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Kidney Damage in the Golden Hamster Following Chronic Administration of Diethylstilbestrol and Sesame Oil.*

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Estrogen induced hyperplasias have been reported repeatedly for various species of animals. The most conspicuous of such changes reported so far for the estrogenized hamster are in the hypophysis. In this gland the pars intermedia develops very extensive adenomas which migrate through the stalk well into the hypothalamus (Vasquez-Lopez,¹ Koneff, Simpson and Evans,² Matthews³). For the hamster the only kidney alteration mentioned in the literature is found in the paper by Vasquez-Lopez where Table I records a "large secondary deposit macroscopically visible in the left kidney" of one of 28 hamsters implanted with 10 mg pellets of diethylstilbestrol or of estradiol benzoate; this particular animal had been treated for 299 days with the natural estrogen.

While a tumor-producing action, in guinea pigs, has been denied for sesame oil by Lipschütz and Vargas⁴ it has been affirmed in man by Conrad, Conrad and Weiss.⁵ To date we have had no opportunity of examining the kidneys of sesame oil-treated control hamsters. We know of no reports in the literature, however, which attribute the formation of renal adenomas, in any species, to treatment with either estrogens, sesame oil, or any other similar oil.

In this laboratory we have examined kid-

neys from 14 hamsters (*Cricetus auratus*) in which group were 4 untreated males, one untreated female, 6 treated males and 3 treated females. On the average the treated animals received a total of 41 mg of diethylstilbestrol in 25 cc of sesame oil followed by a total of 61 mg in the form of microcrystals in 23 cc of saline solution. Injections were made subcutaneously, daily or on alternate days, over a period averaging 379 days. The animals averaged 429 days in age and 112 g in body weight at the time of sacrifice.

Kidney changes were observed in all of the 9 treated animals. Of these changes by far the most conspicuous were adenomas (Fig. 1C) found in each of the 6 males. In size these tumors ranged from small nodules a few cells in width to masses about one-third of the volume of a control kidney. In many of the adenomas were groups of cells showing "colloid degeneration", rare in the cells of intact tubules. Many of the adenomas were in the region of the pelvis, projecting more or less into the renal sinus. The cell arrangement in some of these suggests an origin from the transitional epithelium of the pelvis. Other adenomas occurred in various portions of the kidney cortex. The fact that the adenomas alone of all the kidney tissue contain much sudanophilic substance suggests that sesame oil (also sudanophilic) may be the tumor-producing agent. Experiments are under way to test the relative actions of oil and estrogen and to investigate the cause of the sex difference in kidney response. In one animal the renal tumor had metastasized through the peritoneal cavity to the mesenteries and the spleen.

In 2 males, fibromas were observed in the capsular connective tissue.

No extraglomerular arteriosclerosis was observed, but in the females amyloid infiltration

* The diethylstilbestrol used in this study was supplied through the courtesy of Dr. D. C. Hines of the Eli Lilly Company.

¹ Vasquez-Lopez, E., *J. Path. and Bact.*, 1944, **56**, 1.

² Koneff, A., Simpson, M. E., and Evans, H. M., *Anat. Rec.*, 1946, **94**, 169.

³ Matthews, V. S., 1947 unpublished data.

⁴ Lipschütz, A., and Vargas, L., *C. R. Soc. biol.*, 1939, **130**, 9; Lipschütz, A., Rodriguez, F., and Vargas, L., *C. R. Soc. biol.*, 1939, **130**, 939.

⁵ Conrad, A. H., Conrad, A. H., Jr., and Weiss, R. S., *J. A. M. A.*, 1943, **121**, 237.

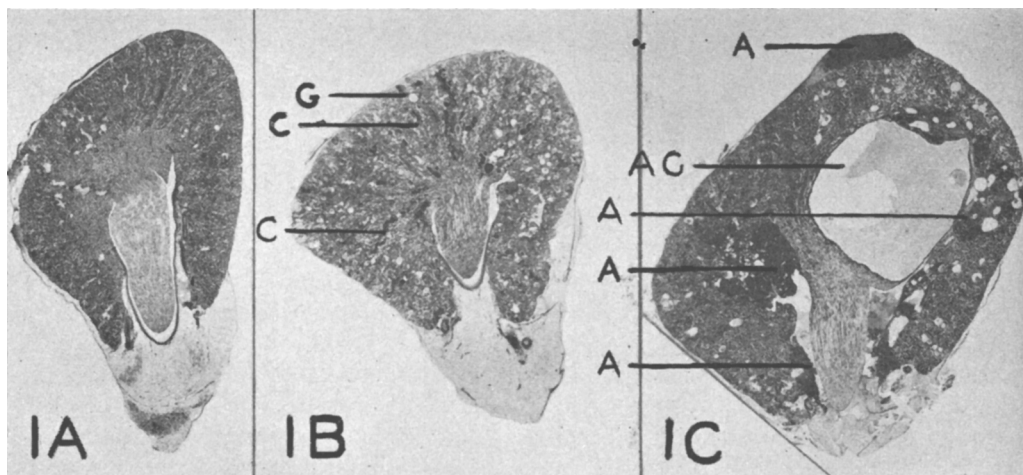


FIG. 1.

Fig. 1, A to C, (all $\times 5$) are transverse sections through kidneys of golden hamsters. 1A represents a normal kidney from a 389-day-old ♀ weighing 136 g; untreated. 1B is from a 364-day-old ♀ weighing 85 g; received 29 mg of diethylstilbestrol in 17 cc of sesame oil over a period of 107 days, followed by 59 mg in the form of microcrystals suspended in 20 cc of saline solution over a period of 215 days. 1C is from a 456-day-old ♂ weighing 130 g; received 55 mg of diethylstilbestrol in 33 cc of sesame oil over a period of 205 days, followed by 58 mg of microcrystals in 19 cc of saline solution over a period of 215 days. A, adenoma; Ac, cyst in adenoma; C, casts in enlarged tubules; G, enlarged capsular space about glomerulus.

was considerable in many glomeruli and around many convoluted tubules. This was associated with large and abundant hyaline casts and tubular atrophy (Fig. 1B). In 2 of the 6 treated males also, amyloid was demonstrated. In one animal it was confined to traces in a few of the glomeruli; in the other animal, No. 49, (the one possessing fewest and smallest adenomas) it was present in somewhat greater amount and found around convoluted tubules as well as in glomeruli. A similar picture of glomerulo-nephritis has been described by Korenchevsky and Ross⁶

in both male and female, normal and gonadectomized, albino rats treated with 0.018 to 0.2 mg of estradiol dipropionate, in sesame oil, weekly for from 21 days to 3¾ months. They make no mention of sesame oil controls or of sexual differences in kidney reaction.

A more detailed account, involving hamsters still being treated, will be published later.

Summary. The kidneys of golden hamsters treated for long periods with diethylstilbestrol and sesame oil tend to undergo marked changes of a destructive character. In the male these changes are primarily in the direction of potentially malignant tumor formation. In the female they are in the direction of glomerulo-nephritis

⁶ Korenchevsky, V., and Ross, M. A., *Brit. Med. J.*, 1940, 1, 645.