Exercise and High Intensity Interval Training (HIIT)
Contributed by Dr. Andrea Sitlinger

1. Why did you choose high intensity interval training (HIIT)? What activities were used for the HIIT portion at home?
HIIT workouts can be done with walking, running, or biking. They can also incorporate strength exercises. The key is getting your heart rate up to a significant level. We choose HIIT because there is a growing body of evidence showing the benefits of high intensity exercise.

2. Please give more details about how to do HIIT at home, especially about how to estimate VO2max levels without measuring CO2.
Using heart rate is an excellent surrogate for VO2max. You want to get to 80-90% of your maximal heart rate.

3. Does 30 minutes at 80 - 85% heart capacity qualify as high intensity?
That is high intensity, but these workouts are specifically short interval very high intensity (80-95% maximal heart rate) followed by active recovery (60 to 70% maximal heart rate).

4. I am newly diagnosed with CLL, on watch and wait. I have heard that rebounding (jumping on a mini trampoline), is good for the lymphatic system because jumping gets the lymph moving. I have used a friend’s rebounder and really enjoyed it. I am considering purchasing one. Do you think this is a good piece of equipment for CLL patients because of the benefits to the lymphatic system?
Jumping (jumping rope, trampoline, etc.) can be a great workout and can even mimic HIIT workouts, so this could be a great exercise. That being said, there is no scientific evidence that shows it results in improved lymphatic drainage.

5. Any thoughts on COVID-19 risk when participating in group cycling or running?
If done outdoors, pretty minimal if you can remain socially distanced. When held indoors, this would be considered a high-risk activity for those with CLL/SLL. It would be very important to wear a well-fitted KKN95 or N95 mask, consider the
case rates in your area at the time, as well as the level of ventilation and how far apart the equipment is spaced out from one another.

6. **Do you have suggestions for HIIT and strength programs such as apps or a website for an at-home program?**
   I personally use the HIIT Workout app, but there many other good apps available. The key for any of them is having a reliable measure of heart rate and variety of exercises.

7. **Is there a place where we can go for a more specific exercise routine?**
   There are a number of HIIT interval books and apps that provide specific workouts and can even change daily.

8. **Is high intensity workouts five times a week a good goal?**
   3-5 times per week is good.

9. **Have you looked at results of your interventions against the increase of absolute lymphocytes? Or is this too small a pilot?**
   We did look at it. But there was too short of an intervention and too small of a sample size for meaningful data currently. We will continue to explore this in the future.

10. **Where does someone with CLL on watch-and-wait for 16 years with no symptoms or treatments fall on the risk framework for immunosuppressed category?**
    Everyone with CLL/SLL is considered moderately to severely compromised, regardless of treatment or disease status.

**Cancer Risk and Age**
*Contributed by Dr. Gordon Saxe*

One of the slides in my presentation showed the striking international correlation between diet and risk of breast cancer. This prompted the following question: Could this correlation be a false one that was due to age differences across the different countries? Breast and many other cancers are known to increase with age. Perhaps the countries with the lowest risk just happened to have younger populations?

This is an excellent question – and one that was raised many years ago by epidemiologists. And it affects many diseases (heart disease, type 2 diabetes, etc.), not just cancer. The way it was addressed in the slide I presented (and in most data that is properly presented) is through “age adjustment,” a statistical process that permits fairer comparisons between populations with different age distributions.
In the example I provided, the breast cancer rates in the different countries were all statistically adjusted to have a standard age distribution, thereby taking age out of the equation.

So no, differences in age distribution across the different countries did not account for the differences in the cancer rates. The differences may have been due to dietary or other factors, but they were not due to age.

**Use of Supplements**  
*Contributed by Dr. Gordon Saxe*

Many people had questions about the use of supplements by patients with CLL/SLL, particularly regarding which ones I recommend and whether any can lead to adverse interactions with medications. These are important questions.

I am generally a minimalist when it comes to supplements and feel that we should strive to get most or all of what we need from healthy food. I prefer that people not rely on supplements when they do not need to. The human body evolved to derive nourishment by eating food, not popping pills or capsules. There are many factors in foods (not just the extracted fraction that we supplement) that come together in food as a whole and may enhance the absorption, metabolism, and safety of the part we are most interested in.

Also, supplements are not always benign. Levels in supplements may be much higher than naturally found in foods. Without other parts of the food to buffer them, may be too high or concentrated and pose a safety risk. While certain foods may also pose problems (such as food allergies or sensitivities) in some individuals, the danger is higher with supplements and therefore, there is a greater burden for safety testing than with food. Yet most supplements have not been adequately tested for either safety or efficacy, despite the hype that sometimes surrounds them and the exorbitant prices that are often charged.

Although food comes first, there can be a time and place when supplements make sense and can be recommended on a case-by-case basis. Some examples:

- A nutritional deficiency that needs more rapid correction than can be achieved with food alone.
- A health condition or symptom(s) normally treated with medication that can be equally improved with a supplement, but with fewer or no side effects.
- When access to healthy food is limited because it is out of season, prohibitively expensive, or when one lives in a “food desert” or institutional setting where it is unavailable.
- For those who are unable or unwilling to consume a healthy diet.
There are also a couple general situations in which I typically recommend supplementation more broadly:

- Vitamin D for those who cannot access high enough amounts from sun exposure or diet.
- B-12 for those following vegan diets.

There is evidence that green tea extract (containing the antioxidant EGCG) may be protective against CLL/SLL. A growing body of evidence also suggests that certain polypore mushrooms (such as Shitake, Maitake, Turkey Tail, Agarikon, and others) may enhance anti-cancer and anti-viral immunity. The use of green tea as a beverage, mushrooms or turmeric in cooking (or as a beverage) is safe for most individuals with CLL/SLL who are in the active surveillance (watch and wait) phase of their disease.

However, the use of supplements should be discussed with your healthcare provider before beginning any treatments for CLL/SLL. They may have concerns about possible adverse reactions with required CLL/SLL medications and, if so, certain supplements may need to be avoided.

Despite the promising possibilities, supplements need to be further studied for safety, possible drug interactions, efficacy, and proper dosing before they can be broadly recommended as preventives or adjunctive treatments for CLL/SLL.

**Vitamin D**
*Contributed by Dr. Gordon Saxe*

Higher blood levels of vitamin D have been associated with decreased incidence of several common malignancies, including cancers of the breast, prostate, and colon, increased antiviral immunity, more efficient calcium absorption and better bone health, and decreased levels of inflammatory biomarkers. Although more research is needed, recent evidence also suggests that vitamin D may be protective against progression of CLL/SLL.

Vitamin D can be obtained by a brief period – 10-20 minutes per day – of judicious sun exposure in the mid-afternoon, between about 11 am and 2 pm – the time of day when natural ultraviolet-B light is at its peak. To optimize the amount of vitamin D formed on the skin, it is best, if possible, to expose the large parts of the skin (torso, arms, and thighs/legs) while protecting the face and any other sensitive areas. And care must be taken to avoid sunburn!

But sunbathing for more than 10-20 minutes a day for those with CLL/SLL is not recommended due to the increased risk of secondary skin cancers. Also, some medications increase sun sensitivity. It is also often impractical in the wintertime or for those who live in the more northern latitudes, whose life circumstances require more...
modest dress, or for those whose schedules do not permit time off to go outside in the afternoon. In this case, one can emphasize dietary intake of foods (such as cold-water fish or mushrooms) that are naturally rich in vitamin D, or if necessary, take a vitamin D supplement. Supplementation is often the safest and most practical approach for many people and the easiest to dose precisely.

A normal vitamin D level is at least 30 ng/ml, although an optimal level is thought to be a little higher, in the range of 40-60 ng/ml. Of course, it is also possible to get too much of a good thing. At present, there appears to be no increased risk of CLL/SLL or any other health condition when vitamin D blood levels are in the optimum range. Instead, there are benefits. However, an excessively high serum vitamin D level (over 100 ng/ml) – while uncommon – may lead to too high a blood level of calcium and, eventually, bone or kidney problems. The risk of too high a level is greatest in those taking vitamin D supplements. But in all cases, a simple vitamin D blood test can tell you if you are in the optimum range.

“Keto” Diets and Fat
Contributed by Dr. Gordon Saxe

In my presentation, I recommended the use of a whole food, plant based (WFPB) diet. However, in recent years, there has also been growing interest in and popularity of “keto” diets. In the popular media, this is often presented as a debate between two irreconcilable positions: Diets that are purely plant-based (i.e., vegan diets) versus those that are based on high intake of meat and animal foods. In my view, this is a false dichotomy!

But first, a little background. It has been recognized for many years that certain conditions, such as obesity and type 2 diabetes, are increased in individuals who have a higher intake of highly processed foods and foods high in simple carbohydrates (sugar, white flour, high-fructose corn syrup, etc.). These foods are associated with higher blood glucose levels, and there is also evidence that chronically high blood glucose levels (which drives fat production in the body, and therefore leads to being overweight and/or obesity) are in turn, linked with an increased risk/progression of certain cancers – possibly including CLL/SLL.

Whole plant foods are high in fiber, complex carbohydrates, water, and various micronutrients, low in total fat, and do not contain simple carbohydrates. Average blood glucose levels are usually lower, and being overweight or obese is much less common in those following WFPB diets when compared to those following diets high in processed foods and simple carbohydrates. But it has also been observed that individuals following keto diets that are high in fat (usually from high intake of meat and animal foods) and devoid of simple carbohydrates – also tend to have lower blood glucose levels and lower rates of being overweight or obese.
How can this be? The human body uses glucose as an energy source, but under certain circumstances, it can also use ketones for this purpose. Like glucose, ketones are energy molecules that can drive many processes (movement, body heat, mental activity, etc.). But unlike glucose, ketones are derived from fat. This can be the fat in high-fat foods (such as animal foods, oils, or nuts) or the fat stores – the adipose tissue – in our bodies. During periods of starvation or fasting, the body draws on its own fat reserves to produce ketones – and thereby meets its need for energy.

There is growing evidence that the risk of some cancers may be reduced, or their growth slowed, when we are in a state of ketosis (i.e., when our primary energy source is ketones rather than glucose). And this has led some people to advocate various ketogenic practices - high protein diets (usually high in animal foods), strict avoidance of simple carbohydrates, and intermittent fasting for cancer prevention.

However, I would suggest that the best keto diet may not be one that is high in meat and animal food, but rather a WFPB diet. As noted, whole plant foods do not contain simple carbohydrates, but do have lots of fiber. The fiber is excellent for the health of the gut, nourishing the beneficial bacteria and other microbes to produce – you guessed it – ketones!

By combining a WFPB diet with gentle intermittent fasting, we will also produce ketones from our own body fat reserves – which is a rejuvenating process. If we add in small amounts of healthy, higher-fat foods (seeds, nuts, small cold-water fish, etc.), we may even further boost our ketones. And with the WFPB diet we can increase all manner of beneficial micronutrients by avoiding simple carbohydrates.

**Clean Water and Glenn’s Journey**
*Contributed by Glenn Sabin, CLL Patient Advocate*

1. **How much water is needed per day to reach the hydration that Glen referred to?**
   There is no magic number, and the amount differs from person to person. But I generally aim for a ½ ounce of water for each pound of body weight.

2. **What is clean hydration?**
   Filtered water and reverse osmosis. Think Dasani or Aquafina but stay away from plastic bottles and instead purchase a system. They are now only a few hundred dollars. Or you can purchase a Zero Water unit that is quite inexpensive and does a great job.

3. **What herbal supplements did Glenn use?**
If people are interested in this topic, I recommend the article *A Case of Complete and Durable Molecular Remission of Chronic Lymphocytic Leukemia Following Treatment with Epigallocatechin-3-gallate, an Extract of Green Tea.*

4. **Could Mr. Sabin elaborate what he did exactly?**
For a limited time, you can download my book as an e-book for free [here](#). I've also shared much of my journey in articles on the CLL Society website including "My Remarkable Journey with Chronic Lymphocytic Leukemia" and "The Impact of Diet on CLL".