nient to culture than the cells normally responsible for producing α1AT, such as hepatocytes and mononuclear phagocytes (*2, 3, 17*). Nevertheless, the fibroblasts produced human α1AT that diffused into the blood and, more importantly, reached the lower respiratory tract of the lung. Although large amounts would have to be produced by such cells in order to effectively treat α1AT deficiency, modifications such as the transplantation of clones containing multiple copies of the integrated gene could make this a feasible approach (*18*).

In addition to the long-term application of this approach to the therapy of hereditary disorders, transplantation of retroviral vector-produced clones secreting other proteins active in the extracellular milieu might provide a new approach to study the in vivo effects of such hormones and growth factors.

REFERENCES AND NOTES

1. J. E. Gadek and R. G. Crystal, in *The Metabolic Basis of Inherited Disease*, J. B. Stanbury, J. B. Wyngaarden, D. S. Frederickson, J. L. Goldstein, M. S. Brown, Eds. (McGraw-Hill, New York, 1982), pp. 1450–1467.
2. R. W. Carrell, *J. Clin. Invest.* **78**, 1427 (1986).
3. J. Travis and G. S. Salvesen, *Annu. Rev. Biochem.* **52**, 655 (1983).
4. J. Bieth, *Front. Matrix Biol.* **6**, 1 (1978).
5. J. E. Gadek, G. A. Fells, R. L. Zimmerman, S. I. Rennard, R. G. Crystal, *J. Clin. Invest.* **68**, 889 (1981).
6. J. E. Gadek *et al.*, *ibid.*, p. 1158.
7. M. Wewers *et al.*, *Am. Rev. Respir. Dis.* **133**, A103 (1986).
8. H. Varmus and R. Swanstrom, in *RNA Tumor Viruses*, R. Weiss, N. Teich, H. Varmus, J. Coffin, Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1984), pp. 423–428.
9. W. F. Anderson, *Science* **226**, 401 (1984).
10. D. A. Williams and S. H. Orkin, *J. Clin. Invest.* 77, 1053 (1986).
11. D. Armentano *et al.*, *J. Virol.*, in press.
12. R. I. Garver, Jr., *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **84**, 1050 (1987).
13. S. J. Chen *et al.*, *ibid.* **82**, 7284 (1985).
14. A. F. Voronova and B. M. Sefton, *Nature (London)* **319**, 682 (1986).
15. S. Hartung, R. Jaenisch, M. Breindl, *ibid.* **320**, 365 (1986).
16. P. W. Kantoff *et al.*, *Trans. Assoc. Am. Phys.*, in press.
17. D. H. Perlmutter, F. S. Cole, P. Kilbridge, T. H. Rossing, H. R. Colten, *Proc. Natl. Acad. Sci. U.S.A.* **82**, 795 (1985).
18. E. Robertson, A. Bradley, M. Kuehn, M. Evans, *Nature (London)* **323**, 445 (1986).
19. M. A. Courtney *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 669 (1984).
20. A. D. Miller, M.-F. Law, I. M. Verma, *Mol. Cell. Biol.* **5**, 431 (1985).
21. R. A. Jorgensen, S. J. Rothstein, W. S. Reznelkoff, *Mol. Gen. Genet.* 177, 65 (1979).
22. R. Mann, R. C. Mulligan, D. Baltimore, *Cell* **33**, 153 (1983).
23. V. Klement, W. P. Rowe, J. W. Hartley, W. E. Pugh, *Proc. Natl. Acad. Sci. U.S.A.* **63**, 753 (1969).
24. J.-F. Mornex *et al.*, *J. Clin. Invest.* 77, 1952 (1986).
25. S. I. Rennard *et al.*, *J. Appl. Physiol.* **60**, 532 (1986).
26. J. P. Michalski, C. C. McCombs, S. Sheth, M. McCathy, R. deShazo, *J. Immunol. Methods* **83**, 101 (1985).

27. We are indebted to G. Fells and R. Seabron for their help in carrying out this work.

4 February 1987; accepted 27 May 1987

Myocardial Failure in Cats Associated with Low Plasma Taurine: A Reversible Cardiomyopathy

P. D. PION, M. D. KITTLESON, Q. R. ROGERS, J. G. MORRIS

Thousands of pet cats die each year with dilated cardiomyopathy, the cause of which is unknown. Although taurine is present in millimolar concentrations in the myocardium of all mammals, taurine depletion has not previously been associated with a decrease in myocardial function in any species. In this study, low plasma taurine concentrations associated with echocardiographic evidence of myocardial failure were observed in 21 cats fed commercial cat foods and in 2 of 11 cats fed a purified diet containing marginally low concentrations of taurine for 4 years. Oral supplementation of taurine resulted in increased plasma taurine concentrations and was associated with normalization of left ventricular function in both groups of cats. Since myocardial concentrations of taurine are directly related to plasma concentrations and low plasma concentrations were found to be associated with myocardial failure in cats, a direct link between decreased taurine concentration in the myocardium and decreased myocardial mechanical function is proposed.

DILATED CARDIOMYOPATHY (DCM), a degenerative disease of the myocardium, results in decreased myocardial contractility (myocardial failure). DCM has been reported in humans, dogs, cats, and other species (*1*). The etiology of primary DCM in most cases, regardless of the species, is unknown and the prognosis is poor (*1*). The incidence of DCM in domestic cats is unknown, but a retrospective study at a large urban veterinary referral center revealed that 193 (3.0%) of 6385 consecutive necropsy reports on pet cats that died between January 1962 and December 1977 indicated a gross pathologic diagnosis of DCM (*2*).

Taurine (2-aminoethanesulfonic acid) is an essential nutrient for cats and possibly primates, including humans (*3*). The most prominent clinical sign associated with taurine deficiency in humans and animals is photoreceptor cell degeneration (*3*). Taurine is not a constituent of mammalian proteins and its major metabolic role has been attributed to bile salt conjugation (*4*). Myocardium and retina have the highest concentration of free taurine in the body, ranging between 100 and 400 times that found in plasma. This concentration gradient is maintained by an energy-dependent transport process that is saturable and is mediated, at least in part, by adrenergic mechanisms (*5*). Taurine may play a role in the inotropic, metabolic, and osmotic regulation of the myocardium (*6*). In addition, congestive heart failure in humans, dogs, and rabbits is associated with increased myocardial taurine concentrations (*7*). Although several studies imply that taurine affects the inotropic properties of the heart in vivo and in vitro in several species, including humans (*8*), the basic physiologic function of taurine in the heart is unknown.

Taurine depletion is difficult to induce in most species. In cats, however, the biosynthesis of taurine is minimal and conjugation of bile acids with taurine is obligatory. Feeding taurine-deficient diets to cats results in low concentrations of taurine in plasma and tissues, including the retina and myocardium (*3, 9*). Taurine depletion for more than 6 months may produce feline central retinal degeneration (FCRD) (*3, 9*). In taurine-depleted rats, no mechanical cardiac abnormalities have been noted, and mechanical function of the heart has not been specifically investigated in taurine-depleted cats (*9*). In this report we present results that implicate low concentrations of taurine in the plasma [and therefore by deduction in myocardial tissues (*5, 9*)] as a major causal factor of DCM in cats.

Twenty-three cases of DCM were diagnosed at the University of California Veterinary Medical Teaching Hospital between 1 December 1986 and 1 April 1987. DCM was diagnosed by echocardiography in 21 client-owned cats (group 1) and in 2 of 11 female cats maintained in a specific pathogen-free (SPF) colony fed a purified diet containing marginal concentrations of taurine (250 or 500 mg per kilogram of dry diet) for 4 years (group 2). M-mode echocardiograms, indirect funduscopic examinations, plasma taurine concentrations, and dietary histories were obtained for all cats.

Four cats died from congestive heart failure within hours of arriving at the clinic.

School of Veterinary Medicine, University of California, Davis, Davis, CA 95616.

One cat, which initially appeared to be responding to therapy, died after 2 weeks from renal failure; another was humanely killed at the owner's request 4 weeks after beginning therapy because of recurrent pleural effusion that was not responsive to aggressive diuretic therapy. Seventeen cats, treated and followed for 10 to 26 weeks, are alive and clinically normal. Serial echocardiographic results and plasma taurine concentrations from these 17 cases are presented.

The echocardiographic criterion for diagnosis of DCM was an end-systolic diameter greater than 12 mm with a shortening fraction [defined as (end-diastolic diameter − end-systolic diameter)/end-diastolic diameter] less than 35% in cats with no evidence of other underlying acquired or congenital anatomic or functional cardiac abnormalities (Fig. 1) (*10*). The echocardiographic variables shown in Fig. 2 are the mean of measurements made by two observers who were unaware of the clinical or therapeutic status of each animal. Plasma taurine concentrations were determined by means of an amino acid analyzer (*11*).

Client-owned cats were treated with crystalline taurine (0.5 g administered orally twice daily) and with furosemide and captopril as needed to control signs of congestive heart failure (*12*). Digoxin (*12*) was continued in one cat that had been treated with this positive inotrope for 2 years prior to supplementation with taurine. Positive inotropic agents were not administered to any other cats. The two cats in group 2 that were found to have DCM after being fed purified diets with marginally low taurine concentrations were treated by increasing the taurine concentration in the purified diet to 5000 mg of taurine per kilogram of dry diet (equivalent to 250 to 500 mg of taurine per day) for 21 days; they were then switched to a diet containing 1500 mg of taurine per kilogram of dry diet. No diuretics, captopril, or inotropic agents were administered to the cats in group 2.

Statistical significance of changes in end-diastolic diameter, end-systolic diameter, and shortening fraction over time with taurine supplementation was performed by analysis of variance with the use of SAS GLM (*13*) on a microcomputer; measurements before treatment were contrasted with measurements after taurine treatment and the significance values were adjusted to consider multiple observations by using the Bonferroni correction (*13*). $P < 0.05$ was considered significant.

All cats except cat 19 with echocardiographic evidence of DCM had low concentrations of plasma taurine (10 ± 6, range = 1 to 20 nmol/ml) (Table 1) when compared to 55 client-owned cats brought to our hospital with diet histories that did not include the commercial foods implicated (Table 1) in producing DCM in association with low plasma taurine concentrations by our studies (82 ± 33, range = 31 to 147 nmol/ml). Eight cats with low plasma taurine and DCM had retinal lesions (FCRD), verifying a long-term taurine deficiency.

Every cat improved clinically (appetite, activity, and respiratory pattern) during the first 2-week period of taurine supplementation, but no cat improved echocardiographically before the second 2-week period (that is, 3 to 4 weeks after beginning taurine supplementation). As shown in Fig. 2 and Table 2, no statistically significant improvement in end-systolic diameter and shortening fraction (that is, the echocardiographic indices of systolic function used in this study) was apparent in the population until periods 3 and 2, respectively. At this time all 17 cats are clinically and echocardiographically normal and are no longer receiving medication for their heart failure.

In primary (idiopathic) DCM in humans and cats there is a remarkable lack of specific light or electron microscopic lesions (*1*). For this reason it is logical to hypothesize a biochemical and not a physical abnormality as the underlying etiology (*14*). A small percentage of cases of DCM in humans and dogs is known to result from carnitine deficiency, and in such cases carnitine supplementation may be curative (*15*). We propose that, in cats, the biochemical abnormality is a deficiency of myocardial taurine and that taurine supplementation reverses the biochemical abnormality and subsequent myocardial failure.

In this study DCM was associated with low plasma taurine concentrations in every case. Rat myocardium in vitro can concentrate taurine to 400 times that of plasma (*5*).

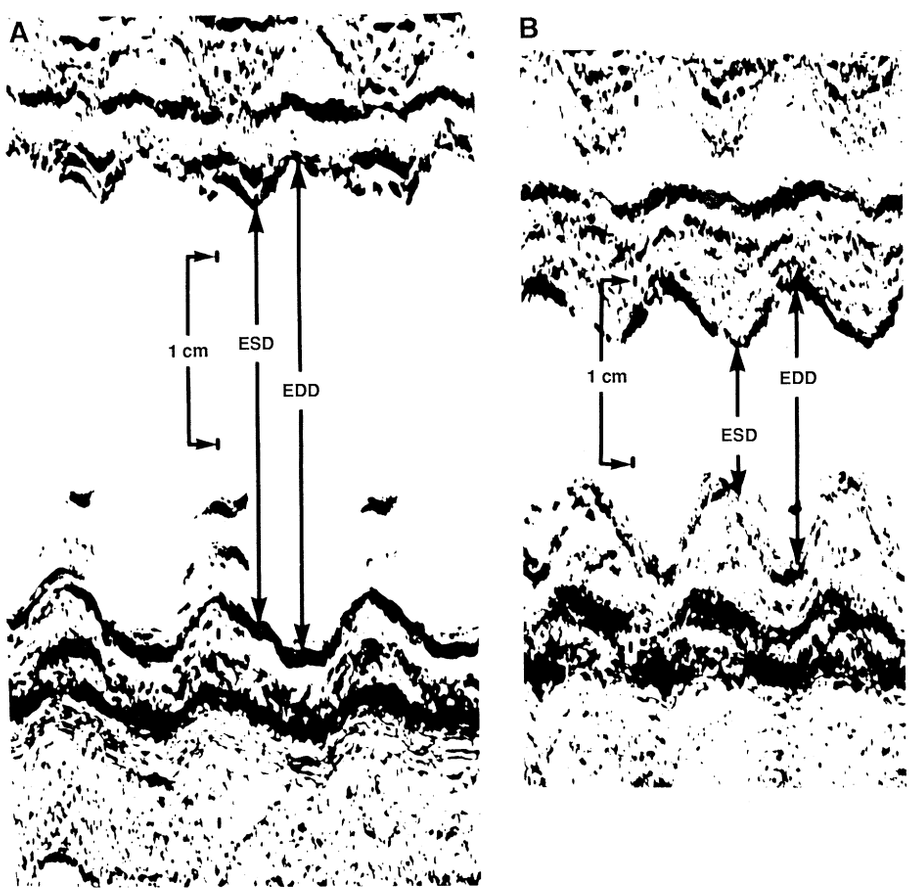

Fig. 1. M-mode echocardiograms from one cat before and after taurine supplementation. M-mode echocardiograms were recorded with a 7.5-MHz focused transducer from the lower right third or fourth intercostal space with cats in left lateral recumbency. Left ventricular end-systolic diameter (ESD) was measured as the distance between the left interventricular septal endocardial surface and the left ventricular free wall endocardial surface at the smallest dimension available and left ventricular end-diastolic diameter (EDD) was measured as the distance between the same surfaces at the onset of the QRS complex on the electrocardiogram (*21*). Shortening fraction (SF) was calculated as: SF = (EDD − ESD)/EDD. (**A**) M-mode echocardiogram from the first client-owned DCM cat treated with taurine at presentation; (**B**) echocardiogram of the same cat as in (A) after 10 weeks of taurine supplementation. The cat's diet was not changed and all other medications were discontinued 5 weeks after beginning therapy. Depth markers are automatically printed on the recording and represent 1 cm.

In normal cats, the ratio between myocardial and plasma taurine concentrations is about 100:1 (*9*). In taurine-depleted cats the ratio is reported to be about 250:1 (*9*). Therefore, the measured plasma taurine concentrations in cats with DCM, which ranged from 1 to 20 nmol/ml, suggests that myocardial taurine concentrations were between 250 and 5000 nmol per gram of tissue (wet weight). Normal cat myocardial taurine concentration is 6,000 to 18,000 nmol per gram of tissue (*9*). It is therefore reasonable to deduce that myocardial concentrations of taurine were subnormal in the cats that we found had chronically low plasma taurine concentrations. With the possible but unlikely exception of the presence of a myocardial taurine transport defect, it is also reasonable to deduce that myocardial taurine concentrations were normal to increased in cats supplemented with taurine.

The end-diastolic diameter was initially enlarged in cats with DCM but decreased after taurine administration (Fig. 2A, Table 2). There are two possible explanations for this decrease. First, both furosemide (a diuretic) and captopril [an angiotensin converting enzyme inhibitor (ATCEI)] decrease intravascular volume and can decrease intraventricular filling pressures and volume (preload). This could have contributed to the observed decrease in end-diastolic diameter in the 14 client-owned cats given these drugs to control signs of congestive heart failure. An alternative explanation, independent of furosemide or captopril, is that the improved systolic performance increased stroke volume (that is, the volume of blood pumped per heart beat), increasing blood flow to the kidneys and glomerular filtration and thus decreasing sodium and water retention. The resultant net sodium and water excretion could have decreased intravascular volume and contributed to the decreased end-diastolic diameter (*16*). Diuretics and captopril decrease intravascular volume and ventricular filling pressures within a few days of starting therapy (*17*). The time course of the decrease in end-diastolic diameter suggests that improved systolic performance rather than diuretic or ATCEI therapy was the major influence since end-diastolic diameter did not decrease significantly until 5 to 6 weeks after the initiation of taurine supplementation, coincident with improved systolic performance.

The end-systolic diameter (Fig. 2B) was initially increased. The magnitude of the increase in end-systolic diameter and the compensatory increase in end-diastolic diameter is characteristic of a profound chronic decrease in myocardial contractility (*16*). The decrease in end-systolic diameter after taurine supplementation could have been the result of improved myocardial function or a decrease in afterload (*16*). The shortening fraction (Fig. 2C) was initially low. Shortening fraction is an index of left ventricular function providing information analogous to the angiographic ejection fraction (*10*). Again, the magnitude and time course of change in end-systolic diameter and shortening fraction suggest a marked improvement in myocardial performance. Captopril can decrease afterload via arteriolar dilation but this effect would be apparent within hours to days rather than weeks (*17*). Similarly, an acute pharmacologic effect of taurine on myocardium can be ruled out since a significant decrease in end-systolic diameter and increase in shortening fraction was not observed before period 3 (5 to 6 weeks) and period 2 (3 to 4 weeks), respectively. These results therefore suggest that taurine supplementation corrects an unexplained myocardial abnormality caused by taurine deficiency.

Table 1. Demographic information, clinical and dietary history, and initial taurine concentration in the 23 cats with DCM. The data under "Outcome" show weeks from time of diagnosis to last observation or A, died of noncardiac cause; B, died within hours of hospitalization; C, humanely killed at the owner's request after 4 weeks of taurine supplementation. Plasma taurine concentrations were measured at the time each cat first arrived at the hospital.

Cat	Outcome	Age (years)	Sex*	Breed†	Taurine (nmol/ml)	FCRD	Diet‡			Diet changed during taurine therapy
							Type	Dry/wet	Time (years)	
1	26	5	F	DSH	5	No	P	D	4	Yes
2	26	5	F	DSH	8	Yes	P	D	4	Yes
3	20	12	FS	DLH	11	No	a	W	3.5	Yes
4	20	5	MC	Siamese	15	No	b	W/D	2	No
5	21	3	FS	Manx	15	No	a	W/D	3	Yes
6	15	7	MC	DSH	2	Yes	a	D/W	5	No
7	18	5	M	Himal/X	4	Yes	d	D	5	Yes
8	27	10	MC	DSH	7	Yes	d	D	10	No
9	16	12	MC	DLH	7	Yes	d	D	12	No
10	16	10	FS	DSH	4	Yes	a	D	3	No
11	20	12	FS	DLH	6	No	b	W/D	1	No
12	15	4	MC	ABY	3	No	a, c	W	1	No
13	17	5	FS	DLH	19	No	d, b	D	5	Yes
14	18	8	FS	DSH	30§	No	a	D	3.5	Yes
15	14	4	FS	DSH	4	No	a	W	3.5	Yes
16	12	2	MC	DSH	15	No	b	W/D	1	Yes
17	16	5	FS	DSH	20	No	a	D/W	1	Yes
18	A	7	FS	DSH	20	Yes	c	W	7	No
19	B	5	M	DSH	51‖	Yes	b	D	4	
20	B	8	FS	DLH	5	NOE¶	a	W	3	
21	B	7	MC	Somali	17	NOE	a	W	3.5	
22	C	4	FS	DSH	13	NOE	f, g	W	4	
23	B	7	FS	DSH	1	NOE	a	W	2	
Average	18.8	6.7			9.7#				4.0	
SD	4.3	2.9			6.2				2.7	

*M, male; MC, castrated male; F, female; FS, spayed female. †DSH, domestic short hair; DLH, domestic long hair; ABY, Abyssinian; Himal/X, Himalayan cross. ‡P, purified; a, Hill's C/D; b, Hill's Science Diet Maintenance; c, Hill's H/D; d, Purina Cat Chow; e, 9 Lives Beef and Liver; f, Carnation Fancy Feast Beef and Liver; g, Blue Mountain Kitty O's; D, dry; W, wet; foods are listed in the order of most to least commonly fed. §Cat's diet was changed to a mixture of foods 2 months prior to presentation. ‖Cat diagnosed as having an aortic thromboembolism; the normal taurine concentration may be explained by release of taurine from ischemic skeletal muscle. ¶NOE, no ophthalmologic examination was performed prior to death. #Cats 14 and 19 were not included in the taurine summary statistics for reasons stated above.

In dilated cardiomyopathy in both humans and cats, two subsets of individuals are recognized: one large subset progresses rapidly to death, the other smaller subset stabilizes and even improves clinically or echocardiographically (*18*). Prior to this study, most cats with DCM could not be stabilized on any method of therapy. Occasionally a cat could be controlled for 6 to 12 months, and rarely for longer than 2 years (*19*).

We retrospectively collected data on a third group of 27 cats diagnosed as having DCM at our hospital between 1 January 1980 and 1 November 1986. Of these cats, 23 (85%) died 32 ± 53 (range = 0.5 to 240) days after first arriving at the hospital. Four of these cats are alive today. Three of the surviving cats have dietary histories that demonstrate a change in diet coincident with improvement of clinical signs. One of these three cats relapsed when it was again fed a diet that we have shown causes low plasma taurine (*20*); subsequent recovery was again associated with dietary alteration. The fourth cat is cat 3 in Table 1. This cat was diagnosed as having DCM in June 1985 and was clinically stabilized on inotropic and diuretic therapy with no evidence of improved myocardial function on repeated echocardiograms. In January 1987 this cat became critically ill with signs of biventricular failure and cardiogenic shock. Supplementation with taurine resulted in normalized echocardiographic parameters of left ventricular function. This cat is now clinically normal and receives no medication.

That low plasma taurine was the primary cause rather than the result of myocardial failure is suggested by the following: (i) all client-owned cats were eating commercial diets that induce low plasma taurine (*20*); (ii) 2 of 11 laboratory cats with experimentally induced low plasma taurine developed DCM; and (iii) affected cats in both groups improved clinically and echocardiographically when supplemented with taurine.

Since our study shows that chronic taurine depletion causes DCM in cats, the possibility that taurine depletion is associated with DCM in other species should also be investigated. However, in view of the metabolic requirements for taurine in the cat compared with other species, such an association seems unlikely. Chronic taurine depletion in the cat may provide a new model for studying ventricular function, potential inotropic agents, and the mechanisms by which taurine affects myocardial function.

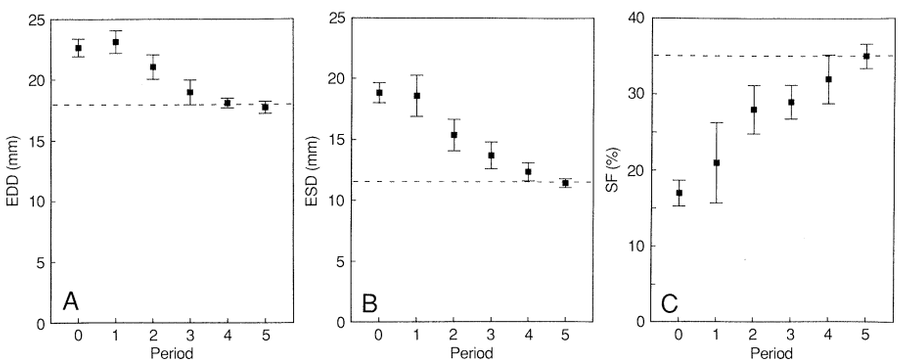

Fig. 2. Mean ± SEM of (**A**) EDD, (**B**) ESD, and (**C**) SF for the 15 taurine-supplemented cats with DCM. Each period represents a 2-week interval except period 5, which represents a 4-week interval including weeks 9 through 12 (that is, period 0 is the date taurine therapy was begun, period 1 represents weeks 1 and 2 after beginning taurine therapy, period 2 represents weeks 3 and 4 after beginning taurine therapy, and so on) (see Table 1). The horizontal dotted lines represent the upper (EDD and ESD) and lower (SF) limits of clinical normality (95% confidence interval) in cats (*8*). The level of significance for differences in echocardiographic parameters determined for each 2-week period after beginning taurine therapy is shown in Table 2.

Table 2. Results of statistical analysis of changes in EDD, ESD, and SF. Each period is contrasted with period 0 (day of original observation). Mean plasma taurine concentrations are reported. Normal plasma taurine concentration for client-owned cats determined in our laboratory is 82 ± 33 nmol/ml.

Period	Weeks	*N*	Probability when contrasted with period 0			Taurine (nmol/ml)		
			EDD	ESD	SF	Mean	SD	Range
0	0	17				9.7	6.2	1–20
1	2	8	1.0000	1.0000	1.0000	551	533	133–1898
2	3–4	8	0.7950	0.0710	0.0370	419	339	72–1058
3	5–6	10	0.0035	0.001	0.0095	574	840	99–2593
4	7–8	8	0.0005	0.0005	0.0015	460	331	75–967
5	9–12	14	0.0005	0.0005	0.0005	521	342	185–1210
Normal		55				82	33	31–147

REFERENCES AND NOTES

1. J. Wynne and E. Braunwald, in *Heart Disease*, E. Braunwald, Ed. (Saunders, Philadelphia, 1984), pp. 1400–1408; L. P. Tilley, S-K. Liu, P. R. Fox, in *Textbook of Veterinary Internal Medicine. Diseases of the Dog and Cat*, S. J. Ettinger, Ed. (Saunders, Philadelphia, 1983), pp. 1029–1051; J. F. Van Vleet and V. J. Ferrans, *Am. J. Pathol.* **124**, 98 (1986); S-K. Liu and L. P. Tilley, *Yale J. Biol. Med.* **53**, 191 (1980).
2. S-K. Liu, Animal Medical Center, New York, personal communication.
3. K. C. Hayes, R. E. Carey, S. Y. Schmidt, *Science* **188**, 949 (1975); K. C. Hayes, *Nutr. Rev.* **43**, 65 (1985); K. Knopf, J. A. Sturman, M. Armstrong, K. C. Hayes, *J. Nutr.* **180**, 773 (1978); B. Rabin, R. J. Nicolosi, K. C. Hayes, *ibid.* **106**, 1241 (1976); H. S. Geggel *et al.*, *N. Engl. J. Med.* **312**, 142 (1985); J. A. Sturman *et al.*, *Int. J. Dev. Neurosci.* **2**, 121 (1984); S. Y. Schmidt, E. L. Berson, G. Watson, C. Huang, *Invest. Ophthalmol.* **16**, 673 (1977).
4. D. A. Vessey, *Biochem. J.* **174**, 621 (1977); R. W. Chesney, *Adv. Pediatr.* **32**, 1 (1985).
5. F. Franconi *et al.*, *Biochem. Pharmacol.* **31**, 3181 (1982); R. J. Huxtable, J. Chubb, J. Azari, *Fed. Proc.* **39**, 2685 (1980); R. J. Huxtable and J. Chubb, *Science* **198**, 409 (1977).
6. J. P. Chovan, E. C. Kulakowski, S. Sheakowski, S. W. Schaffer, *Mol. Pharmacol.* **17**, 295 (1980); J. Chubb and R. Huxtable, *Eur. J. Pharmacol.* **48**, 357 (1978); J. Chubb and R. Huxtable, *ibid.*, p. 369; S. W. Schaffer, J. Kramer, J. P. Chovan, *Fed. Proc.* **39**, 2691 (1980); J. P. Chovan, E. C. Kulakowski, B. W. Benson, S. W. Schaffer, *Biochim. Biophys. Acta* **551**, 129 (1979); W. G. Lampson, J. H. Kramer, S. W. Schaffer, *Can. J. Physiol. Pharmacol.* **61**, 457 (1983); S. W. Schaffer, M. Seyed-Mozaffari, J. Kramer, B. H. Tan, in *Taurine: Biological Actions and Clinical Perspectives*, S. S. Oja *et al.*, Eds. (Liss, New York, 1985), pp. 167–175; M. S. Mozaffari, B. H. Tan, M. A. Lucia, S. W. Schaffer, *Biochem. Pharmacol.* **35**, 985 (1986); J. H. Thurston, R. E. Hauhart, E. F. Naccarato, *Science* **214**, 1373 (1981).
7. R. Huxtable and R. Bressler, *Science* **184**, 1187 (1974); M. B. Peterson, R. J. Mead, J. D. Welty, *J. Mol. Cell. Cardiol.* **5**, 139 (1973); Takihara *et al.*, *Am. Heart J.* **112**, 1278 (1986).
8. J. Azuma *et al.*, *Clin. Ther.* **5**, 398 (1983); J. Azuma *et al.*, *Curr. Ther. Res.* **34**, 34 (1983); J. Azuma *et al.*, *Int. J. Cardiol.* **2**, 303 (1982); J. Azari, T. Reisine, A. Barbeau, H. I. Yamamura, R. Huxtable, *Can. J. Neurol. Sci.* **6**, 223 (1979); J. Azari, P. Brumbaugh, A. Barbeau, R. Huxtable, *ibid.* **7**, 435 (1980); M. J. McBroom and J. D. Welty, *J. Mol. Cell. Cardiol.* **9**, 853 (1977).
9. J. A. Sturman, A. D. Gargano, J. M. Messing, H. Imaki, *J. Nutr.* **116**, 655 (1986); J. A. Sturman, D. K. Rassin, K. C. Hayes, G. E. Gaull, *ibid.* **108**, 1462 (1978).
10. P. R. Fox and B. R. Bond, *Am. J. Vet. Res.* **46**, 1479 (1985); F. S. Pipers and R. J. Hamlin, *J. Am. Vet. Med. Assoc.* **176**, 57 (1980).
11. A Beckman 121MB amino acid analyzer was used [J. A. O'Donnell, Q. R. Rogers, J. G. Morris, *J. Nutr.* **111**, 1111 (1981)].
12. The preparations used were: taurine (Sigma); Furosemide-Lasix (Hoechst-Roussel); Captopril-Capoten (Squibb); Digoxin-Lanoxin (Burroughs Wellcome).
13. G. W. Snedecor and W. G. Cochran, *Statistical Methods* (Iowa State Univ. Press, Ames, 1980), pp. 115–117; P. Spector *et al.*, in *SAS/STAT Guide for Personal Computers*, S. P. Joyner, Ed. (SAS Institute Inc., Gary, IN, ed. 6, 1985), pp. 183–260.
14. D. V. Unverferth and P. B. Baker, *Am. J. Med.* **80**, 22 (1986).
15. L. J. Waber, D. Valle, C. Neill, S. DiMauro, A. Shug, *J. Pediatr.* **101**, 700 (1982); A. M. Glasgow *et al.*, *Pediatr. Res.* **17**, 319 (1983); B. W. Keene, in *Proceedings of the 4th Symposium of the American College of Veterinary Internal Medicine*, San Diego, CA (1986), vol. 2, pp. 9.51–9.54.
16. W. Grossman, E. Braunwald, T. Mann, L. P. McLaurin, L. H. Green, *Circulation* **56**, 845 (1977); J. D. Marsh, L. H. Green, J. Wynne, P. F. Cohn, W. Grossman, *Am. J. Cardiol.* **44**, 1311 (1979).

17. R. Ader *et al.*, *Circulation* **61**, 931 (1980); S. A. Atlas, A. P. Niarchos, D. B. Case, *Am. J. Nephrol.* **3**, 118 (1983); T. W. Smith, E. Braunwald, in *Heart Disease*, E. Braunwald, Ed. (Saunders, Philadelphia, 1984), p. 533.
18. B. R. Bond and P. R. Fox, *Vet. Clinics No. Am.* **14**, 1031 (1984); V. F. Fuster *et al.*, *Am. J. Cardiol.* **47**, 525 (1981).
19. N. K. Harpster, in *Current Veterinary Therapy*, R. Kirk, Ed. (Saunders, Philadelphia, 1987), vol. 9, p. 385.
20. Q. R. Rogers, J. A. Cooke, J. G. Morris, P. D. Pion, unpublished data. When wet (canned) diets a, b, e, and f (Table 1) were fed to 38 normal cats, previously fed various commercial diets, plasma taurine concentrations decreased from 69 ± 35 (mean ± SD) to 18 ± 10 nmol/ml in 3 to 6 weeks ($P < 0.001$). Feeding dry diets a and d to 11 normal cats, previously fed various commercial diets, decreased plasma taurine concentrations from 83 ± 52 to 29 ± 30 nmol/ml in 3 to 6 months ($P < 0.02$). These cats were previously fed various commercial diets including diets a, b, c, d, e, f, and g. In addition, of the cats fed canned diets a and e for 3 to 7 months, two died of DCM and two others have echocardiographically diagnosed DCM.
21. R. A. O'Rourke *et al.*, *Circulation* **69**, 854A (1984).
22. We thank J. G. Fadel for statistical analysis, members of the ophthalmology service of the University of California, Davis, Veterinary Medical Teaching Hospital for performing funduscopic examinations on all cats with DCM, and C. Williams and S. Lee for technical assistance. We especially thank C. Glassauer for her persistent interest in this project and for asking whether taurine deficiency in the cat could cause DCM.

15 April 1987; accepted 25 June 1987

Age and Diet of Fossil California Condors in Grand Canyon, Arizona

STEVEN D. EMSLIE*

A dozen new radiocarbon dates, together with a thorough review of its fossil distribution, shed new light on the time and probable cause of extinction of the California condor, *Gymnogyps californianus*, in Grand Canyon, Arizona. The radiocarbon data indicate that this species became extinct in Grand Canyon, and other parts of the inland West, more than 10,000 years ago in coincidence with the extinction of megafauna (proboscidians, edentates, perissodactyls). That condors relied on the megafauna for food is suggested by the recovery of food bones from a late Pleistocene nest cave in Grand Canyon. These fossil data have relevance to proposed release and recovery programs of the present endangered population of California condors.

DURING THE LATE PLEISTOCENE (Rancholabrean Land Mammal Age) at least two species of large vultures lived in North America. These species were the extinct condor, *Breagyps clarki*, known primarily from Rancho La Brea, California, and the California condor, *Gymnogyps californianus* (*1*), which is near extinction today. These species differed from one another primarily in the bill and cranium; *B. clarki* had an elongated beak that may have allowed it to feed on viscera deep inside carcasses, much as griffon vultures do in Africa today (*2*). Fossils of *G. californianus* have been reported from sites throughout western North America and Florida, of which only two have been radiocarbon dated previously (*3*) (Table 2). The presence of California condor remains on the surface of cave floors, occasionally with archeological artifacts, has led some authors to suggest that until recently *G. californianus* ranged and nested in many areas of the western United States (*4, 5*). This suggestion implies that the condor's decline has occurred only within the past two centuries. With the exception of sites in coastal California and Oregon (*6*) no direct association of condor remains with archeological artifacts are known. Moreover, in dry caves in the western United States it is not unusual to find surface remains of extinct mammals dated at 11,000 to 12,000 years old or older next to artifacts dating from 1,000 to 4,000 years old.

An alternative hypothesis is that the condor was widely extirpated at the close of the Pleistocene in conjunction with the disappearance of many large mammals and birds, but managed to survive in Pacific coastal regions where it still occurs today (*7*). Until now, no reliable method has been available to test either of these hypotheses. The tandem accelerator mass spectrometer (TAMS) provides accurate radiocarbon analysis of very small samples (1 to 3 mg or less) of organic material and provides a means for obtaining dates on many fossil birds. I report the first series of dates completed on a single species of fossil bird in an effort to determine the exact time and cause of the condor's extinction at eight sites in the Grand Canyon of Arizona and at five sites in New Mexico and Texas. This study also provides evidence of the feeding habits of fossil *G. californianus*.

Surface and subsurface fossils of condors were collected from eight caves in Grand Canyon in 1984 (Table 1). Most of these caves are located high on vertical cliffs, inaccessible to all animals except birds and small, cliff-dwelling vertebrates; similar localities are used for nesting by the California condor today (*8*). In all but one cave, only one to four condor bones were found on the surface. The exception, Sandblast Cave (elevation, 900 m), yielded partial skeletons of at least five condors. These remains were deposited in a large packrat midden just inside the entrance of the cave and were found in association with numerous condor eggshell and feather fragments, and bone fragments of large mammals including horse (*Equus* sp.), bison (*Bison* sp.), mammoth (*Mammuthus* sp.), camel (?*Camelops* sp.), and extinct mountain goat (*Oreamnos harringtoni*). Bone porosity indicates young individuals, perhaps near fledgling age. Because the bones are complete and partly articulated, it is reasonable to infer that the condors died in the cave and that this cave was used for nesting by adult condors.

The bones of large mammals associated

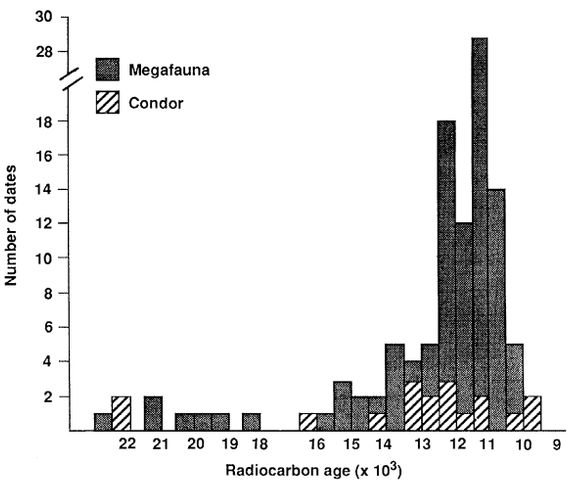

Fig. 1. Distribution of radiocarbon dates on Pleistocene megafauna and California condor, *Gymnogyps californianus*. Megafauna dates are from D. J. Meltzer and J. I. Mead (*12*); only those dates considered most reliable [score of 8 or 9 (*12*, figure 1, p. 163)] are plotted. On the basis of their rating system, all dates of condor bone are rated 7 and all those of tissue are rated 9. Note the break on the vertical axis to account for the large number of dates between 11,000 and 11,500 B.P.

University of Florida, Department of Zoology, Gainesville, FL 32611.

*Present address: Point Reyes Bird Observatory, 4990 Shoreline Highway, Stinson Beach, CA 94970.