The growth maintaining activity and intestinal absorption of ascorbic acid in guinea-pigs

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It has been shown that guinea-pigs develop scurvy on a scorbutic diet in 20–28 days (Evans & Hughes, 1963; Hodges & Hotston, 1970). However, the relationship between the development of scurvy, leucocyte ascorbic acid levels and intestinal absorption of vitamin C has not been accurately established. After maintenance on a normal diet supplemented with vitamin C (50 mg in 100 ml water), 24 guinea-pigs were given a scorbutic diet for two weeks while receiving 20 mg of L-ascorbic daily by stomach tube. They were weighed regularly, food intake was recorded daily, and blood samples were removed at 6 day intervals for estimation of ascorbic acid concentrations. They were then divided into three equal groups receiving 20 mg (control C), 100 mg (hypervitaminotic: HV) and zero (scorbutic: S) ascorbic acid daily. After 7 days the plasma ascorbic acid of the S group began to fall and the group lost weight after 10 days. Plasma ascorbic acid and weight increased after 7 days in the HV group. Leucocyte ascorbic acid levels fell after 10 days in the scorbutic group and increased slightly in the other two groups. On the 28th day two of the S group died. The mean ($\pm$S.E.M.) leucocyte ascorbic acid concentration of the group was $9{\cdot}3\pm1{\cdot}3/10^8$ cells and the plasma ascorbic acid was $0{\cdot}103\pm0{\cdot}016$ mg%. In the HV group the corresponding levels were $32{\cdot}8\pm1{\cdot}7$ $\mu g/10^8$ cells and $1{\cdot}097\pm0{\cdot}145$ mg%. Weight changes for the groups at the end of the period were: C group +23%, HV group +32%, and S group −27% of the initial weights.

On the 28th day the intestinal absorption of ascorbic acid was measured *in vivo* from a loop of the ileum during a 2 h period. The percentage disappearance of ascorbic acid from the loops, the intestinal uptake, and alteration in blood concentrations of ascorbic acid were measured in the different groups. Ascorbic acid uptake from the lumen was least in the scorbutic animals. About three times as much ascorbic acid remained in the lumen of the S group as in the C or HV groups. A larger percentage of ascorbic acid remained in the mucosal cells of the control and scorbutic animals than in the cells of the hypervitaminotic animals. The increase in leucocyte ascorbic acid after the period of intestinal absorption was greatest in the C group and least in the S group, with the values in the HV group coming between. It is concluded that intestinal absorption of vitamin C is diminished in the terminal stages of scurvy. Concurrently leucocyte ascorbic acid concentrations in scorbutic animals fail to increase as easily as those in control or hyperscorbutic animals.

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Liver damage and excretion of bivalent sulphur after exposure to carbon disulphide in fed and fasted rats with and without phenobarbitone pretreatment

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The increased frequency of coronary heart disease in people with a history of exposure to carbon disulphide (CS_2) prompted a study of the toxic effects of CS_2.

Male albino rats (200 to 220 g) were exposed 4 h to CS_2 (2·0 mg/l.) and urine collected in the subsequent 17 h. The animals were then decapitated and the liver taken for histology.

Urine samples were analysed for bivalent sulphur by the catalytic iodine azide reaction which is used in industry to detect excessive exposure (Djuric, Surducki & Berkes, 1965). The net reaction on which the method is based is $I_2+2\ N_3^- \rightarrow 3\ N_2+2\ I^-$. The spectrophotometric method of Strickland, Mack & Childs (1960) was adapted to the bivalent sulphur metabolite(s) of CS_2. The calibration curve was prepared with diethyldithiocarbamate, the reaction product of CS_2 with diethylamine.

Rats were exposed to CS_2 after feeding or after a 24 h fast with or without treatment by intraperitoneal injection of 80 mg/kg or 50 mg/kg phenobarbitone given 24 and 18 h respectively before exposure.

In rats fasted for 24 h before exposure to CS_2 the excretion of bivalent sulphur due to CS_2 exposure fell from 65 μmol/kg found in fed rats to 44 μmol/kg whether or not there had been pretreatment with phenobarbitone. However, in almost all fasted animals pretreated with phenobarbitone the same degree of liver damage was seen as that observed by Bond, Butler, DeMatteis & Barnes (1969), who gave 1·0 ml/kg CS_2 *per os* to fasted phenobarbitone-treated animals. This oral dose was approximately 15 times more than the calculated (72 mg/kg=0·95 mmol/kg) CS_2 retained by the rats during the 4 h exposure to CS_2 vapour. Feeding before exposure decreased or completely prevented liver necrosis.

The observations that phenobarbitone had no effect on the LD50 of CS_2 (Bond *et al.*, 1969) and failed to affect the excretion of the CS_2 metabolite, which accounts for approximately 6% of the body burden, suggests that phenobarbitone may not interfere with the metabolism of CS_2. As CS_2 inhibits at least some of the enzymes which are induced by phenobarbitone (Bond & DeMatteis, 1969) and the extent of microsomal changes depends on the activity of the drug metabolizing enzymes at the time when CS_2 is administered (Bond & DeMatteis, 1969), it is possible that some imbalance in the catabolic and anabolic processes induced by phenobarbitone and intensified by fasting renders the liver cells more sensitive to CS_2.

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Effects of pargyline on body temperature and on hypothalamic levels of monoamines in the rabbit (T)

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Effect of amylobarbitone, dextro-amphetamine and a mixture of these on performance and learning in man (T)

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