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Analysis of 7866 feline and canine uroliths submitted between 2014 and 2020 in the Netherlands

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A B S T R A C T

Analysis of large datasets of uroliths is necessary to illustrate the prevalence and risk factors of urolithiasis. Furthermore, it may help to improve treatment and prevention of urolithiasis. In this study, 7866 uroliths (44.5% feline and 55.5% canine) from veterinary practitioners in the Netherlands between 2014 and 2020 were analysed. Between 2014 and 2020 the distribution over the different types of uroliths remained similar over time. Female cats, obese cats, Domestic Shorthair cats, female dogs, and large breed dogs had an increased risk for struvite. Neutered cats, all cat breeds except Domestic Shorthair, neutered dogs, male dogs, intact male dogs, and small breed dogs had an increased risk for calcium oxalate urolithiasis. Cystine and urate were found predominantly in male dogs. Dalmatians were at highest risk for urate urolithiasis. The findings of this study in the Netherlands were similar to findings in previous studies from different countries. However, urate urolithiasis in the English Cocker Spaniel and cystine urolithiasis in the Yorkshire Terrier were new associations. Body condition score, information about recurrence of urolithiasis, medical history, and diet history should be included in submission sheets in the future to explore other possible associations.

1. Introduction

Urolithiasis is defined as the occurrence of uroliths in the urinary tract. The majority of uroliths can be retrieved from the bladder (Picavet et al., 2007). While relative proportions of urolith types vary, the predominant encountered feline and canine uroliths are struvite and calcium oxalate (CaOx), whereas silica, xanthine, calcium phosphate (CaF), and cystine are less commonly encountered (Houston et al., 2004; Picavet et al., 2007; Osborne et al., 2009). It is of great importance to determine the composition of uroliths to determine the most appropriate treatment and preventive measures for every individual patient with urolithiasis. A few uroliths can be dissolved with a specific diet (for example struvite), whereas other types of uroliths must be surgically removed (Abdullahi et al., 1984). Urolithiasis should not be regarded as a disease with a single cause. Various predisposing factors are associated with the formation of uroliths. Struvite is more often reported in female dogs, medium or large breed dogs, and in cats and dogs with urinary tract infections. On the contrary, male dogs, small breed dogs, and neutered cats are predisposed for CaOx. For cystine, intact male dogs and certain breeds are predisposed. Similarly, for urate, certain breeds are predisposed, especially Dalmatians (Houston et al., 2004; Picavet et al., 2007; Houston et al., 2017). CaF has been reported to occur more often in Cocker Spaniels, Miniature Schnauzers, Yorkshire Terriers, Shih Tzus and Springer Spaniels (Osborne et al., 2009). Furthermore, obese cats and dog are more susceptible to urolithiasis. Obesity is associated with higher food intake, storing larger amounts of fat and a higher excretion of minerals in the urine (Gomes et al., 2018). Whether a dog or cat is obese is determined by the body condition score (9-point scale), where a score around 8 or 9 is considered obese (Bjørnvad et al., 2011). Lastly, the average age of developing urolithiasis in both cats and dogs is reported to be around 7 years, with a higher average age for CaOx (Picavet et al., 2007). Veterinary practitioners should be up to date on trends and associations with predisposing factors of feline and canine urolithiasis to be able to make the right decisions on diagnostics and treatment prior to getting final results of the analysis. Therefore, the aim of this study was to analyse uroliths send in by veterinarians in the Netherlands between 2014 and 2020.

2. Material and methods

The study was approved by the research committee of Utrecht University, and did not require ethical approval according to Dutch legislation.

2.1. Urolith analysis

Retrospective data analysis was performed on data from feline and canine uroliths submitted for analysis to IDEXX laboratories. The

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analysis was conducted in the IDEXX VetMedLab in Ludwigsburg Germany, using infrared spectroscopy. Every urolith was sent in by a veterinary practitioner accompanied by a questionnaire containing information about the patient (breed, age, gender, location of the urolith and overweight yes/no).

Uroliths containing at least 70% of one mineral were classified as that mineral type. Uroliths containing less than 70% of one mineral were classified as mixed. There was no distinction made between compound and mixed, because the layer composition of the uroliths was unknown. Uroliths comprised of calcium oxalate monohydrate, calcium oxalate dihydrate, or a combination were classified as CaOx. Urate uroliths included the uric acid salts sodium, potassium, and ammonium. CaF uroliths included apatite, carbonate, and brushite. Xanthine and hypoxanthine were classified as xanthine.

2.2. Statistical analysis

Data analysis was performed in SPSS (IBM SPSS statistics 25). Age distribution in both species was tested for normality by a Shapiro-Wilk test. As age was not normally distributed in both species, Mann-Whitney *U* tests were performed to compare the average age of cats and dogs, respectively, for different types of uroliths. A multivariable logistic regression was performed for cats and dogs separately to examine the associations of gender, obesity, and neuter status with urolith type. Due to small sample size, silica, xanthine, and cysteine in cats, as well as silica, xanthine, and CaP in dogs were not analysed. The reference urolith type was CaOx in cats and struvite in dogs, because the number of submissions of these uroliths was the highest within each species. A logistic regression was performed to analyse whether there were any associations between breed and urolith type. Only breeds with more than 10 submissions were included in the analysis. For the cats, the reference group was the Domestic Shorthair cat, because the majority of the total submissions was from Domestic Shorthair cats. For the dogs, the reference group was the mixed breed group. For the logistic regression of cats only struvite and CaOx were included in this analysis, because of the small sample size of the other uroliths for some cat breeds. For sample size numbers ≤ 5 a Fisher's exact test was performed, because a logistic regression with numbers below 5 is not accurate (Hsieh et al., 1998). As dogs are also often divided in size groups (based on the average bodyweight), these groups were also analysed with a logistic regression. The groups were:

- Giant: >45 kg.
- Maxi: Between 26 and 45 kg.
- Medium: Between 11 and 25 kg.
- Small: Between 5 and 10 kg.
- Toy: <5 kg.

The small breed group and struvite were used as references, because these had the highest number of submissions. For all analyses, a *P*-value <0.05 was considered significant.

3. Results

3.1. Distribution of feline and canine uroliths

Data obtained consisted of uroliths from 3497 (44.5%) cats and 4369 (55.5%) dogs that had been submitted between the February 20th 2014 and the August 4th 2020.

The distribution of both feline and canine uroliths over time is presented in Figs. 1 and 2.

In the timespan of 6 years the distribution of uroliths in cats remained relatively stable. In dogs the proportion struvite decreased and cystine increased from 2014 until 2016, but from 2016 onwards it remained similar. The composition of the different uroliths submitted between 2014 and 2020 is presented in Table 1. CaOx (68.8%) was the most common urolith type for cats followed by struvite (24.2%), whereas for dogs struvite (40.9%) was the most common urolith followed by CaOx (30.8%).

The majority of the uroliths were retrieved from the bladder (78.7% in dogs and 85.5% in cats) or a combination of the lower urinary tract (15.2% in dogs and 7.6% in cats).

3.2. Feline uroliths

Feline urolith submissions were obtained from 1956 (55.9%) males and 1541 (44.1%) females. From which 1901 (97.2%) of the males, and 1464 (95.0%) of the females were neutered. From all these cats 1481 (42.4%) were overweight (further mentioned as obese).

The average age of submitted uroliths for cats was 7.8 years ($SD = 3.7$). Where the average age of CaOx was significantly higher (8.1 years, $SD = 3.6$) compared to cats with other uroliths (7.0 years, $SD = 3.7$).

Neutered cats had significant lower odds for struvite urolithiasis, which means a higher odds for CaOx urolithiasis, as the reference urolith CaOx has a higher prevalence in neutered cats (69.8%) compared to intact cats (43.9%). Obese cats and neutered cats had significant lower

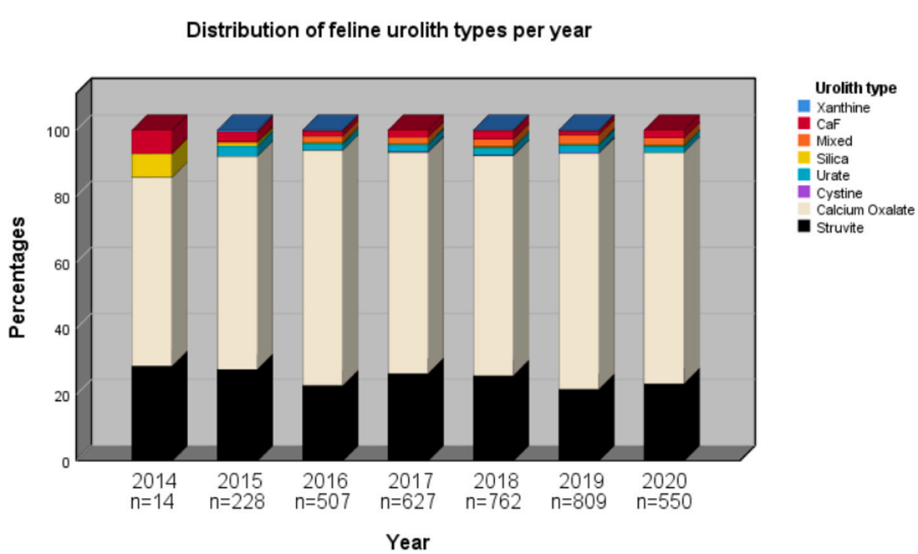

Fig. 1. Distribution of urolith types in cats between 2014 and 2020, distributed to IDEXX laboratories from the Netherlands.

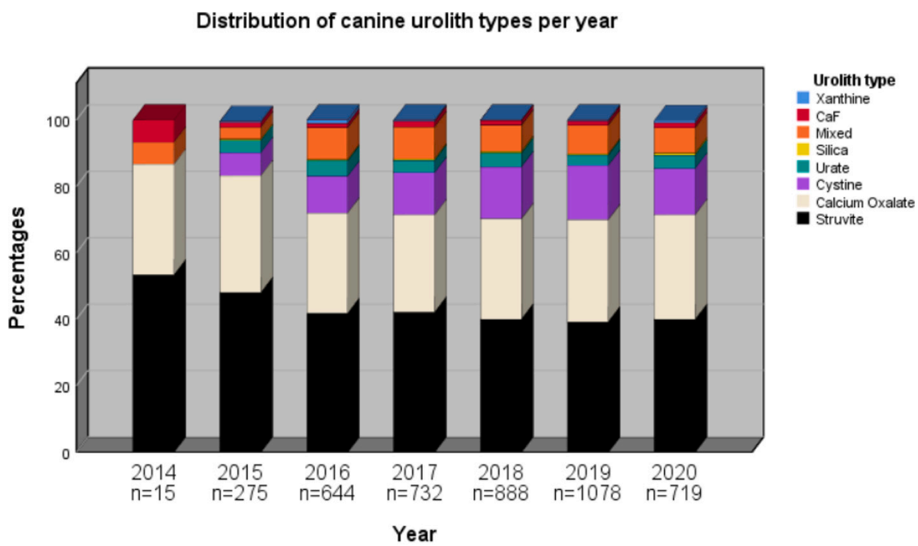

Fig. 2. Distribution of urolith types in dogs between 2014 and 2020, distributed to IDEXX laboratories from the Netherlands.

Table 1
Composition of 7866 canine and feline uroliths submitted to IDEXX laboratories from the Netherlands between 2014 and 2020.

Species difference					
Urolith type	Canine number		Feline Number		Total
CaF	62	(1.4%)	72	(2.1%)	134
CaOx	1347	(30.8%)	2406	(68.8%)	3752
Cystine	601	(13.8%)	4	(0.1%)	605
Mixed	364	(8.3%)	75	(2.1%)	439
Silica	19	(0.4%)	13	(0.4%)	32
Struvite	1789	(40.9%)	845	(24.2%)	2634
Urate	166	(3.8%)	77	(2.2%)	243
Xanthine	21	(0.5%)	5	(0.1%)	26
Total	4369	(100.0%)	3497	(100.0%)	7866

odds for CaF urolithiasis (Tables 2, 3, and 4).

3.3. Analysis of individual cat breeds

In total, cats of 36 breeds were recorded in the database, the most frequent being the Domestic Shorthair with 69.4% of the total submissions. Cats of breeds with less than 10 submissions were not included in the analyses. The British Shorthair, British Longhair, Birman, Maine Coon, Persian Longhair, and Ragdoll all had a significant lower odds for struvite (with CaOx as a reference) compared to Domestic Shorthair cats (Table 5).

Table 2
Difference per urolith type between male and female cats.

Urolith type	Gender			
	Male	Female	Odds ratio (*Confidence interval (CI)*)	P-value
CaF	37 (1.9%)	35 (2.3%)	1.00 *(0.60–1.66)*	NS[a]
CaOx	1401 (71.6%)	1004 (65.2%)	*Reference*	–
Cystine	3 (0.2%)	1 (0.1%)	–	–
Mixed	45 (2.3%)	30 (1.9%)	–	–
Silica	6 (0.3%)	7 (0.5%)	–	–
Struvite	417 (21.3%)	428 (27.8%)	1.46 *(1.25–1.71)*	<0.05
Urate	44 (2.2%)	33 (2.1%)	1.05 *(0.66–1.66)*	NS[a]
Xanthine	3 (0.2%)	2 (0.1%)	–	–
Total	1956 (100.0%)	1541 (100.0%)		

[a] Not significant

Table 3
Difference per urolith type between intact and neutered cats.

Urolith type	Neuter status			
	Intact	Neutered	Odds ratio *(CI)*	P-value
CaF	34 (25.8%)	38 (1.1%)	0.03 *(0.02–0.05)*	<0.05
CaOx	58 (43.9%)	2348 (69.8%)	*Reference*	–
Cystine	1 (0.8%)	3 (0.1%)	–	–
Mixed	4 (3.0%)	71 (2.1%)	–	–
Silica	0 (0.0%)	13 (0.4%)	–	–
Struvite	35 (26.5%)	810 (24.1%)	0.55 *(0.36–0.84)*	<0.05
Urate	0 (0.0%)	77 (2.3%)	1.90 *(0.26–13.91)*[a]	NS[b]
Xanthine	0 (0.0%)	5 (0.1%)	–	–
Total	132 (100.0%)	3365 (100.0%)		

[a] Fisher's exact test
[b] Not significant

Table 4
Difference per urolith type between obese and non-obese cats.

Urolith type	Obesity			
	Non-obese	Obese	Odds ratio *(CI)*	P-value
CaF	58 (2.9%)	14 (0.9%)	0.51 *(0.28–0.95)*	<0.05
CaOx	1430 (70.9%)	976 (65.9%)	*Reference*	–
Cystine	3 (0.1%)	1 (0.1%)	–	–
Mixed	46 (2.3%)	29 (2.0%)	–	–
Silica	9 (0.4%)	4 (0.3%)	–	–
Struvite	420 (20.8%)	425 (28.7%)	1.55 *(1.32–1.82)*	<0.05
Urate	48 (2.4%)	29 (2.0%)	0.87 *(0.54–1.39)*	NS[a]
Xanthine	2 (0.1%)	3 (0.2%)	–	–
Total	2016 (100.0%)	1481 (100.0%)		

[a] Not significant

3.4. Canine uroliths

The canine urolith submissions were obtained from 2289 (52.4%) males and 2080 (47.6%) females. Of these dogs, 1135 (49.6%) of the males, and 1530 (73.6%) of the females were neutered. From all these dogs 1206 (27.6%) were overweight (further mentioned as obese).

The average age of submitted uroliths in dogs was 7.6 years (*SD* = *3.2*). Where the average age of dogs with CaOx was significantly higher (9.1 years, *SD* = *2.8*) compared to dogs with other uroliths (6.8 years, *SD* = *3.1)*. The average age of dogs with cystine was significantly lower (5.6 years, *SD* = *2.6)* compared to dogs with other uroliths (7.9 years,

Table 5
Association of feline breeds and struvite compared to CaOx.

Breed	Prevalence of urolith type within breed			
	CaOx	Struvite	Odds ratio (*CI*)	P-value
Bengal Cat	10/14 (71.4%)	4/14 (28.6%)	0.86 *(0.28–2.83)*[a]	NS[b]
British Shorthair	269/303 (88.8%)	23/303 (7.6%)	0.19 *(0.12–0.29)*	<0.05
British Longhair	24/30 (80.0%)	3/30 (10.0%)	0.28 *(0.08–0.92)*[a]	<0.05
Birman	33/38 (86.8%)	1/38 (2.6%)	0.07 *(0.01–0.49)*[a]	<0.05
Norwegian Forest Cat	28/46 (60.9%)	16/46 (34.8%)	1.26 *(0.68–2.35)*	NS[b]
Maine Coon	62/82 (75.6%)	14/82 (17.1%)	0.50 *(0.28–0.90)*	<0.05
Persian Longhair	88/98 (89.8%)	9/98 (9.2%)	0.23 *(0.11–0.45)*	<0.05
Ragdoll	77/87 (88.5%)	9/87 (10.3%)	0.26 *(0.13–0.52)*	<0.05
Scottish Fold	16/18 (88.9)	2/18 (11.1%)	0.28 *(0.06–1.21)*[a]	NS[b]
Siamese	13/16 (81.3%)	3/16 (18.7%)	0.51 *(0.15–1.80)*[a]	NS[b]
Siberian Cat	18/20 (90.0%)	2/20 (10.0%)	0.25 *(0.06–1.06)*[a]	NS[b]
Crossbred/ unknown	145/240 (60.4%)	47/240 (19.6%)	0.72 *(0.51–1.01)*	NS[b]
Domestic Shorthair	1560/2428 (64.3%)	705/2428 (29.0%)	*Reference*	
Total	2343 (100.0%)	838 (100.0%)		

[a] Fishers exact test.
[b] Not significant

SD = 3.2*)*. The average age for urate was significantly lower (5.2 years, *SD* = 3.0*)* compared to dogs with other uroliths (7.6 years, *SD* = 3.2*)*.

The odds for urate, cystine, and CaOx urolithiasis was significantly lower and the odds for struvite urolithiasis was significantly higher in females. There was a significant higher odds for CaOx urolithiasis and a significant lower odds for struvite in obese and male neutered dogs. There was also a significant lower odds for cystine and a significant higher odds for urate in neutered male dogs. Intact male dogs accounted for 75.7% of the total cystine submissions (Tables 6, 7, and 8).

3.5. Analysis of individual breeds

In total, dogs of 176 breeds were recorded in the database. Dogs of breeds with less than 10 submissions were not included in the analyses. Table 9 presents the significant associations of dog breeds and urolith types.

Table 6
Difference per urolith type between male and female dogs.[a]

Gender				
Urolith type	Male	Female	Odds ratio (CI)	P-value
CaF	26 (1.1%)	36 (1.7%)	–	–
CaOx	1051 (45.9)	296 (14.2%)	0.05 *(0.04–0.06)*	<0.05
Cystine	593 (25.9%)	8 (0.4%)	0.004 *(0.002–0.008)*	<0.05
Mixed	128 (5.6%)	236 (11.3%)	–	–
Silica	17 (0.7%)	2 (0.1%)	–	–
Struvite	317 (13.8%)	1472 (70.8%)	*Reference*	–
Urate	138 (6.0%)	28 (1.3%)	0.04 *(0.03–0.07)*	<0.05
Xanthine	19 (0.8%)	2 (0.1%)	–	–
Total	2289 (100.0%)	2080 (100.0%)		

[a] Not significant

The Cairn Terrier, Chihuahua, Miniature Schnauzer, Jack Russell Terrier, Maltese Dog, Papillon, and Yorkshire Terrier had a significant higher odds for CaOx urolithiasis.

The American Bulldog, Bernese Mountain dog, Dachshund, English Bulldog, Frisian Pointing Dog, Golden Retriever, Labrador Retriever, Pug and Shih Tzu had a significant higher odds for struvite urolithiasis (compared to CaOx). The American Staffordshire Terrier, Basset Hound, Chihuahua, English Bulldog, French Bulldog, Miniature Pincher, Rottweiler, Staffordshire Bull Terrier, Dachshund, and Yorkshire Terrier had a significant higher odds for cystine urolithiasis, with the Miniature Pincher at highest risk. Male dogs accounted for 100% of the cystine submissions for almost all breeds, except the Chihuahua with 6.0% of the submissions from females. The American Bulldog, Dalmatian, English Bulldog, English Cocker Spaniel, and Old English Bulldog had a significant higher odds for urate urolithiasis.

Dalmatians were at highest risk for urate urolithiasis (35/37, 94.6%) with males accounting for 95.0% of the urate submissions.

3.6. Analysis of breed groups

The giant breed group consisted of 33 dogs and from these 33 dogs, 21 (63.6%) had struvite uroliths and none of the dogs had CaOx uroliths (Table 10). CaOx had a significant higher incidence in small breed dogs (40.3% in the toy group and 35.8% in the small breed group, compared to 21.6% in the medium breed group, 8.8% in the maxi breed group, and 0% in the giant breed group). The odds for CaOx urolithiasis was significantly higher in toy dogs compared to small dogs (OR = 2.4, *CI* = *1.9–3.0*). Struvite had a higher incidence in the larger breeds (47.7% in the medium group, 51.6% in the maxi group, and 63.6% in the giant group compared to 20.7% in the toy group and 43.0% in the small group). Medium and maxi dogs had a significant higher odds for struvite urolithiasis compared to CaOx (OR = 1.8, *CI* = *1.5–2.3* and OR = 4.9, *CI* = *3.4–7.0*). The incidence of urate uroliths was the highest in the maxi breed group (17% of the total uroliths detected in the maxi group). The odds for urate urolithiasis was significantly higher in the maxi breed group compared to the small breed group (OR = 7.0, *CI* = *4.8–10.4)*. The odds for cystine urolithiasis was also significantly higher in maxi, medium and toy breed dogs compared to the small breed group, but the toy breeds had the highest odds (OR = 6.5, *CI* = *4.9–8.5*).

4. Discussion

From this study it can be concluded that between 2014 and 2020 the distribution over the different types of uroliths in cats and dogs remained similar over time. The noted changes between 2014 and 2016 were probably due to the small sample sizes in 2014 and 2015. Previous studies reported that the CaOx proportion in cats has changed since 1981. From 1981 the CaOx proportion increased, shifting from a predominance of struvite submissions to a predominance of CaOx submissions around the year 2000. CaOx reached a proportion of 55.0% in 2002 in the USA and reached 61.0% in 2003 in Europe. From 2003 a slight decline of CaOx has been observed, reaching 41.0%. (Houston et al., 2003; Picavet et al., 2007; Osborne et al., 2009; Houston et al., 2017). The increase from 1981 was probably due to the widespread use of struvite preventive diets that promoted calciuria and reduced urinary Mg concentrations (Low et al., 2010). The decrease from 2003 might be due to improvement of these diets to reduce CaOx uroliths (Lulich and Osborne, 2008; Dijcker et al., 2011). The deviation of proportions for both CaOx and struvite could also be due to underrepresentation of struvite in our database. Struvite uroliths are often associated with urinary tract infection (especially in dogs) and could be recognized during microscopic analyses of urinary sediment (Osborne et al., 1996; Palma et al., 2013). This would reduce the need for surgical removal, because a specific diet could dissolve the struvite uroliths (Abdullahi et al., 1984). Analyses of uroliths would not be used and this could have led to underrepresentation of struvite in our study. Not sending in

Table 7
Difference per urolith type between intact and neutered dogs.[a]

Urolith type	Neuter status					P-value
	Male	Female				
	Intact	Neutered	Intact	Neutered	Male odds ratio (*CI*)[b]	
CaF	10 (0.9%)	16 (1.4%)	10 (1.8%)	26 (1.7%)	–	–
CaOx	362 (31.3%)	689 (60.7%)	70 (12.7%)	226 (14.8%)	3.13 *(2.41–4.05)*	<0.05
Cystine	455 (39.4%)	138 (12.2%)	2 (0.4%)	6 (0.4%)	0.50 *(0.37–0.67)*	<0.05
Mixed	52 (4.5%)	76 (6.7%)	62 (11.3%)	174 (11.4%)	–	–
Silica	3 (0.3%)	14 (1.2%)	1 (0.2%)	1 (0.1%)	–	–
Struvite	197 (17.1%)	120 (10.6%)	402 (73.1%)	1070 (69.9%)	*Reference*	–
Urate	70 (6.1%)	68 (6.0%)	3 (0.5%)	25 (1.6%)	1.60 *(1.07–2.39)*	<0.05
Xanthine	5 (0.4%)	14 (1.2%)	0 (0.0%)	2 (0.1%)	–	–
Total	1154 (100.0%)	1135 (100.0%)	550 (100.0%)	1530 (100.0%)		

[a] Not significant.
[b] Odds ratio's from females are not included, because they were not significant

Table 8
Difference per urolith type between obese and non-obese dogs.

Urolith type	Obesity			
	Non-obese	Obese	Odds ratio (*CI*)	P-value
CaF	44 (1.4%)	18 (1.5%)	–	–
CaOx	950 (30.0%)	397 (32.9%)	1.32 *(1.08–1.60)*	<0.05
Cystine	477 (15.1%)	124 (10.3%)	1.08 *(0.81–1.44)*	NS[a]
Mixed	255 (8.1%)	109 (9.0%)	–	–
Silica	16 (0.5%)	3 (0.2%)	–	–
Struvite	1263 (39.9%)	526 (43.6%)	*Reference*	–
Urate	137 (4.3%)	29 (2.4%)	0.71 *(0.46–1.09)*	NS[a]
Xanthine	21 (0.7%)	0 (0.0%)	–	–
Total	3163 (100.0%)	1206 (100.0%)		

[a] Not significant

uroliths for analysis and thus underrepresentation could also be the case for recurrent urolithiasis in the same animal, which occurs more frequently in CaOx, or for dogs with porto-systemic shunting, which often have urate uroliths (Albasan et al., 2009; Caporali et al., 2015). The prevalence of xanthine remained stable since 2014. Following the increased prevalence of leishmaniasis in the Netherlands due to the import of dogs from countries where leishmania is endemic (Mediterranean region), increased prevalence of xanthine urolithiasis could be expected (Herremans et al., 2010), because the drug used against leishmaniasis (allopurinol) is a purine analog, it inhibits xanthine oxidase, decreases the uric acid formation and increases the concentrations of xanthine in the urine (Torres et al., 2016). According to previous studies the risk for CaOx urolithiasis increases with age (Lulich et al., 1999; Picavet et al., 2007). This corresponds with our study, where we found a significant higher average age for dogs and cats with CaOx uroliths. However, a higher average age could also be due to urolith submissions from cats and dogs with recurrence of CaOx uroliths. The recurrence rate of CaOx in dogs is between 48.0% and 57.0% within 3 years after surgical removal and in cats the recurrence rate is 7.1% within 2 years (Albasan et al., 2009). A large number of dogs and cats with second- or third-time diagnosis of urolithiasis in the dataset could lead to a higher average age for dogs and cats with CaOx uroliths in our dataset. In a previous study, the average age of dogs with cystine uroliths was significantly lower (5.9, $SD = 2.5$), this is in accordance with a significant lower average age for cystine uroliths in dogs of 5.6 ($SD = 2.6$) years in this study (Hesse et al., 2016). In this study male dogs had a higher risk for cystine urolithiasis compared to females and intact male dogs had a significant higher risk for cystine urolithiasis compared to neutered male dogs. Almost all cystine uroliths were retrieved from male dogs (98.7%) and intact male dogs (75.7%). Canine cystinuria is caused by a renal tubular defect in reabsorption of cystine and other amino acids. Certain mutations in genes predispose dogs for cysteine urolithiasis. A classification model developed in 2013 indicates four types of genetic defects that can lead to cystine urolithiasis, from which one type is sex-linked to intact male dogs (Brons et al., 2013). This could explain the high percentage of intact male dogs with cystine urolithiasis (Brons et al., 2013; Koehler et al., 2009). In accordance with previous studies, female dogs were at higher risk for struvite urolithiasis compared to male dogs. Struvite is more common in female dogs, because they are more likely to develop urinary tract infection. This is likely due to the anatomy of the female urethra, which is shorter and wider than the male urethra. Urinary tract infection is associated with struvite urolith formation, among other things because of the elevated urine pH that reduces the solubility of magnesium ammonium phosphate (struvite) (Houston et al., 2004). In contrast to female dogs, struvite urolithiasis is not predominantly linked to urinary tract infection in cats. Struvite urolithiasis is found in both male and female cats, although some studies indicate a higher percentage of female cats with struvite urolithiasis (Lekcharoensuk et al., 2000b; Houston et al., 2003; Houston and Moore, 2009; Gomes et al., 2018). Our study also found a significant higher risk for struvite urolithiasis in female cats (OR = 1.46 (1.25–1.71)).

The primary location where uroliths were surgically removed continues to be the bladder for both cats and dogs (78.7% in dogs and 85.5% in cats in our study) which is in agreement with previous studies (Picavet et al., 2007; Low et al., 2010). Nephrolithiasis and ureterolithiasis also occur, but in these cases surgery is more complicated and often requires referral to a specialized clinic performing their own urolith analysis (Ross et al., 1999). Therefore, the nephroliths and ureteroliths could be underrepresented in this study.

The majority of feline urolith submissions were from neutered cats (96.2%). In general neutering is very common in cats both in the USA and Europe, the percentage is approximately 70.0 to 80.0% (Chu et al., 2009; Trevejo et al., 2011; Sánchez-Vizcaíno et al., 2017). However, the high percentage could also be due to neutered cats being more at risk for the development of urolithiasis than intact cats. Previous studies state that neutered cats are more at risk for the development of urolithiasis compared to intact cats. This is suggested to be due to hormonal changes, more inactivity and a higher prevalence of obesity in neutered cats (Picavet et al., 2007; Gomes et al., 2018). Against trend, in this study neutered cats had a 33 times lower risk for CaP urolithiasis. However, there is not a lot of information about CaP urolithiasis available in cats, because it has a very low prevalence (Osborne et al., 2009). Our results corroborate with previous studies (Lekcharoensuk et al., 2000a; Lekcharoensuk et al., 2000b; Okafor et al., 2014) that showed that the risk for CaOx urolithiasis is significantly higher in neutered male dogs and neutered cats (both male and female) compared to intact male dogs and intact cats. The reason for this difference is not yet fully understood. It could be due to the hormonal changes after neutering. In our study we also found a higher risk for urate urolithiasis in neutered male dogs compared to intact male dogs.

Another risk factor for the development of urolithiasis in both cats and dogs is obesity. In our study obese dogs were at higher risk for CaOx

Table 9
Significant associations of canine breeds and CaOx, cystine and urate compared to struvite.

	Breed	*Prevalence of urolith type within breed*			
		Struvite	*CaOx*	*Odds ratio (CI)*	*P-value*
CaOx	American Bulldog	15/40 (37.5%)	1/40 (2.5%)	0.10 *(0.01–0.74)*[a]	<0.05
	Bernese Mountain Dog	23/28 (82.1%)	3/28 (10.7%)	0.19 *(0.06–0.64)*[a]	<0.05
	Cairn Terrier	5/23 (21.7%)	16/23 (69.6%)	4.64 *(1.67–12.77)*	<0.05
	Chihuahua	63/365 (17.3%)	130/365 (35.6%)	2.99 *(2.16–4.16)*	<0.05
	Dachshund	81/186 (43.5%)	32/186 (17.2%)	0.57 *(0.37–0.88)*	<0.05
	Miniature Schnauzer	22/71 (31.0%)	32/71 (45.1%)	2.11 *(1.20–3.69))*	<0.05
	English Bulldog	14/64 (21.9%)	2/64 (3.1%)	0.21 *(0.05–0.92)*[a]	<0.05
	Frisian Pointing Dog	17/21 (81.0%)	1/21 (4.8%)	0.09 *(0.01–0.64)*[a]	<0.05
	Golden Retriever	19/21 (90.5%)	2/21 (9.5%)	0.15 *(0.04–0.66)*[a]	<0.05
	Jack Russel Terrier	79/295 (26.8%)	162/295 (54.9%)	2.98 *(2.21–4.02)*	<0.05
	Labrador Retriever	51/63 (81.0%)	4/63 (6.3%)	0.11 *(0.04–0.32)*[a]	<0.05
	Maltese Dog	48/176 (27.3%)	87/176 (49.4%)	2.63 *(1.81–3.83)*	<0.05
	Papillon	3/31 (9.7%)	17/31 (54.8%)	9.22 *(2.39–28.26)*[a]	<0.05
	Pug	87/125 (69.6%)	12/125 (9.6%)	0.20 *(0.11–0.37)*	<0.05
	Shih Tzu	256/458 (55.9%)	130/458 (28.4%)	0.74 *(0.57–0.95)*	<0.05
	Yorkshire Terrier	24/108 (22.2%)	60/108 (55.6%)	3.63 *(2.22–5.93)*	<0.05
	Mixed	534/1176 (45.4%)	368/1176 (31.3%)	*Reference*	
		Struvite	*Cystine*		
Cystine	American Staffordshire Terrier	16/48 (33.3%)	26/48 (54.2%)	8.19 *(4.25–15.78)*	<0.05
	Basset Hound	6 /17 (35.3%)	6/17 (35.3%)	5.04 *(1.59–15.92)*	<0.05
	Chihuahua	63/365 (17.3%)	134/365 (36.7%)	10.72 *(7.44–15.43)*	<0.05
	English Bulldog	14/64 (21.9%)	34/64 (53.1%)	12.24 *(6.35–23.56)*	<0.05
	French Bulldog	30/99 (30.3%)	25/99 (25.3%)	4.20 *(2.37–7.42)*	<0.05
	Labrador Retriever	51/63 (81.0%)	3/63 (4.8%)	0.30 *(0.09–0.97)*[a]	<0.05
	Pug	87/125 (69.6%)	4/125 (3.2%)	0.23 *(0.08–0.65)*[a]	<0.05
	Miniature Pincher	1/21 (4.8%)	10/21 (47.6%)	50.38 *(6.38–397.70)*[a]	<0.05
	Rottweiler	5/15 (33.3%)	9/15 (60.0%)	9.07 *(2.98–27.60)*	<0.05
	Shih Tzu	256/458 (55.9%)	10/458 (2.2%)	0.20 *(0.10–0.38)*	<0.05
	Staffordshire Bull Terrier	5/21 (23.8%)	10/21 (47.6%)	10.08 *(3.38–30.07)*[a]	<0.05
	Dachshund	81/186 (43.5%)	56/186 (30.1%)	3.48 *(2.34–5.19)*	<0.05
	Yorkshire Terrier	24/108 (22.2%)	12/108 (11.1%)	2.32 *(1.22–5.19)*	<0.05
	Mixed	534/1176 (45.4%)	106/1176 (9.0%)	*Reference*	
		Struvite	*Urate*		
Urate	American Bulldog	15/40 (37.5%)	16/40 (40.0%)	70.81 *(27.69–181.07)*	<0.05
	Dalmatian	0/37 (0.0%)	35/37 (94.6%)	NA[b]	<0.05
	English Bulldog	14/64 (21.9%)	10/64 (15.6%)	51.85 *(39.51–137.80)*	<0.05
	English Cocker Spaniel	24/44 (54.5%)	7/44 (15.9%)	9.31 *(4.00–21.68)*	<0.05
	Old English Bulldog	8/23 (34.8%)	7/23 (30.4%)	65.00 *(18.39–229.72)*	<0.05
	Mixed breed	534/1176 (45.4%)	24/1176 (2.0%)	*Reference*	

[a] *Fisher's exact test.*
[b] *NA = not applicable, as no struvite was found in Dalmatians in this study.*

Table 10
Difference per urolith type between the different breed groups.

Urolith type	Breeds groups				
	Toy	Small	Medium	Maxi	Giant
CaF	22 (3.5%)	32 (1.2%)	8 (1.1%)	2 (0.5%)	0 (0.0%)
CaOx	248 (38.9%)	908 (35.3%)	154 (21.4%)	36 (8.8%)	0 (0.0%)
Cystine	172 (27.0%)	229 (8.9%)	124 (17.2%)	69 (16.9%)	7 (21.2%)
Mixed	55 (8.6%)	245 (9.5%)	50 (6.9%)	13 (3.2%)	1 (3.0%)
Silica	1 (0.2%)	11 (0.4%)	1 (0.1%)	6 (1.5%)	0 (0.0%)
Struvite	127 (19.9%)	1091 (42.5%)	340 (47.2%)	210 (51.3%)	21 (63.6%)
Urate	12 (1.9%)	51 (2.0%)	32 (4.4%)	69 (16.9%)	2 (6.1%)
Xanthine	0 (0.0%)	3 (0.1%)	12 (1.7%)	4 (1.0%)	2 (6.1%)
Total	615 (100.0%)	2538 (100.0%)	713 (100.0%)	407 (100.0%)	33 (100.0%)

urolithiasis and obese cats were at higher risk for struvite urolithiasis. Higher risk for CaOx in obese dogs has been previously described. (Lekcharoensuk et al., 2000a). Higher risk for struvite urolithiasis in obese cats could be due to the fact that a high percentage of cats are obese and obese cats are more likely to eat a large amount of calculogenic minerals. Non-diabetic inactive obese cats drink less, which results in more concentrated urine. In combination with inactivity, the concentrated urine stays in the bladder for a prolonged time, allowing urolith formation. Furthermore, inactivity increases the risk for urinary tract infection (Palma et al., 2009; Gomes et al., 2018). On the other hand, the term obesity is difficult to interpret in our study. Veterinary practitioners only had the possibility to fill in the weight and the option overweight yes or no and not the body condition score. In further studies it would be recommended to add the body condition score (9-point scale) to the questionnaire included with each urolith to determine whether the dogs or cats suffered from obesity.

There were multiple associations for breeds and urolith types in both cats and dogs. For cat breeds, the British Shorthair, British Longhair, Maine Coon, Persian Longhair, and Ragdoll all had a significant lower risk for struvite urolithiasis and a significant higher risk for CaOx urolithiasis compared to Domestic Shorthair cats. This is in agreement with previous studies (Houston and Moore, 2009; Osborne et al., 2009).

For dog breeds, the Cairn Terrier, Chihuahua, Miniature Schnauzer, Jack Russel Terrier, Maltese, Papillon, and Yorkshire Terrier had a significant higher risk for CaOx urolithiasis. Previous studies also reported an increased risk for CaOx regarding these breeds (Lekcharoensuk et al., 2000a; Picavet et al., 2007; Houston et al., 2017). Furthermore, these breeds are all small breed or toy breed dogs. In our study toy and small breed dogs had a higher risk for CaOx urolithiasis compared to medium, maxi, and giant breed dogs. Furthermore, the American Bulldog, Bernese Mountain dog, Dachshund, English Bulldog, Stabyhoun, Golden Retriever, Labrador Retriever, Pug, and Shih Tzu all had a significant higher risk for struvite urolithiasis compared to CaOx. Higher risk for struvite urolithiasis has been described for the Bernese Mountain Dog, Dachshund, Golden Retriever, Labrador Retriever, the Pug, and the Shih Tzu, but not for the other breeds (Houston et al., 2004; Picavet et al., 2007; Palma et al., 2013; Houston et al., 2017). Our study did also find a significant higher risk for struvite urolithiasis in medium and maxi breed dogs and the Frisian Pointing Dog, English Bulldog, and American Bulldog are medium or maxi breed dogs. However, the number of dogs of these breeds was relatively small ($n = 16$ or $n = 18$), this could have influenced the analysis. In accordance with our study, previous studies reported a significant higher risk for cysteine urolithiasis in the American Staffordshire Terrier, Staffordshire Bull Terrier, Basset Hound, Chihuahua, English Bulldog, French Bulldog, Miniature Pincher, Rottweiler, and Dachshund. (Osborne et al., 1999; Hesse et al., 2016; Houston et al., 2017). Cystine urolithiasis in Yorkshire Terriers has been mainly reported in the UK, but in our study there was also a significantly higher risk for Yorkshire Terriers (Hesse et al., 2016).

In this study the American Bulldog, Dalmatian, English Bulldog, English Cocker Spaniel, and Old English Bulldog all had a significantly higher risk for urate urolithiasis. All except the English Cocker Spaniel were previously reported. Only a predisposition for struvite urolithiasis has been reported for the English Cocker Spaniel (Houston et al., 2017). Dalmatians were at highest risk for urate urolithiasis. They are genetically predisposed for urate urolithiasis, as well as the English Bulldog. In other breeds there is an association with liver disease (especially portosystemic shunts) or urinary tract infections (Bartges et al., 1999).

In this study no differentiation was made between compound uroliths and mixed uroliths, because this information was not available. Therefore, mixed uroliths were not taken into the analysis. In further research a distinction between mixed and compound would be beneficial to detect risk factors for the mixed and compound uroliths separately in cats and dogs.

Lastly, in our study the recurrence of uroliths was not included into the analysis, because this information was not available. It could be that there is a different relationship of gender, breed, and neuter status between first time diagnosis of urolithiasis and second- or third-time diagnosis. Medical history and diet history should also be taken into account to provide more insight is possible association.

5. Conclusions

The findings of this study in the Netherlands are similar to findings in previous studies.

From a change in feline and canine urolith composition between 1981 and 2007, it seems like the distribution over the different types of uroliths in both cats and dogs remains similar over time between 2016 and 2020. Obesity, neuter status, sex, age, and breed continue to be associated with certain types of uroliths. New associations of urate urolithiasis in the English Cocker Spaniel and cystine urolithiasis in the Yorkshire Terrier were found in our study. However, further research is necessary to confirm these new findings. Analysis of large datasets needs to be continued to improve the knowledge of the prevalence and risk factors of canine and feline urolithiasis, as well as to discover new associations and trends.

Recommendations for future research:

1) Include the body condition score, recurrence information, medical history, and diet history in the questionnaire. With this information further research can also focus on distinguishing overweight and obese dogs, to identify associations with first time or second time urolithiasis, to be able to assess the effect of underlying diseases on the prevalence of urolithiasis, and to identify associations between certain types of food and urolithiasis.
2) The analysis of the composition of the uroliths needs to distinguish the different layers of the urolith to determine whether it is compound or mixed. In our study we could not analyse the mixed uroliths, because there was no distinction made.
3) A larger number would give more information on certain breeds or urolith types. It could be that some associations of breeds were missed, because they were not taken into the analyses due to a low number of submissions.

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