Paper

Recent shifts in the global proportions of canine uroliths

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Epidemiological surveys are important tools to identify emerging trends in disease. The Minnesota Urolith Centre has been tracking the occurrence of uroliths for over 30 years. To evaluate global changes in the frequencies of canine uroliths, submissions to the Minnesota Urolith Centre in 1999 and 2000 (n=39,965) were compared with submissions in 2009 and 2010 (n=99,598). The proportion of calcium oxalate uroliths rose on every continent except in Europe. Seventy-five per cent of dogs with calcium oxalate uroliths were between 5 and 11 years old. The proportion of struvite uroliths decreased on every continent except in Australia-Oceania. Seventy-seven per cent of all struvite formers were between two and eight years old. The proportion of purine uroliths has declined slightly. Worldwide, uroliths composed of cystine, calcium phosphate, calcium phosphate carbonate and silica remain uncommon. Epidemiological studies of urolithiasis are essential for constructing effective experimental designs and selecting appropriate cases and controls to conduct clinical trials with meaningful results.

Introduction

Epidemiological surveys are important tools to identify emerging trends in disease. The Minnesota Urolith Centre has been tracking the occurrence of uroliths for over 30 years. Since 1981, quantitative analysis of uroliths from over 700,000 animals, of which approximately half a million were dogs, have been performed. During this period, the Minnesota Urolith Centre has reported changes in the relative frequencies of mineral types, and the breeds and ages of dogs forming them (Osborne and others 1999, Osborne and others 2009). Some authors have erroneously reported that our analyses only represent uroliths from the USA. It is true that the majority of submissions represent animals residing in North America; however, the Minnesota Urolith Centre has analysed uroliths from animals residing on all the world's continents except Antarctica.

The aim of the present epidemiological survey was to report the recent changes in the frequencies of canine urolith types worldwide, while taking into account regional differences. Associations of breed, age and sex with urolith type were also reported to help clinicians recognise disease exemplars to improve diagnostic efficiency, and to help researchers identify appropriate canine models for future study.

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Materials and methods

Data source

Medical records of canine uroliths submitted to the Minnesota Urolith Centre were reviewed. To evaluate changes over the past 10 years, data from two periods were compared; submissions from January 1, 1999 to December 31, 2000, and the submissions from January 1, 2009 to December 31, 2010. To maximise submissions, urolith analysis remains at no cost to veterinarians. The information evaluated from each report included quantitative urolith composition; country and continent of origin; and breed, sex and age of the dog from which uroliths were removed. Since data were collected without identifying the dog and owner, the dataset may include recurrent urolith episodes from the same dog. Data were tabulated from two short periods to minimise this overestimation.

Diagnostic criteria

Mineral composition of uroliths was determined by polarisation microscopy and infrared spectroscopy. A urolith without a nidus or shell that contained ≥70 per cent of a single mineral was identified by that mineral. A urolith without a nidus or shell that contained <70 per cent of any single mineral was referred to as a mixed urolith. Compound uroliths were defined as having a central core or outer layer containing ≥70 per cent of a single mineral with an opposing outer layer or central core of a different mineral. Since the outer layer(s) of compound uroliths often form as a consequence of changes in metabolism, disease, medication or diet after formation of the central core, compound uroliths were categorised based on the composition of their central core. For example, a compound urolith with a central core of calcium oxalate and an outer layer of struvite was classified with other calcium oxalate uroliths and not as a compound urolith. This method of subcategorising compound uroliths was proposed because it is likely that if the central core had not been present to serve as a framework for epitaxy, the outer layers may not have formed.

On the basis of mineral composition, uroliths were grouped into the following categories; calcium oxalate consisted of uroliths of monohydrate or dihydrate salts of calcium oxalate; struvite uroliths also included those composed of newberyite ($Mg(HPO_4).3H_2O$), purine uroliths included all uroliths composed of uric acid, salts of uric acid (eg, ammonium urate, sodium urate, calcium sodium urate, etc) and xanthine; calcium phosphate uroliths consisted of calcium phosphate apatite and brushite. Calcium phosphate carbonate, cystine and silica were categorised individually. The category, 'other' consisted of mixed uroliths, drug metabolites and other uroliths of rare or unusual composition.

Statistical analyses

The proportion of urolith types in each study period were calculated in relation to geographic location, breed, age, sex and reproductive status of the dogs from which uroliths were removed. Statistical differences between proportions were assessed with a comparison of two proportion test (Moore andMccabe 1993). Statistical significance was accepted at the 1 per cent level (P<0.01), chosen to take into account the relatively many statistical analyses performed and the large size of the dataset. Urolith exemplars were constructed to represent the most common breed and sex, and the mean age of dogs afflicted with a particular mineral type.

Results

Between January 1, 1999 and December 31, 2000, the Minnesota Urolith Centre analysed uroliths from 39,965 dogs residing on six continents. To identify changes, these results were compared with 99,598 canine urolith submissions received 10 years later (ie, between January 1, 2009 and December 31, 2010). In 1999–2000, the urolith exemplar was a mixed breed (17.6 per cent), female dog (53.7 per cent) with a mean age of 7.2±3.2 years; breed, sex and age were not reported in 4 per cent, 5 per cent and 5 per cent, respectively. The most common urolith at this time was struvite (45.5 per cent) (Table 1). Ten years later, the canine urolith exemplar was unchanged; a mixed breed (18.0 per cent), female dog (51.8 per cent) with a mean age of 7.2±3.7 years (breed, sex and age were not reported in 1 per cent, 2.4 per cent and 4.5 per cent, respectively). However, contrasting with the earlier period, the most common urolith during 2009–2010 was calcium oxalate (45.2 per cent). Compared with the earlier period, canine urolith submissions have increased 2.5 times. Although the majority of uroliths were from dogs residing in North America, the proportion of submissions from North America decreased from 88.2 per cent to 70.7 per cent, while submissions from Africa, Asia and Australia-Oceania increased 7, 22 and 114 times higher compared with submissions 10 years earlier.

In 1999–2000, compound uroliths were diagnosed in 3264 (8.2 per cent of 39,965) canine submissions. The core mineral was calcium oxalate in 42.2 per cent, struvite in 27.6 per cent, purine in 4.5 per cent, calcium phosphate carbonate in 3.2 per cent, silica in 5.2 per cent, calcium phosphate in 1.5 per cent, cystine in 0.3 per cent and a variety of mixed minerals and non-mineral components in 15.5 per cent. In 2009–2010, compound uroliths were diagnosed in 9398 (9.4 per cent of 99,598) canine submissions. The core mineral was calcium oxalate in 39.1 per cent, struvite in 37.7 per cent, calcium phosphate carbonate in 5.6 per cent, purine in 4.7 per cent, silica in 3.7 per cent, calcium phosphate in 1.5 per cent, cystine in 0.3 per cent and a variety of mixed minerals and non-mineral components in 7.4 per cent.

Calcium oxalate

In 1999–2000, calcium oxalate was the second most common urolith. However, in 2009–2010, calcium oxalate surpassed struvite submissions and became the most prevalent urolith. The proportion of calcium oxalate submissions had increased from 40.9 per cent in 1999–2000 to 45.2 per cent (P<0.0001) a decade later. The proportion of calcium oxalate submissions increased on every continent except Europe where it decreased (Table 1); however, the changes were significant (P<0.0001) only in Asia and North America. Not every country in Europe was associated with a decrease in calcium oxalate. Ten European countries (Belgium, Denmark, France, Italy, The Netherlands, Norway, Republic of Ireland, Spain, Sweden and UK) submitted uroliths for analysis during both study periods. Calcium oxalate increased by 8 per cent in The Netherlands (P=0.0032), and by 16 per cent in Spain (P<0.0001); and decreased by 14 per cent in the UK (P<0.0001).

In 1999–2000, the canine calcium oxalate exemplar was an older (mean age of 8.6±2.9 years), male (68.0 per cent of which 77.4 per cent were neutered), miniature schnauzer (20.3 per cent).

In 2009–2010, the canine calcium oxalate exemplar was identical, an older (mean age of 8.4±2.9 years), male (74.2 per cent of which

TABLE 1: Global per cent distribution of types of canine uroliths in 1999–2000 compared with submissions in 2009–2010

	Mineral type									
Continent	CO	MAP	Purine	Cystine	CPC	Silica	CP	Other	Per cent of all submissions	Number of submissions
Africa										
1999–2000	11.1	72.2	5.6	0.0	0.0	2.8	0.0	8.3	0.09	36
2009–2010	25.4	53.3	15.0	1.7	1.7	0.4	0.8	1.7	0.24	240
P value	0.0593	0.0333	0.1251	0.4352	0.4352	0.1193	0.5825	0.0177		
Asia										
1999–2000	28.8	48.4	9.9	2.5	1.0	0.1	0.7	8.6	1.82	729
2009–2010	42.3	42.9	4.8	1.2	1.3	1.4	0.7	5.3	16.05	15982
P value	<0.0001	0.0035	<0.0001	0.0017	0.4166	0.0039	0.9314	0.0001		
Australia-Oceana										
1999–2000	19.4	51.6	12.9	0.0	0.0	0.0	3.2	12.9	0.08	31
2009–2010	22.4	59.3	8.8	3.2	1.2	0.3	0.7	4.1	3.55	3539
P value	0.6821	0.3852	0.4174	0.3142	0.5418	0.7454	0.1005	0.0146		
Europe										
1999–2000	37.7	44.9	7.4	3.4	1.1	0.4	0.7	4.4	9.63	3847
2009–2010	36.7	42.8	10.3	3.8	1.0	0.8	0.6	3.9	9.38	9345
P value	0.3205	0.0241	<0.0001	0.2630	0.4793	0.0027	0.4982	0.2042		
North America										
1999–2000	41.6	45.5	7.6	0.5	0.4	0.7	0.4	3.4	88.16	35236
2009–2010	48.2	41.9	4.2	0.8	1.0	0.6	0.5	2.9	70.68	70394
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0087	0.0116	<0.0001		
South America										
1999–2000	20.9	53.5	15.1	1.2	2.3	0.0	2.3	4.7	0.22	86
2009–2010	41.8	40.8	8.2	2.0	0.0	1.0	0.0	6.1	0.10	98
P value	0.0024	0.0856	0.1389	0.6389	0.1290	0.3476	0.1290	0.6605		
Total										
1999–2000	40.9	45.5	7.6	0.8	0.5	0.7	0.4	3.6	100	39965
2009–2010	45.2	42.8	5.1	1.2	1.0	0.7	0.5	3.4	100	99598
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.3018	0.0026	0.1492		

CO, Calcium oxalate; CP, Calcium phosphate; CPC, Calcium phosphate carbonate; MAP, Magnesium ammonium phosphate (struvite)

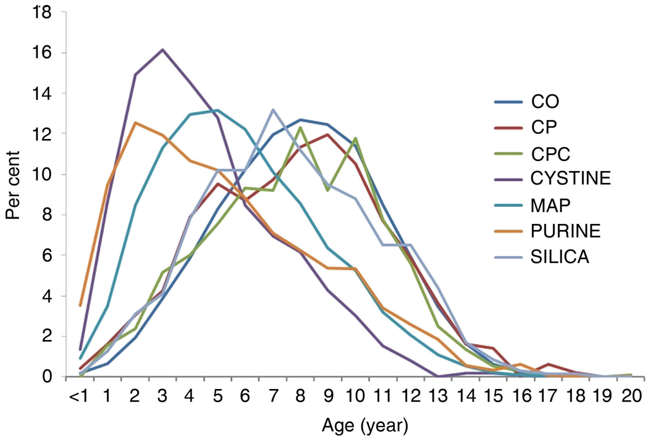

FIG 1: Age distribution of dogs with uroliths. CO, Calcium oxalate; CP, Calcium phosphate; CPC, Calcium phosphate carbonate; MAP, Magnesium ammonium phosphate (struvite)

78.4 per cent were neutered), miniature schnauzer (15.1 per cent). In 2009–2010, the most common pure breed dog with calcium oxalate varied by continent; the Yorkshire terrier was most common in Africa (30 per cent) and Europe (18 per cent), the shih tzu in Asia (17 per cent), the bichon frise in Australia-Oceania (15 per cent), the miniature schnauzer in North America (14.9 per cent) and the Lhasa apso in South America (16 per cent). Worldwide, these five breeds plus the mixed breed dogs accounted for 58 per cent of all calcium oxalate submissions. In addition, 75 per cent of all calcium oxalate dogs were between 5 and 11 years old; less than 1 per cent of dogs with calcium oxalate were less than 1 year old (Fig 1).

Struvite

In 1999–2000, struvite was the most common urolith throughout the world (Table 1). However, compared with submissions in 2009–2010, the per cent of struvite urolith submissions decreased on every continent except Australia-Oceania in which the per cent increased (Table 1); however, the changes were only significant in Asia ($P<0.0035$) and North America ($P<0.0001$). In 2009–2010, struvite became the second most common urolith analysed by the Minnesota Urolith Centre, but was the most common urolith from Africa, Asia, Australia-Oceania and Europe (Table 1).

In 1999–2000, the struvite exemplar was an adult (mean of 6.3±2.9 years), female (88.0 per cent of which 81.8 per cent were neutered), mixed breed (22.3 per cent) dog. In 2009 and 2010, the struvite exemplar was similar, an adult (mean age of 6.2±2.9 years), female (86.1 per cent of which 39.1 per cent were neutered), mixed breed (22.6 per cent) dog. The most common pure breed, struvite-former by continent was the shih tzu in Asia (22.3 per cent), Europe (8.8 per cent) and North America (13.1 per cent), the Jack Russell terrier in Africa (11.7 per cent), the miniature Poodle in South America (12.5 per cent) and the bichon frise (5.6 per cent) in Australia-Oceania. Worldwide, four breeds; mixed, shih tzu, miniature schnauzer and bichon frise accounted for 52 per cent of all struvite uroliths. In addition, 77 per cent of all struvite formers were between two and eight years old (Fig 1). In dogs less than one year old, struvite was the most common urolith (49.3 per cent of 759 submissions), and purine uroliths were the second most common (22.1 per cent).

Purine

In 1999–2000, 7.6 per cent of submissions were purine, and in 2009–2010, the proportion had decreased to 5.1 per cent ($P<0.0001$). Comparing submissions in 1999–2000 with submissions in 2009–2010, the proportions of purine uroliths were significantly lower in Asia ($P<0.0001$) and North America ($P<0.0001$), and significantly higher in Europe ($P<0.0001$). In Europe, the per cent of purine uroliths increased significantly only in the UK ($P\leq0.0001$). By contrast, purine uroliths decreased significantly in Italy ($P=0.0008$).

In 1999–2000, the canine purine exemplar was an adult (mean age of 5.4±2.9 years), male (88.5 per cent of which 68.1 per cent were neutered), dalmatian (20.3 per cent). In 2009–2010, the canine purine exemplar was identical, an adult (mean age of 5.6±3.4 years), male (81.2 per cent of which 63.6 per cent were neutered), dalmatian (28.8 per cent). Dalmatians were the most common purine stone-former on every continent. On the basis of breed, purine uroliths accounted for 97 per cent of uroliths from dalmatians (n=1497), 92 per cent of uroliths from black Russian terriers (n=13), and 35.4 per cent of uroliths from English bulldogs (n=975). In addition, 78 per cent of all dogs with purine uroliths were between one and eight years old.

Xanthine uroliths accounted for 0.9 per cent (27 of 2908) of purine uroliths analysed in 1999–2000, and 2.1 per cent (94 of 4580) of purine uroliths analysed in 2009–2010. Of the 121 xanthine urolith submissions, concurrent allopurinol administration was reported in 71 per cent. No allopurinol administration was reported in 25 xanthine urolith submissions of which 6 were from Cavalier King Charles spaniels, a breed recognised with familial xanthinuria ([b33] van Zuilen and others 1997).

Cystine

In 1999–2000, 0.8 per cent of submissions were cystine. A decade later, the per cent had increased to 1.2 per cent ($P<0.0001$). Compared with submissions in 1999–2000, the proportion of cystine uroliths was significantly higher in North America ($P<0.0001$) and significantly lower ($P=0.0017$) in Asia. Europe had the highest proportion of dogs with cystine uroliths (Table 1).

In 1999–2000, the cystine exemplar was a male (98.3 per cent of which 15.4 per cent were neutered), English bulldog (14.5 per cent), with a mean age of 4.9±2.8 years. In 2009 and 2010, the canine cystine exemplar was identical, a young adult (mean age of 4.9±3.4 years), male (98.1 per cent of which 14.8 per cent were neutered), English bulldog (20.3 per cent). On the basis of geographic location, the most common cystine urolith former in 2009–2010 was the English bulldog in Africa (50 per cent; two of four cystinurics), Europe (24.7 per cent; 88 of 356 cystinurics), and North America (25.1 per cent; 136 of 541 cystinurics), the chihuahua in Asia (18.8 per cent; 35 of 186 cystinurics), and the Staffordshire bull terrier in Australia-Oceania (23.2 per cent; 35 of 186 cystinurics).

In 2009–2010, 92 breeds were diagnosed with cystine uroliths. Although cystine is an uncommon urolith, it occurred in 90 per cent of uroliths from Scottish deerhounds (9 of 10), 63 per cent of uroliths from mastiffs (57 of 91), and 53 per cent of uroliths from Irish terriers (9 of 17). The per cent of cystine uroliths in the Newfoundland, a breed that is recognised to be predisposed to cystinuria (Henthorn and others 2000), was 38 per cent (5 of 13) in 2009–2010, decrease from the 71 per cent (12 of 17) a decade earlier (1999–2000).

Calcium phosphate carbonate

The proportion of calcium phosphate carbonate increased from 0.5 per cent in 1999–2000 to 1.0 per cent ($P<0.0001$) a decade later. By continent, the increase in proportion was only significant in North America ($P<0.0001$). In 1999–2000, the canine calcium phosphate carbonate exemplar was an adult (7.5±4.2 years), female (71.2 per cent of which 70.2 per cent were neutered), mixed breed (13.8 per cent) dog. In 2009–2010, the calcium phosphate exemplar was similar, an adult (mean age of 7.6±3.6 years), female (71.4 per cent of which 33.9 per cent were neutered), mixed breed (18.6 per cent) dog. Worldwide, four breeds (mixed, shih tzu (17.8 per cent), bichon frise (9.7 per cent) and miniature schnauzer (6.7 per cent)) accounted for 53 per cent of all calcium phosphate carbonate uroliths.

Silica

In 1999–2000, 0.69 per cent of submissions were silica. A decade later, the proportion had not changed significantly (0.74 per cent; ($P=0.3018$). By continent, however, the proportion of silica was significantly higher in Europe ($P<0.0027$) and significantly lower in North America ($P<0.0087$). In 1999–2000, the canine silica exemplar was a male (91.6 per cent of which 68.5 per cent were neutered), mixed breed dog (16.4 per cent), with a mean age of 8.6±3.0 years. In 2009–2010, the canine silica exemplar was similar, a male (91.4 per cent of which 64.1 per cent were neutered), mixed breed dog (17.4 per cent), with a mean age of 7.6±3.6 years.

Calcium phosphate

In 1999–2000, 0.40 per cent of submissions were calcium phosphate. In 2009–2010, the per cent had increased to 0.52 per cent (p=0.0026). In 1999–2000, the canine calcium phosphate exemplar was a male (65.1 per cent of which 60.0 per cent were neutered), mixed breed (13.8 per cent) dog, with a mean age of 8.7±3.2 years. In 2009–2010, the canine calcium phosphate exemplar was identical, a male (73.9 per cent of which 64.7 per cent were neutered), mixed breed (16.9 per cent) dog, with a mean age of 8.2±3.3 years. Worldwide, four breeds (mixed, shih tzu (16.7 per cent), Yorkshire terrier (8.1 per cent), and bichon frise (7.3 per cent)), accounted for 49 per cent of all calcium phosphate urolith submissions.

Discussion

Our results are in agreement with observations that calcium oxalate uroliths continue to gain recognition as an emerging problem worldwide (Ling and others 2003, Sosnar and others 2005, Low and others 2006, Hesse and Neiger 2009, Houston and Moore 2009, Rogers and others 2011). In 1981 calcium oxalate uroliths were diagnosed in only 5 per cent of canine urolith submissions to the Minnesota Urolith Centre (Osborne and others 2009). In 2009–2010, 45 per cent of canine urolith submissions to the Minnesota Urolith Centre were calcium oxalate. The prevalence of calcium oxalate uroliths has also risen in cats and human beings (Yasui and others 2008, Osborne and others 2009, Knoll and others 2011).

Research designed to resolve the precise aetiological cascade of risk factors leading to the increase of calcium oxalate is essential to reverse this trend. Our study identified several key factors likely to improve study design. Calcium oxalate uroliths were diagnosed primarily in middle aged and older adults (5–11 years old). Although calcium oxalate uroliths were identified in 136 of 253 breeds, our study is in agreement with others that only a few breeds, particularly the miniature schnauzer, bichon frise, shih tzu, Lhasa apso and Yorkshire terrier, are at high risk (Lekcharoensuk and others 2000, Low and others 2006, Houston and Moore 2009, Rogers and others 2011). Therefore, studying young dogs or breeds unlikely to form calcium oxalate uroliths may provide misleading results contrary to studies evaluating dogs at risk for calcium oxalate (Lulich and Osborne 1992, Stevenson and others 2000, Stevenson and others 2003, Lulich and others 2005). This is supported by a study evaluating thiazide diuretics to minimise urine calcium excretion. Thiazide diuretics were ineffective in healthy beagles (Lulich and Osborne 1992), yet thiazide administration resulted in significantly reduced urine calcium excretion in breeds with spontaneous calcium oxalate uroliths (Lulich and others 2001).

Individual dog breeds represent ideal opportunities for studying genetic determinants of disease because compared with human beings, dogs within a specific breed have relatively little genetic diversity, and disease traits are often controlled by a small number of loci with a strong effect (Lindblad-Toh and others 2005). Based on this premise, dogs may provide an ideal model for studying the genetic determinants and gene-environment interactions that influence calcium oxalate urolithiasis. For these and other comparison studies, controls have often been non-stone formers of similar breed, age and sex to minimise variability between groups (Stevenson and others 2003b, Stevenson and others 2004). This is appropriate because these controls represent the population at risk. However, the tradeoff is that controls, originally presumed to be stone-free, may form calcium oxalate uroliths later in life. Our study supports the premise that matched controls should be of equal age or older than cases, to minimise misclassifying a latent calcium oxalate stone-former as a lifelong, stone-free control. By contrast with selecting controls, when selecting cases, younger stone-formers should be recruited. Results of our study indicated that urolith formation wanes with age (Fig 1). With a reported median recurrence rate of 50 per cent in 2 years (Lulich 2009), recruiting cases <7–9 years old will maximise selection of study participants with active disease and the potential for urolith recurrence.

Our results were in agreement with others that the relative per cent of struvite is decreasing worldwide (Sosnar and others 2005, Low and others 2006, Houston and Moore 2009). A variety of factors may have contributed to this change. The Minnesota Urolith Centre advocates medical dissolution of struvite uroliths except those causing urinary obstruction. With successful dissolution, these uroliths would not be counted because they would not be available for analysis. Since most struvite uroliths in dogs form as a consequence of urinary tract infections with urease-producing bacteria, early recognition and control of bacteriuria would also reduce their occurrence. For those rare cases of sterile struvite uroliths in dogs, diets with reduced magnesium and phosphorus that promote acidification of urine are essential to prevent urolith recurrence (Bartges and others 1992). However, urine acidification is a risk factor for calcium oxalate formation (Lekcharoensuk and others 1998). Therefore, we hypothesise that some dietary strategies to prevent struvite, may indirectly decrease the occurrence of struvite while increasing the occurrence of calcium oxalate.

It is noteworthy that the most common breeds that form struvite uroliths were the same breeds that form calcium-containing uroliths (ie, calcium oxalate, calcium phosphate carbonate and calcium phosphate) (Sosnar and others 2005, Low and others 2006, Houston and Moore 2009, Rogers and others 2011). In this study, the shih tzu accounted for 13.7 per cent of struvite, 17.8 per cent of calcium phosphate carbonate, 16.7 per cent of calcium phosphate, 9.4 per cent of calcium oxalate and 11.4 per cent of all urolith submissions in 2009–2010. We also observed that compared with dogs with struvite uroliths, the mean age of dogs with calcium-containing uroliths was older and the proportion of males was higher. Based on these observations, we hypothesise that several interacting mechanisms account for the shifts in urolith types in breeds at risk for struvite and calcium oxalate. First, these breeds likely possess common structural and/or functional risk factors predisposing to several types of uroliths. Second, young adults are at increased risk for developing urinary tract infections with staphylococcal bacteria that produce the enzyme urease. In one study evaluating the epidemiology of urinary tract infections in dogs with urolithiasis, the mean age of females (6.24 years, n=1933) and males (6.37 years; n=794) with staphylococcal infections were significantly younger than the ages of females (7.63 years; n=235) and males (9.08 year, n=211) with *Escherichia coli* positive cultures (Ling and others 1998). The higher proportion of bacterial urinary infection in female dogs parallels the higher proportion of female dogs with infection-induced uroliths (ie, struvite and calcium phosphate carbonate). Third, we hypothesise that urine calcium in adult dogs, increases with age. This last premise is supported by our study results in which dogs with calcium phosphate carbonate uroliths were older. Calcium phosphate carbonate is an infection-induced stone caused by the same urease-producing bacteria as struvite. Under similar situations, increased urine calcium appears to promote the formation of calcium phosphate carbonate. Increased urine calcium with ageing has also been observed in adult human beings (Kotowicz and others 1990). The association between ageing with fewer urease-producing urinary tract infections and more urine calcium excretion, supports the sex shift to males that is recognised in calcium oxalate urolith-formers. If this hypothesis is true, the clinical implication of these shifts is that the practice of acidifying urine to prevent struvite would be contraindicated in these breeds as they age. This recommendation is based on the observation that hypercalciuria is a consistent abnormality in dogs forming calcium oxalate uroliths (Lulich and others 1991, Lulich and others 2001, Stevenson and others 2004), and because acidification promotes urine calcium excretion by increasing mobilisation of calcium from bone, increasing filtration of ionised calcium from blood, and decreasing renal tubular reabsorption of calcium from ultrafiltrate (Burnell 1971, Sutton and others 1979).

The proportion of purine uroliths had significantly declined in Asia and North America, and significantly increased in Europe (Table 1). Similar declines have been reported in dogs from Canada and the Czech Republic (Sosnar and others 2005, Houston and Moore 2009). In our study, the dalmatian accounted for the majority of purine urolith submissions (66.1 per cent (2021 of 3057) in 1999–2000, and 28.8 per cent (1449 of 5038) in 2009–2010) worldwide. Between 1994 and 2004, the number of dalmatians registered with the American Kennel Club decreased by 98 per cent (AKC News 2005). If this occurred in other geographic locations, the dwindling popularity of dalmatians is likely contributing to the declining proportion of purine uroliths.

The increased proportion of purine uroliths from Europe was unexpected. As in Asia and North America, the proportion of purine uroliths from dalmatians in Europe had decreased (50.9 per cent (145 of 285) in 1999–2000; 43.8 per cent (422 of 963) in 2009–2010). However, purine uroliths in mixed breeds (5.3 per cent (15 of 285) in 1999–2000; 7.7 per cent (74 of 963) in 2009–2010); English bulldogs (5.6 per cent (16 of 285) in 1999–2000; 7.6 per cent (73 of 963) in 2009–2010); and Yorkshire terriers (7.7 per cent (22 of 285) in 1999–2000; 9.0 per cent (87 of 963) in 2009–2010), and other breeds increased. Recently, the Kennel Club of the UK permitted registration of dalmatians resulting from cross breeding with a pointer dog several generations back from the current progeny. Dalmatians and pointers were bred with the intention of producing offspring heterozygous for the fixed autosomal recessive defect of the urate transporter SLC2A9 discovered in this breed (Bannasch and others 2008). The outcome is a dog with the appearance of a dalmatian without hyperuricosuria, and the subsequent risk for purine uroliths. It is anticipated that this will further decrease the proportion of dalmatians with urate uroliths.

Cystine uroliths were primarily detected in young adult males. The highest proportion of cystine uroliths was from dogs residing in Europe. Although a report in 1991 indicated that cystine uroliths occurred in 26 per cent of dogs from Spain (Escolar and others 1991), cystine uroliths were only detected in 4.2 per cent (88 of 2114 submissions in 2009–2010) of urolith-forming dogs from Spain in our study. In 2000, the canine SLC3A1 gene was cloned and sequenced identifying the genetic mutation responsible for cystinuria in Newfoundland dogs (Henthorn and others 2000). Subsequently, a mutation-specific test was developed. However, as in human beings, the mutation responsible for cystinuria appears to be genetically heterogeneous because the test has been effective in identifying Newfoundland dogs with cystinuria and no other affected breeds.

Recent epidemiological reports indicate that silica uroliths remain uncommon (Low and others 2006, Houston and Moore 2009, Osborne and others 2009, Rogers and others 2011). One exception to this generality was a report of dogs in Mexico City in which the proportion of silica uroliths was 14 per cent (Angel-Caraza and others 2010). The authors of that report hypothesised that the high concentrations of silica in drinking water of that region were likely responsible. We agree that dietary factors are an important risk factor for silica formation. However, our study indicated that silica uroliths were uncommon worldwide. Because the Minnesota Urolith Centre receives comparatively few uroliths for analysis from South America, our data may not provide a suitable comparison for the distribution of uroliths affecting dogs in that geographic location.

Trends favouring ownership of breeds prone to urolithiasis may have contributed to the worldwide shifts in urolith types. However, because of the short time-span in which sweeping changes in the proportion of some types of uroliths occurred, other factors are also responsible. It is the authors' interpretation that changes in husbandry and nutrition represent significant contributing factors influencing these epidemiological shifts. Therefore, appropriate changes in husbandry and nutrition may potentially offer solutions for mitigating disease.

Our study has several limitations. Data were derived from submissions to the Minnesota Urolith Centre and not a representative sample from all ages, breeds and geographical locations. Therefore, without knowing the true geographic population of dogs, our results may be influenced by other conditions affecting the study population, such as breed popularity, husbandry practises, sample submission rate and lifespan of the dog. In addition, those areas with highest submissions had the greatest influence on global outcomes. To minimise this effect, changes were also compared between time periods within geographic locations. Few submissions were received from Africa, Australia-Oceania and South America during one or both periods. Therefore, making broad generalisations about these continents may be incomplete because our results may not represent the spectrum of urolithiasis in these locations.

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