

Antioxidant intake from fruits, vegetables and other sources and risk of non-Hodgkin's lymphoma: the Iowa Women's Health Study

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Antioxidant nutrients found in fruits, vegetables and other foods are thought to inhibit carcinogenesis and to influence immune status. We evaluated the association of these factors with risk of non-Hodgkin's lymphoma (NHL) overall and for diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma specifically in a prospective cohort of 35,159 Iowa women aged 55–69 years when enrolled at baseline in 1986. Diet was ascertained using a validated semiquantitative food frequency questionnaire. Through 2005, 415 cases of NHL (including 184 DLBCL and 90 follicular) were identified. Relative risks (RRs) and 95% confidence intervals (CIs) were estimated using Cox regression, adjusting for age and total energy. The strongest associations of antioxidants with risk of NHL (RR for highest versus lowest quartile; *p* for trend) were observed for dietary vitamin C (RR = 0.78; *p* = 0.044), α -carotene (RR = 0.71; *p* = 0.015), proanthocyanidins (RR = 0.70; *p* = 0.0024) and dietary manganese (RR = 0.62; *p* = 0.010). There were no associations with multivitamin use or supplemental intake of vitamins C, E, selenium, zinc, copper or manganese. From a food perspective, greater intake of total fruits and vegetables (RR = 0.69; *p* = 0.011), yellow/orange (RR = 0.72; *p* = 0.015) and cruciferous (RR = 0.82; *p* = 0.017) vegetables, broccoli (RR = 0.72; *p* = 0.018) and apple juice/cider (RR = 0.65; *p* = 0.026) were associated with lower NHL risk; there were no strong associations for other antioxidant-rich foods, including whole grains, chocolate, tea or nuts. Overall, these associations were mainly observed for follicular lymphoma and were weaker or not apparent for DLBCL. In conclusion, these results support a role for vegetables, and perhaps fruits and associated antioxidants from food sources, as protective factors against the development of NHL and follicular lymphoma in particular.

The incidence rate of non-Hodgkin's lymphoma (NHL) increased rapidly over the later half of the 20th century in the United States, and only in the later part of 1990s did the rate of increase level off in developed countries. However, among women aged 55 years and older, incidence rates continued to increase, albeit at a slower pace. The most well-established risk factor for the development of NHL is immunosuppression, including primary immunodeficiency diseases, HIV infection or iatrogenic immunosuppression (e.g. for

organ transplantation or treatment of certain disorders),¹ but these factors account only for a small proportion of patients.² Thus, the etiology of a majority of cases of NHL remains unknown, and diet has been proposed to play a role in the development of NHL, including a protective role of fruits and vegetables.^{3,4}

Reactive oxygen species production, including superoxide radicals, hydrogen peroxide and hydroxyl radicals, can alter DNA and lipid membrane structures, particularly in proliferating cells such as those in the immune system. Cells of the immune system tend to have higher concentrations of nutrients with antioxidant activities,⁵ and lower intakes of antioxidants have been linked to a compromised immune system.^{5–7} This raises the hypothesis that nutrients involved in antioxidant activities may protect against the development of NHL. The major dietary sources of antioxidants are fruits and vegetables, although other foods rich in antioxidants include whole grains, nuts, chocolate and tea. There is growing evidence that higher intake of fruits or vegetables may be inversely associated with risk of NHL,^{8–16} although this evidence has not been universal.^{17–19} While associations with specific types of fruits and vegetables have varied, an inverse

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