Update on Selenium : More is Not Necessarily Better

by
Virgil Simons

David J. Waters, PhD, DVM is Professor and Associate Director of Purdue University's Center on Aging and Life Course and the Executive Director of the Gerald P. Murphy Cancer Foundation, West Lafayette, IN. He has conducted research on selenium and genetic damage in the prostate, which has shown that more selenium is not always better. This work has led to the development of a toenail test, SeleniumHealth™ , that men can use to measure and adjust their selenium intake. I spoke with Dr. Waters about the latest research on selenium and prostate cancer as well as the idea that when it comes to cancer-fighting nutrients, more is not necessarily better.

Q: Dr. Waters, tell us about the SeleniumHealth™ test.

Waters: We have developed a simple toenail test called SeleniumHealth™ that gives every man the opportunity to find out his own selenium level. The SeleniumHealth™ toenail test accurately reflects how much selenium a person has received from his diet and from supplements over the last three months. The goal is to tap into the health benefits of selenium and at the same time avoid oversupplementation. Using the results of the toenail test, you can adjust the amount of selenium you get from food and supplements to the amount that is best for you.

Q: Scientists are hard at work trying to find out more about the cancer-fighting properties of selenium. An example is the SELECT Trial. Can you tell us about that study?

Waters: The Murphy Cancer Foundation is one of more than 400 study sites that have enrolled more than 32,000 men in the largest-ever prostate cancer prevention trial called SELECT. SELECT is a randomized clinical trial designed to determine if daily supplementation with selenium, vitamin E, or both will substantively decrease the number of men who will get prostate cancer. We believe the men in SELECT are real heroes. This 12-year trial has reached its halfway mark and is moving ahead full steam. We and others are anxiously awaiting the final results that will emerge in 2012.

Q: So just how strong is the evidence that low selenium is a risk factor for prostate cancer?

Waters: Over the last 25 years, several epidemiologic studies have documented the link between low selenium and increased risk for cancer. But the evidence goes well beyond these association studies. Perhaps the strongest evidence comes from Larry Clark's Nutritional Prevention of Cancer (NPC) Trial. In 1996, Clark and his colleagues reported the findings from this 13-year, randomized, placebo-controlled study of more than 1000 older Americans. In that study, daily supplementation with 200 micrograms of selenium in the form of selenium-enriched yeast was associated with a significant reduction in the incidence of several cancers, most notably cancer of the prostate (63% risk reduction). These compelling results provided strong rationale to launch the SELECT prostate cancer prevention study. I would also mention that using data from the Physicians Health Study, we estimate that, this year

alone, up to 17,000 men in the United States will develop the aggressive form of prostate cancer because their selenium levels are too low. Among these men, the sobering statistic is that approximately 1/3 will succumb to their cancers despite state-of-the-art care, exercising all available treatment options.

Q: Clearly then selenium is a good thing. So why do men need to bother with testing their selenium levels? Why not just take selenium supplements to crank up your overall selenium intake?

Waters: I can answer this with two simple words: Dose matters. Let me explain. A closer look at the men in Larry Clark's study showed that not everyone benefited from selenium supplementation. Men with the lowest selenium levels prior to the start of the study had an impressive 92% reduction in prostate cancer risk after selenium supplementation. However, those men who had the highest selenium levels prior to the start had no protection from prostate cancer. In fact, these men had an alarming and statistically significant 88% *increase* in overall cancer incidence. These results informed us that more of a good thing is not always a good thing.

Q: More selenium was not better for the men in Larry Clark's study. You have studied the relationship between selenium and prostate cancer in dogs. What do the dogs say?

Waters: The dogs say ditto. We conducted a randomized feeding trial in which elderly beagle dogs received nutritionally adequate or supranutritional levels of selenium for 7 months to mimic the broad range of dietary selenium intake of men in the United States. We studied elderly dogs because, like men, they develop naturally-occurring prostate cancer. By using the aging dog prostate to mimic the aging human prostate, we could study the effects of selenium on prostate cells in an appropriate context – not on the surface of a Petri dish, but deep inside the complex environment of an aging prostate gland prior to onset of cancer. The results of our feeding trial showed an intriguing U-shaped dose response between selenium status (toenail selenium concentration) and the extent of DNA damage within the prostate (measured with alkaline Comet assay). This means the genetic damage in the prostate is most severe at the lowest and highest selenium levels. The dogs tell us that the best place to be is in the mid-range of selenium intake. The implications are clear-cut: *Men need to know their baseline levels of selenium prior to supplementation*. And now they can do just that with the SeleniumHealth™ toenail test.

Q: Who should use the test?

Waters: SeleniumHealth™ is a test for men of all ages because effective cancer prevention begins now. As you know, prostate cancer is a process that takes 20 to 30 years to develop so it's not too early for men in their 30s and 40s to be thinking about selenium and their own personalized prostate protection. SeleniumHealth™ is not a prostate cancer-screening tool like PSA. Cancer screening tools, such as PSA or mammography, are used for the early detection of cancer. In contrast, SeleniumHealth™ tells you whether you have one of the risk factors for cancer – low selenium status. And if your level is low, you can correct it. So you don't have to wait until you are 50 or 60 years old to take the test and get your selenium level right. We think men around age 30 should be turning their attention to things that can lower their risk of prostate cancer.

Q: In that sense, it's like checking your cholesterol.

Waters: Yes, it is. Your physician doesn't guess your cholesterol level. He measures it with a blood test and if it is out of whack, he personalizes a strategy of diet and medication to bring your cholesterol within the desired range. If this seems smart for your heart, then why not personalize your prostate protection? With the results of the toenail test, you can adjust the amount of selenium you get from food and supplements to the amount that is best for you. It's all about you.

Q: In October 2007, *Men's Health* Magazine ran an article entitled "Cancer-Proof Your Body" about 8 things men can do to lower their cancer risk. The article talked about the SeleniumHealth™ toenail test. The heading read "Pop Selenium". That's not really your message, is it?

Waters: We think telling men to "Pop selenium" as an insurance policy is the wrong message. Our message is: "It pays to get your selenium level right". Without measuring your selenium level, you and your physician have no idea whether your selenium falls into a low, optimal, or high range. If your levels are already in the optimal range, then popping selenium could turn out to be precisely the kind of insurance policy you don't want.

Q: I've read recommendations that 200 micrograms is the optimal dose of selenium supplement to use. Would you agree with this?

Waters: A dose of 200 micrograms might be right for some guys, but is probably too much for others. We conducted a study of more than 50 men which showed that men taking the same amount of selenium supplement have very different selenium levels – their levels are all over the map. In scientific slang we call this "biological noise", which probably reflects differences in how much selenium men are consuming in their diet, differences in the form and source of their selenium supplement, and biological differences in how each guy handles selenium. Combine this variability with all of the conflicting recommendations swirling around, and we call selenium "The Noisy Nutrient".

Q: Recently, I heard a news release that taking selenium supplements might cause diabetes. What do you think about this?

Waters: This story came from a recent analysis of Larry Clark's original study. Investigators asked people if they were diabetic before the study started and again about 7 to 10 years later. It turned out that men in the selenium treatment group were 1.5 times more likely to develop diabetes than those who received placebo.

Q: Did the public hear the whole story about this research?

Waters: Unfortunately, what the public heard was "Supplement linked to diabetes" and "200 micrograms of selenium daily raised risk by 50%". But when you take a closer look at the scientific article, you find something quite interesting: It was the selenium status prior to the start of the study that predicted who developed diabetes. *Only those men who started with the highest selenium and then took more selenium had an increased risk for diabetes*; this increase was threefold. Men who had the lowest or middle range selenium did <u>not</u> have a higher risk to develop diabetes than placebo-treated men. So, the actual results of this highly publicized study are in synch with what we've been saying: It's a U-shaped world … more is not always better. The take home message isn't "Stop taking selenium. It's dangerous for

you". Instead, the message should be: "Get your selenium level checked. See how you stack up to other guys." Taking the SeleniumHealth™ test to find out your selenium level is the surest step toward getting the beneficial health effects of selenium while avoiding oversupplementation.

Q: How do men get the test?

Waters: Well, the easiest way is to go to our online site – www.seleniumhealthtest.com – which will enable you to download and print the application form. Follow the instructions and send the completed application along with your toenail clippings (as instructed on the application form) and we will measure your selenium. You will be informed of your results in about 2 weeks. If your levels are outside the optimal range, the Nutritional Guidance Staff at the Murphy Cancer Foundation will recommend how you can adjust your selenium intake. The cost of the test and consultation is less than $100. For a closer look at why men should be tested, read "Straight Talk about Selenium and Your Health" by David J. Waters, at www.gpmcf.org.

Q: The idea of tailoring selenium and other cancer-fighting nutrients according to each person's needs sounds like a good one. Is that the real take home message here?

Waters: Yes. We think that cancer researchers need to turn more of their attention to prevention rather than just treatment. And we mustn't stop there. Now more than ever, we need personalized cancer prevention. We define personalized cancer prevention as a strategy that will enable each person to reduce his or her risk for lethal cancer by matching the dose, duration, and timing of an intervention with their own cancer risk profile. The central tenet of personalized cancer prevention is that average is overrated. Using SeleniumHealth™ to tailor the amount of selenium you are getting from food and supplements enables you to find the amount that is right for you – not the average guy. And that's personalized cancer prevention. In the January 2008 issue of *Nutrition and Cancer,* we discuss the opportunities and challenges of personalized cancer prevention research in our article entitled "The Art of Casting Nets: Fishing for the Prize of Personalized Cancer Prevention", so you can read more about this idea.