

Unique nutrient requirements of cats appear to be diet-induced evolutionary adaptations

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Summary

Cats have requirements for essential dietary nutrients additional to those needed by other animals. The object of this review is to relate the idiosyncratic nutritional requirements of cats to activities of enzymes involved in the pathways of these nutrients. The high protein requirement of cats follows from the lack of regulation of the aminotransferases of dispensable nitrogen metabolism and urea cycle enzymes. The dietary requirements for the amino acids taurine and arginine are consequences of low activities of two enzymes in the synthetic pathways of these two nutrients that have a negative multiplicative effect on the rate of synthesis. Cats have obligatory dietary requirements for vitamin D and niacin due to high activities of enzymes that catabolize the immediate precursors of these vitamins to other compounds. The requirement for preformed vitamin A appears to be the result of deletion of enzymes required for cleavage and oxidation of carotenoids. While the requirement for the long chain n-3 polyunsaturated fatty acids has not been defined, low activities of desaturase enzymes indicate that cats may have a greater dietary need for these nutrients than other animals to maintain normal plasma concentrations.

The present day nutrient requirements of domestic cats support the thesis that their idiosyncratic requirements arose from evolutionary pressures from a rigorous diet of animal tissue. These changes favoured energy conservation by deletion of redundant enzymes and modification of enzyme activities to result in metabolites more suited to the cat's metabolism. However, our retrospective viewpoint allows only recognition of association rather than cause and effect.

Keywords: dietary adaptation, enzyme adaptation, carnivore, nutritional peculiarities, feline evolution

Introduction

Modern molecular techniques (e.g. Johnson and O'Brien 1997; Murphy *et al.* 2000) have provided new insights into the evolution of cats and have supplemented

concepts built from fossil records. Animals with feline traits appeared ~30 MYBP (million years before the present), but ancestors of modern cats were not evident until the mid-Miocene period (15–20 MYBP). Dental and other characteristics suggest that these animals became true carnivores in a nutritional context at least 15 MYBP. DNA studies of the 37 species of modern cats present today indicate that they evolved from approximately eight phylogenetic lineages within the past 10 to 15 MYBP (Johnson and O'Brien 1997; Slattery and O'Brien 1998). Within these lineages or species clades, speciation is comparatively recent; most fossil records of extant cats are less than 2 MYBP. The oldest fossil records are only 3–5 MYBP and some first appear as recently as <100 000 years ago.

Domestic cats evolved within the past 4000 years from the African wild cat *Felis sylvestris libyca*. Comparative genomics using cat-human radiation hybrid mapping have shown that the domestic cat genome organisation is remarkably conserved compared with the human (Murphy *et al.* 2000) and of all non-primate species examined, cats display the fewest number of chromosomal changes relative to humans (O'Brien *et al.* 1999).

The domestic cat (*Felis catus*) is the only member of the family *Felidae* whose nutrition has been studied in any detail. The limited information available supports the view that other felids have nutritional requirements similar to those of domestic cats. It has generally been assumed that animals whose diet contains a wide range of foods are better able to survive under changing environments than those that depend on a single or limited range of foods. Many highly successful mammals, such as rodents, are omnivorous in their dietary habits and adapt to varying diets and protein levels by modulating their metabolism. What is the basis for the success of true carnivores that are extreme specialists and have survived and evolved using a single type of food? A simple answer could be that animal tissue provides complete nutrition, and the restricted food source is a trade off for the high nutritive value of the food. Animals that eat other animals are not faced

with deficiencies of essential nutrients, provided there is an abundance of prey. However, a diet of only animal tissue does not provide the balance of nutrients demanded by the body cells. If strict carnivores evolved adaptive metabolic pathways to handle this imbalance of nutrients, then these adaptations were a possible key to the success of carnivores.

High protein requirement and amino acid metabolism

Animal tissue, especially from non-domesticated animals, is low in carbohydrates and contains an excess of protein relative to the total energy content. When the protein ($N \times 6.25$) requirements of growing kittens are compared to other species, kittens require about 1.5 times the protein in the diet needed by chicks or pigs. These latter species are depositing much more of the food nitrogen in tissue than kittens, but the protein requirement for adult maintenance is about 2 to 3 times higher in cats than in adult non-carnivores. This high protein requirement could be due to either (i) a higher than normal requirement for one or more of the essential amino acids, or (ii) a higher than normal requirement for nitrogen. We have measured the amino acid requirements of kittens for growth and found these (with one exception) to be similar to those of other mammals (Rogers and Morris 1979). This anomalous high amino acid requirement does not account for the high protein requirement and, therefore, we are left with the second alternative: that cats require a high protein diet because they have a high requirement for nitrogen.

Most animals when given diets low in protein, or when starved, conserve nitrogen by reducing the activities of the aminotransferases of general nitrogen metabolism (Harper 1965; Kaplan and Pitot 1970). In addition, nitrogen is conserved by a reduction in the activities of the urea cycle enzymes. However, when cats were given high (70%) and low (17%) crude protein diets there was little or no adaptation in the activities of the aminotransferases to dietary protein (Rogers *et al.* 1977). Similarly, there was no adaptation of the urea cycle enzymes to variation in protein level in the diet. Ammonia resulting from the deamination of amino acids by cats is continually diverted to urea and lost from the body pool rather than contributing nitrogen for the synthesis of dispensable amino acids. The high protein requirement of cats is for dispensable nitrogen. The aminotransferases of the essential amino acids are regulated; otherwise, cats would have a high requirement for these essential amino acids as well as for nitrogen (Rogers and Morris 1980).

A side benefit of the lack of regulation of the aminotransferases of general nitrogen metabolism is that cats (and other true carnivores) during starvation are better able to maintain glucose levels in the blood than omnivorous animals.

Arginine

In our studies referred to above to determine the essential amino acids for growing kittens, we used the following protocol. Kittens were given diets in which all the nitrogen was in the form of amino acids. Individual amino acids under study were removed from the diet and the performance of these kittens was compared to kittens given an identical diet that contained the amino acid. For all diets (with one exception) when an essential amino acid was deleted the food intake would decline by the second day, and there would be a progressive slow body weight loss, but no other clinical signs. However, when arginine was deleted from the diet there was a rapid over-night loss of body weight that continued over the next few days (Morris *et al.* 1979).

For many mammals, such as young and adult humans, adult pigs and pre-ruminant lambs, arginine is not an essential amino acid in the diet. The endogenous rate of synthesis is commensurate with the needs of these animals. Initially it had been assumed that net endogenous arginine in these animals came from the urea cycle in the liver (Drotman and Freedland 1972). However, because of the high activity of hepatic cytosolic arginase (an enzyme that catalyzes arginine degradation to ornithine and urea), virtually none of the arginine synthesized in the liver escaped to the peripheral tissues (Featherstone *et al.* 1973). In those animals that are independent of dietary arginine, the arginine for the peripheral tissues is produced through the combined interaction of the intestine and kidneys. Glutamate and glutamine are metabolized in the intestinal mucosa, producing citrulline (Windmueller and Spaeth 1974, 1975; Windmueller 1980). Citrulline produced in the intestine is converted to arginine in the kidneys by the same pathway the urea cycle uses to generate arginine. Because arginase activity in the kidney is low, arginine can escape and supply the peripheral tissues.

For young growing rats, the rate of endogenous synthesis of arginine is sub-optimal for maximal growth and supplementation with dietary arginine enhances growth rate. Arginine-deficient rats exhibit no obvious clinical signs of arginine deficiency other than decreased growth rate. In contrast, when growing kittens that have been deprived of food overnight consume an arginine-free meal a life-threatening situation occurs. Kittens exhibited progressive clinical signs of salivation, neurological changes, hyperaesthesia, emesis, coma, tetany and death within an hour of consumption of as little as 5 g of a diet devoid of arginine but otherwise complete (Morris and Rogers 1978a,b). These clinical signs were compatible with those of hyperammonaemia in other species, and analysis of the plasma showed that the degree of hyperammonaemia was related to the severity of the clinical signs. In addition, there was a marked decrease in the concentration of arginine in plasma, and hyperglycemia.

Was the hyperammonaemia a result of increased production of ammonia, or decreased disposal of ammonia, or both? Amino acids ingested after overnight food deprivation are rapidly deaminated as a source of energy (facilitated by the high activity of the aminotransferases) and so increase ammonia production. In other animals, this ammonia would be converted into urea. However, overnight food deprivation in cats results in a decrease in circulating levels of amino acids, especially arginine. The liver is also depleted of arginine and other urea cycle intermediates, leading to a reduction in the rate of ammonia removal. When cats ingest a meal containing all the essential amino acids, arginine has an anaplerotic effect on the urea cycle, and allows normal disposal of the ammonia from deaminated amino acids. Humans that ingest an arginine-free diet even after an overnight fast do not experience a rise in plasma ammonia concentration because endogenous synthesis can provide the intermediates for the urea cycle (Carey *et al.* 1987).

The activities of two enzymes in the intestinal pathway of citrulline synthesis were found to be markedly lower in cats than in species such as rats. Costello *et al.* (1980) demonstrated that the activity of ornithine aminotransferase (OAT), required for the conversion of ornithine to citrulline, was low in cats. Rogers and Phang (1985) reported that the activity of pyroline-5 carboxylate synthase (required for ornithine synthesis) was only 5% on a body weight basis of that in rats. As previously indicated, rats do not synthesize adequate arginine for maximal growth. The low activities of these two enzymes in cats have a multiplicative effect and result in negligible production of citrulline in the intestine, rendering cats totally dependent on dietary arginine.

Kittens given an arginine-free diet supplemented with citrulline did not develop hyperammonaemia, and had normal growth rates because citrulline supplied urea cycle intermediates and was converted to arginine in the kidneys (Morris *et al.* 1979). Similarly, when ornithine was substituted for arginine in the diet, cats did not develop hyperammonaemia, but they did not grow. While ornithine had an anaplerotic effect in the urea cycle and facilitated ammonia removal, it was not converted to citrulline in the intestinal mucosa because of the low activity of OAT.

Most natural proteins contain sufficient arginine to prevent hyperammonaemia in cats. However, cats given a diet in which casein was the sole protein source developed hyperammonaemia and exhibited emesis. A 50:50 mixture of isolated soy protein and casein provides sufficient arginine to prevent hyperammonaemia.

A rationale can be provided for the maintenance of high activities and lack of regulation of aminotransferases of dispensable nitrogen metabolism and urea cycle enzymes in cats. Cats need to be metabolically capable, even after prolonged fast, of

handling a high protein meal. Activities of these enzymes need to be maintained at a high level for rapid gluconeogenesis and ammonia disposal. Animal tissues are well supplied in arginine, providing arginine to the liver and urea cycle. While cats consume only animal tissue, there is no risk of hyperammonaemia, and no selection pressure to maintain citrulline synthesis. Reduced synthesis of these redundant enzymes conserves energy for cats. Within the order carnivora, cats are more sensitive than dogs and ferrets to hyperammonaemia resulting from consumption of an arginine-free diet. Cats are exquisitely sensitive to arginine deficiency, for there is no other example in a mammalian species where consumption of a single meal lacking an essential nutrient can lead to death.

Taurine

One of the first workers to attempt studies on the nutrition of cats using purified diets was Patricia Scott. Scott *et al.* (1964) reported that cats given a diet based on casein developed progressive retinal degeneration, which was not corrected by the addition of vitamin A to the diet. However, cats reared on a meat-based diet were normal. Later, Hayes *et al.* (1975) reported that a dietary deficiency of taurine produced feline central retinal degeneration. Besides the effects of a deficiency of taurine on the retina, Sturman *et al.* (1987) showed that there was impairment of reproduction in queens and developmental defects in kittens. Pion *et al.* (1987) further demonstrated that taurine deficiency was associated with dilated cardiomyopathy in cats and the condition could be reversed by supplemental taurine.

Why are cats sensitive to taurine deficiency when taurine is not considered an essential dietary nutrient for mammals except for human infants? Taurine is a β -sulphonic amino acid, that is not a constituent of polypeptides, but occurs as a free amino acid in animal tissues. Taurine is not oxidized by mammals, but is used as a conjugate for the bile acids. Cats and dogs obligatorily use taurine to conjugate bile acids, whereas many other animals including humans, can use either glycine or taurine for the conjugation. In bovines, the hepatic cholyl-CoA:amino acid N-acyltransferase enzyme is capable of conjugating CoA adducts of bile acids to both glycine and taurine (Vessey 1979). However, the affinities of the enzyme for taurine and for glycine depend on species (Vessey 1978) and in cats and dogs, the enzyme has a low affinity for glycine. Unlike taurine-replete cats, the bile of taurine-depleted cats contains free bile acids along with very low concentrations of glycocholate (Hickman *et al.* 1992).

Mammals synthesize taurine by the oxidation of the sulphur amino acid cysteine. Cats possess all the enzymes of the pathway for taurine synthesis, but the activities of two enzymes in the pathway from cysteine to taurine are low. These enzymes are cysteine dioxygenase (CD) that catalyzes the oxidation of cysteine to cysteinesulphinic acid (CSA) and cysteinesulphinic acid decarboxylase (CSAD) that

catalyzes the conversion of CSA to hypotaurine. When the activities of two enzymes in a pathway are greatly reduced (as in this case and citrulline synthesis) there is a multiplicative effect and the traffic along this pathway becomes insignificant. Therefore, most of the sulphur amino acid catabolism is not along the CSA pathway. Park *et al.* (1999) demonstrated that in cats >80% of the cysteine is metabolized by the direct desulphydration pathway, and <20% is metabolized by the transamination pathway. The desulphydration pathway is catalyzed by cysteinodesulphydrase that releases the amino group of cysteine as ammonia, whereas the transamination pathway is catalyzed by cysteine aminotransferase coupled with β -mecaptopyruvate sulphurtransferase and transfers the amino group to α -ketoglutarate. Both pathways produce pyruvate from cysteine, which can be oxidized as a source of energy.

The low enzyme activities of the synthetic pathway limit the endogenous synthesis of taurine, but it is the combination with the extremely low affinity in cats of the cholyl-CoA:amino acid N-acyltransferase for glycine that results in the depletion of the body taurine pool. We have found that the recovery of taurine by the enterohepatic circulation is a function of the diet, particularly the protein component. Diets that contain a high percentage of indigestible protein increase CCK secretion and favour a flora that degrades taurine (Morris *et al.* 1994). Therefore, the dietary requirement for taurine is not fixed, but depends on the dietary ingredients and the method by which they are processed. This factor has special significance in preparation of commercial diets for cats: canned diets need almost twice the concentration of taurine as expanded diets to maintain normal taurine concentrations in plasma. Taurine is well supplied in animal tissue, but may become limiting when the diet contains animal tissue to which significant amounts of vegetable matter have been added, or the animal tissue has been processed to produce Maillard products.

When cats consume a diet of animal tissue, adequate taurine is ingested to meet the body needs without synthesis. Under these conditions it is energetically advantageous for cats to use pathways of cysteine catabolism that produce a substrate (pyruvate) that can be oxidized as a source of energy. Cats derive no benefit from conversion of cysteine to taurine to be excreted in the urine.

Vitamins

The dietary requirements of cats for certain vitamins differ both qualitatively and quantitatively from those of most other mammals. These peculiarities can be related to differences in enzyme activities in the pathways of synthesis of these vitamins.

Vitamin A

The inability of cats to use carotenoids as a source of vitamin A was one of the first of the nutritional

peculiarities of cats that were identified by Gershoff *et al.* (1957). It appears that cats cannot undertake either the symmetrical or the asymmetrical cleavage of the carotene molecule, the first step in the conversion of carotenoids to retinal. The enzyme responsible for symmetrical cleavage of β -carotene has been known for more than 40 years, but it had never been isolated from any species or characterised. Recently the gene for β , β -carotene 15,15'-dioxygenase was cloned from chickens (Wyss *et al.* 2000), and the homology between chicken and mouse sequences was found to be 81% (Wyss *et al.* 2001). While this enzyme is rather well conserved in evolution across these species, it appears to have been deleted from the normal tissue sites of the duodenal villi, liver, and tubular structures of the lung and kidney of cats. As animal tissue contains only low concentrations of carotenoids, the ability of cats to produce retinal from carotenoids is redundant, and maintenance of this enzyme or the asymmetric cleavage enzyme would be an unwarranted energetic cost.

Another peculiarity of vitamin A metabolism that cats share with some of the other carnivores is the high level of retinal esters (predominately retinyl stearate and palmitate) in the plasma. In humans and rats, almost all the vitamin A in plasma is combined with retinal-binding protein, and esters are present in significant concentrations only when toxic levels of vitamin A are ingested.

As many commercial cat foods, particularly canned foods in the United States, contain appreciable amounts of liver, and as much of this liver comes from pigs (receiving diets high in vitamin A) we investigated the potential for vitamin A toxicity in adult cats. Seawright *et al.* (1970) demonstrated that excessive intakes of vitamin A in growing kittens given a diet of liver led to the formation of exostoses on the cervical vertebrae. Our approach was to examine the effects of long term excess dietary vitamin A (300 and 600 mg retinal equivalents (RE) = 1 and 2 million IU of vitamin A/kg diet) on teratology. Over a 3 year period and multiple pregnancies, total fatal and non-fatal malformations in the kittens born to queens from the control (6 mg RE), 306 mg RE and 606 mg RE groups were: fatal, 1.5, 1.6 and 9.1% respectively of kittens born; non-fatal, 0, 1.1 and 5.2 % respectively (Freytag *et al.* 2001). While there is a significant increase in malformation rates with high intakes of vitamin A, these rates are low compared to other species. When compared to rats (the most tolerant species tested to date) given a similar dose only during gestation, the incidence of a specific malformation (cleft palates) in the offspring was 80% compared to 2.9% in kittens from queens in the 606 mg RE group.

There were no apparent deleterious effects of the high intakes of vitamin A on the queens (Freytag *et al.* 1998). Cats given high dietary intakes of vitamin A excreted large amounts of conjugates in the urine, and while liver stores of vitamin A progressively increased, over a three-year period, there were no obvious signs of toxicity.

Evolutionary pressures may have rendered cats more tolerant than other species to excess vitamin A in the diet. As cats use only pre-formed retinyl esters, they lack control over the conversion of carotenoids to retinal, which is one of the controls that prevents toxicity in other animals that utilise carotenoids. An all-animal tissue diet could potentially expose cats to high retinyl ester loads, especially if they exhibited a predilection for viscera. High retinyl ester loads may have induced enhanced capacity in cats for retinyl conjugation and excretion. The studies of Freytag *et al.* (unpublished) support this conclusion, as cats given radiolabelled retinal excreted large quantities of an unidentified polar conjugate in urine that is not present in the urine of other animals.

Vitamin D

For most animals, vitamin D is a conditional nutrient as normal exposure to sunlight negates a dietary requirement. While cats are covered with hair, which would impede UV light reaching the skin, the propensity for cats to lie in the sun and expose their ventral abdomens (which have less hair than the rest of the body) suggested that cats may synthesize vitamin D. Sheep synthesize vitamin D on exposed parts of the body, despite their heavy pelage. However, kittens, both shaved and unshaved, exposed to direct sunlight were found not to be able to synthesize vitamin D (Morris 1999). Cat skin contains a low concentration of 7-dehydrocholesterol, the precursor for pre-vitamin D (How *et al.* 1994; Morris 1999). However, when vitamin D-deficient kittens were exposed to UV light and given a diet containing an inhibitor of the enzyme 7-dehydrocholesterol- Δ^7 -reductase (which catalyses the conversion of 7-dehydrocholesterol to cholesterol), the concentration of 7-dehydrocholesterol in skin was greatly augmented. Also, the concentrations of 25-hydroxycholecalciferol in the plasma of these kittens increased to normal levels indicating synthesis of vitamin D. Similar kittens exposed to UV light without the inhibitor in their diet maintained low levels of 7-dehydrocholesterol in skin and deficient plasma levels of 25-hydroxycholecalciferol.

How do cats in the wild obtain their vitamin D if they are unable to undertake endogenous synthesis? The vitamin D requirement of growing kittens is similar to that of other animals (Morris *et al.* 1999). Analyses of the vitamin D concentration of potential prey of cats (rodents and birds) indicated that the prey could provide adequate amounts of the vitamin without the need for endogenous synthesis. The cat's obligatory dietary requirement for vitamin D is an example where synthesis is prevented by the high activity of an enzyme that reduces the availability of the precursor substrate.

Cats appear to be more tolerant of excess vitamin D in the diet than other mammals (Sih *et al.* 2001). The possible reasons for this tolerance have not been investigated. Retinoic acid and 1,25 dihydroxyvitamin

D use specific nuclear receptors that are members of the steroid superfamily of ligand-activated transcription factors which may provide a common link for the cat's tolerance to excesses of both vitamins.

Niacin

In most species, the niacin equivalence of a food is the sum of nicotinamides in the food and the potential endogenous synthesis of nicotinic acid from tryptophan. The molar yield of nicotinic acid from tryptophan varies with species, but the dietary niacin requirement is inversely related to the hepatic activity of the enzyme picolinic carboxylase (Ikeda *et al.* 1965; Scott 1986). This enzyme catalyzes the conversion of the intermediate (2-amino-3-carboxymuconic acid semialdehyde) in the tryptophan degradative pathway to glutaryl CoA, instead of allowing it to condense to quinolinic acid, the immediate precursor of nicotinic acid. Cats possess all the enzymes of the pathway of niacin synthesis, but the activity of picolinic carboxylase is extremely high (highest of all animals studied) precluding any measurable nicotinic acid synthesis. The absolute requirements of niacin and vitamin D by cats are examples of high activities of enzymes reducing the availability of the precursors required for synthesis of the vitamins.

Coat colour in cats

Owners of cats and dogs frequently report that when their pets are given certain commercial and therapeutic diets they undergo a change of coat colour. Black-coated cats and dogs change to reddish brown, and other coat colours lose their intensity. The public often refers to this colour change as 'red hair'. We have observed grey coat in newborn kittens that should have had solid black coats, but we have attributed this colour change to a deficiency of copper, resulting in low activities of the copper-containing enzyme tyrosinase.

In an experiment that used a gelatin-based purified diet, we noticed that the coat of a black cat changed to reddish brown. When the protein source in the diet was changed to a casein-lactalbumin mixture, the coat colour change was prevented. As all ingredients other than protein in the diet were held constant, the factor causing the production of red hair was attributed to the protein component of the diet. Compared to other proteins, gelatin (and collagen) is low in both phenylalanine and tyrosine. Tyrosine is not an essential amino acid for growing kittens (Rogers and Morris 1979), but tyrosine can supply about half of the total aromatic amino acid requirement (Williams *et al.* 1987). Tyrosine is the precursor of DOPA (3,4-dihydroxyphenylalanine) and melanin, the pigment of hair and skin. As phenylalanine is obligatorily metabolized to tyrosine, the sum of both amino acids has to be considered in estimating the potential tyrosine for melanin synthesis. Amino acid-based diets, in

which essential amino acids were supplied at levels that slightly exceeded the NRC (1986) recommendations, also produced a change of black hair coat to reddish brown. However, addition of phenylalanine or tyrosine to these diets prevented the change in hair colour (Yu *et al.* 2001).

Two forms of melanin occur in hair as co-polymers: cysteine-containing phaeomelanin, which is reddish brown and eumelanin, which is black-brown in color (Ito *et al.* 1993, Ozeki *et al.* 1997). Completely black hair is high in eumelanin, and hair in which phaeomelanin predominates has a reddish colour. The quantity of phenylalanine plus tyrosine in the diet that is required to prevent 'red hair' is > 16.5 g (12 g phe + 4.5 g tyr) and < 24 g of phe, but we are further refining this range of values. The requirement found in short term experiments for maximal growth and nitrogen balance by Williams *et al.* (1987) and used by the NRC (1986) is 8.5 g of phe + tyr (4.0 g phe + 4.5 g tyr). Thus, the requirement for maximum expression of coat colour is more than twice that required for growth. We are unaware of a requirement for a secondary function in any animal being so much greater than the requirement for growth. Presumably, this large difference is due to the K_m for tyrosine of the enzymes involved in eumelanin synthesis being very much higher than the K_m of those involved in tissue growth. This view is supported by plasma concentrations of tyrosine. At dietary concentrations of phe + tyr that did not support black hair, the mean concentrations of tyr in plasma of these cats remained approximately constant, and it was not until plasma concentrations increased from this plateau value that there was consistent maintenance of hair colour. There are other examples of nutrients (e.g. histidine) where the requirement of cats depended on the function being studied (Quam *et al.* 1987). However, aromatic amino acids and hair colour provide a greater disparity than any other example.

Other nutrient requirements of cats

Essential fatty acids

There is consensus that cats, in common with all other mammals, require linoleate in the diet. However, the exact requirements of cats for long chain polyunsaturated fatty acids (PUFAS) is not clear. There is also consensus that cats have a limited capacity to synthesize arachidonate from linoleate, and probably eicosapentaenoate and docosahexaenoate from δ -linolenate (MacDonald *et al.* 1983; Bauer 1997). This limited synthetic capacity was attributed to low desaturase activities of cat liver (Rivers *et al.* 1975, Sinclair *et al.* 1979) and it was assumed that the diet of cats had to contain a source of animal fat to supply arachidonate. Subsequently, the essentiality of arachidonate was questioned when McLean and Monger

(1989) demonstrated that queens given a diet with vegetable fat only could produce up to two litters of kittens. Pawlosky and Salem (1994), demonstrated that cats possess low $\Delta 6$ -desaturase activity and are capable of limited synthesis of arachidonate. This group later demonstrated that reproduction was supported in queens given an arachidonate-free diet containing 7 g linoleic acid/kg diet, contributed by 30 g corn oil/kg diet (Pawlosky *et al.* 1996). Lower concentrations (0.087 g/kg diet) of linoleate in the diet were inadequate for reproduction. Reproduction in toms appears normal when consuming an all-vegetable fat diet containing linoleate (MacDonald *et al.* 1984; Morris unpublished). The testes of toms receiving a linoleate-containing diet had higher levels of arachidonate (indicating synthesis) than those of cats given a linoleate-free diet. The requirement for long chain n-3 fatty acids (eicosapentaenoic and docosahexaenoic) that are not present in vegetable fats has not been studied.

Carbohydrate

There are many interesting aspects of carbohydrate metabolism in cats, for example the absence of hexokinase activity in the liver (Ballard 1965) which is consistent with the low glucose load from an all-animal tissue diet. However, most of the other enzyme modifications relative to carbohydrate metabolism are in degrees of adaptation (Meyer and Kienzle 1991) rather than the extreme examples previously cited.

Conclusions

This overview of some of the idiosyncratic nutritional requirements of domestic cats attempts to link the dietary essentiality of these nutrients to differences in the activities of key enzymes. The inability of cats to regulate the aminotransferases and urea cycle enzymes explains the high protein requirement of cats. Five nutrients that are essential in the diet of cats, but not in the diet of many other animals, result from limited or total lack of synthesis. Two of these nutrients are amino acids (arginine and taurine) whose essentiality can be related to low activities of two enzymes in the pathway of synthesis. The other three nutrients are vitamins. In the case of niacin and vitamin D high activities of enzymes result in degradation of the immediate precursors for their synthesis; the third, vitamin A, has to be present pre-formed in the diet rather than supplied as carotenoids because of the complete deletion of an enzyme required for the oxidation of carotene to retinal. These nutrients do not become limiting to cats that consume an all-animal tissue diet. It is suggested that evolutionary pressures have resulted in deletion or modulation of these enzymes to provide metabolites more suited to the metabolism of cats.

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