TABLE VI. Relative Potencies of Certain 4-Methyl Aromatic Steroids.

Compound designation	Chick androgenic activity Testosterone=1	Estrogenic activity subcutaneous inj. (mouse) Estrone=1	Estrogenic activity subcutaneous inj. (rat) Estrone=1	Pituitary inhibition (parabiosis) Testosterone=1	Pituitary inhibition (parabiosis) Estrone=1
II	1/30	*Ca* 1/5000		1/20	
III	<1/200				
IV	<1/200	1/8000	1/1000		1/500
V	1/10	1/2000			
VI		<1/20,000			

timate would indicate a pituitary suppressing activity essentially related to the estrogenic potency.

Compound IV did not have any anti-estrogenic activity for total doses from 0.05 to 2 mg. Compound VI was less than 1/20,000th as active as estrone when injected into the immature mouse.

Discussion. The data summarized in Table VI indicate clearly that the 3-deoxy-4-methyl steroids show weak estrogenic potency and in the case of 4-methylestra-1,3,5(10)-trien-17β-ol (II), some androgenicity. The pituitary inhibition is definite for II and IV.

Summary. 4-Methylestra-1,3,5(10)-trien-17β-ol (II) and androst-3,5-dien-17β-ol (V) were 1/30th and 1/10th as androgenic as testosterone in chick's comb inunction assay. Subcutaneous injection of 4,17α-dimethylestra-1,3,5(10)-trien-17β-ol, II and V showed 1/8000th, *ca* 1/5000th and 1/2000th the estrogenic potency of estrone, respectively, by a mouse uterine test. By parabiosis assays in the rat, II was approximately 1/20th as pituitary inhibiting as testosterone, while IV was 1/500th as active as estrone.

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Effects of Endotoxin on Turkey Poults.* (27641)

R. A. BALL, J. H. SAUTTER, R. E. BURGER, AND B. S. POMEROY

Divisions of Veterinary Pathology and Bacteriology, College of Veterinary Medicine and Department of Poultry Husbandry, College of Agriculture, University of Minnesota, St. Paul

During studies on dissecting aneurysm in turkeys, methods were sought for the experimental production of the disease. In discussing experimental aortic dissecting aneurysms in animals, Hall(1) mentions the production of aortic medionecrosis in rabbits by the action of adrenalin and also by the use of the exotoxin of *Corynebacterium diphtheriae.* Endotoxins from Gram-negative bacteria are also known to produce necrosis and hemorrhage in a variety of experimental animals. Clinically, the pathological effects of generalized Gram-negative infections are associated with septic shock, attributed largely to the action of endotoxin(2,3,4). The present paper deals with a qualitative survey of the effects of endotoxin on turkey poults.

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Materials, methods, and results. Experi-

ments 1 and 2: Broad Breasted White (BBW) poults, 12 weeks old, were used in attempts to produce the generalized Shwartzman phenomenon. The birds were reared in conventional batteries with raised wire-mesh floors, then transferred to conventional growing batteries. Both sexes were included. The diet was one used in a previous experiment(5). Thirteen poults were used per experiment, 8 receiving endotoxin† intravenously (IV), and 5 controls which were injected IV with saline or were uninjected. Rectal temperatures were obtained with clinical mercury thermometers. In the first experiment, 8 birds were injected with 20 μg of endotoxin IV (*via* wing vein) as a preparatory dose, and with 50-300 μg IV 20 hours later as a provocative dose. The temperature responses are shown in Fig. 1. Poults receiving endotoxin showed a slight and transient depression at the height of the temperature response. This experiment was run in early spring. Exp. 2 was similar to the first experiment, but was run in the summer as a check on possible seasonal change. Ringer(6) has suggested that blood pressure varies seasonally; it was thought body temperature variation might also occur. Also, endotoxin heated to 80°C for 5 minutes was employed as this was believed to enhance the lethal effect of endotoxin for rabbits(7). Temperature responses are shown in Fig. 2. Transient depression was again noted in many of the birds at the height of the temperature response. Controls, injected with n-saline, failed to give a pyrogenic response.

Experiment 3: Thirteen BBW poults, 12 weeks old were used in an attempt to produce vascular collapse and shock by IV injection of large (1,000-15,000 μg) single doses of endotoxin. The average individual weight of the poults was 3.7 kg. The 8 poults receiving endotoxin showed no unusual signs or temperature deviations as compared with 5 controls. Attempts to produce aortic rupture by administration of 150 μg of adrenalin chloride‡ IV to 5 poults, 36 hours after they had received endotoxin were unsuccessful. However, no signs of internal hemorrhage or aortic rupture were produced and histological sections of aorta did not differ from control birds.

Experiment 4: Twelve New Hampshire hens were used in an attempt to reproduce necrosis and hemorrhage in an avian mesodermal tumor by one IV injection (20-500 μg) of endotoxin as has been reported in mammals (4). The birds were acquired as avian leukosis suspects. The birds showed no response to the endotoxin, and were sacrificed 72 hours after injection. Three of the 12 showed lesions of avian leukosis in the liver, mesentery, and kidneys, but none of the neoplasms showed hemorrhage or necrosis.

Experiment 5: Nine rabbits were used in an attempt to determine whether turkey serum exerted any protective action against the endotoxin when given to rabbits. Turkey serum was obtained, asceptically, by venipuncture, from healthy 12-week-old male and female turkeys. Endotoxin was added to the serum to give a final concentration of 50 μg endotoxin/ml serum. The mixture was incubated for 30 minutes at room temperature. Six rabbits received a preparatory dose of 25 μg (0.5 ml serum) and a provocative dose of 100 μg endotoxin (2.0 ml serum) each. The other 3 rabbits received 2.0 ml of turkey serum alone in one IV injection. Of the 6 rabbits receiving endotoxin-serum, 4 failed to develop the generalized Shwartzman phenomenon but did exhibit a mild pyrogenic response. Two of the 6 showed such a severe reaction to one injection of endotoxin-serum that debility prevented their receiving the provocative dose. Of the 3 rabbits receiving turkey serum alone, one developed a marked pyrogenic response. The other 2 rabbits showed a moderate pyrogenic response.

Discussion. The pathogenesis of many Gram-negative infections has been attributed mainly to the endotoxins liberated by the microorganisms within the host's blood stream. Turkeys are susceptible to generalized Gram-negative infections with high morbidity and

† Endotoxin used was Bactopolysaccharide, source: *E. coli* 0111:B4 (Difco Laboratories, Detroit, Mich.). Merthiolate was added to a final concentration of 1:1,000. Potency was verified by production of the characteristic generalized Shwartzman reaction in the rabbit.

‡ Parke-Davis & Co., Detroit, Mich.

mortality such as fowl cholera and fowl typhoid. Hence, the lack of ability to produce a generalized Shwartzman reaction or vascular collapse from large single doses of endotoxin is of interest. Failure to elicit a marked response does not prove that endotoxin is not concerned with the pathogenesis of such infections. The bird may possess different physiological mechanisms for dealing with endotoxin(8). The high body temperature of the bird may confer resistance. The possibility of the birds being previously exposed to Gram-negative organisms with the development of resistance should not be overlooked.

Adrenalin was used for two reasons: (1), if weakening of the aortic wall had resulted from the action of the endotoxin, a sudden increase in blood pressure from adrenalin might produce aortic rupture; (2), it has been shown that adrenalin itself will produce aortic medionecrosis in the rabbit(1,9). The failure of adrenalin itself to produce aortic lesions might have been due to the use of only one injection, whereas Lorenzen(9) used repeated injections in his experiments.

The small number (3) of adult chickens having avian leukosis does not permit definite conclusions; however, none of the 3 developed necrosis or hemorrhage at the site of the tumor following IV administration of endotoxin. Thus, it would appear that this mesodermal tumor does not respond as do certain mammalian mesodermal tumors.

The results with the control poults show that the normal turkey poult usually shows an afternoon rise in temperature of as much as 0.5-1.0°F when the environmental temperature is held rather constantly at 70°F. This agrees with the data given for the chicken(10, 11,12). Hence, such experiments should be carried out at other times. The afternoon body temperature rise is probably associated with muscular activity, because birds held alone in cages, under standard conditions, with a minimum of muscular activity, did not show this rise.

Whereas Landy(13) and Smith(8) report that the chicken does not give a thermal response to endotoxin, these experiments show that the turkey does so. Although Figs. 1 and 2 show that the birds receiving endotoxin

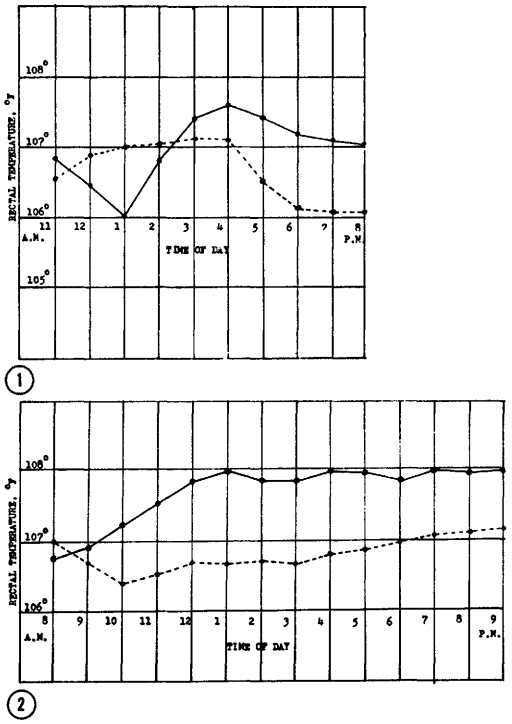

FIG. 1. Avg rectal temperature response in turkey poults following administration of a second dose of endotoxin 20 hr after initial dose. Temperatures of injected birds are represented by a solid line; those of controls by a broken line.

FIG. 2. Twenty μg of endotoxin were used as the preparatory dose followed 15 hr later by the provocative dose of 60 μg. The graph above shows the avg temperature responses following final dose at 8 A.M. Solid line denotes injected birds; broken line the controls.

have only approximately 0.8°F increase over the controls, this is significant because of 16 injected birds, 15 were within 0.3°F of the temperature mean given, whereas the temperatures of the control birds showed much greater variation. The reason for the peculiar initial temperature drop, shown in Fig. 1, of the birds receiving endotoxin is not clear; however, it occurred in every bird receiving endotoxin and in none of the controls. In the second experiment in late spring, it was not possible to reproduce this initial thermal response. In Exp. 3, the tolerance of turkey poults to as high as 15,000 μg of endotoxin is remarkable, in view of the fact that much smaller doses will kill dogs, rabbits, and other mammals, producing vascular collapse and irreversible shock.

Summary. Attempts to produce the gener-

alized Shwartzman phenomenon in the turkey poult were unsuccessful. Large (1,000-15,000 μg) single doses of endotoxin, administered intravenously, failed to produce vascular collapse or other clinical signs in the poult. Attempts to reproduce a syndrome with lesions similar to aortic dissecting aneurysm as it occurs under field conditions, by use of endotoxin alone, or in combination with adrenalin, were unsuccessful. These experiments cast some doubt on the likelihood of Gram-negative organisms or sensitization by them being responsible for the naturally-occurring syndrome of dissecting aneurysm.

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Human Adenovirus Complement-Fixing Antibodies in New York Family Dogs. (27642)

L. E. CARMICHAEL AND FRANCES D. BARNES (Introduced by James A. Baker)

Veterinary Virus Research Institute, New York State Veterinary College, Cornell University, Ithaca, N. Y.

Reports of human adenovirus complement-fixing (CF) and neutralizing antibodies in farm and laboratory dogs have suggested the possibility that canines may act as healthy carriers(1,2). Serological studies in Sweden, however, failed to show CF antibody in dogs, despite the prevalence of adenovirus infections in the human population(3). In addition to public health considerations attending possible adenovirus infections in dogs, demonstration of a high incidence of adenovirus antibodies in dogs would also probably have implications as regards infectious canine hepatitis (ICH), since prior immunological experience with certain human adenoviruses alters the response of dogs to ICH virus(2).

Dogs have been shown to be susceptible to human adenovirus types, for both CF and neutralizing antibodies develop following a single inoculation. The course of the disease in dogs is entirely without clinical signs and criteria for adjudging infection are therefore serological or based upon virus isolation. Reports of human adenovirus isolation from experimentally infected dogs are conflicting(1, 2). Whereas one group reported persistence of virus in excretions and secretions for periods up to 7 days(1), attempts to isolate virus from inoculated dogs in our laboratory failed when specimens were tested later than 24 hours after exposure to adenovirus types 4 and 7(2). In addition, contact transmission to susceptible littermate dogs did not occur. This suggested that dogs probably do not act as carriers or reservoirs of human adenovirus types, despite the ease with which they may become infected.

In an effort further to assess the role of dogs as asymptomatic carriers of human adenoviruses, serums were selected from sam-