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Vitamin C, disease, and surgical trauma

Vitamin C is concerned with the integrity of connective tissue constituents, particularly collagen and intracellular cement substance, but its precise mode of action is still not clear.¹ The Medical Research Council study in Sheffield during the second world war showed that a daily dietary intake of 10 mg ascorbic acid could prevent or cure overt signs of scurvy.² In Britain today scurvy is seen only rarely—mainly in mentally handicapped children and elderly people. Experimentally, it has developed in human volunteers fed on a diet containing no vitamin C, the normal body pool of 1500 mg being depleted at the rate of about 3% daily.³ Clinical manifestations of scurvy appear after 84-97 days, when the body pool is less than 300 mg: they include fatigue, petechial haemorrhages, follicular hyperkeratosis, aching limbs, swollen and bleeding gums, and effusions into the joints. But even before physical signs appeared in the volunteers psychometric tests⁴ showed personality changes, notably hypochondriasis and depression, followed by a decline in psychomotor performance that was associated with reduced arousal and motivation. A severe depressive state is reported as a striking clinical feature in chronic scurvy, but this clears after a few days of vitamin C treatment.⁵

Anaemia is common in vitamin C deficiency, which may cause continued gastrointestinal haemorrhage once this has been precipitated by gastric irritants such as aspirin.⁶ The anaemia is usually normocytic or macrocytic with normoblastic or macronormoblastic erythropoiesis, but true megaloblastic anaemia also occurs.^{7 8} The anaemia is usually due to several factors: haemolysis, bleeding, dietary deficiency of iron, and derangement of red cell metabolism have been incriminated.⁹ Megaloblastic change possibly results from either an associated dietary folate deficiency or the impairment of folate metabolism in scurvy.¹⁰ In the absence of vitamin C tetrahydrofolates are oxidised to 10-formyl folic acid, and an important role of vitamin C in metabolism is probably maintaining an available metabolic pool of folate.

Increasing the vitamin C content of the diet fed to guinea pigs increases the wound strength in healing skin.¹¹ Though in man wound healing can proceed satisfactorily with low intakes of vitamin C—less than 10 mg daily—more may be needed in special circumstances. Thus biopsy specimens taken before and after treatment from paraplegic patients with pressure sores showed more intense staining for collagen when they had taken 1 g of ascorbic acid for three days, an effect not produced by placebo.¹² Though none of the patients showed evidence of vitamin C deficiency, the increased intake could

have helped clinically. Crandon and his colleagues¹³ suggested that surgical operations result in increased requirements for vitamin C, and that deficiency is a common and important factor in wound complications after operation. Their findings have been questioned, however, owing to the difficulties of interpreting the alterations in the concentrations of ascorbic acid in the buffy layer or plasma that accompany postoperative metabolic and haematological changes. Recently Irvin and his co-workers¹⁴ in Sheffield have reassessed ascorbic acid requirements after operation in patients grouped according to the severity of the surgical trauma. The leucocyte ascorbic acid (LAA) concentrations were significantly reduced after operation. The reductions were unrelated to the severity of surgical trauma or to the volume of blood transfused at operation, but there was a significant inverse correlation between LAA concentrations and white blood counts. The authors conclude that postoperative leucocytosis due to surgical trauma and the release by the bone marrow of leucocytes with a low ascorbic acid content may partly account for the postoperative changes in LAA measurements. Nevertheless, surgical operations were evidently followed by an authentic increase in ascorbic acid requirements since circulatory LAA concentrations fell by 42% on the third day. The results of the Sheffield study support the argument for ascorbic acid supplements in patients having surgery even though their benefits have not been assessed.

In a series of aged hospital patients the death rate was 47% in the four weeks after admission for those whose initial LAA concentration was under 0.68 μmol (12 μg)/10⁸ leucocytes but only 10% when it was over 1.42 μmol (25 μg)/10⁸ leucocytes ($P < 0.01$).¹⁵ The mortality rate turned out, however, to be related not to LAA concentration directly but to the severity of the illness, which in turn influences the tissue stores of vitamin C.¹⁶ In the follow-up study administration of vitamin C failed to produce an increase in LAA concentrations in many of the patients nor did it influence the death rate. Thus the disturbances of metabolism that occur in many diseases—as well as several drugs, including tetracycline¹⁷—are likely to depress the LAA concentration. But how far do ascorbic acid concentrations in the tissues influence the course of diseases (and the efficacy of treatment) as well as the rate of wound healing? This is a question we cannot answer until we have more sensitive tests to detect impaired collagen function. Meanwhile we need further evaluations of the effects of vitamin C supplements on wound healing in patients undergoing surgery.

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