

Within the past four decades, the efforts of investigators worldwide have established the amino acid homocysteine as an important factor in arteriosclerosis and diseases of aging. After its discovery in 1932, homocysteine was demonstrated to be an important intermediate in the metabolism of amino acids. However, little was known about the broader biomedical significance of homocysteine until 1962, when children with mental retardation, accelerated growth, dislocated ocular lenses, and frequent vascular thrombosis were found to excrete homocysteine in the urine. My study of two patients with homocystinuria caused by different inherited enzymatic disorders in 1968 disclosed advanced widespread arteriosclerotic plaques in both cases. This discovery led to the conclusion that homocysteine causes vascular disease by a direct effect on the cells and tissues of the arteries. This interpretation suggests that homocysteine is important in the pathogenesis of arteriosclerosis in persons with hereditary, dietary, environmental, hormonal, metabolic, and other factors predisposing them to hyperhomocysteinemia. Within the past decade, many major clinical and epidemiological studies have proven that hyperhomocysteinemia is a potent independent risk factor for vascular disease. According to the homocysteine theory of arteriosclerosis, insufficient dietary intake of the B vitamins, folic acid and pyridoxine, caused by losses of these nutrients during processing of foods, leads to elevation of blood homocysteine and vascular disease in the general population. The significant decline in cardiovascular mortality since the 1960s in the United States is attributable to voluntary fortification of the food supply by synthetic pyridoxine and folic acid. Since 1998 when folic acid was mandated for addition to flour and refined grain foods by the US Food and Drug Administration, mortality from cardiovascular and cerebrovascular disease has dramatically declined further. The recent Swiss Heart Study showed that B vitamins slowed restenosis in patients with coronary arteriosclerosis treated with angioplasty. Currently, more than 20 prospective, worldwide, interventional trials involving at least 100,000 participants are examining whether lowering plasma homocysteine levels with supplemental B vitamins will prevent mortality and morbidity from arteriosclerotic vascular disease.

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