

LETTERS TO THE EDITORS

PHYSIOLOGY

An Exteroceptive Block to Pregnancy in the Mouse

EXPERIMENTS on the effect of certain oral progestogens during early pregnancy, in continuation of previous observations¹ on non-pregnant animals, involved placing a recently mated female receiving oral progestogen with a strange male. In a number of the mice the procedure resulted in failure of pregnancy from the first mating and a new mating within 3-6 days. Control experiments showed that the same effect was produced by dosage with inert material or even without any treatment other than the introduction of a strange male at 24 hr. after mating. 20 out of 49 females behaved in this way, a far greater proportion than could be attributed to the expected incidence of anovular cycles. Only about 8 per cent of young females, as used, return to oestrus within 4-5 days if removed from the male after their first mating, or copulate again at this time if they are left with the male. Moreover, among the suspect females there was a failure of the pseudo-pregnancy which might have been due to poor stud males. Experiments were therefore undertaken to explore this effect.

Two test situations were devised. Situation *A* was as already mentioned, that is, the recently mated female was paired with a strange partner 24 hr. after copulation with the stud male. Situation *B* was one of proximity without contact, the female being housed in a small cage inside a stock box containing other mice which could climb about the cage but not enter it.

The stud males and all the females were albinos. The test males were either albino or wild-type. Young virgin females were mated in pairs with a stud male; the females were removed from the male when the vaginal plug was found and housed together overnight. 24 hr. later they were presented with the test situation. The females were generally left in the test situation for 7-10 days, and they were then removed to normal mouse boxes. The pregnant females were isolated before parturition, and females which became pseudopregnant or in which the pregnancy had been blocked received a fertility test with a stud male. The few females which proved to be infertile were excluded. Daily vaginal smears were examined.

The results of these investigations are briefly summarized in Table 1.

Pregnancy was blocked and implantation inhibited in nearly 30 per cent of females by the introduction of a strange male within 24 hr. of coitus; it was so blocked even by the presence of a castrated male. Pregnancy was not affected by the return of the female to her original stud male or by the presence of a strange female, whether parous or ovariectomized. Contact between the sexes was not necessary for this effect. Pregnancy was also blocked when the female was caged inside the male stock box. Among parous females, pregnancy was less readily blocked than among non-parous by contact with a strange male,

Table 1. PREGNANCY BLOCK IN THE MOUSE
The females were separated from stud males on finding vaginal plug, and housed together until presented with the test situation 24 hr. later

Test situation	Females having blocked pregnancies	
	Proportion	Per cent
<i>A</i> Housed with :		
Strange normal male (albino)	19/69	28
Strange wild-type male	25/35	71
Castrated male (albino)	13/50	26
Another female (parous or ovariectomized)	0/48	—
Original stud male	0/32	—
<i>B</i> . Proximity without contact : that is, in cage inside stock box containing :		
Albino males	8/32	25
Wild-type males	52/68	76
Females	0/49	—

but apparently broke down as easily when the female was housed inside the male stock box. This suggests that the latter situation supplies a stronger stimulus.

In both test situations the superiority of the wild-type males over the albinos as pregnancy blocking agents was highly significant. The reason for this difference is not understood, and as yet male mice of other strains have not been tried. Two different strains of females, one albino and the other pink-eyed champagne, were tested in small numbers in situation *B*. Both exhibited pregnancy block in similar proportions to those found for the original mice.

The use of the genetically marked wild-type test males showed that superfetation did not occur. Of 35 females, 15 mated with the test male. All 15 gave birth to black-eyed young only (123 young). This includes one female in which coitus with the test male took place within a few hours of introduction, her litter of 8 black-eyed young being born 19 days later, 20 days after finding the vaginal plug from the stud albino male.

No mutual reaction between females as regards pregnancy block was indicated either when the test situation involved other females or when the mated females were themselves placed singly, in pairs, or in threes in the test situation. It is well established, however, that females exert a powerful effect upon one another in terms of the oestrous cycle² and the incidence of mammary cancer³, and that the presence of a male tends to synchronize the cycle of non-pregnant females⁴.

Further experiments designed to throw light on the mechanism involved in this pregnancy block of exteroceptive origin are in progress. The pituitary and the hypothalamus are probably both implicated.

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¹ Bruce, H. M., *Studies on Fertility*, 10, 158 (1958).

² Lee, S. van der, and Boot, L. M., *Acta Physiol. Pharm. Neerl.*, 4, 430 (1955); 5, 213 (1956). Whitten, W. K., *J. Endocrinol.*, 14, 160 (1956); *Nature*, 180, 1436 (1957); *J. Endocrinol.*, 17, 307 (1958). Dewar, A. D., *ibid.*, 18, 186 (1959).

³ Mühlbock, O., *J. Endocrinol.*, 17, vii (1958).

⁴ Whitten, W. K., *J. Endocrinol.*, 13, 399 (1956).