REPRODUCTIVE DECLINE IN AGED FEMALE RATS

H. C. MAIBENCO AND R. H. KREHBIEL

Department of Anatomy, School of Basic Medical Sciences,
College of Medicine University of Illinois at the Medical Center,
Chicago, Illinois 60680, U.S.A.

(Received 14th July 1972)

Reproductive decline in older female rodents has been interpreted as being due to deficiencies in various segments of the reproductive tract. Previous observations, such as those of Ingram, Mandle & Zuckerman (1958), Block & Flury (1959), Finn (1962), Blaha (1964) and Conners, Thorpe & Soderwall (1970) among others, have attributed deficiencies to one or all of the reproductive organs. In the present observations of a colony of aged females, examples of deficiencies at all levels of the reproductive tract were found. There were, however, a number of these animals which did produce a normal complement of ova and which fostered their continued development.

Sixty-six virgin or multiparous rats, aged 18 months or older, were caged with males and matings were noted as having taken place by the presence of spermatozoa in the vaginal smear. The females were subjected to laparotomy or were killed at intervals from 1 hr following mating until term (Table 1). An additional fifteen rats, 18 months or older, were bilaterally ovariectomized. Three weeks after spaying, these females were started on hormone replacement therapy in the form of 2 mg progesterone daily.

On Days 5 and 6 of progesterone treatment, each animal received 0·5 µg oestradiol propionate. On Day 6, needle stabs (six) were made in each uterine horn. On Days 9 and 10, the animals were killed. Most of the animals were injected with either Evan’s blue or pontamine blue just before being killed to facilitate the observation of any decidual reactions.

In thirty-five of sixty-six animals, evidence of pregnancy was observed (Table 1). Ova were found in the normal stages of cleavage and in the appropriate segment of the oviducts, with the following exceptions. Five of the twenty animals examined during the tubal period had a purulent salpingitis. Corpora lutea were absent in three rats. In two females, mating occurred after 09.00 hours. Ovulation was taking place in these two animals when they were killed 1 hr after mating.

Thirty-six animals were examined on Days 4 to 9 of pregnancy. The uteri obtained during Days 4 and 5 (preimplantation stages) were serially sectioned. In the six negative cases, various degrees of leucocytic infiltration were found in the mesometrial segment of the lumen. In some, the migration of lymphocytes was massive. Abnormal ova were surrounded by polymorphonuclear leucocytes. When implantation had occurred in the animals killed on Days 6 to 9 of pregnancy, the average number of decidual reactions per uterine horn

121
(5-6) was comparable to that in younger females of the species and the number of resorption sites was not above average.

In ten females, pregnancy was allowed to proceed until blood was found in the vaginal smears (Days 10 to 12 of pregnancy). The percentage of absorbing sites in these animals was much higher than in earlier stages (twenty-two out of forty-eight). In three rats, no uterine enlargement was found. At term, one rat littered eight normal young and another died while delivering three young.

In contrast to the number of decidual reactions induced by the presence of ova, only four reactions occurred following a total of 180 needle stabs in thirty uterine horns of ovariectomized rats receiving replacement hormones.

A higher incidence of leucocytic infiltration and infection was found in the reproductive tracts of aged females than was normally present in the young adult rat. Such an unfavourable tubal or uterine environment was undoubtedly a contributing factor to the failure of ova to survive. This observation appears to agree with that of Greenwald (1965). Irregularities in the oestrous cycle,

### Table 1. Ova found in the reproductive tract of aged female rats

<table>
<thead>
<tr>
<th>Pregnancy state</th>
<th>No. of animals mated</th>
<th>No. of uterine horns containing ova</th>
<th>No. of ova found</th>
<th>No. of abnormal ova</th>
<th>No. of ova/horn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubal period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days 1 to 4</td>
<td>20</td>
<td>15 (12)*</td>
<td>58</td>
<td>23</td>
<td>3.9</td>
</tr>
<tr>
<td>Uterine period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days 4 to 9</td>
<td>36</td>
<td>32 (16)</td>
<td>179</td>
<td>26</td>
<td>5.6</td>
</tr>
<tr>
<td>Uterine period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days 10+</td>
<td>10</td>
<td>11 (7)</td>
<td>48</td>
<td>22</td>
<td>4.4</td>
</tr>
</tbody>
</table>

* Figures in parentheses indicate number of females in which either one or both sides of the reproductive tract contained ova.

infrequency of mating and variations in egg transport also contributed to the loss of ova. Conners et al. (1970) found the number of copora lutea in ‘senescent hamsters’ to be comparable to that present in young females. The total number of ova which entered the uterus in the present study was not determined. The number of implantation sites (Table 1) indicates that a normal complement of ova can survive tubal transport and the uterine environment in certain old female rats and induce a decidual reaction.

The findings in this study indicate that the ability of the uterus of aged spayed animals receiving hormones to produce a decidual reaction in response to traumatic stimuli is minimal. These findings agree with observations made by Soderwall, Kent, Turbyfill & Britenbaker (1960), Finn (1966) and Blaha (1967). In contrast to this apparent failure, our findings agree with those of Finn (1962) in that, in certain pregnancies of older females, the reproductive system fosters normal development through the implantation period. The differences in the reproductive capacity of older female rats may be due to genetic or molecular factors not yet elucidated.
This work was supported by grants 1 RO 1 HD 00974 from the National Institutes of Health and Grad. Rsch. 2 41 33 10 3 21 from the University of Illinois at the Medical Center.

REFERENCES


