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Variation of Response to Infection With *Treponema Pallidum* Between an Albino and a Brown Breed of Rabbit.

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This experiment was undertaken for the purpose of comparing the course of syphilitic infection in 2 different breeds of rabbit, one a pure albino and the other a brown variety, inoculated under identical conditions with a virulent strain of *Treponema pallidum*. The animals were normal young males. The body weight of the albinos varied from 1430 to 1860 gm., that of the brown rabbits from 1340 to 2130 gm. During the experiment they were housed under uniform conditions in a light and well ventilated room, and fed on the same diet.

Experimental. The strain of *Treponema pallidum* used was that originally isolated by Nichols¹ from the spinal fluid of a patient with syphilitic neurorecurrence. This strain, now 17 years old, has had many passages through rabbits and has attained a high degree of virulence for this animal. The strain was brought to China in September, 1927. The immediate source of virus for this experiment was one of the third group of rabbits through which the strain had passed in this country. This animal was a brown breed and

¹ Nichols, H. J., *J. Exp. Med.*, 1914, xix, 362.

showed clinical evidence of orchitis 28 days after inoculation. When the orchitis was progressing, the right testis was excised under ether anesthesia, finely minced with scissors, and ground up in a sterile mortar with sterile physiologic sodium chloride solution. Of the more fluid portion of this emulsion, 0.3 cc. was inoculated into the right testis of each of 8 albino and 9 brown rabbits. The inoculations were all made on February 24, 1928. The emulsion contained from 2 to 3 actively motile organisms to the microscopic field. One animal in each group of rabbits died of pulmonary disease soon after inoculation. These are not included in the results of the experiment.

Results. The data on the natural course and character of the infection among the individual animals in the 2 groups (Group A—Albino, Group B—Brown) have been tabulated in the accompanying table.

TABLE I.
Comparison of Primary and Metastatic Lesions in Albino and Brown Rabbits Inoculated Intratesticularly with Treponema Pallidum.

Rabbit	Primary Orchitis		Metastatic Lesions					Period of Observation
	Time of Appearance	Duration days	Testis		Bone	Skin	Eye	
Orchitis			Duration days					
Group A Albino								days
1	+(11)	77	+(63)	74	0	0	+(230, 298, 324,* 338*)	338
2	+(11)	84	+(60)	10	0	0	+(95)	338
3	+(11)	168	+(109)	21	+(46)	0	+(165)	179
4	+(11)	112	+(42)	67	0	0	+(123,300)	338
5	+(14)	95	+(53)	56	0	0	0	258
6	+(11)	84	+(63)	59	+(56)	0	+(130)	338
7	+(14)	158	0		0	0	+(74,130)	186
Average	(11.5)	111.1	(55.7)	47.8	+28%	0	+85.7%	
Gr. B Brown								
8	+(7)	88	+(53)	42	+(46)	0	+(223)	338
9	+(11)	119	+(46)	49	0	0	0	172
10	+(14)	32	+(26)	12	0	0	0	338
11	+(11)	56	+(60)	10	0	0	0	338
12	+(14)	81	+(95)	14	0	0	0	195
13	+(14)	81	0		0	0	0	167
14	+(18)	26	+(39)	14	0	0	0	338
15	+(14)	74	+(42)	60	+(56)	+(42)	0	338
Average	(12.8)	69.6	(45)	28.5	+25%	+12.5%	+12.5%	

* Recurrent keratitis.

The figures in parenthesis indicate the number of days after inoculation.

All of the animals developed a typical syphilitic orchitis of the inoculated testis from 11 to 18 days after inoculation. There was no significant difference between the 2 groups in the length of the period of incubation; however, the primary reaction of the albinos was characterized by a much greater enlargement and induration of the testis than that of the brown rabbits. All but one of the former developed scrotal chancres from 1 to 3 cm. in diameter, which healed slowly, while only 2 of the brown animals had scrotal ulcers comparable to those of the albinos. The average duration of the primary lesions was significantly longer in the albino than in the brown group.

The incidence and character of the metastatic testicular lesions in both groups were generally uniform, although those of the albino rabbits were of somewhat longer duration. There were 2 cases of periosteal and bone lesions in each group, and one metastatic skin lesion among the brown animals.

It was in the number and character of the metastatic eye lesions that the two breeds presented the most remarkable variations in their respective reactions to the infection. Six of the 7 albino rabbits manifested syphilitic lesions of the eyes.² With one exception (Rabbit 2) all of these were well defined cases of interstitial keratitis. In the case of Rabbit 2 there was pronounced ciliary congestion without clinically detectable involvement of the cornea or iris. In Group A there were several instances of transient mild degrees of pericorneal vascular injection which have not been included in the accompanying table. Rabbit 9 was the only animal of brown breed that developed keratitis. Rabbit 15 of the same group had a slight transient congestion of the right eye over the superior rectus muscle at its corneal margin, which was of doubtful significance. Otherwise there was no other instance of clinically detectable ocular lesions in Group B.

During the period of the most active clinical lesions the albino rabbits were in poor general condition. They were less active than before the onset of the disease and their hair lost its usual sleekness, turning a dirty yellow color in irregular patches on the abdomen, flanks and legs. The brown animals remained vigorous and well groomed.

The animals were under observation for a period of 338 days after inoculation, with the exception of 3 rabbits of each group that died before the expiration of this time at intervals of from 167 to 258 days after inoculation. The deaths of 5 of these occurred in

² Brown, W. H., and Pearce, L., *J. Exp. Med.*, 1921, xxxiv, 167.

the month of August following severe diarrhoea. No gross lesions of significance were found at necropsy. Since the only case of keratitis in Group B occurred as late as 223 days after inoculation it is possible that had they survived longer 3 of the brown animals might have developed similar lesions. It is to be noted, however, that 4 animals of this group, in addition to Rabbit 8 of the brown breed, which reacted with a keratitis, survived for the full period of the experiment without showing lesions of the eyes.

Recurrence of generalized metastatic lesions occurred only in Rabbit 1 in the form of keratitis of both eyes.

Conclusion: The evidence as presented above indicates that under the conditions of the experiment the albino rabbits offered less resistance to infection with *Treponema pallidum* than did the brown breed of rabbit. This difference was manifested particularly in the magnitude and duration of the primary orchitis and in the incidence of metastatic keratitis. The albino group with more pronounced primary testicular reactions developed a high incidence of eye lesions. Six of the 7 animals, or 85.7%, developed metastatic lesions of the eye, while in the brown group whose primary response to infection was less pronounced, one out of 8 animals, or 12.5%, manifested ocular lesions.

While other factors of which we are not cognizant may have entered into the conditions influencing the course of the disease in these rabbits, the one known variable was that of breed. Whether the variations in the disease phenomena observed between the pigmented and non-pigmented breeds would be found constant, or relatively so, under similar conditions is a doubtful question. It is worthy of note, however, that in this experiment clinical variations occurred during the natural course of the disease where no attempt was made to modify the defensive mechanism of the hosts following unilateral intratesticular inoculation with equal amounts of the same virus at the same time. These divergent reactions must be attributed to some inherent constitutional factor of the host and not to strain specificity of the infecting organism.