Genetic variation in spontaneous ovulation rate and LH receptor induction in mice

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Summary. Selection for litter size (Line S1) and for post-weaning body weight gain (Line G) increased spontaneous ovulation rate in mature females by 69 and 73%, respectively, over that of randomly bred control mice (Line C). Inbreeding from S1 mice with selection for litter size produced highly inbred lines with elevated ovulation rates. Inbreeding from Line C mice produced a 21% divergence among lines, but did not depress the mean ovulation rate. Crosses of these lines revealed little heterosis in ovulation rate. LH receptors were induced by treating females from 22 days of age with diethylstilboestrol for 4 days and FSH for 2 days. The in-vitro binding of ^{125}I -labelled hCG per μg DNA decreased 56% in response to selection for litter size and increased 57% in response to selection for body weight gain, indicating high susceptibility of this trait to genetic change. Inbreeding from Line C mice produced a 135% divergence amongst lines, but did not depress the mean LH receptor induction. Body weight had significant effects on ovulation rate and LH receptor induction.

These results show that selection for litter size and for rapid post-weaning body weight gain increases ovulation rate, but we suggest that different mechanisms are involved in these responses.

Introduction

Ovulation rate, the number of eggs ovulated at oestrus, is a major determinant of reproductive rate in mammals. Ovulation rate has been increased by selection in mice (Bradford, 1969; Land & Falconer, 1969) and pigs (Cunningham, England, Young & Zimmerman, 1979). Heritability estimates of ovulation rate vary from 0 to 42%, and average about 20%. Ovulation rate has also been increased by selection for litter size in mice (Falconer, 1960; Bradford, 1968; Land, 1970; Durrant, Eisen & Ulberg, 1980) and in sheep (Turner, 1969; Quirke, Bradford, Famula & Torell, 1982). Ovulation rate in mice has also been increased by selection for body weight gain (MacArthur, 1944; Land, 1970; Bradford, 1971; Durrant *et al.*, 1980). Ovulation rate in mice tends to be inherited in an additive manner (Bradford & Nott, 1969), although there is evidence for non-additive gene action controlling the spontaneous ovulation rate of Wistar rats (Land, de Reviers, Thompson & Mauléon, 1974).

The spontaneous ovulation rates of the mouse lines S1, G and C differ, at least in part, because of differences in the regulation of gonadotrophic and steroid hormones, as well as in ovarian sensitivity and responsiveness to these hormones (Spearow & Geschwind, 1979; Spearow, 1980). Genetic variation in ovarian responsiveness to gonadotrophins within this population seems to be mediated largely by differences in the number of developing follicles, and the rate of induction of LH receptors. One of the final steps by which FSH stimulates follicular maturation is by increasing

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the number of LH receptors (Richards, 1978), which are essential for follicles to respond to the LH surge and to ovulate. However, the genetics of LH receptor induction are not understood.

In the present study we have used mice to examine the effects of selection for litter size and for rapid post-weaning body weight gain, and of inbreeding and crossing on spontaneous ovulation rate and on one of its components, the induction of ovarian LH receptors. The study also investigated the possibility of developing inbred lines with high ovulation rates.

Materials and Methods

Lines of mice. The mice used were developed in a study of the long-term effects of selection for reproduction and growth, and of the effects of inbreeding in the different lines. The lines involved were: C, an unselected control, and lines inbred from it (C2, C6, C8, C12 and C17); S1, selected for large litter size, and lines inbred from it (S12 and S15); and G, selected for rapid post-weaning body weight gain. Several crosses among these lines were also used. Ovulation rate was determined on reciprocal crosses of C17 and C6 as well as of C2 and C6. Since few reciprocal crosses were examined and no differences were apparent, the data from the F1s of C6 × C17 and C2 × C6 were pooled with, and reported as, their reciprocal. No reciprocal crosses were tested for the induction of LH receptors. Line C was developed with no intentional selection but with random mating, while Lines S1 and G were developed with both selection and random mating from the same base population (a four-way cross of strains C57BL/6J, AKR/J, C3H/J, and DBA/2J), as described by Bradford (1968, 1971), Eklund & Bradford (1977), and Barria & Bradford (1981). Lines C2 to C17 were developed by initiating full sib matings in 18 litters of Line C at generation 50. Full sib matings were continued with no intentional selection for litter size. Lines were culled due to low fertility or infertility until, at generation 8 of inbreeding, 5 partly inbred C lines remained. Lines S12 and S15 were developed from Line S1 (generation 34), using sib mating and selection for large litter size. Their performance through the first 10 generations has been described by Eklund & Bradford (1977). The lines have been continued with sib mating. The ovulation rate experiments were conducted after 50 generations of selection and random mating in Lines C, S1 and G, after 5–6 generations of inbreeding of Line C mice, and after 20–21 generations of inbreeding and selection of Line S1 mice. The LH receptor induction experiments were conducted two generations later. The housing and management of these mice has been previously reported by Bradford (1968, 1971). Lights were on from 05:00 to 19:00 h, and the temperature was maintained between 22 and 24°C. White diet (Simenson Laboratories, Gilroy, California) with an approximate analysis of 24% crude protein, 6% crude fat, 3.5% fibre and 5% ash was fed *ad libitum*.

Spontaneous ovulation rate. Virgin females, 8–10 weeks old, were housed in groups of 3–5 with one male. The day of oestrus was determined by the presence of a vaginal plug before 11:00 h on the morning of oestrus. Spontaneous ovulation rate was determined after killing the mice that morning by counting ova in the cumulus clump (Land & Falconer, 1969) under a dissecting microscope.

LH receptor induction. LH receptors were induced by treating females from 22 days of age with a subcutaneous Silastic implant (8 mm × 1.575 mm i.d., 3.175 mm o.d.; Dow Corning, Midland, Michigan) of diethylstilboestrol for 4 days, and 2 subcutaneous injections of 15 µg ovine FSH (NIH-FSH-S12) per day for the last 2 days. This treatment bypasses much of the normal feedback regulation of follicular development which occurs between the pituitary and the ovary, and has been previously shown to mature follicles and to induce LH receptors (Spearow, 1980).

LH receptor binding analysis. Highly purified hCG (CR117), (15 µg) was labelled with 1 mCi ¹²⁵I by the low temperature chloramine-T method of Catt, Dufau & Tsuruhara (1972). Iodinated hCG was separated from free iodine on a 6 cm Sephadex G50 column. The specific activity of ¹²⁵I-labelled hCG (46.4 c.p.m./pg hCG-CR117) was determined by a self-displacement radioreceptor assay. After cervical dislocation of each mouse, its ovaries were cleanly excised and homogenized

in cold 0.01 M-phosphate-buffered saline with 0.1% gelatin, pH 7.2. ^{125}I -labelled hCG, 200 000 c.p.m., in 1% BSA-PBS was added without (total binding) or with 1 μg crude hCG (non-specific binding) to three-tenths of an homogenized ovary (final volume 400 μl). After an overnight incubation at 22°C, 2.5 ml cold PBS-gelatin was added, the tubes were centrifuged at 2500 g for 30 min, the supernatant aspirated, and the pellet washed again with another 2.5 ml PBS-gelatin. After another centrifugation and aspiration step radioactivity in the pellet was counted in a gamma counter.

Statistical analyses. Data on spontaneous ovulation rate and on LH receptor induction were evaluated first using all data, and then separately for each group of comparisons by analysis of variance, analysis of covariance, Scheffé's multiple range test, and/or by F test. When appropriate, the data for each group were analysed with a one-way analysis of variance. The variances among lines for spontaneous ovulation rate were not equal, mainly due to the higher variation in C6, C17 S1, and especially G mice. Since the variance did not seem to be a function of the mean, a log transformation was not performed. The condition of equality of variances was not met for hCG binding on a per ovary or a per μg DNA basis ($P < 0.001$) but log transformation improved the equality of variances for these data ($P < 0.05$) and so the actual tests of significance for all LH receptor data were conducted after log transformation. Since the regression of these traits on body weight was significant and did not differ between lines, except for spontaneous ovulation rate among Lines C, S1 and G, the performance for mice of each line was also corrected using the appropriate pooled within-line regression to the mean body weight for that group. The mean body weights to which the lines in Tables 1(a), 1(b), 1(c), 1(d), and all of Table 2 were adjusted was 24.6, 23.1, 25.4, 24.3 and 11.5 g, respectively. The final comparison of the appropriate line means was made with a Scheffé's multiple range test, or with an F test for individual pair-wise comparisons.

Results

Spontaneous ovulation rate

The spontaneous ovulation rates of the different lines and crosses are shown in Table 1. A one-way analysis of variance of ovulation rate revealed significant differences among Lines C, S1 and G; 78% of the variation was among lines. Selection for litter size (Line S1) increased ovulation rate over that of the randomly selected control mice (Line C) ($P < 0.001$). Selection for body weight gain (Line G) increased ovulation rate over that of Line C mice ($P < 0.01$) but not over that of the litter size line.

Inbreeding of Line C mice produced significant differences among lines in ovulation rate, with 16% of the variance among lines. The lines ranked as follows in order of increasing ovulation rate: C2, C6, C8, C12 and C17, with C2 and C6 mice ovulating significantly fewer ova than did C17 mice. Inbreeding from Line S1 produced a slight divergence of spontaneous ovulation rate, with Line S15 ovulating more ova than S12 ($P < 0.1$). Inbreeding did not depress the mean ovulation rate in the C mice. However, inbreeding from S1 mice significantly decreased the ovulation rate in S12 ($P < 0.01$) but not in S15 mice.

There was no consistent heterosis for ovulation rate as measured in the F1 mice: 4 out of 6 crosses showed no heterosis, S12 $\times$ C17 mice showed significant negative heterosis (-5%) and S12 $\times$ S15 mice showed significant positive heterosis (7%) for ovulation rate. However, the ovulation rate of S12 $\times$ S15 mice was not different from that of the mice in Line S1.

Selection for litter size, followed by inbreeding with continued selection for litter size within and amongst lines, produced greatly inbred lines (S12, S15) with high ovulation rates. Furthermore, when crossed to unselected lines (C17 and C8), the mice of Lines S12 and S15 generally improved the ovulation rates of their progeny over that of the C-derived parent.

Table 1. Spontaneous ovulation rate and body weight of 8–10-week-old mice of various lines and crosses

	Line or cross	Generation	No.	Ovulation rate		Body wt (g)
				Observed	Corrected for body wt	
(a)	C	55	19	10.3 ± 0.3 ^a	10.3 ± 0.3 ^a	24.6 ± 0.5 ^a
	S1	50 + 51	18	17.6 ± 0.5 ^b	16.8 ± 0.3 ^b	25.9 ± 0.7 ^a
	G	58	9	17.8 ± 1.5 ^b	10.7 ± 0.9 ^a	44.7 ± 2.1 ^b
(b)	C	55	19	10.3 ± 0.3 ^{ab}	9.9 ± 0.4 ^{ab}	24.6 ± 0.5 ^{bc}
	C2	5 + 6	19	9.2 ± 0.3 ^a	9.7 ± 0.4 ^a	21.1 ± 0.4 ^a
	C6	5 + 6	28	9.5 ± 0.2 ^a	9.9 ± 0.3 ^{ab}	21.6 ± 0.4 ^a
	C8	5 + 6	26	10.0 ± 0.4 ^{ab}	10.3 ± 0.3 ^{ab}	22.0 ± 0.4 ^{ab}
	C12	5 + 6	22	10.6 ± 0.3 ^{ab}	9.6 ± 0.4 ^a	26.7 ± 0.6 ^c
	C17	5 + 6	25	11.4 ± 0.4 ^b	11.4 ± 0.3 ^b	23.1 ± 0.5 ^{ab}
(c)	S1	50 + 51	18	17.6 ± 0.5 ^b	17.2 ± 0.4 ^b	25.9 ± 0.7 ^b
	S12	20 + 21	21	15.7 ± 0.2 ^a	15.7 ± 0.4 ^a	25.3 ± 0.3 ^{ab}
	S15	20 + 21	23	16.7 ± 0.4 ^{ab}	17.0 ± 0.3 ^b	24.3 ± 0.4 ^a
(d)	C2 × C6	F1	6	10.0 ± 0.6 ^{ab}	10.8 ± 0.5 ^{ab}	22.1 ± 1.1 ^{ab}
	C6 × C8	F1	9	10.3 ± 0.4 ^{ab}	11.0 ± 0.4 ^a	22.7 ± 0.5 ^{ab}
	C17 × C6	F1	23	9.7 ± 0.3 ^a	9.7 ± 0.3 ^a	21.1 ± 0.6 ^a
	S12 × C17	F1	22	12.9 ± 0.2 ^c	12.9 ± 0.3 ^b	24.3 ± 0.3 ^b
	S15 × C8	F1	7	12.7 ± 0.7 ^{bc}	13.0 ± 0.5 ^b	23.4 ± 1.0 ^{ab}
	S12 × S15	F1	29	17.3 ± 0.3 ^d	15.9 ± 0.3 ^c	27.9 ± 0.4 ^c

Values are mean ± s.e.m.

Means within the same table section and column not sharing a common superscript are significantly different ($P < 0.05$) according to Scheffé's multiple range test.

Body weight

As shown in Table 1, a one-way analysis of variance revealed dramatic differences in the body weights of mice in the various groups ($P < 0.001$). While the body weight of Line G females was greater than that of Line S1 and Line C females ($P < 0.001$ for both), the difference (1.3 g) in mean body weight between S1 and C females was small ($P < 0.2$), but agreed well with the value of 1.4 g ($P < 0.01$) reported by Eklund (1975) for a larger sample.

While inbreeding from Line C mice produced a significant divergence in body weight, inbreeding from Line S1 mice did not. The lines ranked in increasing order as follows: C2, C6, C8, C17, C12. The body weight of F1 females was significantly lower than the mid-parental value for C17 × C6 mice (−6%) and higher for S12 × S15 mice (12%), but the average of all crosses showed no heterosis.

The effect of body weight on ovulation rate

The pooled within-line regression of ovulation rate on body weight for all lines was $b = 0.35 \pm 0.03$ ($P < 0.001$). The slope of this regression was positive in all lines and did not differ significantly amongst lines. Correction for body weight affected the ovulation rate of S1 mice very little but eliminated the difference between mice in Lines G and C. While the ovulation rate of G mice was similar to that of S1 mice before correction, it was lower after correction. The increased ovulation rate of the mice in Line G but not that of mice in Line S1 was associated with increased body weight.

The ovulatory performance of the inbred lines and crosses was also affected by differences in body weight. The pooled within-line regression of ovulation rate on body weight for lines inbred from Line C was $b = 0.26 \pm 0.03$ ($P < 0.001$) and did not differ amongst lines. The variation in

body weight did not account for the increased ovulation rate of C17 mice, but it did appear to account for the reduced ovulation rate of the smaller mice in Lines C2 and C6. The pooled within-line regression of ovulation rate on body weight for lines inbred from Line S1 was $b = 0.30 \pm 0.068$ ($P < 0.01$), and did not differ amongst lines. After correction for body weight, the ovulation rate of S12 mice was less than that of S1 or S15 mice. Correction for the effect of body weight with the overall pooled within-line regression also eliminated the heterosis in the ovulation rate of S12 $\times$ S15 F1 females. Therefore, the only cross showing positive heterosis in ovulation rate may have done so due to heterosis in body weight.

LH receptor induction

The in-vitro binding of ^{125}I -labelled hCG by ovarian homogenates from immature females treated with diethylstilboestrol (4 days) and FSH (2 days) is shown in Table 2. The actual tests of significance, as reported in Table 2, were obtained from analysis of log-transformed data (not shown). The effect of body weight on LH receptor induction was considered on a per μg DNA and on a per ovary basis. Considering all lines and crosses, the regression of hCG binding per μg DNA on body weight (155.2 ± 38.7 c.p.m./ μg DNA/g body weight) was significant and did not differ amongst lines. For all lines and crosses, the slope of the regression of hCG binding per ovary on body weight (2171 ± 670 c.p.m. ^{125}I -labelled hCG/g body weight) was different from zero ($P < 0.01$) and did not differ between lines. The body weights of mice in these lines differ due to genetic differences in growth performance as well as individual differences due to environmental or error effects. Nevertheless, such correction does help to determine whether the observed changes in LH receptor induction were associated with changes in body weight. Therefore, the log-transformed binding of ^{125}I -labelled hCG per μg DNA and per ovary was considered both before and after correction for the effect of body weight (not shown) using the pooled within-line regressions.

Table 2. Body weight and number of LH receptors in the ovaries of 26-day-old mice pretreated with diethylstilboestrol (4 days) and FSH (2 days)

			Specifically bound ^{125}I -labelled hCG (c.p.m.)			
Line			No.	Per ovary	Per μg DNA	Body wt (g)
(a)	C		14	13408 ± 1714^b	908 ± 119^b	10.5 ± 0.2^a
	S12 $\times$ S15	F1	14	5779 ± 490^a	400 ± 38^a	9.8 ± 0.2^a
	G		19	32547 ± 34175^c	1506 ± 176^c	14.2 ± 0.5^b
(b)	C12		6	28439 ± 2363^b	1943 ± 181^b	11.9 ± 0.6^b
	C17		8	10065 ± 2052^a	718 ± 179^a	10.6 ± 0.5^a
(c)	S12		14	3539 ± 310^a	332 ± 24^a	11.4 ± 0.4^b
	S15		17	5728 ± 481^b	466 ± 36^b	10.1 ± 0.4^a
(d)	C6 $\times$ C8	F1	9	24578 ± 4412^a	1845 ± 317^a	11.1 ± 0.3^a
	S12 $\times$ C8	F1	7	16954 ± 3418^a	1124 ± 238^a	11.6 ± 0.5^{ab}
	S15 $\times$ C12	F1	6	27198 ± 6935^a	1666 ± 337^a	12.7 ± 0.4^b

Values are mean $\pm$ s.e.m. raw data.

Means within the same table section and column not sharing a common superscript are significantly different ($P < 0.05$) when the raw data for body weight or the log-transformed data for hCG binding per ovary or per μg DNA were analysed by F tests (for Tables 2b and 2c) or by Scheffé's multiple range test (for Tables 2a and 2d).

All S-derived mice had fewer LH receptors per μg ovarian DNA and per ovary than did Line C mice ($P < 0.05$ for all comparisons). Line G females bound more ^{125}I -labelled hCG per μg DNA and per ovary than did S-derived ($P < 0.01$) or C females ($P < 0.05$). Correction of the log-

transformed ^{125}I -labelled hCG binding per μg DNA for the effect of body weight, using the pooled within-line regression, eliminated the differences between G and C mice but not between S12 $\times$ S15 F1s and either G ($P < 0.1$) or C ($P < 0.01$) mice. Correction of the log-transformed hCG binding per ovary for the effect of body weight eliminated the differences between C and S12 $\times$ S15 F1 or G mice, whereas G mice continued to bind more hCG than did the S12 $\times$ S15 F1s ($P < 0.01$). Therefore, body weight seemed to affect the induction of LH receptors in Lines C, S12 $\times$ S15 F1 and G, but only in Line G could the increased induction of LH receptors be accounted for by changes in body weight.

Inbreeding produced a divergence of line performance, but did not depress the mean LH receptor induction. Correction of the log-transformed LH receptor induction for body weight had only a small effect and did not change the ranking of the inbred lines. The number of LH receptors per μg DNA or per ovary was higher in C12 than in C17 mice both with and without correction for the effect of body weight ($P < 0.01$). This represents a 135% divergence of inbred lines in 7–8 generations of inbreeding from a common outbred stock. The log-transformed binding of ^{125}I -labelled hCG, both with and without correction for the effect of body weight, was greater in S15 than in S12 mice both on a per μg DNA ($P < 0.05$) and a per ovary basis ($P < 0.01$). The S12 $\times$ S15 and S15 $\times$ C12 F1s showed a significant heterosis in LH receptors per ovary but not per μg DNA. After correction for the effect of body weight, only the S12 $\times$ S15 F1s showed heterosis for LH receptor per ovary ($P < 0.05$).

Discussion

Selection of mice for litter size or for body weight gain increased spontaneous ovulation rate. The observation that selection for litter size increases spontaneous ovulation rate agrees well with earlier studies in these same lines of mice (Bradford, 1969), in other lines of mice (Falconer, 1960; Land & Falconer, 1969; Durrant *et al.*, 1980), and in sheep (Turner, 1969; Quirke *et al.*, 1982). The finding that selection for body weight gain increased ovulation rate agrees with the results of previous studies (MacArthur, 1944; Fowler & Edwards, 1960; Falconer, Edwards, Fowler & Roberts, 1961; Durrant *et al.*, 1980).

Inbreeding generally produced a divergence of ovulation rate amongst lines, suggesting that at the initiation of inbreeding Lines S1 and C were segregating at loci controlling ovulation rate. The smaller divergence among S1-derived lines could be due to the smaller number of S1-derived lines that were sampled, or the 34 generations of selection preceding intensive inbreeding from S1, which could have fixed loci before the initiation of inbreeding. Inbreeding did not depress the mean spontaneous ovulation rate; the fact that it produced a divergence without depressing the mean value indicates a large amount of genetic variation in this trait, and suggests that these genetic differences are controlled by genes which act additively. These conclusions are consistent with the absence of significant heterosis in the F1s of 4 out of 6 cases, and support earlier observations on crosses of other lines of mice from the same base population (Bradford & Nott, 1969). Conversely, inbred strains of Wistar rats show evidence of non-additive gene action affecting spontaneous ovulation rate (Land *et al.*, 1974). Nevertheless, the present results suggest that selection for litter size with inbreeding could produce lines with elevated ovulation rates in other species, e.g. specialized dam lines or crosses. Whether this can be achieved in a particular population probably depends on the type of genetic variation controlling ovulation rate and on the genetic load in the population.

The present study demonstrates a large amount of genetic variation in the number of induced LH receptors. The induction of LH receptors decreased in response to selection for litter size, increased in response to selection for body weight gain, and diverged in response to inbreeding. LH receptors are induced by FSH, and down-regulated by LH. Furthermore, the induction of LH receptors by FSH is potentiated by oestrogen (Richards, 1978). The genetic differences in the

number of ovarian or testicular LH receptors found in untreated animals (Purvis, Clausen & Hanson, 1978; Spearow, 1980; Amador & Bartke, 1981, 1982) could, in part, be due to genetic differences in serum gonadotrophin concentrations (Bartke, Robertson & Dalterio, 1979; Bindon, Blanc, Pelletier, Terqui & Thimonier, 1979; Quirke, Hanrahan & Gosling, 1979; Spearow, 1980; Wolfe *et al.*, 1981) or the down-regulation of LH receptors by LH or hCG (Amador & Bartke, 1981). The present study suggests that the 6–9-fold differences in LH receptor induction by diethylstilboestrol and FSH are a major source of genetic variation in the number of LH receptors found in untreated animals.

Inbreeding produced a large divergence in LH receptor induction per μg DNA without depressing the mean value, suggesting that this trait is under additive genetic control. This conclusion is supported by the absence of significant heterosis in hCG binding per μg DNA. While the hCG binding per ovary also diverged in response to inbreeding, heterosis was observed in this trait in the F₁s of the S12 $\times$ S15 and S15 $\times$ C17 crosses. Correction of the LH receptor per ovary for the effect of body weight eliminated this effect in S15 $\times$ C17 F₁s, suggesting that the observed heterosis in this cross is due to an effect of body weight. In contrast, the observed heterosis in hCG binding per ovary but not per μg DNA in the S12 $\times$ S15 F₁s suggests heterosis in follicle number or ovarian size, rather than in LH receptor induction per cell.

The divergence produced by inbreeding in LH receptor induction was much greater than that in spontaneous ovulation rate. The most obvious explanation is the homeostatic mechanisms regulating ovulation rate: even if selection increased the ovarian responsiveness to gonadotrophins, spontaneous ovulation rate would not increase without concomitant changes in the feedback regulation of blood gonadotrophic hormone concentrations.

Natural ovulation rate increased in S1 and G mice, while the induction of LH receptors increased in Line G, but decreased in all S1-derived lines. This suggests either that LH receptor induction and spontaneous ovulation rate are independent, or negatively associated, or that the spontaneous ovulation rates in Lines S1 and G have been increased by different mechanisms. Spearow (1980) has suggested that the increased ovulation rate in Line S1 involves a decrease in the induction of LH receptors, resulting in a decreased oestrogen production rate, thereby decreasing the relative feedback on serum FSH. In contrast, the increased spontaneous ovulation rate of mice in Line G seems to be due to an increased induction of LH receptors, thereby increasing ovarian responsiveness, and to another way of decreasing the relative negative feedback on serum FSH.

Body weight was positively associated with spontaneous ovulation rate in all strains, confirming the observations of Falconer & Roberts (1960), Land (1970) and Durrant *et al.* (1980) on other genetically heterogeneous mouse populations and of Quirke *et al.* (1982) on sheep. Based on indirect evidence, Land (1970) concluded that the components of ovulation rate, FSH activity and ovarian sensitivity were positively correlated genetically and phenotypically with body weight. The suggestion by Durrant *et al.* (1980) that selection for litter size or for body weight increased ovulation rate via increasing ovarian sensitivity seems less than conclusive. The ovulatory responses to gonadotrophins were generally less than the spontaneous ovulation rate and differed only slightly amongst strains. Moreover, since follicular maturation was induced with a single massive injection of 0.5 mg FSH, which has a short half-life, it is unclear which aspect of ovarian sensitivity or responsiveness was being measured. The present study clearly shows that body weight affects ovarian function, at least in part, by influencing the induction of LH receptors by FSH and oestrogen.

The correlated responses in ovulation rate and/or body weight in the present study are very asymmetric, depending on whether selection was for litter size or for gain. Adjusting ovulation rate in Line G mice for body weight removes the differences from that of Line C mice, suggesting a fairly direct association between body weight and ovulation rate in these lines. Adjusting for body weight in Line S1 does not affect ovulation rate, again suggesting that selection for litter size or for gain increases ovulation rate by different mechanisms.

Several types of evidence suggest that increased ovulation rate, ovarian responsiveness to

gonadotrophins and increased body weight may all be, in mice of Line G and in sheep (Quirke *et al.*, 1982), pleiotrophic effects of nutritional or metabolic changes. Line G mice differ from those of Line C in feed intake, feed efficiency, body composition, and in energy metabolism and its hormonal regulation (Mears & Mendel, 1974; Meyer & Bradford, 1974). Increased food intake (flushing) increases ovulation rate in sheep (Coop, 1966). Increased availability of gluconeogenic precursors via the feeding of sodium monensin results in an increased ovarian responsiveness to gonadotrophins (Bushmich, Randel, McCarter & Carroll, 1980). Furthermore, changes in energy balance seem to be closely related to changes in the resumption of ovarian function in post-partum dairy cows (Butler, Everett & Coppock, 1981).

In contrast, the difference in ovulation rates in mice of Lines S1 and C is clearly not related to differences in body weight. Some genetic differences in ovarian responsiveness are not associated with body weight; there are very large differences amongst other inbred strains of mice in ovarian responsiveness to gonadotrophins, whether they are corrected for the effect of body weight or not (Spearow, 1981).

Since all lines, whether inbred or outcrossed, had similar regressions of ovulation rate on body weight, the effects of body weight seem to be the same whether the differences in body weight are genetic or environmental in origin. Body weight clearly must be considered when trying to increase ovulation rate by genetic selection. However, statistical correction of ovulation rate for body weight may be undesirable since it could remove the genetic variation in ovulation rate due to genetic differences in body weight. The development of selection criteria that permit (1) screening of many individuals for the necessary genetic variation in ovulation rate and its components, (2) correction for maternal effects, and (3) selection based on the rate-limiting genetic differences rather than environmentally caused differences, should result in a faster improvement of ovulation rate. A more complete understanding of the physiological and biochemical mechanisms mediating genetic differences in ovulation rate and body weight, and their effects on the efficiency of reproduction, are needed before methods for increasing ovulation rate can be recommended.

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