Reproduction and growth of mice and rats under conditions of simulated increased gravity

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OYAMA, JIRO, AND WILLIAM T. PLATT. Reproduction and growth of mice and rats under conditions of simulated increased gravity. Am. J. Physiol. 212(1): 164–166. 1967.—Mating studies were performed on rats and mice subjected to chronic centrifugation at various g loads. Rats conceived and delivered viable pups at 2.5 and 3.6 g but not at 4.7 g. Newborn pups, however, survived only when they were removed intermittently from the centrifuge during the first several weeks of exposure. Newborn mice, in contrast, exposed continuously to 2.5 g from birth were able to survive and grow. Growth rates of animals born and reared on the centrifuge were lower than those of controls. Measurements were made of changes in food and water consumption and body mass of rats born at and adapted to 2.5 g when shifted to 3.6 g or returned to normal gravity. A transient increase in food and water consumption of animals returned to normal gravity was the only significant change observed. Results of this study show that rats and mice can reproduce under conditions of simulated increased gravity.

METHODS AND MATERIALS

Animals. Sprague-Dawley rats and Swiss-Webster mice were employed throughout this study. All animals were fed Purina laboratory chow and water ad lib. The diet of pregnant and lactating animals was supplemented with a commercial powdered milk concentrate (Milkmans, Foremost Dairy, San Francisco, Calif.).

Animal centrifuges. Rat studies were performed at either 2.5, 3.6, or 4.7 g on an 8.5-ft radius centrifuge which has been previously described in detail (5). The centrifuge was operated at a constant 40 rpm with a different radius being employed for each g level. Mice studies were performed only at 2.5 g on a 4.5-ft radius centrifuge of similar design. The same radius was employed for both mice and rats at 2.5 g. The centrifuges were operated continuously except for approximately 20-min periods each day when they were stopped to service and weigh the animals. Stimulation of day-night cycling was achieved by an automated 12-hr on-off (6 AM–6 PM) lighting system.

RESULTS

Breeding experiments. The breeding performance of rats chronically exposed to three different g loads is summarized in Table 1. Both females and servicing males were centrifuged at least 2 months before matings were attempted. The data show that rats can mate and successfully deliver their young at 2.5 and 3.6 g. However, the newborn rats only survived at 2.5 g and only under special conditions, as will be noted below. Pregnancy was indicated by the weight of the mated females which increased significantly a week before parturition. In initial experiments, pregnant rats were individually isolated through term and after delivery of their young. In later experiments, several mothers with their litters were grouped together since this appeared to enhance the survival of the newborn rats. The average litter size could only be estimated since there was a tendency of some mothers to devour their young immediately after

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REPRODUCTION UNDER INCREASED GRAVITY

TABLE 1. Effect of increased g load on reproduction

<table>
<thead>
<tr>
<th>g</th>
<th>Avg No. Per Litter</th>
<th>Survivors</th>
</tr>
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<tbody>
<tr>
<td>2.5</td>
<td>12</td>
<td>15*</td>
</tr>
<tr>
<td>3.6</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>4.7</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

* Intermittently removed from centrifuge during first several weeks. † Continuously subjected to 2.5 g from birth.

delivery. These animals were excluded in calculating the average litter size.

All attempts to raise rats born on the centrifuge were unsuccessful whenever the centrifugation was continuous since the rats usually succumbed within the first 48 hr of exposure. Therefore, both newborn rats and mothers were removed from the centrifuge for periods ranging from 16 to 18 hr/day during the first several weeks. Under such conditions newborn rats did survive and grow.

Only a limited number of breeding experiments were run on mice (Table 1), all of which were done at 2.5 g.

Mice were able to mate, deliver their young, and have them survive while being continuously subjected to 2.5 g from birth. The ability of the newborn mice to survive under these conditions was in distinct contrast to that of the rats.

Growth of survivors. The growth curves of the first male and female rat survivors at 2.5 g are shown in Fig. 1. These rats were the only ones to survive in the litter. Brother and sister were mated three times. Of 11 rats obtained from the second mating, 2 males and 4 females survived. The growth curves of this second generation of rats which were born on the centrifuge are shown in Fig. 2. This group was centrifuged 6 hr/day for the first 3 weeks. For comparison, the growth curve of a group of 36 noncentrifuged female rats is also presented. A very similar growth pattern (Fig. 3) was obtained with another litter of first-generation rats born and reared at 2.5 g. These pups, in contrast to the previous group, were subjected to 6 hr of centrifugation at 2.5 g each day from birth for the 1st week. During the 2nd week they were subjected to 16 hr/day, and from the 3rd week onward...
were centrifuged continuously except for the time taken to service the centrifuge. It is clear that female rats born and reared at 2.5 g have a lower rate of growth than non-centrifuged female rats.

Figure 4 shows the growth curves of five female and seven male mice born and reared at 2.5 g. Mice were exposed continuously to 2.5 g from day of birth except for approximately 20 min each day when the centrifuge was stopped for servicing of animals. These mice were a third generation of animals successively born and reared at 2.5 g. Both male and female mice were weighed together until they were weaned. It is seen from the growth curves that both male and female centrifuged mice are lower in body weight than their corresponding non-centrifuged controls.

Response to changes in g load. To see how rats born and reared on the centrifuge react to changes in g, rats were centrifuged at 2.5 g. Both male and female mice were weighed together until they were weaned. It is seen from the growth curves that both male and female centrifuged mice are lower in body weight than their corresponding non-centrifuged controls.

REFERENCES

DISCUSSION
Results of this study show that both mice and rats can be subjected to relatively high g fields without impairing their ability to mate and produce litters. Rats were able to do so at 2.5 and 3.6 g but not at 4.7 g. Although no tolerance limit was established for mice in this study, there is little doubt that it is higher for mice than for rats. This is supported by the observation that newborn mice can survive almost continuous exposure to 2.5 g from birth; whereas newborn rats cannot survive at 2.5 g unless the exposure is intermittent during the first several weeks. Although no experiments have been made so far, it appears likely that at some level below 2.5 g newborn rats will be able to survive continuous centrifugation. The reason for their inability to survive continuous centrifugation has not been clearly determined. In some cases it was clear that the mother had abandoned her litter. In other cases, apparently viable and healthy litters which were being nursed by their mothers died within the first 72 hr. Autopsies performed on the newborn rats which died did not reveal the cause of death. Histological examination of the lungs of some but not all the newborn rats revealed variable degrees of focal atelectasis. Although respiratory failure may have been contributory, death may have been due to a generalized failure in body function resulting from an inability of newborn rats to maintain an adequate body temperature. Preliminary studies in our laboratory have shown that centrifuged rats show a marked and sustained depression in their deep body temperature. Several attempts were made exposing newborn rats to oxygen-rich atmospheres but this did not improve their survival. An interesting observation, however, assessed only in qualitative terms, was that more newborn rats appeared to survive when several mothers were present together. A possible factor contributing to this increase in survival may have been that the chances of the newborn being nursed were increased under these conditions. As in our previous studies in which animals were exposed to simulated increased gravity from weaning age, animals born and reared under simulated increased gravity conditions were significantly smaller in body size than control animals. Contrary to the initial inanition and transient decrease in body mass experienced by either weanling or mature rats when first subjected to centrifugation, newborn rats showed a continuous and steady increase in body mass from the 1st day onward. The newborn rats furthermore showed no head nystagmus or other vestibular effects as were observed in weanling and mature rats.