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Cerebrovascular Accidents (CVA) or strokes are the third leading cause of death and the primary cause of disability in adults. As the clock ticks and each minute of every day, another person has a stroke. Four of five American families will be affected by stroke during their lifetime (16). Fortunately, many of the 550,000 strokes, new or recurrent, that occur each year are preventable using basic preventative measures, which could be easily incorporated into dietary health management with proper stroke prevention education. At this point, stroke costs the U.S. approximately \$30 billion annually in health care costs and losses in productivity. 3 million Americans are left currently disabled due to the preventable effects of stroke (16). Stroke risk factors include: age (over 55), previous stroke or transient ischemic attack, hypertension, heart disease, diabetes, carotid artery disease, ethnicity, smoking, hypercholesterolemia, family history, obesity, alcoholism, and a sedentary lifestyle (16). Preventative medicine education for stroke awareness is very poor in the U.S. to the point where 38% of adults over age 50 did not know where a stroke occurs. 19% of adults were unaware that there are preventative measures for stroke. In fact, a simple measure of calling 911 during a stroke, can save your brain, yet only 40% of adults over 50 would call 911 when they experienced stroke-like symptoms, (one-sided weakness, numbness, or paralysis of face, arm, or leg; sudden blurred or decreased vision monocularly or binocularly; difficulty speaking or understanding simple statements; dizziness, loss of balance, or loss of coordination, especially with other symptoms; and most importantly a sudden severe, unexplainable headache: "the worst headache of your life") (16). Many strokes can be prevented, and using several easy dietary methods.

Current research dictates that there are several dietary preventative measures that can reduce the likelihood of having a stroke. The Framington Study indicates that men who consume 3 or more servings of fruits and vegetables have a 22% lower risk of stroke and are half as likely to die from stroke, if one occurs, and a similar study for women showed similar results (7). Similarly, salt reduction, by mechanisms of reducing overall blood pressure, can afford reductions in stroke potential in adults (2, 4). However, it is important to consider what aspects of diet can promote the best means of stroke prevention.

While antioxidants have often been seen as fad vitamins, recently antioxidants have been shown to have dramatic effects on preventing strokes, both new and recurrent (3, 5). One of the primary ways of preventing strokes is with prevention of chronic vascular stenosis, secondary to atherosclerosis of cerebral vasculature. There are two main mechanisms that provide primary stroke protection: LDL oxidation prevention and prevention of hyperhomocysteinemia (11). Three categories of agents which provide this protection against stroke are: 1) dietary antioxidants (vitamins B-complex, C, E, and beta-carotene), 2) vitamin B12, and 3) the flavonoids. Each category can be shown to be beneficial to stroke prevention, both primary (1st strokes) and secondary (recurrent stroke), and some prove to be beneficial on other diseases such as coronary artery disease, and free-radical induced mutagenic carcinogenesis.

Dietary antioxidants, such as vitamins E, C, B-complex, and beta-carotene, have been shown to be important in blocking critical steps in the formation of atherosclerotic plaques.

Atherosclerotic plaques have been shown to form from free-radical oxidation of lipids, thereby forming fatty plaques on vessel walls, leading to vascular stenosis. Vitamin C, a water-soluble vitamin has been important in reducing the free-radical formation in aqueous phase (12). Beta-carotene and vitamin E have been shown to block free radical oxidation in the lipid-phase of LDLs. Studies have shown that low levels of beta-carotene have a higher relative risk for CVA

(R.R. = 1.53, $p=0.02$), as does low levels of vitamin C (R.R. = 1.25, $p = 0.38$), and the combined condition with low beta-carotene and vitamin C has an even higher relative risk of 1.96 ($p = 0.02$) (9). A diet low in both beta-carotene and vitamin C has almost double the risk for having a stroke or ischemic heart disease (6). Yet, scientists have also found that beta-carotene doses as delivered in pill or supplement form, can actually do more damage than harm. In fact, large doses of beta-carotene can lead to increased risks of heart attack and cancers (8). Studies show that large doses of beta-carotene deplete the body of vitamin E, which can increase your risk for cancer (9). Thus, one should eat lots of fruits, vegetables, whole grains and beans since vegetables contain many other phytochemicals that are known to prevent heart attacks and cancers, rather than just taking beta-carotene in a pill form, may serve to better prevent against heart attacks and cancers.

Another antioxidant that has recently been identified in the prevention of atherosclerotic plaques is vitamin B12. Vitamin B12 is a vitamin that is not found in common vegetable sources, and is often formed in both small and large intestinal bacteria, though it is only absorbed in the small intestine. It is said that those who are "vegan" tend to absorb vitamin B12 at higher rates than do those who are not "vegan" (14). Vitamin B12 is important for both cell division and for blood formation, especially in iron absorption, and deficiencies in the vitamin B12 can lead to improper iron absorption as well as deficits in sulfur amino-acid metabolism. Low serum vitamin B12, or genetic defect in uptake or utilization of B12 proteins, such as an intrinsic factor deficiency, can lead to a condition known as hyperhomocysteinemia, a condition in which there is an over-excess of homocysteine in the blood, indicating a problem in sulfur-amino acid metabolism (13). Hyperhomocysteinemia increases the risk of stroke as it causes an increased formation of a cyclic reactive form of homocysteine that can react with low-density lipoproteins. Such oxidation can lead to atheroma formation, (macrophagocytic lipid aggregations, secondary to increased LDL uptake by these macrophages), as well as intimal injury, oxidation of cholesterol and unsaturated lipids, platelet aggregation, thrombogenic factors, myointimal hyperplasia, deposition of sulfated GAG's, fibrosis, and calcification of atherosclerotic plaques (11). The chronic effects of the buildup of these toxic thiolactone derivatives of sulfur amino acid metabolites can lead to ongoing vascular stenosis, leading to ischemic diseases of many organs, especially cerebral and cardiac tissues. Extra dietary vitamin B can also afford a drop in thrombomodulin, an important factor in the clotting cascade. The drop in thrombomodulin levels reflect decreased vessel endothelial injury, which preventing induction of the clotting cascade (15).

One of the newest, and yet oldest, treatments for stroke prevention is the dietary intake of plant compounds called flavonoids. Flavonoids are antioxidant compounds that are characterized by their polyphenolic chemical structure. Flavonoids are responsible for primary anti-oxidative effects by attracting oxygen free radicals before these free radicals can cause cellular damage. Over 4,000 flavonoids have been discovered, and they are found in fruit, vegetables, seeds, nuts, flowers, and bark. The best sources of flavonoids in human consumables are red wine, tea, onions, and the ubiquitous agent of health care: APPLES! Flavonoids have also been found to aid in vascular smooth muscle relaxation, which can reduce blood pressure, and thereby reduce the risk of stroke (9). Common flavonoids are quercetin, kaempferol, myricetin, luteolin, and apigenin, which tend to be found in vegetables and fruit. Using fruit and vegetable intake as a measure of flavonoid uptake, it was found that men without strokes had consumed on average 77.2 g per day of solid non-citrus fruit, as compared to high stroke risk men with an intake of

57.4 g per day (9). It was also found that those in the stroke-free category had also consumed more citrus fruit (vitamin C), more vegetables (beta-carotene, and others), and more tea (other flavonoids). More surprising was that when looking at the sources of flavonoids directly, in the same study, it was learned that 70% of flavonoid intake was on tea alone, and about 10% from apples (9). (Both black and green teas provide the same amount of dietary flavonoids.) The protective benefits of flavonoids provide the strongest proof for their importance: the men who were stroke-free in the study, who consumed flavonoids in the top quartile of intake, had a 73% less risk of stroke (9). Flavonoids are beneficial not only for stroke, but in terms of cancer and coronary heart disease prevention, as well, using similar prevention of lipid oxidation mechanisms like vitamin B12 and beta-carotene (9).

In essence, it is important to look at one's diet as crucial in stroke prevention, while there are familial risk factors for stroke, one can cut their non-genetic risk in half by simply watching their diet and insuring proper intake of antioxidants and other vitamins. A big concern then is raised with why then shouldn't we increase our levels of these compounds using pill-style supplementation, rather than eating vegetables and fruits and maintaining adequate overall vitamin intakes. As we saw in the case of vitamin E and beta-carotene, large doses of beta-carotene can actually increase one's risk for stroke since large doses of beta-carotene can deplete the body of vitamin E (8, 9). Obviously, in compounds such as vitamin B12, which is primarily from fortified foods and from endogenous sources such as enteric bacteria, it is important to look for foods high in vitamin B12. Obviously, in patients with intrinsic factor deficiency, both forms of supplementation will prove insufficient, and other means of increasing vitamin B12 are necessary. Most importantly, we know so little in respect to the flavonoids and other phytochemicals of fruit and vegetable origin and their systemic effects, that there are many great, but undiscovered benefits of eating large quantities of them. Lastly, fruits and vegetables serve as sources of fiber, which will have a too fold effect: 1) By allowing for the "fullness" feeling after eating, they will prevent eating more than necessary, and can help to reduce fat intake, and are great snacks. For those with chronic hemorrhoids, dietary fiber can soften stool and prevent many common causes of hemorrhoids. Fiber also helps to reduce cholesterol levels, since it can reduce fat intake, and by the same mechanism can promote better health, preventing atherosclerosis (1, 7). There are great benefits to these treatments in addition to just stroke prevention with these vitamin and antioxidant supplements. Coronary Artery Disease (CAD), ischemic heart disease, and cancers of free-radical mutagenic origin can be greatly prevented using similar measures of increasing intake of these antioxidants (10). Since stroke is a definitively predictable illness for 550,000 Americans, if we watch what we eat, and have a bit more fruit and vegetables in our diet, we can spare ourselves many of the problems associated with stroke. Remember: A diet with apples, oranges, more fruit and more vegetables a day will keep the neurosurgeon away.

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