Taurine Deficiency Syndrome in Cats

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Taurine deficiency has been an important nutritional problem in cats since its discovery in 1975. Following the original descriptions of clinical blindness and retinal degeneration,[4,5,18] the number of deficiency signs has increased substantially, to include reproductive failure and growth retardation,[25,27] CNS dysfunction, deformed spinal skeleton,[25] dilated cardiomyopathy,[15] platelet hyperaggregation,[7] and potentially impaired immune function.[19] This review briefly describes the deficiency syndrome in cats, comments on possible reasons that this species is subject to taurine depletion, and discusses the dietary requirement for taurine in this species.

TAURINE CHEMISTRY

Taurine (2-aminoethanesulfonic acid) is a sulfur-containing β-amino acid that resembles alanine, except that the carboxyl group is replaced by a sulfonyl group and the amino group resides on the β (second) carbon, not on the α carbon typical of most other amino acids.

In tissues and biological fluids, taurine remains as the major free amino acid unincorporated into protein, only rarely being incorporated into low molecular weight peptides.[14] At a physiological pH, taurine is fully charged as a zwitterion (Fig. 1). Its sulfur moiety can be oxidized to sulfate by intestinal bacterial flora but not by mammalian cells themselves.

MINIMAL TAURINE SYNTHESIS IN THE CAT

The peculiar susceptibility of feline species to taurine deficiency has been addressed previously.[6] It is the consensus that cats, like several

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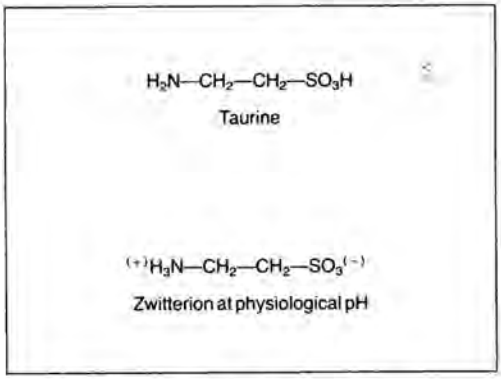

Figure 1. Taurine structure.

species including man, cannot synthesize appreciable amounts of taurine,[8] even though they seem to require substantial amounts of this sulfur amino acid for biological functions. In most species such as dogs, rats, and birds, taurine is readily synthesized as an end product in the transulfuration pathway originating with methionine (Fig. 2).[10] Because this synthetic pathway is limited in the cat, which requires a dietary source of taurine for normal health, taurine can be considered an essential nutrient in this species.

Methionine is considered an essential sulfur amino acid for all mammalian species, and cysteine may qualify in the neonate, since enzyme activity (cystathionase) needed for conversion of methionine to cysteine is poorly developed in the newborn.[23] In addition, the limiting step in taurine biosynthesis is the decarboxylation of cysteinesulfinic acid by CSA decarboxylase, an enzyme whose activity is low in cats.[11] Taurine synthesis also depends on age and varies from organ to organ and from species to species[30] (Table 1). Since taurine synthesis in newborn kittens is especially limited by the low level of CSAD,[23] kittens (and other mammals) depend on their mother's milk for an initial supply of taurine. In other words, in the case of cats, any taurine needed in excess of that readily synthesized must come from the diet.[11] This realization focused our attention on the demand for taurine in the metabolism of cats and the possible imbalance between the dietary taurine supply and whole body needs.

Low Supply, High Demand

It soon became apparent that the bile acid pool in cats was somewhat unique in that essentially all the bile acids were conjugated with taurine,[16] unlike in most species, including humans, that can also conjugate with glycine when necessary, or the rabbit, which conjugates its bile acids almost exclusively with glycine under normal circumstances. In essence, as available taurine becomes limited in cats, the bile acid pool, and to a lesser extent even the retina, conserve taurine, while most

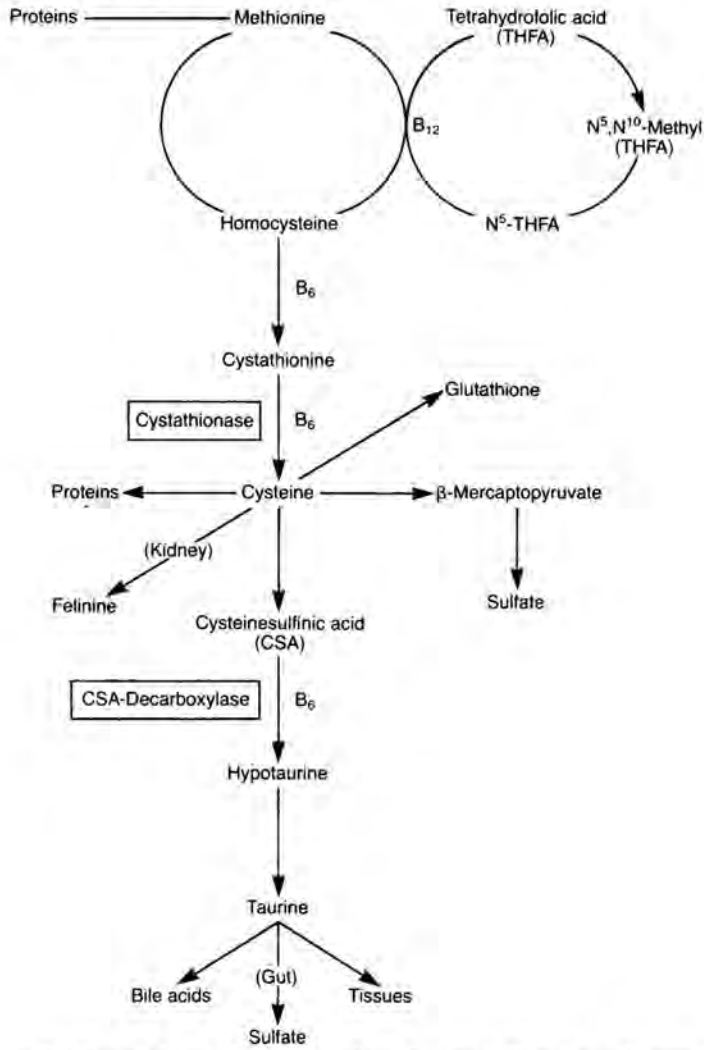

Figure 2. Taurine biosynthesis depends on the transsulfuration pathway originating with methionine. Key vitamin B_6-dependent enzymes are encased. Note the additional competition for cysteine due to the exceptional production of glutathione, felinine, and protein for hair production.

tissues deplete their concentration to 10 per cent of normal or less.[23] It is interesting that in both cats[16] and monkeys,[21] the chenodeoxycholic acid pool conserves its taurine much better than the cholic acid pool. In kittens, the bile acid pool, retina, and olfactory bulb maintain their taurine concentration most avidly.[22] This suggests that taurine is quite important for bile metabolism and retinal function and may also play a special role in olfaction. A second consideration is that kittens grow quickly, increasing the demand for taurine by a rapidly expanding muscle mass. Yet a third factor that requires further documentation is the

Table 1. *Activity of Cysteinesulfinic Acid Decarboxylase (CSAD) in Various Adult Mammals**

SPECIES	BRAIN	LIVER
Cat	59†	4
Rat	63	468
Dog	54	412
Monkey		
Rhesus	5	5
Cynomolgus	1	0
Cebus	2	2
Human	7	<1

* *Adapted from* Hayes KC, Sturman JA: Ann Rev Nutr 1:401, 1981.
† nmol CO_2/hr/mg protein

possibility that taurine and, even more likely, the cysteine-containing peptide, glutathione (GSH), act as primary conjugators for detoxifying xenobiotics and other metabolites for biliary excretion.[3] This would increase the cat's requirement for cysteine and taurine, necessitated by the absence of the more traditional glucuronyl transferases serving this function in other species.[2]

DIET SUPPLY

Ordinarily, the cat, as an obligate carnivore, would not have a taurine problem because its natural diet of meat and fish contains a high concentration of taurine (Table 2). In contrast, the plant kingdom is essentially devoid of taurine. So when cat diets were commercially formulated, based on cereals and grains, or when processed dog foods were fed,[1] the present-day crisis evolved. Thus, when cats are fed certain diets arbitrarily restricted by the designs of people, like a vegetarian diet, the problem may develop. Surprisingly, the problem has not been resolved, since several commercial diets of both canned and dry varieties are fortified with taurine yet still fail to maintain normal plasma taurine levels.[15] Apparently, much of the taurine in these processed diets is unavailable (Table 3) or, if absorbed, is rapidly metabolized. Further research is needed to explain this phenomenon.

TAURINE FUNCTION IN CELLS AND ORGAN SYSTEMS

It needs to be stated that the molecular action of taurine is still unresolved. However, the various investigations involving the deficiency syndrome in cats provide several clues. The retinopathy has been investigated most intensively. The primary defect appears to reside in the structural integrity of the photoreceptor cell outer segments and the underlying structure of the tapetum lucidum.[5,6] When retinal taurine concentration is reduced to 50 to 75 per cent of normal, the structure and function (as measured by electron microscopy and electroretinography) deteriorate progressively. If the early deterioration is not corrected by dietary taurine supplementation, the photoreceptor cells eventually at-

Table 2. *Taurine Content in Meat and Fish*

	UNCOOKED	BAKED	BOILED
Meat			
Beef	14–47*	7–18	4–9
Pork	11–69	7–39	3–18
Chicken	30–38	14–31	7–18
Fish			
Cod (frozen)	23–40	26–33	13–20
Clams (fresh)	145–370	59–170	26–79

* mg/100 g wet weight
Adapted from Roe DA, Weston MO: Nature 205:287, 1965.

rophy and disappear, causing irreversible blindness (Fig. 3). The implication is that taurine modulates the structural integrity by means of control over ionic flux (Ca^{++}, Na^{+}, K^{+}) in the retina and possibly by zinc-taurine-cysteine interactions in the tapetum.[24]

Taurine-deficiency cardiomyopathy of cats represents a failure in contractility,[15] presumably due to abnormal calcium-ion balance in the myocardial cell. The development of cardiomyopathy probably requires lengthy and severe taurine depletion, since moderately severe depletion with purified diets does not generally result in clinical evidence of heart failure, even when other signs of deficiency exist and even though the taurine concentration in cardiac muscle has been reduced to less than 10 per cent of normal.

In the cardiovascular realm, however, we recently found that platelets from modestly depleted cats, with plasma taurine levels less than 20 μmol/l, were twice as prone to collagen-induced aggregation as control cats. In addition, platelet production of thromboxane (TXB_2) was elevated, whereas the platelet GSH concentration was decreased by taurine deficiency.[7] Again, platelet aggregation and TXB_2 production are linked to intracellular calcium metabolism in the platelet, both of which are modulated by the redox status (GSH content) of platelets.[28] It was not possible to assess whether the higher GSH associated with taurine supplementation represented increased GSH synthesis from cysteine or de-

Table 3. *Taurine Content of Cat Foods*

DIET TYPE	TAURINE CONCENTRATION	
	as fed (mg/100 g)	*dry wt basis* (mg/kg)
Dry, n = 7	88 (68–120)*	994 (771–1365)
Semimoist, n = 2	78 (70–86)	1182 (1068–1296)
Canned		
Pure-fish formulas, n = 6	91 (73–118)	4121 (3309–5359)
Meat-based formulas, n = 10	53 (33–72)	2392 (1495–3293)

* Mean value (range). Samples include most major cat food companies and products such as Cadillac, Bright Eyes, Fancy Feast, Friskies, Kal-Kan, Purina, Amore, 9-Lives, Sweet Life, Hi-Tor, and IAMS.

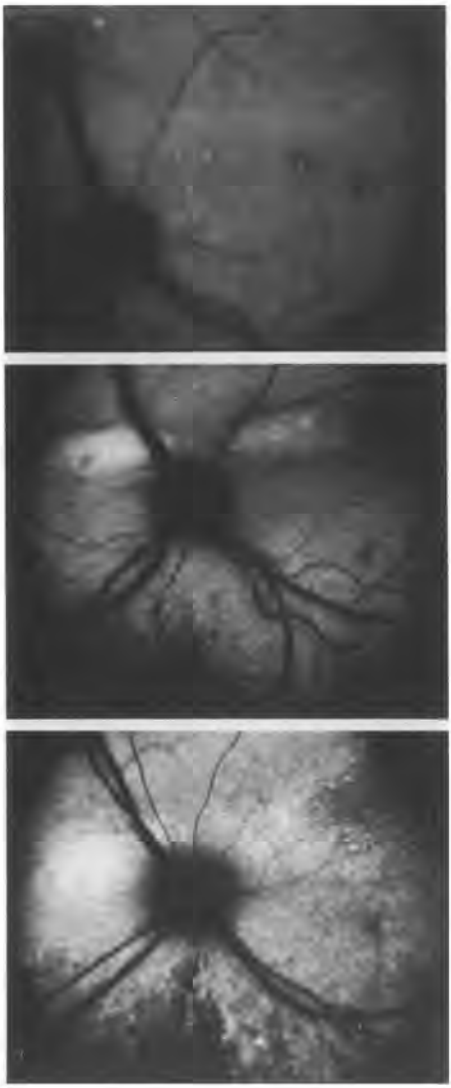

Figure 3. Feline central retinal degeneration is a progressive blindness in cats resulting from taurine depletion. The progressive loss of photoreceptors (especially cones) can be detected early *(top)* or in more advanced stages *(middle, bottom)* as a focal to zonal hyper-reflective area in the area centralis (dorsolateral quadrant) of the retina.

creased catabolism of GSH due to a direct effect of taurine on reducing platelet aggregation. Nonetheless, it serves to focus attention on the taurine-calcium-sulfhydryl connection. The implications for cats may be significant, because this species is prone to thromboembolism,[29] generally in association with cardiomyopathy but possibly as a primary event linked to the role of taurine in platelet aggregation. Episodes of embolism might be prevented by adequate taurine nutrition.

Growth depression in kittens is another aspect of taurine deficiency that has been well documented[25,26] (Table 4). Kittens born and suckled by depleted queens gain less weight than normal (Fig. 4). In our lab, deficient kittens that are born alive are 30 to 50 per cent smaller than

Table 4. *Effect of Dietary Taurine (500 ppm) on Weight Gain in Kittens of Different Age Groups**

	BODY WEIGHTS (G)		WEIGHT GAIN	WEIGHT GAIN
	Initial	*Final*	(g/day)	(%/day)
Newborn (0–3 wk)†				
Plus taurine	147 ± 19	335 ± 13	8.9 ± 1.1	6.2 ± 1.5
No taurine	150 ± 16	258 ± 22‡	5.1 ± 0.4‡	3.4 ± 0.3‡
Pre-weanling (5 day–6 wk)†				
Plus taurine	147 ± 17	546 ± 11	10.8 ± 0.7	7.4 ± 1.4
No taurine	144 ± 16	371 ± 35‡	6.1 ± 0.6‡	4.3 ± 0.6‡
Weanling (9–16 wk)†				
Plus taurine	847 ± 25	1774 ± 75	19.3 ± 0.3	2.3 ± 0.1
No taurine	797 ± 43	1240 ± 90‡	9.2 ± 0.1‡	1.2 ± 0.1‡

* N = 4 per group.

† Kittens were hand-fed purified liquid formula diets or were weaned onto a solid diet. The protein source was casein, which contributed a percent of the total calories from protein as follows: newborns, 36%; preweanling, 32%; weanling, 27%.

‡ Significantly less than supplemented kittens: $P < 0.05$.

control kittens. Severe depletion of the queen during pregnancy can often produce fetal death and malformations.[27] When kittens survive to be suckled, they frequently develop a spastic posterior gait and thoracic kyphosis, attributed to dyplasia of the cerebellar granule cell layer (Fig. 5). These defects represent a failure in cell division and cell differentiation, processes that depend on precise modulation of the intracellular calcium pool.

The impaired immune function in taurine-deficient cats is less well defined. However, white blood cells, like platelets, are readily depleted of taurine,[12] and the biocidal activity of neutrophils from taurine-deficient cats is depressed.[19] We have observed a high incidence of conjunctivitis and a peculiar suppurative arthritis in peripheral joints of neonates born to deficient queens, possibly related to immunosuppression and consequent susceptibility to infection.

Thus, the expression of this unique nutritional deficiency is widespread in cats, affecting many organ systems. Since taurine is present in most cells and presumably impacts calcium metabolism in these cells, the scope of the deficiency should not be surprising. In fact, careful scrutiny of other systems, e.g., olfactory, adrenal, kidney, gonads, bile (hepatic function), where taurine is found in high concentrations should extend the list of potential metabolic defects in this species when the taurine supply is inadequate.

CLINICAL ASSESSMENT AND TREATMENT

Unfortunately, taurine depletion is not readily measured, since the assay for taurine requires either routine plasma amino acid assessment with an ion-exchange chromatography method or with a specific HPLC assay.[9,13,20] Until further information is generated, both feline central

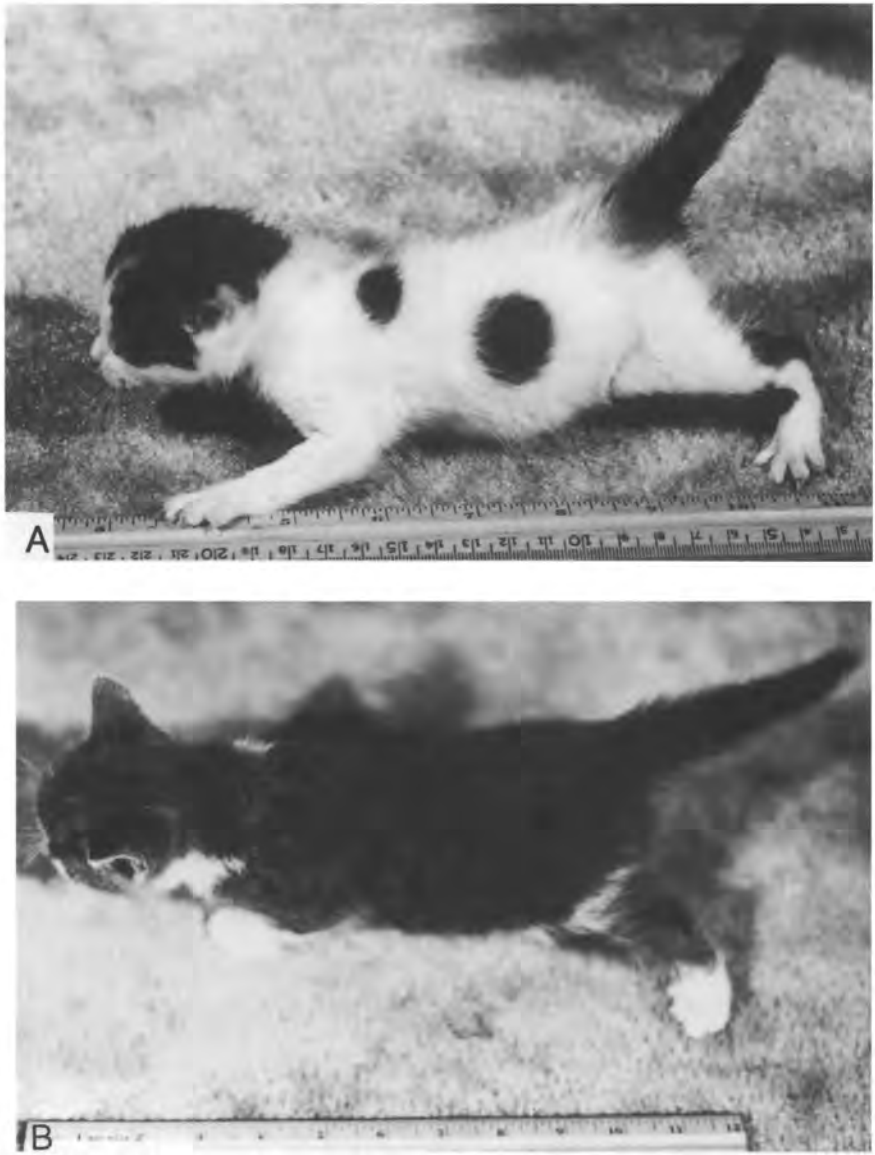

Figure 4. Kittens from severely taurine-deficient queens *(A)* are often 30–50 per cent smaller than normal *(B)* and gain weight more slowly. The contrast is apparent in this comparison of 10-day-old kittens. (Courtesy of J.A. Sturman.)

retinal degeneration, which is readily observed with an opthalmoscope (Fig. 3), and/or dilated cardiomyopathy (detected by echocardiography) in cats should be taken as evidence of taurine deficiency. A fasting plasma sample sent to an appropriate laboratory for taurine analysis provides the necessary confirmation. When plasma taurine is measured, careful sample preparation is necessary to exclude platelet aggregation and clotting.

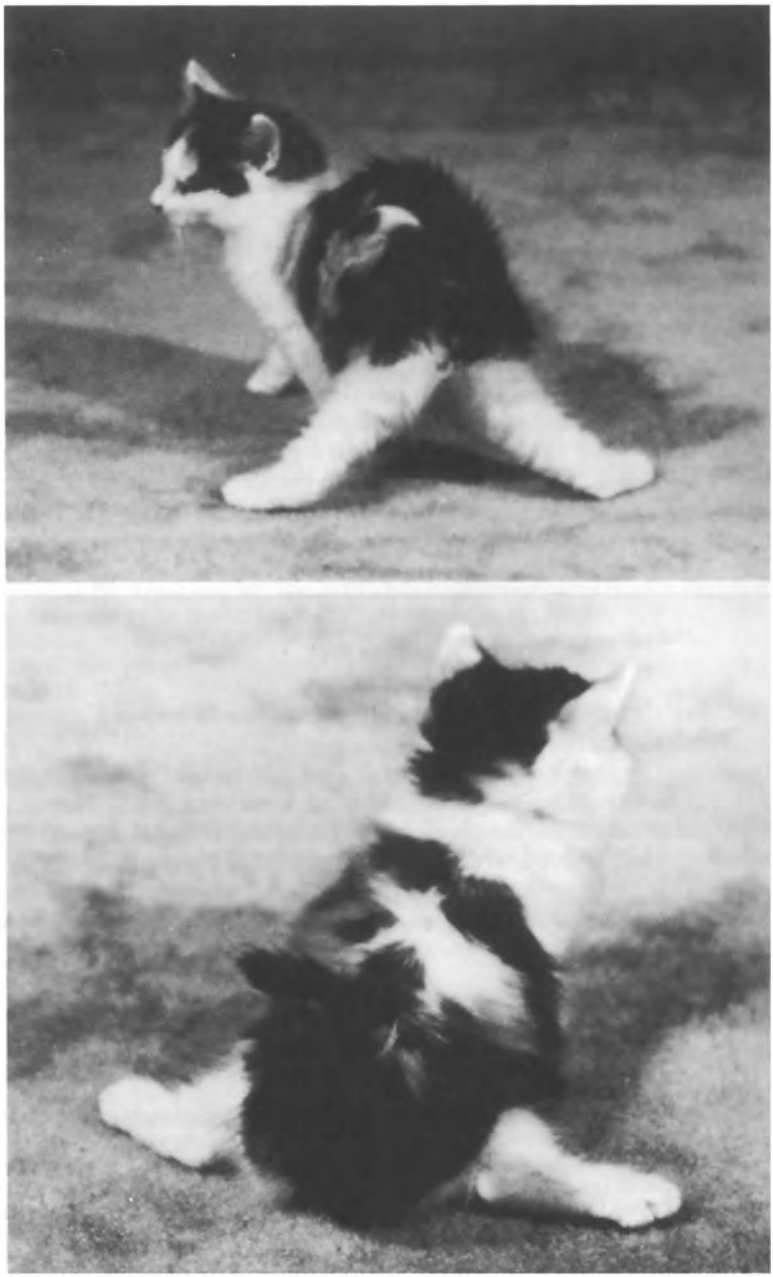

Figure 5. This 8-week-old taurine-deficient kitten demonstrates the spastic posterior paresis and excessive abduction characteristic of the impaired development of the cerebellum in this syndrome. (Courtesy of J.A. Sturman.)

Otherwise, the plasma taurine concentration is apt to be contaminated by platelet or white blood cell taurine, since both platelets and white blood cells represent an extremely rich source of taurine.[7,12] Normal values for plasma taurine in cats appear to range between 50 and 120 μmol/l, with a mean value between 70 and 80 μmol/l. One to 10 μmol/l are typical values in depleted cats. Diet history should be taken and the cat fed a diet that specifies on the label that it is "nutritionally complete." Major cat food manufacturers are aware of the taurine problem and have taken measures to fortify their formulas appropriately.

As noted in Table 3, the "normal" recommended dietary allowance of 500 to 700 mg/kg (dry weight basis) was exceeded by essentially all diets tested. This is particularly true of the all-fish diets, but other canned diets have been fortified to protect against the unavailability of taurine associated with processing, a problem already mentioned and not understood at this time.[15] Canned diets containing more than 2000 mg/kg and dry diets with more than 1000 mg/kg are presumably adequate under any circumstances. Supplements of fresh cooked fish, meat, or poultry are ready souces of this most interesting sulfonic amino acid (Table 2). The dietary requirement for cats is thought to be about 50 mg of taurine per day, available in 3 tablespoons of minced clams.

SUMMARY

Taurine deficiency occurs in a large number of cats fed unfortified commercial diets. Deficiency arises because cats are unable to absorb all the taurine in processed diets and/or are unable to synthesize the deficit between absorption and requirement, which makes taurine an essential amino acid for cats. Taurine-depleted cats develop retinal degeneration, cardiomyopathy, altered white-cell function, and abnormal growth and development. Taurine deficiency is best estimated from the plasma-taurine concentration, with values less than 30 μmol/l considered deficient.

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