TCDD Exposure Triples Risk of Graves' Disease

VITALS

Major Finding: Graves' disease was diagnosed in 54 of 23,939 veterans exposed to Agent Orange and 148 of 200,109 nonexposed veterans (OR 3.05).

Data Source: Electronic database analysis of veterans born between 1925 and 1953.

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BY MIRIAM E. TUCKER

BOSTON — Vietnam veterans exposed to Agent Orange were found to have a threefold increased risk of Graves' disease in an analysis of electronic medical records of more than 200,000 vets who served during the Vietnam era.

The herbicide Agent Orange was sprayed over South Vietnam between 1962 and 1971, ultimately covering nearly 20% of the country's surface. Much of the concern over its use stemmed from the dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin, TCDD) it was contaminated with during production. Its persistent toxicity in biological tissue has been known for 35 years, Dr. Ajay Varanasi said at the annual meeting of the American Association of Clinical Endocrinologists.

Evidence of thyroid tissue damage arising from TCDD has been observed in animals and humans, said Dr. Varanasi of the State University of New York at Buffalo and the VA Western New York Health Care System.

The study included Department of Veterans Affairs electronic medical records data from 224,048 veterans born between 1925 and 1953 who were followed in upstate New York. Of those, 23,939 were classified as having been exposed to Agent Orange. Only about 10% of veterans from the Vietnam era actually set foot in Vietnam, but it can be assumed that nearly all who did were exposed to Agent Orange, he noted.

The exposed group did not differ significantly from the 200,109 nonexposed veterans in terms of age (average 62 years), race (1/5 were African American), smoking history (more than 90% were smokers), and sex (92% of the exposed and 89% of the nonexposed were men).

Diabetes, however, was significantly more common among the exposed, 24% vs. 14%. The substantial increase in type 2 diabetes among Vietnam veterans has been described previously and is well recognized, he noted.

Graves' disease was diagnosed in 54 exposed and 148 nonexposed vets, for an odds ratio (OR) of 3.05. Hypothyroidism was significantly more prevalent in the nonexposed group, with 7,273 receiving the diagnosis vs. 740 exposed veterans (OR 0.85). There were no significant differences in the rates of thyroid cancer (OR 1.16) or thyroid nodules (OR 1.14).

In a multivariate analysis, Agent Orange exposure was independently associated with an increased risk of Graves' disease (OR 2.76), whereas smoking history (OR 1.42), diabetes (OR 1.05), and race (OR 1.22 for African American vs. other) were not, Dr. Varanasi reported.

Recent literature indicates that TCDD can have both immune-suppressing and immune-promoting effects in humans. The dioxin may play a role in normal immune responses as well (Trends Immunol. 2009;30:447-54).

Data also suggest that TCDD exposure can promote Th17-cell differentiation and expansion. In one study, the proportion of peripheral Th17 cells in patients with autoimmune thyroid disease was higher than in controls, and the proportion of these cells in patients with intractable Graves' disease was higher than in patients with Graves' that was in remission (Thyroid 2009;19:495-501).

An increased prevalence of combined thyroid disorders—thyrotoxicosis, goiter, hypothyroidism, and thyroid adenoma—was seen in accidentally exposed German workers (Occup. Environ. Med. 1994;51:479-86). However, other studies of TCDD and thyroid function have produced less-consistent findings (Occup. Environ. Med. 1999;56:270-6).

"Our finding of an increased prevalence of Graves' disease in Vietnam veterans potentially exposed to TCDD warrants further investigation," Dr. Varanasi concluded. ■