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Effect of Gonadal Hormones on Experimental Infection of Rats with *Brucella abortus.**

LEONORA H. PUGH. (Introduced by R. P. Reece.)

From the New Jersey Agricultural Experiment Station, New Brunswick, N.J.

Ascoli[1] noted that there was a sex difference in the resistance of albino rats to intraperitoneal inoculations of *Brucella abortus*. Further studies involving over 1000 rats showed that the mature male rat is more resistant than the mature female and immature males and females to an intraperitoneal infection with a virulent strain of *Br. abortus*. This evidence suggested that androgen might account for the difference in resistance.

Several investigators have studied the effects of the estrogens on the course of experimental infections. In studies on tuberculosis, contradictory results have been obtained. Aycock and Foley[2] noted a decrease in resistance to tuberculosis in guinea pigs receiving α-estradiol dipropionate. Estrogenic substances were found to increase resistance in mice to *Diplococcus pneumoniae* Type I[3] and to streptococcus infections.[4] Testosterone propionate increased resistance in mice to *D. pneumoniae* Type I[3] and to streptococcus infections.[4] Progesterone had no effect on the resistance to pneumococcal infection in mice.[3] *In vitro,* it was found that estrogens have a bactericidal action on Gram positive organisms, but have no effect on Gram negative organisms.[5]

Experimental. Albino rats from our colony were castrated at two age levels: sexually mature rats with an average weight of 150 g and sexually immature rats with an average weight of 80 g. The castration was performed 1 to 7 days before administration of the hormone. For each trial, the animals were divided into 3 groups: castrates receiving hormone, untreated castrates, and untreated intact animals, 5 or more animals were included in each group. In one trial estradiol dipropionate (Diovocylin†) was usually administered 2 days before infection by subcutaneous injection in oil at a dose level of 0.005 mg per rat. Mature males and females and immature females were used in this trial. In the other trial testosterone propionate (Perandren†) was administered by subcutaneous injections in oil at 2 dose levels; 0.5 mg per rat per day for 10 days (immature males and females) and 0.1 mg per rat per day for 10 days (mature males and immature males and females). Following the above treatments, the rats in all groups were injected intraperitoneally with approximately 4000 million *Br. abortus* organisms suspended in sterile saline. The number of survivors 5 days after infection was recorded.

The results given in Table I showed that all rats receiving testosterone propionate at both dose levels exhibited increased resistance to the infection. Of those rats receiving estradiol dipropionate, immature castrated females showed decreased resistance, and mature castrated females showed increased resistance to the infection. There was no significant difference in the group of mature males.

Another experiment was run on 15 immature intact males and 22 immature intact females. One half of each group was injected subcutaneously with 2.5 mg testosterone pro-

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1 Ascoli, A., PROC. SOC. EXP. BIOL. AND MED., 1947, **63**, 326.

2 Aycock, A. L., and Foley, G. E., *J. Clin. Endocrinol.*, 1945, **5**, 337.

3 von Haam, E., and Rosenfeld, I., *J. Infect. Dis.*, 1942, **70**, 243.

4 Foley, G. E., and Aycock, W. L., *Endocrinol.*, 1940, **35**, 139.

5 Faulkner, G. H., *Lancet*, 1943, **2**, 38.

† Furnished by Ciba Pharmaceutical Products, Inc., through the courtesy of Dr. E. Oppenheimer.

TABLE I.
Influence of Gonadal Hormones on Resistance to *Brucella abortus* Infection in Rats.

Age level and sex	Intact Controls	Castrates				
		Controls	Estradiol dipropionate: 0.005 mg 2 days before infection	Estradiol dipropionate: 0.005 mg 7 days before infection	Testosterone propionate: 5 mg	Testosterone propionate: 1 mg
Immature males	1/5*	4/5			2/5	
	2/6	2/5				1/7
Immature females	3/8	0/6			0/8	
	3/6	2/3				0/5
	3/5	5/11		8/11		
		2/8	3/8			
Mature males	0/4	1/5				1/6
		3/14	4/14			
Mature females	5/6	6/13	2/13			

* Number deaths/total number rats.

TABLE II.
Results Obtained Using 2.5 mg Testosterone Propionate 6 Hours Before *Brucella abortus* Infection in Rats.

		No. rats	No. deaths	% mortality
Immature intact males	Treated	8	7	87.5
	Controls	7	7	100
Immature intact females	Treated	11	7	63.6
	Controls	11	11	100

pionate in oil 6 hours before infection. All rats were infected with 3800 million *Br. abortus* organisms via the intraperitoneal route. After 5 days, the mortality rate was as follows: males and females receiving no hormonal injection, 100%; males receiving testosterone propionate, 87.5%; females receiving testosterone propionate, 63.6%. (See Table II) These results indicate that the androgen increased the resistance of the females to the infection.

Discussion. It was thought that there might be some correlation between the effect of castration and subsequent hormone therapy on the size of the adrenal cortex and the resistance to infection. According to Dougherty *et al.*,[6] the release of antibodies from the lymphocytes is controlled by adrenocortical hormone. Can it be assumed that, if the adrenal cortex is larger than normal and contains more lipoid, the animal is more resistant to infectious diseases? This might account for the fact that the female of the species in general is more resistant to infection than the male. In all species investigated the adrenal cortex of the female is larger than that of the male.[7] In this experiment there was no correlation between the size of the adrenal cortex and the resistance to infection.

Summary. Testosterone propionate significantly increased the resistance to experimental *Br. abortus* infection in the small number of rats used in this experiment. The effect was more pronounced in the females than in the males. This correlates with the fact that A.L.D. for *Br. abortus* for mature male rats is twice that for mature females and immature male and female rats.

[6] Dougherty, T. F., Chase, J. H., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 135.

[7] Giroud, A., and Santa, N., *C. R. Soc. Biol.*, 1940, **133**, 420.