

From Chapter Seven, Antivirals & Immune Modulators:

**~ Increasing Absorption & Decreasing Drug Side Effects ~**

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Regardless of the drugs you choose to use, one of the most important things you can do to improve your chances of benefiting from them is to improve your body's capacity to absorb and process and transport them, while lowering the likelihood that they will cause side effects and toxicity. And the way you do this is with nutrients. As already mentioned in *Chapters Three and Five*, there are many ways in which nutrients can affect drug use in the body. First, where intestinal damage or atrophy is present they can help to repair the intestines and boost the capacity for proper absorption of drugs. Malabsorption is, unfortunately, a not uncommon problem in people living with HIV which can greatly diminish how well a drug is taken up by the body. When it is present, you won't be receiving the full dose of the drugs you're swallowing. Even if you're doing everything else right in terms of your scheduling and dosing of drugs, it won't do you any good if they're not getting through the intestinal wall into the bloodstream. When drugs are only partially absorbed, the effect will be the same as taking a dose that's too low. They will work less well, allowing greater viral activity and speedier development of resistance. Since some of these drugs are in forms that are difficult for the body to absorb in any case, worsening the situation with intestinal malabsorption is, to say the least, a very bad idea. Ensuring that your body has an optimal supply of all the nutrients needed for intestinal health is, thus, crucial for maintaining long-term drug effectiveness.

Unfortunately, the one very important agent that could help ensure the absorptive capacity of the small intestine is very likely to be present in inadequate levels in people living with HIV. This agent is L-glutamine, the amino acid already discussed in *Chapter Six* as having many important uses for health maintenance in HIVers. Glutamine is required for the constant rebuilding of intestinal cells. These cells are regenerated every 3-4 days. The energy which allows this process to occur comes from glutamine. If glutamine concentrations are low, the result is intestinal tissue atrophy and decreased absorption of both nutrients and drugs. Maintaining intestinal health by ensuring the presence of optimal levels of glutamine in the body may be one of the most important things you can do to lessen the chances for resistance developing. If the absorptive capacity of the intestines is good, then you will actually be getting the dose of the drug that was intended, rather than a suboptimal level that could hasten the development of resistance. Other nutrients necessary for the proper building of intestinal tissue may also be in short supply so a total approach to building and maintaining healthy intestines should be an integral part of anyone's antiretroviral drug program. [For more information on what may be needed to repair the intestines, see *Chapter Nine, Treatments for Intestinal Damage*; for more information on glutamine, see *Chapter Six, Glutamine*.]

Second, loss of body cell mass, increases in total body water, and other changes in body composition can change your body's ability to respond to drug therapies and increase their toxicity.<sup>1</sup> There are many reasons for this, not the least of which is that the body may become less able to properly transport drugs because its levels of certain critical proteins are inadequate.

For example, the levels of albumin, the most plentiful protein dissolved in the blood, may be too low in those whose protein stores have diminished. Albumin serves as a transport protein which carries fatty acids, bilirubin, certain hormones, and, yes, indeed, many drugs through the body. If the internal decline that ultimately results in wasting is too far along, there may be insufficient albumin to transport drugs properly. This may be another reason why those in earlier disease stages seem to generally benefit more from antiretroviral drugs than those in advanced disease stages. In addition to their better immune function (which contributes to the viral suppression effort), they also have more intact bodies which are better able to use the drugs. Those in later disease stages are far more likely to have experienced loss of body cell mass and the other negative body changes that prevent optimal use of drugs. Thus, maintaining your body by preventing internal decline and wasting in all the ways discussed in *Chapter Two* is also very important if you wish to gain the most benefit from drugs.

Third, good nutrition and nutrient supplementation can help to maintain a body that is healthy enough to withstand the assault of drugs, to the greatest extent possible. The simple fact is that what could keep many people from using antiretroviral drugs long-term is the toxicity and side effects that they can cause. If we can use good nutrition to help reduce such problems, we will greatly increase the chances for long-term effective use of the drugs. In addition to this general body support with nutrition, it is important to look at the specific effects of certain drugs in order to design a program that can help the body to tolerate them. As discussed in *Chapter Four*, certain nutrients may increase tolerance for and/or help to counter the negative effects of a number of the antiretroviral drugs. Ensuring an optimal supply of such nutrients is an obvious step for anyone taking those drugs. [For details on particular nutrients and the drugs with which they are needed, see *Chapter Four, Increasing Drug Efficacy and Tolerance.*]

Fourth, good nutrition, in general, and certain specific nutrients, in particular, are important to provide protection for the organs that have to filter drugs out of the body, including both the kidneys and the liver. Drinking plenty of healthful fluids is very important to health, in general, and will be particularly important for long-term use of the drugs such as indinavir that can affect the kidneys. Many people simply don't drink enough liquids. They may have gotten away with this prior to their use of a drug that has the potential to cause kidney problems. But putting a kidney stressing drug into the body could result in rapid development of kidney stones or other problems if their inadequate fluid intake continues. For example, reports from the community have made it very clear that the amount of water drunk by those taking indinavir can make a dramatic difference in their ability to tolerate the drug. In some cases, people who initially developed serious kidney problems (and experienced the excruciating pain that can go with that) were able to resume their use of indinavir by simply increasing their water intake. Don't risk ever experiencing such problems. Drink large amounts of water every single day. Period.

The other organ that you must protect is the liver. Many of the drugs in common use can adversely affect liver function. Doing everything possible to repair the liver and support its ability to process drugs effectively should always be part of any program that includes such drugs. This may both increase the chances for continued use of the drugs (since liver damage could quickly preclude their use) and help to eliminate or lessen certain side effects. As an example of the latter, high triglyceride levels are commonly seen with protease inhibitors. Since the liver

controls blood fats in the body, giving it the support necessary for continued optimal functioning may help to address this problem.

As discussed in more depth in *Chapter Nine*, there are a number of things that can help to repair the liver and promote its long-term health. Among these are using the nutrients that promote maintenance of optimal levels of glutathione, the intracellular antioxidant that is very important for liver health. Included would be vitamin C, L-glutamine, alpha-lipoic acid, and N-acetyl-cysteine. Using sylimarin, the milk thistle-derived extract that can reduce inflammation and promote liver repair might also be quite useful. Thus, the use of these healing agents might be very important to allow people to continue long-term use of the drugs that can cause liver problems. [For details, see *Chapter Nine, Treatments for Liver Damage.*]

A substantial percentage of people on various versions of HAART (highly active antiretroviral therapy) also experience some version of fat redistribution problems in their bodies. This syndrome, now commonly referred to as lipodystrophy, may include fat wasting in the arms, legs, face, and buttocks; and/or abnormal fat accumulation in the abdomen, breasts, and over the shoulders. Many people also develop insulin resistance, blood sugar elevations, and blood fat elevations (high cholesterol and/or triglycerides) problems. There are possible therapies, including human growth hormone (to decrease fat accumulation) and agents aimed at increasing insulin sensitivity or decreasing elevated blood fats. For details, see *Lipodystrophy, Possible therapies for body changes and blood fat and blood sugar problems.*

Some protease inhibitors seem to cause increased intestinal gas and bloating. For many people, this can create a problem that is both embarrassing (a lovely rotten-egg, sulfurous-smelling gas that occurs throughout the day and night) and uncomfortable or even painful. Some people have felt that the problem is severe enough to warrant discontinuation of the drugs. The most effective approach to this seems to be taking pancreatic enzymes with every meal. Dennis Rosa-Re, MD, a physician with a large HIV practice in Fort Lauderdale, Florida, recommends Ultrase MT-20, a potent pancreatic enzyme which contains the fat-digesting enzyme lipase. It is available by prescription and will usually be reimbursed. He has found that most of his patients have been able to eliminate the gas when they take 1-3 enzymes with each meal. Now being tested is a potentially even more effective enzyme product called Pancrecarb. It contains a potent amount of lipase combined with bicarbonate that helps to ensure that the small intestine is not too acidic for the enzyme to work its best. The developer believes that the result of the combination will be that you can actually use lower doses of lipase for better results. Trials are currently underway to prove this, but the product is already approved for cystic fibrosis and, thus, available "off-label" for your doctor to prescribe. Over-the-counter enzyme formulas may also work as long as they contain sufficient lipase, but since the prescribable forms are likely to be covered by your insurance, they will be the preference of most.

For those for whom the enzymes are insufficient to address the problem, a community-derived solution that seems to work for many is adding to the enzyme therapy the use of glutamine (in doses of 10-20 grams/day, taken in three doses, mixed into a liquid). Some people also add a high-colostrum whey protein product. The particular whey protein product used by the people I know has been Optimune, made by Optim Nutrition of Salt Lake City, Utah. Doses of 2-3 scoops (10-15 grams) of the Optimune are mixed into a drink and consumed once per day. I do not know why this combination would work to reduce the gas and bloating but enough people

have reported the effect to me that it seems worth passing on. If this is a problem for you, it might be worth a try. [For more information on glutamine, see *Chapter Six, Glutamine*. For more information on whey protein products, see *Chapter Nine, Treatments for Diarrhea and Treatments for Cryptosporidiosis, Bovine Colostrum*.]

The bottom line is that if we wish to create the possibility that people will be able to use antiretroviral drugs long-term, it is terribly important to do everything possible to help reduce their toxicity and increase the body's tolerance for them. Overall, following the guidelines presented in other chapters for preventing body damage, maintaining body cell mass, and ensuring optimal levels of nutrients throughout the body (with a particular emphasis on those that may help with the particular drugs you are taking) may be the most important things you can do gain the most long-term benefit from drugs with the least adverse effects.

1. Hayes JR and Borzelleca JF. Nutrient interaction with drugs and other xenobiotics. *J Am Diet Assoc* 85:335-339, 1985.