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# Prevalence of Urolithiasis in Client-owned Chelonians and Its Association with Selected Housing and Dietary Parameters in African Spurred Tortoises (*Centrochelys sulcata*)

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## Abstract

There is limited information on the prevalence and etiology of urolithiasis, although it is considered a common condition in chelonians. Several hypotheses regarding urolith formation in chelonians have been proposed, but none has been tested by epidemiological research. The objective of this study was to evaluate the prevalence of urolithiasis in a large number of chelonians and to evaluate the association between housing and dietary conditions and urolithiasis in African spurred tortoises (*Centrochelys sulcata*). Records of all client-owned chelonians that underwent radiographs at two institutions were extracted. Univariable and multivariable logistic regression models were built to explore associations between the presence of urolithiasis and husbandry variables. Prevalence of urolithiasis was 4.4% (95% confidence interval (CI): 3.3–5.9%; 46/1,033) among all chelonians. Terrestrial chelonians had 64 times the odds (odds ratio (OR): 64.2; 95% CI: 15.4–266.6; $P < 0.001$) of presenting urolithiasis compared with aquatic chelonians. African spurred tortoises had 22 times the odds (OR: 22.3; 95% CI: 7.7–64.5; $P < 0.001$) of presenting urolithiasis compared with other terrestrial chelonians. African spurred tortoises living in a confined indoor area had 3 times the odds of presenting urolithiasis compared with the tortoises living outdoors (OR: 3.01; 95% CI: 1.06–8.55; $P = 0.038$), and African spurred tortoises that were not fed any fruit had 0.31 times the odds of presenting urolithiasis compared with the tortoises fed fruit (OR: 0.31; 95% CI: 0.10–0.99; $P = 0.049$). Certain chelonians in captivity are at higher risk than others of suffering urolithiasis. African spurred tortoises in a confined indoor area had the highest risk of developing urolithiasis. As a precaution, avoiding fruit should be considered in the diet of African spurred tortoises.

**Keywords:** Calculi, chelonians, epidemiology, stone, urinary, urolithiasis

## Introduction

Urolithiasis is considered a common disorder in chelonians (Keller, 2019; Johnson and Watson, 2020; Takami *et al.*, 2021). In a survey of necropsies of captive tortoises in the United Kingdom performed almost 50 yr ago (Keymer, 1978), urolithiasis was diagnosed in 4.2% (6/144) of chelonians necropsied. In a retrospective study including client-owned chelonians from a veterinary teaching hospital in the United States (Keller *et al.*, 2015), the prevalence of urolithiasis in chelonians was estimated to be 5.1% (40/789), with the most common species affected being desert tortoises (*Gopherus agassizzi*: 77.5%, 31/40) and African spurred tortoises (*Centrochelys sulcata*: 7.5%, 3/40). In that study, the prevalence was calculated over the total of the chelonians examined, regardless of whether diagnostics were performed (Keller *et al.*, 2015). A retrospective study including three veterinary hospitals in Japan and spanning 20 yr (Takami *et al.*, 2021) identified 101 cases of urolithiasis in chelonians: the African spurred tortoise was the most common species with urolithiasis in the study, representing 41.6% of cases (42/101), followed by the Indian star tortoise (*Geochelone elegans*: 29.7%, 30/101). The total number of chelonians examined in the study was not reported; thus, incidence or prevalence of urolithiasis could not be determined.

There are currently different hypotheses to explain the etiology of urolithiasis in reptiles (Keller *et al.*, 2015; Keller, 2019). Uroliths of chelonians are mainly formed of urates (i.e., uric acid salts), with <10% formed of calcium carbonate or other crystals (Osborne *et al.*, 2009; Keller *et al.*, 2015). They are found in the distal urinary tract (urinary bladder or cloaca), rather than in the kidneys or ureters (Keller *et al.*, 2015), indicating that crystallization of uric acid likely occurs in the bladder. In theory, any increase in concentration of uric acid in the urine (e.g., diets too high in protein, or insufficient urine production), change in the solubility of uric acid (e.g., low urine pH, lower environmental temperature), or decrease in urine excretion could result in excessive formation of crystals in the urinary bladder. Authors have reported dehydration as a risk for the formation of uroliths, suggesting that this pathological process can occur from inappropriate environmental and dietary water (Johnson and Watson, 2020). Nutritional imbalance has also been reported as a risk factor (Boyer and Scott, 2019; Johnson and Watson, 2020). These theories are mainly based on case reports and have not been evaluated by epidemiological research.

The objectives of the present study are 1) to evaluate the prevalence of urolithiasis in client-owned chelonians and 2) to evaluate the association of urolithiasis with housing and dietary conditions in African spurred tortoises.

## Material and Methods

**Study design:** A retrospective unmatched case-control study was performed by collecting data from chelonians presenting to two related institutions, Tai Wai Small Animal & Exotic Hospital, Hong Kong, and Island Exotics, Hong Kong, between 31 July 2014 and 31 December 2018. Medical records from one of the veterinary hospitals (Island Exotics) were included from the date of its opening (1 June 2016).

**Medical record search and inclusion criteria:** The electronic medical record database of each institution was searched by one investigator (VC) for the following keywords: "chelonian," "turtle," "terrapin," "tortoise," and "reptile." The medical record of each chelonian seen during the period of interest on which radiology was performed was extracted. Only animals with a minimum of dorsoventral radiographs in their records (either performed in the hospital or at a referring clinic) were included in the study.

**Data extraction and variable classification:** All data were entered manually in an electronic spreadsheet by the same investigator. The following variables were extracted: age, sex, body weight, species, species habitus, husbandry variables (i.e., diet, housing, ultraviolet B [UVB] exposure, heat exposure), and diagnosis. Extracted variables were classified into categories for further analysis. Habitus of each species was classified as primarily aquatic or terrestrial, depending on the natural history of the species. Sex was classified as female, male, or undetermined. Dietary information from terrestrial chelonians was extracted by categorizing as "present" or "absent" to each of one of the following dietary items: presence of vegetables, presence of pellets, presence of hay, presence of fruits, and presence of calcium supplementation. Any combination of presence or absence of the dietary items was possible. The frequency or amount of each of these variables could not be reliably extracted. Housing information from terrestrial chelonians was classified into the following categories: confined indoor (i.e., living in a vivarium or a tank), free-roaming indoor, and free-roaming outdoor. Animals that received one or more water baths per week were classified as "soaking weekly or more." Animals that had a UVB bulb in their living environment were classified as "UVB light present." Animals that were exposed to sunlight (minimum of once a week) were classified as "sun exposure." The final diagnosis or diagnoses was extracted as reported on the medical record.

**Statistical analysis:** Continuous variables were summarized as either means or medians and SDs, depending on their distribution. For categorical variables, the percentages of patients in each category were calculated. Univariable and multivariable logistic regression models were built to identify predictors associated with urolithiasis. Initially, univariable models were built including only one predictor variable to calculate unadjusted odds ratio (OR), 95% confidence intervals (CIs), and $P$ values. For continuous variables (age and body weight), variables were included in the univariable models both as continuous and after binning them in quartiles. Multivariable logistic regression models were subsequently developed including variables that had an arbitrary $P$ value cutoff point of 0.1 and variables deemed clinically relevant (Mickey and Greenland, 1989; Hosmer and Lemeshow, 2000). The Hosmer–Lemeshow statistic and the Nagelkerke $R^2$ were used to assess goodness of fit and to compare the logistic regression models. Results of the final multivariable model were provided as adjusted odds ratio, 95% CIs, and $P$ values. Data were analyzed with commercial software (SPSS statistics, version 22.0, IBM Corp.). Two-tailed values of $P < 0.05$ were considered significant.

## Results

**Population summary:** The initial database included 1,033 chelonians from 49 species. Of these animals, 438 (42.4%) were red-eared sliders (*Trachemys scripta elegans*), 118 (11.4%) African-spurred tortoises, 70 (6.8%) golden coin turtles (*Cuora trifasciata*), 67 (6.5%) leopard tortoises (*Stigmochelys pardalis*), 62 (6%) Reeve's turtles (*Mauremys reevesii*), 32 (3.1%) Indian star tortoises, 30 (2.9%) Chinese striped neck turtles (*Mauremys sinensis*), 27 (2.6%) yellow-marginated box turtles (*Cuora flavomarginata*), 21 (2%) radiated tortoises (*Astrochelys radiata*), and 18 (1.7%) fly river turtles (*Carettochelys insculpta*). Other species are reported in Table S1. Overall, 496 (48.0%) chelonians were female, 266 (25.8%) were male, and 271 (26.2%) were of undetermined sex. Seven-hundred thirty-seven (71.3%) chelonians were predominantly aquatic and 296 (28.7%) were predominantly terrestrial. Age and body weight were not normally distributed (Shapiro–Wilk test, $P < 0.001$ for both variables). Median age ($n = 1{,}030$) was 8 yr (0.1–61.0 yr) and median body weight ($n = 1{,}020$) was 1.0 kg (0.0–50.0 kg).

**Table 1.** Results of univariable and multivariable binary logistic regression describing the association between urolithiasis and housing and dietary factors in chelonian species. Adjusted odds ratios were only reported if the variable was included in the final multivariable model.

| | Urolithiasis | No urolithiasis | OR | 95% CI | *P* value | aOR[a] | 95% CI | *P* value |
|---|---|---|---|---|---|---|---|---|
| Age (yr) | 6.5 (1.0–14.0) | 5.0 (0.1–20.0) | 1.05 | 0.96–1.17 | 0.28 | 1.12 | 0.99–1.26 | 0.065 |
| Weight (kg) | 4.3 (0.1–30.8) | 4.5 (0.0–50.0) | 0.99 | 0.96–1.04 | 0.83 | | | |
| Sex, *n* (%) | | | | | | | | |
| Unknown | 19 (38.8) | 30 (61.2) | Ref | | | Ref | | |
| Male | 11 (25.0) | 33 (75.0) | 0.53 | 0.22–1.28 | 0.16 | 0.41 | 0.15–1.09 | 0.07 |
| Female | 10 (40.0) | 15 (60.0) | 1.05 | 0.39–2.82 | 0.92 | 0.90 | 0.31–2.63 | 0.85 |
| Diet component, *n* (%) | | | | | | | | |
| Vegetables | 37 (35.9) | 66 (64.1) | Ref | | | | | |
| No vegetables | 3 (20) | 12 (80) | 0.44 | 0.12–0.17 | 0.23 | | | |
| Pellets | 24 (30.8) | 54 (69.2) | Ref | | | | | |
| No pellets | 16 (40.0) | 24 (60.0) | 1.50 | 0.68–3.32 | 0.32 | | | |
| Hay or grass | 19 (35.2) | 35 (64.8) | Ref | | | | | |
| No hay or grass | 21 (32.8) | 43 (67.2) | 0.90 | 0.42–1.93 | 0.79 | | | |
| Fruits | 9 (52.9) | 8 (47.1) | Ref | | | Ref | | |
| No fruits | 31 (30.7) | 70 (69.3) | 0.39 | 0.14–1.12 | 0.08 | 0.31 | 0.10–0.99 | 0.049 |
| Calcium supplementation | 4 (44.4) | 5 (55.6) | Ref | | | Ref | | |
| No calcium supplementation | 36 (33.0) | 73 (67.0) | 0.62 | 0.16–2.44 | 0.49 | 0.47 | 0.11–2.03 | 0.31 |
| Housing, *n* (%) | | | | | | | | |
| Outdoor free roaming | 10 (25.0) | 30 (75.0) | Ref | | | Ref | | |
| Indoor free roaming | 9 (32.1) | 19 (67.9) | 1.42 | 0.49–4.14 | 0.52 | 1.64 | 0.51–5.34 | 0.41 |
| Indoor confined | 21 (42.0) | 29 (58.0) | 2.17 | 0.87–5.39 | 0.09 | 3.01 | 1.06–8.55 | 0.038 |
| Sun exposure | 21 (38.2) | 34 (61.8) | Ref | | | | | |
| No sun exposure | 19 (30.2) | 44 (69.8) | 1.75 | 0.81–3.79 | 0.16 | | | |
| UVB present | 16 (27.6) | 42 (72.4) | Ref | | | | | |
| No UVB | 24 (40.0) | 36 (60) | 0.70 | 0.32–1.50 | 0.36 | | | |
| Soaking weekly or more | 9 (31) | 20 (69) | Ref | | | | | |
| No soaking | 31 (34.8) | 58 (65.2) | 1.19 | 0.48–2.92 | 0.71 | | | |

OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; Ref, reference category.
[a] The final multivariable model was considered properly fitted: Hosmer–Lemeshow = 0.81; Nagelkerke $R^2 = 0.14$.

**Prevalence of urolithiasis:** Of 1,033 chelonians in total that underwent radiographic exams, 46 chelonians suffered from urolithiasis. Except for two turtles (one Chinese striped neck and one Amboina box turtle [*Cuora amboinensis*]) and three other terrestrial species (two Indian star tortoises, one leopard tortoise, and one pancake tortoise [*Malacochersus tornieri*]), all of the other 40 chelonians diagnosed with urolithiasis were African spurred tortoises. Prevalence of urolithiasis was 4.4% (95% CI: 3.3–5.9%; 46/1,033) among all chelonians, 0.3% (95% CI: 0.0–1.0%; 2/737) among aquatic chelonians, 14.9% (95% CI: 11.0–19.4%; 44/296) among terrestrial chelonians, and 33.9% (95% CI: 25.4–43.2%; 40/118) among African spurred tortoises. Terrestrial chelonians had 64 times the odds (OR: 64.2; 95% CI: 15.4–266.6; $P < 0.001$) of presenting urolithiasis compared with aquatic chelonians. African spurred tortoises had 22 times the odds (OR: 22.3; 95% CI: 7.7–64.5; $P < 0.001$) of presenting urolithiasis compared with other terrestrial chelonians.

**Housing and dietary conditions of African spurred tortoises:** The vast majority of African spurred tortoises (87%, 103/118) were fed vegetables in their diets. Seventy-eight (66%) and 54 (46%) of the animals were fed tortoise pellets and hay, respectively. Seventeen tortoises (14%) were fed fruits and nine (8%) had calcium supplementation. Fifty tortoises (42%) lived indoors in a confined enclosure (i.e., in a terrarium), 40 tortoises (34%) lived free roaming outdoors, and 28 tortoises (24%) lived free roaming indoors. About half of the tortoises (47%, 55/118) had some degree of exposure to natural sunlight, whereas the remaining animals had no exposure to natural sunlight. Half of the tortoises (49%, 58/118) were exposed to a UVB, whereas the remaining animals had no exposure to UVB. One fourth of the tortoises (26%, 29/118) were soaked in water weekly or more often, whereas the other tortoises were not routinely soaked in water. Stratification of housing and dietary conditions by presence or absence of urolithiasis is reported in Table 1.

**Association between housing and dietary conditions and urolithiasis in African spurred tortoises:** In the univariable logistic regression analyses, none of the predictor variables showed a statistically significant association with urolithiasis. A multivariable logistic regression model was further built including variables that were considered clinically relevant as confounders independently of their statistical significance (age, sex, and calcium supplementation) and variables that had a $P$ value in the univariable models $<0.1$ (housing condition and fruit provision; Table 1).

Based on the multivariable model, African spurred tortoises living in a confined indoor area had three times the odds of presenting urolithiasis compared with animals living outdoors (OR: 3.01; 95%CI: 1.06–8.55; $P = 0.038$). Chelonians that were not fed any fruit had 0.31 times the odds of presenting urolithiasis compared with chelonians fed fruit (OR: 0.31; 95% CI: 0.10–0.99; $P = 0.049$).

## Discussion

In this study, African spurred tortoises were identified as the species most at risk of suffering urolithiasis compared with other terrestrial chelonians commonly kept as pets, with odds of having a urolith >20 times higher than in other terrestrial species. African spurred tortoises were heavily represented in two of the previous studies on chelonian urolithiasis from the United States and Japan (Keller *et al.*, 2015; Takami *et al.*, 2021).

Currently, there is limited information on the prevalence of urolithiasis in wild terrestrial chelonians. In one study describing postmortem findings in 24 dead desert tortoises, 3 (12.5%) of them had urolithiasis (Homer *et al.*, 1998). Besides this small study, we could not retrieve any additional published survey of postmortem or radiographs in wild chelonians that could help establish the prevalence of urolithiasis in a noncaptive environment. The prevalence of urolithiasis in African spurred tortoises observed in our study (34%) was almost three times higher than in that survey, suggesting that captivity may play a role in the development of urolithiasis. There are three overarching factors that could explain the high prevalence of urolithiasis observed in African spurred tortoises in this study: decreased elimination, excessive production, or decreased solubility of uric acid salts.

Because the main risk factor identified in our study was housing in a confined indoor environment, a potential reason for development of urolithiasis could be the space available for the tortoises to roam. A larger available space to roam could influence development of uroliths in several ways, such as increased thermoregulation opportunity or more physical activity. This latter factor may be particularly important. Wild tortoises tend to travel long distances (Berry, 1986; Drabik-Hamshare and Downs, 2017). For example, the desert tortoise home range is on average 20 ha and this species commonly travels a distance of 460–823 m/day, with some males covering up to 1,000 m/day (Berry, 1986). The leopard tortoise, a sub-Saharan chelonian, has a home range that varies from 13 to 200 ha depending on its location (Drabik-Hamshare and Downs, 2017). This species is nomadic and travels from 50 m/day up to 8,000 m/day (Drabik-Hamshare and Downs, 2017). Such an extensive amount of traveling could stimulate drinking and voiding urine, helping to excrete some of the uric acid before it crystallizes into urates. Reproducing these home ranges in captivity is near impossible, even in a zoological collection. However, specific treatments, such as treadmill walking, could be instituted in tortoises at risk of developing urolithiasis to increase the turnover of urine in the urinary bladder.

One of the other risk factors identified in our study was the inclusion of fruits in the diet of the tortoises. In mammals, fructose metabolism produces urate as a byproduct. During the initial phosphorylation of fructose in the liver by the enzyme fructokinase, ATP is used rapidly and both ATP levels and intracellular phosphate levels decrease (Maenpaa *et al.*, 1968). The rapid decrease of phosphate stimulates the enzyme adenosine monophosphate deaminase, which catalyzes the degradation of adenosine monophosphate to inosine monophosphate and finally to uric acid (Lanaspa *et al.*, 2012). In humans, for example, it has been shown that after ingestion of 0.5 g/kg of oral fructose, uric acid levels rise dramatically in both serum and urine (Perheentupa and Raivio, 1967). If a similar process were to occur in tortoises, the increase in uric acid levels in the urine could result in further urate deposition on a previously existent urolith, or in formation of a new urolith. Older publications on dietary needs of chelonians recommend fruits as part of the captive diet for African spurred tortoises (Stauffer, 2003), but more recent recommendations limit fruits to a small portion of the diet and fruits are to be kept as an occasional treat (Boyer and Boyer, 2019). Because we found potential evidence of increased risk of urolithiasis in African spurred tortoises fed fruit and there is a physiological pathway to explain this process, it is prudent to avoid inclusion of fruit in the diet of chelonians at risk of urolithiasis.

A decrease in solubility of the uric acid that is normally excreted through the urine could also contribute to urolith formation in chelonians. Changes in solubility of uric acid could result in the formation of excessive urates (uric acid salts) and overcoming the capacity of chelonians to eliminating them. Several factors influence the solubility of uric acid, including temperature, pH, and its concentration. Chemical studies showed that when urates are suspended in a solution, decreasing temperatures lead to a decrease in their solubility (Iwata *et al.*, 1989; Chhana *et al.*, 2015). In the present study, we could not explore the actual temperature at which tortoises were kept, due to the wide variability on how temperature was reported in the medical records.

Urate solubility is also widely influenced by pH (Shekarriz and Stoller, 2002). Uric acid in urine supersaturates at pH $<$ 5.5, whereas at a pH $>$ 6.5 most uric acid is in the form of urates (Shekarriz and Stoller, 2002). In fact, in humans, urine with an acidic pH tends to promote the formation of uric acid stones (Kamel *et al.*, 2002; Wagner and Mohebbi, 2010). In chelonians, limited publications are available for the normal range of the pH of urine. In wild desert tortoises, urine pH has shown seasonal variation and was found to be between 5.6 and 7.3 (Christopher *et al.*, 1994). Although anecdotally it is believed that alkalinization of the urine could help dissolution of chelonian uroliths (Eisenbarth *et al.*, 2022), the majority of uric acid at a pH $>$ 6.5 is in the form of urates, the component of most tortoise uroliths. In fact, it is possible that both a pH lower than normal and a pH higher than normal could be responsible for urolithiasis in chelonians.

The concentration of uric acid also influences its solubility (Shekarriz and Stoller, 2002). One of the main factors that has been recommended to prevent this disease is adequate humidity to prevent chronic dehydration (Keller, 2019; Johnson and Watson, 2020). In our study, although a comprehensive assessment of ranges of humidity to which the tortoises were exposed was not possible, exposure to weekly baths did not influence the risk of developing this disease.

This study has some limitations. One limitation of our study is the retrospective nature of the data collection, which may have introduced imprecisions in the characterization of the various categories used for the analysis. In addition, the sample size for some species was small, which may have limited our ability to draw conclusions about the prevalence of urolithiasis in those species. Finally, the study was conducted in a single institution, which may limit the generalizability of our findings to other populations of chelonians.

Based on our study, some chelonian species in captivity are at higher risk than others of suffering urolithiasis. In addition, it seems that the amount of space available, more than any other housing requirement, plays a role in the development of urolithiasis. As a precaution, until more evidence on their safety is available, fruits should be avoided in the diet of African spurred tortoises. Considering the retrospective nature of this study, further evidence is required to consolidate these findings.

## Supplemental Material

Table S1. Chelonian species or genera included in the study in decreasing order of frequency. Genera were reported when a more precise classification based on the medical records was not possible.

### Literature Cited


Berry KH. 1986. Desert tortoise (*Gopherus agassizii*) relocation: implications of social behavior and movements. Herpetologica, 42(1):113–125.

Boyer TH, Boyer DM. 2019. Tortoises, freshwater turtles, and terrapins. *In* Divers SJ, Stahl SJ (eds): Mader's Reptile and Amphibian Medicine and Surgery. 3rd ed. W.B. Saunders, St. Louis, MO, USA:168–179.

Boyer TH, Scott PW. 2019. Nutrition. *In* Divers SJ, Stahl SJ (eds): Mader's Reptile and Amphibian Medicine and Surgery. 3rd ed. W.B. Saunders, St. Louis, MO, USA:201–223.

Chhana A, Lee G, Dalbeth N. 2015. Factors influencing the crystallization of monosodium urate: a systematic literature review. BMC Musculoskelet Disord, 16(1):296.

Christopher MM, Brigmon R, Jacobson E. 1994. Seasonal alterations in plasma $\beta$-hydroxybutyrate and related biochemical parameters in the desert tortoise (*Gopherus agassizii*). Comp Biochem Physiol Part A: Physiol, 108(2–3):303–310.

Drabik-Hamshare M, Downs CT. 2017. Movement of leopard tortoises in response to environmental and climatic variables in a semi-arid environment. Mov Ecol, 5(1):5.

Eisenbarth JM, Gauntt DM, Rivas AE. 2022. Dual-energy computed tomography for diagnosis and monitoring attempted medical management of a large urate urolith in a desert tortoise (*Gopherus agassizii*). J Herpetol Med Surg, 32(1):26–34.

Homer BL, Berry KH, Brown MB, Ellis G, Jacobson ER. 1998. Pathology of diseases in wild desert tortoises from California. J Wildl Dis, 34(3):508–523.

Hosmer DW, Lemeshow S. 2000. Applied Logistic Regression. Wiley, New York, NY, USA.

Innis C. 1997. Observations on urinalyses of clinically normal captive tortoises. Proc Assoc Reptile Amphib Vet:109–112.

Iwata H, Nishio S, Yokoyama M, Matsumoto A, Takeuchi M. 1989. Solubility of uric acid and supersaturation of monosodium urate: why is uric acid so highly soluble in urine? J Urol, 142(4):1095–1098.

Johnson JG, Watson MK. 2020. Diseases of the reptile renal system. Vet Clin North Am Exot Anim Pract, 23(1):115–129.

Kamel KS, Cheema-Dhadli S, Halperin ML. 2002. Studies on the pathophysiology of the low urine pH in patients with uric acid stones. Kidney Int, 61(3):988–994.

Keller KA. 2019. Urolithiasis (cystic calculi and cloacal uroliths). *In* Divers SJ, Stahl SJ (eds): Mader's Reptile and Amphibian Medicine and Surgery. 3rd ed. W.B. Saunders, St. Louis, MO, USA:1355–1356.

Keller KA, Hawkins MG, Weber III ES, Ruby AL, Guzman DS-M, Westropp JL. 2015. Diagnosis and treatment of urolithiasis in client-owned chelonians: 40 cases (1987–2012). J Am Vet Med Assoc, 247(6):650–658.

Keymer I. 1978. Diseases of chelonians:(1) Necropsy survey of tortoises. Vet Rec, 103(25):548–552.

Lanaspa MA, Sanchez-Lozada LG, Choi YJ, Cicerchi C, Kanbay M, Roncal-Jimenez CA, Ishimoto T, Li N, Marek G, Duranay M, Schreiner G, RodriguezIturbe B, Nakagawa T, Kang DH, Sautin YY, Johnson RJ. 2012. Uric acid induces hepatic steatosis by generation of mitochondrial oxidative stress: potential role in fructose-dependent and-independent fatty liver. J Biol Chem, 287(48):40732–40744.

Liptovszky M, Bende B. 2016. Urolithiasis in a zoo-housed African spurred tortoise (*Geochelone sulcata*). Magyar Állatorvosok Lapja, 138(3):177–182.

Maenpaa PH, Raivio KO, Kekomaki MP. 1968. Liver adenine nucleotides: fructose-induced depletion and its effect on protein synthesis. Science, 161(3847):1253–1254.

Mickey J, Greenland S. 1989. A study of the impact of confounder-selection criteria on effect estimation. Am J Epidemiol, 129(1):125–137.

Osborne CA, Albasan H, Lulich JP, Nwaokorie E, Koehler LA, Ulrich LK. 2009. Quantitative analysis of 4468 uroliths retrieved from farm animals, exotic species, and wildlife submitted to the Minnesota Urolith Center: 1981 to 2007. Vet Clin North Am Small Anim Pract, 39(1):65–78.

Perheentupa J, Raivio K. 1967. Fructose-induced hyperuricaemia. Lancet, 2(7515):528–531.

Shekarriz B, Stoller ML. 2002. Uric acid nephrolithiasis: current concepts and controversies. J Urol, 168(4):1307–1314.

Stauffer KE. 2003. Captive care of the African spurred tortoise, *Geochelone sulcata*. J Herpetol Med Surg, 13(4):38–44.

Takami Y, Koieyama H, Sasaki N, Iwai T, Takaki Y, Watanabe T, Miwa Y. 2021. Survey of tortoises with urolithiasis in Japan. J Vet Med Sci, 83(3):435–440.

Wagner CA, Mohebbi N. 2010. Urinary pH and stone formation. J Nephrol, 23(16):S165–S169.