

The DASH to lower blood pressure

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uring 1997 epidemiologic studies continued to show that an elevated serum blood homocysteine concentration increases the risk of coronary artery disease. People carrying the gene for homocystinuria have the highest concentrations of serum homocysteine, but milder increases occur far more frequently and (in the absence of renal failure) are most often due to inadequate vitamin B₁₂ and, especially, folic acid nutrition. Indeed, levels of serum homocysteine and methylmalonic acid — the latter is selectively increased in people with vitamin B₁₂ deficiency — are emerging as better tests of vitamin B₁₂ and folic acid status than are blood levels of the vitamins themselves. Research continues in an attempt to find whether a common mutation in methylenetetrahydrofolate reductase, an enzyme that enables folate to metabolize homocysteine, constitutes a disease risk factor in increasing the folic acid requirement.

Surveys continue to indicate that large numbers of Canadians, Americans and Europeans are still eating foods deficient in folic acid. This is important both for preventing congenital neural tube defects and — quite possibly — cardiovascular disease.

Although it is well known that obesity or excessive sodium and alcohol consumption can increase blood pressure, there is epidemiologic evidence that decreased consumption of certain other nutrients — fibre, potassium, magnesium, and calcium — can have the same effect.

Prospective clinical trials testing the antihypertensive effect of one or another of these nutrients have produced only small or inconsistent results, so a multicentre feeding study was developed. The Dietary Approaches to Stop Hypertension (DASH) trial was designed to determine the effect on blood pressure of entire dietary patterns that combine some or all of these nutrients.¹

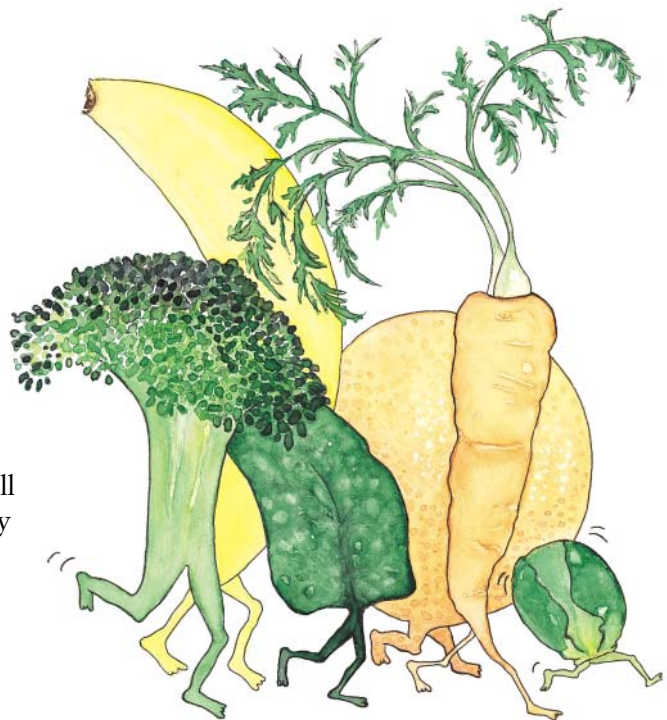
The study comprised a 3-week run-in phase during which all 459 subjects consumed a control diet typical of that of many Americans and Canadians: fibre intake was 9 g/d, cholesterol 300 mg/d, calcium 450 mg/d, magnesium 165 mg/d, potassium 44 mmol/d (1700 mg) and sodium 130 mmol/d (3000 mg). Participants had 1.6 servings of fruits and juices each day, and 2 servings of vegetables.

For the 8-week intervention period, subjects either continued

on the control diet or switched either to a diet high in fruits and vegetables (more than doubling their intake of fibre, magnesium and potassium) or to one that combined this approach with increased intake of dairy products (increasing calcium intake to more than 1200 mg/d) while lowering fat and cholesterol intake.

The subjects, whose average age was 44, were marginally overweight (body mass index 28 kg/m²) and were normotensive or only borderline hypertensive; they were not taking any antihypertensive medications. The starting average blood pressure level for the group was 131/85 mm Hg. Sodium and energy intakes for all diets were similar, and no significant weight loss occurred during the trial.

Although the control diet had no consistent effect on blood pressure, the combined diet reduced systolic and diastolic blood pressure by 5.5 and 3.0 mm Hg, respectively, compared with concurrently measured control-group values. The fruits-and-vegetables diet reduced



blood pressure to a lesser extent. Of particular interest to physicians, the blood-pressure-lowering impact of diet was greatest for subjects with the highest initial blood pressures. Thus, among the 133 subjects with a blood pressure of 140/90 mm Hg or higher, the combination diet reduced the systolic and diastolic blood pressure by 11.4 and 5.5 mm Hg more respectively than the control diet. This effect is similar in magnitude to single-drug therapy for mild primary hypertension.

The DASH trial indicates that a mildly deficient intake of certain dietary ingredients — especially in combination — can create or worsen primary hypertension. Both obese and normal-weight hypertensive patients may now be informed that adherence to a healthy diet can improve blood pressure as effectively as single-drug therapy.

This is an interesting illustration of a “pragmatic” clinical trial. Until quite recently trials that were not double blind or that altered more than a single treatment variable at a time were considered suspect. Pragmatic trials are now scientifically credible, so it has become feasible to test the effectiveness of multifaceted treatments and approaches that match real clinical experience. The DASH trial was difficult and undoubtedly costly, but trials using this pragmatic approach — particularly in nutrition — can be enormously useful because they allow for the synergism expected of nutrient and metabolic effects, and they permit better extrapolation to the clinical situation.

As attempts to use diet to control blood pressure continued in 1997, other research was supporting the theory that appropriate antioxidant therapy can inhibit atherosclerotic heart disease.² Several secondary prevention trials using vitamin E are under way, and their results are awaited with interest.³

It is unlikely, however, that the current crop of antioxidant trials will either establish or discredit nutritional antioxidant therapy for chronic disease. For one thing, we still don't know what forms, doses and combinations of nutrients to test. For another, there is still much to learn about the pathophysiology of the diseases being considered for treatment by using nutritional approaches. For example, consider the recent, widely publi-

cized trial involving the use of vitamin E and selegiline in treating Alzheimer's disease (AD). That trial tested a biologically improbable hypothesis — that vitamin E alone can dramatically reduce the rate of cognitive decline in established AD — and it obtained an implausible result: no effect on cognitive function but, after adjustments for baseline mental status, a delay in the time to hard primary outcomes such as severe mental decline, institutionalization because of loss of function, or death.⁴

But hard outcomes are influenced by more than one factor in AD.

Given the evidence that potent antioxidant therapy can reduce serious cardiovascular events, the authors should have formally recorded the baseline cerebrovascular and cardiovascular status of their trial participants and examined their data for evidence that vitamin E conferred its benefit in patients with obvious atherosclerosis. It could act indirectly, by reducing the frequency of silent brain infarcts, or directly, by reducing cardiac events. But this type of analysis was not done.

Moreover, given what we know about the interaction of antioxidants and other nutrients, it is archaic to continue designing nutritional interventions in the same way drug trials are designed. The diet of patients with AD is frequently poor.⁵ The most efficient test — the DASH trial demonstrated this — would be a pragmatic trial that incorporated combined nutritional therapies, such as high-dose vitamin E combined with ascorbic acid, folic acid and vitamin B₁₂, within the context of a generally excellent diet.

References

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