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The Relative Roles of External Taurine Concentration and Medium Osmolality in the Regulation of Taurine Transport in LLC-PK1 and MDCK Cells

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ABSTRACT

Taurine is a β-sulfonic amino acid that serves as a nutrient important for developing brain and retina and as an osmolyte in the medullary collecting duct. The activity of the taurine transport system is regulated by substrate supply and by the external osmolality; these two stimuli induce changes in taurine transport. Increased medium osmolality (500 mosmol) stimulates taurine uptake into MDCK cells but not LLC-PK1 cells. The enhanced taurine uptake that occurs in response to hyperosmolality is localized primarily to the basolateral surface of MDCK cells, whereas the adaptive response to medium taurine concentration is expressed on both the apical and the basolateral surfaces of both cell lines. The response of MDCK cells to medium osmolality requires protein synthesis and RNA transcription and is expressed in the presence of microtubular toxins. When cell monolayers were loaded with taurine by incubation in high-taurine medium before increasing medium osmolality, the expected increase in taurine uptake was blunted. Similarly, increased external β-alanine (500 μM) also prevented the anticipated increase in taurine accumulation in response to hypertonicity; aminoisobutyric acid and betaine (500 μM) partially prevented the increase in taurine transport after hypertonicity, whereas L-alanine had no effect. The concentration of taurine or structurally similar analogs in the external medium might modify the response of taurine accumulation after exposure to hypertonic medium, in that taurine-replete cells behave differently than taurine-depleted cells. These studies indicate that there are at least two distinct mechanisms involved in the regulation of taurine transport: external taurine concentration and medium osmolality, with taurine concentration seeming to be the predominant stimulus. Thus, the changes in cell taurine transport depend on the physiologic stimulus as well as the cell studied, a phenomenon that might be related to the renal tubular site of origin. (***Pediatr Res* 37: 227–232, 1995**)

Abbreviations

GABA, aminoisobutyric acid
act D, actinomycin D
cyt D, cytochalasin D
Colch, colchicine
Cyclo, cyclohexamide
GPC, glycerophosphocholine
EBSS, Earle's balanced salt solution

Taurine, a β-sulfonic amino acid that is found in millimolar intracellular concentrations in the kidney of many mammalian species, is postulated to have several key functions in the kidney; among these are the function of a nutritional substrate, as well as that of an osmolyte (1). Taurine is transported by the renal tubular cell by a sodium- and chloride-dependent transporter, which accepts the β-amino acid taurine and structural analogs such as β-alanine (2–5).

The kidney taurine transporter serves at least two important functions: *1*) to reabsorb filtered taurine as a nutrient (this occurs in the proximal tubule and has been shown to be functionally immature in the neonatal rat, to be regulated by dietary taurine intake, and to be abnormal in the hypertaurinuric mouse model) and *2*) to offer protection to medullary collecting duct cells or to MDCK (Madin-Darby canine kidney) cells in response to increased external osmolality by serving as an osmolyte. In addition to sorbitol, inositol, glycerophosphorylcholine, and betaine, taurine is increased in the inner medulla of salt-loaded rats and MDCK cells. In the first example, taurine transporter activity changes in response to taurine supply, and in the latter, in response to external tonicity. We have been interested in contrasting the nature of the stimulus as well as the cell type: the proximal tubular cell, in

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which regulation of taurine transport by substrate concentration may be most important, in comparison with the collecting duct or distal cell, in which regulation by external osmolality is of greater importance to cell survival.

Taurine transport is regulated by the dietary intake of taurine in the rat (6), by the extracellular concentration in kidney cells in culture (7), and by medium osmolality in MDCK cells (8). We have previously demonstrated that taurine transport in both MDCK and LLC-PK1 cells is increased after incubation of cell monolayers in taurine-free medium and is decreased after incubation of cells in high levels of extracellular taurine (8). The adaptive response to medium taurine concentration was prevented when protein synthesis and protein export were inhibited (9). Inhibition of RNA transcription had no effect on the ability of the cells to respond to medium taurine concentration (9).

The following studies were performed to examine the interaction between medium hypertonicity and medium taurine concentration in regulation of taurine transport in cultured renal epithelial cells.

METHODS

Cell culture methods. LLC-PK1 and MDCK cell lines were obtained from American Type Culture Collection (Rockville, MD) and maintained in 5% CO_2, 95% air. Standard medium, consisting of Dulbecco's modified Eagle's medium (1000 mg/L glucose, 584 mg/L L-glutamine, and 110 mg/L sodium pyruvate) in a 1:1 mixture with Ham's F12 Nutrient Mixture (GIBCO/BRL, Life Technologies, Grand Island, NY), plus 10% FCS and penicillin (100 U/ml) and streptomycin (100 μg/mL), was used for routine cell carriage (7). Cells were subcultured by trypsinization and seeded onto 0.4-μm polycarbonate filter supports (Costar, Cambridge, MA, Transwell) (10). For experiments, medium was replaced with a hormonally defined, serum-free formulation consisting of Dulbecco's modified Eagle's medium/F 12 with insulin (5 μg/mL), transferrin (5 μg/mL), prostaglandin E1 (2.5×10^{-5} mg/mL), hydrocortisone (5×10^{-8} M), and thyroxin (5×10^{-12} M).

Transport studies. Uptake studies were performed on confluent monolayers 10–14 d after seeding. Briefly, cells were washed with EBSS at 37°C. Uptake was initiated by the addition of EBSS with or without sodium, pH 7.4, with 50 μM taurine (0.5 μCi ^{3}H-taurine) at 37°C (10). Uptake was terminated by the removal of uptake solution followed by three rapid washes with cold EBSS. The uptake solution contained ^{14}C-inulin (0.1 μCi/mL) in addition to ^{3}H-taurine. Luminal uptake was measured by addition of uptake solution on the upper surface of the monolayer with an equal volume of EBSS on the lower chamber. For basolateral uptake, the uptake solution was added to the lower chamber and the EBSS with or without sodium to the upper chamber. The contralateral solution was sampled for contamination with ^{14}C-inulin as a measure of monolayer integrity as well as contamination by the extracellular space. Monolayers were considered to be intact if the inulin leakage was less than 1% (10, 11). Cells were solubilized in 1% SDS in 0.2 N NaOH. An aliquot was dispersed into Optifluor (Packard Instrument Co., Meriden, CT) and then radioactivity counted in a Packard Tricarb 2000-CA Liquid Scintillation Analyzer (Packard Instrument Co., Downers Grove, IL).

Total cell protein was measured by a modification of the Lowry method (12). Duplicate 10-μL samples of cell homogenate and standards were pipetted into a 96-well microtiter plate. A 0.4-mL volume of solution A, consisting of 2% Na_2CO_3, 1.0% $CuSO_4$, and 2.0% $KNaC_4H_4O_6$ (100:1:1) was added to each well, followed by 0.04 mL of 1.0 N Folin-Diocalteau phenol reagent. After a 30-min incubation, the OD was measured using an automated microtiter plate spectrophotometer at a wavelength of 680. The protein concentration of the samples were determined by linear regression analysis from standards of BSA. Uptake was then expressed as pmol of taurine per mg of cell protein per min.

Adaptive response to medium substrate concentration. Confluent cell monolayers were exposed for 24 h to hormonally defined, serum-free medium with 0, 50, or 500 μM taurine. Uptake studies were performed after two 37°C washes in EBSS.

Response of cells to hypertonicity. Cell monolayers were exposed for 24 h to standard, hormonally defined, serum-free medium with 50 μM taurine or with medium made hypertonic to 500 mosmol by the addition of raffinose. Monolayers were then gently washed twice in 37°C EBSS followed by measurement of taurine uptake in the presence and absence of sodium. MDCK monolayers were incubated in the presence of either act D (0.5 μg/mL) (9, 13), which inhibits RNA transcription; Cyclo (70 μM) (9, 13), which inhibits protein synthesis; and two inhibitors of microtubular depolymerization, cyt D (10 μM) (14) and Colch (50 μM) (9), for 2 h before and during a 12-h incubation in either standard or hypertonic medium.

Materials. Media, penicillin/streptomycin, trypsin, and FCS were purchased from GIBCO (Grand Island, NY). Radiolabeled taurine and inulin were purchased from New England Nuclear Corp. (Boston, MA). Insulin, hydrocortisone, thyroxin, prostaglandin E1, EBSS, choline chloride, choline bicarbonate, and other chemicals were from Sigma Chemical Co. (St. Louis, MO) and transferrin was from Calbiochem (La Jolla, CA).

Data analysis. Data comparisons were made by *t* test for independent data and by analysis of variance with assistance from the computer program STATVIEW 512+ (Brainpower, Inc., Calabasas, CA).

RESULTS

Effect of hypertonicity and medium taurine concentration on taurine uptake in LLC-PK1 and MDCK cells. LLC-PK1 and MDCK cells were incubated for 24 h in either standard, serum-free, hormonally defined medium or in medium to which raffinose was added to achieve a final medium osmolality of 500 mosmol. In addition, the medium taurine concentration was varied so that the concentration of taurine was either 0, 50, or 500 μM. Taurine uptake was measured in the presence of sodium after the 24-h incubation (Fig. 1*A* and 1*B*).

Taurine uptake by the apical surface of MDCK cells was unchanged after exposure to hypertonic medium when taurine was also present at 50 and 500 μM. Exposure of MDCK cell monolayers to hypertonic medium without taurine resulted in

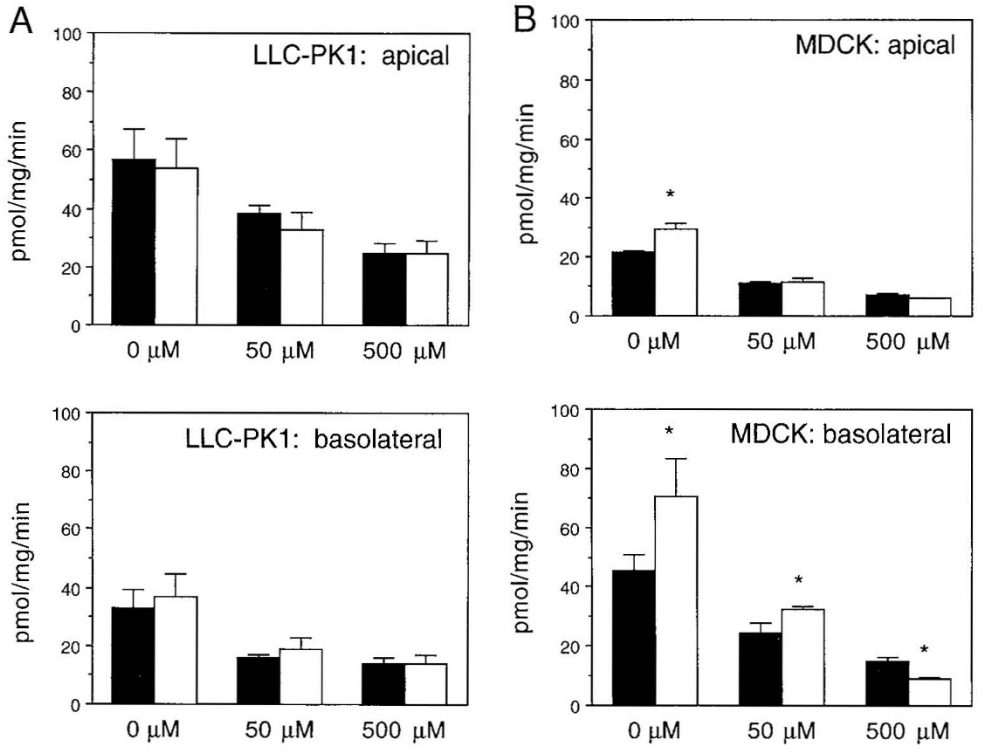

Figure 1. Polarity of taurine transport in LLC-PK1 (*A*) and MDCK cells (*B*) in response to variation in medium taurine concentration and medium tonicity. Confluent monolayers of LLC-PK1 and MDCK cells were incubated for 24 h in either standard osmolality, serum-free medium (*black bars*) or serum-free medium made hypertonic to 500 mosmol (*open bars*) by the addition of raffinose. To either medium was added no taurine (0 μM) or 50 or 500 μM. Apical and basolateral taurine uptake was measured for 15 min in LLC-PK1 and assessed at 20 min in MDCK cells by incubation in uptake solution (EBSS, 50 μM taurine). Values represent the mean ± SEM of six filters. An *asterisk* indicates a p value of ≤0.001.

enhanced taurine uptake compared with control (Fig. 1*B*). Taurine accumulation by the basolateral surface of MDCK cells was increased after 24 h in hypertonic medium containing 50 μM taurine or no taurine (Fig. 1*B*). Therefore, apical taurine accumulation by MDCK cells was not increased after increased medium osmolality, except when taurine was absent from the medium.

Conversely, taurine uptake by either the apical or the basolateral surface of LLC-PK1 cells was not different from controls after incubation in hypertonic medium (Fig. 1*A*); the adaptive response of cell monolayers to changes in medium taurine concentration was expressed by both surfaces of LLC-PK1 cells, with relatively greater transporter activity on the apical surface compared with the basolateral surface, as was previously demonstrated (11). To summarize, taurine accumulation by either apical or basolateral surfaces of LLC-PK1 cells does not appear to be regulated by hypertonic external medium, regardless of the medium taurine concentration.

Time course of the response to hypertonicity in MDCK cells. Taurine uptake by the basolateral cell surface was measured at 2, 4, 8, 12, and 24 h after incubation of MDCK cells in hypertonic medium (Fig. 2). A significant increase in basolateral taurine accumulation was present by 4 h and was fully expressed by 12 h (Fig. 2). Therefore, the increase in taurine accumulation was observed within the initial 4 h after changing the medium and was maintained for a period of at least 24 h.

Role of protein synthesis, RNA transcription, and microtubular function on adaptation to medium hypertonicity. Previous studies in LLC-PK1 cells demonstrated that the adaptive response to changes in medium taurine concentration required intact microtubular apparatus as well as a functional protein-assembly mechanism. We examined whether RNA synthesis, protein translation, and an intact cytoskeleton were necessary for expression of the response to hypertonicity. MDCK monolayers were incubated in the presence of either act D (0.5 μg/mL), which inhibits RNA transcription (9, 13);

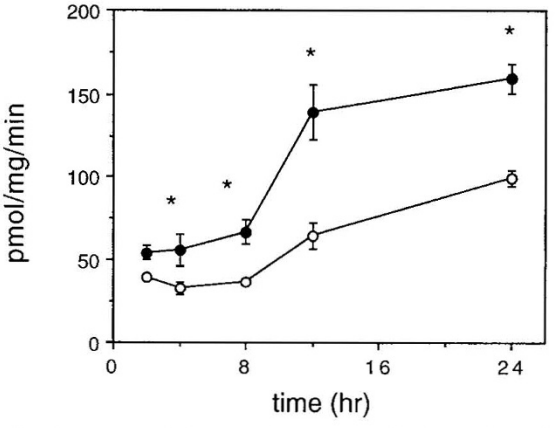

Figure 2. Time course of basolateral taurine uptake in MDCK cells after incubation in control (*open circles*) or hypertonic (*black circles*) medium. Taurine accumulation at 20 min (standard uptake buffer, 50 μM taurine) was measured 2, 4, 8, 12, and 24 h after addition of hypertonic medium to both wells and compared with that in cells grown in isotonic medium. Values represent the mean ± six filters. An *asterisk* indicates $p < .01$ by analysis of variance and then nonpaired t test compared with the control.

Cyclo (70 μM), which inhibits protein synthesis (9, 13); or two inhibitors of microtubular depolymerization, cyt D (10 μM) (14), or Colch (50 μM) (9), for 2 h before and during a 12-h incubation in either standard or hypertonic medium. Taurine accumulation by the basolateral cell surface was 95% of baseline (monolayers in isotonic medium) in the Cyclo-treated group and 103% of baseline in the act D–treated group compared with an increase in taurine uptake of 161% of baseline in the control group (Fig. 3). Exposure to hypertonicity in the presence of cyt D and Colch increased taurine accumulation to 319% and 330% of baseline values, respectively (Fig. 3). To summarize, incubation in the presence of either Cyclo or act D prevented the adaptation of MDCK cells to hypertonicity, whereas incubation with cyt D or Colch did not prevent the observed increase in basolateral taurine accumulation. Thus, expression of the adaptive response to hypertonicity requires functions of RNA transcription and protein synthesis.

The importance of medium taurine concentration before exposure to hypertonic medium. We postulate that the primary stimulus for regulation of taurine transport is an intracellular taurine pool. To examine whether taurine availability would affect the response to hypertonicity in various taurine concentrations, MDCK cell monolayers were either taurine depleted (deprived) or taurine loaded for 24 h before manipulation of medium osmolality. The increase in taurine accumulation that occurs after exposure to hypertonicity was markedly blunted if cells had been previously loaded with taurine as compared with those incubated in the absence of taurine (Fig. 4*A*). In addition, taurine loading also prevented the expected increase in taurine accumulation after 24 h in the absence of medium taurine, irrespective of medium osmolality (Fig. 4*B*). As expected, uptake was lower in both groups exposed to 500 μM taurine (Fig. 4*B*).

Effect of other osmolytes and amino acids on the ability of MDCK cells to respond to hypertonicity. To examine whether taurine decreases the response of MDCK cells to hypertonicity

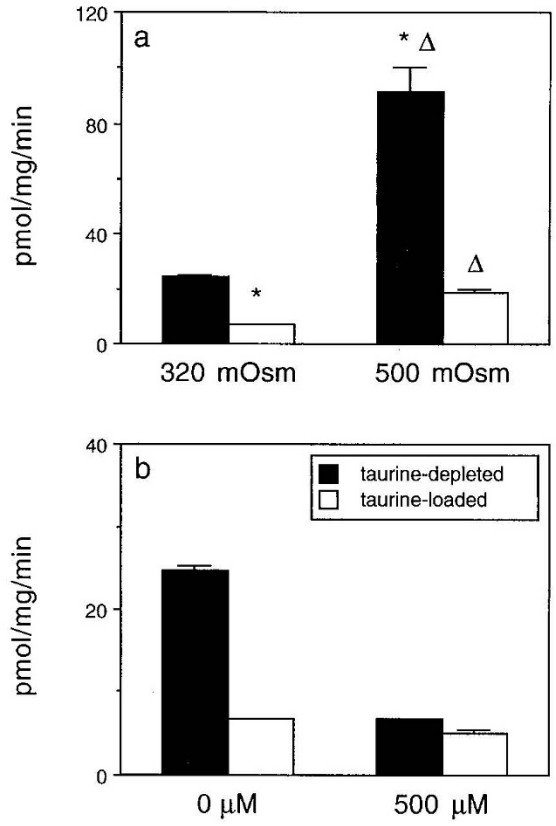

Figure 4. Effect of medium taurine concentration on the response of MDCK cells to hypertonic medium (*a*) or changes in medium taurine concentration (*b*). Confluent MDCK cells were either taurine depleted by incubation in isotonic, taurine-free medium for 24 h (*black bars*) or taurine loaded by incubation in isotonic medium containing 500 μM taurine (*open bars*). After the first 24-h incubation, medium was changed to either isotonic or hypertonic medium containing no taurine or 500 μM taurine. Basolateral taurine uptake was measured at 20 min (EBSS, 50 μM taurine). Values represent the mean ± SEM for four filters. An *asterisk* denotes statistical significance ($p \leq 0.05$) compared with the taurine-depleted, 320 mosmol group; Δ denoted statistical significance when compared with the taurine-loaded, 320 mosmol group.

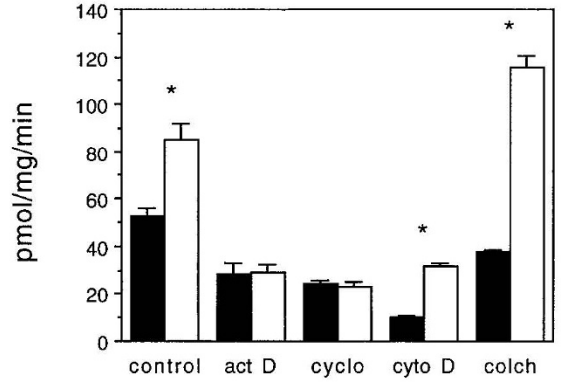

Figure 3. Effect of inhibitors on basolateral taurine uptake in MDCK cells. Confluent, filter-grown MDCK cells were incubated in the presence of one of the following: act D (0.5 μg/mL), Cyclo (*cyclo*), (70 μM), cyto D (10 μM), or Colch (*colch*) (50 μM) 2 h before and during a 12-h incubation in either isotonic (*black bars*) or hypertonic (*open bars*) serum-free medium containing 50 μM taurine. After removal of medium, basolateral taurine accumulation was measured at 20 min (EBSS, 50 μM taurine). Values represent the mean ± SEM for four filters. An *asterisk* indicates statistical significance with $p \leq 0.5$ when the monolayers in hyperosmolar medium are compared with those in normotonic medium for each experimental group.

because of its role as an osmolyte or as a substrate for the β–amino acid transporter, we incubated cells with another osmolyte, betaine, and a substrate which has been shown to share the betaine transporter, GABA, in addition to a structural analog of taurine, β-alanine, and a dissimilar compound, L-alanine. MDCK cells were incubated in the presence of standard, serum-free, hormonally defined medium containing 500 μM taurine, GABA, betaine, L-alanine, or β-alanine for 24 h; then bathing medium was changed to either standard or hypertonic medium with the same added amino acid for an additional 24 h. Basolateral taurine accumulation was measured and compared with control (0 μM taurine). The adaptive response of MDCK cells to hypertonicity was prevented by β-alanine but not by L-alanine (Fig. 5). In addition, both GABA and betaine prevented the increase in taurine accumulation after exposure to hypertonic medium, but not to the same degree as β-alanine. One might conclude that structural similarity and transporter homology are important in the ability of taurine to down-regulate the response of MDCK cells to high external osmolality; however, the presence of other osmolytes or similar compounds also causes down-regulation of taurine

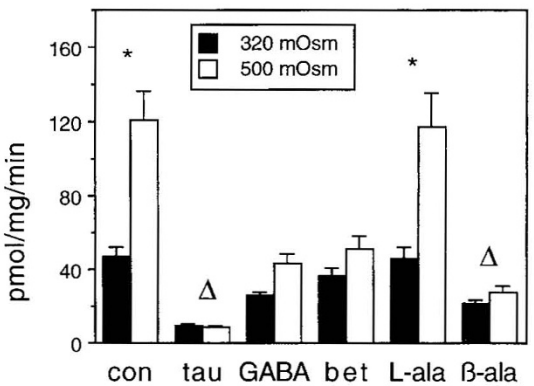

Figure 5. Effect of other solutes on the hypertonic adaptation of taurine transport in MDCK cells: MDCK cells were incubated for 24 h in either isotonic (*black bars*) or hypertonic medium (*open bars*) containing 500 μM taurine, GABA, betaine, L-alanine, β-alanine, or no added amino acid. Values represent the mean ± SEM of four filters. An *asterisk* represents statistical significance ($p \leq 0.05$) when the 320 mosmol and 500 mosmol values for each group are compared and Δ denotes statistical significance compared with the 320 mosmol control.

transport. Perhaps these compounds have an effect in the intracellular taurine pool and affect the expression of the taurine transporter in a similar fashion. These questions remain to be answered.

DISCUSSION

Increased medium osmolality (500 mosmol) stimulates taurine uptake into MDCK cells, a canine kidney cell line that originated from the distal tubule, most likely the collecting duct. LLC-PK1 cells, which are from the porcine proximal tubule, do not exhibit increased taurine accumulation after exposure to hypertonic medium. In contrast, both cell lines respond to changes in external taurine concentration with reciprocal changes in taurine accumulation (11). The enhanced taurine uptake that occurs in response to hyperosmolality is primarily localized to the basolateral surface of MDCK cells, whereas the adaptive response to medium taurine concentration is expressed on both the apical and the basolateral surfaces of LLC-PK1 and MDCK cell lines (8, 11). The response of taurine transporter activity to increased external medium tonicity is dissimilar in these two cultured renal epithelial cell lines and may be related to the renal tubular site of origin; however, one must be cautious in drawing conclusions about the intact renal tubule from data in continuous cell lines.

Although methylamines and polyols such as glycerophosphocholine and sorbitol are the major osmolytes accumulated by the renal medulla during antidiuresis, the adaptative accumulation of these osmolytes after exposure to hypertonicity is relatively slow (days); therefore, accumulation of amino acids such as taurine may play a more important role in the acute adaptation to high medium osmolality in the renal medulla, as has been demonstrated in the cerebral cortex (15, 16). In comparing the renal tubular handling of taurine and betaine, the accumulation of betaine is enhanced after long-term exposure of MDCK and PAP-HT25 cells (of papillary origin) to hyperosmolar medium (17, 18). In addition, the cellular content increased by 24 h in hypertonic medium and continued to increase over the next 5 d (19). Like taurine, betaine accumulation by MDCK cells is primarily localized to the basolateral surface (20). Kinetic analysis reveals the presence of two distinct transport systems for betaine, a high-affinity system and a low-affinity system (20). After exposure of MDCK cells to medium made hypertonic by the addition of NaCl, the V_{max} of both the low-affinity and the high-affinity systems is increased (20). The increased V_{max} was noted to peak at 24 h and then to decline if betaine was present in the medium, presumably after sufficient osmolyte was accumulated within the cell (18, 20). Uchida *et al.* (8, 21) reported that exposure of MDCK cells to medium made hypertonic by the addition of raffinose increases the V_{max} for basolateral taurine uptake in MDCK cells, and this is accompanied by increased expression of a mRNA, which imparts taurine transporter activity when injected into *Xenopus* oocytes. Therefore, basolateral taurine transport and betaine transport increase when MDCK cells are exposed to a hypertonic environment.

Medium taurine concentration modifies the response of MDCK cells to hypertonic medium. As previously shown by others (8), incubation of MDCK cells in taurine-free medium further enhanced the adaptive response to hypertonicity, so that the two stimuli seemed additive. Our studies confirm their data. In addition, high medium taurine concentration in the face of hypertonicity blunts the enhanced basolateral uptake of taurine. One might speculate that in the presence of high medium taurine, adequate taurine is accumulated in the cell without the need to increase taurine transport. One stimulus for regulation of taurine transport, at least in response to medium taurine concentration or substrate supply, is the intracellular content of taurine. Uchida *et al.* (8) reported that cell taurine was unchanged in MDCK cells after incubation for 48 h in either isotonic or hypertonic taurine-free medium; however, the cellular taurine content was 2-fold greater in monolayers incubated in hypertonic medium containing 50 μM taurine compared with isotonic medium containing 50 μM taurine. Cellular taurine content is probably not the only stimulus that increases taurine transport, because taurine accumulation by MDCK cells was enhanced after exposure to hypertonic medium, despite intracellular taurine levels that were comparable to control.

Medium taurine regulates taurine transport in LLC-PK1 cells by a mechanism that requires functional protein synthesis but not RNA transcription (9). In contrast, the response of MDCK cells to hypertonic medium is prevented by act D, an inhibitor of RNA transcription, as well as cycloheximide, an inhibitor of protein synthesis. As previously noted, injection of mRNA from MDCK cells exposed to hypertonic medium into *Xenopus* oocytes has demonstrated increased taurine transporter activity caused by increased message. Thus, the mechanisms involved in increased taurine transport induced by changes in medium osmolality seem to be distinct from those involved in the response to changes in medium taurine concentration. RNA transcription is required for the osmolar response but not for the adaptive response to changes in substrate concentration.

Structural analogs of taurine such as β-alanine also blunted the adaptive response to hypertonic medium. Interestingly, the presence of 500 μM GABA, which is not known to function as

an osmolyte, blunted the response to hypertonic medium as well as reduced taurine uptake by the monolayers exposed to isotonic medium. GABA has been shown to competitively inhibit taurine uptake and has been proposed to be a potential substrate for the β-amino-acid transporter (2). In addition, GABA is postulated to be transported by the betaine transporter (8). Betaine also reduced the increase in taurine accumulation typically expressed after exposure to hypertonicity. The ability of betaine to alter taurine transport may be related to its known function as an osmolyte rather than as a substrate of the β–amino acid transport system. There may be regulatory mechanisms that enable one osmotically active substance to affect the accumulation of another.

Indeed, the presence of one osmolyte has been shown to alter the accumulation of another (15, 22). Renal medullary cells incubated in high extracellular osmolality (700 mosmol) in the presence of 0, 0.5, and 15 mM betaine exhibit reciprocal changes in the cell sorbitol content and very small, yet significant, changes in cell GPC and inositol content (15, 22). This was not observed when inositol concentration was varied between 0 and 15 mM. In addition, the intracellular concentration of betaine increases when sorbitol is decreased; similarly, the accumulation of sorbitol is increased with low betaine (15, 22). Potential mechanisms by which the accumulation of one osmolyte can affect the accumulation of another include changes in the transport of the substrate, alterations in the availability of substrate for synthesis, and inhibition of enzymes involved in the synthesis of the osmolyte (22).

The accumulation of osmolytes has been studied in LLC-PK1 and MDCK cell lines. After culture in high medium NaCl, LLC-PK1 cells exhibit increased intracellular *myo*-inositol, betaine, and GPC with no change in intracellular sorbitol. MDCK cells accumulated *myo*-inositol, betaine, and GPC and did not accumulate sorbitol (18). Therefore, the accumulation of an amino acid or organic osmolyte may depend on intrinsic cell characteristics as well as the influence of other osmotically active agents in external medium or present within the cell.

The signal for the adaptive response to dietary taurine or external taurine concentration is most likely intracellular taurine concentration. The cell response seems to require intact protein synthesis as well as a functional cytoskeletal system, presumably to allow for synthesis and export of transporters that are targeted to the membrane. This constitutes the early response to alterations in taurine supply. A less rapid mechanism has been proposed to account for the most delayed response to dietary manipulation seen in the rat in which new message synthesis is likely to contribute (23). It seems likely that the mechanism by which elevated external tonicity increases taurine transport is different from that which responds to alterations in taurine supply. Addition of raffinose to the medium increases taurine transporter message expression in MDCK cells (8). This response may be modified if intracellular taurine is already increased. Thus, these two stimuli must interact. The mechanisms have yet to be elucidated; however, evidence exists for a protein kinase C–dependent pathway in regulation of taurine transporter activity (9).

In conclusion, there are at least two distinct mechanisms involved in the regulation of taurine transport: external taurine and medium osmolality. The response to medium osmolality requires protein synthesis and RNA transcription and remains intact in the presence of microtubular toxins. The increase in taurine transport that occurs after increased external osmolality is expressed by the basolateral surface of MDCK cells but not by LLC-PK1 cells. The concentration of taurine in the external medium may modify the change in taurine uptake after hypertonic medium. That is, taurine-replete cells behave differently than taurine-depleted cells. In addition, taurine supply has a more generalized effect on taurine uptake in that it induces changes in accumulation by both surfaces of LLC-PK1 and MDCK cells. The adaptation that follows manipulation of taurine concentration does not seem to require RNA synthesis for expression, yet the adaptation is absent when protein synthesis or exocytosis is inhibited. Thus, the cell processes leading to changes in taurine transport at the membrane are divergent, depending on the physiologic stimulus as well as the cell studied.

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