

# Eating Bran Lowers Mortality in Type 2 Disease

Whole grains may protect against systemic inflammation.

BY ROBERT FINN

FROM CIRCULATION: JOURNAL OF THE AMERICAN HEART ASSOCIATION

Consumption of whole grains, especially the bran component of whole grains, was associated with a significant decrease in the risk of all-cause mortality and cardiovascular disease-specific mortality in women with type 2 diabetes who were followed as part of the Nurses' Health Study.

After adjustment for age, women in the highest quintile of whole grain, cereal fiber, bran, and germ consumption had 16%-31% lower all-cause mortality than women in the lowest quintile, Dr. Meian He of the Harvard School of Public Health, Boston, and colleagues reported.



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After further adjustment for lifestyle and dietary risk factors, only bran consumption remained significantly associated with mortality.

Compared to women in the lowest quintile of bran consumption, those in the highest quintile had a 28% decrease in the risk of all-cause mortality and a 35% increase in the risk of mortality associated with cardiovascular disease.

"To my knowledge, this is the first study of whole grain and its components and risk of death in diabetic patients," Dr. Lu Qi, also of the Harvard School of Public Health and the study's senior author, said in a statement.

"These findings suggest a potential benefit of whole grain, and particularly bran, in reducing death and cardiovascular risk in diabetic patients," Dr. Qi said.

The Nurses' Health Study began in 1976 with 121,700 female registered nurses aged 30-55 years.

Data on participants' medical history, lifestyle, and medical diagnoses have been updated every 2 years.

For this study, the investigators focused on 7,822 women diagnosed with type 2 diabetes between 1976 and 2006.

They excluded women diagnosed with diabetes before age 30 years and those with a history of cardiovascular disease or cancer reported on the 1980 questionnaire, when diet was first assessed [doi:10.1161/CIRCULATION-AHA.109.907360].

Women completed semi-quantitative food frequency questionnaires every 2 or 4 years between 1980 and 2002.

Investigators used data on how often they consumed certain foods and beverages to estimate each woman's average intake of whole grains, as well as her intake of bran and cereal fiber.

## VITALS

**Major Finding:** Women with type 2 diabetes in the highest quintile of bran consumption had a 28% lower risk of all-cause mortality and 35% lower risk of cardiovascular disease-specific mortality than women in the lowest quintile.

**Data Source:** The Nurses' Health Study.

**Disclosures:** The study was funded by the National Institutes of Health, the American Heart Association, and the Boston Obesity Nutrition Research Center. The investigators reported that they had no other disclosures.

Investigators followed the women for 26 years, for a total of 70,102 person-years.

During that time, 852 women died, 295 of cardiovascular disease.

They adjusted for age, smoking status, body mass index, alcohol intake, physical activity, parental history of myocardial infarction, menopausal status, use of hormone therapy, duration of diabetes, and various dietary factors including total energy intake, and intake of polyunsaturated fat, saturated fat, trans fat, magnesium, and folate.

Several different mechanisms could explain the association between bran consumption and mortality in women with diabetes, Dr. He and colleagues wrote. Their earlier research suggested that consumption of whole grains might protect against systemic inflammation and endothelial dysfunction.

"Diabetes is thought to be a chronic state of inflammation characterized by moderately increased levels of chemical markers for inflammation and endothelial dysfunction," Dr. Qi said in the prepared statement, which was issued by the American Heart Association, one of the study's sponsors.

"Those markers have been found to be related to increased risk of CVD in both diabetic and nondiabetic populations," Dr. Qi said. ■

# Agent Orange Exposure Increases Risk of Graves' Disease

BY MIRIAM E. TUCKER

FROM THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

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 the production process.

Awareness of its persistent toxicity in biological tissue now spans at least 35 years, Dr. Ajay Varanasi said at the annual meeting.

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 (about 1 in 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, which acts primarily by binding to the transcription factor aryl hydrocarbon receptor (AhR) and prolonging its activation, 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).

**In a multivariate analysis, Agent Orange exposure was independently associated with an increased risk of Graves' disease, whereas smoking history and race were not.**

Data also suggest that TCDD exposure, along with endogenous AhR ligands, 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).

"In view of known immune-modulating effects of TCDD, our finding of an increased prevalence of Graves' disease in Vietnam veterans potentially exposed to TCDD warrants further investigation," Dr. Varanasi concluded. ■

**Disclosures:** This study was funded by the Department of Veterans Affairs, and Dr. Varanasi stated that he had no other disclosures.