THE INDUCTION BY IRRADIATION WITH NEUTRONS OF HEREDITY CHANGES IN MICE

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In a previous paper by Snell and Aebersold1 the production in male mice by irradiation with neutrons of an initial period during which small litters are sired, followed by a period of complete sterility, followed, in turn, for the smaller doses, by a resumption of normal fertility, has been described. This paper is concerned with the appearance of sterility and of heredity changes in the descendants of the irradiated males.

The twelve irradiated males were from the C stock, homozygous for the mutant genes b and c. Before the onset of sterility they were mated as often as possible to females of the P stock (genotype aabbCCddppss), or in a few cases to females of the M stock (genotype aabbCCddppss). F1 animals were mated to mice of the P (or M) stock to give the second generation, designated as the F2. F2 mice of the appropriate sex were selected and back-crossed and to their F1 parent to give the F3 generation, among the individuals of which new recessive mutations may be expected to become phenotypically visible if any such have been induced by the treatment. The advantages of this type of cross in a search for induced mutations have been discussed in a previous paper by Snell.2

In order to make a rapid test of the semi-sterility of F1 males, they were mated to females of the Pch stock as well as to the females from the P (and M) stocks. The Pch stock was selected because of its fertility.

The results of the tests for sterility and semi-sterility are summarized in table 1.

| TABLE 1 |
|---------------------|---------------------|---------------------|---------------------|---------------------|
|                   | F1 test             |                   |                   |                   |
|                   | TOTAL NO.           | NO. TESTED         | NO. STERILE       | NO. SEMI-Sterile   |
|                   | g  d  ?             | FOR FERTILITY      | g  d             | g  d             |
| (a) Sired during pre-sterility period | 16  25  3 | 10  23  0 | 0  3  1 | 3 |
| (b) Sired during post-sterility period | 13  10  | 2  5  0 | 0  0  0 | 0 |
| F1 control        | 43  28  5          | 19  3  0          | 0  0  0          | 0  0          |

The nature of semi-sterility in mice has been discussed in previous papers by Snell3 and Snell, Bodemann and Hollander.4 In the experiment here described, 62 F2 and 68 F3 litters by F1 control females averaged 9.3 young per litter, and 16 F2 and 68 F3 litters by F1 control males averaged 9.6 young per litter.
young per litter. The consistent production of litters considerably smaller than this may be regarded as evidence of semi-sterility due to a translocation. Experience has shown that a mouse whose litters average below 7 should be subjected to further tests for semi-sterility. Cases of sterility and semi-sterility found in the present experiment are listed below.

\( \varnothing R_{18} \)= (Dose applied to father, 140 "r.") Fourteen litters of \( R_{18} \) by normal females averaged 6.0 young. Incompleted tests indicate that \( R_{18} \)’s tendency to produce small litters is transmitted to about one-half his progeny. In addition to the normal and semi-sterile offspring of \( R_{18} \), 5 out of 63 offspring that have been raised to maturity have shown conspicuously slow growth and have remained stunted throughout life. \( R_{18} \) is clearly semi-sterile. Further tests are in progress.

\( \varnothing R_{12} \)= (Dose applied to father, 110 "r.") Fifteen litters of \( R_{12} \) by normal females averaged 3.3 young. Incompleted tests indicate that \( R_{12} \)’s tendency to produce small litters is transmitted to about one-half his progeny. Further tests are in progress.

\( \varnothing R_{14} \)= (Dose applied to father, 110 "r.") Sterile. He was killed at eight months of age. There were no motile sperm in the sperm ducts. The testes were slightly below normal size. Sections show a very few spermatids, some in rather advanced stages, but no mature spermatozoa. The interstitial cells appear normal.

\( \varnothing R_{28} \)= (Dose applied to father, 110 "r.") This male though placed with six different females produced only one litter, a litter of 2, which was not raised. He was killed at eight months. Many motile sperm were present in the sperm ducts.

\( \varnothing R_{30} \)= (Dose applied to father, 110 "r.") Sterile. Male \( R_{30} \) was killed at eight months. A few immotile sperm were found in the left vas deferens, and a very few motile sperm in the left epididymis. No sperm were found in the right sperm tract. Sections of the testis showed a limited number of normal appearing spermatozoa to be present, but all of those observed were still attached.

\( \varnothing R_{58} \)= (Dose applied to father, 140 "r.") Five litters averaged 4.4 young. The semi-sterility is definitely transmitted. Further tests are in progress.

\( \varnothing R_{61} \)= (Dose applied to father, 120 "r.") Sterile. No sperm were present in the sperm ducts. Sections of the testes show spermatogonia and spermatocytes but no spermatids. Many of the tubules show hyaline degeneration of the germinal epithelium. The interstitial cells are normal or slightly increased in number.

In addition to the above, one test female, \( R_{2} \), produced nine litters averaging 5.7 young; one test male, \( R_{16} \), produced one litter of 4 and was then lost; one test female, \( R_{57} \), produced 4 litters averaging 6.8 young and was then discarded; one control female, \( R_{64} \), produced 3 litters
averaging 6.7 young and was then discarded; one control female, \( R_65 \), produced 13 litters averaging 5.9 young; one test \( F_1 \) of unrecorded sex, \( R_90 \), was found with a tail one-half normal length, shown by examination under the microscope to be a congenital defect and not the result of eating by the mother, but was missing three days later. Test female \( R_2 \) and control female \( R_65 \) were tested further by matings of their progeny. Of 10 tested sons and daughters of \( R_2 \), only 1, a daughter, produced litters below normal size, and 3 grandsons by this daughter were normal. Fifty-one litters by 9 sons and daughters of \( R_65 \) averaged normal size. Females \( R_2 \) and \( R_65 \) were, therefore, probably genetically normal despite the small size of their own litters. Similar cases among \( F_1 \) females have been noted previously by Snell\(^4\) in the control group of a similar experiment. Aside from the above, all \( F_1 \) mice were phenotypically normal and produced litters averaging more than 7 young.

In the search for recessive visible mutations, 33 \( F_1 \) experimental animals (13 \( \delta \) and 20 \( \varnothing \)) were tested. Back-cross matings between these mice and 83 of their offspring (17 sons and 66 daughters) yielded 842 \( F_2 \) mice. The majority of these were observed at birth and again at about three weeks of age. No mutations were found, though there were a few minor variations that failed to reappear. Twenty-five control mice mated to 39 of their offspring gave 467 \( F_3 \) mice, all normal.

**Summary and Conclusions.**—Out of the 44 \( F_1 \) animals in the experimental group there are thus 3 proven semi-sterile individuals (\( \varnothing R_8 \), \( \varnothing R_{12} \), \( \varnothing R_{58} \)), 1 almost completely sterile male (\( R_{28} \)) and 3 completely sterile males with abnormal spermatogenesis (\( R_{14}, R_{30}, R_{61} \)). There are no cases of complete sterility and probably no cases of semi-sterility in the control, and while there are insufficient \( F_1 \) males in the untreated group to furnish an adequate control for the sterile males in the experimental group, the control groups of two other comparable experiments by Snell\(^2\) and Hertwig\(^4\) serve to show that in \( F_1 \) males from untreated parents, sterility is very rare. In quite extensive tests, no evidence was found for the occurrence of recessive visible mutations following irradiation with neutrons.

The similarity of the results found by Hertwig\(^4\) and Snell\(^2\) following irradiation with x-rays and the results here reported following irradiation with neutrons is noteworthy. Both treatments result in the production of translocations and of sterile \( F_1 \) males, and both fail to produce recessive mutations, at least in detectable numbers. Snell\(^2\) found that a dose of about 700 r of x-rays applied to male mice caused translocations in about 33% of their offspring. This is a much higher incidence than the 9.1% (or 15.1% if \( \varnothing R_{28} \) and \( \varnothing R_{16} \) are included) found in the present experiment among animals sired during the initial fertile period. Yet Snell and Aebersold found that the reduction in \( F_1 \) litter size during the initial fertile
period was about the same in the two cases. Only further tests can show whether or not this represents a real difference between the effects of the two treatments.

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**IMAGINAL DIFFERENTIATION INAUGURATED BY OXYGEN IN DROSOPHILA PUPAE**

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The imaginal differentiation of the abdominal ectoderm of a Drosophila pupa depends upon a factor localized in the anterior part of the pupa. This factor acts during a critical period in pupal development. When the anterior part of the pupa is removed by means of a ligature before the critical period, the abdominal ectoderm is incapable of differentiation. On the other hand, imaginal differentiation takes place when the anterior part of the pupa is removed after the critical period.¹ Furthermore, it has been found that the differentiation of an eye anlage transplanted into an abdomen also depends upon the action of the pupal differentiation factor.¹ Such a differentiation center localized in the anterior part has not only been demonstrated for flies but also for Lepidoptera.²,³ Thus the action of the imaginal differentiation center seems to be necessary for the developmental processes leading to imaginal completion.

We have already said that eye transplants can differentiate only after they are activated by the pupal differentiation center. The same has been found in skin transplants in the Micro-Lepidopteran Galleria.⁴ Since the transplanted tissues lie free in the body cavity it was thought that the surrounding blood carried an "imaginal metamorphosis hormone" which is responsible for the differentiation of the transplants. The