Autoimmune thyroid disease, Vitamin B-12, atrophic gastritis, H. pylori, anemia and the Israeli Air Force

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Web version of this article is at: http://www.denvernaturopathic.com/AITDandB12.htm

The city of Kfar Saba lies to the northeast of Tel Aviv on the way to Nabulus. Translated from Hebrew, Kfar Saba means 'grandfather's village.' Googling and reading about Kfar Saba is easier than figuring out how to write this article. It starts out simple enough though.

The American Journal of Medical Science published a paper last year written by several researchers from Kfar Saba. Their paper reported a high prevalence of vitamin B-12 deficiency in people suffering from autoimmune thyroid disease. Of the 115 people in the study, all of who had autoimmune thyroid disease (AITD), 32 of them had low vitamin B-12 levels. That's 28%, slightly more than 1 in 4. Of those patients who were B-12 deficient, 31% had pernicious anemia. So, there is a clear relationship between vitamin B-12 absorption and autoimmune thyroid disease, that is what most people who are hypothyroid have.

The land of Kfar Saba was bought up in 1892 by Zionist settlers who apparently never settled there. They sold it in 1896 to the Baron Rothschild who resold it in 1903 to settlers from Petah Tikva who sold it yet again. Back then, the area was so remote and desolate, no one was willing to settle there. When settlements were finally established, the Ottoman government refused to grant building permits. It wasn't until 1912 that permanent houses were built on the land. Today 81,000 people live in Kfar Saba.

Vitamin B-12 acts as a coenzyme in the transformation of homocysteine to methionine. This is reaction is essential to make S-adenosylmethionine (SAMe) which is needed to make myelin. Without myelin, nerves do not work properly. This is why B12 deficiency causes neuropathies. SAMe is also involved in making certain neurotransmitters. These neurotransmitters are important for maintaining mood, explaining why depression is associated with B12 deficiency. This is why people take SAMe as an antidepressant.

Vitamin B-12 is the biggest vitamin in size and finding it in food is complicated. Neither plants nor animals make vitamin B-12. Only bacteria and archaea can make it. If you haven't heard of archea, don't be alarmed, I didn't recognize the term either. Archaea are single celled organisms genetically about halfway between prokaryotic and eukaryotic organisms. They adapt to live in extreme environments, like the geysers in Yellowstone, and aren't relevant to this discussion unless you want to consider Kfar Saba of the 1890s an extreme environment. Meat and dairy are the only reliable food source of vitamin B-12 in our diets. They contain B-12 only because feed is either fermented or enriched. Tempeh, a mold and soy bean product, may contain vitamin B-12, but only if allowed to

ferment to a degree past where most Americans will eat it.

To move vitamin B-12 out of food into the blood system is complicated. Many things can go wrong in this process preventing absorption. As vitamin B-12 is pulled out of food in the stomach, proteins secreted in the digestive tract, called salivary R-binders, attach to it. Acid from the stomach and pancreatic proteolytic enzymes are both needed to releases the B-12 from these 'binders.' Without both, the B-12 will not be absorbed.

Once free of the R-binders, B-12 is grabbed up by chemical called B-12 intrinsic factor. B-12 needs to attach to intrinsic factor to be absorbed through the intestine into the blood. Specialized cells called parietal cells that line the stomach secrete intrinsic factor. The vitamin B12 and intrinsic factor complex can only be absorbed through a short section of the small intestine, called the terminal ileum. This is way down near the appendix. Even with adequate dietary B-12, moving it into the blood stream still requires that the stomach generates both acid and intrinsic factor, a pancreas that generates the enzymes to release B-12 from the binding proteins, and small bowel capable of absorbing the B-12. Any of these can be a weak link leading to B-12 deficiency.

When I mentioned that I was reading about Kfar Saba, Dr. Bloom, she informed me that she once lived there. Well actually her mother, my mother-in-law, had an apartment in Kfar Saba in the 1970s. I never knew.

B-12 deficiency leads to a form of anemia called megaloblastic anemia in which red blood cells become swollen and bloated. On a complete blood count, the Mean Corpuscular Volume (MCV) increases and the Red Blood Cell (RBC) count decreases. The most common cause of B-12 deficiency is atrophic gastritis, a condition that damages the parietal cells preventing them from making intrinsic factor. We call this condition pernicious anemia. Sometimes the term pernicious anemia is used incorrectly to refer to any B-12 deficiency anemia, but technically, pernicious anemia is caused by atrophic gastritis.

Atrophic Gastritis is usually the result of an autoimmune process in which the immune system inappropriately makes antibodies that attack the parietal cells or intrinsic factor itself. Approximately 90% of individuals with pernicious anemia have antibodies for parietal cells, however only 50% of individuals with these antibodies have pernicious anemia.

This Kfar Saba study is not the first to report an association between autoimmune thyroid disease and B-12 deficiency. An Italian study, published in the Archives of Internal medicine back in 1999 reported that 22 out of 62 autoimmune thyroid disease (AITD) patients had confirmed atrophic gastritis. Antiparietal cell antibodies were found in 68% (15/22) of patients with atrophic gastritis. Anemia was observed in 82% (18/ 22) of patients with AITD and atrophic gastritis. It was not just macrocytic, B-12 deficiency anemia, AITD patients also have a higher incidence of iron deficiency anemia.

Autoimmune gastritis also causes iron deficiency anemia. Atrophic gastritis causes about one quarter of all cases of chronic iron deficiency anemia. Destruction of the parietal cells stops acid production in the stomach. An acidic stomach is necessary to absorb iron. Thus, atrophic gastritis can trigger both iron deficiency and B-12 deficiency. This complicates things. Iron deficiency causes microcytic anemia, a form of anemia where the red blood cells shrivel up in size. The Mean Corpuscular Volume (MCV) decreases. If B-12 and iron deficiencies coexist, the combined average volume of big and small red blood cells expressed as MCV may appear normal. The only hint on the lab numbers may be an elevated RDW, but that is more detail than you will want.

Other conditions besides autoimmune attack can cause atrophic gastritis. The first that comes to mind is Helicobacter pylori. In fact, these infections may be a more common cause of atrophic gastritis than we initially thought.

Helicobacter pylori infections cause about one quarter of all cases of atrophic gastritis. Treating and curing the H. pylori infection will usually improve the damaged tissue but not all the time. One study showed reduction in tissue damage in only about half of the patients cured of H. pylori infection.

Here is where it starts to get complicated. There appear to be several diseases that seem closely related. Autoimmune thyroid disease no longer appears to be lone entity. One in four people with AITD, that is who make antibodies that attack their thyroid, also make antibodies that attack the parietal glands in the causing B-12 deficiency.

Rena tells me that she used to stay at her mom's apartment in Kfar Saba when on weekend leave. This is back when she served in the Israeli Air Force in the 1970s. This side story is suddenly more than a distraction, it is getting complicated as well.

There is also celiac disease. People with celiac disease have a higher than normal incidence of autoimmune thyroid disease, about twice the expected. It works both ways; people with thyroid disease are also more likely to have celiac disease. Celiac disease also increases risk of B-12 deficiency. According to one study, 12% of celiac patients will be B-12 deficient. There are two possible explanations for this increase. First, celiac disease inflames the terminal ileum where B-12 is absorbed. Second, celiac disease patients may make antibodies against parietal cells and so cause atrophic gastritis. It turns out that only about 10% of the B-12 deficient celiac patients have atrophic damage in the stomach, so the first scenario, damage to the colon prevents absorption, is probably more often the reason.

A 2005 study looked at 190 patients with chronic unexplained iron deficiency anemia. Eight (5%) of the patients had celiac disease. Forty (27%) had autoimmune atrophic gastritis of whom 22 also had low serum vitamin B12 levels. Of the entire 190 patients, 29 (19%) only had H. pylori infection. But, H. pylori infection co-existed along with one of these other causes in 77 people (51%). None of the patients with celiac disease

responded or improved with iron supplements. Most (71%) of the patients with autoimmune atrophic gastritis also failed to respond. About the same lack of response (68%) was seen with H. pylori infection. But of the patients who tested negative for these three conditions (AITD, H. Pylori and celiac), almost all (89%) responded to iron supplements. Killing off the H. pylori improved the response to iron supplements.

Though it sounds possible, studies tell us that there is no relationship between autoimmune thyroid disease and H. Pylori infection.

The primary symptom of both iron deficiency and B-12 deficiency anemis and of autoimmune thyroid disease is the same. All three cause fatigue. Vitamin B-12 deficiency will also often present with neurologic symptoms, typically peripheral numbness or neuropathy. Helicobacter pylori infection presents with upper gastrointestinal symptoms. Celiac disease traditionally has been associated with digestive complaints, most commonly, chronic diarrhea. This opinion has shifted and it is now believed that digestive complaints are not that common in celiac disease, occurring in less than 20% of patients. Osteopenia and osteoporosis are common in celiac patients. The explanation typically given is that this results from chronic malabsorption of calcium. It may also be a result of low vitamin B-12 levels which lead to increased homocysteine levels which are linked to osteoporosis.

This adds a level of complexity to analyzing anemia in patients. First, there is need for vigilance in all cases of autoimmune thyroid disease watching for symptoms of anemia. It would be reasonable to test either B-12 or homocysteine routinely in this patient population. Also, iron and ferritin levels. Atrophic gastritis, of either autoimmune or infectious origin, can cause both iron and B-12 deficiency and there is no reason that both deficiencies can't occur at the same time.

Over the last few weeks, we have hosted participants from the Building Bridges for Peace program in our home. Past newsletters have described our involvement with this program. Participants come from the Israeli and Palestinian communities in Israel to Colorado each summer. Looking at old photos of Rena during her Air Force days when she spent her free time in Kfar Saba, I contemplate how our knowledge and understanding can grow and change during a lifetime. It is not just about vitamin B-12 chemistry that I am thinking.

No one ever promised that biology, medicine or life would be simple. Yet if one pays attention, it certainly can be interesting. As time goes on, we can work to learn more and understand the complexity of life more completely. Doing so allows us to practice better medicine, among other things.

Prior newsletter on Building Bridges for Peace:
http://www.denvernaturopathic.com/news/BBfP.html

Building Bridges for Peace:
http://s-c-g.org/

Photos of Rena during her Air Force days:
http://www.denvernaturopathic.com/RenaAirForcephotos.htm