Evaluation of calciotropic hormones in cats with odontoclastic resorptive lesions

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Objective—To assess associations between epidemiologic and laboratory variables and calciotropic hormones in cats with odontoclastic resorptive lesions (ORLs).

Animals—182 client-owned cats older than 1 year of age with oral disease.

Procedure—Information on medical history, behavior, living environment, and feeding management was assessed by use of a questionnaire. After induction of general anesthesia, oral examination was performed following standardized protocols and included dental probing and full-mouth radiography. Laboratory analyses included evaluation of FeLV-FIV status, serum biochemical analyses, CBC, urinalysis, and serum concentrations of intact parathyroid hormone (iPTH), parathyroid hormone-related peptide (PTHrP), 25-hydroxyvitamin D (25-OHD), free thyroxine (fT_4), and ionized calcium (iCa).

Results—ORLs were identified in 72.5% of cats. Mandibular third premolars were the most commonly affected teeth. Cats with ORLs were significantly older (mean, 9.2 years) than cats without ORLs (mean, 6.6 years). Multivariate logistic regression analysis revealed that 25-OHD, urine specific gravity, jaw-opening reflex on probing, and missing teeth were significant variables, even after accounting for age. Cats with ORLs had significantly higher mean serum concentration of 25-OHD (112.4 nmol/L) and significantly lower mean urine specific gravity (1.0263), compared with cats without ORLs (89.8 nmol/L and 1.0366, respectively).

Conclusions and Clinical Relevance—Results did not indicate associations between iPTH, PTHrP, or fT_4 and development of ORLs. In affected cats, the importance of high serum 25-OHD and low urine specific gravity has not been determined. (*Am J Vet Res* 2005;66:1446–1452)

Feline **odontoclastic resorptive lesions (ORLs)** are a common and frustrating condition in small animal practice, resulting in loss of teeth caused by progressive resorption of dental hard tissues. Depending on the population of cats studied and investigative methods applied, 20% to 75% of domestic cats worldwide may have 1 or more ORLs.[1]

Resorption of cementum and superficial dentin in humans may be self-limiting.[2] In cats, although attempts at repair by fibroblasts, cementoblasts, and osteoblasts can be identified, the resorption of permanent teeth is usually progressive and continues until the roots are completely resorbed or the crown breaks off, leaving root remnants in the alveolar bone.[1] The focus of previous research has been resorption that commences at the gingival margin.[3] Although the periodontal space is narrow in mandibular premolars and molars in adult cats,[4] fusion of the tooth roots with alveolar bone, also frequently observed, has not been explored in the literature. A recent histologic study[5] revealed that early lesions of ORLs are noninflammatory in nature. When clinically and radiographically healthy teeth from adult cats with ORLs on other teeth were histologically evaluated, periodontal ligament degeneration with gradual narrowing of the periodontal space and ankylotic fusion of the tooth root with alveolar bone were identified. Ankylosed teeth are at risk of being incorporated into the normal bone remodeling process, and affected tooth roots may be subject to resorption and replacement by bone.[6]

Although information on the pathogenesis of feline ORLs has become increasingly available, the etiology has remained speculative.[1] Retrospective studies[7,a] of zoo and museum collections of feline skulls reveal a low prevalence of ORLs prior to the 1960s, suggesting that increased recognition of ORLs during the past 4 decades might be associated with aspects of domestication, such as altered feeding practices, neutering, and vaccinations.[1] In an epidemiologic study,[8] increased prevalence of feline ORLs was significantly associated with a calcium-deficient diet, decreased radiopacity of lamina dura and alveolar bone, and horizontal alveolar bone loss. However, permanent teeth have not been observed to undergo resorption in cats and dogs with nutritional secondary hyperparathyroidism,[1] and in humans with hyperparathyroidism, radiographically apparent bone resorption is usually not accompanied by tooth resorption.[9,10] Furthermore, no apparent association has been found between ORLs and serum biochemical markers of bone turnover in domestic cats.[11]

In general, the roots of teeth are resistant to resorption, even during systemic diseases that are associated with marked bone resorption. The most important systemic stimulators of osteoclastic bone resorption are **parathyroid hormone (PTH)** and **1,25-dihydroxyvitamin D_3 ($1,25[OH]_2D_3$)**, whereas the most important

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local stimulators are **prostaglandin (PG)** E_2 and **interleukin-1 (IL-1)**.[12] The thyroid hormones, vitamin A, and **parathyroid hormone-related peptides (PTHrP)** also systemically increase osteoclastic activity. There is an extensive list of potential local regulators, including other cytokines and growth factors. Many of these factors have dual activity, in the sense that they stimulate bone resorption both directly and indirectly by increasing endogenous PG production.[12]

In humans, pathologic tooth resorption is usually limited to 1 tooth and associated with a history of physical trauma (eg, contusion, subluxation, luxation, avulsion, orthodontic tooth movement, bleaching, or partial vital pulpectomy).[2] In domestic cats, resorption typically affects multiple permanent teeth at various sites in the mouth.[1] Because trauma and periodontal inflammation are not likely to cause resorption of multiple teeth, ORLs in cats may be associated with metabolic or systemic disorders. To the authors' knowledge, no study has been performed to assess calciotropic hormones in cats with and without ORLs. The purpose of the study reported here was to assess associations between epidemiologic and laboratory variables and calciotropic hormones in cats with ORLs.

Materials and Methods

Data were collected from cats older than 1 year of age evaluated from 1997 to 2001 at 4 private animal care facilities (Mesa Veterinary Hospital, Mesa, Ariz; South West Veterinary Specialty Center, Tucson, Ariz; Aid Animal Dental Clinic, Scottsdale, Ariz; and Main Street Small Animal Hospital, San Diego, Calif) and 1 veterinary teaching hospital (Matthew J. Ryan Veterinary Hospital, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pa) for prophylactic or therapeutic treatment of oral cavity disease. Informed client consent was obtained prior to inclusion of any cat in the study.

Information on the cat's medical history, environment, behavior, and feeding management was requested from owners by use of a standardized questionnaire that included questions about history of home dental care, oral cavity disease, urogenital disease, food intolerance, infections and skin disease, vomiting, and indoor versus outdoor status; vaccination against agents of upper respiratory tract infections, panleukopenia virus, FeLV, infectious peritonitis virus, and rabies virus; other animals in household; hunting for prey; eating grass and house plants; toys available and chewing on toys; and feeding canned versus dry food, commercial treats, meat (including fish), giblets, table foods, and dairy products.

Food was withheld for 12 hours, and blood and urine samples were collected prior to or at the time of anesthetic induction. A rapid immunoassay[b] was used for simultaneous detection of FeLV antigen and FIV antibody in serum. Urine was collected via cystocentesis and evaluated immediately by means of reagent strips[c] and refractometry. Serum biochemical analyses[d] and CBCs[e] were performed in-house or at local laboratories by use of routine automated techniques. Differential counts of WBCs were evaluated manually.

Serum concentrations of intact PTH, PTHrP, **25-hydroxyvitamin D (25-OHD)**, fT_4, and **ionized calcium (iCa)** were assessed at the Animal Health Diagnostic Laboratory of Michigan State University. Serum iPTH[f] and PTHrP[g] concentrations were measured by use of immunoradiometric assays. Serum iCa[h] concentrations were determined with a selective ion electrode-dialysis membrane. Assays for iPTH, PTHrP, and iCa have been validated for use in domestic cats.[13]

Serum 25-OHD[i] concentrations were determined by use of **radioimmunoassay (RIA)**. After extraction from serum with acetonitrile, 25-OHD was reconstituted in assay buffer and assayed. Radioimmunoassay revealed cross-reaction with 25-OHD_2, 25-OHD_3, and their metabolites. There was no appreciable cross-reaction with vitamin D_2 or vitamin D_3. The intra-assay **coefficients of variation (CVs)** at 60 and 161 nmol/L were 9.1% and 8.7%, respectively, and the interassay CVs were 13% and 13%, respectively. When samples were diluted 1:2 and 1:4 with water, recovery was 99% and 89%, respectively, indicating good parallelism. Sensitivity of the assay at 90% B/B0 (bound with x amount of hormone divided by bound at zero [without any hormone]) was 7 nmol/L.

Serum fT_4[j] concentrations were measured by use of RIA after dialysis. The fT_4 by dialysis assay, designed for human diagnostic testing, uses a dialysis cell (Nelson cell) with 200 µL of sample placed above the dialysis membrane with 2.4 mL of physiologic dialysate solution. Dialysis proceeded for 16 to 18 hours at 37°C, at which time the dialysate (800 µL) was assayed in duplicate via an iodine I 125-T_4 RIA procedure. The intra-assay CVs were 12%, 11%, and 8% at 8, 53, and 102 pmol/L, respectively. The interassay CVs were 24%, 11%, and 14% at 7, 56, and 110 pmol/L, respectively (n = 10). When T_4 was added to the dialysate (range, 13 to 77 pmol/L), the assay was able to quantify 83% to 91% of the additional T_4.

Three board-certified veterinary dentists and a veterinarian with a special interest in veterinary dentistry performed the oral examinations on cats. Standardized protocols were used for recording oral disease. The crown surfaces of all teeth were evaluated with a dental explorer, and full-mouth dental radiographs were obtained with dental radiographic film or a digital dental radiography system. Cats with missing teeth were considered ORL-free if clinical and radiographic evidence of root remnants or resorbing roots were absent in the area of a missing crown. Oral variables recorded included whether the tooth was affected or unaffected by ORLs, determined by use of a described staging system.[1] Also recorded were the number of missing teeth (tooth crown not visible or evident), stomatitis (inflammation of nongingival oral mucosae and oral inflammation other than isolated contact ulcers), and the presence of a jaw-opening reflex as a result of dental or periodontal probing.

Statistical analyses—Differences between cats with and without ORLs were assessed by use of the χ^2 or Fisher exact test (2 × 2 tables) for categoric data and a Student *t* test for continuous data. Categoric data are given as percentage frequency of occurrence. Continuous data are given as mean ± SD. Where applicable, data are presented as **odds ratios (ORs)** with 95% **confidence intervals (CIs)**. Multivariate logistic regression analysis was used to identify factors that had significant relationships with ORLs after taking other variables into account. Model selection was determined by use of simultaneous inclusion and backward elimination. Significance was defined as $P < 0.05$. All analyses were performed with statistical software.[k]

Results

One hundred eighty-two cats were enrolled in the study. One hundred thirty-two of 182 (72.5%) cats had ORLs, whereas 50 of 182 (27.5%) cats were free of ORLs. The most commonly affected teeth were the mandibular third premolars (103/706 [14.6%] teeth), mandibular first molars (80/706 [11.3%] teeth), and maxillary fourth premolars (74/706 [10.5%] teeth; **Table 1**). The most commonly missing teeth in cats

with ORLs were the maxillary second premolars (112/825 [13.6%] teeth) and the mandibular third premolars (106/825 [12.8%] teeth). Of the 50 cats without ORLs, 20 had complete permanent dentition, whereas 30 had teeth missing without clinical or radiographic evidence of roots, root remnants, or resorbing roots. Teeth most commonly missing in cats without ORLs were the maxillary second premolars (19/134 [14.2%] teeth) and the mandibular (17/134 [12.7%] teeth) and maxillary first incisors (13/134 [9.7%] teeth). Cats with ORLs had significantly ($P < 0.001$) more teeth missing (mean ± SD, 6.3 ± 5.3 teeth) than cats without ORLs (2.7 ± 4.1 teeth). A jaw-opening reflex in response to probing was significantly ($P = 0.002$) more common in cats with ORLs (34.2%), compared with cats without ORLs (10.6%; OR, 4.4; 95% CI, 1.5 to 15.1). Stomatitis was not associated with ORLs.

Mean ± SD age of the study cats was 8.5 ± 4.1 years (range, 1.3 to 17.6 years). Cats with ORLs were significantly ($P < 0.001$) older (mean, 9.2 ± 4.0 years) than cats without ORLs (mean, 6.6 ± 3.7 years). Weight, sex, and breed were not associated with ORLs.

The majority of cats in the study (> 90%) received no oral care at home. Cats with ORLs vomited more often (mean, 2.2 ± 3.7 times) each month than cats without ORLs (mean, 0.9 ± 1.7 times; $P = 0.007$). Cats with ORLs were significantly ($P = 0.006$) more likely to have a history of oral disease (67.6%) than cats without ORLs (42.2%; OR, 2.9; 95% CI, 1.3 to 6.2). Cats with ORLs were significantly ($P = 0.04$) less likely to be vaccinated against agents of upper respiratory tract infections (66.7% vaccinated), compared with cats without ORLs (84.6% vaccinated; OR, 0.36; 95% CI, 0.11 to 1.0). Differences in other medical history and enviromental variables between cats with and without ORLs were not significant.

Differences in feeding canned and dry diets between cats with and without ORLs were not significant. Both groups of cats had almost equal access to dry diets (> 90%; **Table 2**). Cats with ORLs were more likely to be fed raw or heat-processed meat or fish than cats without ORLs (OR, 2.6; 95% CI, 1.1 to 7.1). Only cats with ORLs received giblets. Differences in other feeding management variables between cats with and without ORLs were not significant. Chicken was the most commonly fed meat product. Liver was the most commonly fed giblet. Milk was the most commonly fed dairy product.

Serum samples were tested for FeLV antigen (n = 137 cats) and FIV antibodies (138). No cat yielded positive results for FeLV antigen. Four of 104

Table 1—Frequency of missing teeth or teeth with odontoclastic resorptive lesions (ORLs) in cats with and without ORLs.

		Cats with ORLs				Cats without ORLs	
Tooth location		**No. affected**	**(%)***	**No. missing**	**(%)***	**No. missing**	**(%)***
Maxilla	I1	36	5.1	79	9.6	13	9.7
	I2	29	4.1	53	6.4	9	6.7
	I3	36	5.1	75	9.1	11	8.2
	C	53	7.5	27	3.3	2	1.5
	P2	34	4.8	112	13.6	19	14.2
	P3	70	9.9	50	6.1	9	6.7
	P4	74	10.5	16	1.9	7	5.2
	M1	11	1.6	70	8.5	11	8.2
Mandible	I1	36	5.1	70	8.5	17	12.7
	I2	15	2.1	52	6.3	6	4.5
	I3	20	2.8	44	5.3	6	4.5
	C	73	10.3	18	2.2	3	2.2
	P3	103	14.6	106	12.9	11	8.2
	P4	36	5.1	14	1.7	3	2.2
	M1	80	11.3	39	4.7	7	5.2
Total		**706**	**100**	**825**	**100**	**134**	**100**

*Percentage of all affected or missing teeth.
I1 = First incisor. I2 = Second incisor. I3 = Third incisor. C = Canine. P2 = Second premolar. P3 = Third premolar. P4 = Fourth premolar. M1 = First molar.

Table 2—Feeding management of cats with and without ORLs.

	Cats with ORLs		Cats without ORLs		
Diet	**N**	**%**	**N**	**%**	***P* value**
Canned food	82/109	74.6	28/46	60.9	NS
Dry food	108/110	98.2	42/46	91.3	NS
Commercial treats	40/108	37.0	16/46	34.8	NS
Meat	39/110	35.5	8/46	17.4	0.035
Giblets	8/108	7.4	0/46	0.0	NS
Table foods	8/107	7.5	5/46	10.9	NS
Dairy products	27/108	25.0	10/46	21.7	NS

N = Number of cats fed the food item divided by the population of cats with and without ORLs. NS = Not significant.

Table 3—Results of serum biochemical analyses (mean ± SD) in cats with and without ORLs.

Analyte	Cats with ORLs	Cats without ORLs	*P* value
BUN (mg/dL)	26 ± 7.8	22.43 ± 5.1	< 0.001
Phosphorus (mg/dL)	5.11 ± 1.1	4.63 ± 0.99	0.009
Calcium-to-phosphorus ratio	1.88 ± 0.51	2.13 ± 0.58	0.005
Total calcium (mg/dL)	9.12 ± 0.89	9.35 ± 0.85	NS
Ionized calcium (mmol/L)	1.26 ± 0.1	1.24 ± 0.11	NS
Calcium-phosphorus product	46.4 ± 9.9	43.2 ± 9.7	NS
Creatinine (mg/dL)	1.7 ± 0.54	1.56 ± 0.36	NS
Magnesium (mg/dL)	2.71 ± 1.02	2.44 ± 0.72	NS
Total protein (g/dL)	6.91 ± 0.99	6.89 ± 0.88	NS
Sodium (mEq/L)	149.2 ± 4.3	149.2 ± 4.4	NS
Potassium (mEq/L)	4.06 ± 0.43	4.09 ± 0.4	NS
Sodium-to-potassium ratio	37.02 ± 3.8	36.82 ± 3.7	NS
Albumin (g/dL)	2.89 ± 0.45	2.95 ± 0.43	NS
Globulins (g/dL)	4.01 ± 0.8	3.93 ± 0.8	NS
Albumin-to-globulin ratio	0.75 ± 0.18	0.78 ± 0.19	NS
Glucose (mg/dL)	158.8 ± 74.4	146.1 ± 41.9	NS
Bilirubin (mg/dL)	0.454 ± 0.87	0.378 ± 0.35	NS
Alkaline phosphatase (U/L)	33.7 ± 22.6	38.3 ± 19	NS
Asparatate aminotransferase (U/L)	27.6 ± 16.5	25.7 ± 11.5	NS
Alanine aminotransferase (U/L)	47.5 ± 35.7	55.8 ± 46.9	NS
γ-glutamyltransferase (U/L)	2.42 ± 6.1	2.2 ± 2.9	NS
Creatine kinase (U/L)	301 ± 461	194 ± 176	NS
Amylase (U/L)	913 ± 277	856 ± 268	NS
Lipase (U/L)	69.2 ± 58.8	61.4 ± 47.9	NS
Cholesterol (mg/dL)	153.3 ± 48.6	149.1 ± 56.4	NS
Osmolality (mosm/kg)	302.2 ± 8.5	299.7 ± 6.2	NS

See Tables 1 and 2 for key.

Table 4—Serum concentrations (mean ± SD) of calciotropic hormones in cats with and without ORLs.

Analyte	Reference range	Cats with ORLs	Cats without ORLs	*P* value
25-hydroxyvitamin D (nmol/L)	65–170	112.4 ± 47.1	89.8 ± 33.4	< 0.001
Intact parathyroid hormone (pmol/L)	0–4	2.97 ± 3.53	2.66 ± 2.84	NS
Parathyroid hormone–related peptide (pmol/L)	< 1	0.078 ± 0.281	0.072 ± 0.274	NS
Free thyroxine (pmol/L)	10–50	34.2 ± 9.0	35.5 ± 11.2	NS

See Tables 1 and 2 for key.

Table 5—Results of multivariate logistic regression analysis of variables associated with ORLs in cats.

Variable	Estimate	SE	*P* value	Odds ratio	95% Confidence interval
Intercept	34.817	13.839	0.0119	NS	NS
Age (y)	0.204	0.065	0.0016	1.2	1.1–1.4
No. of missing teeth	2.144	0.651	0.001	8.5	2.4–30.6
Jaw-opening reflex on probing	–0.375	0.134	0.0053	0.69	0.5–30.89
Serum 25-OHD (nmol/L)	0.022	0.007	0.0023	1.02	1.01–1.04
Urine specific gravity (units X 100)	0.128	0.058	0.027	1.14	1.02–1.27

25-OHD = 25-hydroxyvitamin D.
See Tables 1 and 2 for remainder of key.

(3.8%) cats with ORLs yielded positive results for FIV antibodies. None of the 34 cats without ORLs had positive results for FIV antibodies. Infection with FeLV or FIV antibody status was not associated with ORLs.

Mean urine specific gravity was significantly (P = 0.002) lower in cats with ORLs (1.026 ± 0.016), compared with cats without ORLs (1.037 ± 0.02). Differences in other urine variables were not significant. Mean serum concentration of BUN was significantly higher in cats with ORLs than in cats without ORLs (**Table 3**). Mean serum phosphorus concentration was significantly higher and mean calcium-phosphorus ratio was significantly lower in cats with ORLs, compared with cats without ORLs. Differences in other serum biochemical variables between cats with and without ORLs were not significant. There were no hematologic differences between cats with and without ORLs.

Mean 25-OHD serum concentration was significantly higher in cats with ORLs, compared with cats without ORLs, although neither exceeded the reference range (**Table 4**). There were no significant differences in serum concentrations of iPTH, PTHrP, or fT_4 between cats with and without ORLs.

Results of multivariate logistic regression analysis indicated that the following variables were associated

with ORLs: age, jaw-opening reflex on probing, missing teeth, urine specific gravity, and serum 25-OHD concentration (**Table 5**). Each 1-year increase in age was associated with an increased risk of ORLs from 8% to 40%. Risk of ORLs was 8.5 times as great with the presence of a jaw-opening reflex on probing, compared with the absence of that reflex. Each missing tooth was associated with an increased risk of ORLs from 1% to 27%. Each decrease of 0.01 in urine specific gravity was associated with an increased risk of ORLs from 10% to 47%. Each increase of 1 nmol/L in serum 25-OHD concentration was associated with an increased risk of ORLs from 1% to 4%.

Discussion

It has been reported[14] that ORLs may occur on certain teeth more than others and that the disease is associated with increasing age and missing teeth. On the basis of results of dental probing with a hand instrument and examination of dental radiographs, 72.5% of cats in the present sample population had ORLs. Cats with ORLs were significantly older and had significantly more teeth missing, compared with cats without ORLs. The most commonly affected teeth were the mandibular third premolars. As in previous studies,[14-16] ORLs were not associated with sex, breed, or weight. A jaw-opening reflex was significantly more frequent in cats with ORLs, compared with cats without ORLs, a finding that differed from results of a longitudinal study[17] in which no correlation between jaw-opening reflex and ORLs was identified.

In a study[18] that made limited use of dental radiography, a higher prevalence of ORLs was found in cats infected with FIV (6/10), compared with age-matched cats free of FIV (3/9). In the present study, dental radiographs were taken in all cats to assess the presence of ORLs; no cat had positive results for FeLV, and only 4 of 104 (3.8%) cats with ORLs had positive results for FIV antibodies. Similar prevalences of FeLV (0% to 2%) and FIV infection (6.5% to 7.5%) were found in a random population of healthy cats in Australia.[19] Thus, it appears unlikely that virus-induced immunosuppression initiates ORLs.

In a human patient, herpes zoster was associated with root resorption of permanent teeth.[20] A recent investigation[21] found that 88% of cats with stomatitis were shedding both feline calicivirus and feline herpesvirus-1 in saliva. In another study,[22] ORLs were found in 43% of cats with chronic oral inflammation, but stomatitis was detected in only 3%[15] and 17%[23] of cats with ORLs in other studies. The high prevalence of ORLs in cats with stomatitis is not surprising, considering the high prevalence of ORLs in the general cat population. In the present study, stomatitis was not associated with ORLs.

Feeding noncommercial foods and treats has been associated with increased risk of ORL, whereas decreased risk has been associated with mixing noncommercial and commercial cat foods or treats.[24] In a recent study,[25] cats fed a mixed diet (dry and soft food) had higher prevalence of ORLs, compared with cats fed only dry food. In the present study, cats with ORLs were more likely to be fed canned diets than cats without ORLs, but this difference was not significant, and both groups had almost equal access to dry diets. Feeding a dry-food–only diet is not associated with lower prevalence of ORLs.[26] Furthermore, coating the surface of dry kibbles with an acidic substance to preserve the food and enhance its palatability does not predispose the teeth to development of ORLs,[1,27] and there is no correlation between specific oral bacteria and the pH of the tooth surface in cats.[28] Dietary acidification may predispose cats to hypercalcemia, calciuria, and calcium oxalate urolithiasis.[29]

Feeding of raw liver has been associated with ORLs in cats.[3,30] Feeding a diet with high phosphorus and low calcium content (eg, skeletal meat, heart, liver, or kidneys) may increase the prevalence of ORLs.[8] Although a correlation has not been found between ORLs and serum calcium concentration, a homemade diet low in calcium and with an incorrect calcium-to-phosphorus ratio has been significantly associated with ORLs.[8] In the present study, cats with ORLs were significantly more likely to be fed raw or heat-processed meat, compared with cats without ORLs, and only cats with ORLs received any giblets, with liver being the most commonly fed giblet. Consumption of table foods, cheese, and butter has also been associated with increased risk of ORLs.[24] In the present study, there were no significant differences in consumption of table foods or dairy products between cats with and without ORLs.

Although the mean serum 25-OHD concentration was significantly higher in cats with ORLs, compared with cats without ORLs, there were no significant differences in mean serum concentrations of iPTH, PTHrP, or fT_4. Mean serum calcium-to-phosphorus ratio was significantly lower in cats with ORLs, compared with cats without ORLs, but no significant differences in mean serum concentrations of total calcium and iCa were found. Although higher serum 25-OHD concentrations were detected in cats with ORLs, homeostatic regulation of serum total calcium and iCa was maintained within physiologic ranges, presumably through enhanced metabolism of vitamin D or by regulation via other hormones responsible for calcium homeostasis.

Biosynthesis of vitamin D_3 in the skin was long believed to occur in cats, until it was revealed that cats are not able to adequately synthesize vitamin D_3 in the skin and depend on dietary intake.[31-33] A direct linear relationship between plasma concentrations of 25-OHD and dietary intake of vitamin D_3 has been detected in cats,[34] and the reference range for serum 25-OHD in adult cats is considered to be 80 ± 12 nmol/L.[35] The National Research Council proposed a minimum vitamin D requirement for growing kittens of 500 U/kg of diet dry matter.[36] In studies[32,37] that evaluated the vitamin D_3 content of commercial cat foods, 31% were in excess of the Association of American Feed Control Officials' maximal allowance of 10,000 U/kg of diet dry matter. It has been suggested that the high concentrations of vitamin D_3 in commercial cat foods likely come from the raw ingredients and not from overzealous vitamin supplementation.[32] Chronic excess intake of vitamin D may cause vomiting, hypercalcemia, hyperphosphatemia, azotemia, proteinuria, calciuria, phosphaturia, decreased urine specific gravity, and cal-

cification of soft tissues.[38]

In the present study, owners reported that cats with ORLs vomited significantly more often than cats without ORLs, a finding that has been reported.[39] Mean serum concentrations of BUN and phosphorus were significantly higher in cats with ORLs, compared with cats without ORLs. However, BUN and serum phosphorus concentrations were not found to be significantly associated with ORLs when tested by use of the multivariate logistic regression model, which indicated that higher concentrations in cats with ORLs could be associated with other factors, such as age. Higher mean serum creatinine concentrations were detected in cats with ORLs, compared with cats without ORLs, but the difference was not significant. Urine specific gravity was significantly lower in cats with ORLs than in cats without ORLs as determined via univariate analysis, and this variable remained significantly associated with ORLs as determined via multivariate analysis. Although renal variables remained within physiologic range, one may speculate whether there is a predisposition to impairment of renal function in cats with ORLs. Renal function tests (eg, creatinine clearance, urine protein-to-creatinine ratio, and assay for microalbuminuria) have not been performed in this sample population to support a relationship between ORLs and renal efficiency. The detection of serum iPTH concentrations within the reference range in most cats in the present study is not consistent with renal secondary hyperparathyroidism, which would be expected in cats with chronic renal failure.

It has been reported that cats without ORLs are more likely to be fed diets with higher magnesium, calcium, phosphorus, and potassium content, compared with cats with ORLs.[40] In the present study, although no significant differences were found in mean serum concentrations of magnesium, calcium, iCa, and potassium between cats with and without ORL, mean serum concentration of phosphorus was significantly higher and mean calcium-to-phosphorus ratio was significantly lower in cats with ORLs. Although diets were not evaluated in this study for their mineral or vitamin content, decreased calcium-to-phosphorus ratios in cats with ORLs may have been caused by vitamin D–induced enhancement of phosphate reabsorption in the kidney rather than from decreased dietary calcium intake.

In humans, resorption of multiple permanent teeth has been reported to occur more often in females and abnormal concentrations of circulating sex hormones have been suggested to play a role.[41] With the exception of 2 sexually intact males, all cats in the present study were neutered. Whether neutering reduces estrogen production and increases vitamin D activity remains speculative. Results of previous studies[14-16] indicate that neutering of domestic cats is not associated with increased risk of ORLs.

Results of histologic studies[42-47] using light microscopy have characterized the effects of excess vitamin D and vitamin D metabolites on the periodontium in rats and dogs; changes include periodontal ligament degeneration and calcification, hypercementosis, hyperosteoidosis along alveolar socket walls and alveolar crests, narrowing of the periodontal ligament space, dentoalveolar ankylosis, and root resorption.[42-47] These induced changes in periodontal tissues in experimental animals resemble many radiographic and histologic features of teeth from cats with ORLs.[m] Could chronic dietary intake of excess vitamin D explain the apparent increase in prevalence of ORLs reported in the last 4 decades, and are the results reported here supportive of such a hypothesis? Although one might argue that increased vitamin D–associated factors are a result of the higher mean age of cats with ORLs, compared with cats without ORLs, multiple logistic regression analysis identified serum 25-OHD as a significant variable, even after taking age and other variables into account.

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