-1
Insulin

Increased Myeloid Differentiation and Proliferation
Defective Stem Cell Function
Impaired Bone Marrow Niche
Increased ROS and DNA Damage
“Hyper-aging” Profile
Inflammation
Driving MPN Mutant Cell Growth

MPN Development

Acquisition of the JAK2v617f mutation

Suppressed growth WT

Auto-production of inflammatory cytokines

TNF-α

Induce bystander cell production of inflammatory cytokines

Inflammatory cells
Production of IL-6, IL-8, IL1B, bFGF, LCN2

BM Stromal Cells
Production of TNF-α, VEGF, TGF-b, BMP2, RUNX2, osteoprogenin, collagen type I

Koschmieder et. al. Leukemia 2016
Inflammation contributes to...

Symptoms

Nutritional Deficiencies

Low blood counts

Thrombosis

Organ Dysfunction

Sequelae of Inflammation

Thromb Haemost. 2010;104(1):151-6
Leukemia 2012(26): 563–571
JCO 2015 33(20):2288-2295
Foods With Independent Anti-Inflammatory Potential

- Fruits/Berries
- Green Leafy Vegetables
- Turmeric/Curcumin
- Nuts
- Dark Chocolate
- Oily Fish
- Green Tea
- Garlic
- Many other herbs and spices
- Whole Grains

*Just to name a few*...
### Intermittent Fasting: Anti-Inflammatory

#### Improved Microbiome
- Reduced Inflammation
  - IL-6 ($p < 0.001$), CRP ($p < 0.001$) and homocysteine ($p < 0.01$) levels

#### Reduced Inflammation
- Improved Insulin Sensitivity
- Lowers Resting HR

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BMI and Symptom Burden

AACR 2019 abstract, being presented later this month
The NUTRIENT Trial
Nutritional Survey: Part IA

- An internet-based survey hosted by the Mayo Clinic Survey Research Center
- Promoted on multiple MPN-based forums, Facebook pages and websites during February of 2017.
- 55-item questionnaire regarding nutritional and supplement use habits, needs and preferences

N=1329 Respondents
75% Female
Median age 60 years
Respondents represented MPN patients from 40 countries
### Food allergies and/or Intolerances

<table>
<thead>
<tr>
<th>Food allergies and/or Intolerances</th>
<th>Frequency among all respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>8.3%</td>
</tr>
<tr>
<td>Wheat</td>
<td>6.9%</td>
</tr>
<tr>
<td>Fruit</td>
<td>4.1%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>2.8%</td>
</tr>
<tr>
<td>Soy</td>
<td>2.3%</td>
</tr>
<tr>
<td>Peanuts</td>
<td>1.7%</td>
</tr>
<tr>
<td>Egg</td>
<td>1.4%</td>
</tr>
<tr>
<td>Tree Nuts</td>
<td>1.4%</td>
</tr>
<tr>
<td>Fish</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

### Dietary Restrictions

<table>
<thead>
<tr>
<th>Dietary Restrictions</th>
<th>Frequency among all respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low salt</td>
<td>6.6%</td>
</tr>
<tr>
<td>Gluten-free</td>
<td>6.5%</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>6.0%</td>
</tr>
<tr>
<td>Vegetarian</td>
<td>5.7%</td>
</tr>
<tr>
<td>Low fat</td>
<td>5.3%</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>5.1%</td>
</tr>
<tr>
<td>Lactose intolerant</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

34.0% of patients endorsed **using diet** to help control their symptoms or MPN disease.
Nutritional Survey in Chronic Blood Cancers

<table>
<thead>
<tr>
<th>Correlative</th>
<th>Mean symptom burden (MPN-10)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Not Following Diet</td>
<td>Following Diet</td>
</tr>
<tr>
<td>Diabetic diet</td>
<td>3.33</td>
<td>4.67</td>
</tr>
<tr>
<td>Lactose Intolerant</td>
<td>3.35</td>
<td>3.87</td>
</tr>
<tr>
<td>Food Intake (Dichotomous)</td>
<td>Never</td>
<td>At Least Once Per Week</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3.62</td>
<td>3.11</td>
</tr>
<tr>
<td>Fast Food</td>
<td>3.24</td>
<td>3.59</td>
</tr>
<tr>
<td>Fried Foods</td>
<td>3.22</td>
<td>3.46</td>
</tr>
<tr>
<td>Rice</td>
<td>3.57</td>
<td>3.30</td>
</tr>
<tr>
<td>Soda</td>
<td>3.22</td>
<td>3.72</td>
</tr>
<tr>
<td>Food Intake (Continuous)</td>
<td>Pearson Correlation</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>-</td>
<td>-0.139</td>
</tr>
<tr>
<td>Baked Goods</td>
<td>-</td>
<td>-0.070</td>
</tr>
<tr>
<td>Dairy other than Cheese (milk, cream)</td>
<td>-</td>
<td>-0.069</td>
</tr>
<tr>
<td>Fast Food</td>
<td>-</td>
<td>0.104</td>
</tr>
<tr>
<td>Fried Foods</td>
<td>-</td>
<td>0.086</td>
</tr>
<tr>
<td>Pasta</td>
<td>-</td>
<td>-0.072</td>
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<tr>
<td>Pre-made Snack Foods</td>
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<td>0.067</td>
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<tr>
<td>Soda</td>
<td>-</td>
<td>0.121</td>
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<tr>
<td>Refined Sugars</td>
<td>-</td>
<td>0.075</td>
</tr>
<tr>
<td>Tacos</td>
<td>-</td>
<td>0.068</td>
</tr>
</tbody>
</table>

Foods associated with worsened symptom score in **red**, foods associated with improved score in **green**
96.2% of MPN patients endorsed being willing to restrict their diet if it helped to control symptom burden.

98% of patients were willing to restrict their diet if they could help their MPN to stabilize or reduce the risk of their MPN getting worse.
Patients desire a tailored dietary intervention which addresses their needs and preferences.

Patients express concern over the lack of resources regarding diet.

Patients frequently have food restrictions or intolerances that are related to their MPN disease course and symptoms.

Patients are enthusiastic regarding participation and execution of a dietary intervention.

Patients desired the ability to connect with each other and with researchers.

Patients desire a tailored dietary intervention which addresses their needs and preferences.

- MPN participants recruited from the “We are MPN” participant conference in Irvine, California in April 2017.
  - N=13, 77% female, 45% from the Irvine, California area.
Primary Endpoint: combined >70% Dietary Adherence and >5/10 patient-reported feasibility

Meeting with a nutritionist for diet education

- Blood draw
- BMI

- 24-Hour Diet recall
- MPN-10

MPN Nutritional Trials

NUTRIENT Study

UCI/Mays Collaboration

Enrollment N=30

Screening Visit

Month 1 Month 2 Month 3 Month 4

Myeloid Hematologic Neoplasm Patients n=15

Age-Matched Healthy Controls n=15

Screening

Registered Dietician Visits

Daily Ketone Assessment

Dietary Intervention

Phlebotomy

NUTRIENT Study

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Dietary Intervention

Phlebotomy
Increased Hematopoietic Cell Diversity
Reduction in Inflammatory Symptoms
Impaired Bone Marrow Niche
Decreased ROS and DNA Damage

Nutritional Ketosis Fasting

Reduced Reactive Oxygen Species
Improved Antioxidant Potential
NAD⁺/NADH

Histone Demethylation
HDAC

NFκ-B
NLRP3 Inflammasome

Ketones

Acetoacetate

B-hydroxybutyric Acid

HSC

IL-6, TNF-α

Mays Cancer Center
UT Health San Antonio
MD Anderson Cancer Center
Potential changes with a Diet….

Dietary Intervention

- NFkB Activation
- NLRP3 Inflammasome Function
- HDAC Function

HSC

- CBC hyper-/Hypo-proliferation
- IL-1, IL-6, IL-8, TNF-a, CRP
- Disease Symptom Burden

- TET2
- ASXL1
- DNMT3A
- IDH1/2

Reduction in Genetic Marker Alterations
So, Dr. Scherber, What Should I Eat?

No data yet on what diet is best
But you can’t go wrong with general principals:

Eat Lots of:
- Grilled chicken
- Salmon
- Eggs
- Various spices
- Berries

Limit intake of:
- Sweetened beverages
- Processed foods
- Fast food
- Fries
Intent to treat analysis demonstrated significant survival advantage for patients with higher QOL at baseline (HR 1.47, p=0.02)

Scherber et al. Haematologica 2017. 102 (S1) E1351
Early data suggests nutrition may play an important role in the care of MPN patients. Efforts to look at this closer are ongoing – not enough evidence to suggest dietary change as of yet! For now, a healthy diet and focusing on QOL is key!
Questions/Comments

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