Health and Wellness: Beyond the Medicine Cabinet

April 25, 2022

10 AM PT, 11 AM MT
12 PM CT, 1 PM ET
Pre-Event Notes

- The audience is muted
- Please direct your questions to CLL Society staff and speakers using the Q&A function (located at the bottom of your screen) at any time throughout the presentation
- Questions can only be seen by staff and speakers. We will do our best to answer as many questions as possible
- Please complete the short survey emailed after the event. Your response will help CLL Society plan future events
- The virtual event is being recorded and will be available on our website
- Closed captions are available. If you want to turn them on or off, go to Live Transcript and Show Subtitle or Hide Subtitle
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Speakers

Glenn Sabin
CLL Patient Advocate

Gordon Saxe, MD, PhD, MPH
Preventive and Integrative Physician
UC San Diego Health

Andrea Sitlinger, MD
Assistant Professor of Medicine
Duke University School of Medicine

CLL Society Staff

Welcome
Robyn Brumble, MSN, RN
Director of Scientific Affairs and Research
CLL Society

Moderator
Brian Koffman, MDCM (retired)
MS Ed
Executive Vice President and Chief Medical Officer
CLL Society
• CLL Society encourages all patients to discuss with the healthcare team about what would be their best approach to diet, exercise, lifestyle changes and supplements to help with the management of their CLL/SLL.

• Healthy decisions can be very beneficial but should always be coordinated with the doctors and their team who are managing their CLL/SLL.
Leveraging Lifestyle for Immunity and Resiliency

Glenn Sabin
CLL Patient Advocate

April 25, 2022
Diet in the Prevention of Cancer

Gordon Saxe MD, PhD

April 25, 2022
Cancer: A Bolt From Out of the Blue?
**International Variation in Prostate Cancer**

<table>
<thead>
<tr>
<th>Country</th>
<th>Rate per 100,000</th>
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<tr>
<td>China</td>
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</tr>
<tr>
<td>Sweden</td>
<td>55.3</td>
</tr>
<tr>
<td>United States</td>
<td>102.1</td>
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Cancer Development: Initiation vs. Promotion

- **Initiation:**
  - Mutation in cell that predisposes it to become cancerous

- **Promotion:**
  - Proliferation of mutated cell that causes it to form a cancer

- If we stop promoting initiated cells, we may be able to slow the growth of cancers and possibly even cause them to stop growing or regress
Cancer Development: Initiation vs. Promotion

- Mutated cells are like individual pieces of grass and the cancer is like an entire lawn
  - We’re highly skilled at mowing the grass
  - But maybe we should also try to stop overwatering the lawn?
What are the promoting factors?
Possible Nutritional Cancer Promoters

- Obesity
- Excess calories
- Sugar and refined/processed foods
- Excessive protein or fat
- Inflammatory fats (high in omega-6, low in omega-3)
- Dairy/casein
- Deficiency of fibrous plant foods
- Deficiency of phytonutrients
- Vitamin D deficiency
- Gut microbiome imbalance
Nutrition and CLL

- Western diets linked with higher incidence of CLL
- Obesity may be a risk factor for poor outcome
- Research planned at UC San Diego to examine diet – CLL connection
Effect of adoption of a whole food, plant-based diet and stress reduction on rate of progression of advanced prostate cancer

Saxe GA, Hebert JR, Carmody JF, Kabat-Zinn J, Rosenzweig PH, Jarzobski D, Reed GW, and Blute RD, “Can Diet in Conjunction with Stress Reduction Affect the Rate of Increase in Prostate Specific Antigen after Biochemical Recurrence of Prostate Cancer?” J Urology, 166(12): 2202-7, 2001
Figure 1. Rate of Change in PSA by Patient: Pre-study vs Intervention

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Pre-Study</th>
<th>Intervention</th>
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<tbody>
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</table>
Reversal of coronary artery disease

Coronary angiography reveals a diseased distal left anterior descending artery (A). Following 32 months of a plant-based nutritional intervention without cholesterol-lowering medication, the artery regained its normal configuration (B).
The Five Pillars of a Cancer Preventive Diet
Pillar # 1:

Whole, unrefined, unprocessed
Pillar # 2: Plant-based
Pillar # 3:

Locally grown and in season
Pillar # 4:

Organic, biodynamic, sustainable
Pillar # 5: Balanced
Foods with Possible Anti-cancer Properties

- Whole grains, vegetables, and beans/legumes
- Fruits, seeds, and nuts
- Dark leafy greens
- Brassica (cabbage family vegetables)
- Allium (onion family vegetables)
- Polypore mushrooms (e.g. shitake, maitake)
- Sea vegetables
- Fermented/probiotic plant foods (miso, sauerkraut)
- Green tea (contains EGCG)
- Various herbs (turmeric)
Brilliant—cold porridge and stale bread again!
UC San Diego Study on a Natural Approach to COVID Vaccine Enhancement in CLL Patients

• **Research question:**
  - Can taking capsules of polypore mushrooms for several days at time of COVID vaccination increase antibodies and improve overall vaccine response?

• **Study design:**
  - Double-blind, placebo-controlled randomized clinical trial
  - May also involve recruitment at sites beyond Southern California

• **For more info:**
  - CLL Society will share additional information as it becomes available
Learning Objectives

• General Health Benefits of Exercise

• Difficulties to Fitness in CLL

• Potential Additional Benefits of Exercise in CLL

• How Exercise can be Feasible in CLL
Why is Physical Activity Beneficial?

What are the health benefits of physical activity?

- Dementia by up to 30%
- Hip fractures by up to 68%
- Depression by up to 30%
- All-cause mortality by 30%
- Cardiovascular disease by up to 35%
- Type 2 diabetes by up to 40%
- Colon cancer by 30%
- Breast cancer by 20%

Regular physical activity reduces your risk of...

Physical Activity Cross Sectional Study at Duke CLL Clinic

• Physical Activity Surveys
• Grip strength
• 6 minute walk test (6MWT)
• Timed Get Up and Go
• Short Physical Performance Battery (SPPB).
  • Four meter gait speed test
  • Chair Stands
  • Balance Testing
• Predicted aerobic fitness ($VO_{2peak}$)
  • calculated from a validated algorithm using the 6MWT, age, body weight, resting heart rate, and gender.

Go4life National Institute on Aging at NIH
https://go4life.nia.nih.gov/exercise/chair-stand/
Results

• Surveys both had 90% validity and full completion.

• The surveys were positively associated with each other

• Activity results from all patients were 60% to 70% of age-predicted normative values.
  • 48% of patients were inactive or engaged in light activities
  • 28% moderate intensity activities (by SBAS)

• Aerobic Capacity/Strength ($\text{VO}_{2\text{peak}}$) was 64±13% of normative values.

• The surveys and physical function tests did not correlate.

Randomized Controlled Trial of the Effects of Aerobic Exercise on Physical Functioning and Quality of Life in Lymphoma Patients

- 122 patients were recruited
  - 62 patients in the control group
    - 10 CLL patients
  - 60 patients in the exercise intervention
    - 4 CLL patients

- Intervention
  - Stationary bike 3 times per week for 12 weeks
  - Intensity of exercise increased each week

Results/Conclusions

Immediately Post Intervention
• Better outcomes were found in the following:
  • Physical functioning
  • Overall quality of life
  • Fatigue
  • Happiness
  • Depression
  • General health
  • Cardiovascular fitness
  • Lean body mass

6 Months After the Intervention
• Still found improvements in the following:
  • Overall quality of life
  • Happiness
  • Depression

• No increased risk of disease recurrence or progression

IMMUNE SYSTEM: FIGHTING CANCER FOR YEARS
How exercise may influence the landscape of the immune system

Visualizing the potentially favorable effects of exercise on an immune system confronted with cancer within the cellular microenvironment.

**LEUKEMIA/LYMPHOMA INFLUENCE**

- Reactive oxygen species
- CD64+ and CD64+ and ↑ TNF-α
- Neutrophil function:
- ↓ IL-1β and TNF-α
- Indicating tolerance from inflammation

**POTENTIAL INFLUENCE OF EXERCISE**

- ↑ Clearance of old neutrophils
- Replacement of old neutrophils with younger, more functional neutrophils

**Cytokines**

- CCL22
- CCL17

**Cytokines from macrophages**

- Migration of Treg cells which limit immune activation and immune responses

- ↑ TNF-α causing T cell exhaustion and immune tolerance

**Increased M2 macrophages**

**Inflammatory macrophages (M1) and anti-inflammatory macrophages (M2)**

**Lower levels of unstimulated reactive oxygen intermediates.**

**T cells**

- NHL cells with ↑ TGF-β, IL-9, and PD-1 ligands induce Treg induction

- ↑ T cell, NK cell, neutrophil, and macrophage function, thus limiting inflammation. ↑ tumor cell recognition and killing

**Natural killer cells**

- ↑ NK cell recognition and killing of tumor cells

**Macrophages**

**Neutrophils**

**Cancer cell**

A pilot study of high-intensity interval training in older adults with treatment naïve chronic lymphocytic leukemia

- Treatment Naïve
- Average age
  - 64 yo for the intervention
  - 66.5 yo for the control group
Pilot Study of Exercise

Recruitment

~2 weeks

12 weeks

CLL-Ex = 3x week exercise
CLL-Con = No Supervised Exercise

T0 Testing
- CPET
- Strength
- Body Comp
- Bloods
- Activity Levels

T1 Testing
- CPET
- Strength
- Body Comp
- Bloods
- Activity Levels

T2 Testing
- CPET
- Strength
- Body Comp
- Bloods
- Activity Levels

12 weeks

CLL-Ex = No Supervised Exercise
CLL-Con = No Supervised Exercise

11:23137
The Exercise Prescription

- **5 minute warm-up**
  - 2x per week: 60 minute exercise session: 30 minutes HIIT
  - 1x per week: 30 minute HIIT session alone

- **HIIT**
  - 60-90s intervals alternating between:
    - High intensity: heart rate corresponding to 80–90% of VO$_2$ reserve
    - Active recovery: 50–60% VO$_2$ reserve

- **Strength**
  - Sets = max repetitions possible at 70% of maximal weight.
  - Once able to perform 20 repetitions or more, the weight was increased for the next session by 2–5 kg.

- **5 minute cool down**

Results

• 99 +/- 3.6% of the prescription was completed amongst the patients.

• 100% of participants completing > 80% of high-intensity intervals at the prescribed heart rate.

• No serious/major injuries.

• 100% of HIIT participants reported minor muscle soreness due to the resistance and aerobic exercise but were considered normal reactions to exercise training.

More Results

<table>
<thead>
<tr>
<th></th>
<th>Maximal Strength</th>
<th>Muscular Endurance</th>
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</thead>
<tbody>
<tr>
<td>Leg Press</td>
<td>35.4%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Chest Press</td>
<td>56.1%</td>
<td>21.7%</td>
</tr>
<tr>
<td>Seated Row</td>
<td>39.5%</td>
<td>29.2%</td>
</tr>
</tbody>
</table>

- in vitro NK-cell cytolytic activity against cancer cell lines
  - The K562 cell line 20% higher, OSU-CLL cell line 3.0% higher, and autologous B-cells 14.6% higher than controls.

- Aerobic capacity actually decreased marginally (3.8%) in the exercise group compared to control.
Conclusion

• Exercise can be beneficial in a number of domains for CLL patients.

• Exercise is feasible and safe!

• There may be immune system benefits though this needs to be explored further.
Poll Questions
Audience Questions & Answers
This program was made possible by grant support from

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Thank You for Attending!

Please take a moment to complete our post-event survey, your feedback is important to us.

If you’re question was not answered, please feel free to email asktheexpert@cllsociety.org.

Join us on May 16th for our upcoming webinar on clinical trials.

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