

Agent Orange Exposure Increases Veterans' Risk Of Aggressive Recurrence Of Prostate Cancer

ScienceDaily (Apr. 23, 2009) — Veterans exposed to Agent Orange are at increased risk of aggressive recurrence of prostate cancer, researchers report.

A study of 1,495 veterans who underwent radical prostatectomy to remove their cancerous prostates showed that the 206 exposed to Agent Orange had nearly a 50 percent increased risk of their cancer recurring despite the fact that their cancer seemed relatively nonaggressive at the time of surgery. And, their cancer came back with a vengeance: the time it took the prostate specific antigen, or PSA, level to double – an indicator of aggressiveness – was eight months versus more than 18 months in non-exposed veterans.

"There is something about the biology of these cancers that are associated with prior Agent Orange exposure that is causing them to be more aggressive. We need to get the word out," says Dr. Martha Terris, chief of urology at the Charlie Norwood VA Medical Center in Augusta and professor of urology at the Medical College of Georgia School of Medicine.

Dr. Terris, corresponding author on the study published in the May issue of *British Journal of Urology International*, says she wants her colleagues following prostate cancer patients with Agent Orange exposure to know those patients may need more meticulous scrutiny and so-called salvage therapy quickly if their prostate cancer returns. "Not only are their recurrence rates higher but their cancers are coming back and growing much faster when they do come back," the Georgia Cancer Coalition Distinguished Scholar says.

The PSA of prostate cancer patients is typically measured every three months for two years after surgery then every six months for life. After surgery to remove the diseased prostate, the PSA should be zero, but any prostate cancer cells left behind continue to make PSA, a red flag of recurrence, Dr. Terris says. The PSA often "percolates along" so physicians tend to watch it for a while to determine if additional therapy is needed. However in patients with Agent Orange exposure, radiation or hormone therapy to kill remaining cells may need to be done sooner rather than later, she says.

Increasing evidence is emerging that exposure to Agent Orange, a herbicide and defoliant used during the Vietnam War, increases risk for a variety of health problems, including prostate cancer, although the exact mechanism is unclear. Dioxin, its known carcinogen, also is found in herbicides and pesticides used by U.S. farmers, forestry and chemical plant workers who studies have shown to have an increased cancer risk. Scientists suspect dioxin activates regulatory regions of genes to enable the uncontrolled cell division that is a cancer hallmark.

Dr. Terris led a separate study of 1,653 veterans at VA medical centers in five cities between 1990 and 2006 that also showed recurrence rates were higher and recurring cancers were more aggressive with Agent Orange exposure. Dr. Sagar R. Shah, MCG urology resident, presented the findings at the 2007 annual meeting of the American Urological Association.

This new study – which includes the VA Medical Center in Augusta, Veterans Affairs Greater Los Angeles Healthcare System, Veterans Affairs Palo Alto Healthcare System and six affiliated medical schools – included new patients as well as longer follow up on many of the original study patients. As with the previous study, prostate cancer seemed to have a similar course in blacks and whites, but Agent Orange exposure was more common in blacks, who were more likely to be ground troops in Vietnam.

Plenty of questions remain, such as what happens to patients whose primary treatment is standard radiation or brachytherapy, where rice-size radiation pellets are implanted in the prostate, rather than surgery, Dr. Terris says.

She also wants to know whether the veterans' degree of exposure is related to the severity of their cancer. Everyone has some dioxin exposure; "Even if you never set foot in Vietnam or outside the United States," she says. So she is now measuring levels in the body fat – which is like a repository for what the body has been exposed to – to determine how levels correlate to their cancer severity.

Prostate cancer is the most common cancer in men and trails lung cancer as the second leading cause of cancer death.

The study was funded by the Department of Veterans Affairs, the National Institutes of Health, the Georgia Cancer Coalition, the Department of Defense Prostate Cancer Research Program and the American Urological Association/Astellas Rising Star in Urology Award.

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