Proceedings of the Nutrition Society (1997), **56**, 1013–1024

Fatty acid metabolism in domestic cats (*Felis catus*) and cheetahs (*Acinonyx jubatas*)

BY J. E. BAUER

Comparative Nutrition Research Laboratory, Department of Small Animal Medicine and Surgery, Texas A & M University, College Station, Texas 77843-4474, USA

The obligatory carnivorous nature of cats probably emerged as part of the slow adaptational process of these animals in becoming efficient predators rather than the result of a specific dietary requirement. Loss of the ability to produce needed nutrients from plant precursors was peripheral to this evolutionary change, but a lasting effect of it. As a result, present-day cats must meet their nutritional needs in the context of specialized requirements for dietary fat and other nutrients. These needs are most readily met by consumption of other mammalian tissues. High dietary concentrations of protein and special requirements for arginine, taurine, and retinol uniquely characterize feline nutrition. Like other mammals, cats cannot synthesize the essential fatty acid (EFA), linoleic acid (18:2*n*-6; LA). However, unlike other mammals, cats also have a limited capacity to synthesize arachidonic acid (20:*n*-6; AA) from LA and, similarly, eicosapentaenoic acid (20:5*n*-3; EPA) and docosahexaenoic acid (22:6*n*-3; DHA) from α-linolenic acid (18:3*n*-3; ALA). These features of fatty acid metabolism underscore the reliance of cats on other mammals to make these important fatty acids for them.

The provision of the dietary EFA to domestic cats (*Felis catus*) is of interest to veterinarians and animal nutritionists, especially in view of their domestication and role as exclusive household companions. Among other members of the Felidae family, comparative differences are also of interest, not only because optimal nutritional care of captive zoological species must be provided, but also because reproductive performance depends on adequacy of the EFA. The importance of this latter concept with respect to endangered species such as the cheetah (*Acinonyx jubatas*) needs little added emphasis. Although most studies of feline fatty acid metabolism have been conducted in *Felis catus*, opportunities to investigate this topic in other species, when presented, have furthered our understanding of the unique lipid metabolic pathways of the order Carnivora. Results of recent studies in cheetahs from our laboratory are the focus of the present discussion, along with a review of fatty acid metabolism in cats.

ESSENTIAL FATTY ACID CHEMISTRY

Mammalian EFA are straight-chain polyunsaturated hydrocarbons with all their double bonds in the *cis*-configuration. A convenient shorthand notation is often used by indicating the number of C atoms in the acyl chain and the number and position of the double bonds (Fig. 1). Designation of the double-bond placement depends on the point of reference used in the molecular structure. The usual chemical convention is to number the C atoms from the functional group (in this case, the carboxyl group) onward. Using this system, LA has double bonds between C-9-10 and C-12-13 and is designated Δ9,12-18:2. This notation is referred to as the Δ-notation.

By comparison, an alternative ω-notation begins by numbering the C atoms at the methyl end of the molecule (the last or ω-C from the functional carboxyl group). Thus, LA is referred to as 18:2*n*-6. Placement of the first double bond is between C-6-7 counted from

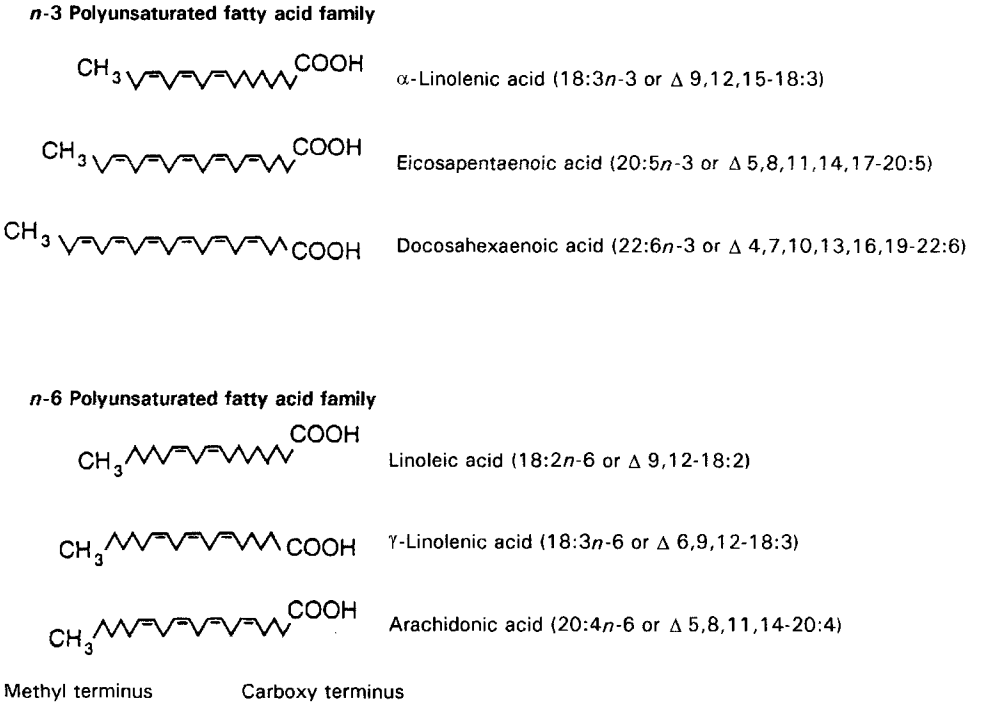

Fig. 1. Structure of the *n*-3 and *n*-6 polyunsaturated fatty acid families. Because all metabolic modifications to these molecules occur at the carboxyl terminus, the methyl terminus remains invariant. Thus, *n*-3 fatty acids give rise to other *n*-3 fatty acids and similarly for the *n*-6 and other families. Fatty acid structures can be specified using the ω-notation in the form of A:B*n*-C, where A is the number of carbon atoms in the chain, B is the number of double bonds, and C is the position of the first double bond from the methyl terminus. All double-bond placements are specified by this notation since it is only applied to straight-chain carbon fatty acids having methylene-interrupted double bonds in their structure. The alternative Δ-notation is described in detail on p. 1013. It numbers the carbon atoms from the carboxyl terminus and indicates the location of each double bond.

the methyl terminus. Since the double bonds occur in methylene interrupted sequence, only the first double bond position needs to be stipulated.

Each nomenclature has its advantages and both are used here. The Δ-notation readily demonstrates fatty acid regulation due to desaturase enzyme activities, since these steps are specific for double-bond placement from the carboxyl end. By contrast, the ω-notation shows the relationship within a specific fatty acid family and highlights metabolic relationships as a result of chain elongation and desaturation reactions which may occur. Appreciation for both nomenclatures provides a better understanding of the possible metabolic conversions that may occur.

ESSENTIAL FATTY ACIDS IN CATS: LACK OF Δ-6 DESATURATION

Although the dietary essential nature of C_{18} fatty acids in mammals has been recognized since the 1920s (Burr & Burr, 1929), in the early 1970s, observations by Rivers & Crawford at the Nuffield Institute of Comparative Medicine in London indicated that domestic cats additionally appeared to require a dietary source of long-chain (i.e. $> C_{18}$) polyunsaturated fatty acids (Sinclair, 1994). Initial attempts at devising semi-purified diets containing vegetable oils that cats would eat led these investigators to a series of

experiments on feline EFA metabolism. The first biochemical evidence was published in 1975 when cat liver preparations were observed to apparently lack the Δ-6 desaturase enzyme needed for AA synthesis from LA and EPA from ALA (Rivers *et al.* 1975). This reaction characterizes the first enzymic step in the metabolic cascades that provide long-chain polyunsaturated fatty acids for important neurological tissues and precursors for physiological mediators of cell function (i.e. eicosanoids and prostaglandins; Fig. 2). Clinically, animals fed on the experimental diets in this study had dry, lustreless-hair coats, dandruff, behavioural infertility, and hepatic lipid infiltration. Stimulated by these observations a series of published studies by Rivers and his colleagues (Rivers *et al.* 1976*a*,*b*; Hassam *et al.* 1977; Frankel & Rivers, 1978; Rivers & Frankel, 1980, 1981; Rivers, 1982) demonstrated an EFA requirement for cats, a deficiency of which could be caused by feeding hydrogenated coconut oil as the only fat source. What made these studies unique by contrast to other mammals, was that a similar deficiency syndrome was observed when other groups of cats were fed on diets containing the requisite LA and ALA. Thus, the possibility of a dietary requirement for long-chain polyunsaturated fatty acids derived from the C_{18} precursors emerged. In terms of practical diets these fatty acids would be animal-derived.

Although the diets used in the studies described previously were probably marginal in dietary taurine (Hayes *et al.* 1975; MacDonald *et al.* 1984*a*), possibly marginal in vitamin E (Stephan & Hayes, 1978), and excessive in vitamin D contents (MacDonald *et al.* 1984*a*), some of these concerns were addressed in later reports. It was found that taurine supplementation did not change the fatty acid profiles seen earlier (Rivers & Frankel, 1980). The authors did recognize that vitamin D levels may have been excessive in their earlier work. However, vitamin E levels were corrected (Rivers & Frankel, 1980) and the previously observed fatty acid changes occurred again, even when hydrogenated coconut oil, which would not readily deplete vitamin E stores, was the source of fat. In addition, when γ-linolenic acid (18:3*n*-6)-containing oils were added to the diets the reproductive

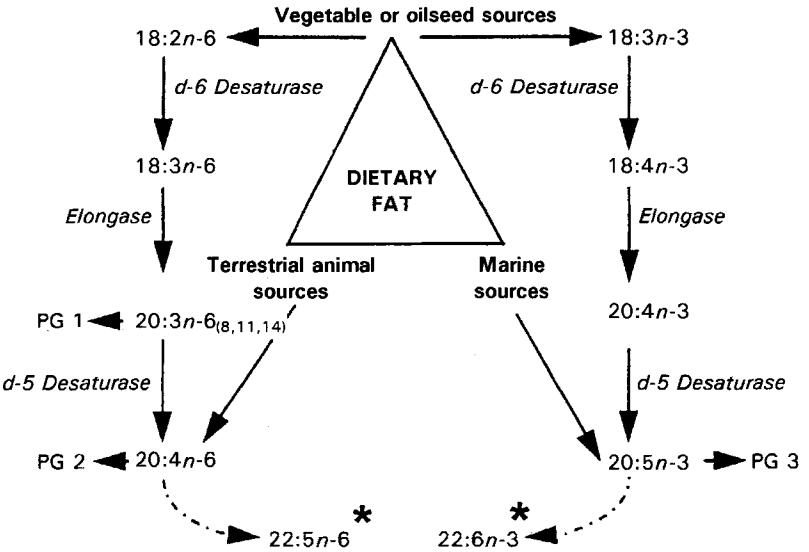

Fig. 2. Predominant pathways of essential fatty acid metabolism in mammals. d-6 desaturase, Δ-6 desaturase; d-5 desaturase, Δ-5 desaturase; elongase, chain elongase; PG, prostaglandin. * For details of a new pathway for C_{22} polyunsaturated fatty acid synthesis, see Voss *et al.* (1991).

clinical picture improved. This fatty acid may have improved AA status to some extent by virtue of bypassing the Δ-6 desaturase step (see discussion of Δ-5 desaturation below; Rivers & Frankel, 1980).

Reports from two other laboratories a few years later additionally described effects of EFA-deficient diets, LA-replete diets, and LA and AA-replete diets in cats. In the USA, Rogers and colleagues (MacDonald *et al.* 1983*a*,*b*, 1984*b*) reported that EFA deficiency resulted in similar symptoms to those reported by Rivers and co-workers. By contrast, diets containing 50 g safflower oil plus 300 g hydrogenated beef tallow (6·7 % energy as linoleate)/kg prevented all clinical symptoms except reproduction problems in females (MacDonald *et al.* 1983*b*). Workers in Australia (Sinclair *et al.* 1979, 1981; McLean & Monger, 1989) reported that cats maintained for up to 8 years on diets containing 50 g safflower oil/kg did not suffer the severe symptoms reported by Rivers and his colleagues (Rivers & Frankel, 1980). These cats appeared normal except for some dulling of hair coats and a general inability of females to produce more than two litters. It was speculated that the severity of symptoms was attenuated by the possibility of inadequate amounts of taurine and some vitamins as acknowledged in the earlier studies. Nonetheless, it was clear that amounts of what would be adequate LA for other mammalian species did not maintain the cat in optimal health.

Possible explanations of the observed differences from various laboratories include the possibility that diets differing in their relative fatty acid profiles or other nutrients may have led to variable capacity of cats to synthesize AA. Indeed, certain *n*-3 fatty acids such as ALA (Holman & Mohrauer, 1963; Mohrauer & Holman, 1963; Hwang & Carroll, 1980; Monger, 1986) may be involved in regulation of the Δ-6 desaturase enzyme. For that matter, AA itself may regulate this enzyme. Evidence for limited Δ-6 desaturase activity was obtained when production of small amounts of Δ 5,8,11-20:3 (20:3*n*-9) was seen in cats fed on LA diets containing no AA (Sinclair *et al.* 1979; Rivers & Frankel, 1981; MacDonald *et al.* 1983*a*). This fatty acid is produced from oleic acid by the same enzymic pathway as AA from LA. Limited Δ-6 desaturase activity in cats has recently been confirmed using sophisticated stable isotope techniques combined with GC and mass spectrometry (Pawlowsky *et al.* 1994) but generally appears only when diets are completely devoid of AA. Thus, the picture that has emerged is that cats cannot synthesize enough AA to maintain tissue concentrations at the levels needed for health in the absence of a small dietary supply (MacDonald *et al.* 1984*b*).

BEYOND Δ-6 DESATURASE: EVIDENCE FOR Δ-5 DESATURASE BUT NOT Δ-8 DESATURASE ENZYMES

The studies designed to show the lack of the Δ-6 desaturase in cats summarized previously also led to certain additional observations relating to the existence of other mammalian desaturase enzyme activities. Because Δ-6 desaturation appeared limited in cats, when diets rich in LA were fed an alternative chain elongation was observed, resulting in the modest accumulation of 20:2*n*-6 and the appearance of the novel fatty acid, Δ 5,11,14-20:3. This latter fatty acid was most probably the result of Δ-5 desaturation of 20:2*n*-6 produced via chain elongation of accumulated dietary LA (18:2*n*-6; Sinclair *et al.* 1981; MacDonald *et al.* 1984*b*; Fig. 3). Further evidence for this enzyme activity was also obtained after injection of ^{14}C-labelled 20:3*n*-6 (Δ 8,11,14-20:3) with the appearance of liver AA (Sinclair *et al.* 1981). This group also showed that when ^{14}C-labelled 18:3*n*-6 was fed, levels of Δ 8,11,14-20:3 and AA increased in erythrocyte lipids (Fig. 2). Although other mammals can also synthesize Δ 5,11,14-20:3, it is usually not detectable in animal

tissues. For example, normal human erythrocytes contain no more than 0·1 mol/100 mol total fatty acids in this form (MacDonald *et al.* 1984*b*). Thus, when it occurs, small but significant amounts of this fatty acid in the presence of dietary LA are a hallmark of limited Δ-6 and active Δ-5 desaturase enzyme systems.

The existence of a Δ-8 desaturase (Fig. 3), although suggested as an alternative pathway for the formation of Δ 8,11,14-20:3 and AA (Sinclair *et al.* 1981) has not been established. If it were present in cats to any considerable degree, AA synthesis from LA might occur by this alternative pathway. Also, studies of mammalian tissues, including liver, brain and mammary tissues *in vivo* and *in vitro* with 20:1*n*-9 or 20:2*n*-6 indicate that the addition of another double bond is in the Δ-5 position (Cook, 1991). On the other hand, low-level Δ-8 desaturation has been reported in tumours, testes (Albert & Coniglio, 1977; Cook, 1991), human bladder and colon (Nakazawa *et al.* 1976), although no evidence has been found for any appreciable activity in cats to date (MacDonald *et al.* 1983*a*).

FAT IN THE DIETS OF CHEETAHS AND OTHER LARGE CATS

A dramatic series of bottle-neck events occurring 10 000 years ago contributed to the near extinction of cheetahs. They are the only surviving species of this genus (O'Brien *et al.* 1985; Menotti-Raymond & O'Brien, 1993). Cheetahs appear to have limited genetic diversity (O'Brien & Wildt, 1983). Reproductive failures (O'Brien *et al.* 1985) and numerous diseases complicate their captive management (Munson, 1993). Observations of feeding patterns and behaviours of these animals and other large cats have provided a few clues to their dietary fat needs. It has been estimated that large cats obtain 60 % of their total energy from dietary fats and that diets up to 67 % energy as fat are efficiently digested and utilized (Scott, 1968). The apparent digestibility of crude fat by captive wild felids has been reported to be 95–99 % when fed on a meat-based diet containing 160 g crude fat/kg (Barbiers *et al.* 1982). The recommendation for domestic cats is currently 90 g/kg DM (about 19 % dietary energy as fat; Association of American Feed Control Officials, Inc.,

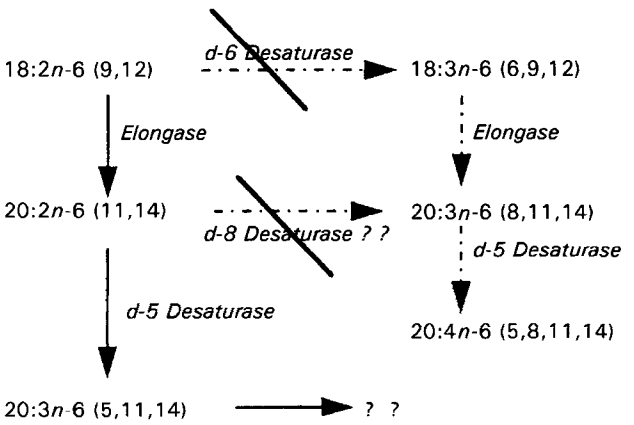

Fig. 3. Pathways of linoleic acid (18:2*n*-6) metabolism in cats. Low Δ-6 desaturase (d-6 desaturase) activity in cats favours chain elongation of 18:2*n*-6 to eicosadienoic acid (20:2*n*-6) and its subsequent desaturation via Δ-5 desaturase (d-5 desaturase) to novel fatty acid 20:3*n*-6 (Δ-5,11,14). Accumulation of this latter fatty acid appears unique to cats. Also, an alternative path for 20:4*n*-6 synthesis is shown via Δ-8 desaturase (d-8 desaturase). However, the lack of 20:4*n*-6 accumulation when 18:2*n*-6 is fed indicates that d-8 desaturase activity is low in cats.

1997), although they can tolerate amounts as high as 67% dietary energy as fat (MacDonald *et al.* 1984*a*).

In addition to the domestic cat, the lion (*Panthera leo*) also appears to lack the ability to desaturate fatty acids at the Δ-6 position. However, the cheetah belongs to a different genus from either the lion or the domestic cat and demonstrates other adaptive differences from these species. As the single surviving species of its genus, cheetahs may be markedly divergent in both anatomy and behaviour from other genera among Felidae (Kingdon, 1977). For example, the cheetah's ecology and ethology place it at the opposite end of the felid spectrum compared with leopards and it appears to be less capable of adapting to a human-dominated environment (Myers, 1974). The cheetah is diurnal, does not conceal its food, nor does it scavenge, whereas the leopard is nocturnal with a wide food spectrum covering forty different types of prey from fish to terrestrial animals, caches food, and is an opportunistic scavenger (Myers, 1974). In view of these differences, the fatty acid patterns seen in cheetahs may also be different from those of other cats. Some evidence exists that cheetahs may not have an active Δ-6 desaturase enzyme, although further information is needed to better establish this phenomenon in this genus (Davidson *et al.* 1986*a*).

Another difference among cats is that cheetahs are more frequently robbed of their kills. They must compensate for this problem by being extraordinarily efficient hunters (Kingdon, 1977). In this way, for better or worse, the freshness of their food supply is assured. From the perspective of dietary fat requirements, the possibility exists that their long-chain polyunsaturated fatty acid supply must be oxidatively unspoiled. One study in which liver fatty acid profiles of two cheetahs culled in the wild *v.* one captive animal showed markedly lower amounts of nearly all highly-unsaturated long-chain fatty acids in the captive animal tissues (Davidson *et al.* 1986*b*). These authors noted that this animal had been fed in captivity most of its life and that the possibility of dietary fatty acid deterioration may have been a factor in the observed differences.

SERUM LIPID AND LIPOPROTEIN DISTRIBUTIONS IN NORMAL AND HYPERLIPIDAEMIC CAPTIVE CHEETAHS

Backeus *et al.* (1997*a*,*b*) recently described fasting hyperlipidaemia in four related captive cheetahs. Samples from these studies were recently characterized in our laboratory (Backeus *et al.* 1997*a*,*b*; Bauer, unpublished results). The first syndrome was identified in an 11-year-old male at the Oklahoma City Zoological Park (OCZP) that was subsequently diagnosed with azotaemia and isosthenuria consistent with uncompensated renal failure. The animal was humanely killed 44 weeks after the initial illness, when 2 weeks of treatment involving immobilization for intravenous and subcutaneous fluid therapy every second day failed to resolve the azotaemia. Other problems diagnosed included severe gastric gland atrophy and venous occlusive disease. At necropsy, severe mucosal thickening of the gastric and small intestinal mucosa was noted. The other three animals were male littermates, 3 years of age, located at the Milwaukee County Zoological Park. They are great nephews of the first animal (Backeus *et al.* 1997*b*). Sera from two of these littermates were grossly hyperlipaemic, while the third had elevated serum triacylglycerol concentrations. A complete clinical report of the findings in these animals has been published (Backeus *et al.* 1997*b*).

Sera from a group of twenty-eight normal, healthy adult cheetahs from two zoological collections in North America were collected during routine health examinations for comparison with the hyperlipidaemic cats (Backeus *et al.* 1997*a*). Seven animals were from OCZP and twenty-one were from White Oak Conservation Center in Yulee, Florida.

Table 1. *Representative fatty acid composition of the Nebraska Brand diets* fed to the cheetahs (*Acinonyx jubatus*)*

Fatty acid types	Composition (mol/100 mol fatty acids)
Total saturated	35·3
Total monounsaturated	38·9
n-6 Polyunsaturated	
18:2*n*-6 (Δ9,12)	11·5
20:2*n*-6 (Δ11,14)	0·3
20:3*n*-6 (Δ8,11,14)	0·2
n-3 Polyunsaturated	
18:3*n*-3 (Δ9,12,15)	10·3
20:5*n*-3 (Δ5,8,11,14)	0·1
22:5*n*-3 (Δ4,7,10,13,16)	1·0
18:2*n*-6 : 18:3*n*-3	1·1

* Central Nebraska Packing Inc., North Platte, NB, USA.

Fresh sera were analysed for lipoprotein distributions immediately after overnight delivery of the refrigerated (not frozen) specimens to our laboratory. Remaining samples were then stored at −90° until the time of lipid extraction and fatty acid analysis. All animals including the hyperlipidaemic cats had been maintained on the same type of commercial diet (Nebraska Brand, Exotic Canine Diet; Central Nebraska Packing Inc., North Platte, NB, USA). Three of the animals had been fed on a 50:50 (w/w) mixture of the Exotic Canine Diet and an Exotic Feline Diet from the same manufacturer. All meat and meat by-products in both diets were of equine origin and the diets had been fed on a long-term basis. While different lots of the diet were fed to the animals, fatty acid analysis of three separate batches revealed nearly identical concentrations of LA (23 g/kg DM) and ALA (21 g/kg DM) reflecting the horsemeat-based formula since horse tissues are replete in LA and ALA (Table 1).

Serum lipids and lipoprotein distributions of the cheetah sera demonstrated fasting hyperlipidaemia in the four affected animals. In the normal group, lipoprotein distributions were similar to our earlier study of domestic cats (Bauer, 1992; Table 2). By contrast, the hyperlipidaemic cats had marked elevations of chylomicrons, while the beta and pre-beta fractions (i.e. LDL fractions) were only mildly elevated. These findings are consistent with either a decreased clearance of exogenous triacylglycerol as transported in the chylomicron fraction, or increased or altered production of this lipoprotein. These metabolic alterations may have been the result of intestinal mucosal pathology noted in the one cat that had been necropsied because this tissue is a known site of lipoprotein synthesis. Analysis of post-heparin plasma specimens for lipoprotein lipase (*EC* 3.1.1.34) and hepatic lipase (*EC* 3.1.1.3) activities as well as lecithin–cholesterol acyltransferase (*EC* 2.3.1.43) may shed additional light on these possibilities. Samples for this purpose are currently being analysed in the laboratory.

FATTY ACID METABOLISM IN NORMAL AND HYPERLIPIDAEMIC CAPTIVE CHEETAHS

Because of the uniqueness of Felidae with respect to Δ-6 desaturase enzyme activities, previous reports of reproductive failures (O'Brien *et al.* 1985), and the need for a dietary source of AA to assure reproduction in females (MacDonald *et al.* 1984*a*), the fatty acid composition of serum phospholipid subfractions was investigated in the cheetah sera.

https://doi.org/10.1079/PNS19970106 Published online by Cambridge University Press

Table 2. *Serum triacylglycerol (TAG), total cholesterol concentrations, and lipoprotein distributions via agarose gel electrophoresis in hyperlipidaemic and normal cheetahs* (Acinonyx jubatus) (Adapted from Backeus *et al.* 1997*a*)

	TAG (mmol/l)	Cholesterol (mmol/l)	Lipoprotein distribution (%)			
			Chylomicron	Beta	Pre-beta	Alpha
Hyperlipidaemic						
No. 5158·28	16·0	14·3	25·0	32·0	23·5	21·0
No. 3760	55·7	22·1	20·8	38·6	15·3	25·2
No. 3759	8·0	10·4	20·5	41·0	17·3	21·1
No. 3758	1·3	6·0	5·6	29·5	20·5	44·4
Mean	25·5*	14·9†	18·0†	34·9†	19·2†	27·9†
SD	7·6	2·7	8·5	5·8	3·6	11·2
Normal						
Mean	0·8	4·3	0·0	19·4	12·6	68·0
SD	0·1	1·2	0·0	5·6	7·9	10·0

Mean value was significantly different from normal cheetah mean (one-tailed *t* test): $*P < 0{\cdot}05$.
Mean values were significantly different from normal cheetah means (two-tailed *t* test): $\dagger P < 0{\cdot}05$.

Serum total phospholipid (PL)-fatty acid compositions were examined after total lipid extraction (Bauer, 1991) and fractionation by TLC (Bauer *et al.* 1997). Fatty acids were analysed by capillary GC (Bauer *et al.* 1996) and confirmed by GC–mass spectroscopy when necessary (J. E. Bauer, B. L. Dunbar, K. E. Bigley and R. D. Stipanovic, unpublished results).

Overall, serum PL were enriched in LA, ALA, and AA (Bauer *et al.* 1996; Table 3). However, only small relative amounts of EPA, 22:5*n*-3 and DHA were seen compared with domestic cats fed on commercially-prepared diets. These latter diets contained amounts of long-chain *n*-3 polyunsaturated fatty acids (Rivers & Frankel, 1980), in contrast to the cheetah diet (Table 1). However, because the cheetah diets contained high dietary ALA, its conversion to long-chain metabolites would be expected and higher amounts would have been observed if Δ-6 desaturase were active in these cats. This observation supports limited Δ-6 desaturase activities in cheetahs. Of additional interest was the presence of the LA chain-elongation product, 20:2*n*-6 (Δ11,14-20:2), and its Δ-5 desaturation product 20:3*n*-6, (Δ 5,11,14-20:3; Table 3). Since diet analysis revealed the absence of any 20:3*n*-6 (Table 1), the presence of these two fatty acids additionally supports the likelihood of limited Δ-6 desaturase but active Δ-5 desaturase activities in cheetahs. This finding is similar to the domestic cat and lion noted earlier.

When hyperlipidaemic samples were compared with those from normal animals, significant relative increases in 18:1*n*-9, LA, and DHA were seen in the PL fraction of affected animals. Decreases in both AA and 22:4*n*-6 also occurred. The *n*-3 polyunsaturates, ALA and EPA, were unchanged. Relative amounts of 22:5*n*-3 were decreased and DHA were elevated in the hyperlipidaemic cheetahs (Table 3). Furthermore, when desaturation indices (products : substrate for desaturase enzyme reaction) were calculated for the Δ-6 (AA + 20:3*n*-6/18:2*n*-6) and Δ-5 (AA/20:3*n*-6) desaturase enzyme reactions, both were significantly lower compared with those for normal animals.

Despite the possibility of limited Δ-6 desaturase activities in normal cats, elevations of LA in conjunction with decreases in AA and lower desaturation indices support the contention that hyperlipidaemic cheetahs may have yet further inhibitions of both Δ-6 and Δ-5 desaturase enzymes. Whether this possibility is an effect of the syndrome or its cause cannot be determined by this evaluation. Nonetheless, the reported pathology of intestinal

Table 3. *Selected fatty acid composition (mol/100 mol) of serum phospholipid fraction of hyperlipidaemic and normal cheetahs* (Acinonyx jubatas) *and domestic cats* (Felix catus)

(Mean values and standard deviations; values without standard deviations are average values calculated from individual mean values)

	Hyperlipidaemic (*n* 4)		Normal (*n* 28)		Domestic cats† (*n* 4)	
Fatty acid	Mean	SD	Mean	SD	Mean	SD
Total saturated	48·0		48·4		46·1	
Total monounsaturated	14·3		13·0		13·1	
18:1*n*-9 (Δ 9)	9·9*	0·5	8·2	0·8	–	
n-6 Polyunsaturated (total)	30·2		30·0		28·1	
18:2*n*-6 (Δ 9,12)	17·5*	1·7	12·5	1·7	11·8	0·9
20:2*n*-6 (Δ 11,14)	0·4	0·03	0·4	0·1	–	
20:3*n*-6 (Δ 5,11,14)	0·2	0·02	0·2	0·07	Trace	
20:3*n*-6 (Δ 8,11,14)	1·1	0·3	1·1	0·2	1·1	0·2
20:4*n*-6 (Δ 5,8,11,14)	10·5*	1·4	15·0	2·1	14·3	1·1
22:4*n*-6 (Δ 7,10,13,16)	0·4*	0·1	0·6	0·1	0·9	0·3
AA + DGLA:LA (Δ-6 index)	0·7*	0·1	1·3	0·2	1·3	
AA:DGLA (Δ-5 index)	10·3*	2·5	14·3	1·4	13·0	
n-3 Polyunsaturated (total)	5·4		4·9		12·9	
18:3*n*-3 (Δ 9,12,15)	2·9	0·7	2·3	0·7	0·3	0·1
20:4*n*-3 (Δ 5,8,11,14)	0·7	0·2	0·6	0·2	8·0	1·6
22:5*n*-3 (Δ 4,7,10,13,16)	0·9*	0·1	1·4	0·3	0·8	0·1
22:6*n*-3 (Δ 4,7,10,13,16,19)	0·7*	0·3	0·4	0·2	4·1	0·4
EPA + DPA:ALA (Δ-6 index)	0·6*	0·1	0·9	0·3	–	

AA, arachidonic acid (20:4*n*-6); DGLA, dihomo-γ-linolenic acid (20:3*n*-6 (Δ 8,11,14)); Δ-6 index, products AA + DGLA : substrate, 18:2*n*-6, of the Δ-6 desaturase enzyme reaction; Δ-5 index, ratio of product AA: substrate, DGLA, of the Δ-5 desaturase enzyme reaction; EPA, eicosapentaenoic acid (20:5*n*-3); DPA, docosapentaenoic acid (22:5*n*-3); ALA, α-linolenic acid (18:3*n*-3); Δ-6 index, products EPA + DPA : substrate, ALA, of the Δ-6 desaturase enzyme reaction.

Mean values were significantly different from those for normal cheetahs: $*P < 0{\cdot}05$.

† Adapted from Rivers & Frankel (1980). Cats had been fed on commercially-prepared cat foods.

mucosa and liver in the one affected animal on post-mortem examination may compromise lipid metabolic enzymes and lipid metabolism, thereby resulting in the lipid alterations seen in the hypertriacylglycerolaemic specimens.

Of related interest, it has been reported recently that obese children with hypertriacylglycerolaemia (>1·6 mmol/l) have lower AA levels compared with a cohort group with triacylglycerol contents ≤ 1·6 mmol/l (Desci *et al.* 1997). However, when compared with normal-weight children, AA levels were higher in the combined obese cohort. These investigators suggested that enhanced Δ-6 desaturase activities may exist with obesity. It should be noted that the cheetahs in our studies were not overweight. However, a similar inverse relationship of low AA and high plasma triacylglycerol concentrations was observed.

An alternative explanation is that increased utilization of AA and other long-chain polyunsaturated fatty acids may be occurring. This possibility would mask the interpretive value of the calculated desaturation indices resulting in apparent decreases. In this case, AA may be utilized for the synthesis of physiologically-active eicosanoids in response to some underlying metabolic alteration. However, it does not explain the significant increase in LA in the affected animals, especially because similar diets had been fed to both normal and affected cheetahs in this study. How this latter change might relate to hyper-

triacylglycerolaemia is not known. It is possible that both increased utilization of AA and decreased conversion of LA may be occurring simultaneously, thereby accounting for the fatty acid profiles observed. Reduced lipolysis of dietary LA is consistent with this possibility and is presently being evaluated in our laboratory.

CONCLUSION

Evidence has been obtained that fatty acid metabolism of cheetahs is similar to that of domestic cats and lions in that cheetahs appear to have limited Δ-6 desaturase but active Δ-5 desaturase enzyme activities. In addition, Δ-8 desaturase activities appear limited overall. Thus, a dietary requirement for long-chain polyunsaturated fatty acids derived from C_{18} *n*-6 and possibly *n*-3 fatty acids most probably exists for this species. Further, characterization of a hyperlipidaemic syndrome in four related male cheetahs resulted in relatively-elevated substrate fatty acids and decreased products of the important desaturation reactions compared with normal animals fed on similar diets. An investigation of lipid metabolic enzymes in the affected cheetahs is ongoing in our laboratory. Nonetheless, future collaborative studies such as ours will be needed to further our understanding of lipid metabolism in the big cats. In the meantime, the similarities of cheetahs to domestic cats with respect to lipid metabolism will provide us a continued foundation from which to understand diet, health, and disease states in Felidae species.

The author thanks collaborators, K. A. Backeus, J. P. Hoover, M. T. Barrie, J. McCann, S. Citino, R. Wallace and G. A. Campbell for their efforts in assuring freshly collected sera and plasma so that the timely laboratory analysis of cheetah samples could be performed. Expert technical assistance of B. Dunbar and K. Gerlich-Bigley is also acknowledged as is that of Dr R. D. Stipanovic of the USDA-ARS Cotton Pathology Research Laboratory in College Station, Texas for the GC–mass spectrometry fatty acid analysis and confirmation of unique lipid structures. The studies were supported in part by the Oklahoma City Zoological Park and the Mark L. Morris Professorship in Clinical Nutrition.

REFERENCES

Albert, D. H. & Coniglio, J. G. (1977). Metabolism of eicosan-11,14-dienoic acid in rat testes. Evidence for delta 8-desaturase activity. *Biochimica et Biophysica Acta* **489**, 390–396.

Association of American Feed Control Officials, Inc. (1997). *Official Publication – Association of American Feed Control Officials, Inc.* pp. 141–142. Atlanta: AAFCO, Inc.

Backeus, K. A., Hoover, J. P., Bauer, J. E., Barrie, M. T., McCann, J., Citino, S. & Wallace, R. (1997*a*). Serum lipoproteins, thyroid hormones and resting cortisols in normal Cheetahs (*Acinonyx jubatas*). *Journal of Zoologic and Wildlife Medicine* (In the Press).

Backeus, K. A., Hoover, J. P., Bauer, J. E., Campbell, G. A. & Barrie, M. T. (1997*b*). Hyperlipidemia in four related male Cheetahs. *Journal of Zoologic and Wildlife Medicine* (In the Press).

Barbiers, R. B., Vosburgh, L. M., Ku, P. K. & Ullrey, D. E. (1982). Digestive efficiencies and maintenance energy requirements of captive wild felidae: cougar (*Felis concolor*); leopard (*Panthera pardus*); lion (*Panthera leo*) and tiger (*Panthera tigris*). *Journal of Zoological Animal Medicine* **13**, 32–37.

Bauer, J. E. (1991). Serum lipoprotein alterations of rabbits fed high fat soy protein–dextrose diets. *Nutrition Research* **11**, 771–782.

Bauer, J. E. (1992). Diet-induced alterations of lipoprotein metabolism. *Journal of the American Veterinary Medical Association* **201**, 1691–1694.

Bauer, J. E., Backeus, K., Dunbar, B. L., Hoover, J. P., Barrie, M. T., Citino, S. & Wallace, R. (1996). Serum lipid fatty acids in captive cheetahs: evidence of *n*-6 and *n*-3 chain elongation and Δ-5 desaturation. *Proceedings of 14th Annual American College of Veterinary Internal Medicine FORUM*, p. 752. Lakeland, CO: American College of Veterinary Internal Medicine.

Bauer, J. E., McAlister, K. G., Rawlings, J. M. & Markwell, P. (1997). Molecular species of cholesteryl esters formed via plasma lecithin : cholesterol acyltransferase in fish oil supplemented dogs. *Nutrition Research* **17**, 861–872.

Burr, G. O. & Burr, M. M. (1929). A new deficiency disease produced by the rigid exclusion of fat from the diet. *Journal of Biological Chemistry* **82**, 345–367.

Cook, H. W. (1991). Fatty acid desaturation and chain elongation in eucaryotes. In *Biochemistry of Lipid, Lipoproteins and Membranes*, pp. 141–169 [D. E. Vance and J. Vance, editors]. Amsterdam: Elsevier Science.

Davidson, B. C., Cantrill, R. C. & Varaday, D. (1986*a*). The reversal of essential fatty acid deficiency symptoms in the cheetah. *South African Journal of Zoology* **21**, 161–164.

Davidson, B. C., Morsbach, D. & Cantrill, R. C. (1986*b*). The fatty acid composition of the liver and brain of southern African cheetahs. *Progress in Lipid Research* **25**, 97–99.

Desci, T., Molnar, D. & Koletzko, B. (1997). Long-chain polyunsaturated fatty acids in plasma lipids of obese children. *Lipids* **31**, 305–311.

Frankel, T. L. & Rivers, J. P. W. (1978). The nutritional and metabolic impact of γ-linolenic acid on cats deprived of animal lipid. *British Journal of Nutrition* **39**, 227–231.

Hassam, A. G., Rivers, J. P. W. & Crawford, M. A. (1977). The failure of the cat to desaturate linoleic acid: Its nutritional implications. *Nutrition and Metabolism* **21**, 321–328.

Hayes, K. C., Carey, R. E. & Schmidt, S. Y. (1975). Retinal degeneration associated with taurine deficiency in the cat. *Science* **188**, 949–951.

Holman, R. T. & Mohrauer, H. (1963). A hypothesis involving competitive inhibitions in the metabolism of polyunsaturated fatty acids. *Acta Chemica Scandinavica* **17**, 5540–5590.

Hwang, D. H. & Carroll, A. E. (1980). Decreased formation of prostaglandins derived from arachidonic acid by dietary linolenate in rats. *American Journal of Clinical Nutrition* **33**, 590–597.

Kingdon, J. (1977). *East African Mammals: An Atlas of Evolution in Africa*, vol. 3(A), pp. 397–413. New York: Academic Press.

MacDonald, M. L., Anderson, B. C., Rogers, Q. R., Buffington, C. A. & Morris, J. G. (1983*a*). Essential fatty acid requirements of cats: Pathology of essential fatty acid deficiency. *American Journal of Veterinary Research* **45**, 1310–1317.

Macdonald, M. L., Rogers, Q. R. & Morris, J. G. (1983*b*). Role of linoleate as an essential fatty acid for the cat independent of arachidonate synthesis. *Journal of Nutrition* **113**, 1422–1433.

MacDonald, M. L., Rogers, Q. R. & Morris, J. G. (1984*a*). Nutrition of the domestic cat, a mammalian carnivore. *Annual Reviews of Nutrition* **4**, 521–562.

MacDonald, M. L., Rogers, Q. R., Morris, J. G. & Cupps, P. T. (1984*b*). Effects of linoleate and arachidonate deficiencies on reproduction and spermatogenesis in the cat. *Journal of Nutrition* **114**, 719–726.

McLean, J. G. & Monger, E. A. (1989). Factors determining the essential fatty acid requirements of the cat. In *Nutrition of the Dog and Cat. Waltham Symposium* no. 7, pp. 329–342 [I. H. Burger and J. P. W. Rivers, editors]. Cambridge: Cambridge University Press.

Menotti-Raymond, M. & O'Brien, S. J. (1993). Dating the genetic bottleneck of the African cheetah. *Proceedings of the National Academy of Sciences USA* **90**, 3172–3176.

Mohrauer, H. & Holman, R. T. (1963). The effects of dose level of essential fatty acids upon the fatty acid composition of the rat liver. *Journal of Lipid Research* **4**, 151–159.

Monger, E. A. (1986). Polyunsaturated fatty acid metabolism in the cat. PhD Thesis, University of Melbourne, Australia.

Munson, L. (1993). Diseases in captive cheetahs: results of the Cheetah SSP Pathology Survey 1988–1992. *Zoologic Biology* **12**, 105–124.

Myers, N. (1974). Status of the leopard and cheetah in Africa. In *The World's Cats*. vol. 3, *Proceedings of Third International Symposium on the World's Cats*, 1974, pp. 53–69 [R. L. Eaton, editor]. Seattle, WA: Department of Zoology, University of Washington.

Nakazawa, I., Mead, J. F. & Yonemoto, R. H. (1976). In vitro activity of the fatty acyl desaturases of human cancerous and noncancerous tissues. *Lipids* **11**, 79–82.

O'Brien, S. J., Roelke, M. E., Marker, L., Newman, A., Winkler, C. A., Meltzer, D., Colly, L., Everman, J. F., Bush, M. & Wildt, D. E. (1985). Genetic basis for species vulnerability in the cheetah. *Science* **227**, 1428–1434.

O'Brien, S. J. & Wildt, D. E. (1983). The cheetah is depauperate in genetic variance. *Science* **221**, 459–462.

Pawlowsky, R., Barnes, A. & Salem, N. Jr (1994). Essential fatty acid metabolism in the feline: relationship between liver and brain production of long chain polyunsaturated fatty acids. *Journal of Lipid Research* **34**, 2032–2040.

Rivers, J. P. W. (1982). Essential fatty acids in cats. *Journal of Small Animal Practice* **23**, 563–576.

Rivers, J. P. W. & Frankel, T. L. (1980). Fat in the diet of dogs and cats. In *Nutrition of the Dog and Cat*, pp. 67–99 [R. S. Anderson, editor]. Oxford: Pergamon Press.

Rivers, J. P. W. & Frankel, T. L. (1981). The production of 5,8,11-eicosatrienoic acid (20:3*n*-9) in the essential fatty acid deficient cat. *Proceedings of the Nutrition Society* **40**, 117A.

Rivers, J. P. W., Hassam, A. G., Crawford, M. A. & Brambell, M. R. (1976*a*). The absence of Δ-6 desaturase activity in the cat. *Proceedings of the Nutrition Society* **35**, 69A.
Rivers, J. P. W., Sinclair, A. J. & Crawford, M. A. (1975). Inability of the cat to desaturate essential fatty acids. *Nature* **258**, 171–173.
Rivers, J. P. W., Sinclair, A. J., Moore, D. P. & Crawford, M. A. (1976*b*). The abnormal metabolism of essential fatty acids in the cat. *Proceedings of the Nutrition Society* **35**, 68A.
Scott, P. P. (1968). The special features of nutrition of cats with observations on wild felidae nutrition in the London Zoo. *Symposium of the Zoological Society of London* **21**, 21–36.
Sinclair, A. J. (1994). John Rivers (1945–1989): His contribution to research on polyunsaturated fatty acids in cats. *Journal of Nutrition* **124**, 2513S–2519S.
Sinclair, A. J., McLean, J. G. & Monger, E. A. (1979). Metabolism of linoleic acid in the cat. *Lipids* **14**, 932–936.
Sinclair, A. J., Slattery, W. J., McLean, J. G. & Monger, E. A. (1981). Essential fatty acid deficiency and evidence for arachidonate synthesis in the cat. *British Journal of Nutrition* **46**, 93–96.
Stephan, Z. F. & Hayes, K. C. (1978). Vitamin E deficiency and essential fatty acid (EFA) status of cats. *Federation Proceedings* **37**, 2588.
Voss, A., Reinhard, M. Sankarappa, S. & Sprecher, H. (1991). The metabolism of 7,10,13,16,19-docosapentaenoic acid to 4,7,10,13,16,19-docosahexaenoic acid in rat liver is independent of 4-desaturase. *Journal of Biological Chemistry* **266**, 19995–20000.