Melamine Toxicity—Stones vs. Crystals

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The recent article “Melamine Toxicity” by Skinner et al. unfortunately confuses the outcomes of two separate forms of melamine toxicosis, namely typical response to either ingestion of melamine alone vs. co-ingestion of melamine and cyanuric acid. The authors repeatedly (and incorrectly) refer to stone formation following co-ingestion of melamine and cyanuric acid. In their discussion of the clinical case reports of the pet food recall Skinner et al. state that “Stones in the distal tubules of affected animals also contained melamine and cyanuric acid.” Those cases reported crystals within tubules, not stones. Figure 1, shows what these crystals typically look like (crystals from the cat reported in [1]).

In their discussion of the experimental studies in cats, rats, pigs and fish the authors incorrectly state that co-administration of melamine and cyanuric acid produced renal stones. The experimental studies of animals dosed with melamine and cyanuric acid, however, report intra-

tubular crystal formation, not stones [1–3]. No stones were found in those experimental animals; however, melamine-cyanurate crystal spherulites were present.

With regard to ingestion of prolonged melamine only, Skinner et al. incorrectly state that toxicity is “characterized by crystal formation and stones.” This statement is misleading as crystals have not been routinely reported with melamine only exposure. Although some crystals are probably involved in stone formation, however neither their appearance and composition nor their abundance has been characterized. In the discussion of the analysis of the stones in Chinese infants, the authors of the review describe “melamine-urate crystals,” however no reports have been published characterizing such crystals. The composition of the stones has been described by several authors [4–7].

Unfortunately, the authors have confused the basic difference between the two toxicities. Ingestion of melamine alone has repeatedly been shown to cause stone formation, stones that are measured in centimeters. Co-ingestion of melamine and cyanuric acid results in the formation crystals of melamine-cyanurate measuring between 20 and 200 μm . Those intratubular crystal spherulites cause rapid renal failure in a mechanism that is similar to acute uric acid nephropathy. This type of renal failure has not been reported with ingestion of melamine alone.

Finally, citation 15 is missing the author of the presentation from which the figure was adapted [8].

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Fig. 1 Appearance of crystals in frozen section of cat kidney

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