Failure of Orchiectomy to Affect Degenerative Joint Disease in STR/1N Mice. (27069)

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Osteoarthritis is a genetically governed disease in laboratory mice. Among several endocrine or metabolic parameters studied that might conceivably have a major influence on the genesis of the lesions, only one, in our hands, has proved important: spontaneous degenerative joint disease is more frequent in male than in female mice(1). Other investigators have found that orchiectomy, performed early in life, markedly reduced the occurrence of joint lesions in C57 black and DBA mice(2); administration of 17-ethyl-19-nortestosterone largely reversed this finding (3). Furthermore, although bone length was not measured, histologic findings suggested that epiphyseal growth was retarded by orchiectomy in mice. During the course of other studies, it was surprising to note that neither the reported diminution of osteoarthritis nor retardation of bone growth occurred following early castration in STR/1N mice, a strain particularly prone to this disorder. For this reason, it seemed worthwhile to place these findings on record.

Methods and materials. Five groups of STR/1N mice were raised until 16 months of age: 1) non-breeder males; 2) sexually active males; 3) males orchiectomized at 4-6 weeks of age; 4) breeder females and 5) virgins. They were housed concurrently in groups of 4-6, usually 5, and fed Purina laboratory chow. The uneven numbers of males (Table 1) resulted from an intercurrent uropathy to which intact males of the strain are susceptible. Skeletons were prepared by maceration with papain; osteoarthritis of the knees, evaluated on a 0 to 4 severity scale, and femur lengths were measured as in previous studies(4). For reasons discussed elsewhere(4), the data concerning the joint disease were tested statistically by the ridit method of Bross(5), rather than by conventional procedures applicable to continuous values following a normal distribution.

Results. The frequency and severity of osteoarthritis of the knees were significantly ($p. <.05$) less in females than in males (Table 1). Breeding was without influence on the joints in females; in breeder males, the median osteoarthritis score was somewhat less than in non-breeders (Fig. 1) although the signifi-

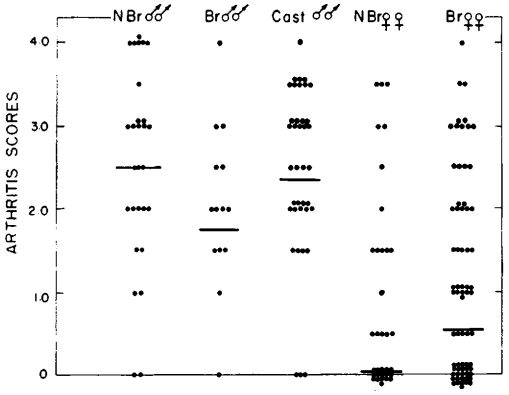

FIG. 1. Distribution of osteoarthritis scores of each knee in 5 groups of STR/1N mice. Horizontal lines represent median score for each group. Br: breeder; N Br: non-breeder; Cast: castrate.

TABLE I. Osteoarthritis, Femur Length and Body Weight in STR/1N Mice, 16 months old.

Group—(No. mice)	Osteoarthritis (Ridits)*			Femur Length‡ (mm)	Final Body‡ Wt (g)
	Mean	Upper CL	Lower CL		
♂ ♂ Non-breeders—(14)	.498†	—	—	15.86 ± .09	44.4 ± .9
♂ ♂ Breeders—(7)	.352	.487	.217	15.65 ± .09	41.9 ± 1.7
♂ ♂ Castrate—(19)	.474	.554	.394	16.27 ± .05	53.2 ± 1.1
♀ ♀ Non-breeders—(17)	.183	.264	.102	15.69 ± .05	45.4 ± 1.6
♀ ♀ Breeders—(34)	.207	.259	.155	15.81 ± .04	47.3 ± 1.2

* Both knees; CL: 95% confidence limits.
‡ Mean ± standard error.
† The identifiable distribution to which no confidence limits are attached.

cance of this finding is questionable in view of the small number of animals in this group. Castrate males had articular lesions as often and severe as intact males. They were significantly (p. $<.01$) larger (mean femur lengths) and heavier than were the intact males.

Discussion. It is difficult to interpret the failure of orchiectomy to reduce the amount of joint disease in STR/1N mice in view of different findings by others already noted. It is conceivable that strain differences have an important role in determining the effect of the testes on osteoarthritis. The apparent arthritis-sparing influence of femaleness in STR/1N mice was not simulated by removal of the testes; presumably an ovarian contribution must be involved in the sex difference.

The increased length of the bones in the castrate mice does not lend support to the view (3) that the growth-promoting effects of testicular or other hormones have an important enhancing effect on degenerative joint disease in mice. Castration prevented the obstructive uropathy already referred to. This lesion was absent from the intact animals that survived for 16 months and so were included in this study. For this reason, any debility attending the uropathy can be excluded as a contributory factor to the bone growth or articular findings. The greater obesity of castrate than intact males probably does not account for the failure of orchiectomy to reduce the amount of joint disease. Not only are the STR/1N females as obese as the males, but other studies (4) on males of several strains, including STR/1N, have shown that obesity *per se* does not have deleterious effects on the joints of mice. The relatively lower body weights in intact males than in females in the present experiment, on the basis of past experience, is the result of a decline from peak values that occurs in this strain in the second year of life. Femur lengths were comparable in intact animals of both sexes. We have found this true also in other strains, although body weight and tail-snout lengths are generally less in female mice than in males.

Summary and Conclusions. Osteoarthritis of the knees was less frequent and severe in 16 month old female than male STR/1N mice. Orchiectomy, performed at 4-6 weeks of age, failed to reduce the amount of joint disease in males. Femur length was increased in the castrate animals.

Mrs. Priscilla Auvil and Mr. Fred Bell, Jr. gave capable technical assistance.

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Received September 25, 1961 P.S.E.B.M., 1961, v108

Erythropoietic Activity of Tissue Homogenates.* (27070)

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An erythropoietically active factor has been unequivocally demonstrated in the plasma of a wide variety of mammals, including the human, by many investigators. Early attempts to find a similar factor in tissues, using extraction procedures effective for plasma, were not successful(1). Current tissue work employing other extraction methods and assays of increased sensitivity have been more fruitful. Naets(2) has demonstrated erthropoietic activity in saline extracts of dog kidney, liver

* Studies supported by contract with School of Aviation Medicine, U. S. Air Force, and grant from Hematology Research Foundation.