Silica Urolithiasis in Dogs Fed an Atherogenic Diet[1] (37268)

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Siliceous urinary calculi are known to occur in cattle (1, 2) and sheep (3) and can be produced experimentally in rats (4) but so far they have not been found in dogs. This report describes the occurrence of silicon containing stones in the kidneys, urethra and bladder of dogs fed a semisynthetic atherogenic diet. The diet was formulated by Malmros and Sternby (5) and has been shown by them and us (6) to induce atherosclerosis in dogs when fed for a year or longer. We previously reported changes in lipid composition and metabolism which take place in arteries (7), leukocytes (8) and kidneys (9) of these dogs as well as alterations which occur in plasma lipids and lipoproteins (10) in response to this diet. Kidney stones were first observed in 3 of the 5 original dogs maintained on the diet for 12 to 16 mo (9) but a thorough analysis of the stones was not attempted at that time. Recently, we placed another group of dogs on this diet and the ensuing urolithiasis is described below.

Methods and Results. The experimental diet contained 16% hydrogenated coconut oil, 5% cholesterol, 20% casein, 29% sucrose, 3% salt and vitamin mixture and 27% nonnutritive bulk. Eight adult male mongrel dogs were placed on this diet for an intended period of 15 mo. However, 3 dogs died prematurely at 4, 9 and 12 mo, respectively, each one showing the presence of renal and cystic calculi, bladder ulceration and perforation, and severe peritonitis on postmortem examination. Of the remaining 5 dogs examined at the end of the experiment, 4 were found to have similar stones in the renal pelvis and 3 had stones in the bladder.

The stones removed from the renal pelvis at autopsy were typically hard, dense, and irregularly shaped, varying in size up to about 5 mm. They had smooth brown surfaces with sharp edges but had no recognizable crystalline structure when viewed grossly or microscopically. When stones were present in the bladder they were usually lighter brown or yellow and generally found as clumps or loose aggregates of smaller stones.

Microscopic examination together with systematic chemical analyses failed to clarify the nature of the stones, the ground calculus material being nonreactive in each of the chemical tests for common calculi components (11). The possibility that silicon might be the major component of this inorganic material was then considered, since the pelleted diet contained 3% talc or magnesium silicate ($Mg_3Si_4O_{11}\cdot H_2O$) and 12% silicic acid ($SiO_2\cdot xH_2O$) as nonnutritive bulk constituents. The solubility of a large portion of the calculus material in hydrofluoric acid reinforced this hypothesis. The subsequent identification of Si as the only major inorganic element was made by emission spectrographic analysis[2] of kidney stones taken from two dogs. Trace amounts (1–500 ppm) of Cu, Fe, Mg, K, Na and Ca were also found. Other elements looked for but not detected were Ag, Al, As, B, Ba, Be, Bi, Cb, Cd, Co, Cr, Ge, In, Li, Mn, Mo, Ni, Pb, Sb, Sn, Sr, Ti, V, W, Zn and Zr.

Discussion. Although canine silica urolithiasis has not been previously reported, the ability of dogs to adsorb Si from ingested particulate silica and soluble silicates with subsequent excretion of Si in the urine has been established by King, Stantial and Dolan

[1] This work was supported in part by Grant No. HL-6835 from the U.S. Public Health Service.

[2] Emission spectroscopy was performed by National Spectrographic Laboratories, Inc., Cleveland, OH 44128.

(12). Formation of silica calculi must also be rare in man but the occurrence of a urinary calculus identified by X-ray diffraction and refractive index as opaline silica ($SiO_2 \cdot xH_2O$) was reported in a human patient by Herman and Goldberg (13). This man had been taking 30–35 antacid tablets a day for 2–3 yr, each tablet containing 0.5 g magnesium trisilicate ($Mg_2Si_3O_8 \cdot xH_2O$). Other studies have shown that subjects ingesting 5 g of a commercial magnesium trisilicate product for each of 4 days absorbed more than 5% of the silicon calculated as SiO_2 (14).

Our dogs consumed a daily average of 400 g of the atherogenic diet and were therefore ingesting 12 g of talc/day. This amount on its own is almost as much as the 15 g/day of $Mg_2Si_3O_8 \cdot xH_2O$ ingested by the human subject (13) who developed the SiO_2 calculus. In addition to the 12 g of magnesium silicate or talc, each dog consumed approximately 48 g a day of silicic acid, a form of silicon which is known to be readily absorbed by dogs (12).

Silica urolithiasis has thus been produced in dogs fed a silica containing atherogenic diet. Possible impairments in kidney function and morphology are being investigated. Whether the absorption of silicon compounds into the blood or subsequent renal damage plays any role in this type of experimental atherogenesis seems unlikely but is not yet known. In view of our findings we suggest that silicon compounds should not be included in diets to be fed to dogs for long periods of time. The suitability of replacing the talc and silicic acid with additional cellulose is now being studied with this diet.

Summary. Obstructive calculi, shown by emission spectroscopy to contain silicon as a major component, were observed in the kidneys, bladders and urethras of dogs fed a semisynthetic atherogenic diet. Deposition of these stones was due in part to the presence of large amounts of silicates in the diet as nonnutritive bulk constituents. The occurrence of silica urolithiasis, previously unreported in dogs, suggests that silicon containing compounds should not be included in formulated diets fed to dogs for prolonged periods.

1. Connell, R., Whiting, F., and Forman, S. A., Can. J. Comp. Med. **23**, 41 (1959).

2. Bailey, C. B., Science **155**, 696 (1967).

3. Jubb, K. V. F., and Kennedy, P. C., "Pathology of Domestic Animals," 2nd ed., Vol. 2, p. 324. Academic Press, New York (1970).

4. Emerick, R. J., Kugel, E. E., and Wallace, V., Amer. J. Vet. Res. **24**, 610 (1963).

5. Malmros, H., and Sternby, N. H., Progr. Biochem. Pharmacol. **4**, 482 (1968).

6. Robertson, A. L., Butkus, A., Ehrhart, L. A., and Lewis, L. A., Atherosclerosis **15**, 307 (1972).

7. Butkus, A., Robertson, A. L., Ehrhart, L. A., and Lewis, L. A., Exp. Mol. Pathol. **16**, 311 (1972).

8. Ehrhart, L. A., Balachandran, R., Butkus, A., Lewis, L. A., and Robertson, A. L., Lipids **6**, 895 (1971).

9. Butkus, A., Robertson, A. L., Ehrhart, L. A., and Lewis, L. A., Exp. Mol. Pathol. **17**, 55 (1972).

10. Butkus, A., Ehrhart, L. A., Robertson, A. L., and Lewis, L. A., Lipids **5**, 896 (1970).

11. Henry, R. J., "Clinical Chemistry: Principles and Technics," 914 pp. Harper and Row, New York (1964).

12. King, E. J., Stantial, H., and Dolan, M., Biochem. J. **27**, 1007 (1933).

13. Herman, J. R., and Goldberg, A. S., J. Amer. Med. Ass. **174**, 1206 (1960).

14. Page, R. C., Heffner, R. R., and Frey, A., Amer. J. Digest. Dis. **8**, 13 (1941).

Received Jan. 16, 1973. P.S.E.B.M., 1973, Vol. 143.