BRIEF COMMUNICATION

ON THE INCIDENCE OF SPONTANEOUS DECIDUALIZATION IN THE RAT*

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(Received 27th June 1967)

Recently, in a brief communication, Coppola, Ball & Brown (1966) reported an incidence of 17% spontaneous deciduomata in pseudopregnant rats. One to three discrete zones of decidualization per uterus were observed. One of us, (M.C.S.), who has been concerned with the problem of decidualization for many years, has never observed as high an incidence of spontaneous decidualization. Because of the importance of the decidual response and decidual induction as a model system in the study of nidation (Shelesnyak, 1957) and of mammalian tissue growth and differentiation (Shelesnyak, 1962), it is essential to have a reliable index of the efficiency, or lack thereof, in induction of the decidual response under experimental conditions. Any degree of spontaneous decidualization would decrease the reliability of the experimental system by making unreliable such usual criteria as the weight of the uterus and/or the proportion of the uterus undergoing the decidual transformation.

The reported high incidence of spontaneous decidualization in pseudopregnant rats therefore warranted re-investigation of the incidence in our own colony. The rats of the Biodynamics colony, originally of Wistar stock, have been colony-bred for the past 15 years. They were maintained in air-conditioned quarters under a natural light-cycle, or, during the last 3 years, under a timed cycle of 14 hr of artificial light and 10 hr of darkness. Purina Laboratory Chow and tap water were freely available. Pseudopregnancy was induced by electrical stimulation of the cervix uteri on the days of pro-oestrus and oestrus (Shelesnyak, 1931), or by mating with vasectomized male rats. Routine daily vaginal smearing was performed, the first day of the leucocytic vaginal smear being designated as Day L₁. Rats were examined for decidual reactions by autopsy or by laparotomy on Day L₁₈. In our experience, this would be the time of maximal decidual development (Lobel, Tic & Shelesnyak, 1965).

The data, assembled in Table 1, were collected over the past 8 years from groups of animals used as untreated controls in various experiments as well as from animals observed specifically for occurrence of spontaneous decidual reactions. Of 280 female rats examined, 5% showed apparently spontaneous decidual reactions. In only one rat did response occur in each uterine horn.

* This work is supported by grants-in-aid from the Population Council and The Ford Foundation, New York.
and in only two rats were there as many as two areas of decidualization. In eight of the fourteen animals showing responses, the sole area of response was the utero-cervical junction. Histological examination of many such responses revealed them, in approximately one-half the cases, to be fluid-filled cysts rather than decidual nodes.

Since most of the animals referred to in Table 1 were examined only by laparotomy, zones of suspected decidual responses were not subjected to histological examination for verification of the response. The figure of 5% is, therefore, likely to be an overestimate of the incidence of spontaneous decidualization. The only previous study of the incidence of spontaneous decidualization in pseudopregnant rats, of which the authors are aware, is that of Evans (1928) in which an incidence of 3 to 3.7% was reported for normal rats of the Long-Evans strain. In vitamin E deficient rats, the incidence was elevated to between 52 and 61%. The increased incidence was attributed to greater responsiveness of the uteri under conditions of vitamin E deficiency.

**Table 1**

**INCREASE OF APPARENT SPONTANEOUS DECIDUALIZATION IN PSEUPO-PREGNANT RATS**

<table>
<thead>
<tr>
<th>Pseudopregnancy induced by:</th>
<th>No. of ♀♀</th>
<th>No. of ♀♀ with responses</th>
<th>Percentage of uterine horns with responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrical stimulation</td>
<td>208</td>
<td>10</td>
<td>4-8</td>
</tr>
<tr>
<td>Sterile mating</td>
<td>72</td>
<td>4</td>
<td>5-6</td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>14</td>
<td>5-0</td>
</tr>
</tbody>
</table>

We believe that spontaneous decidualization does not occur at all in the pseudopregnant rat. Apparently spontaneous responses may be the reaction to mild infections or to irritation caused by debris descending into the uterus after ovulation. Indeed, in a group of rats which had the ampulla of one oviduct removed on the morning of oestrus for recovery of ova, all animals exhibited massive decidualization, but only in the uterine horn on the operated side, although the uterus had not been exposed or touched in the operation (P. F. Kraicer, personal communication).

In another series of experiments, eleven pseudopregnant rats were subjected to bilateral ovariectomy on the morning of Day L₄, taking precautions to avoid touching, stretching or otherwise subjecting the uterus to direct stress. All of the rats received daily injections of progesterone (s.c., 4 mg in 0.1 ml of peanut oil U.S.P.), from Day L₄ to L₇ inclusive. On autopsy, on Day L₈, eight of the eleven rats exhibited decidual responses, which, in four cases, were massive. The debris occasioned by the surgery is assumed to have been the causative agent.

Although Blandau (1949) has suggested that "the slightest disturbance of the superficial epithelium is sufficient to instigate the decidual reaction", it is apparent, from the work of Alden (1959) that the mere introduction of foreign objects such as unfertilized sea urchin eggs or two-celled mouse eggs, does not induce decidual responses, although two-cell rat eggs may do so. It is evident,
therefore, that some degree of specificity in the stimulation of the decidualization is exhibited, although such specificity may be masked by treatments which enhance uterine sensitivity. An example of this is provided by formation of deciduomata brought about by unfertilized rat ova under conditions of progesterone supplementation (Alloiteau, 1958).

Any claim of spontaneous decidualization must be regarded with suspicion and the cause sought in unrecorded parasitic or bacterial infections or other source of irritation of the uterus, or tissue detritus which undergoes lysis with consequent liberation of amines.

We thank Joseph Shalom for technical assistance.

REFERENCES


EVANS, H. M. (1928) Spontaneous deciduomata in pseudopregnancy with low vitamin E. Am. J. Physiol. 85, 149.


