Those Darned Free Radicals

Sean Strub is dangerously low in glutathione to quash these cell-damaging molecules

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Laboratory analyses of blood and other medical measurements, which help health practitioners make diagnoses and detect toxic effects of medication, can also help people with HIV track their health. Judy Shabert, MD, MPH, RD, is a researcher and clinical instructor of obstetrics and gynecology at Harvard University Medical School. She specializes in the nutritional aspects of HIV disease, particularly oxidative stress and wasting. She analyzes the glutathione blood levels of POZ founder Sean O. Strub.

According to a newly marketed blood test, Sean has alarmingly low levels of the antioxidant glutathione. There has recently been a rush of enthusiasm for measuring blood levels of this previously ignored nutrient in the wake of published findings from a Stanford University study showing an apparently powerful link between higher levels of glutathione and survival in PWAs. The study focused on about 100 people (almost all men) with less than 200 CD4 cells. The researchers found that after three years, 85 percent of those who had initially tested high on their glutathione levels survived, compared to only 18 percent of those who had tested low. The precise reason for this astonishing survival difference has not been established, but it is known that glutathione is very important to the body for several reasons.

First, it is considered by most researchers to be the most important antioxidant inside the body's cells. Antioxidants -- including not only glutathione but also vitamin C, selenium, vitamin E and others -- are needed to prevent the damage to the body's cells and tissues that free radicals can cause. Free radicals -- unstable molecules that result in part from certain immune responses -- are present in large amounts in PWAs because of their bodies' ongoing fight against the virus. The result is a much-greater-than-average need for antioxidants, including glutathione.

Unfortunately, a combination of many factors -- including the body's elevated use of nutrients to power the immune response, replace and repair damaged and destroyed cells, and break down medications -- creates in almost all HIV positive people deficiencies of many nutrients, including these critically important antioxidants. The result: Many PWAs are unable to counter the chain of damage that free radicals can cause. This may be a large part of the explanation for the apparent link between high glutathione levels and much higher survival rates.

In addition, glutathione is absolutely necessary to help the liver neutralize the breakdown products

of medications and clear toxic compounds from the body. In fact, the liver cells contain more glutathione than the body's other cells because of this need to protect the body from toxins, a need greatly increased in the many PWAs, including Sean, who are taking a number of strong medications. Chronic use of drugs that are particularly likely to lower glutathione levels in the liver -- particularly acetaminophen (contained in Tylenol and other pain-killers) and alcohol -- can cause serious liver injury and should be avoided by PWAs as much as possible.

When we look at Sean's glutathione level, we are getting an indirect reading of his nutritional status, a direct measure of the amount of free-radical damage his body is combating and an indication of the potential his liver has for continuing to break down the drugs he's taking and eliminate toxic by-products. (However, because this particular version of the test is so new, validation from laboratories throughout the country is still lacking. It may take pressure on insurance companies to obtain reimbursement for this test.)

Unfortunately, Sean is typical of many PWAs in whom the level of this vital compound is quite low. His blood glutathione level is only 0.508 micromoles per milliliter, on a test for which the reference range (the amount found in healthy people) is 0.72 -- 1.40, a result that means his level is completely inadequate to meet his body's needs. The percentile score of 0.15% means that only 0.15 percent of the population as a whole would fall below Sean's level.

Research has shown that glutathione levels are low in PWAs even in early disease stages, and generally worsen over time. The levels of glutathione in both red blood cells and lung secretions of PWAs are only, on average, half of those seen in HIV negative people. The fact that Sean's level is even lower is not at all surprising, since he has been living with HIV for so many years. However, the finding should provide the motivation to supplement with the nutrients that can help raise his glutathione level, thus restoring full antioxidant protection to the body and boosting the liver's ability to handle toxic drugs.

Directly supplementing glutathione itself may ultimately prove effective, but so far there is only preliminary evidence for this approach and questions about how well it is absorbed; a clinical trial is planned. Meanwhile, a form of specially processed whey (milk protein) called Immunocal has shown glutathione-boosting effects in a small study of children with AIDS wasting.

For now, the most important supplements are n-acetyl-cysteine (NAC), glutamine, alpha-lipoic acid and vitamin B-6. The body actually creates glutathione from three amino acids -- cysteine, glutamate and glycine. Cysteine is the primary rate-limiting amino acid in the body's production of glutathione. In other words, the amount of glutathione you can produce will depend on the amount of cysteine the body has available. Unfortunately, it is neither safe nor effective to give high doses of cysteine itself, since it can be caustic to tissue and much of it is converted in the stomach into a form which the body cannot use. Thus, NAC, which can effectively provide cysteine for the body and doesn't usually cause side effects when given in appropriate doses, is used instead. Doses of 2,000 -- 3,000 mg of NAC per day can help provide enough cysteine to boost glutathione back toward normal levels. Because vitamin B-6 is also needed to maintain cysteine levels in cells, taking 25 mg of B-6 three times per day is an important accompaniment to any use of NAC.

The second-most important ingredient in the body’s recipe for glutathione production is glutamine, used as a source for the glutamate that actually helps create the glutathione molecule. Glutamine is often low in PWAs because of its multiple uses in the body. Besides supplying glutamate, it is needed for the production of muscle protein -- crucial for the prevention of wasting. Glutamine is also necessary to keep the cells in the small intestine healthy. Inadequate glutamine can cause those cells to die, thus impeding the body’s absorption of both nutrients and drugs. This nutrient is also required for the production of secretory immunoglobulin A (sIg-A), a type of antibody that provides immune defense in the lungs, and the gastrointestinal tract (from the mouth to the intestines). And last but definitely not least, glutamine is a major energy source for immune-system cells. With all these demands for glutamine, it is no surprise that many PWAs fall short, often requiring supplementation at levels of 15 -- 20 grams per day until glutathione is restored, followed by doses of 10 -- 12 grams per day for maintenance.

Research has shown that use of alpha-lipoic (thioctic) acid, a fatty acid that is an important antioxidant, both raises glutathione and helps to maintain it at optimal levels. Doses of 300 -- 600 mg per day, taken in conjunction with the NAC, glutamine and B-6, could help restore Sean’s glutathione to the level he needs for body protection, liver support and -- it is fondly to be hoped -- survival.

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