

Letters to the Editor

Scorbutogenic Guinea Pig Diet

Dear Sir:

Attention needs to be drawn to the totally inadequate dietary controls used in the study of M. B. Garvey, L. H. Dennis, and M. E. Conrad in the November issue, thus nullifying most, if not all, of the authors' conclusions (Labile Factor Depression in Scorbutic Guinea Pigs. *Am. J. Clin. Nutr.* 22: 1423, 1969).

The authors produced scurvy in 400- to 500-g guinea pigs "by feeding them a scorbutogenic diet for 1 month." (No further description of the deficient diet is given to allow evaluation of the nutritional adequacy of the diet or repetition of the work, unfortunately.) The deficient animals developed many of the usual symptoms of scurvy plus the new findings of "a moderately severe deficiency of labile factor (V) and fatty metamorphoses of the liver," which the authors attribute (without sufficient evidence, I feel) to a lack of vitamin C.

Unfortunately, the "control" animals were not given supplements of pure ascorbic acid, which would have served as the proper control. Rather, the "control animals were fed the same diet supplemented with green leafy vegetables" (amount unspecified and rich in many nutrients other than vitamin C). Thus, a basic tenet of nutritional experimentation was overlooked and the authors do not really prove the reported changes they found were due to a lack of vitamin C.

The study, in order to be acceptable, needs to show results with control animals fed pure ascorbic acid, and only then are the conclusions proved. Of course, the conclusions may well be right, but the evidence published in this paper is insufficient to prove anything. When such studies are published, complete details of the composition of the basal diet should also be given just as carefully as the details of other procedures (in this case, the blood studies). The guinea pig's nutritional requirements are very complex and several more essential nutrients than vitamin C—such as folic acid, choline, vitamin K, and iron, to name a few—may well

be deficient in the scorbutogenic diet unless proven otherwise.

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Author's Reply

Dear Sir:

The guinea pigs were fed a commercial ascorbic acid-deficient diet for guinea pigs containing a surplus of vitamin diet fortification mixture with ascorbic acid omitted (Nutritional Biochemicals Corporation, Cleveland, Ohio). Control animals were fed the same diet but given cabbage leaves thrice weekly as a supplement. As Dr. Briggs indicates, the addition of ascorbic acid rather than cabbage leaves would provide more absolute control. However, if the changes observed were not caused by vitamin C deficiency, they would seem to be caused by a new and unidentified deficiency state. We believed that the data were adequate to show 1) normal guinea pigs have an unusually low concentration of factor VII, 2) the hemorrhagic manifestations of scurvy were not caused by disseminated intravascular coagulation, and 3) insight into the seemingly more marked hemorrhagic manifestations in guinea pigs than humans.

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Urinary Creatinine Excretion

Dear Sir:

When it is impossible to collect timed specimens, the excretion of urinary compounds in random urine samples is usually expressed as per gram creatinine in so-called creatinine ratios. This procedure is based on the assumed constancy of creatinine excretion (1). Investiga-



tions by Vestergaard (2) on the constancy of urinary creatinine excretion over short collection periods have revealed an hour to hour variation, which frequently exceeds 100%. Bleiler (3) states that the use of creatinine excretion as a reference in interpreting the excretion of other urinary constituents may be invalid when based on single or random urine samples.

Moreover, the level of urinary creatinine excretion is generally agreed to be dependent on the muscle mass. This, however, is a disadvantage in nutritional surveys as the level of protein intake has a well-known influence on muscle development. Therefore, as creatinine excretion is dependent on the nutritional status any urinary creatinine ratio used in the assessment of the nutritional status is unduly influenced.

We wish to report on an alternative way to express the excretion of urinary compounds that seems to be less dependent on muscle development. Two extreme nutritional groups of children in Kenya were studied. One was comprised of poorly nourished children of squatters. Children from an orphanage who received an adequate diet were selected as the control group. In both groups 3-hr urine specimens were collected in which the creatinine concentration and the osmolarity were estimated. The osmolarity was determined by the boiling point elevation, although other methods might also be equally accurate. The total urinary solute and the absolute creatinine excretion over the collection period were thus calculated. The total solute excretion was very similar in both groups, but the creatinine excretion was significantly lower in the group of malnourished children. These findings indicate that urinary compounds expressed in ratios with creatinine in the denominator are relatively too high in malnourished children who have a low creatinine excretion due to poor muscular development. This influence of poor muscular development on urinary

creatinine ratios, therefore, can be abrogated by using osmolarity in lieu of creatinine.

However, the constancy of the total solute excretion in a given period is, like creatinine, not entirely independent of diet. To a large degree the osmolarity of urine is influenced by the intake of electrolytes and to a lesser extent by nitrogen-containing compounds. Considering the large endogenous variations in creatinine excretion and its dependence on muscle mass, osmolarity ratios might be of value in nutritional field studies, provided the intake and output of electrolytes are as well balanced and constant as they are in most communities of the developing countries where nutritional surveys are done. Excessive mineral intake seldom occurs.

Although the suggested method of expressing urinary compounds as osmolarity ratios gave very promising results in our study, further investigations in other parts of the world under different nutritional and climatic conditions are essential before its application on a large scale can be recommended.

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