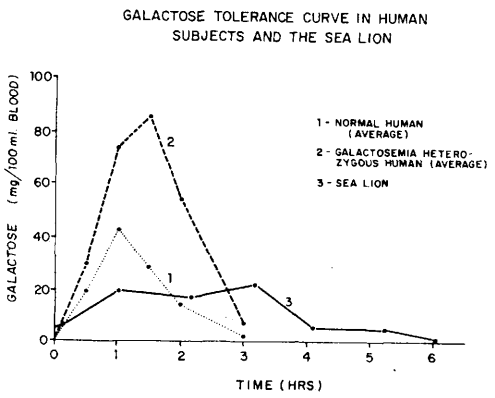

FIG. 1. Galactose tolerance curves in human subjects and a sea lion. Galactose levels after administration of .91 g of galactose/kg body weight are compared with results reported on human subjects receiving approximately twice this dose of galactose.

1 and are compared with average normal galactose tolerance tests and tests on heterozygotes carried out under similar conditions in human subjects by Donnell *et al* (6). The capacity of the sea lion to metabolize galactose is clearly demonstrated by these studies, the curve returning to baseline levels after 4 hours. The somewhat prolonged elevations of blood galactose levels may be due to the long intestinal tract of this species, resulting in long-continued absorption of the monosaccharide.

These studies indicate that although, unlike most other mammals, the infant sea lion is not presented with a large quantity of dietary galactose, the enzymes of galactose metabolism remain intact. Unlike the human, in which galactokinase activities are several-fold higher in infants than in adults(4), sub-adult sea lion galactokinase activity was approximately the same as that found in the infant sea lion. This suggests that the persistence of the enzymes of galactose metabolism in the sea lion may be a necessity because of the relatively high galactose content of mucopolysaccharides of various aquatic organisms (7,8). These findings indicate that the sea lion is not a suitable species to serve as a model for the study of the pathophysiology of galactosemia.

Summary. Studies on the enzymes, galactokinase and galactose-1-phosphate uridyl transferase have shown that these enzymes are present in the blood and liver of sea lions. A galactose tolerance test on a sea lion has revealed that these animals are able to metabolize galactose.

1. Pilson, M. E. Q., Kelly, A. L., Science, 1962, v135, 104.

2. Sunshine, P., Kretchmer, N., ibid., 1964, v144, 850.

3. Beutler, E., Baluda, M. C., Clin. Chem. Acta, 1966, v13, 369.

4. Ng, W. G., Donnell, G. N., Bergren, W. R., J. Lab. & Clin. Med., 1966, v19, 115.

5. Roth, H., Segal, S., Bertoli, D. Analyt. Biochem., 1965, v10, 32.

6. Donnell, G. N., Bergren, W. R., Rolden, M., Pediatrics, 1959, v24, 418.

7. Muramatsu, T., J. Biochem., 1965, v57, 223.

8. Enomotto, N., Tomiyasu, Y., Nippon Suisan Yakkaishi, 1962, v28, 510.

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Aortic Ruptures in Turkeys Induced by Diethylstilbestrol and Dienestrol Diacetate.* (31555)

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The administration of diethylstilbestrol (DES) to turkeys by either the parenteral (1,2) or oral(3) routes causes mortality from aortic ruptures. The possibility that other synthetic estrogens might induce aortic rhexis in turkeys has not been investigated. This paper describes experiments which were conducted to determine if dienestrol diacetate (DD) was comparable to DES in ability to cause such lesions.

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Materials and methods. Broad-Breasted

Bronze male turkeys were purchased at one day of age from a commercial hatchery, and raised by conventional poultry husbandry methods which were described previously(2). The poults were changed to a 19% protein diet containing 0.5% NaCl(4) at 4 weeks of age, and to a 23% protein diet containing 3% NaCl and 6% animal fat(4) at 6 weeks of age. At this time the turkeys were assigned to groups and treatments with estrogens were initiated.

Experiment 1. Each group of birds consisted of 6 poults. The feed of 4 groups of turkeys was supplemented with 16 g of pure DES powder/100 lb of feed(3). The feed of a second 4 groups of birds contained 256 mg DD†/lb of feed and the diet of another 4 groups of turkeys included 526 mg DD/lb of feed. Four additional groups served as controls and received no treatment.

Body weights and incidence of aortic ruptures were recorded. The experiment was terminated when the turkeys were 12 weeks of age.

Experiment 2. Each group of turkeys consisted of 10 poults. The feed of 2 groups of turkeys was supplemented with 16 g of liquid DES/100 lb of feed(3). Another 2 groups of birds were fed 512 mg DD/lb of feed, and the diet of a third 2 groups of turkeys was supplemented with 1024 mg DD/lb of feed. One group of poults served as controls and received no treatment. This experiment was repeated 3 times.

Total serum lipid(5) and cholesterol(6) determinations, body weights, and indirect systolic blood pressure measurements(7) were recorded. The experiment was terminated when the turkeys were 11 weeks of age.

Results. Exp. 1. Thirty-three percent of the turkeys fed 16 g pure DES powder/100 lb of feed died of aortic ruptures. Thirteen percent of the poults fed 526 mg DD/lb of feed died of aortic rhexis while none died that were fed 256 mg DD/lb of diet.

Weight gains of turkeys were increased by feeding 256 mg DD/lb of feed, but they were decreased by all other treatments (Table I).

† Lipamone, American Scientific Laboratories, Bloomfield, N. J.

TABLE I. Body Weights and Mortality from Aortic Ruptures Among Turkeys Fed DES and DD (Exp I).

Treatment	Wt (lb)‡	% Aortic rupture
0	8.6^{bc}	0^{a}
16 g DES*	7.6^{a}	33^{b}
256 mg DD†	9.2^{c}	0^{a}
526 mg DD†	8.1^{ab}	13^{ab}

* Per 100 lb of feed.
† Per pound of feed.
‡ At 12 wk of age.
Means with different superscripts are significantly different according to Duncan's Multiple Range Test.

Exp. 2. Thirty-nine percent of the turkeys fed 16 g liquid DES/100 lb of feed died of aortic ruptures. Thirty-four percent of the poults fed 512 mg DD/lb of feed died of aortic rhexis, and 47% of the birds given feed containing 1024 mg DD/lb of feed died of the syndrome.

Administration of DES and both levels of DD caused hyperlipemia, hypercholesterolemia, and relative hypotension that did not differ materially with the estrogen and dose level employed (Table II).

Discussion. Estrogenic compounds have been used to increase the finish and carcass quality of turkeys. Both DES and DD, at low levels, have been used for this purpose(8). In this study it was found that a low level of DD (256 mg/lb of feed) produced increased weight gains in turkeys, but no mortality from aortic rupture. High levels of DD (512 and 1024 mg/lb of diet) caused mortality from aortic rupture and decreased weight gains. This is similar to a previous report(3) in which increased weight gains and no mortality followed the feeding of a low level of DES to turkeys; however, mortality from aortic rhexis and decreased weight gains ensued when high levels of DES were fed in the feed. Apparently the induction of aortic rupture by the feeding of estrogens is dependent upon the incorporation of a sufficient quantity of the hormone in the feed to produce reduced weight.

Summary. High levels of dienestrol diacetate in the feed of turkeys (512, 526, 1024 mg/lb) caused aortic ruptures and decreased weight gains, while a low level (256 mg/lb of feed) caused no mortality and increased

TABLE II. Serum Composition, Body Weights, Blood Pressure, and Mortality from Aortic Rupture Among Turkeys Fed DES and DD (Exp II).

Treatment	Wt (lb)‡	Total lipid‡ (mg/100 ml serum)	Total cholesterol‡ (mg/100 ml serum)	Systolic blood pressure‡ (mm Hg)	% Aortic rupture
0	5.9[a]	673[a]	155[a]	230[a]	0[a]
16 g DES*	5.1[b]	14,536[b]	911[b]	176[b]	39[b]
512 mg DD†	5.4[ab]	12,671[b]	1,150[b]	177[b]	34[b]
1024 mg DD†	4.7[b]	16,548[b]	958[b]	175[b]	47[b]

* Per 100 lb of feed.
† Per pound of feed.
‡ At 10 wk of age.
Means with different superscripts are significantly different according to Duncan's Multiple Range Test.

weight gains. Comparable mortality, hyperlipemia, hypercholesterolemia, and hypotension resulted from the feeding of 16 gm diethylstilbestrol/100 lb and 512 or 1024 mg dienestrol diacetate per pound of feed.

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1. Beall, C. W., Simpson, C. F., Pritchard, W. R., Harms, R. H., Proc. Soc. Exp. Biol. and Med., 1963, v113, 442.
2. Simpson, C. F., Harms, R. H., Neal, F. C., ibid., 1964, v116, 334.
3. Simpson, C. F., Harms, R. H., ibid., 1966, v122, 1162.
4. ———, Poultry Sci., 1964, v43, 681.
5. Sperry, W. M., Brand, F. C., J. Biol. Chem., 1955, v213, 69.
6. Pearson, S., Stern, S., McGavack, T. H., J. Clin. Endocrinol. and Metab., 1952, v12, 1245.
7. Simpson, C. F., Harms, R. H., Proc. Soc. Exp. Biol. and Med., 1965, v119, 509.
8. Carter, R. D., Wyne, J. W., Chamberlin, V. D., McCartney, M. G., Poultry Sci., 1958, v37, 1284.

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Role of the Granulocyte in the Pyrogenic Response to Intra-Cisternal Endotoxin. (31556)

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Intravenously administered endotoxin may produce fever indirectly by releasing endogenous pyrogen, an intermediate substance presumably derived from granulocytes, into the peripheral circulation(1). That this represents the sole or even major mechanism of the production of fever by endotoxin has been questioned following the observation that endotoxin injected into the basal cistern via chronically implanted catheters regularly produces high sustained fevers with short latent periods(2-4). However, the importance of granulocytic pyrogen cannot be excluded in this model since an inflammatory response about the tip of the chronically implanted catheter could provide a readily available local source of the granulocytic pyrogen. The present study was performed to define the role of the granulocyte in the production of the febrile response to intracerebrally administered endotoxin.

Materials and methods. Glassware was rendered pyrogen-free in a dry-air oven at 180°C overnight. Physiological saline for injection and diluent was sterile and pyrogen-free. *Escherichia coli* endotoxin (Difco, lipopolysaccharide 0127B8) was diluted to 1.0 μg/ml.

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