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The action of vitamin C on blood vessels

The relationship between vitamin C, fat, and blood vessels is now becoming much clearer.

Zaitsev, Myasnikov, and Sheikman,¹ in 1964, gave animals an atherogenic diet containing ¹⁴C-labelled cholesterol and showed that the cholesterol was deposited on the aorta. If, however, the animals were given vitamin C as well as the diet, the cholesterol was found in the liver and the adrenals, but not on the aorta. Thus, vitamin C is responsible for the transport of cholesterol to the liver.

Personal observations² that in young healthy people the serum cholesterol went down after the administration of vitamin C, while in atherosclerotic patients it tended to rise, suggested that this was due to mobilization of arterial cholesterol and, in effect, confirmed the Russian experiment in human subjects. Sokoloff, Michiteru, and Saelhof³ treated elderly atherosclerotic patients with vitamin C over a 2½ year period, and was able to produce striking improvement in the patients' clinical condition without making much impression on the serum cholesterol, thus supporting the hypothesis that the arterial cholesterol was being mobilized, with resulting circulatory improvement.

An isolated serum cholesterol determination is therefore of no value, because it gives no indication of the state of the arteries. Of much greater value would be the study of the behavior of the serum cholesterol after vitamin C, because this would give some indication of the amount of cholesterol on the arteries. However, this is really academic, because the important factor is that while vitamin C is being given, the cholesterol is being directed away from the arteries.

Vitamin C also acts on the other components of fats. It reduces the β -lipoproteins,¹ enhances the activity of lipoprotein lipase, and therefore brings down the triglycerides.³ In addition to this, it provides the ground substance for the blood vessel walls. In other words, it has a controlling influence on all the factors which become abnormal in atherosclerosis.

Thus a balance exists between vitamin C and fat. If the balance permanently favors vitamin C, the cholesterol will always be delivered to the liver, the β -lipoproteins will remain low, the lipoprotein lipase activity will be high, so the triglycerides will be low, and the arteries will be well supplied with ground substance, so they will remain clean. If, on the other hand, the balance favors the fats, there will be a gradual accumulation of cholesterol in the arteries, the other

fat fractions will gradually become abnormal, and the arteries will lose their ground substance, so atherosclerosis will result.

The difficulty in proving any hypothesis relating to atherosclerosis, however logical it may be, is very great, because of the widespread incidence and insidious onset of the disease. No adult can be guaranteed to be "normal" and there is no absolute method of demonstrating "normality."

However, the same cannot be said of the veins. Deep vein thrombosis has a very similar epidemiologic distribution to atherosclerosis, and it has two advantages over the arteries where studies are concerned: the shortness of the time exposure to risk and the convenience of methods for studying the development of thrombi.

A double-blind trial has been done⁴ on patients who were vulnerable to a deep vein thrombosis, using vitamin C (1 Gm. daily) and a placebo. ¹²⁵I-fibrinogen was used to detect the development of thrombi. The incidence of deep vein thrombosis in the vitamin C group was halved, as measured by this method, but what was much more striking was the reduction in physical signs. This was a reflection of the marked reduction in the degree of radioactivity found in the positive legs in the vitamin C group and, therefore, in the extent of the thrombus. A rise of more than 15 per cent was regarded as positive, but six of the vitamin C patients had rises of less than 25 per cent, and were therefore only just in the positive range. None of the vitamin C patients had a rise of more than 80 per cent, while several of the placebo patients had rises of more than 200 per cent.

Vitamin C therefore has a powerful antithrombotic effect. Whether this action is directly on the coagulation system, or a consequence of its action on the blood fats, is a matter for speculation and study. Carnivorous animals, which synthesize their own vitamin C, are not troubled with atherosclerosis or other thrombotic disease, and yet their coagulation system is, if anything, more active than ours.⁵ This would suggest that in man the action of vitamin C is initially on the abnormal blood fats and then, indirectly, on the coagulation system.

The protective action is a rapid one. In the study described above, the patients were divided into three main groups. Patients for hip arthroplasty were given vitamin C from the time they were seen in the outpatient department and up to six weeks' treatment was given (average 15 days). Patients

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having a prostatectomy received vitamin C after admission and had an average of seven days' preoperative treatment. Patients who had a coronary thrombosis did not have their vitamin C until after the catastrophe had occurred. Although the numbers were small, there was virtually no difference in the degree of protection afforded by vitamin C in the three groups.

Thus, provided that the vitamin C is given as quickly as possible after people are admitted to hospital with a condition which exposes them to a deep vein thrombosis, they should be protected. The trial has now been followed up by the administration of vitamin C routinely in our surgical and orthopedic wards and deep vein thrombosis has now disappeared from these wards.

Andrews and Wilson,⁶ giving 200 mg. of vitamin C daily to geriatric patients, found that it did not provide any protection against thrombotic disease. Sokoloff and associates,³ giving 1 to 3 Gm. daily to elderly atherosclerotic patients, were able to protect all their 60 patients for up to 2½ years (i.e., the end of the trial) from further thrombotic episodes. Routine administration of 500 mg. daily to our surgical patients produced a very occasional case of deep vein thrombosis, but since we have increased the dose to 1 Gm. daily we have had no further cases. This suggests that in the elderly and most vulnerable cases, at least 1 Gm. daily is needed to provide protection against thrombotic disease.

There are certain points of interest which should be mentioned: (1) Smokers have lower vitamin C levels than non-smokers.⁷ (2) A man who has had a coronary thrombosis is almost invariably told to lose weight. His low-calorie diet contains an abundance of vitamin C-containing foods. (3) Women who take contraceptive pills have a lowering of their vitamin C levels.⁸

Thus, vitamin C protects the capillaries by a direct action

on the vessel walls. Its protective action on the veins and the arteries is a combination of its action on the vessel walls and the blood fats, with an indirect action on the coagulation system. The capillary defect is an acute deficiency, while thrombosis is a long-term negative balance, of vitamin C.

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Some aspects of the left atrial sound

The atrial sound is the presystolic vibration associated with atrial systole. It is also known as the fourth sound, but this term is confusing since it is the initial sound of the complete cardiac cycle. It is a low-frequency vibration, between 25 and 100 Hz, and usually near the threshold of human hearing. The peak vibrations of the atrial sound coincide with the peak of the atrial beat (the "a" wave of apex displacement) which is the outward movement of the left ventricular apex caused by left atrial contraction. The time relationship of the atrial sound with the P wave of the electrocardiogram is variable and incompletely understood. When an atrial sound is recorded in the normal subject it usually occurs at about 0.12 to 0.16 sec. after the onset of the P wave. In patients with heart disease the interval may be shorter or longer than this, but never less than 0.07 sec. The more severe forms of left ventricular disease are associated with shorter intervals.¹ Recovery of heart function after myocardial infarction^{2,3} and with the treatment of hypertension⁴ leads to progressive lengthening of the interval between the P wave

and the atrial sound, which may become incorporated in the first sound.

The atrial sound is best detected by examining the patient in the left lateral position. In cases with a pathological atrial gallop it is often easier to feel the atrial beat with the fingers on the cardiac apex than to hear it. The sound is most easily heard with the bell of the stethoscope placed very lightly over the cardiac apex, and is usually filtered out by firm pressure which converts the skin of the chest wall into a diaphragm.

The healthy young ventricle fills readily in early diastole, with a prominent rapid filling wave of apex displacement often accompanied by a physiological third heart sound. The atrial contribution to ventricular filling is relatively small: the "a" wave of apex displacement is small and any accompanying sound vibrations are inaudible clinically. The diseased left ventricle fills less readily in early diastole, the rapid filling wave is attenuated and the physiological third sound is lost, while the contribution from left atrial systole increases, producing a large apical "a" wave often accom-