CARBOHYDRATE, PROTEIN AND FAT ABSORPTION IN CHRONIC URAEMIA

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Comprehensive and systematic investigations concerning the absorption of the digestion products of carbohydrate, protein and fat are not yet available. The following remarks are intended to review the sparse findings published to date.

Carbohydrate Absorption

In 1969, Madzarovova-Nohejlova reported on the determination of disaccharidase activities in small intestinal biopsies of 30 patients with renal disease, 15 of whom had normal blood urea levels, whereas in 15 cases serum urea values were in the range of 55 to 210 mg/100 ml. The patients without renal insufficiency showed normal enzyme activities whereas there was a significant reduction in lactase activity and cellobiase activity. In the presence of structural changes of the mucosa, the activities of trehalase, sucrase and maltase were diminished, too. In 11 of the 15 patients with renal insufficiency, Madzarovova-Nohejlova (1969) also observed an inadequate low rise in blood glucose following an oral lactose test.

Figure 7. Mean blood glucose level (± SEM) after oral administration of 100 g lactose to 13 chronic uraemic patients with a mean inulin clearance of 7.5 ± 3.5 ml/min.
We failed to confirm this frequent lactose malabsorption in chronic renal insufficiency. In 13 patients, who had a mean inulin clearance of $7.5 \pm 3.5$ ml/min, lactose malabsorption was consistently absent (Figure 7). In a group of 10 patients with chronic uraemia Bloch et al (1973) likewise failed to observe lactose malabsorption. McNair and Olsen (1974) investigated 32 uraemic patients and found lactose malabsorption in not more than 2 of the cases.

Denneberg et al (1974) also failed to confirm the significant fall in lactase and cellobiase activity reported by Madzarova-Nohejlova (1969). These workers had examined the small intestinal biopsy specimens of 12 chronic haemodialysis patients and of 6 chronic uraemic patients receiving conservative treatment. Diminished lactase activity was found in only 5 of the 18 patients studied, whereas maltase and sucrase activity was reduced in two-thirds of the patients. Isomaltase was decreased in 5, and trehalase in 9 patients. Normal activity of all the 5 disaccharidases studied was consistently found in 4 of the 18 patients.

McNair and Olsen (1974) investigated the biopsy specimens of 15 uraemic patients. In contrast to the above findings of Denneberg et al (1974) these workers observed diminished activity of sucrase and maltase, and also of lactase, in not more than 2 cases. In a lactose tolerance test these 2 patients were the only ones to exhibit lactose malabsorption, as has been mentioned before, whereas normal sucrose tolerance tests were obtained in all the 15 patients studied.

Furthermore Berlyne (1972) and Mallick et al (1972) showed the same response of the blood glucose level to Caloreen, a dietetic carbohydrate containing a variety of glucose polymers, as to glucose after oral load.

Despite the fall in trehalase activity demonstrated by Denneberg et al (1974) in every second patient with renal insufficiency, it appears that trehalose malabsorption does not become manifest in uraemia because of the findings of Pointner et al (1974), who observed a normal trehalose tolerance in every single one of his 9 chronic haemodialysis patients.

By contrast, our findings in 5/6-nephrectomised rats (Grimmel et al, 1974, 1976) are in good agreement with those of Denneberg et al (1974) in patients with chronic renal insufficiency. We also observed a significant fall in maltase and sucrase activity, whereas lactase and cellobiase failed to show a change in activity.

Accordingly, it may be stated in summary that, although falls in the activity of disaccharidases, varying according to kind of enzyme and observed frequency, have been demonstrated by individual workers, significant disaccharide intolerances are not likely to develop in uraemia because of the large functional reserve of the small intestine.

As regards monosaccharide absorption, the findings available in the literature are even sparser.

In 1973, Bloch et al investigated a 63-year old female patient with phenacetin-induced nephropathy who had a serum creatinine value of 7.6 mg/100 ml and a serum urea value of 130 mg/100 ml. Using segmental small intestinal perfusion,
a glucose absorption of 50.87 mg/cm/h was found, being in the lower normal range of 60.84 ± 11.3 mg/cm/h. This is, in fact, the only direct absorption study at all in chronic renal insufficiency published to date.

Denneberg et al (1974) performed oral glucose tolerance tests with a 30 g/m² loading dose in 12 chronic haemodialysis patients and they found that the rise in blood glucose was smaller than in healthy individuals. On the contrary Hampers et al (1972) and Cerletty and Engbring (1967) reported higher mean glucose levels in uraemic patients after oral load of 100 g glucose. Bloch et al (1973) saw a diminished glucose level in only 1 of 14 patients with chronic renal insufficiency who had received an oral loading dose of 50 g glucose; similarly, the xylose absorption was reduced in only 1 of 13 patients, when the blood level was determined after a 25 g oral loading dose. In the study of McNair and Olsen (1974) it was found that a glucose-galactose tolerance test involving administration of 25 g each to 32 patients with chronic uraemia produced a normal though delayed rise in blood glucose.

However, when assessing such divergent indirect absorption studies, allowance should be made for stomach emptying, small intestinal passage and the hormonal regulation of the blood glucose level. To summarise, it would seem that absorptive derangements of monosaccharides — if present at all — are not critical in extent in states of uraemia.

Protein Absorption

In as much as Bergström et al (1972) have described a consistently positive nitrogen balance after administration of both oral and intravenous doses of the eight essential amino acids plus histidine to patients with severe renal insufficiency, it might be concluded that serious disturbance of amino acid absorption appears to be non-existent in uraemia, too.

Gulyassay et al (1972) determined plasma levels of tryptophan after administering an oral load to both normals and end stage uraemic patients and patients on chronic haemodialysis, respectively. The plasma curve was considerably below normal levels in both groups, indicating either impaired transport by the small intestine or accelerated metabolism of tryptophan in patients with advanced uraemia. Since the plasma levels of ¹⁴C after oral administration of the non-metabolised synthetic amino acid ¹⁴C-cycloleucine were the same in controls and in patients on chronic dialysis, Gulyassay et al (1972) suggest that accelerated metabolism rather than delayed absorption may be the more important cause for the blunted plasma tryptophan levels in the patients.

However, when using the everted sac technique in 5/6-nephrectomised rats with chronic renal insufficiency, Kassler et al (1973) demonstrated a significant fall in arginine absorption.

Denneberg et al (1974) estimated 5 dipeptidase activities in small intestinal biopsy specimens of 18 uraemic patients. Fifty per cent of the patients studied
showed decreased activities of glycyl-leucine-dipeptidase and alanyln-proline dipeptidase. The activity of alanyl-glutamine dipeptidase was depressed in 8, that of valyl-glutamine dipeptidase in 4, and of glutamyl-valine dipeptidase in 3 of the 18 patients. Normal activities of all dipeptidases under study were present only in 4 patients.

Using the animal model of rats in whom chronic renal insufficiency was induced by 5/6-nephrectomy, we determined the activities of 11 more dipeptidases (Grimmel et al, 1974, 1976). With two exceptions, there was no evidence of significant uraemia-induced alterations. However, in uraemic rats the mean activity of leucylproline dipeptidase and methionyl-proline dipeptidase was significantly elevated.

It can be stated in summary that in contrast to findings from animal experimental studies the dipeptidase activities in patients with chronic renal insufficiency may apparently be depressed, depending on the individual enzyme, to a variable extent. Whether in uraemia such reduced enzyme activities may also lead to serious derangements in dipeptide absorption appears unlikely by analogy with the disaccharides; absorptive studies which might throw light on this question have not been done so far. With respect to amino acid substitution therapy in uraemic patients, the performance of such studies would be important since there is evidence that amino acids, when given in the form of dipeptides, are more rapidly absorbed by animals and human individuals than when given in the free form (Matthews et al, 1968, 1969; Craft et al, 1968; Hellier et al, 1972; Silk, 1974), even in sprue patients (Adibi et al, 1974).

Fat Absorption

Based on the fact that steatorrhoea is not usually observed in patients with chronic renal insufficiency, it may be concluded that here again disturbances, if present at all, do not appear to be critical. In a group of 20 uraemic patients, who received a potato-egg diet supplying 80—100 g of fat per day, Kassler et al (1973) failed to observe an increased faecal fat excretion except in one patient, in whom there was a slight increase beyond the normal limit of 7 g/day. In a group of uraemics, studied by Denneberg et al (1974), the faecal fat likewise was pathological in only one out of 14 patients. According to Bloch et al (1973), steatorrhoea was found in 3 of 14 uraemic patients, and the vitamin A test was abnormal in 2 of 16 patients. Magas et al (1971) studied the absorption of $^{131}$I-labelled triolein by measurement of faecal radioactivity in 26 patients with chronic renal failure and found minimally abnormal values in only 4 cases.

However, when assessing indirect absorption tests, it should be borne in mind that disturbances in exocrine pancreatic function may be one of the factors influencing the result.

Sommer et al (1976), employing the model of the 5/6-nephrectomised rat, measured the re-esterification of palmitic acid and observed a significant uraemia-
induced decrease.

Thus, summarising, we may say that — as far as relevant studies have been done — they seem to indicate that uraemia-induced disorders affecting the absorption of all organic food constituents are demonstrable to a variable extent. But quantitatively they do not play a significant role.

References

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CHAIRMAN Thank you Dr Grimmel for your paper. I think we will discuss this together with the next one by Dr Hesch.