

type POW strain and were found to be antigenically similar.

Grateful acknowledgement is made to Mr. Thomas Watthews, Mr. Robert Means, and Mr. J. W. Wilcox for identification and collection of specimens; to Dr. Doris Collins for histopathologic examinations; and to Mrs. Ruth Swift, Mr. Albert Roz, and Mr. George Rayner for excellent technical assistance.

1. Whitney, E., *Am. J. Trop. Med. and Hyg.*, 1963, v12, 417.
2. McLean, D. M., Donohue, W. L., *Canad. Med. Assn. J.*, 1959, v80, 708.
3. McLean, D. M., de Vos, A., Quantz, E. J., *Am.*

J. Trop. Med. Hyg., 1964, v13, 747.

4. Thomas, L. A., Kennedy, R. C., Eklund, C. M., *Proc. Soc. Exp. Biol. and Med.*, 1960, v104, 355.
5. Whitney, E., *Am. J. Vet. Res.*, 1965, in press.
6. ———, *Am. J. Trop. Med. and Hyg.*, 1964, v13, 123.
7. Clarke, D. H., Casals, J., *ibid.*, 1958, v7, 561.
8. Sever, J. L., *J. Immunol.*, 1962, v88, 320.
9. Kent, J. F., Fife, E. H., Jr., *Am. J. Trop. Med. and Hyg.*, 1963, v12, 103.
10. MacPherson, I. A., Stoker, M. G. P., *Virology*, 1962, v16, 147.

Received February 26, 1965. P.S.E.B.M., 1965, v119.

Alteration of Sex Characteristics of Turkey Poult with Diethylstilbestrol.* (30203)

CHARLES F. SIMPSON, R. H. HARMS AND H. R. WILSON

Department of Veterinary Science, University of Florida, Gainesville

Injection of male turkeys with diethylstilbestrol (DES) causes the development of aortic ruptures, hyperproteinemia, hypercholesterolemia, and hyperlipemia(1). Although lipid metabolism in the chicken appears to be controlled by the ovarian hormones, concentration of blood lipids of immature male and female birds is not remarkably different from that found in other species such as man (2). However, blood lipid levels of avian females during periods of egg formation are greatly elevated as compared to chickens not in production.

Few trials have been described in which turkeys were injected with DES for long periods of time, and there are conflicting reports concerning the value of DES in stimulating growth and fat deposition in turkeys (3). The present work was conducted to determine the influence of this estrogen on immature turkeys.

Materials and methods. Male and female Broad-Breasted Bronze turkeys were purchased at one day of age from a commercial hatchery. They were raised by routine poul-

try husbandry methods which have been reported previously(1). Two experiments were conducted which were identical except that they were separated by an interval of 5 months. There were 80 males and 80 females in each experiment, consisting of 16 groups, each containing 10 poult. Eight turkeys in each group were injected with DES, and 2 turkeys served as controls. Birds were started on DES at various ages. Four groups of males received the first injection of 30 mg of DES in liquid form† at 6 weeks of age, and 2 groups had an initial injection at 8 weeks. Another 2 groups were first injected at 10 weeks of age. The same numbers and groups of females were subjected to the identical treatment schedule. Treatment with DES and collection of blood serum for total cholesterol determinations(4) were repeated weekly until the experiment terminated at 18 weeks of age. Oviduct and testes of treated and control turkeys were compared.

Results. About 8 days following the first DES injection, all treated male birds began to strut, as evidenced by pronounced spreading of the tail feathers and dropping of the wing tips. Strutting was spontaneous; how-

*Supported in part by a grant from Nat. Heart Inst., U.S.P.H.S. Florida Agr. Exp. Stations Journal Series No. 2116.

† Caponade, Vineland Laboratories, Vineland, N. J.

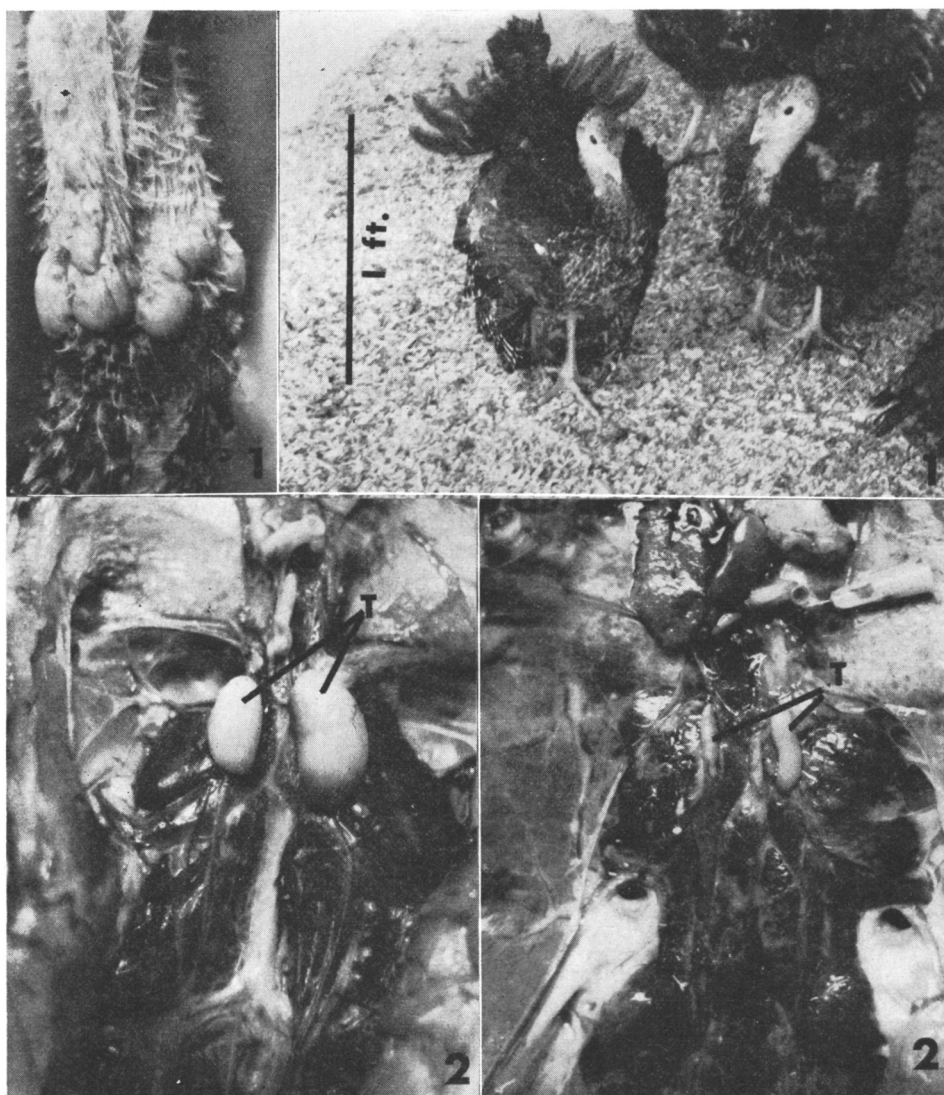


FIG. 1. Nine and one-half weeks old female after receiving 4 injections of DES. Notice strutting and development of thickenings in neck region (enlarged in photo at left).

FIG. 2. Left, testes (T) of normal 15½ weeks old turkey. Right, testes (T) of bird of same age following 8 weekly injections with DES. Both photos were taken at the same magnification.

ever, the act was readily prompted by stimulatory influences, such as whistling by the caretaker. About the same time the skin in the neck region became thickened and red, sac-like lobes appeared. Rectal prolapses were common after males had been treated with DES for 3 weeks. Gobbling sounds were first emitted by males about 7 days after strutting commenced or about 15 days after the first treatment with DES. Treated

poults displayed a precocious mating instinct.

Ninety-five per cent of the female turkeys treated with DES reacted in a manner not greatly different from males. They demonstrated secondary male characteristics. They strutted, had enlarged and flaccid vents, gobbled when stimulated, displayed precocious mating actions, and developed thickenings of the neck region (Fig. 1). Females did not demonstrate these characteristics as soon, or

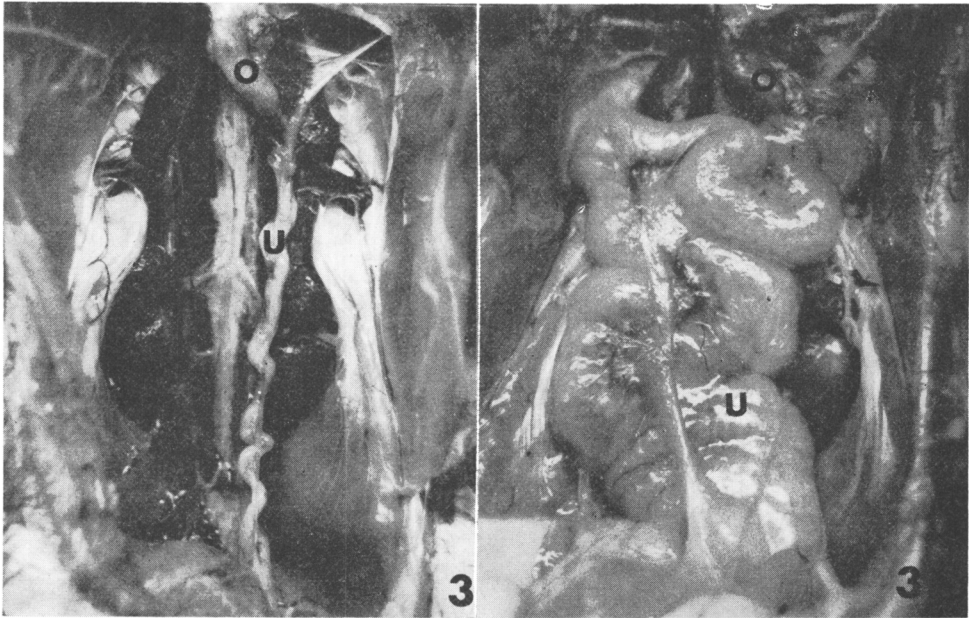


FIG. 3. Left, oviduct (U) and ovary (O) of normal 15½ weeks old turkey. Right, organs of bird of same age following 10 weekly injections with DES.

as markedly as males, but they were nevertheless easily detectable. Males showed these influences of DES treatment about one week before they became evident in females. Treated males and females emitted predominantly gobbling sounds, but occasional chirping vocal sounds were also heard.

Diethylstilbestrol had an effect on the gonads of all injected turkeys. The testes were atrophied, but this was not marked until turkeys had been treated for 4 or 5 weeks. After 8 injections with 30 mg of DES, testes were $\frac{1}{3}$ the size of controls (Fig. 2). Females developed pronounced hypertrophy of the oviduct following 3 treatments with the estrogen. The average weight of the oviduct of a 15½-week-old female injected for 6 weeks was about 30 g as compared to 0.5 g for controls (Fig. 3). When poults were killed at 15 weeks of age, 20% had cystic testes or ovaries.

Treated males and females had increased deposits of body fat as compared to controls. Total serum cholesterol levels were markedly elevated in both treated males and females, and there were no differences due to sex. Following 10 injections with DES, the average serum cholesterol levels were significantly

increased (947 mg/100 ml *vs* 135 mg for controls). These results indicate that DES has an effect on the metabolism of both males and females.

Age at the time of first injection apparently had no influence on behavior induced by the estrogen. However, poults injected at 6 weeks of age did not achieve body weights of untreated birds, when comparisons were made at 15½ weeks of age.

Discussion. Immature male and female turkeys apparently assumed masculine secondary sex characteristics, such as strutting and development of thickenings of the neck region when treated with DES. However, feminizing effects were also manifested in both sexes, as indicated by oviduct hypertrophy or testicular atrophy. This is interesting because the same signs described here have been reported to occur in a 6-month-old female turkey given androgen(5). Therefore, each sex of turkey contains the mechanism capable of mediating the behavior of the opposite sex. It is believed that tissues mediating masculine behavior in females are very responsive to estrogens(6).

Secondary sex characteristics have been reversed in other species by hormonal injection

tions(7). Male rats developed maternal instincts when injected with testosterone in specific sites in the hypothalamus.

Summary. Male and female turkeys were started on weekly injections of diethylstilbestrol at 6, 8, and 10 weeks of age. Such treatments caused the development of secondary male characteristics consisting of gobbling, strutting, development of thickenings of the neck region, prolapsed rectums, and precocious mating actions. There were also feminizing effects from DES treatments consisting of atrophy of the testes in males and hypertrophy of the oviduct in females. Increased fat deposition and hypercholesterolemia also occurred in treated birds.

The technical assistance of J. W. Carlisle, C. J. Miller, and R. G. Overcash is acknowledged.

1. Simpson, C. F., Harms, R. H., Neal, F. C., *Proc. Soc. Exp. Biol. and Med.*, 1964, v116, 334.
2. Lorenz, F. W., Chaikoff, I. L., Entenman, C., *J. Biol. Chem.*, 1938, v126, 763.
3. Creger, C. R., Mitchell, R. H., Jones, M. L., Atkinson, R. L., Quisenberry, J. H., Couch, J. R., *Poultry Sci.*, 1960, v39, 1041.
4. Pearson, S., Stern, S., McGavack, T. H., *J. Clin. Endocrinol. and Metab.*, 1952, v12, 1245.
5. Herrick, E. H., *Poultry Sci.*, 1951, v30, 758.
6. Young, W. C., *Sex and Internal Secretions*, Williams & Wilkins Co., Baltimore, 1961, v2, 3rd Ed., 1198.
7. Fisher, A. E., *Scien. Am.*, 1964, v210, 60.

Received March 19, 1965. P.S.E.B.M., 1965, v119.

Antiphlogistic Effects of Antiserotonin (SQ 10,643) and Aminopyrine in Rats *Versus* Endotoxin and Other Agents. (30204)

BERNARD RUBIN AND MARGARET H. WAUGH (Introduced by Bradford N. Craver)

The Squibb Institute for Medical Research, New Brunswick, N. J.

Rubin *et al* have described(1) the relatively specific and highly potent antiserotonin properties of SQ 10,643 [2'(3-dimethylaminopropylthio) cinnamanilide HCl] on certain smooth muscle organs and tissues as well as the moderate antianaphylactoid activity of this compound. Furgiele *et al* have reported(2) on some of the central effects of SQ 10,643 in experimental animals.

Antopol and Chryssanthou have reported (3) that pretreatment of rabbits with either SQ 10,643 or with aminopyrine only slightly inhibited the Schwartzman phenomenon, whereas pretreatment with both compounds markedly inhibited the Schwartzman phenomenon. These results tend to support the roles of serotonin and bradykinin in the Schwartzman phenomenon(3) since the combined effect of the antiserotonin compound, SQ 10,643(1), and of the antibradykinin(4), analgesic-antipyretic compound, aminopyrine, appeared to have been more than additive.

This report is concerned with the local anaphylactoid response of the rat's paw to injected serotonin, bradykinin, histamine, or

E. coli endotoxin and with the degrees of inhibition produced by pretreatment with SQ 10,643, aminopyrine, or with both SQ 10,643 and aminopyrine.

Methods. Male rats of the Sprague-Dawley Strain, ranging in weight from 170 to 275 g, received intraplantar injections (0.055 ml) of an aqueous solution of one of the following phlogistic agents: serotonin creatinine sulfate (10 γ as base), synthetic bradykinin (50 γ), histamine diphosphate (150 γ as base), or *E. coli* endotoxin, (2.0 mg). These injections were made with hypodermic syringes and 26 gauge needles that were directed towards the ankle-joint of the right hind foot. The left hind foot of each rat served as a non-injected control. The latero-medial diameter of each ankle-joint was determined to the nearest 0.1 mm with vernier calipers. Determinations of the widths of the ankle-joints were made 1, 2, 3, 4, 5, 22-24 hours, and in some tests 48 hours after injection of the phlogistic agent.

The endotoxin employed was Bacto lipopolysaccharide W, *E. coli* 0127:B8 (Difco Labs.). Preliminary trials in 40 rats (5 rats