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REVIEW

Drugs That Deplete-Nutrients That Heal

A review of Drug-Induced Nutrient Depletion Handbook, 1999-2000

by Ivy Greenwell

Ross Pelton and three other pharmacists with a holistic orientation have given us a valuable gift: a reference guide that lists not only the common side effects of various widely used drugs, but also the nutrients that these drugs deplete, whether by interfering with absorption, or by inhibiting transport or metabolism.

The knowledge that long-term use of many drugs leads to nutritional deficiencies of specific nutrients is not new; it has been documented by a large number of studies done over the last three decades. And yet this information is not generally communicated to the patients taking these drugs. In the case of the elderly, who are already likely to suffer from nutritional deficiencies, the ravages of the multiple drugs typically prescribed for aging-related diseases could lead to serious consequences. In addition, the elderly are more likely to use non-prescription drugs such as non-steroidal anti-inflammatories or antacids. Generally, they are completely unaware that these might make them deficient in calcium, phosphorus, folic acid and iron.

The elderly are only one example. Women are another group of drug consumers who should be especially concerned with drug-induced nutrient depletion. Few women know that oral contraceptives lower the levels of such vital nutrients as Vitamin B2, B6, and B12, Vitamin C, folic acid, magnesium and zinc. Mainstream hormone replacement (chiefly Premarin, but also Estratab and raloxifene) can also lead to deficiencies in Vitamin B6, magnesium and zinc. Heart patients, diabetics, epileptics and heavy users of corticosteroids and anti-inflammatories are also particularly at risk for drug-induced nutrient deficiencies.

This is a fairly technical reference guide, written so as to be an adequate source for pharmacists, physicians, nurses and other health professionals. At the same time, however, the authors rightly insist that every individual who takes medication should have access to this information. Armed with this knowledge, patients can then act to protect their health by modifying their diets and/or taking supplements.

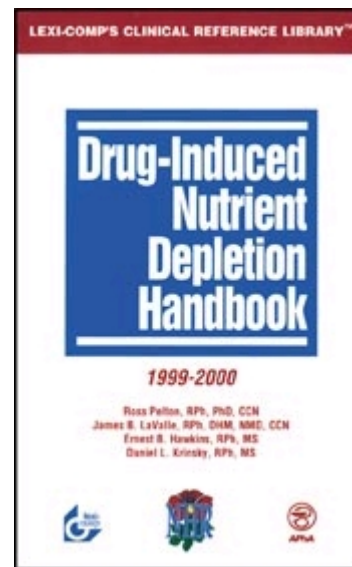
At the same time, the authors are careful not to overstate their case by blaming too many problems on drug-induced nutrient depletion. They state, "This book does not suggest that drug-induced nutrient deficiencies are the source of people's medical problems. Many people have high stress, pollution, poor diets and other negative influences on their health. When individuals take medications that create an additional nutrient depletion, it may be the proverbial straw that breaks the camel's back."

For instance, a person suffering from high blood pressure and heart disease is likely to be deficient in coenzyme Q10, folic acid and magnesium. Unfortunately, the drugs commonly prescribed for cardiovascular disease and hypertension tend to deplete those very nutrients. Some of the side effects of those drugs may in fact stem from drug-induced nutrient deficiencies. To compound the irony, chances are that if the patient had been taking CoQ10, folic acid and magnesium, there may not have been a need for these dangerous drugs. Thus, millions of people develop serious disorders in which nutrient deficiencies play a significant role; the same people then end up taking medications that often further deplete various critical nutrients.

Pelton openly states his pro-supplement philosophy. Most Americans would benefit from taking nutritional supplements. Those who take prescription drugs have a particular need for learning more about nutrient depletion so that they can counteract it.

The structure

Since this is a reference guide, efficient organization is crucial. Pharmacists and physicians need to be able to tell at a glance



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which drugs deplete which nutrients, and the consequent problems that may arise from this deficiency. For professionals, probably the most useful part of this handbook is the chart of drugs listed by category (ACE inhibitors, non-steroidal anti-inflammatories, antibiotics, corticosteroids, beta blockers, diuretics, etc.), the nutrients they deplete, and the possible deficiency symptoms. A layman, on the other hand, is probably more likely simply to look up the name of his medication in the index, go to the page describing the drug and the nutrients it depletes, and then, if there is sufficient interest, go to the section that describes the functions of various nutrients. Both prescription and over-the-counter drugs are included. Two other features make this handbook of special interest: an appendix on herb-caused nutrient depletion (diuretic and tannin-containing herbs are special culprits), and the food-drug interaction chart. There is also a brief section on chemotherapy drugs, but it should be stressed that cancer patients should seek more comprehensive sources and professional advice before making any decisions about taking supplements.

The handbook also includes abstracts of various studies that the authors use to document their summaries of drug-induced nutrient depletion. It is to the authors' credit that they include negative findings as well. As the authors explain, "Conflicting studies do not necessarily negate positive studies. Oftentimes there are differences in dosages, ages and health conditions of subjects, number of participants, etc."

The inclusion of the abstracts is of great value, since the story that emerges in the abstracts is sometimes more complex than that which can be summarized in the statement that such and such drug depletes such and such nutrient. In the case of magnesium and estrogens, for instance, we learn that estrogens actually enhance magnesium uptake and utilization by both soft tissues and bone, which may significantly contribute to premenopausal women's resistance to heart disease and osteoporosis. But when magnesium is deficient in the diet, the estrogen-induced higher utilization of magnesium may result in incorrect calcium-magnesium ratio in the serum, favoring greater coagulation and raising the risk of thrombosis. The authors of this study warn against excess calcium supplementation in the face of magnesium deficiency. The practical implications for women who take either oral contraceptives or hormone replacement therapy are clear, and enormously important. Thus, those readers who bother to study at least some of the abstracts can gain valuable knowledge that is not easily accessible elsewhere.

One of the most informative and enjoyable parts of the book is the section dealing in depth with various nutrients. The book may be worth buying for the sake of this section alone, even for someone who avoids taking prescription drugs. The authors are to be applauded for providing more precise and up-to-date information about vitamins and minerals than can be found in typical popular sources. There is no "dumbing down" here, only solid explanation derived from the latest research. Some of this information may be too technical for the average reader without any background in biochemistry. Those who enjoy digging deeper, however, will feel gratified.

Let us now take a look at several highlights from this in-depth section.

Coenzyme Q10

A large number of drugs deplete Coenzyme Q10. These include such widely used tricyclic antidepressants as Elavil (amitriptyline) and Tofranil (imipramine), the anti-psychotic drug Haloperidol, cholesterol-lowering statin drugs such as Lovastatin and Pravastatin, beta-blockers, anti-diabetic sulfonylurea drugs such as Glucotrol (glipizide) and Micronase (glyburide), and the anti-hypertension drug Clonidine. These common drugs, as well as several others, interfere with the body's synthesis of CoQ10 and may cause a deficiency of this crucial compound, so important for energy production and protection against free radicals. This drug-induced depletion can be particularly serious in the elderly, who already suffer from aging-related CoQ10 deficiency.

It is particularly ironic that drugs prescribed to heart patients result in lower levels of CoQ10, since the heart has an enormous need for CoQ10 for its energy production. In fact, a CoQ10 deficiency first manifests itself in cardiovascular symptoms. The authors warn, "The results of some studies suggest that congestive heart failure is primarily a coenzyme Q10 deficiency disease." The same may be true of cardiomyopathy, heart muscle impairment which may lead to heart failure. The authors also list other symptoms of CoQ10 deficiency, including angina, cardiac arrhythmias, mitral valve prolapse, high blood pressure (which may lead to stroke), gum disease, low energy and a weak immune system (which may result in greater susceptibility to cancer). Recently it has also been discovered that CoQ10 is very important for brain health, and may help prevent Parkinson's disease and Alzheimer's disease.

The importance of CoQ10 can hardly be overemphasized. As its name indicates, it is a co-enzyme—a substance that works with an enzyme, or a variety of enzymes, to produce a chemical reaction. CoQ10 is a required cofactor in energy production in the mitochondria, and thus plays a critical role in the synthesis of ATP, our "energy molecule," the chemical fuel used by all cells. Thus it is not surprising that one tell-tale symptom of CoQ10 deficiency is lack of energy and a feeling of "running on empty"—something that users of beta-blockers and other anti-hypertensive drugs often complain about. It's very simple: no system in our body can run efficiently and defend itself against damage and disease if we don't produce enough energy in our mitochondria, and we can't produce enough energy without sufficient CoQ10. While CoQ10 is especially important for



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Being fat-soluble, CoQ10 is also an antioxidant, protecting the lipids in all cell membranes, especially the mitochondrial membranes. CoQ10 performs two chief functions in the mitochondria: it helps produce ATP, and it quenches some of the free radicals that are a by-product of the energy-producing cycle. CoQ10 is also a part of our primary antioxidant network, enhancing the effectiveness of other antioxidants, including Vitamin E, which it closely resembles in chemical structure.

While normally we can synthesize CoQ10, this synthesis is a complicated 17-step process that depends on adequate nutrition, with sufficient vitamins and trace elements. Thus, malnutrition is one of the reasons for CoQ10 deficiency. Another major reason is the use of one of the many very commonly prescribed drugs.

Anyone with cardiovascular problems would be wise to use CoQ10 supplements. The authors point out that CoQ10 helps protect against the toxic side effects of beta blockers. Likewise, high doses help prevent heart damage in patients receiving anti-psychotic agents or certain chemotherapy drugs such as adriamycin.

While organ meats and seafood provide some dietary CoQ10, it is impossible to obtain enough CoQ10 from the diet, particularly as we grow older-and if we take one of the many CoQ10-depleting medications that are so commonly prescribed for aging-related disorders. These drugs often only mask the symptoms and compound the underlying problem by lowering the levels of the very nutrient needed to raise cellular energy levels and increase antioxidant protection-CoQ10.

Again, one of the huge ironies of mainstream medicine is that many physicians have not even heard of CoQ10. They are not aware that declining levels of CoQ10 play a significant part in the susceptibility to the diseases of old age, and that so many drugs aimed at controlling the symptoms of these diseases further depress CoQ10 levels. Heart patients and diabetics are in critical need of effective CoQ10 supplements.

Folic acid deficiency: yet another case of drug-induced depletion

Another sad case of drug-induced nutrient deficiency involves the depletion of folic acid (also known as folate and folacin) by a myriad of commonly used drugs. These include aspirin and other salicylates, ibuprofen, indomethacin and other non-steroidal anti-inflammatories. Celebrex unfortunately also depletes folic acid. Methotrexate, used in the treatment of rheumatoid arthritis and various cancers such as leukemia and lymphoma, is notorious for depleting folic acid. Likewise, the use of corticosteroids, barbiturates such as phenobarbitol, sulfa drugs such as Bactrim, certain antibiotics, diuretics and oral contraceptives can cause a deficiency of folic acid. The widely used anticonvulsive drug Dilantin (phenytoin) and related drugs also deplete folic acid.

The authors point out that folic acid deficiency is one of the most common vitamin deficiencies. In fact, it may be the number one vitamin deficiency in North America. It is shocking to realize how long it has taken the FDA to mandate adding folic acid to commercial grain products, chiefly white flour and breakfast cereal. The mandated level of enrichment is still so low that unless one eats lots of spinach, broccoli, beans, beets, yeast, eggs and organ meats such as liver and kidneys, one is likely to need folic acid supplements. At present, only about a quarter of the adult U.S. population takes supplements that contain folic acid.

Why the enormous importance of this B vitamin? Folic acid happens to be one of the chief methylating agents. It is only recently that we have begun to understand the role played by methylation in protecting our DNA against damage. Folic acid is also crucial for the conversion of homocysteine to methionine, thus lowering the levels of this harmful atherogenic compound. Deficient methylation is one of the key dysfunctions brought on by the aging process. In a vicious circle, many of the diseases of aging are due to a significant degree to deficient methylation.

In addition, folic acid also plays a crucial role in the production of nucleic acids (DNA and RNA) and in cell division. It is well known that adequate levels of folic acid are needed for the prevention of terrible birth defects known as neural tube defects such as spina bifida and the especially horrifying anencephaly, in which a large part of the brain fails to develop at all. The handbook points out the less known fact that other birth defects such as cleft palate and cleft lip may also be prevented by providing folic acid during pregnancy. Low birth weight and various pregnancy complications are also associated with low levels of folic acid.

In addition, folic acid appears to help protect against colon cancer and cervical dysplasia, a precancerous condition. The authors state, "Some professionals believe that the folic acid depletion caused by oral contraceptives is linked to the high incidence of cervical dysplasia and hysterectomies" in the United States. Large doses of folic acid can reverse cervical dysplasia. Long-term cigarette smokers might also gain a degree of cancer protection if they take folate supplements.

Folic acid may also help alleviate arthritis and depression. By lowering homocysteine, this inexpensive B vitamin aids in the prevention of heart disease and stroke, and possibly also osteoporosis and Alzheimer's disease.

Since folic acid is necessary for the synthesis and maturation of red blood cells (erythrocytes), its deficiency results in a shortage of these cells, and hence inadequate oxygenation of all tissues. Folic acid also plays a role in the maturation of white blood cells (leukocytes), thus enhancing the immune response.



The handbook points out the less known fact that other birth defects such as cleft palate and cleft lip may be prevented by providing folic acid during pregnancy

Symptoms of folic acid deficiency include elevated homocysteine, anemia, headaches, fatigue, depression, hair loss, insomnia and increased susceptibility to infection.

Again, there are medical ironies here. Folic acid is helpful in relieving arthritic pain, but the drugs commonly prescribed for arthritis deplete folic acid. The cells of the intestinal lining have a special need for folic acid because of their high rate of replication; sulfasalazine, a drug commonly prescribed for colitis, can cause a deficiency of folic acid, ultimately delaying healing.

It is likely that thousands of premature deaths of heart disease and stroke could be prevented through adequate supplementation with folic acid. Some multivitamins and B-complex vitamins include only 100 mcg of folic acid; 400 mcg is a better level, and there is much to be said for using even more than that. It is a tragedy that this very inexpensive and non-toxic vitamin is not more widely used-especially by those who need it the most, including millions of users of anti-inflammatory drugs and oral contraceptives.

Drugs and magnesium

Another extremely common dietary deficiency involves magnesium. A USDA survey reported that 75% of Americans consume less than the RDA of magnesium. Again, a large number of commonly prescribed drugs deplete magnesium. These include oral contraceptives and both conjugated estrogens (Premarin) and esterified estrogens (Estratab). Various antibiotics, such as tetracyclines and doxycycline, also deplete magnesium. Diuretics are another class of

magnesium-depleting drugs, as is digoxin, used in the treatment of congestive heart failure. Corticosteroids also deplete magnesium.

While the need for calcium has received tremendous publicity, magnesium remains relatively neglected. The irony here is that excess calcium supplementation may lead to magnesium deficiency (it also interferes with zinc and iron absorption). Magnesium is important not only for the bones and teeth, but plays an essential part in a myriad of physiological functions. The authors state that magnesium "is a cofactor in over 300 enzymatic reactions in the body." Without magnesium, there would be no transmission of neural signals or muscular activity, to give just two examples. Furthermore, magnesium is a cofactor for the phosphorylation reactions needed to produce ATP, our chemical fuel. This essential mineral is also involved in the synthesis of DNA and RNA, and in various detoxification processes, as well as in blood sugar control. The authors call magnesium "a nutritional superstar when it comes to cardiovascular disease." Magnesium deficiency goes hand in hand with atherosclerosis, heart attack, hypertension and stroke. Low levels of magnesium can cause a life-threatening cardiac spasm.

The authors warn: "It is now recognized that many heart attacks happen to individuals with relatively healthy hearts. It is a magnesium deficiency that causes a cardiac spasm, which results in death." This happens because magnesium is a natural calcium channel inhibitor. When the levels of magnesium fall too low, too much calcium can enter the cells of the heart muscle, resulting in a dangerous cramp.

A minor version of the muscular cramps caused by magnesium deficiency are the leg cramps that tend to disrupt the sleep of the elderly. Other symptoms of magnesium deficiency include insomnia, restlessness, irritability, nervousness, anxiety, depression, fatigue and osteoporosis. Migraines and PMS appear to be related to magnesium deficiency. Interestingly, so is asthma. Some diabetics show a magnesium deficiency. Magnesium is also important for the kidneys. It helps prevent the formation of kidney stones.

The authors stress the importance of magnesium for the prevention of osteoporosis. They state, "Magnesium may be more important than calcium for bone health." Why? Without magnesium, there can be no normal calcium metabolism. Magnesium is involved in the skeletal bone-crystal (hydroxyapatite) formation. Pelton and colleagues are emphatic: "Calcium supplements are only minimally effective when taken alone." If magnesium is deficient, calcium may be deposited not in the bones, but in soft tissue, including the arteries, joints, brain and kidneys. Magnesium is also necessary for the synthesis of vitamin D, and it plays a role in maintaining tooth health, since it is magnesium that helps bind calcium to the tooth enamel, creating a barrier to tooth decay.

All in all, magnesium is by itself one of the best "drugs" that nature has provided. It could eliminate the need for all kinds of cardiovascular drugs, for instance. The authors give the following examples: like aspirin, magnesium inhibits platelet aggregation; like Coumadin, magnesium thins the blood; like Procardia, a calcium channel blocker, magnesium prevents excess calcium uptake; like Vasotec, an ACE inhibitor, magnesium relaxes blood vessels.

One could add to this the blood-pressure lowering activity of magnesium, which could eliminate the need for the anti-hypertensive drugs, when the treatment with magnesium is combined with other alternative health measures. Likewise, diabetics could reduce or eliminate their need for insulin and other anti-diabetic drugs if they followed a treatment that includes magnesium, known to help

stabilize blood sugar. Since magnesium relaxes bronchial muscles, this versatile mineral is also a valuable part of alternative treatment for asthma, bronchitis and emphysema. Asthmatics would do well to supplement with magnesium, especially considering that corticosteroids lower magnesium levels. Insomniacs, migraine sufferers, PMS sufferers, fibromyalgia patients and those prone to kidney stones should also seriously consider taking magnesium supplements.

Magnesium is cheap; drugs are expensive. Need more be said?

Zinc

Zinc deficiency is also rampant both in the United States and all over the world. It increases with age due to poor absorption and the inadequate diet of many elderly people. Vegetarian and semi-vegetarian diets, low in animal protein and high in phytate-containing grains, often lead to zinc deficiency. Zinc-depleted soils are also a factor, as is food processing. Zinc deficiency is often seen in conditions such as alcoholism, diabetes, liver and kidney diseases, macular degeneration, inflammatory bowel diseases and melanoma.

Like magnesium, zinc can be depleted by a variety of drugs. These include corticosteroids, oral contraceptives, oral estrogens used in hormone replacement therapy (including the designer estrogen raloxifene), ACE inhibitors such as Lotensil (benazepril) and Altace (ramipril), diuretics such as Hydrex (benzthiazide), triamterene, and Bumex (bumetanide), the cholesterol-lowering drug cholestyramine resin, and the anti-ulcer drug Cimetidine.

Zinc deficiency affects every cell in the body, since zinc is needed for the activity of well over 300 enzymes. One of them is alcohol dehydrogenase, which detoxifies alcohol. Another important zinc-dependent enzyme is alkaline phosphatase, essential for the use of phosphates in bone metabolism. Other enzymes include the cytochrome C system, the extremely important antioxidant enzyme zinc/copper superoxide dismutase, carbonic anhydrase, which helps excrete carbon dioxide, and carboxypeptidase, necessary for the digestion of proteins. DNA methyltransferase, one of the most important enzymes regulating gene expression, contains zinc.

Zinc also plays a part in the synthesis and/or function of several hormones. Zinc is a component of insulin, and may also help regulate insulin receptors. In addition, zinc facilitates the action of thyroid hormones by promoting the conversion of thyroxine (T4) to the more active triiodothyronine (T3). Zinc is also needed for the production of a thymus hormone, thymulin.

Zinc plays a pivotal role in the synthesis of DNA and RNA, protein synthesis and cell division. In addition, zinc helps protect DNA from damage.

Another well-known function of zinc is the enhancement of immunity. Yes, zinc lozenges and zinc nasal spray do work to reduce the duration and severity of the common cold. But zinc plays a more general role in the immune system: it helps regulate the activities of T lymphocytes, natural killer cells, interleukin 2 and more. Zinc also regulates the levels of vitamin A by controlling its release from the liver; vitamin A likewise has a significant impact on the immune system.

Deficiency symptoms include slow wound healing, poor sense of smell and taste, problems with skin, hair, and nails (zinc is highly concentrated in skin, hair and nails), low immune response and frequent infections, night blindness, excessive sensitivity to light, depression and even lethargy, anemia, menstrual and fertility problems, male sterility, various pregnancy complications and joint pain (zinc has some anti-inflammatory activity). Benign prostate enlargement may reflect zinc deficiency. Even stretch marks during pregnancy are due partly to zinc deficiency (pregnant women have a higher risk of being deficient in zinc). White spots on fingernails are a telltale sign of zinc deficiency.

Seafood (including the legendary oysters), eggs and meat are the best dietary sources of zinc. Unfortunately for strict vegetarians, plant food provides very little zinc, and then in a form not well absorbed by the human body. The good news is that there exists an excellent zinc supplement, zinc monomethionate, which is well absorbed even in the presence of fiber, and very affordable. Again, for literally pennies a day one can prevent a multitude of problems.

One gets the impression that this book is only a first step, a modest beginning of a more thorough exploration of multiple physiological consequences of nutrient deficiencies, many of them caused or exacerbated by prescription drugs. The main problem is that we still do not have enough research into the full effects of various drugs. Their impact on the levels of certain nutrients has simply not yet been studied. As the authors point out, drug companies are generally not required to do nutrient depletion studies, and the funding for such research is difficult to obtain. In the authors' words, "We actually believe that the problem of drug-induced nutrient depletions is substantially larger and more widespread than what is reported in this book."

Let us hope that we will see more research in this important area, and more updates of this useful book. (At press time, Natural Therapeutics Pocket Guide-also co-authored by the same group of doctors in addition to Nancy Ashbrook Willis, BA, JD-was in its last printing stages. Look for a review of this book in an upcoming issue of Life Extension magazine -Eds.).

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