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The fertility of mice selected for large or small body size

By RUTH E. FOWLER and R. G. EDWARDS*

Institute of Animal Genetics, Edinburgh, 9

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Selection for large or small body size results in considerable changes in the adult body weight of the selected lines. Examples of the effects of selection for body size are to be found among domestic livestock (Comstock, Winters, Jordan & Kiser, 1942; Krider, Fairbanks, Carroll & Roberts, 1946; Dickerson & Grimes, 1947; etc.) and experimental animals, e.g. the mouse (Goodale, 1938; MacArthur, 1944*a*, *b*, 1949; Falconer, 1953, 1955). The usefulness of selection programmes is limited if fertility is impaired, and changes in body size are often associated with changes in reproductive traits such as the time of onset of sexual maturity, litter size, etc. (e.g. Hertzer & Brier, 1940; Phillips & Zeller, 1943; MacArthur, 1944*a*, *b*, 1949). The present paper describes the effects of long-term selection for large and small body size on the reproductive physiology of two unrelated strains of mice.

MATERIAL

Two strains of mice, both selected by Dr D. S. Falconer of this Institute, were available. Strain *N* had been selected for large (line *NL*) or small (line *NS*) body size, and an unselected control line (*NC*) had been constructed at a later date than the selected lines. The origin and history of strain *N* were described by Falconer (1953, 1955). Strain *C* had also been selected for large and small body size (lines *CL* and *CS* respectively), no control line being available. The strain is described by Falconer (1960) (the lines here designated *CL* and *CS* were those selected on a normal diet, their full designation being *CFL* and *CFS*). Selection was based on body weight at 6 weeks of age in strain *N*, and on weight gain between 3 to 6 weeks of age in strain *C*.

Most of the data were derived from strain *N*. During the course of selection, the generation interval in the small line had increased due to delay in the arrival of first litters. The contemporaneous generations available for a comparative study were 25–31 in *NS*, 18–25 in *NC*, and 34–40 in *NL*. Considerable differences in body weight existed between the three lines at the time of this study (see Table 5), the response to selection being apparently complete.

Strain *C* had been selected for fewer generations, and both large and small lines were still responding to selection. The mice used came from generations 16–20 in *CL*, and 16–19 in *CS*. There was no evidence of delay in sexual maturity in line

* Present address: Dr and Mrs R. G. Edwards, National Institute for Medical Research, The Ridgeway, Mill Hill, London, N.W.7.

CS. Considerable differences in body weight also existed between *CL* and *CS* mice at the commencement of this work.

The mice used were between 6 and 25 weeks of age. All of the females were nulliparous.

THE MEASUREMENT OF FERTILITY

The interval between pairing males and females and the arrival of the subsequent litter was recorded as an overall indication of the fertility in each line, and of the interval between pairing and mating. ('Pairing' is used to describe placing a male and female together in the same cage; 'mating' to mean that copulation has occured as judged either by the arrival of a litter or the finding of a vaginal plug.)

The length of the oestrous cycle was determined by the vaginal-smear technique, details of our accuracy with this technique being given elsewhere (Fowler & Edwards, 1957). Smears from some mice were recorded daily for up to 10 consecutive days. Single smears from other mice were taken as an estimate of the number of mice in oestrus at a particular time. The frequency of oestrus was also measured by pairing females with outbred males of high sexual activity, the females being examined daily for vaginal plugs. This method will be referred to as 'mating performance'.

Ovulation was studied by autopsying mice at approximately 18 hr. after mating. The autopsies were carried out during late afternoon to ensure that ovulation was complete. The recently ovulated eggs were counted, and many of them were examined under the phase-contrast microscope to ensure that fertilization was normal. The number of eggs ovulated was related to the weight of the animal at ovulation.

Other mice that had mated were allowed to carry their foetuses to late stages of gestation or to full term. The proportion of mice with implanted embryos could thus be compared with the proportions which mated and ovulated. Embryonic mortality during pregnancy and parturition was estimated by comparing the mean number of eggs ovulated with mean litter size (living offspring only). Foetal mortality after implantation was measured by counting the numbers of living and resorbing foetuses in mice autopsied during late pregnancy. Foetuses which die between 8 and 11 days' gestation can usually be recognized as a 'mole' during late gestation (Fortuyn, 1919; Huggett & Pritchard, 1944); those which die earlier might leave no trace and thus be excluded from our estimates.

Some females were treated with exogenous hormones. The intraperitoneal injection of pregnant mares' serum (PMS) followed after an interval of 40 hr. by human chorionic gonadotrophin (HCG) induces oestrus and ovulation in adult mice (Fowler & Edwards, 1957). The number of eggs ovulated was found to be largely controlled by the amount of PMS injected. The method was adapted to obtain an estimate of the amount of follicle-stimulating hormone (FSH) secreted by the five lines. It is generally assumed that the number of eggs ovulated during natural oestrus is controlled by the amount of endogenous FSH available. The

mean number of eggs ovulated after natural oestrus was therefore compared with the numbers ovulated after different amounts of PMS, in order to estimate the amount of endogenous FSH.

As will be shown later, many *NS* mice had no implanted embryos after natural mating. Some of these mice were therefore given 2 mg. progesterone in sesame oil daily from day 2 to day 12 inclusive after mating in attempts to maintain their pregnancies (see Smithberg & Runner, 1956, 1957). Other *NS* mice were given PMS and HCG to induce mating and ovulation, and were likewise treated with progesterone.

RESULTS

Fertility in Strain N

The fertility of paired mice

The fertility of pairs of mice of the large, control and small lines, judged by the proportion which produced litters after a period of 2–3 months, is shown in Table 1. Control mice were uniformly fertile, whereas a number of pairs in the large and small lines were sterile.

Table 1. *The incidence of sterility and the time of arrival of first litters in pairs of* NL, NC, NS, CL, *and* CS *mice*

Line	Gens.	No. of pairs	Percentage sterile pairs	Time after pairing when first litters arrived (days)				
				20–21	22–23	24–27	28–35	35
Strain *N*								
Large (*NL*)	37–40	43	18·6	3	9	12	9	2
Control (*NC*)	18–25	47	0	15	21	5	3	3
Small (*NS*)	25–31	67	17·9	0	9	21	15	10
Strain *C*								
Large (*CL*)	16–20	36	5·6	14	13	4	0	3
Small (*CS*)	16–19	25	0	6	10	6	2	1

The interval between pairing the mice and the arrival of the first litter is also shown in Table 1. If the mice mated during the first oestrus period of the female, and assuming that the oestrus cycle was normal, then the expected time of arrival of the first litter would be from 20 to 23 days after pairing. Almost all of the *NC* litters arrived within this period, as compared with approximately one-half of *NL* litters. *NS* litters were even more delayed. Previous work has shown that after eleven generations of selection the delay in arrival of first litters in *NS* mice was already evident, though not so extreme as in the present study, and that no delay existed in line *NL* (Falconer, 1953).

The oestrous cycle

Details of the oestrous cycle during a period of 10 days in large and control mice are given in Table 2. Mice of the large line had a slightly longer cycle than those

Table 2. *The oestrous cycle and mating performance in strain* N *mice*

A. Oestrous cycle judged by vaginal smears

Line	No. of females	No. with cycles	Cycle length (days) 4–5	6–7	8 or more	No. of females recorded once	No. in oestrus
Large (*NL*)	12	10	1	6	3	63	11
Control (*NC*)	6	6	4	1	1	44	10
Small (*NS*)	34*	4	–	–	–	12	0

B. Mating performance

Line	No. of females	Days between pairing and mating 1–2	3–4	5–8	> 8	No. not mating
Large (*NL*)	30	9	14	4	1	2
Control (*NC*)	30	11	13	2	3	1
Small (*NS*)	57	3	8	9	11	26

* Smears recorded for 5 consecutive days.

of the controls. Vaginal smears of the small line were discontinued after 5 days: only 4/34 mice had an oestrous smear during this period, the remainder being in dioestrus. Observations on mice recorded for 1 day only, given in the same Table, agree with the above data. The relation between the oestrous cycle of *NS* mice and their age and body weight is shown in Table 3; the presence of a cycle was independent of age or weight.

Table 3. *The oestrous cycle and mating performance of* NS *females in relation to age and body weight*

A. Oestrous cycle

No. of females	Age in days	Weight (g.)	No. of mice with oestrous smear within 5 days
10	42–63	10·9 ± 0·5	1
9	64–108	12·8 ± 0·4	1
15	109 and older	13·4 ± 0·5	2

B. Mating performance

	No. of females	Mean age (days)	Mean weight (g.)
Mated within 16 days of pairing	31	105·2 (Range 58–176)	13·1 ± 0·3
Failed to mate within 16 days of pairing	26	103·9 (Range 55–163)	12·8 ± 0·4

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The mating performance of females of the three lines, when paired with outbred males for 16 days, is given in Table 2. Both *NL* and *NC* females mated in nearly equal proportions (28/30 and 29/30 respectively) and at approximately the same time. *NL* females had also mated during their first oestrus when paired with outbred males, whereas when paired with *NL* males there was a delay (Fig. 1).

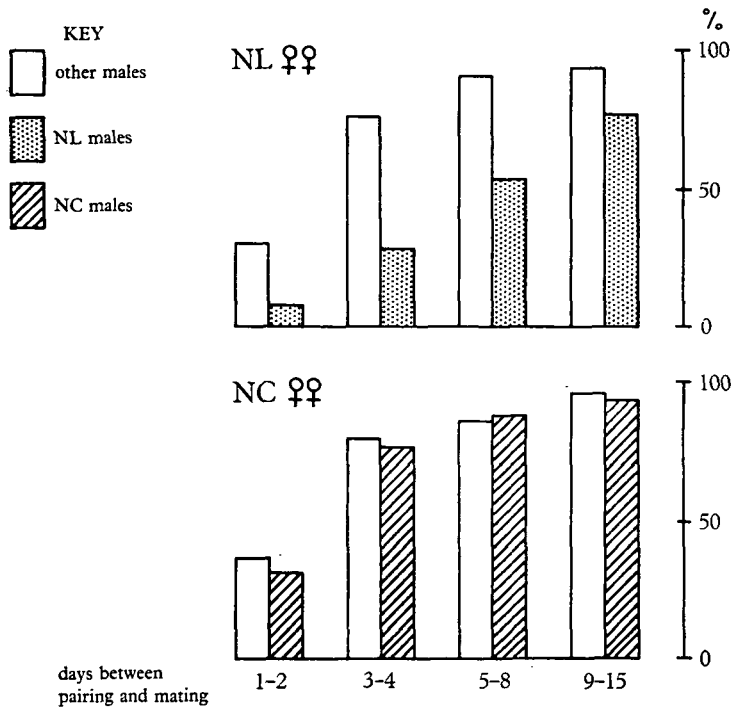

Fig. 1. Accumulative proportion of strain *N* females that had mated to strain *N* or other males at various intervals after being paired. Data on other males taken from Table 2; data on strain *N* males derived from Table 1 (19 days, i.e. the mean gestation period, being subtracted from the interval between pairing and the arrival of the first litters). *NS* males not shown. Many *NS* females failed to produce litters after mating (see text) and the data in Table 1 could therefore not be modified for inclusion.

This difference suggests that the delay noted above (Table 1) was due to *NL* males rather than to the females.

Only slightly more than one-half of the *NS* females mated, many of the matings were delayed, and no relation could be found between mating and age or body weight (Table 3). This evidence confirmed the data from vaginal smears, that selection for small body size had resulted in a lengthened or delayed oestrous cycle.

Male libido

The sterility in some of the *NL* pairs was not due to an abnormal oestrous cycle, nor, as shown below, to foetal mortality during pregnancy. Male sterility was thus suspected as the cause of infertility in this line. To measure the libido of *NL* males,

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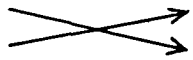
Table 4. *Mating performance of* NL *males compared with those of another strain when paired with* NL *females*

	No. of pairs	No. mating within 10 days	Females which had not mated exchanged males	No. of pairs	No. mating within 10 days
NL males	14	6		2	1
Other males	15	13		8	7

one group of *NL* females was paired with *NL* males, and another group with outbred males of another strain. Results are shown in Table 4. *NL* males were obviously less active. When the unmated females were exchanged, most of them mated within 10 days. Furthermore, twelve females from sterile *NL* pairs all mated to outbred males within 5 days of pairing, and all produced litters. Lastly, as shown above, *NL* males were evidently responsible for the delay in the arrival of first litters in *NL* pairs.

NS males from sterile pairs were paired with females of another strain. All of the males sired litters. None of the sterility in the small line during the present investigation was due to male infertility.

Table 5. *Ovulation, mean egg number, and body composition in strain* N *and strain* C *mice*

Strain and line	No. of females		Mean no. of eggs ovulated	Body weight (g.)		Fat in carcass* (g.)
	Mated	Ovulated		Mean	Range	
Strain *N*						
Large (*NL*)	29	29	10·9 ± 0·3	30·1 ± 0·6	24·1 – 36·5	7·2
Control (*NC*)	25	25	7·7 ± 0·3	20·1 ± 0·4	16·2 – 25·0	1·9
Small (*NS*)	32	25	4·5 ± 0·2	13·3 ± 0·3	10·5 – 16·5	1·8
Strain *C*						
Large (*CL*)	22	22	14·8 ± 0·3	35·9 ± 1·9	27·8 – 61·6	3·1
Small (*CS*)	24	24	8·6 ± 0·1	17·6 ± 0·5	14·3 – 22·5	1·2†

	Regression of egg no. on body weight	Ratios of egg no. to body weight	
		Including fat	Excluding fat
Strain *N*			
Large (*NL*)	0·03 ± 0·10	0·36	0·48
Control (*NC*)	0·07 ± 0·15	0·38	0·42
Small (*NS*)	0·08 ± 0·12	0·34	0·39
Strain *C*			
Large (*CL*)	0·01 ± 0·06	0·41	0·45
Small (*CS*)	‡0·49 ± 0·14	0·49	0·52

* Fowler (unpublished)
† Estimates based on males
‡ Significantly different from zero ($P < 0·01$)

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Ovulation and fertilization

The proportion of mice that ovulated after mating is shown in Table 5. All of the *NL* and *NC* mice possessed recently ovulated eggs. In contrast, approximately one-quarter of the *NS* mice failed to ovulate. A scatter diagram of the number of eggs ovulated in relation to body weight is shown in Fig. 2. The mean numbers of

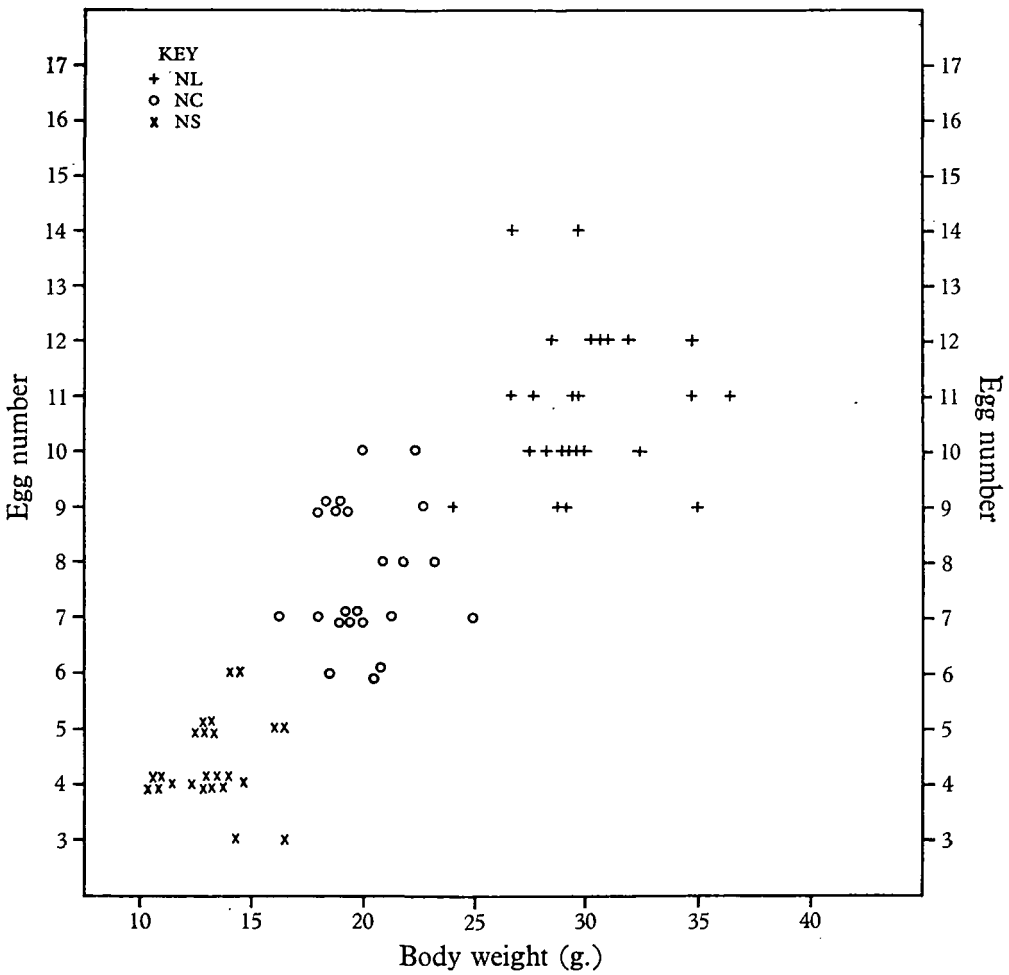

Fig. 2. The relation between the number of eggs recovered after natural mating and body weight in strain *N* females. Each point represents one female.

eggs ovulated, mean body weights, and the regression of egg number on body weight, are given in Table 5. Considerable differences in the numbers of eggs ovulated existed between the three lines, though the egg number per gram of body weight was similar in each line. The number of eggs ovulated was positively correlated with body weight within each line, though the correlations and regressions did not differ significantly from zero. The failure of many *NS* mice to ovulate, and the small number of eggs ovulated, was not due to a deficiency of oocytes, for treat-

Table 6. *Mean numbers of eggs ovulated by strain* N *and strain* C *mice in response to various amounts of PMS and HCG, and estimates of FSH in PMS equivalents*

Strain	Line	No. of mice	Mean no. of eggs ovulated: 6 i.u. PMS 6 i.u. HCG	3 i.u. PMS 3 i.u. HCG	1 i.u. PMS 2 i.u. HCG	½ i.u. PMS 2 i.u. HCG	¼ i.u. PMS 2 i.u. HCG	Mean no. of eggs ovulated during natural oestrus	Regression of egg no. on dose of PMS	Estimates of FSH in PMS equivalents*
N	Large (*NL*)	63	—	20·1 ± 1·6	13·8 ± 1·1	9·4 ± 0·7	—	10·9	3·72	0·6 ± 0·2
	Control (*NC*)	52	—	23·6 ± 3·1	10·7 ± 1·3	9·4 ± 1·3	6·8 ± 1·0	7·7	6·88	0·4 ± 0·1
	Small (*NS*)	61	—	12·4 ± 2·5†	10·2 ± 1·3	10·3 ± 0·9	7·0 ± 1·0	4·5	—‡	≪ 1/4
C	Large (*CL*)	49	32·3 ± 3·5	21·3 ± 1·8	13·6 ± 1·3	12·6 ± 0·8	—	14·8	3·63	1·2 ± 0·3
	Small (*CS*)	24	—	21·9 ± 4·7	8·8 ± 1·1	8·3 ± 1·6	—	8·6	5·81	0·8 ± 0·2

* See text for description.

† All treated mice ovulated except in this group where 6/20 failed to ovulate.

‡ Regression not calculated because of evidence of suppression of ovulation after 3 and 1 i.u. PMS. Moreover, considerable extrapolation would be required to reach the number of eggs ovulated during natural oestrus.

ment of these mice with gonadotrophins (see below) induced the ovulation of large numbers of eggs. In each of these lines, more than 95% of the eggs recovered after natural mating were fertilized.

The injection of PMS and HCG was used to estimate the amount of FSH secreted by mice of the three lines. Amounts of PMS between $\frac{1}{4}$ and 6 i.u. were injected, and the mean numbers of eggs ovulated at each dose level are given in Table 6. The number of eggs ovulated at each dose level was independent of body weight, both within and between lines, and of the stage of the oestrous cycle of the mice when PMS was injected. The relationship between egg number and dose of PMS was approximately linear in all lines except *NS*, where there was evidence of excess of PMS in the injections (see below). The regression of the numbers of eggs ovulated on dose of PMS was therefore calculated. The amount of PMS equivalent to the mean number of eggs ovulated during natural oestrus could then be derived from the regression equation. These equivalents are given in Table 6.

Small mice evidently received too much PMS when 1 or 3 i.u. were injected, for some failed to ovulate and others ovulated very few eggs. Excess gonadotrophin is known to cause premature luteinization of follicles, thereby suppressing ovulation (Noble, Rowlands, Warwick & Williams, 1939).

Maternal factors and implantation of the embryos

Control mice evidently had little difficulty in maintaining their pregnancies to and beyond implantation (Table 1). Similarly, large mice also maintained their pregnancies with little difficulty, for 28/30 females with vaginal plugs gave birth to litters.

In the small line, only 14 out of 34 females autopsied eight or more days after mating possessed implanted embryos. This degree of infertility could not be explained by failure to ovulate, for less than one-quarter of the mice failed to ovulate after natural mating (Table 5). Six non-pregnant mice autopsied 8 days after mating had no active corpora lutea. Seventeen mice of the small line were therefore given 2·0 mg. progesterone daily from day 2 until day 12 after mating. At autopsy on day 12, the proportion of mice with implanted embryos was considerably increased (Table 7B). The mean number of implanted embryos was not significantly higher.

A further thirty-nine mice of the small line, including eighteen which had failed to mate during 16 days of pairing with outbred males, were given 1 i.u. PMS and 2 i.u. HCG to induce mating and ovulation. Thirty-two of them mated, and these were divided into two groups: one received progesterone, the other received no further treatment. Progesterone treatment increased the proportion of mice with implanted embryos (Table 7C), no significant difference being found between the mean numbers of embryos implanted in the two groups. We have no evidence of the effect of progesterone on pregnancy in *NL* and *NC* mice induced to mate by exogenous gonadotrophins, but other data (Fowler & Edwards, 1960) have shown that fertile mice show no increase in fertility when given progesterone. The data from these *NS* mice were therefore considered to support the observations on mice

Table 7. *The proportion of* NS *mice with implanted embryos, and the mean number of embryos implanted*

A. Mice autopsied at various stages of pregnancy after mating during natural oestrus

	Time when autopsied (days gestation)			
	8–10	11–14	15–18	Total
Number of mice	11	13	10	34
Number with implanted embryos	5	6	3	14
Percentage with implanted embryos	45·5	46·2	30·0	41·2
Number resorbing all embryos	0	1	0	1

B. Comparison between untreated mice and those given progesterone after natural mating

	No. of mice	No. with implanted embryos	% with implanted embryos	Mean no. of implanted embryos
Natural mating, no further treatment	34	14	41·2	4·3 ± 0·3
Natural mating, 2mg. progesterone from day 2 to day 12	17	14	82·4	4·9 ± 0·3

C. Comparison between gonadotrophin-treated mice given no further treatment and those given progesterone

	No. of mice	No. with implanted embryos	% with implanted embryos	Mean no. of implanted embryos
Gonadotrophins and no further treatment	17	6	35·3	9·2 ± 1·8
Gonadotrophins, 2mg. progesterone from day 2 to day 12	15	13	86·7	7·2 ± 1·1

that mated during natural oestrus, i.e. that some mice of the small line fail to secrete adequate amounts of progesterone after mating.

Foetal mortality and mean litter size

Usually only a small proportion of foetuses die after implantation, although all foetuses are resorbed in a few mice. In control and large lines, there was no evidence of the resorption of all foetuses, for almost all mice carried their embryos to full term. In line *NS*, mice were autopsied at various intervals during pregnancy, and the proportion with implanted embryos after 15 days was lower than those autopsied earlier (Table 7A). This difference was probably due to sampling, however, for foetuses which die after implantation can usually be detected in the uterus until parturition. Nevertheless, one of the nine pregnant mice autopsied between 11 and 14 days' gestation was resorbing all of its foetuses.

The proportion of foetuses dying in pregnancies maintained to full term was estimated from the difference between the mean number of eggs ovulated and mean litter size (Table 8). Mortality was highest in the large line, and lowest in the small line. The proportion of foetuses which died after implantation was found

Table 8. *Estimates of embryonic and foetal mortality in the selected lines*

Strain and line	Mean no. of eggs ovulated	Mean litter size	Total mortality (%)	Foetuses dying after implantation*	
				Numbers	Percentage
Strain *N*					
Large (*NL*)	10·9	7·9 ± 0·5	27·5	15/116	12·9
Control (*NC*)	7·7	6·7 ± 0·4	13·0	—	—
Small (*NL*)	4·5	4·0 ± 0·2	11·1	3†/27	11·1
Strain *C*					
Large (*CL*)	14·8	9·2 ± 0·6	37·8	—	—
Small (*CS*)	8·6	6·2 ± 0·3	27·9	—	—

* Dashes indicate no observations

† Excluding one female resorbing all foetuses

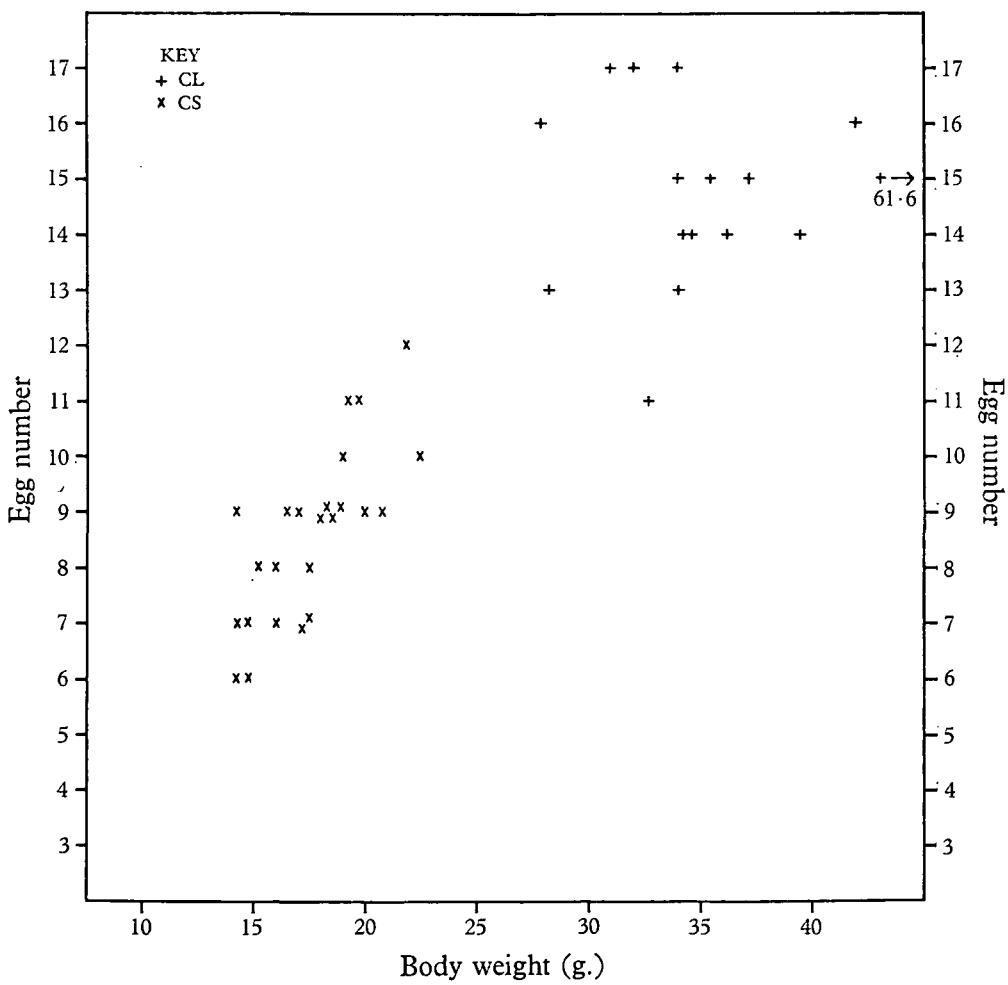

Fig. 3. The relation between the number of eggs recovered after natural mating and body weight in strain *C* females. Each point represents one female.

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by autopsying *NL* and *NS* mice during late gestation. Results are given in Table 8, the incidence of resorbing foetuses being similar in the two lines.

Fertility in Strain C

The oestrous cycle of *CL* and *CS* females was normal as judged by the proportion of females giving birth to litters within 25 days of pairing (Table 1). Ovulation was also normal, all mated mice having recently ovulated eggs in the ampullae of the Fallopian tubes (Fig. 3 and Table 5). In the large line, the number of eggs ovulated was not significantly correlated with body weight. In contrast, the correlation in *CS* mice differed significantly from zero (Table 5).

In relation to body size, more eggs were ovulated by females of strain *C* than by those of strain *N*. Differences in the egg-number/body-weight ratios appeared to be mainly due to differences in the amount of fat in the carcasses of the two strains (Table 5). Estimates of the amount of FSH secreted by *CL* and *CS* mice are given in Table 6; the estimates (1·2 and 0·8 PMS equivalents in *CL* and *CS* respectively) were higher than those for strain *N*.

No sterility was observed in *CS* pairs, and only two out of thirty-six *CL* pairs failed to produce litters. Estimates of the incidence of foetal mortality between ovulation and birth in the two lines are shown in Table 8. More than 35% of *CL* embryos died during pregnancy.

The major differences in fertility between strains *N* and *C* were: the absence of any sterility in the males and females of strain *C*, the positive correlation between egg number and body weight in line *CS*, and the higher incidence of foetal mortality in *CL* mice.

DISCUSSION

Different factors were responsible for the infertility in the large and small selected lines of strain *N*. In the large line, the low libido of certain males led to total sterility, or, if less extreme, to delay in the arrival of first litters. The incidence of embryonic mortality between ovulation and birth was also higher in this line than in control and small lines. The higher rate of embryonic mortality was probably due to the presence of the larger number of embryos at implantation (Bowman & Roberts, 1958) rather than to differences in maternal capabilities or variation in embryonic vitality.

The factors causing sterility in the small line of strain *N* strongly suggest a deficiency in gonadotrophin secretion. Thus, the absence of oestrous cycles and failure to ovulate after mating imply deficiencies in circulating follicle-stimulating and luteinizing hormone respectively. Moreover, these mice evidently secreted considerably less FSH than $\frac{1}{4}$ i.u. PMS equivalent, which was lower than the amount estimated in mice of the other lines. The levels of prolactin in many mice of the small line also appeared to be inadequate to maintain functional corpora lutea, and the absence of luteal secretions, which was undoubtedly the cause of failure at implantation, could be remedied by exogenous progesterone.

Selection for small body size has thus apparently impaired the secretion of

gonadotrophins by the anterior pituitary. The decreased growth-rate of these mice might also be due to hypo-functioning of the anterior pituitary, leading to insufficient secretion of growth hormone. A similar conclusion was drawn by Baird, Nalbandov & Norton (1952), who reported that the pituitaries of pigs selected for low rates of gain contained less growth hormone per unit tissue than those selected for high rates of gain. Preliminary experiments (unpublished) indicate that small mice will respond to exogenous growth hormone if sufficiently high doses are given, high doses probably being required because of the species specificity of growth hormones (e.g. Li & Papkoff, 1956; Li, Papkoff & Jordan, 1959).

If increasing sterility accompanies reduced growth-rate, limits will be imposed on the effectiveness of continued selection. Mice which are sterile or semi-sterile will leave few or no offspring for subsequent generations. Falconer (1955) has shown that selection in *NS* mice was impeded in this way: the smallest of the selected mice left fewer offspring than the less small. Extreme sterility could be overcome by ovary transfer, or by inducing oestrus and ovulation with gonadotrophins and then transferring the eggs into fertile mice. Sterility may also limit the effectiveness of selection for large size, if the low libido of some males was due to considerable fat deposition.

In contrast to strain *N*, infertility in pairs of strain *C* mice was negligible. Strain *C* had not reached such an advanced stage in the response to selection as strain *N*, and may become infertile in later generations. A significant positive correlation between egg number and body weight could only be established for line *CS* out of all five lines. Egg number may be correlated with body protein rather than with total body weight, for *CS* mice contained little fat, and the egg-number/body-weight ratios were similar for both strains when fat was excluded. This effect of fat was especially notable in the two large lines; the largest mice of these lines, i.e. those which probably contained the greatest proportion of fat (Fowler, 1958), ovulated the same number of eggs as mice weighing 10–20 g. less.

Estimates of the amount of FSH secreted by mice of strain *C* were higher than those of strain *N*. The level of FSH secretion might be determined by the size of the pituitary (Ladman & Runner, 1959). Moreover, mice of strain *C* deposit more protein than those of strain *N* (Fowler, 1958), and the amount of protein deposited during growth is probably regulated by the amount of pituitary growth hormone available (e.g. Li & Evans, 1948; Greenbaum & McLean, 1953). Inherited differences in the rate of deposition of protein and in the numbers of eggs ovulated indicate a higher level of pituitary activity in strain *C*.

SUMMARY

The fertility of two unrelated strains of mice (strains *N* and *C*) which had both been selected for large and small body size has been studied.

The fertility of pairs of mice in the large or small lines of strain *C* was unimpaired by selection. In strain *N*, some of the pairs in the large and small lines, but not in the control line, were sterile. Sterility in the large line was due to the low libido of

the males, and not to female infertility. Sterility in the small line was probably due to hypo-functioning of the anterior pituitary of some females: the oestrous cycle was delayed or absent, some mice failed to ovulate after mating, and a high proportion of those mating had no implanted embryos at 12 days' gestation. Oestrus and ovulation could be induced in mice of the small line of strain *N* by exogenous gonadotrophins, and the proportion of mice with implanted embryos was considerably increased by progesterone supplements.

The number of eggs found after natural mating was considerably higher in large mice than in small mice, and was significantly correlated with body weight in the small line of strain *C* only. The egg-number/body-weight ratio was higher in the lines of strain *C* than in those of strain *N*, though the ratios were similar when carcass fat was subtracted from total body weight.

The amount of endogenous follicle-stimulating hormone secreted by the mice of the five lines was estimated by inducing ovulation with various amounts of exogenous gonadotrophins, and comparing the number of eggs found after each dose with the mean number ovulated after natural mating. Estimates of the amount of follicle-stimulating hormone secreted by mice of strain *C* were higher than those for mice of strain *N*.

Differences in the rates of growth and in the numbers of eggs ovulated after natural mating indicate a higher level of pituitary activity in strain *C* than in strain *N*.

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