Sanford Medical Center

Aunt Cathy's Guide to Nutrition:

SOME Drug / Nutrition Interactions of Interest



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This paper is <u>not</u> intended to be a complete review and it is presented here without references. It is intended to be just a closer look at a collection of medication/nutrition interactions that have been especially problematic for my patients, and some suggestions for minimizing problems. There are (of course) <u>many</u> other drug/nutrition interactions that are not covered here and that I don't know a thing about. ^(C). Drug/Drug interactions are also not included here. As always, it is not intended to take the place of advice from your health care provider.

Anti- Seizure/Epilepsy Medications

<u>All seizure medications cause vitamin D to turn over faster</u>, so the intake needed to maintain healthy blood levels of vitamin D are higher than usual.

Vitamin D inadequacy is common in the general population, and it is especially prevalent among people taking seizure-control medications.

Vitamin D deficiency is associated with <u>many</u> health problems, including increased risk of cancer, congestive heart failure, impaired immune function, depression, muscle weakness, osteoporosis, falls, pain, and increased risk of all autoimmune disorders, such as Type I diabetes, MS, arthritis, lupus and more.

RDA/RDI/AI levels at the moment are not associated with optimal vitamin D levels even among healthy people, and they are very unlikely to assure adequacy among people using these medications.

Recommended in general: maintain a blood level at about 40-50 mg/dL. Ideally, get a blood level to determine current status and give a therapeutic dose to correct low levels (e.g. 50,00 iu/week x 8 weeks followed by a re-check.) Then provide an intake level sufficient to

maintain the 40-50 range (which may be found to require supplementation to provide 2000-5000 iu/day.) Please see my "Top Five" paper for more on this topic.

All seizure medications cause decreased absorption of biotin (vitamin B7).

Biotin is involved in many metabolic pathways, including the TCA Cycle to make ATP (making usable energy from food), and gluconeogenesis (making glucose out of amino acids.) Deficiency in general seems to be uncommon in healthy people, but when it does occur it has been known to result in a number of serious problems. It has been shown to contribute to depression, hallucinations, increased infections, poor muscle control, loss of hair, skin problems, seizures and developmental delay in infants. Eggs, nuts and legumes like peanuts are among the very best dietary sources. Eggs do contain a protein called avidin that makes biotin be poorly absorbed if the egg is eaten raw, but cooked eggs are excellent sources of biotin ... and also safer to eat in terms of food-borne illness risk. The yolk has most of the biotin.

The intake of biotin assumed to meet the needs of most healthy people is about 30 mcg/day. In addition to all seizure medications, alcohol also impairs absorption of biotin. Additionally, chronic antibiotic use decreases the biotin usually produced by bacterial activity in the large intestine. People with intestinal absorption problems (such as inflammatory bowel disease) have also been observed to become deficient in biotin. It appears that biotin supplementation can be useful for people with diabetes in particular.

Because a very high biotin intake has no known detrimental effects, supplementation at or above levels recommended for healthy people is very reasonable for anyone on chronic seizure medications or in other situations described above. Not all multivitamins contain 30 mcg biotin. However, it is easy to provide it singly if desired. For example, there are over-the-counter biotin supplements that provide 600 mcg, and it can also be found in variable amounts as a part of "B-complex" vitamin supplements. The "B-<u>100</u> Complex" type of supplement may include 300 mcg of biotin along with many other B vitamins.

Some Specific Seizure Medications That Interact with Nutrients.

Phenytoin (Dilantin)

<u>Folic acid</u> deficiency is associated with use of this medication if appropriate supplementation is not provided. However, there are some safety issues to consider:

When <u>starting</u> the prescription for phenytoin, it is recommended that people <u>start folic</u> <u>acid supplementation right away</u>. If a person is <u>already on the drug and found to be folic acid</u> <u>deficient</u>, generous and rapid folic acid supplementation can cause problems. In the latter case,

the physician can introduce supplemental folic acid slowly to avoid breakthrough seizures, and to work up to achieving a normal blood folic acid level. This is important because it is clearly not safe to simply let the person remain folic acid deficient. Folic acid deficiency is associated with birth defects, poor DNA production, depression, high homocysteine level, increased risk of stroke and impaired immune function.

The 1998 introduction of fortification of grain products with a well-absorbed form of folic acid in the US improves the odds of preventing some of the folic-acid related problems in the US today. However, requirements continue to be higher than for people not using phenytoin. The usual intake suggested for most healthy people is 400 mcg folic acid /day, with 600 mcg recommended in pregnancy. "Prenatal vitamins" often have 800 mcg of folic acid, but they often do not contain many other nutrients. For that reason, just recommending a prenatal vitamin is not a good solution to this problem. A better approach would be to provide as complete a regular multivitamin with minerals daily as possible, and add one or more tiny 400 mcg folic acid tablets.

Other food sources include leafy greens and orange juice, but it is not clear that folates in the form found naturally in foods are as well absorbed as supplemental forms among people using this medication. And, as it is well known that there is significant genetic variation in one's ability to obtain folic acid from non-supplemented food sources, it is reasonable to be generous.

Folic acid supplementation is simple, easy and safe at intake levels of 1000 mcg/day from supplements and fortified foods. That "upper limit" is based on the possibility that higher amounts <u>might</u> "mask" vitamin B12 deficiency, as recognized by elevated blood cell size. It was not due to any observed toxicity of the vitamin. However, large red blood cell size (Mean Cell Volume on a laboratory test) is a very late appearing symptom of vitamin B12 deficiency and it should not be relied upon to detect deficiency. Instead, steps described later should be able to prevent vitamin B12 deficiency, so the "masking deficiency of vitamin B12" concern is no longer an issue. There is also no evidence that naturally occurring folates in foods pose any threat to health.

In view of the well documented effect of phenytoin on folic acid status, it is reasonable to monitor this, e.g. via erythrocyte folate levels, to determine the amount of supplementation needed by an individual already on the drug. <u>Before starting phenytoin</u>, and in the absence of the ability to monitor the situation with laboratory assessment, it is reasonable to just begin a generous intake and maintain it ... e.g. a regular intake of 1000 mcg supplement daily. This amount can be provided in a tiny pill by prescription ... and that level of supplementation is available over-the-counter in Europe and elsewhere because of the excellent safety profile. One could also achieve an intake level around that amount (1200) in the USA from, for example, taking a standard multivitamin plus two tiny 400 mcg folic acid tablets without prescription.

The use of this medication is associated with birth defects and a Fetal Phenytoin Syndrome has been described. Relative inadequacy of many B vitamins (including folic acid) induced by use of this medication appears to be contributory to the degree of damage. For this reason, optimizing nutrition status in women of childbearing age is especially important. But really ... it is mighty important for everyone. [Please see my "Folic Acid Absorption" cartoon paper for further detail.]

<u>Vitamin B12</u> absorption is also impaired, so monitoring adequacy of vitamin B12 is important. As noted, normal Mean Cell Volume (red blood cell size) is NOT a useful assessment of adequacy ... by the time the cells are large, a lot of other damage has already occurred, and not all of it is repairable. A serum B12 level would be a much better test. [To obtain the most reliable and specific <u>functional</u> measure of vitamin B12 status, one could get a methylmalonic acid (MMA) level, which is more sensitive than a serum vitamin B12 level. However, this is not as available and it is more expensive.]

Vitamin B12 is affected by other medications as well, and by age and by certain dietary practices. Please see more detail about vitamin B12 in the section below called "Gastro-esophageal reflux (GERD) hyperacidity," and see my "Vitamin B12" paper and "Vitamin B12 Absorption" cartoon paper for further details.

Thiamin (Vitamin B1) levels in the blood are depleted by the use of phenytoin.

<u>Riboflavin (Vitamin B2)</u> can also be depleted because the drug increases production of a liver enzyme that destroys it. Supplementation of both is in order.

<u>Vitamin B6 (pyridoxine</u>) is also affected by intake of phenytoin, but there is a special caveat about taking the "B-100 complex" type of supplement: with this particular medication 100 mg vitamin B6 may be too high. Vitamin B6 increases the breakdown rate of phenytoin, so taking relatively high doses (e.g. 50-100 mg) may be a factor in decreased effectiveness of the drug. As described earlier, the "B-100 Complex"-type of supplement would provide 100 mg, so this would not be the best choice in this instance.

However, this does NOT mean that people should be made deficient of vitamin B6.

This vitamin is critical for many metabolic functions, including all protein metabolism, energy metabolism, DNA production and nervous system function. The usual recommendation for most folks is 1.5-2.0 mg/day. That amount should certainly be provided. If a person requires an additional generous vitamin B6 for other medical reasons, it might result in needing a different (higher) dose of Dilantin.

<u>Phenytoin impairs production of carnitine</u>, and carnitine adequacy is needed for the drug to work most efficiently. Carnitine inadequacy effects on metabolism are described below in the section on valproic acid, another seizure medication. Supplementation of carnitine is strongly recommended. Please see my Carnitine handout for more details.

Primidone (Mysoline) This medication has also been shown to impair vitamin B12 status.

Phenobarbital Vitamin B2 (riboflavin) can be depleted because the drug increases production of a liver enzyme that destroys it. Supplementation is in order.

Valproate / Valproic Acid (Depekene) Inadequate carnitine increases the liver toxicity of the drug and also contributes to very low blood sugar in certain contexts. Carnitine deficiency contributes to the side effects of lethargy and excessive weight gain noted with this medication. High triglycerides and poor control of insulin-treated diabetes have also been seen. Impaired production of carnitine can also lead to "breakthrough seizures" because inadequacy also impairs the utilization of the seizure medication itself. Please see my carnitine paper for specific details.

Stomach Acid Blockers for

Hyperacidity or Gastroesophageal Reflux Disease (GERD)

Proton Pump Inhibitors (PPIs) block production of stomach acid by over 90%. However, the form of vitamin B12 found naturally in foods of animal origin requires stomach acid for absorption.

The <u>crystalline vitamin B12</u> form found in pills (e.g. multivitamins or just vitamin B12 alone) or in <u>fortified</u> foods bypasses this problem, so supplementation in pill form is strongly advised. Vitamin B12 supplements are very tiny, very safe, cheap and easy to use. The form of vitamin B12 added to food is also of this type so loss of stomach acid does not interfere with vitamin B12 absorption from this source. This includes, for example, fortified cereals, infant formulas and vitamin-supplemented beverages.

[The <u>amount</u> of vitamin B12 provided in these forms needs to be considered when determining adequate intake. For example, if one drinks a fortified beverage, what number of

ounces would achieve the recommended amount? Eight ounces (1 cup) of some products provide 100%, but many products provide that amount only in about a quart a day. Check the label, or just add additional vitamin B12 via a multivitamin or a separate vitamin B12 pill. Vitamin B12 is extremely non-toxic.]

As described earlier related to phenytoin (Dilantin) use, vitamin B12 deficiency is associated with birth defects, poor DNA production, depression, high homocysteine level, increased risk of stroke, and serious neurologic damage. Deficiency is often missed until significant damage has occurred, in part because common blood tests like Mean Cell Volume (that identify overt deficiency by enlarged cell size) only pick up very late- appearing symptoms.]

Vitamin B12 absorption can be impaired by factors other than

absent stomach acid, so the above recommendations related to PPI use

will NOT correct other factors that interfere.

For example, loss of production of ar stomach-produced substance called Intrinsic Factor (IF) will impair absorption of vitamin B12 in the intestine. Intrinsic Factor may be inadequate among:

1. <u>elderly</u> people because of changes due to stomach atrophy affecting IF production.

2. people with a potentially debilitating autoimmune condition called "Pernicious Anemia," that

causes inability to produce IF in the stomach.

- 3. people with surgical removal of the stomach (gastrectomy.)
- 4. people who have had certain forms of gastric bypass surgery.

Additionally, the terminal ileum (the last part of the small intestine) is the only location in the GI tract where vitamin B12 can be absorbed. That means that damage or interference there can also make even generous oral intake of vitamin B12 inadequate. People with intestinal conditions such as inflammatory <u>bowel disease or who have "short bowel" due to intestinal surgery will</u> generally need to obtain vitamin B12 via another route.

<u>Vitamin B12 shots or special sublingual or nasal application forms</u> are needed if the absorption problems are not resolved. As discussed later, <u>this may be also be needed when the medication **Metformin (Glucophage)** is used. The interference with vitamin B12 absorption in the intestine in this case is caused by a different type of problem, and estimates are that up to a third of people using this medication chronically may be vitamin B12 deficient.</u>

Vitamin B12 deficiency takes a long time (e.g. two years) to become evident, and the consequences of inadequacy are very serious. For this reason, it is critical that people using PPIS or who have "achlorhydria" (inadequate production of stomach acid for any reason) assure an adequate oral intake of an absorbable form of vitamin B12.

Other conditions may require an administration route that bypasses the GI tract.

PPIs can also result in decreased absorption of inorganic iron and zinc

due to decreased acidity. Organic forms (like heme-iron and zinc in meat and lactoferrin in mother's milk) are not affected, but plant forms and pill/supplement forms (like ferrous sulfate, etc.) can be significantly less well absorbed. However, other dietary features can modify this effect in either direction. For example, adding meat to the meal improves absorption due to the presence of "Meat Protein Factor," and the addition of acidic foods (like orange juice and vitamin C) also enhances absorption of inorganic iron and zinc somewhat in this context.

Conversely, substances naturally occurring in certain plant foods, such as phytates, oxalates and tannins, will significantly impair absorption of inorganic iron and zinc. Interestingly, milk consumption also significantly impairs absorption of inorganic iron and zinc. Please see my "Nutrition Support of Iron Deficiency Anemia" paper for more details on this.

<u>Calcium</u> supplements are also less well absorbed, but a generous intake and -- more importantly --assuring a generous vitamin D intake will prevent problems. Most of the differences in absorption of various forms of supplemental calcium are only clinically important in the absence of the normal hormonal regulation of calcium absorption by vitamin D. When vitamin D status is adequate, the role of relative acidity in calcium absorption is much less important.

<u>Magnesium</u> absorption can also be impaired by these medications, and intake is often suboptimal in the US. Assuring a generous intake is a very good idea. Poor magnesium status increases risk of insulin resistance, osteoporosis and leg cramps. [More on this later ... please see my Calcium and Magnesium papers for more detail.]

Bacterial overgrowth can result from use of PPI acid blockers, which can sometimes lead to diarrhea and malabsorption of nutrients in general. This is also seen in achlorhydria due to aging. Hydrochloric acid in the stomach is actually a part of the immune system because the low pH kills many bacteria and other micro-organisms that may be consumed with food.

<u>Acid Blockers: H2 Blockers</u> These acid-reduction medications block production of stomach acid by ~65-70%. They present less overt risk of impairment of vitamin B12 from

natural food sources than acid reduction with PPIs, but supplementation in pill or other supplement form is strongly advised. Again, supplementation is very safe, cheap and easy to do.

Chronic Antibiotic Use

There are many types of antibiotics and many different reasons for using them.

For example, conditions associated with chronic use of antibiotics include:

Spinal Cord Injury including Spina Bifida, and others at risk of kidney/urinary tract infections, Tuberculosis, Cystic Fibrosis, Inflammatory Bowel Disease, Chronic Ear Infection, Immune System Issues (e.g. HIV/AIDS, Hypogammaglobulinemia, etc.) and Severe Acne.

General for All Chronic Antibiotics:

Vitamin K

Antibiotics impair the expected vitamin K production by intestinal bacteria. This is not new. **However, that source is now known to be generally poorly available for <u>everyone</u>. This is fairly new.**

However, people taking chronic antibiotics will be getting <u>absolutely none</u> from that source. Supplementation with generous vitamin K is recommended for everyone, and for this population in particular. Vitamin K is very NON-toxic, although people often assume that it is toxic because it is fat soluble. No upper end of safety has ever been established for it because no one has ever taken enough to cause problems. [The only safety issue involving vitamin K is the (often misunderstood) interaction with the drug warfarin (Coumadin) which will be discussed later.]

The current recommended intake of vitamin K levels for the healthy population appears to underestimate the amount needed to assure optimal blood levels of this vitamin. See my Vitamin K papers for more detail. **Vitamin K deficiency contributes to osteoporosis, arterial calcification, kidney calcification, risk of diabetes and certain cancers.** Note that these health risks all are increased long before coagulation time is effected so one's <u>coagulation time is not a</u> good way to monitor a person's vitamin K adequacy.

Impairment of Absorption of Folic Acid

The 1998 introduction of fortification of grain products with a well-absorbed form of folic acid in the US improves the odds of preventing some of the folic-acid related problems. However, requirements continue to be higher for people chronically taking antibiotics than for people not using these medications. Generous supplementation is recommended. It is also safe, easy and inexpensive. As described earlier, the results of folic acid inadequacy includes birth defects, poor DNA production, depression, high homocysteine level, increased risk of stroke, and serious neurologic damage.

Two Specific Interactions of Interest:

Tetracycline

Tetracycline reduces absorption of folic acid, but B vitamins in general also reduce absorption of tetracycline, so they should not be taken <u>at the same time.</u> As always, this does <u>not</u> mean that a person should be made to be vitamin deficient in order to optimize drug absorption. It just means that attention should be paid to maintaining both general vitamin adequacy and efficacy of the tetracycline dose used.

Isoniazid (Nydrazid, Laniazid)

Vitamin B6 (pyridoxine) levels in the blood are decreased by these TB medications. It used to be a well known interaction when tuberculosis was very common, but it fell off our radar when TB became quite rare. Only we old guys remember it from that time period. However, TB is now back (for a variety of reasons) and the awareness of vitamin B6 supplementation also needs to come back whenever these medications are used. Some of the neurologic and birth-defect symptoms described as side effects of isoniazid appear to be related to the relative vitamin B6 deficiency associated with its use.

In any case, assuring adequacy of vitamin B6 is very important in this situation, and as is the case for other B vitamins, this can be done easily, cheaply and safely. It does not impair the efficacy of the drug. Pyridoxine is known to be safe at up to 200 mg/day. The usual recommended intake is between 1.5-2 mg/day. It is usually given at 10-50 mg/day to patients on isoniazid.

There are many interactions with nutrition seen with chronic antibiotic

use, but this is a quick overview so I have focused on only a few examples. Health care professionals will want to familiarize themselves with the ones they see often in their practice and that will be far more than can be covered here. Luckily, this kind of specific information is now easy to get on the Internet. S

Anti-coagulants: Warfarin (Coumadin)

Since 2005, our understanding about the role(s) of vitamin K and the natural means by which we get it have undergone tremendous change. As described earlier (in the section on antibiotics,) it is now known that there are many important functions of vitamin K besides the well-recognized role in blood coagulation, making us aware that inadequacy of the vitamin is very detrimental to health. [For example, vitamin K is a cofactor necessary to activate osteocalcin/calcitonin to allow calcium to be moved from the bloodstream into the bones. Failure to manage calcium levels in blood and bone contribute to a variety of health problems.]

Additionally, during this same period our assumptions about the availability of vitamin K made by intestinal bacteria have changed markedly. And even the importance of assuring ADEQUACY of vitamin K (and not just consistency of intake) as a key factor in the safety of warfarin use has now been shown. That is, persons with adequate/normal vitamin K status have been shown to be far less vulnerable to extremes of coagulation volatility that is a danger associated with the use of this drug.

Misunderstandings about the interaction of warfarin with vitamin K are extremely common and they result in very serious health consequences. This particular anticoagulant works by interfering with the availability of vitamin K as a cofactor in the cascade of events that produces a blood clot. **The official recommendations from the manufacturers are that people should take a consistent and adequate amount of vitamin K.**

A consistent and <u>adequate</u> vitamin K intake will do much to prevent volatility in blood clotting that can be associated with wide swings in vitamin K intake. That is, maintaining adequacy of vitamin K seems to buffer the degree of variation in coagulation associated with daily differences in vitamin K intake.

However, the official recommendation above is very often misinterpreted by users of the medication and by health professionals, and the belief continues to be commonly expressed that one should "avoid all sources of vitamin K." Some people are even told that they should avoid taking vitamins ... even if the vitamin product did not contain vitamin K! (Until very recently, MANY common multivitamin brands did NOT contain vitamin K.) Interestingly, as noted above, providing a daily standard amount of vitamin K actually makes the drug safer to use, especially in elderly people. Additionally, it prevents the serious (but not uncommon) consequences of accidentally (or intentionally) inducing a Vitamin K deficiency that results in increased risk of the following health problems:

Osteoporosis

Calcification of kidneys and kidney stones Artery damage (Calcification of arteries, increased arterial inflammation and risk of plaque build-up, high blood pressure and varicose veins.) Cancer of the liver and colon Type II Diabetes Pre-eclampsia in pregnancy

The Role of Vitamin K in Blood Clotting:

Remember that vitamin K does not MAKE you clot your blood ... it just needs to be available if you WANT to clot your blood.

[If it MADE people clot their blood, we could expect to have big problems after eating a big spinach salad. Vitamin K is just a cofactor (a tool) needed to do the job, not the thing that initiates the process.]

Recommendations for people not using warfarin:

People <u>not</u> using warfarin (that is ... most everyone):

Take a generous amount of vitamin K. A good daily amount would be about twice the current recommendation for most healthy people (because that level appears to be set too low to assure optimal blood levels.) Dark leafy greens are great foods for many reasons, and they are the richest dietary source. Supplemental vitamin K is an option as well. Remember that vitamin K is NOT toxic and no upper tolerance level has ever been set because no one has ever had problems. **The ONLY vitamin K safety issue is the potential interaction with the drug warfarin.**

Recommendations for people who may be going to start taking warfarin

People not using warfarin yet but who may starting it:

Before starting the drug do as described above for people not on the medication to assure an adequate vitamin K level. The doctor will set the appropriate drug level needed to control coagulation for a person (you) who has adequate vitamin K status.

[This prevents setting the drug prescription based on a person's unrecognized inadeaquate vitamin K level.] Then continue to take in a consistent but adequate amount as a vitamin K supplement while on the drug. Now, many doctors are regularly prescribing a daily vitamin K supplement when they initiate any warfarin prescription in order to reduce the health risks associated with this medication.

Recommendations for people <u>currently using</u> warfarin:

Do not make any changes in your vitamin K intake without the approval of your physician.

If your vitamin K level is low, he/she will want to gradually "walk up" the vitamin K intake until you are in the healthy range. This can be monitored just as it was when one initially starts on the medication. Abrupt changes from low to normal-high vitamin K are not safe when one is on warfarin. There may be other factors to consider in a person's particular situation

Once the low vitamin K level is corrected by the physician, he/she will want you to continue to take in a consistent but adequate amount as a vitamin K while on the drug. As noted, this will often include a prescription for daily vitamin K supplement in order to maintain the health risks. Additionally, there is no reason to discontinue assuring a consistent and adequate amount of vitamin K if the warfarin is discontinued.

An additional reason to avoid banning dark leafy greens from the diet:

Inducing a vitamin K deficiency by banning vitamin K-rich foods also **decreases intake of lutein**, the dark green pigment of the foods that provide vitamin K. It is a potent antioxidant with important roles in prevention of oxidative damage to cell membranes, especially in macular degeneration and the development of complications of diabetes.

Vitamin K-rich foods are naturally very low in fat and calories, and they are very "nutrient dense." Removing them unnecessarily from people's diet is not in their best interests.

Similarly, telling people to "stop taking a multivitamin to avoid taking in vitamin K" means that one has just removed all the <u>other</u> nutrients they would have received by taking the multivitamin. This includes 400 iu vitamin D, and although the 400 iu amount in the multivitamin is not even sufficient as a maintenance level in terms of blood vitamin D level, in many people it may be the ONLY vitamin D they do get. It is especially not benign to remove this source of vitamin D and other nutrients such as vitamin B12 in a form that is absorbed best by elderly people or those on PPIs.

Other types of anti-coagulants

Many <u>other anticoagulants</u> (e.g. Plavix, Aspirin, Aggrinox) do not work by means of interacting with vitamin K. They operate entirely differently, in a way that does not involve tinkering with vitamin K availability. That means that there is <u>absolutely no reason at all</u> to restrict vitamin K for these patients. Encourage intake of foods rich in vitamin K for many reasons, including the other nutrients and lutein that are well-represented in those foods. A multivitamin with minerals that also includes vitamin K is a very good idea as well, in part because there are a lot of people who don't go anywhere near those dark leafy greens even if we nag at them. Additionally, it appears that the amount of vitamin K needed to assure a healthy blood level is higher than 90-120 mcg, the amount currently recommended for healthy people.

Diuretics: Furosemide (Lasix) Use

Magnesium is a mineral cofactor in over 300 metabolic pathways, including energy and protein metabolism, bone health and nervous system function. Use of furosemide (Lasix) increases losses of potassium and also magnesium. The potassium part is well known to health professionals so I won't address it here, but the magnesium losses are much less well known. At a cellular level, potassium metabolism cannot operate normally in the absence of adequate magnesium. The foods that are well-known to be rich in potassium (e.g. potatoes, milk, bananas, orange juice, etc.) do not happen to be rich in magnesium.

The best foods sources of magnesium are the part of the plant that will be "the baby plant" ... that is, the part that is a seed, bean, germ, or nut. Increasing intake of these foods can be very helpful for many health reasons. This includes, for example, decreasing risk of developing Type II diabetes, and improving management of diabetes if it is already established. The fairly recent recognition of these foods as the best magnesium sources and the importance of magnesium adequacy is a main reason why "whole grains" ... the kind that still have the **germ** included ... and eating nuts are being encouraged.

Most multivitamins contain 0- 25% of the recommended magnesium intake. (Most contain <u>zero</u> potassium, by the way.) For people <u>not</u> on furosemide, the amount of magnesium provided in a multivitamin may be sufficient <u>if</u> food magnesium sources are generally good. However, **it is unlikely to be sufficient if furosemide is in the picture as well.**

In this context, supplementation of a separate magnesium oxide or magnesium chloride to provide about 400 mg/day more is a good idea for people on this medication, unless the person has poorly functioning kidneys. Four hundred is just the usual recommended amount for healthy people and readily available over the counter ... it is not a high "therapeutic" level. [Note that magnesium sulfate and magnesium citrate are poorly absorbed sources of magnesium, and they contribute to loose stools. That is why they are used for constipation problems and for cleansing the bowel prior to having a colonoscopy. The unabsorbed particles attract water to the intestine. They are not as effective as dietary supplements.]

The addition of a medication that increases urinary losses of magnesium can result in very low levels. Consider that **magnesium intake is generally low in many Americans** (e.g. NHANES: Most Americans obtain less than 2/3 of the recommended amount of magnesium.) This is not good because, as noted, **magnesium inadequacy contributes to diabetes** (because insulin receptors are magnesium dependent) and also to energy metabolism in general, all protein metabolism, and nerve function. It is hugely important in pregnancy.

At the same time, we rarely look closely at a nutrient that is not easy to evaluate meaningfully. For example, **blood magnesium levels in general do not reflect cellular magnesium levels**, so an "OK" blood magnesium level does not tell us about magnesium intake adequacy. The blood Mg level is controlled by the kidney, and it will stay in the normal range even if cells are not getting enough for optimal functioning.

My experience has been that most people are given advice about bananas for potassium (courtesy of a successful advertising campaign of the Chiquita people.) But the magnesium loss is left out of the conversation in part because it is hard to measure with a lab. The other reason is that people have not been told what foods are rich sources of magnesium and how to assess magnesium intake meaningfully.

The practical answer is to ask about the amount of those "baby plant" foods that a person eats. Regularly eating a good amount of nuts, seeds, legumes (like beans, peanuts, peas and lentils) and whole grains is the best indication that one has a healthy dietary magnesium intake. [One large study from Harvard, for example, found that eating an ounce of nuts or peanuts four times a week or more was associated with 25% less risk of developing type II diabetes in a 16 year period.] These foods are also very rich sources of many other nutrients in addition to magnesium.

The asking about these foods is key because details of a person's actual diet are rarely evaluated in the brief amount of time allotted to a clinic visit. Just saying "eat a balanced diet and exercise!" does not provide enough specific information to protect people from the increased risk of magnesium inadequacy associated with this medication.

Encouraging a generous intake of these same foods (along with a multivitamin with minerals) is especially important for your patients on furosemide or any other diuretic that is described officially as causing potassium loss in the urine. If the patient is unable or unwilling to eat a generous amount of these foods, consider adding a 400-500 mg magnesium supplement as described (unless there is a question of kidney failure.)

For more on these nutrition issues, please see my other papers, which include:

Overview Papers:

My Current Top Five Easy Ways to Improve Your Family's Nutrition (subject to change at any moment! ③)

Thinking about Other Nutrition Issues in Diabetes

Top Ten Pregnancy Nutrition Recommendations

Why Are Children with Chronic Illnesses or Handicapping Conditions at High Risk of Receiving Suboptimal Nutrition?

Single Nutrient Topics:

Magnesium

Folic Acid

Calcium A Short Carnitine Discussion that Might Be Helpful

Vitamin B12 Nutrition Support of Iron Deficiency Anemia

Vitamin K: New Issues in Cardiovascular Health, Renal Health, Osteoporosis, Liver & Colon Cancer, Diabetes, Pregnancy and Varicose Veins

Vitamin K: Focus on the Vitamin K and Warfarin/Coumadin Anticoagulant Drugs Issue