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Fasting Reverses the Renal Adaptation to Altered Dietary Sulfur Amino Acid Intake[1] (41464)

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Abstract. We have previously shown that there is renal adaptation to alterations in dietary sulfur amino acid intake. While ingesting a low-methionine, low-taurine diet, urinary and plasma taurine concentrations fall, and the accumulation of taurine by collagenase-isolated tubules is greatly enhanced. On a taurine and methionine-supplemented diet (3%, w/w), urinary and plasma taurine values are increased, and accumulation by tubules is diminished. This study was planned to evaluate the effect of fasting on the adaptation to dietary intake change. Rats were given a high-taurine diet (HTD), low-taurine diet (LTD), or a normal diet (NTD) from age 56 to 70 days of life. Half of the rats in each dietary group were fasted for 72 hr and they lost 13 ± 1% of body weight. Plasma taurine values fell in all three fasted groups, and urinary taurine excretion rose in LTD and fell in HTD-fasted animals. Renal cortex taurine fell in all fasted groups, indicative of taurine release. The *in vivo* tissue distribution ratio remained unchanged in fasted LTD and NTD animals, but rose into the normal range in fasted HTD animals. The initial rate of uptake (5 min) by isolated tubules was reduced in LTD-fasted and increased in HTD-fasted cortex. Kinetic analysis indicated that the K_m of uptake was unaffected, but the V_{max} was changed after fasting. Fasting also reverses the adaptive response detected in isolated renal brush border membranes. The renal adaptive response is found at the level of the isolated brush border membrane vesicle, indicating that this membrane surface is involved. A 72-hr fast appears to blunt the adaptive response of the kidney to altered dietary amino acid intake at the level of the luminal surface. The signal for this adaptation and its blunting remains uncertain.

The adaptive response of the renal tubular epithelium to dietary change has recently received considerable attention. Renal tubular epithelial transport adapts to dietary phosphate restriction, and the phosphaturic response to parathyroid hormone (PTH) is largely abolished in rats on a low dietary intake of phosphate (1, 2). Even in the X-linked hypophosphatemic mouse, with a massive renal tubular phosphate leak, enhanced phosphate reabsorption is found when these animals are fed a phosphate-restricted diet (3). Sodium-dependent uptake of phosphate by proximal tubule cell brush border membrane vesicles is enhanced in membranes from phosphate-depleted animals (4, 5). However, this renal adaptation to phosphate deprivation and blunting of the phosphaturic response to PTH can be ablated if the phosphate-depleted animals are fasted for several days (6, 7). Upon fasting, urinary phosphate excretion increases, and the phosphaturic response to PTH is restored. Little is known about the transport events related to dietary changes in amino acid intake.

We have recently demonstrated that renal adaptation of β-amino acid transport can be found if animals are placed on a diet with minimal quantities of methionine and cysteine and devoid of taurine, or if they are given a diet containing large amounts (3%) of taurine (8–10). Similar adaptive responses have been reported by Rozen *et al.* (11). With dietary restriction, plasma and urinary taurine levels fall, and uptake of

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taurine by isolated tubule segments is enhanced. Taurine supplementation results in an elevation in plasma and urinary taurine concentrations, and *in vitro* isolated tubule accumulation is diminished. The effect of fasting on this adaptive process to altered dietary amino acid intake has not been previously examined. In this paper, we report that fasting of animals on a low-taurine or high-taurine diet almost completely abolishes the adaptive response to dietary alteration in both isolated tubules and isolated brush border membrane vesicles.

Methods. All studies were performed on 10-week-old Sprague–Dawley rats (Sprague–Dawley, Madison, Wisc.), which were initially fed Lab-Blox Chow (Libertyville, Ill.). Rats for experimental use received the diet for 14 days from ages 56 to 70 days of age. Rats were fed one of three diets: normal taurine (sulfur amino acid) diet (NTD) containing 20% soy protein, plus 0.5% methionine to supply sufficient methionine for taurine biosynthesis; low-taurine (sulfur amino acid) diet (LTD) containing 20% soy protein plus no added methionine; and high-taurine (sulfur amino acid) diet (HTD) containing 20% soy protein plus 0.5% methionine and 3.0% taurine. This diet contains normal amounts of methionine. Experimental diets were obtained from ICN, Cleveland, Ohio, and the details of the diet are given elsewhere (9).

On Day 70 of life, the animals were divided into two groups. The control groups continued to ingest the diet *ad lib*. The experimental groups were placed in metabolic cages and given only distilled H_2O. After 72 hr all rats were weighed and transferred to clean metabolic cages; urine was collected over 3–6 hr. Plasma and urine were collected as previously described (12). Plasma and urine creatinine and taurine concentrations were determined so as to estimate the fractional excretion of taurine. Creatinine was measured as described (12), and taurine was measured in a Beckman-120 amino acid analyzer (13).

Transport studies were performed in isolated renal cortex tubules, as previously described (14, 15). Minced cortex was digested in 0.375% collagenase II (Worthington, N.J.) at room temperature in Krebs–Ringer bicarbonate medium. After filtration through three layers of surgical gauze, the filtrate was spun at 1600 rpm three times. The final suspension of tubules contained 1 ml of fetal calf serum per 20 ml final volume, and there were 8–12 mg of tubules per milliliter of incubation medium. Tissue and medium were constantly gassed with 95% O_2:5% CO_2. Concentrative uptake studies were performed as described (14, 15). Concentration-dependent uptake was measured using unlabeled taurine in concentrations ranging from 0.009 to 20 m*M* plus 1.0 μCi of [1-^{14}C] taurine. Initial rate kinetics was measured after 5 min of incubation, as it has previously been established that taurine uptake reaches steady state after 20 min incubation (9, 14, 15).

After 5 min incubation, intracellular taurine concentration was measured from isolated tubules placed in tared centrifuge tubes and rotated for 10 min at 4°C and 38,600*g*. A medium sample was taken and the tubules were then placed in boiling water. With disruption of the pellet and denaturing of the tissue, another sample, representative of intracellular taurine, was taken. Uptake of taurine was measured by determining distribution ratio (cpm/ml ICF to cpm/ml of medium). The percentage of trapped medium in the pellet was determined using radiolabeled polyethylene glycol, as previously described (14). Since polyethylene glycol can be used as a marker of the extracellular fluid (ECF), the proportion of ECF in a pellet can be derived. Moreover, by knowing the concentration of taurine in the medium, the amount of intracellular taurine can be derived after subtracting the amount of extracellular taurine present in the pellet prior to boiling.

Brush border membrane vesicles (BBMV) were isolated by a modification of the technique of Booth and Kenny (16). After homogenization of renal cortex in a 300 Tris–Hepes–mannitol (THM) solution, and the removal of cellular debris by a low-speed centrifugation (500*g*), membranes were incubated in 10 m*M* $CaCl_2$. This incubation results in the precipitation of all membranes other than the brush bor-

TABLE I. WEIGHT OF RATS (g) ON VARIOUS DIETS AND EFFECT OF FASTING

Diet	Control (fed)	Prefasting	72-hr fast
HTD	261.7 ± 23.6 $n = 8$	253.8 ± 32.5 $n = 8$	223.7 ± 18.3* $n = 8$
NTD	262.7 ± 20.6 $n = 8$	283.5 ± 20.5 $n = 8$	244.8 ± 17.7* $n = 8$
LTD	280.1 ± 19.8 $n = 8$	277.3 ± 22.9 $n = 8$	246.4 ± 15.7* $n = 8$

Note. Rats were 70 to 74 days of age at time of study, and fasted animals had food removed for exactly 72 hr prior to study. Results are means ± SE. HTD, High-taurine diet; NTD, normal taurine diet; LTD, low-taurine diet.

* $P < 0.005$ by paired t test.

der membrane. Following centrifugation at 15,000*g*, a second $CaCl_2$ precipitation step was carried out to further purify the BBMV. Membrane purity was assessed using the ratio of the activity of several marker enzymes in the brush border fraction (pellet) to the homogenate (3–7). Membrane protein concentration was assessed by the Lowry method (3).

Taurine uptake by BBMV was measured by incubation in a medium containing 100 m*M* NaCl, various concentrations of cold, and [1-^{14}C]taurine at 25°, followed by rapid filtration through a cellulose nitrate membrane (0.45-μm pore size) in a 12-port manifold. The filters were dried overnight, dissolved in aquasol and counted. The uptake of taurine is expressed as pmol/mg protein/time.

All chemicals were reagent grade, and radionuclides were obtained from New England Nuclear, Boston, Massachusetts. Fetal calf serum was obtained from Flow Labs. Cellulose nitrate membranes and the 12-port manifold were obtained from the Millipore Corporation.

Lineweaver–Burk plots were drawn from concentration-dependent uptake data, and "apparent" K_m and V_{max} were ascertained. Statistical significance was determined by Students' t test and by comparison or regression coefficient and analysis of variance.

Results. Animal weights were influenced by fasting. Rats fed HTD, LTD, and NTD had comparable weights prior to fasting (Table I). With a 72-hr fast, the weights were significantly lower than in the fed state. Accordingly, fasting results in a 6.33 to 19.00% (mean 13.35 ± 1.06

TABLE II. PLASMA AND URINE TAURINE CONCENTRATIONS ON VARIOUS DIETS AND AFTER A 72-hr FAST

	LTD	NTD	HTD
Plasma, on diet (μmol/liter plasma H_2O)	225 ± 6 $n = 3$	244 ± 48 $n = 3$	1365 ± 104* $n = 3$
Plasma, postfasting (μmol/liter plasma H_2O)	167 ± 21 $n = 8$	192.4 ± 22 $n = 8$	262.5 ± 25** $n = 8$
Urine, on diet (μmol/mg creatinine)	0.55 ± 0.11* $n = 8$	4.92 ± 1.55 $n = 3$	211 ± 57* $n = 3$
Urine, postfasting (μmol/mg creatinine)	3.04 ± 1.26** $n = 8$	10.2 ± 2.7 $n = 8$	16.55 ± 2.4** $n = 8$
Fractional excretion of taurine on diet	0.014 ± .004* $n = 8$	0.106 ± .013 $n = 3$	0.604 ± .031* $n = 3$
Fractional excretion of taurine postfasting	0.093 ± .009** $n = 8$	0.168 ± .023 $n = 5$	0.138 ± .012** $n = 8$

Note. Values represent mean ± SE.

* Different from NTD, $P < 0.05$.

** Different from fed state, $P < 0.01$.

(±SE)%) fall in body weight, despite free access to water.

The plasma and urinary taurine concentrations and the fractional excretion of taurine is shown in Table II. Animals fed LTD and NTD have significantly lower plasma levels than do HTD-fed animals ($P < 0.001$). With fasting, plasma taurine levels were comparable in each group and were comparable to normal values obtained in our lab of 160 to 360 μmol/liter plasma H_2O (9, 12, 13). The plasma taurine value in fasted LTD animals is lower, but not significantly different from fasted NTD and HTD animals. Urinary taurine in the fed LTD animals was 0.55 ± 0.11 μmol/mg creatinine, similar to values found previously by us of 0.61 ± 0.11 μmol/mg creatinine in 8-week-old rats fed LTD (9). This value is significantly lower than for rats fed either NTD ($P < 0.05$) or HTD ($P < 0.005$). Upon fasting, urinary taurine increased in LTD rats and fell in HTD rats, and the values were similar to those found in animals fed a normal diet. Although fasted LTD animals still have the lowest excretion and fasted HTD animals still have the highest excretion, these values did not differ from levels in fasted NTD animals. A significant difference ($P < 0.02$) between LTD and HTD animals was found, but the ratio of HTD to LTD urinary excretion fell from 383.2 to 5.44 after fasting. The fractional excretion of taurine was reduced in LTD-fed animals and increased in HTD-fed animals, when compared to NTD-fed animals. After fasting, the fractional excretion of taurine was the same in all three groups and very similar to values previously reported by us (9).

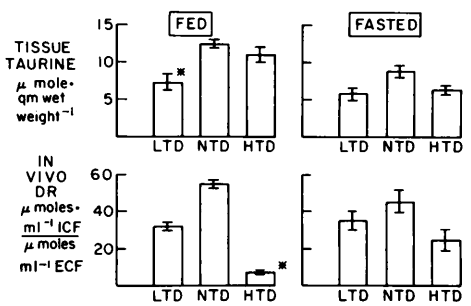

FIG. 1. Upper portion: The tissue taurine concentration (μmol/g wet weight) in animals fed the three diets and after fasting. Lower portion: The *in vivo* taurine distribution ratio (μmol/ml tissue intracellular fluid divided by μmol/ml extracellular fluid) in animals fed the three diets and after 72 hr of fasting. Each point represents the mean ± SE of three determinations.

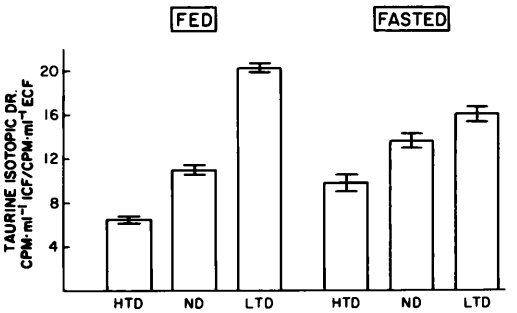

FIG. 2. The taurine isotopic distribution ratio for tubules incubated for 5 min in 0.01 m*M* taurine. The values shown represent the mean ± SE of at least 12 determinations. The uptake after fasting in LTD and HTD animals is significantly different from the values obtained from animals remaining on their diet. LTD, low-taurine diet; NTD, normal taurine diet; HTD, high-taurine diet.

The influence of fasting on the concentration of taurine in the renal cortex (μmol/g wet weight) is shown in Fig. 1. Tissue concentrations of taurine prior to fasting are similar in NTD- and HTD-fed animals. Taurine content is significantly lower in LTD-fed animal cortex than in NTD tissue ($P < 0.01$). After 72 hr of fasting, the concentration of taurine in renal cortex is always lower than in the fed state, regardless of the diet. Cortex taurine values are reduced by 20.2% in LTD-fed animals (NS), by 30.2% in NTD-fed animals ($P < 0.005$), and by 41.1% in HTD-fed animals ($P < 0.01$). When tissue taurine is expressed per milligram protein, the reduction in tissue taurine concentration is found after fasting.

When the ratio of tissue taurine (μmol/ml ICF) to plasma taurine (μmol/ml ECF) is compared before and after fasting (Fig. 1), a significant increase in this ratio is found only in animals on the HTD. With fasting, the *in vivo* distribution ratio in animals fed the HTD more resembles that in fasted animals fed the LTD or NTD.

In Vitro Studies. The initial rate of uptake *in vitro* incubated at 10 μ*M* taurine in tubules is shown in Fig. 2. The distribution ratio is significantly higher in LTD-fed

TABLE III. KINETIC CHARACTERISTICS OF TAURINE ACCUMULATION IN TUBULES FROM FED OR FASTED ANIMALS

	Initial rate			
	K_{m_1}	K_{m_2}	V_{max_1}	V_{max_2}
HTD, fed	0.155	2.72	0.706	6.30
P value	<0.01	NS	<0.01	<0.01
HTD, fasted	0.062	2.36	1.05	8.49
NTD, fed	0.084	2.66	1.01	10.98
P value	NS	NS	NS	NS
NTD, fasted	0.067	2.68	1.02	10.82
LTD, fed	0.055	2.30	1.28	14.55
P value	NS	NS	NS	<0.05
LTD, fasted	0.063	2.65	1.17	11.23

Note. Data were derived by linear regression analysis of points depicted in Fig. 2. K_m is measured in millimol/liter and V_{max} in micromol/ml ICF/5 min. All lines had correlation coefficient (r) of >0.99. *P* values were determined by comparison of regression coefficient and analysis of variance.

animals and significantly lower in HTD animals. After fasting, these distribution ratios approximate the values found in animals fed the NTD; uptake in tubules from animals fasted after taking the LTD are significantly lower than those found in the fed state ($P < 0.001, n = 12$). Uptake in tubules from fasted HTD animals is significantly higher than in HTD-fed animals ($P < 0.005, n = 12$). After fasting, uptake by LTD and HTD are not significantly different from uptake by NTD tubules. However, uptakes by tubules from fasted LTD and fasted HTD are different from each other.

In Table III are shown the effects of fasting on the "apparent K_m" and V_{max} of uptake under all three diets. From these data, it can be seen that fasting significantly alters the "apparent K_m" of the high-affinity system in rats fed the HTD, but does not change the K_m in any of the other animal groups. The "apparent K_ms" of the low-transport system are unaltered by fasting or dietary change. The V_{max} of transport is changed by fasting both in LTD- and HTD-fed animals. By switching from the HTD to fasting, the V_{max} of accumulation by both uptake systems increases. Changing from the LTD to fasting lowers the V_{max} of the high-K_m system. In both the LTD and HTD animals, the V_{max} of accumulation following fasting appears to be similar to that found in animals fed the NTD diet. Accordingly, the kinetics of transport after fasting over a wide range of taurine concentrations is similar to the kinetics of uptake in animals on a normal diet, and the renal adaptation to dietary alteration appears to be reversed. An examination of the influence of fasting on uptake by tubules over a variety of concentrations is shown in Fig. 3. This Eadie–Hofstee plot demonstrates that uptake in tubules from animals on each of the diets is accomplished by at least two processes. Fasting does not alter this finding of uptake by at least two uptake systems, but does change the V_{max} of accumulation.

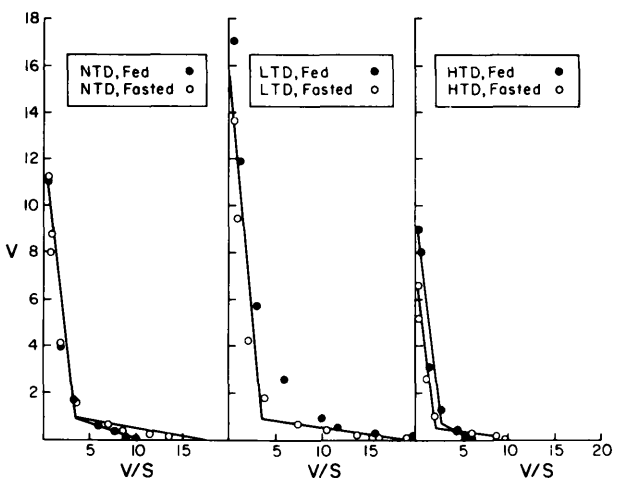

FIG. 3. Eadie–Hofstee plots of the initial rate of uptake of taurine at concentrations between 0.005 and 20 m*M* by collagenase-isolated tubules. Uptake was measured as described in the text. Note the retention of both uptake limbs after fasting. Each point is the mean of 12 determinations.

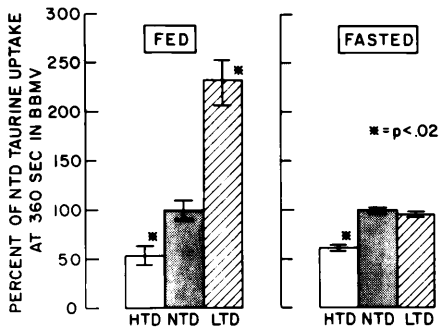

FIG. 4. The uptake of taurine accumulated by brush border membrane vesicles (BBMV) isolated from rats fed each diet. Data are expressed as the percentage of uptake compared to NTD-fed kidney vesicles and represents the mean ± SE. Each point is the mean of at least six determinations. LTD, low-taurine diet; NTD, normal taurine diet; HTD, high-taurine diet.

BBMV were enriched as compared to homogenates by at least sevenfold using γ-glutamyl transferase and 5'-nucleotidase as marker enzymes. The activities of marker enzymes of the basal-lateral membrane, nucleus, lysosome, and microsome were less in the BBMV pellet than in the homogenate.

The peak rate of uptake of taurine by BBMV prepared from animals fed each of the diets and in animals fed each diet and later fasted is shown in Fig. 4. The uptake of taurine by BBMV from rats fed the LTD is 135.2 ± 10.6 pmol/mg protein/360 sec or 230% of the value in BBMV isolated from animals fed the NTD (64.8 ± 8.1 pmol/mg protein/min). The uptake in BBMV from rats fed the HTD was reduced to 54.2 ± 10% of the value in NTD-fed animals. Uptake by BBMV from rats fed either the LTD or HTD is significantly different from uptake by NTD-fed BBMV ($P < 0.001$). With fasting, the increased uptake found in BBMV fed the LTD is no longer detected and the amount of taurine accumulated is comparable to that found in membranes from the NTD animal. Although the uptake of taurine by BBMV from fasted HTD animals is still lower, these differences are less marked than in the fed state (Figs. 4, 5).

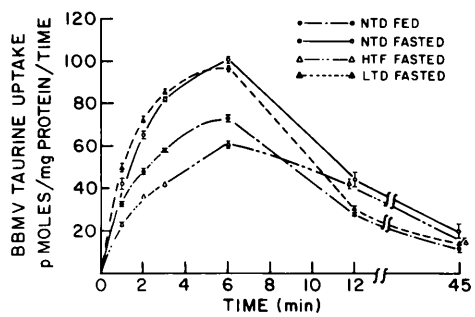

FIG. 5. The uptake of taurine over time by vesicles incubated in a medium containing 10 μ*M* taurine. For statistical analysis, see text. Each point represents the mean ± SE of at least six determinations.

The time course of taurine uptake by BBMV is shown in Fig. 5 and indicates a slight increase in uptake in fasted LTD and NTD animals, as compared to uptake in fed animals ($P < 0.005$), but no differences in uptake by NTD compared to LTD vesicles over the entire time course of uptake. Taurine uptake by BBMV from HTD rats is significantly lower until 12 min, after which these differences disappear. Nonetheless, the peak rate (360 sec) of taurine uptake by BBMV from fasted HTD rats is 61.7 ± 1.3 pmol/mg protein/360 sec in comparison to 30.4 ± 3.8 pmol/mg protein/360 sec in fed HTD rats, significant at $P < 0.001$.

Discussion. Variation in dietary sulfur amino acid intake leads to adaptation in renal taurine transport. This adaptation occurs with 6 days on an LTD and with 3 days on an HTD. Therefore, 14 days of dietary taurine manipulation ensures full expression of this renal adaptive response (10). Lifelong exposure to the LTD results in animals that are significantly smaller than normal (8, 9), since they receive inadequate concentrations of methionine and cysteine in their diet during a critical growth period (17). In this study, 70-day animals have been fed on the LTD only from Days 56 to 70; thus, they are fully grown prior to initiating the diet with reduced values for sulfur amino acids. Accordingly, weights are similar in LTD, HTD, and NTD-fed animals at the onset of this study. These animals were chosen for the study since they are comparable groups in which to examine the phenomena of renal adaptation to dietary alteration. Since the animals weigh the same, pair-feeding is unnecessary, and the influence of fasting can be studied directly.

When animals are fed an LTD, they have

a decline in urinary taurine excretion and enhanced tubular uptake of taurine; after the rats are fed an HTD, urinary taurine excretion increases and tubular taurine uptake falls. This observation was previously made in 4- and 8-week animals (8, 9). A major component of the tubular transport of taurine by isolated cortical tubules occurs across the luminal membrane. The study of Balaban *et al.* (18) indicates that the tubular lumina of short tubule segments isolated by the collagenase method remain open, thus permitting luminal uptake. This study was performed using rabbit tubules, however, which may have different uptake patterns than tubules from the rat. Roth *et al.* (19) have shown that α-methyl-D-glucoside is actively accumulated by isolated rat renal tubules and make the point that this accumulation must occur across the apical surface of the tubule, since the indicator dilution studies of Silverman *et al.* (20) demonstrate no active accumulation of this hexose across the antiluminal membrane. Moreover, in this study, the uptake of taurine by tubules parallels the pattern of reabsorption found after ingestion of each diet. Finally, the kinetics and sodium dependency of taurine uptake by tubules is quite similar to the pattern of uptake we have found in isolated BBMV (21).

Fasting of animals for 3 days blunts this renal adaptive response to dietary alteration of sulfur amino acid intake. No large differences in plasma and urine taurine levels are found among the three dietary groups. The fractional excretion rises in fasted LTD animals and falls in fasted HTD animals to reach the level of taurine excretion seen in NTD animals. There is concordance of *in vitro* uptake by collagenase-isolated tubules as demonstrated by enhanced uptake after the LTD, diminished uptake after the HTD, and the return of these two adaptive responses toward normal after fasting. The mechanism of this ablation of renal adaptation remains uncertain.

Nonetheless, as we were concerned about which membrane surface was exposed by the tubule method, we performed parallel studies in isolated brush border membrane vesicles (BBMV). Taurine uptake is greater in BBMV from LTD and reduced in BBMV from HTD-fed animals, as compared to NTD-fed animals. With fasting, these differences disappear when vesicles from NTD and LTD animals are compared. With respect to the HTD, fasting results in the following changes: (i) it significantly increases the uptake of taurine by BBMV as compared to HTD-fed animals; (ii) it reduces, but does not eliminate, the significant difference between HTD and NTD vesicle uptake. Concordance between *in vivo* urinary excretion and BBMV uptake is again found, and the changes noted on utilizing the various diets with feeding and fasting are parallel in tubules and vesicles. Hence, it is probable that the renal adaptation to altered dietary sulfur amino acid intake and its reversal by fasting occurs at the brush border surface. Whether any adaptation is evident in basal–lateral membranes cannot be ascertained by these studies.

The return of the plasma and urine concentrations and *in vitro* taurine accumulation to approximate the concentrations and distribution ratios found in animals on a normal diet is similar to the findings in phosphate-depleted animals postfasting (6, 7). However, plasma taurine level fell in all three groups of animals. One possible explanation for this loss of the adaptive response upon fasting is the catabolism that these animals experience with the release of intracellular stores of taurine. Evidence of catabolism is provided by the fall in weight in these fasted animals, which amounts to a mean of 13.3% of initial body weight. Animals fed the HTD obviously will have a decline in plasma and urinary taurine content with 72 hr of fasting. With fasting, this reversal of the diminished taurine reabsorption in HTD animals is paralleled in tubules where greater uptake and a higher V_{max} of transport are found, as well as a higher *in vivo* distribution ratio. Further, BBMV uptake is higher in fasted HTD animals.

A second explanation for the changes in tubular taurine reabsorption caused by fasting involves an alteration in intracellular metabolism with a resultant diminished level of high-energy compounds required

for active transport. Kempson *et al.* (22) have shown that reversal of renal adaptation to phosphate depletion by fasting may involve a rise in the level of oxidized nucleotides (NAD^+) which in turn alters transport. Such a change in metabolism could explain the decline in taurine accumulation found in LTD animals *in vitro* and the augmented taurine excretion in these animals with fasting. However, it would not explain the augmented taurine uptake found in HTD-fed animal tubules postfasting or the more efficient resorption found. It is unlikely that fasting would cause opposite intracellular events in LTD and HTD, or that the same intracellular event would lead to completely opposite patterns of taurine uptake. Thus, catabolism with release of intracellular taurine and the development of almost equivalent plasma taurine values seems to be a more plausible explanation for the findings in the three dietary groups following fasting.

One can also examine an *in vivo* tissue-to-ECF distribution ratio by knowing the tissue and plasma taurine values pre- and postfasting. This ratio is 32.1 in LTD, 55.4 in NTD, and 7.76 in HTD-fed animals; the latter value indicates the blunting of uptake in these animals fed excessive dietary taurine. With fasting, the *in vivo* distribution ratios for taurine are unchanged in LTD (34.8) and NTD (45.1) groups, but are quite different in HTD at 23.5. It is difficult to understand how depletion of substrates, used for amino acid transport or to maintain membrane transport activity, could account for this higher *in vivo* distribution ratio in HTD-fed animals. The signal for these changes at the level of the renal epithelium and at the brush border membrane is unknown at present.

We have examined the uptake of D-glucose and α-aminoisobutyric acid (α-AIB) by tubules prepared from animals on each of the three diets and note small changes in the uptake pattern of these substances (A. Friedman and R. Chesney, unpublished observation). In general, glucose and α-AIB uptake by tubules was increased by 10–15% in those rats on the LTD and decreased by 8–12% in those on the HTD, but the magnitude of these changes was far less than that found when examining taurine uptake. Since these changes were small, we did not examine the effect of fasting on the uptake of these substances accumulated by a different system within the tubule. It is clear, however, that fasting will block the adaptive response to other substances as seen with phosphate restriction (6, 7, 22).

In conclusion, the response of the kidney to excess dietary taurine and to taurine deprivation with regard to urinary excretion pattern and uptake by renal tubules and brush border vesicles is lost after fasting. The reversal of renal adaptation caused by a 72-hr fast suggests the possibility that normalization of plasma levels may serve as a tocsin for this reversal of adaptation. Nonetheless, further studies are indicated to better understand the membrane or intracellular signals for this adaptive response and its ablation by fasting.

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