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Mutation induced in germ cells of the foetal female mouse

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INTRODUCTION

In Great Britain by far the greater part of the genetically effective dose of man-made radiation to the human population is due to high-intensity irradiation of the gonads in medical radiology; about a third of it is received by post-natal males, a third by post-natal females, and a third by foetuses, mainly in the later stages of gestation (Osborn & Smith, 1956).

When estimating the genetically effective dose it has usually been assumed that all human germ cells, at whatever stage of development, are equally sensitive to the mutagenic action of radiation, but this assumption is unsupported by data. In their absence it has been thought desirable to obtain data from some other mammal; and for this reason several studies have been made of induced mutation in the mouse, using the specific-locus method. The earlier studies were all of mutation induced in spermatogonia of adult males (Russell, 1951; Russell, Russell & Kelly, 1958; Carter, Lyon & Phillips, 1956, 1958). Recently, however, this work has been extended to cover mutation induced in spermatogonia of the foetal male (Carter, 1958), in postspermatogonial cells of the adult male (Russell, Bangham & Gower, 1958) and in oöcytes of the adult female (Carter, 1958; Russell, Russell, Gower & Maddux, 1958; Russell, Russell & Cupp, 1959). The main conclusions that can be reached are:

(i) *Radiation intensity.* When spermatogonia of the adult male or oöcytes of the adult female are irradiated, the yield of mutation per rad is dependent on the intensity of the radiation, being higher when the dose is administered at a high intensity. This effect was not found in postspermatogonial cells. Other germ-cell stages have not yet been tested.

(ii) *Germ-cell stage.* With high-intensity exposures, (*a*) spermatogonia of the adult male and oöcytes of the adult female show similar induced mutation rates, (*b*) postspermatogonial cells show a higher rate, and (*c*) spermatogonia of the foetal male show a lower rate. For low-intensity exposures, (*a*) and (*b*) are true, but (*c*) has not yet been tested.

In none of this work was the mutability of the germ cells of foetal females studied; the experiment now reported partly fills this gap.

MATERIAL AND METHODS

Strain C3H females $12\frac{1}{2}$ days pregnant by Strain 101 males were placed in the low-intensity γ-radiation field from a cobalt-60 source and irradiated for six successive 16-hour nights, in the course of which their foetuses accumulated a whole-body dose of 300 rad. In female mouse foetuses of up to about 14 days' gestation the germ cells are present as oögonia, thereafter entering meiotic prophase and reaching the pachytene stage at about the time of birth, after 19 or 20 days' gestation (Snell, 1941). The irradiated germ cells were therefore oögonia and early oöcytes. After irradiation the foetuses were brought to term, and 6 weeks later they were mated to males homozygous for the recessive genes *a*, *b*, c^{ch}, *d*, *se*, *p* and *s*. They were allowed to breed for up to 7 months. The progeny were scanned for the mutant phenotype associated with the seven marked loci; mutants were tested genetically.

RESULTS AND CONCLUSIONS

The data are shown in Table 1, which also summarizes earlier data on specific-locus mutation in the female mouse. Four mutations were found in the new experiment. The observed mutation rate was higher, by a factor of 3, than that

Table 1. *Mutation at seven specific loci in germ cells of the female mouse*

Age of mouse irradiated	Radiation			Progeny examined	Mutations at loci *a b c d se p s*	Source of data*
	Type	Intensity	Dose			
Adult	γ, Co-60	50 rad/16 hr.	600 rad	10,117	– – – 1 – – –	(a)
Adult	γ, Cs–137	86 r/week	258 r	26,468	– 1 – 1 – –	(b)
—	—	—	0 r	40,918	– – – – – – –	(b)
Adult	X, 250 Kv.	96 r/min.	400 r	1,729	– – – – – – 1	(b)
—	—	—	0 r	5,845	– – – – – – –	(b)
Adult	X, 250 Kv.	92 r/min.	400 r	6,130	– 2 – 1 1 2	(b)
Foetus	γ, Co-60	50 rad/16 hr.	300 rad	18,753	– 1 2 1 – – –	(c)

* Sources of data: (a) Carter, 1958; (b) Russell, Russell & Cupp, 1959; (c) Carter, this paper.

Table 2. *Comparison of induced mutation rate in the foetal female with those in the adult*

Mutations observed in the new experiment	4
Mutations expected if adult females had been exposed:	
To acute X-irradiation	12·5
To chronic γ-irradiation	1·3

found when oöcytes of the adult female were chronically γ-irradiated, and lower by a factor of 3 than that found when they were acutely X-irradiated (Table 2). In each case the difference approaches, but does not attain, statistical significance.

It is clear, however, that the germ cells of the foetal female mouse, irradiated under the conditions of the experiment, are not grossly more sensitive than those of the adult.

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