BRIEF COMMUNICATION

DELAYED IMPLANTATION IN THE SPAYED,
PROGESTERONE TREATED ADULT MOUSE

K. YOSHINAGA* AND C. E. ADAMS

A.R.C. Unit of Reproductive Physiology and Biochemistry, University of Cambridge†

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The influence of the time of spaying on the occurrence of delayed implantation has been intensively studied in the rat. Although it was originally reported that early spaying (Day 1 or 2 of pregnancy) followed by progesterone treatment did not lead to a delay in implantation, whereas spaying at a later stage (Day 4) did (Canivenc, Laffargue & Mayer, 1956; Cochrane & Meyer, 1957), further work on rats revealed that spaying before Day 4 generally resulted in delayed implantation (Psychoyos & Alloiteau, 1962; Nutting & Meyer, 1963; Mayer, 1963). Failure to observe delayed implantation more universally in the early experiments has been ascribed in part to incomplete ovariectomy. As the influence of the time of spaying on implantation has apparently not been examined in the adult mouse, the present work was undertaken. Endocrinological aspects of delayed implantation have been studied in the immature mouse (Smithberg & Runner, 1956, 1960) and in pregnant, lactating mice (Bloch, 1958).

A total of fifty-seven adult female mice (TO strain) was used. After establishing the pattern of the oestrous cycle over three cycles, the females were placed with fertile males on the day of pro-oestrus. The following morning they were examined for the presence of a copulation plug or of spermatozoa in the vaginal smear (Day 1 of pregnancy). Mated females were allocated at random to one of five groups and spayed on Day 1, 2, 3, 4 or 5 of pregnancy. Spaying took place between 10.00 and 13.00 hours.

Progesterone (0.5 mg in 0.05 ml arachis oil) was given daily subcutaneously, beginning on the day of spaying. On Day 8 laparotomy was performed to determine whether implantation had occurred. When implantations were present the animals were killed; otherwise a single injection of oestradiol-17 β (0.05 μ g) was given, followed by daily progesterone injections for a further 4 days. Autopsy was performed on Day 12 and the number of implantations then recorded. A thorough examination was always made for ovarian remnants, especially in those mice in which implantation was not delayed. No remnants were found.

The results are summarized in Table 1; they refer only to those forty mice in which implantations were observed either on Day 8 or 12. Spaying during the

* Population Council Fellow (1964–65).

† Postal address: 307 Huntingdon Road, Cambridge.

first 4 days of pregnancy resulted in delayed implantation to a varying degree, a delay being noted in five out of eight, six out of nine, eight out of eight, and two out of seven of the mice spayed on Days 1, 2, 3 and 4 respectively. Thus implantation was delayed in all of the mice that were spayed on Day 3, but only in about two-thirds of those animals that were spayed on Day 1 or 2. Spaying on Day 5 when followed by progesterone treatment did not interfere

TABLE 1
THE OCCURRENCE OF DELAYED IMPLANTATION IN SPAYED ADULT MICE
TREATED WITH PROGESTERONE IMMEDIATELY AFTER SPAYING

Spaying on Day	No. of mice	Day 8		Day 12	
		No. with implants	Mean No. of implants	No. with implants	Mean No. of implants
1	8	3	5.3(3 to 8)	5	5.2(1 to 10)
2	9	3	6.0(5 to 7)	6	5.7(2 to 10)
3	8	0	0.0	8	5.8(1 to 11)
4	7	5	5.8(3 to 10)	2	5.0(2 to 8)
5	8	8	5.9(4 to 9)	0	0.0

All the mice were examined on Day 8; those in which implantation had not occurred were given a single injection of 0.05 μ g oestradiol and progesterone treatment was continued to Day 11 (ranges in parentheses).

with implantation at all. In all treatment groups the mean litter size was relatively constant, and was not significantly different from control material.

Smithberg & Runner (1956) observed delayed implantation in prepubertal mice in which ovulation was induced with gonadotrophins. In such animals either intact or spayed 24 to 48 h p.c. implantation was observed following progesterone treatment alone though it was more common when oestrogen was also given (Smithberg & Runner, 1960). In spayed, lactating mice, undergoing delayed implantation, progesterone treatment alone did not lead to implantation which, however, followed the injection of oestrogen (Bloch, 1958). The occurrence of delayed implantation during lactation has been ascribed to a reduced secretion of oestrogen in mice (Whitten, 1955). It is apparent that oestrogen, as well as progesterone, plays an important role in implantation in mice. Moreover, our results, which are in keeping with the above observations, show that the hormonal requirements for implantation in spayed mice vary according to the time of spaying with a significant change in uterine condition occurring on Day 3.

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