# Effect of Coprophagy on Utilization of Urea by the Rat. (24932)

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Our recent studies as well as elsewhere(1) have demonstrated a growth stimulatory effect of urea, in rats, when added to diet containing minimum level of essential amino acids but lacking in non-essential amino acids. This growth response was attributed to extra nitrogen supplied by urea used for synthesis of non-essential amino acids. The way in which *in vivo* synthesis of non-essential amino acids from urea proceeds is not clear but it is logical to assume that the first step is splitting of urea by urease. Presence of this enzyme was demonstrated in gastrointestinal tract of ruminants as well as many simple-stomached animals, including cats, dogs, mice, rats and guinea pigs. The source of urease in monogastric animals was debatable for some time but it is apparent from latest experiments, reviewed by Kornberg and Davies(2), that *in vivo* breakdown of urea is due ultimately to the presence of urea-splitting organisms in the intestinal tract rather than to gastric urease *per se*. The beneficial effect of intestinal bacteria by splitting down urea and thus making available to the host extra nitrogen for synthesis of amino acids is comparable with bacterial synthesis of vitamins in the intestinal tract. The most recent studies pertaining to the latter problem(3,4) have demonstrated that availability to the host of certain vitamins that are produced by intestinal synthesis is considerably reduced if not completely abolished, when the animals are prevented from eating their feces (coprophagy). Our purpose was to find out whether prevention of coprophagy in the rat would have a similar depressing effect on utilization of urea. The use of urea in nutrition studies with man(5) and the fact that man, in general, does not practice coprophagy makes this question one of fundamental as well as practical importance.

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*Methods.* Twenty-four male weanling albino rats (purchased from Holtzman) were divided into 4 groups consisting of 6 animals each. Each rat was housed in individual wire screen-bottom cage in room at 72°C and was permitted to eat and drink *ad lib.* The first 2 groups of rats were given a synthetic diet containing essential amino acids at their minimal required levels while the other 2 groups were fed a comparable ration supplemented with urea. Composition of basal diet and the amino acid mixture has been described previously(6). In one group of rats on each diet, coprophagy was prevented. This was accomplished by placing a plastic feces collection cup over the anus and tail of the rat, as described by Barnes *et al.*(7). Emptying of feces from the cups and weighing of animals was done every other day during 19-day experimental period. Then the animals were bled and the blood saved for cholesterol analyses.

*Results.* Results are presented in Table I. Rats which ingested a complete diet containing urea as source of "non-essential" nitrogen, gained an average of 52 g while those fed a ration devoid of urea gained only 37 g during 19-day experimental period. When coprophagy was prevented in animals on the former diet there was no change in growth response to urea, as is evident from body gain of 51 g. Similarly treated animals, which were fed a regimen devoid of urea, gained 32 g which is somewhat lower but probably not significantly different from the gain of control animals which had access to their feces.

Rats fed urea-supplemented diet consumed more food and utilized it more efficiently than did animals on a urea-free diet. Coprophagy did not seem to affect either consumption or utilization of the diets.

Serum cholesterol values (Table I) followed, in general, the weight gains of the animals. Since body weight was invariably related to amount of food consumed it is pos-

TABLE I. Average Weight Gain, Food Consumption, Food Efficiency and Blood Serum Cholesterol in Conventional and Coprophagy-Prevented Rats, Fed Urea-Free or Urea-Supplemented Diets.*

| Diet | Coprophagy | Wt gain (g) | Food intake (g) | Food efficiency | Serum cholesterol (mg/100 ml) |
|---|---|---|---|---|---|
| Basal | + | 37 ± 2† | 152 | .24 | 104 |
| | — | 32 ± 1 | 142 | .23 | 93 |
| Basal + urea | + | 52 ± 3 | 178 | .29 | 113 |
| | — | 51 ± 1 | 174 | .30 | 113 |

* Six rats with avg initial wt of 52 g were used in each exp. † Stand. error of mean.

sible that the latter also affected cholesterol values.

*Discussion.* Our experiments confirm previous observations(1) of growth promoting effect of urea when fed with the diet which was deficient in non-essential amino acids. The present study further shows that prevention of coprophagy apparently does not reduce availability of urea to the animals. This finding is contrary to previous observations on the effect of coprophagy on availability of intestinally synthesized vitamins(3,4). The probable explanation of this difference lies in the animals' ability or inability to absorb nutrients from the intestinal tract. Intestinal synthesis of vitamins occurs, for the most part, in the large intestine where their absorption is apparently low.

Effective utilization of urea by animals that had no access to their feces suggests the possibility that following enzymatic splitting of urea by intestinal microorganisms, the released ammonia is immediately absorbed by the intestine rather than incorporated into the microbial protein. The ammonia is then transported *via* blood to the liver where it can be used for biosynthesis of non-essential amino acids or reconverted back to urea. This interpretation is in accord with the demonstration of bacterial urease throughout the gastrointestinal tract(2), including the stomach, and the rapid absorption of ammonia from the cecum and other parts of the gastrointestinal canal(8).

*Summary.* 1. Addition of urea to a synthetic amino acid diet lacking in non-essential amino acids stimulated growth of young rats. 2. The growth-stimulatory effect of urea was not affected by prevention of coprophagy in the animals.

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