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Concerning the Possibility of a Nut . . .

The findings reported by Fraser et al[1] from the Adventist Health Study revive our interest in looking for data from prospective studies that show diet factors associated with favorable blood cholesterol or lipoprotein levels in free-living populations eventually lead to lower rates of coronary heart disease (CHD). Most of what we know about the effects of diet factors, particularly the saturation of fat and cholesterol, on serum lipid parameters derives from metabolic ward–type studies.[2,3] Alas, such findings, within a cohort studied over time have been disappointing, indeed the findings have been contradictory. For example, in Framingham, Mass, the more saturated fat one ate, the more cholesterol one ate, the *more calories one ate*, the lower the person's serum cholesterol. The *opposite* of what one saw in the 26 metabolic ward studies, the opposite of what the equations provided by Hegsted et al[2] and Keys et al[3] would predict. Only the international comparisons showed that the world could be lined up on cholesterol intake or saturated fat intake, and it would correlate with the rate of CHD.[4] Of course, since these countries differed in many other ways, the possibility that some unidentified factor might explain the rate of CHD, loomed in one's thoughts. Eventually, diet intervention trials were done, and where the follow-up got out beyond 3 years, they all show the same thing. The larger the percentage fall in cholesterol, the larger the percentage fall in CHD.[5]

See also p 1416.

In view of this, this study fails to describe a relationship of those traditional dietary constituents, saturated fat and cholesterol, known to have an adverse effect on blood lipids, and thereby, on the subsequent development of coronary disease end points. Only the Western Electric study[6] has shown dietary cholesterol to be related to the later development of CHD in a population study. However, the authors of this Adventist study did show a slight increase in definite nonfatal myocardial infarction with eating cheese one to two times per week (RR = 1.97; 95% confidence interval, 1.27 to 3.04) and, in men, a relationship of eating beef to fatal CHD. Whole wheat bread, thank goodness, lowered the nonfatal coronary disease rate.

The big finding was nuts. Nuts, eaten five or more times a week, apparently independently (Cox proportional hazard model analysis adjusted by age, sex, smoking, exercise, relative weight, and high blood pressure) lowered the coronary fatal and nonfatal end points in half. But these are the Seventh-Day Adventists who already have a seventh of our heart attack rate, who live 7 years longer than we do. How could you cut this rate even lower, in half? Is this the first article showing a dramatic fall in coronary disease rates in men and women who are already at low risk?

The first reaction of a population watcher is that there just has to be some other factor related to nut ingestion confounding this relationship. The two factors that jump to mind are exercise and weight. In Framingham, for example, we found that the people who ate the most cholesterol, ate the most saturated fat, ate the most calories, weighed the least, and were the most physically active. This article showed that the people who eat the most nuts weigh the least. However, in the Cox model, neither exercise nor weight explained the impact on coronary disease. As to what other factors associated with nut eating explain the benefit, the authors give us a preview of a feeding trial, using walnuts, that at least shows a favorable change in the blood lipids eating nuts. Is this due to the polyunsaturated or monounsaturated fat in nuts? Is it some exotic fiber component? Hopefully, this anecdote will allay speculation about some other exotic confounder like television watching, nose-picking, or any myriad number of factors *not* routinely measured in this study.

I suppose that the ARCHIVES will be bombarded by the usual letters about

an article such as this by those cheerful folk who will want to know if the fall in coronary death rate in the nut eaters was offset by an increase in accidental, violent, or suicidal death. Perhaps there was a social price to pay, at least from the peanuts that, after all, are legumes.

Should dietitians everywhere tremble? Has the magic bullet arrived? Is it the humble nut? Should fat people eat fat-rich nuts to lose weight and atherosclerosis, or do nuts only work in vegetarians? Should nuts replace oat bran as the shield that I can load up on each day which will let those hot dogs just bounce right off my chest, no trouble. Will this article affect the stock market sending the lipid-drugs reeling when that well-balanced report appears in the *Wall Street Journal?* So many questions, so little time. In the meantime, hold the cheese, I will have my nuts (walnuts?) on whole wheat, please.

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Does Human T-Cell Lymphotropic Virus Type I and Human Immunodeficiency Virus Type 1 Coinfection Accelerate Acquired Immunodeficiency Syndrome?

The Jury Is Still Out

In this issue of the ARCHIVES, Gotuzzo et al[1] provide evidence that human immunodeficiency virus type 1 (HIV-1) and human T-cell lymphotropic virus type I (HTLV-I) coinfection is associated with a more severe clinical course with shortened survival for acquired immunodeficiency syndrome (AIDS). The teleological attraction of epidemiologic findings such as this, as with prior population studies of coinfected persons,[2-4] is that in vitro molecular and biochemical studies suggest that other viruses can enhance the replication and expression of HIV-1. Viruses for which this effect has been demonstrated include HTLV-I,[5] HTLV type II (HTLV-II),[6] cytomegalovirus,[7] human herpes virus type 6,[8] herpes simplex virus,[9] and Epstein-Barr virus.[10] For example, the envelope peptides of both HTLV-I and HTLV-II have been reported to activate T cells, resulting in enhanced HIV-1 expression.[6] In addition, the *tax* gene product of HTLV-I (the regulatory element of HTLV-I that promotes HTLV-I replication) stimulates HIV-1 proviral expression by activating the major promoter element of HIV-1, the long terminal repeat.[11] We now know that HTLV-I and human herpes virus type 6 can infect and coexist in cells infected by HIV-1, making these interactions more plausible.[12] Although suitable animal models for these interactions have been lacking, there is evidence in cats that coinfection of feline immunodeficiency virus with feline leukemia virus potentiates the immunoablative effects of feline immunodeficiency virus.[13]

See also p 1429.

There is a growing body of evidence that HTLV-I itself adversely affects the host immune system, albeit in a more subtle fashion than that observed for HIV-1. There are anecdotal case reports from HTLV-I endemic areas of *Pneumocystis carinii* pneumonia and other AIDS-defining illnesses in HTLV-I– infected persons without leukemia.[14] In addition, persons who are HTLV-I infected are more likely to have anergy based on skin test responses.[15,16] Autoimmune conditions such as arthritis[17] and iritis[18] are more frequent in HTLV-I infection, and the pathogenesis of HTLV-I–associated myelopathy/tropical spastic paraparesis is thought to result from immunologic hyperstimulation from HTLV-I infection.[19] Infective dermatitis of children is a recently described HTLV-I–associated condition characterized by persistent refractory cutaneous infections with saprophytic staphylococcal and streptococcal bacteria, which appear to result from a defect in immunity.[20] Recent findings that some patients with this condition subsequently progress to leukemia[21] raise the possibility that HTLV-I–associated immunosuppression may play a role in the pathogenesis of HTLV-I–associated adult T-cell leukemia. In vitro laboratory studies show that HTLV-I induces the expression of a variety of cytokines and lymphokines, including the elevation of the immunosuppressive tumor growth factor beta-1 in cases of adult T-cell leukemia.[22,23] One of the most intriguing aspects of HTLV-I infection is the finding that peripheral blood lymphocytes from HTLV-I/II–infected persons undergo spontaneous proliferation when placed in tissue culture without other stimulating factors.[24,25] Levels of spontaneous lymphocyte proliferation are highest in patients with HTLV-I–associated myelopathy/tropical spastic paraparesis, significantly elevated in healthy carriers of HTLV-I, and