MeritCare Medical Center

Aunt Cathy's Guide to:

Thinking About OTHER Nutrition Issues in Celiac Disease

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1. General Nutrition Adequacy Issues

It is important for individuals avoiding gluten to take a close look at the nutritional adequacy of the foods remaining in the diet. This may mean getting some help from a Registered Dietitian, as not all the threats to complete nutrition are obvious. Any diet that eliminates a number of common foods has the potential to leave some gaps in nutrient intake.

In addition to general nutritional adequacy, there are diet/nutrition factors besides gluten control that can provide additional benefit to people with celiac disease. Many chronic health conditions have an inflammatory component. CD, MS, diabetes, rheumatoid arthritis, inflammatory bowel disease and lupus, for example, all have the potential to result in increased inflammation. It is now recognized that inflammation is an important contributor to heart disease as well, so the recommendations included here to decrease inflammation and to protect tissues from the negative effects of inflammation are of great potential benefit.

2. Omega-3 and Omega-6 Fats in the Diet and the Problem of Inflammation.

One of the most important issues in controlling inflammation is the ratio of two different families of certain polyunsaturated oils in our diets. The two families are called omega-3 and omega-6 fats, and in America we tend to eat far more omega-6 fats than omega-3 fats - - in fact we eat them in a ratio of 10-to-1! There is a clear benefit for all of us in moving toward a ratio of 4-to-1 (as in the heart healthy "Mediterranean Diet.")

Some researchers believe that for people with inflammatory conditions, a ratio of 2-to-1 may be even more beneficial. This is because certain inflammatory substances (prostaglandins) are made out of these fats, and the ones made out of omega-6 fats are much more inflammatory than the ones made out of omega-3 fats. That means that **by altering the ratio of these fats in our diet, we can decrease the degree of inflammation experienced.** In brief here is how to change the ratio:

A. Replace corn oil (high in omega-6 and very low in omega-3) in cooking and baking with **olive oil** (neutral, so it displaces the high omega-6 oils) or **canola oil** (an oil with a better ratio of omega-3 and omega-6 fat.)

B. Incorporate **ground flax seed** and **fatty fish** like salmon in the diet. These are terrific sources of omega-3 fat. **Flax oil** is a good source of omega-3 fat, but the rest of the flax seed is very nutrient dense as well, including nutrients that are often low in the diets of Americans, like magnesium and chromium. Additionally, it has some substances (lignans) that appear to decrease risk of breast cancer. For that reason, **the ground flax has a better benefit-to-cost ratio that buying flax oil or flax oil capsules**.

C. If eating fish is not attractive (or if you are worried about mercury), you should consider taking **fish oil or krill oil capsules.** These are labeled "EPA and DHA" and a Consumer Reports survey showed that all the brands in the US were safe and equal in quality, with price being the only difference. The price ranged from 6 cents each to 60 cents each, so check out a local warehouse-type or discount store for the best buy. The fish oil capsules tend to be a bit large for some folks to easily swallow. Because the benefits of taking fish oil (for nearly everyone,) are being recognized, more and more products are becoming available. Many new forms are already available, including smaller capsules, liquids and pastes that are citrus flavored and not fishy-tasting. You can find many products on line just by Googling fish oil or omega 3.

   Although flax is rich in a certain omega-3 fat (linolenic acid --- a vegetable oil,) **there is a special benefit to taking in at least some of the omega-3 fat in the forms found in fish (EPA and DHA.) Think of EPA as standing for "Environmental Protection Agency" – protecting your internal environment!** Even the American Heart Association (a very conservative organization) recommends that most people take 1000 mg of fish oil daily. Fish oil is also being used to decrease risk of cancer and as an adjunct to chemotherapy. The form of fat that is DHA in fish is also particularly important in brain / neurologic health. Some people have been found to be unable to make enough EPA and DHA out of the vegetable oil linolenic acid (the one in flax and canola) so taking some in a ready-to-go form is a wise idea.

3. Fiber Issues.

Unless carefully planned, the gluten-free diet can also be low in **dietary fiber**, including the kind that "moves things along" (like cellulose in wheat bran), and the kind that helps to lower cholesterol. That type is called "water soluble fiber", and it includes Guar gum, Legumes, Oat bran and Pectin – which can be remembered by the acronym "GLOP." Some of the cholesterol eaten and some that enters the intestinal tract in the form of bile from the liver can be thought of as "getting stuck in the GLOP" and excreted instead of being absorbed into the body.

People with celiac disease obviously cannot have wheat bran, and the oat bran can be iffy because of cross contamination, so they need to work a little harder to obtain the many benefits of foods that contain both kinds of dietary fiber. Legumes are one option … dried beans and peas (like chili beans, navy beans, pinto beans, split peas, etc.) are great sources of fiber and additionally they are very nutritious. This is because any plant part that is actually what turns into a baby plant is full of all the nutrients needed by the new plant. In grains it is the "germ." The rest of any grain is

primarily starch and the fibrous coating. Other foods that are high in both fiber and nutrients like this are nuts and seeds (like the flaxseed discussed earlier.)

4. Increased "Free Radical" Production and Protection by Antioxidants:

Just running your body produces a certain type of waste product called **"free radicals."** They can cause injury to cells, but normally they are kept from causing injury by substances that we eat or make collectively called **"antioxidants."** They include certain vitamins (like vitamins C and E), and a substance made with the mineral selenium (glutathione peroxidase.) There is some new evidence that assuring adequacy of selenium may be a therapeutic tools to prevent both tissue damage and complication of CD such as autoimmune thyroid diseases (AITD.)

A number of substances in plants (certain **phytochemicals**) are now known to be terrific antioxidants, and there is a lot of interest in these plant substances for promoting good health in general. The plant pigments (coloring agents) especially, such as "lutein" in leafy greens, "lycopene" in tomatoes and "anthocyanins" in blueberries are examples of some very promising protective substances. **Eating plenty of brightly colored vegetables and fruits is a very good idea for many reasons for everyone.**

Inflammatory conditions result in a much greater production of free radicals than is usual. For this reason, people with inflammatory conditions like CD and diabetes should aim for a much more generous intake of antioxidants than usual to minimize the increased risk of cell damage. In this situation, a reasonable and safe daily amount of vitamin E is 400 iu, vitamin C 500-1000 mg, and selenium 100-200 mcg, plus lots of brightly colored fruits and vegetables. The vitamin C, E and selenium amounts shown above are higher than the usual Recommended Dietary Allowance (RDA) amount, because the RDA is designed to meet the needs of folks without a chronic inflammatory disease. Do not take more than this (especially of selenium) without consulting your health care provider.

Even more potent antioxidants are the phytochemicals that are pigments (coloring agents) naturally occurring in plants. For example, lycopene, the red color in tomatoes, is 200 times more potent as an antioxidant than vitamin E, and it has been shown to help minimize the oxidation damage from excess free radicals related to CD.

[Neurologic impairment due to vitamin E and copper deficiencies in celiac disease. Neurology 2009 Sept 9; 71(11):860-1. Selenium deficiency in celiac disease: risk of autoimmune thyroid diseases. Minerva Med. 2008 Dec;99(6):643-53. Lycopene, quercetin and tyrosol prevent macrophage activation induced by gliadin and IFN-gamma. Eur J Pharmacol. 2007;566(1-3):192-9.]

5. Vitamin K Inadequacy: A Newly Recognized National Problem Needing Special Attention in Celiac Disease

Eating leafy green vegetables has an additional benefit because it is now recognized that **vitamin K is often inadequate in Americans**. Dark leafy greens are broccoli are the very best natural sources. At the moment, **vitamin K is not included in most multivitamins** because the serious inadequacy

problem is only newly recognized. It has now been discovered that inadequate vitamin K contributes to osteoporosis, arterial calcinosis (an independent risk factor for cardiovascular disease,) kidney calcinosis and liver cancer as well as pregnancy problems and bleeding problems, so eating these foods is very important for everyone. Additionally poorly controlled CD greatly increases the risk of vitamin K deficiency. For more on this, including issues for people using the blood-thinning medication Coumadin, please see my handout just on vitamin K.

[Celiac disease with diffuse cutaneous vitamin K-deficiency bleeding. Adv Ther. 2007 Nov-Dec;24(6):1286-9. Coagulopathy due to celiac disease presenting as intramuscular hemorrhage. J Gen Intern Med. 2007 Nov;22(11):1608-12.]

6. Re-emergence of Iodine Insufficiency in the USA

Another new problem on the horizon for <u>everyone</u> is a re-emergence of iodine deficiency disease in the United States and the world. In short, the problems are these: Certain regions are known to have inadequate iodine in the soil and this results in IDD (Iodine Deficiency Disease) if iodine is not provided in some other way. Iodizing salt has been the traditional approach, but that intervention was initiated before we advised people to cut way back on salt consumption to help control high blood pressure. [see iodine map on the last page.]

Additionally, there is a popular fad of using exotic "gourmet" salts from around the world, most of which are not iodized. "Sea salt" is usually not iodized, but some brands are. Even the common salt at the grocery store looks pretty similar … iodized vs non-iodized … and folks are no longer being reminded to pick the iodized version. Most vitamins, (including many prenatal vitamins) contain no iodine because of the assumption that the iodization of salt program "took care of" the widespread public health problem of iodine deficiency.

Recently the World Health Organization increased the iodine recommendation for pregnant women, in part because they found that even in regions where salt was regularly iodized, the amount was insufficient for the best pregnancy outcome. (Iodine deficiency is actually the number one cause of preventable mental retardation in the world.) Thyroid function is very reliant on adequacy of both iodine and selenium. So, in addition to issues in brain development of infants, iodine deficiency can rob people of energy because of hypothyroidism.

What is the connection to celiac disease? Well, people with celiac disease are not protected from this deficiency, nor is the issue likely to be in the radar of most health care professionals yet, so I am bringing it up here. It is not unreasonable to suppose that any person with nutrient absorption problems would have an increased risk of poor iodine status beyond that of the general public. Additionally, as described above, there is the suggestion of a possible connection to autoimmune thyroid disease for selenium deficiency. Selenium and iodine work together for the thyroid to function. I have not seen any specific celiac/iodine connection in the scientific literature, but the whole issue is <u>very</u> new. In general, in the US most men tend to get an adequate amount of iodine, but <u>many</u> women do not … this is probably just a reflection of how much total food one typically eats.

[Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. Am J Clin Nutr. 2009 Feb;89(2):668S-72S. Iodine Content of prenatal multivitamins in the United States. NEJM. 2009;360:939-940. Iodine status of the U.S. population, National Health and Nutrition Examination Survey 2003-2004. Thyroid. 2008 Nov;18(11):1207-14.]

7. "Eat Right" AND take a Multivitamin with Minerals AND take extra vitamin D!

It is now well recognized throughout the scientific community that most people would benefit from taking a standard multivitamin with minerals. The old advice to "just eat right" has been found to be extremely unlikely to assure optimal health in most people**. The new advice is "Eat right … and take a multivitamin with minerals … and take additional vitamin D"** References for these audacious claims are in the handouts in great number.

There are many reasons for the recommendation that everyone should take a multivitamin with minerals even if one does "eat right," including significant individual variability in absorbing certain vitamins in the forms found in foods. For example, **folic acid** and **vitamin B-12** are actually more reliably absorbed in the pill form than in the forms found in foods. There are **1)** genetic reasons, **2)** aging-related reasons, **3)** drug interaction reasons, and **4)** intestinal injury (e.g. CD) reasons that make it hard for some people to absorb adequate amounts of these vitamins from the usual food sources. It is wise to simply assure an intake at (at least) the RDA level of these two vitamins in the form found in vitamin pills because this form bypasses the problem in all of the above situations except for intestinal injury from poorly controlled CD.

Both of these vitamins have been shown to be critical to cardiovascular health because they prevent the build-up of a substance called "**homocysteine**" and other problems that the high homocysteine level reflects. It is prudent to simply prevent the problem. Inadequate folic acid is a known risk factor for cancer of the breast, colon and prostate, and for depression and birth defects. Vitamin B-12 is critical for neurologic health. Assuring adequacy of these vitamins in an easy-to-absorb form has broad benefits. If your CD is not in good control, a much more generous intake is certainly needed. These nutrients are commonly inadequate in newly diagnosed individuals with CD … poor control would mimic that situation.

[Effect of B vitamin supplementation on plasma homocysteine levels in celiac disease. World J Gastroenterol. 2009 Feb 28;15(8):955-60. Celiac disease and ischemic stroke. Rev Neurol(Paris);2009 Jan 12. Vit A Celiac Disease Presenting as Xeropthalmic Fundus. Retina;2008 Mar 28(3):525-5. Undiagnosed coeliac disease and nutritional deficiencies in adults screened in primary health care. Scand J Gastroenterol. 2007 Jan;42(1):60-5; Celiac sprue, hyperhomocysteinemia, and MTHFR gene variants. J Clin Gastroenterol. 2006 Aug;40(7):596-601; Prevalence of hyperhomocysteinemia in adult gluten-sensitive enteropathy at diagnosis: role of B12, folate, and genetics. Clin Gastroenterol Hepatol. 2005 Jun;3(6):574-80.]

Additionally, inadequate vitamin D intake is now recognized as a serious under-diagnosed and widespread problem with a great many serious health consequences. These include congestive heart failure, heart attack, MS, diabetes, osteoporosis, muscle/nerve pain, muscle weakness, rheumatoid arthritis and cancer of the breast, prostate, colon and pancreas, to name a few. Note the many "autoimmune" conditions listed. It appears that vitamin D deficiency can be a trigger for the development of many of these conditions in genetically susceptible people, just as certain viruses can trigger them.

Over 200 tissues in your body have receptors looking for vitamin D in order to operate correctly. The current RDA is 200-400 iu of vitamin D, and it is now known that in the northern third of the US especially, **this amount is inadequate to maintain appropriate blood levels of the vitamin.** [see map]

This is also true in people who are elderly, or have dark skin, or who are covered up or out of the sun**. In these situations, 1000-2000 iu/day has been shown to be needed in several recent studies.** Some individuals have been shown to require **5000-6000 iu/day** to maintain appropriate blood levels of vitamin D … and people with celiac disease are sometimes members of this group. In fact, while getting a vitamin D level for some other health problem for a patient, I have seen many levels that are extremely low. In some of these cases, the low vitamin D level turned out to be the clue that caused celiac disease to be identified.

It is now known that the upper level of safety for vitamin D is actually over 10,000 iu daily chronically, so the amount above is nowhere near a dangerous amount, particularly when it is shown to be needed by a particular person just to maintain normal levels. What is a real and present danger now all around the world is inadequacy. **The World Health Organization (WHO) estimates that half of the world's population has inadequate vitamin D levels for a wide variety of reasons … even in the sunny equatorial regions.**

There are few foods that are naturally good sources of vitamin D—liver and salmon are the only one that one might actually eat, so the 400 iu provided by a vitamin pill is a good place to start. Milk is fortified with vitamin D (it doesn't have it naturally) and only a few other foods are fortified, such as some orange juice and some yogurt. So, while milk is one of the "very best" dietary sources in the US, **one cup has only 100 iu of vitamin D added to it.** Note that milk "straight from the cow" does not contain any vitamin D, so some of our farm families get none and are quite unaware if it.

It is clear that relying on milk to provide the target amount of vitamin D described is unrealistic without additional vitamin supplements on the team. If you are in an at-risk group (e.g. dark skin, living up north, etc.) it is necessary to take an additional vitamin D supplement even if you drink a lot of milk and take a multivitamin. And now that we know that people all over the world are living with vitamin D inadequacy, that whole "at risk" concept is not very useful. We should consider ourselves to be "at risk" unless we have some evidence to the contrary.

For people who are eliminating wheat, rye, barley and often oats from their diet, and often dairy foods as well for other reasons, there is great potential for failing to obtain the best health-promoting level of a number of nutrients. Not all of these will be corrected with the multivitamin with minerals, but it is certainly a good start. You do not need to buy an expensive product – the best-known discount and warehouse stores have very good ones that are well absorbed (contrary to the information provided by people selling more expensive products.)

An important CD note regarding vitamin D is that the recommended amounts described are not taking any malabsorption into account. If your CD is in good control, those levels (1000-2000 iu) could be fine. If your CD is NOT in good control, you could easily have a seriously inadequate intake. However, having intestinal symptoms of celiac disease is not necessary for it to result in severe vitamin D deficiency. In some cases the only symptom of celiac a person had was the pain and bone damage from vitamin D deficiency. Additionally, there was no difference in some studies of nutrient status between people with partial villous atrophy compared with those who had severe villous atrophy. So although avoiding gluten is clearly the most

important factor in CD, it appears that generous supplementation of vitamins is a very reasonable adjunct factor in making CD hurt people less even if they have the gluten–free diet well in place.

Interference with absorption of bone-related nutrients (vitamins A,D, K and the minerals calcium, phosphorus and magnesium in particular) are all seen commonly in celiac disease. For example, poor bone density was found in 75% of newly diagnosed children, but it was still very common (40%) among those who were not newly diagnosed and who were said to be following the gluten restricted diet.

Assessment 0f bone mineral density in children with celiac disease. Pol Merku Kekarski. 2008 Mar 24(141);219-26. Severe primary hypothyroidism masked by asymptomatic celiac disease. Endocr. Pract. 2008 Apr 14(3);347-50. Adult celiac disease with severe or partial villous atrophy: a comparison study. Gastroenterol Clin Biol. 2008 Mar;32(3):236-42. A correlation of symptoms with vitamin D deficiency and system response to cholecalciferol treatment: a randomized controlled trial. Endocr Pract. 2009 May-Jun;15(3):203-12. Resistance to vitamin D treatment as an indication of celiac disease in a patient with primary hypoparathyroidism. Clinics(Sao Paulo)2009 Jan;64(3):259-61. Disabling osteomalacia and myopathy as the only presenting feature of celiac disease: a case report. Cases J 2009 Jan 7;2(1)20. Osteoporosis in celiac disease and in endocrine and reproductive disorders. World J Gastroenterol. 2008 Jan 28;14(4):498-505;Bone in celiac disease. Osteoporos Int. 2008 Apr 17. Osteomalacic myopathy associated with coexisting celiac disease and primary biliary cirrhosis. Med Princ Pract 2008; 17(5):428-8.

Because a low vitamin D level is so dangerous and it is very common, it is a VERY good idea to ask your health care provider to check your blood vitamin D level at least annually in the winter. Ask him/her to order a "25-hydroxy cholecalciferol level" --- the form of vitamin D that tells if you have enough on board.

Please share this handout with him/her as well so that it is clear how important this is. Interestingly, it is looking like EVERYONE should probably have vitamin D levels checked annually – not just folks with CD -- because they are finding what has been described as "an unrecognized epidemic of vitamin D deficiency" in the US and around the world. Because the symptoms are nearly always invisible, and the problem is very common and very dangerous, the only way to be sure that any individual is "OK" is to check the blood level. Until fairly recently this has rarely been done.

8. New investigations into milk intolerance in CD: Casein and/or Lactose

Many people with CD experience some difficulty drinking milk at all, let alone drinking 10 cups a day. For them, it is useful to remember that there is no reason why one must take their vitamin D supplement in a form that involves drinking milk. The form in milk is just a supplement of vitamin D – it is not naturally there. All that is required is that one make sure to get the nutrients one would expect to get from milk -- i.e. calcium, phosphorus, potassium, vitamins D and B12 and B2 (riboflavin) – from some other sources. A Registered Dietitian can help figure out lots of ways to reach a nutrition goal.

The milk-intolerance itself has often been attributed to lactose intolerance – trouble digesting milk sugar because of intestinal injury. This causes cramps, gas and diarrhea. Certainly some individuals may be lactose intolerant for reasons unrelated to CD, but that would likely be a minority of them. So, it has been hard to explain the continued gastro-intestinal distress when the individual has been controlling the CD diet very well and there is no expectation of intestinal injury that would lead to lactose intolerance. **Now there is a new clue:**

It appears that for many people with CD, there is an actual intolerance of the cow's <u>milk protein</u> that is similar in many respects to the intolerance of gliadin protein in gluten. In that situation, it would be especially inappropriate to try to meet one's vitamin D requirement in the form of dairy foods. It appears that it is the **casein** part of the protein that is the problem … that is, the curds rather than the whey. (The whey part is primarily a protein called lactoglobulin.) **That means that foods made from milk that happen to be very low in lactose could still be a problem for some people with CD.** For example, cheese is very low in lactose, but the protein is almost all casein. I have included some highlights of a study that looked at this recently:

Mucosal reactivity to cow's milk protein in coeliac disease. Clin Exp Immunol. 2007 Mar;147(3):449-55. Patients with coeliac disease (CD) on a gluten-free diet may still have gastrointestinal symptoms. On clinical grounds cow's milk (CM) protein sensitivity may be suspected. Here, using rectal protein challenge, we investigated the local inflammatory reaction to gluten and CM protein in adult patients with CD in remission. … Casein, in contrast to alpha-lactalbumin, induced an inflammatory response similar to that produced by Cow's milk. **A mucosal inflammatory response similar to that elicited by gluten was produced by CM protein in about 50% of the patients with coeliac disease.** Casein, in particular, seems to be involved in this reaction.

One practical suggestion that comes from this research is that people who continue to have celiac symptoms in spite of careful avoidance of gluten should do a trial of strictly avoiding casein for a few weeks to see if symptoms improve. If it doesn't help, then that is not the problem so dairy foods can be re-introduced. But if it <u>does</u> result in improvement, consider removal of milk protein from the diet and replacing of the nutrients usually contributed by milk in the American diet as described earlier. **And as emphasized earlier, it is NOT SAFE to simply remove this kind of food and then not replace the nutrients.**

9. A Mineral of Special Note: Magnesium

Magnesium is critical for over 300 processes in the body. And yet, according to a large national survey by the CDC (the NHANES Report), **this important mineral is low in the diets of the <u>majority</u> of Americans**. Inadequacy contributes to diabetes, obesity, migraine, muscle spasms, poor pregnancy outcome, and many other problems, but it is often unrecognized. Because one of the most important dietary sources is the "germ" part of whole grains, **there is a greater likelihood of poor intake among people avoiding gluten.** Other good sources include nuts and legumes, but many people do not eat much of these foods for a variety of reasons. **Most multivitamins with minerals contain very little magnesium** -- often only 10-25% of the recommended amount for healthy people. For these reasons, some folks will need an additional magnesium supplement of 200-300 mg/day in the form of magnesium oxide or magnesium chloride. Others can do well with just some diet tinkering. Check out the Magnesium handout on the website for the particulars and specific recommendations.

10. Iron, Copper and Zinc

These three minerals have all been found to be problematic in celiac disease, especially when The diet is poorly managed and intestinal damage is present. It is well known that the first recognized symptom of celiac disease is often anemia**. Iron deficiency because of intestinal injury can be a cause of this. However, newly recognized as a factor in this picture is copper deficiency,** which can result in inability to transport iron well and therefore looks like iron-deficiency anemia. This is one reason why treatment with supplemental iron alone can often be ineffective. Another is that chronic inflammation alone can result in an anemic state in spite of iron status.

Additionally, there are many factors that affect both iron and zinc absorption … enhancing it or impairing it. Both are affected by the same factors, but often only iron status is measured in the form of hemoglobin or hematocrit measures**. A good rule of thumb is to assume unrecognized zinc inadequacy when one is known to be iron deficient**. As zinc is a factor in over 200 enzyme systems in the body, including the immune system, making DNA, growth, and wound healing (including intestinal injury repair), inadequacy can be globally damaging. If one supplements zinc, however, it is important to also supplement copper, because supplementation of zinc alone can interfere with copper absorption.

New reports also suggest that there may be an increased urinary loss of copper in the urine of women with celiac disease … a factor separate from the question of impaired absorption. And in addition to the anemia issue, unrecognized copper deficiency can also result in irreversible muscle/nerve damage.

I have additional information available on line with lots of information about factors that affect absorption of these nutrients that can be used to help improve the situation: "Nutrition Support of Iron Deficiency" is on line with other handouts of potential interest as described at the end of this paper.

[Copper deficiency in celiac disease. J Clin Gastroenterol. 2009 Feb;43(2):162-4. Serum zinc in small children with celiac disease. Acta Paedoiatr 2009 Feb 98(2); 343-5. Anemia of chronic disease and defective erythropoietin production in patients with celiac disease. Haematologica. 2008 Dec;93(12):1785-91.Neurologic disorders in adults with celiac disease. Can J Gastroenterol 2008 Nov 22(11);909-11, .Serum copper, ceruloplasmin and 24-h urine copper evaluations in celiac patients. Dig Dis Sci. 2008 Jun;53(6):1564-72. Copper Deficiency in Celiac Disease: A Report of 5 Cases and a Review of the Literature. J Clin Gastroenterol. 2008 May 15. Anemia of chronic disease. Haematologia 2008:dec 93(12);1785-91. Neurologic impairment due to vitamin E and copper deficiencies in celiac disease. Neurology 2008 Sept 9; 71(11):860-1. The soluble transferrin receptor (sTfR)-ferritin index is a potential predictor of celiac disease in children with refractory iron deficiency anemia. Clin Chem Lab Med. 2005;43(1):38-42.Hematologic manifestation of childhood celiac disease. Acta Haematol. 2004;111(4):211-4.Refractory iron deficiency anemia as the primary clinical manifestation of celiac disease. J Pediatr Hematol Oncol. 2003 Feb;25(2):169-72. Efficacy of gluten-free diet alone on recovery from iron deficiency anemia in adult celiac patients. Am J Gastroenterol. 2001 Jan;96(1):132-7.]

11. A Newer Topic: Carnitine and Celiac Disease

Carnitine (also called L-carnitine) is a substance one produces in the liver and kidneys, but which is also found in meats. It is important for getting fuel into your muscles, so having an inadequate amount contributes substantially to fatigue and even to heart muscle problems (cardiomyopathy.) Normally we hear little about it because most folks take in or produce all they

need. However, in a number of health conditions, adequacy may require an additional supplemental intake. For several years there has been interest in evaluating the possibility of a relative carnitine deficiency in people with CD.

[Encephalopathy due to carnitine deficiency in an adult patient with gluten enteropathy. Clin Neurol Neurosurg. 2006 Dec;108(8):794-7. Plasma carnitine ester profile in adult celiac disease patients maintained on long-term gluten free diet. World J Gastroenterol. 2005 Nov 14;11(42):6671-5. Carnitine deficiency in patients with coeliac disease and idiopathic dilated cardiomyopathy. Nutr Metab Cardiovasc Dis. 2005 Aug;15(4):279-83. Intestinal permeability in long-term follow-up of patients with celiac disease on a gluten-free diet. Dig Dis Sci. 2005 Apr;50(4):785-90. Serum carnitine and selenium levels in children with celiac disease. Indian J Gastroenterol. 2004 May-Jun;23(3):87-8. Plasma L-carnitine levels in children with celiac disease. Minerva Pediatr. 1992 Sep;44(9):401-5 Serum carnitine and selenium levels in children with celiac disease. Indian J Gastroenterol. 2004 May-Jun;23(3):87-8.]

A recent prospective investigation looking specifically at carnitine supplementation in CD patients with fatigue found that they benefitted from supplementation. I have included the complete abstract of the research study below so that you can share this information with your health care provider. This benefit in fatigue-reduction is consistent with applications in many other conditions in which fatigue is a common problem. I listed a few examples of those after the abstract below.

L-Carnitine in the treatment of fatigue in adult celiac disease patients: a pilot study. Dig Liver Dis. 2007 Oct;39(10):922-8. **BACKGROUND:** Fatigue is common in celiac disease. L-Carnitine blood levels are low in untreated celiac disease. L-Carnitine therapy was shown to improve muscular fatigue in several diseases. AIM: To evaluate the effect of L-carnitine treatment in fatigue in adult celiac patients. **METHODS:** Randomised double-blind versus placebo parallel study. Thirty celiac disease patients received 2 g daily, 180 days (L-carnitine group) and 30 were assigned to the placebo group (P group). The patients underwent clinical investigation and questionnaires (Scott-Huskisson Visual Analogue Scale for Asthenia, Verbal Scale for Asthenia, Zung Depression Scale, SF-36 Health Status Survey, EuroQoL). OCTN2 levels, the specific carnitine transporter, were detected in intestinal tissue. **RESULTS:** Fatigue measured by Scott-Huskisson Visual Analogue Scale for Asthenia was significantly reduced in the L-carnitine group compared with the placebo group (p=0.0021). OCTN2 was decreased in celiac patients when compared to normal subjects (-134.67% in jejunum), and increased after diet in both celiac disease treatments. The other scales used did not show any significant difference between the two celiac disease treatment groups. **CONCLUSION**: **L-Carnitine therapy is safe and effective in ameliorating fatigue in celiac disease. Since L-carnitine is involved in muscle energy production its decreased absorption due to OCTN2 reduction might explain muscular symptoms in celiac disease patients. The diet-induced OCTN2 increase, improving carnitine absorption, might explain the L-carnitine treatment efficacy.**

A few examples of related elated applications of carnitine in the treatment of fatigue: Efficacy of l-carnitine administration on fatigue, nutritional status, oxidative stress, and related quality of life in 12 advanced cancer patients undergoing anticancer therapy. Nutrition. 2006. Levocarnitine administration in elderly subjects with rapid muscle fatigue: effect on body composition, lipid profile and fatigue. Drugs Aging. 2003. Safety, tolerability and symptom outcomes associated with L-carnitine supplementation in patients with cancer, fatigue, and

carnitine deficiency: a phase I/II study. J Pain Symptom Manage. 2006. Double-blind, multicenter trial comparing acetyl l-carnitine with placebo in the treatment of fibromyalgia patients. Clin Exp Rheumatol. 2007. L-carnitine decreases severity and type of fatigue induced by interferon-alpha in the treatment of patients with hepatitis C. Neuropsychobiology. 2003.

12. Effects of Gluten Exposure on Absorption of Nutrients in the Intestine

As a recap, poor control of gluten intake results in **poor absorption of essentially all nutrients**, whether in food or taken as supplements. Several examples of this were described earlier, but the poor absorption would affect all nutrients, so your body would not have a "level playingfield" to do all the things it needs to do. This includes brain function as well. So, as always, gluten avoidance remains the cornerstone of nutrition for Celiac Disease. All the other issues described above are just the icing on the (gluten-free) cake.

[Metabolic and nutritional features in adult celiac patients. Dig Dis. 2008;26(2):128-33.Affective and psychiatric disorders in celiac disease. Dig Dis. 2008;26(2):140-8.]

MAPS of INTEREST: VITAMIN D and IODINE

VITAMIN D:
https://www.health.harvard.edu/newsweek/images/latitude-vitaminD.jpg
Except during the summer months, the skin makes little if any vitamin D from the sun at latitudes above 37 degrees north (in the United States, the shaded region in the map) or below 37 degrees south of the equator. People who live in these areas are at relatively greater risk for vitamin D deficiency.

(Actually, that's where **I** live … but you can see why it's a really big deal Up North!")

IODINE: Map showing spatial correlation between the former "Goiter Belt" in the northern U.S. and areas where the iodine content of drinking water is naturally low.
www.uwsp.edu/gEo/faculty/ozsvath/images/goiter_belt.htm