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Effects of Reduced Food Intake on Reproduction in Mice

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Abstract

The effect of undernutrition on the reproductive performance of the Quackenbush strain of mice was studied using four dietary levels: *ad libitum* (8·0 g per mouse per day; D_{100}), 85% (D_{85}), 70% (D_{70}), and 55% (D_{55}) of *ad libitum* food intake.

Dietary restriction for 60 days at the 55% level resulted in an increase in the length of the oestrous cycle compared with other dietary levels, whereas D_{85} and D_{70} mice did not differ from the control group. When the underfed mice were fed *ad libitum* their reproductive performance did not differ from that of the D_{100} mice.

In a second experiment mice were fed the restricted diet for 2 weeks before males were introduced. The males were fed *ad libitum* except for a 5-day mating period, when they were removed and replaced by another group of males. On days 1, 7, and 16 of pregnancy approximately 10 mice per dietary level were killed and the ovulation rate, implantation rate, and late embryonic survival were estimated. The remainder of the mice were allowed to litter for studies of the litter size, birth weight and sex ratio.

Dietary restriction did not affect the ovulation rate and only 45% restriction resulted in a decreased implantation rate. The late embryonic survival was reduced at all levels of restricted food intake, but sex ratios were unaffected by dietary intake. Dietary restriction of 30% and 45% decreased the littering rate and increased foetal resorption.

The litter size decreased at all levels of dietary restrictions, but the birth weight was reduced only with moderate (D_{70}) and severe (D_{55}) restrictions.

The litter size and the pup weight of the D_{70} and D_{55} mice following *ad libitum* refeeding were greater than those of their counterparts maintained on restricted feeding.

Introduction

Many investigators have studied the effects of undernutrition on reproductive performance of laboratory rodents. Irregularity, increased cycle length and cessation of oestrous cycles have been reported in underfed laboratory mice (Mulinos *et al.* 1939; Carr *et al.* 1949; Rinaldini 1949) and rats (Cooper *et al.* 1970).

A detrimental effect of inanition on ovulation rate has been shown in the rat (Cooper *et al.* 1970) and mouse (Lamond and Bindon 1969). When treated with gonadotrophins, hypophysectomized mice fed *ad libitum* produced more ova per ovulating mouse than those on restricted feeding (Fielden and Brumby 1962).

The long-term effect of undernutrition on implantation rate in mice does not seem to have yet been reported. However, McClure (1961*a*, 1961*b*, 1966) has shown that fasting for 48 h around the time of mating and implantation reduced the implantation rate.

Berg (1965) surprisingly did not demonstrate any difference in the embryonic survival of fully fed and 75% restricted rats on day 13 of gestation, but Cooper *et al.* (1970) reported a decreased number of viable foetuses on day 19 with increased dietary restriction.

The effects of low levels of food intake on the litter size vary according to the severity and the period of treatment (Chow 1964; Berg 1965; Widdowson and Cowen 1972; Chow and Rider 1973; Wodzicka-Tomaszewska *et al.* 1974; Smart and Silence 1977). Dietary restriction of 50% in rats during pregnancy only resulted in significantly reduced foetal weights on days 17–22 of gestation (Durst-Zivkovic 1977).

Reduced birth weight due to undernutrition has been reported by many workers (Widdowson and Cowen 1972; Chow and Rider 1973; Smart and Silence 1977); however, Wodzicka-Tomaszewska *et al.* (1974) reported no difference in the birth weights of pups born to control mice and mice underfed for 18 days before mating.

In most works cited here restriction was applied after animals became pregnant or for the pre-mating period only, and the oestrous cycle, litter size and birth weight were recorded. However, no single work has investigated all of these parameters simultaneously in any one species. Varying dietary levels and different strains have been used and as a result the comparison of findings in one species is difficult.

The purpose of the present paper was to study the effects of three levels of food intake—85%, 70% and 55% of *ad libitum*—as compared to *ad libitum* feeding for a period of three litters on the incidence of oestrus, ovulation rate, implantation rate, late embryonic survival, litter size, birth weight, and sex ratio of the Quackenbush strain of mice and to investigate the effect of rehabilitation on some of these features.

Materials and Methods

Albino mice of the Quackenbush strain, 6–7 weeks old, were caged in an air-conditioned room at 23°C and under a lighting regime of 12 h light–12 h dark, the period of light being from 0600 to 1800 h. The animals were fed 'rat and mouse cubes' (Bunge, Australia Pty Ltd) and water was supplied *ad libitum*.

Experiment 1

Food consumption measurement

To measure the average daily food consumption per mouse, 60 mice were allotted to four replicates in cages containing 1, 2, 4 and 8 mice. Diet was supplied daily for 10 days at the rate of 40 g per mouse. Unused food was removed at 1100 h each day, weighed and the difference taken as the *ad libitum* food intake of each cage. No attempts were made to measure the amount of food wasted in the bedding.

Experiment 2

Underfeeding and the incidence of oestrus

Ninety mice were randomly allotted to four dietary levels and caged in groups of five mice per cage: 20 mice on *ad libitum* feeding (8·0 g per mouse per day; D_{100}), 20 mice on 85% (6·8 g per mouse per day; D_{85}), 20 mice on 70% (5·6 g per mouse per day; D_{70}) and 30 mice on 55% (4·4 g per mouse per day; D_{55}) of *ad libitum* feeding.

The mice in all dietary groups were fed *ad libitum* for an initial period of 30 days during which their oestrous cycle behaviour was studied. The stages of the oestrous cycle were identified by vaginal smear, taken daily between 0900 and 1000 h. The oestrous cycle was classified into five stages: pro-oestrus, oestrus, metoestrus, and day I and day II dioestrus according to the vaginal cell types found (Bingel and Schwartz 1969). At the end of the preliminary 30-day period of *ad libitum* feeding the mice were fed the four dietary levels and their oestrous cycle behaviour was then studied for 60 days.

Effect of dietary rehabilitation on fertility after restricted feeding for 60 *days*

At the end of the experimental period the female mice were fed *ad libitum* for 2 weeks before one male was introduced to each cage. The females were allowed to produce one litter and upon littering the litter size, birth weight, sex ratio and prenatal period were compared. The prenatal period was calculated from the time of introduction of the male to parturition.

Experiment 3

In total 640 mice (160 mice per dietary level) were allotted at random to the four dietary levels and all diets were fed for a period of 2 weeks before males were introduced. The males were fed *ad libitum* except for a 5-day mating period, when they were removed and replaced by another group of males. This tended to compensate for differences in male fertility and the possible effects of underfeeding on male fertility. Because of the difficulty in obtaining fresh males some of these males were re-used after at least 2 weeks of *ad libitum* feeding. Females were checked daily at 0800 h for the presence of a copulatory plug; the day the plug was found was counted as the first day of pregnancy.

Ovulation rate

On day 1 of pregnancy approximately 11 female mice per dietary level were killed and the numbers of corpora lutea in the ovaries were counted with the aid of a magnifying lamp. This count was taken as a measure of ovulation rate.

Implantation rate

On day 7 of pregnancy another 11 or 12 females per dietary level were killed and their uteri were inspected for implantation sites. The number of implantation sites was taken as a measure of implantation rate.

Late embryonic survival (LES)

On day 16 of pregnancy 11 or 12 females per dietary level were killed and the number of live embryos counted to determine the LES.

The remainder of the experimental animals in each treatment group were allowed to deliver their litters (if any). Upon delivery the number of offspring, sex ratios, and total weight of the litter were recorded. The litter was removed on the day of delivery, males were introduced and the same procedures were repeated for the second and third pregnancies.

Recovery Experiment

When almost all D_{100} and D_{85} mice had completed their third pregnancies there were 32 mice on D_{70} and 101 mice on D_{55} dietary levels that had not littered for either first, second or third pregnancies. The mice in each group were divided at random into two subgroups, one of which was fed *ad libitum* and the other retained on the restricted diet. Males were introduced to both subgroups 2 weeks after *ad libitum* feeding was begun. The animals were allowed to litter and the litter size, birth weight and sex ratio were determined.

Statistical Analysis

The data were analysed by the analysis of variance and the least significant differences (l.s.d.) calculated.

Results

Experiment 1

Food consumption measurement

At densities of 1, 2, 4, and 8 mice per cage the mean food consumption increased with density, being 6·2, 6·5, 7·7 and 8·4 g per mouse per day for the four groups respectively (l.s.d. = 0·7 with $P = 0{\cdot}05$, and 1·0 with $P = 0{\cdot}01$). In the other experiments *ad libitum* feeding was taken to be 8·0 g per mouse per day.

Experiment 2

Underfeeding and the oestrous cycle

The mean oestrous cycle length at each dietary level is given for the pretreatment (30-day) and treatment (60-day) periods (Table 1). Cycle length in the D_{55} mice was significantly extended ($P < 0{\cdot}01$).

Table 1. Effect of dietary level on the oestrous cycle length of mice

Values given are mean numbers of days ± s.e.

Dietary level	No. of mice	Pretreatment period (30 days)	Treatment period (60 days)	Difference
D_{100}	20	6·7±0·4	8·9±0·5	2·2±1·2
D_{85}	20	7·1±0·4	9·3±0·5	2·2±1·2
D_{70}	20	7·3±0·4	10·1±0·2	2·8±1·2
D_{55}	30	7·3±0·3	15·0±1·7	7·7±1·0

L.s.d. = 3·4, $P = 0{\cdot}01$, d.f. = 86.

Fertility upon ad libitum *feeding*

After *ad libitum* feeding there were no significant differences among the four groups in the litter size, birth weight and sex ratio (Table 2), although two mice in the D_{85} group did not litter. D_{100} mice had significantly longer prenatal periods than mice in the other groups.

Table 2. Litter size, birth weight, sex ratio and prenatal period for the first pregnancy upon dietary rehabilitation

Values given are means ± s.e.

	Dietary level			
	D_{100}	D_{85}	D_{70}	D_{55}
No. of mice	20	20	20	30
Litter size	10·9±0·9	8·7±0·9	9·4±0·9	9·6±0·7
Birth weight (g)	1·8±0·1	1·8±0·1	1·9±0·1	1·8±0·1
Sex ratio (%)	54·8±3·3	49·0±3·4	45·4±3·2	50·1±2·6
Prenatal period[A] (days)	32·3±1·6	27·3±1·6	25·3±1·6	25·3±1·3

[A] For D_{85}, l.s.d. = 4·7, $P = 0{\cdot}05$, d.f. = 82.
For D_{70}, l.s.d. = 6·0, $P = 0{\cdot}01$, d.f. = 82.
For D_{55}, l.s.d. = 5·0, $P = 0{\cdot}01$, d.f. = 82.

Experiment 3

Ovulation rate

The range and the mean ovulation rate for each dietary level over three consecutive pregnancies (L_1, L_2, and L_3) are shown in Table 3. Each mean ovulation rate is the average of either 11 or 12 records except for the $D_{55} \times L_3$ mean which is the mean of two records (13 and 20).

Dietary restriction over three pregnancies did not have any significant effect on the ovulation rate (Table 3). The ovulation rate increased with parity, the mean ovulation rate of the third pregnancy (17·6) being greater than the means of the first (13·1) and second (14·4) pregnancies. There was no interaction of dietary levels and litter sequence on ovulation rate.

Implantation rate

The range and the mean implantation rate (the total number of implantation sites in the uterine horns on day 7 post-coitum) for each dietary level are shown in Table 4. The mean implantation rates in this table represent either 11 or 12 records except for the $D_{55} \times L_3$ mean which represents only two records (0 and 11).

Table 3. Ovulation rate (number of corpora lutea in the ovaries) of mice fed four dietary levels and analysis of variance of the effect of the dietary levels on the ovulation rate

Litter sequence		Dietary level D_{100}	D_{85}	D_{70}	D_{55}
L_1	Number of mice	11	11	11	11
	Mean number of corpora lutea	13·0	12·0	14·5	13·1
	Range	9–17	0–19	8–21	10–18
L_2	Number of mice	12	12	12	12
	Mean number of corpora lutea	14·7	15·9	14·0	13·0
	Range	10–18	8–22	9–20	7–24
L_3	Number of mice	12	12	12	2
	Mean number of corpora lutea	19·7	18·7	15·2	16·5
	Range	11–24	10–26	9–26	13–20

Source of variation	d.f.	m.s.s.	*F*
Litters	2	204·57	11·71 ($P < 0·01$)
Dietary levels	3	17·01	0·97 n.s.
Interaction	6	28·78	1·65 n.s.
Error	119	17·47	—

L.s.d. ($L_1 - L_3$) = 2·0, $P = 0·01$, d.f. = 119.
L.s.d. ($L_2 - L_3$) = 2·4, $P = 0·01$, d.f. = 119.

There was no significant difference between implantation rates of mice on D_{100} (11·8), D_{85} (11·0), and D_{70} (10·1) dietary levels but D_{55} (6·7) mice had a significantly ($P < 0·01$) lower implantation rate than other dietary levels. Parity did not have an effect on the implantation rate and no interaction was observed between parity and dietary level.

Late embryonic survival (LES)

The range and the mean LES of mice over a period of three litters on four dietary levels are given in Table 5. Analysis of variance showed a marked effect ($P < 0·01$) of dietary level on the LES with no significant effect of either litter sequence or its interaction with the diet. The mean LES of D_{100}, D_{85}, D_{70} and D_{55} mice over three litters was 12·5, 11·2, 10·8 and 10·5 respectively.

Food restriction of 30% (D_{70}) and 45% (D_{55}) significantly lowered the number of live embryos in the uterus on day 16 of gestation compared to *ad libitum* feeding ($P < 0{\cdot}01$). Restriction of 15% (D_{85}) also reduced the LES but the effect was not so pronounced ($P < 0{\cdot}05$). There were no significant differences among the LES values of the mice fed at the 85%, 70%, and 55% levels.

Table 4. Implantation rate of mice fed four dietary levels

Values in parentheses are the numbers of animals in each group with no implantation sites

Litter sequence		Dietary level D_{100}	D_{85}	D_{70}	D_{55}
L_1	Number of mice	11	12	11	11
	Mean number of implantation sites	11·1	10·3	12·4	8·6
	Range	0–14 (1)	0–15 (2)	8–15 (0)	0–12 (3)
L_2	Number of mice	12	12	12	12
	Mean number of implantation sites	12·2	11·1	9·0	5·2
	Range	3–15 (0)	0–16 (1)	0–14 (3)	0–12 (5)
L_3	Number of mice	12	12	12	2
	Mean number of implantation sites	11·8	11·6	9·2	5·5
	Range	0–17 (1)	0–18 (1)	0–14 (3)	0–11 (1)

L.s.d. = 3·3, $P = 0{\cdot}01$, d.f. = 119.

Table 5. Late embryonic survival of mice fed four dietary levels

Litter sequence		Dietary level D_{100}	D_{85}	D_{70}	D_{55}
L_1	Number of mice	11	11	12	11
	Mean number of live embryos	11·9	10·4	10·5	9·4
	Range	9–19	5–13	6–13	0–13
L_2	Number of mice	12	12	12	12
	Mean number of live embryos	12·7	11·3	10·2	10·7
	Range	10–16	7–14	8–13	7–13
L_3	Number of mice	12	12	12	1
	Mean number of live embryos	13·0	11·8	11·7	12·0
	Range	6–18	7–18	10–14	—

L.s.d. ($D_{100} - D_{85}$) = 1·2, $P = 0{\cdot}05$, d.f. = 119.
L.s.d. ($D_{100} - D_{70}$) = 1·6, $P = 0{\cdot}01$, d.f. = 119.
L.s.d. ($D_{100} - D_{55}$) = 1·8, $P = 0{\cdot}01$, d.f. = 119.

Littering and resorption rates

The littering rate did not differ significantly between the D_{100} and D_{85} feeding levels and the small resorption rates were negligible (Table 6). The resorption rate was determined using the littering rate and the embryonic survival rate on day 16.

An effect of the D_{70} diet on the littering and resorption rates appeared at the second litter but there was no increased effect on the third litter. The most marked effect was seen with D_{55} where the littering rate was reduced at the first and second litters to 62·4 and 67·3% respectively and then fell to 6·1% at the third litter. Foetal resorption was high at the first and second litters but oestrous suppression, fertilization, and/or implantation failure appeared after the first litter and accounted for most of the reproductive failure following the second pregnancy.

Litter size, birth weight, and sex ratio

An overall analysis of variance showed that the dietary level had a significant effect ($P < 0{\cdot}01$) on the litter size and birth weight but had no significant effect on the sex ratio (Table 7).

Table 6. Littering and resorption rates of mice fed four dietary levels over three litter periods

Dietary level	First litter			Second litter			Third litter		
	Total No. of females	% female littering	% foetal resorption	Total No. of females	% female littering	% foetal resorption	Total No. of females	% female littering	% foetal resorption
D_{100}	138	98·6	1·4	112	99·1	0·9	85	97·6	2·4
D_{85}	134	100·0	0·0	109	99·1	0·9	87	100·0	0·0
D_{70}	137	96·4	3·6	108	78·8	21·2	61	80·3	19·7
D_{55}	117	62·4	30·7	49	67·3	32·7	33	6·1	26·5

Table 7. Mean litter size, birth weight, and sex ratio of mice fed four dietary levels over three litter periods

Dietary level	First litter			Second litter			Third litter		
	Mean litter No.[A]	Mean birth wt[B] (g)	Sex ratio ♂ : ♀	Mean litter No.[A]	Mean birth wt[B] (g)	Sex ratio ♂ : ♀	Mean litter No.[A]	Mean birth wt[B] (g)	Sex ratio ♂ : ♀
D_{100}	9·8	1·71	0·48	10·2	1·74	0·48	10·4	1·70	0·44
D_{85}	8·2	1·69	0·50	8·7	1·69	0·48	7·8	1·69	0·49
D_{70}	7·2	1·55	0·49	6·7	1·58	0·49	5·9	1·55	0·49
D_{55}	5·4	1·45	0·51	4·1	1·47	0·40	6·0	1·33	0·58

[A] L.s.d. = 1·0, $P = 0{\cdot}01$, d.f. = 15. [B] L.s.d. = 0·1, $P = 0{\cdot}01$, d.f. = 15.

Reproductive performance upon dietary rehabilitation

Performance of the D_{70} mice. Sixteen females from the D_{70} diet were subsequently fed *ad libitum* ($D_{70}N$) and all became pregnant and littered. Only 12 of 16 (75%) mice which had remained on this level of food intake ($D_{70}R$) became pregnant and littered; two resorbed and two had not become pregnant when all of the $D_{70}N$ mice had completed their litters. The mean litter size of the $D_{70}R$ group (5·4) was significantly less than that of the $D_{70}N$ group (9·7) (l.s.d. = 4·1; $P = 0{\cdot}01$; d.f. = 26). The mean birth weight was significantly greater for the $D_{70}N$ group (1·9 g) than for the $D_{70}R$ group (1·5 g) (l.s.d. = 0·3; $P = 0{\cdot}01$; d.f. = 26). No significant difference was observed between the sex ratio of the $D_{70}N$ (0·50) and $D_{70}R$ (0·39) groups.

Performance of the D_{55} mice. Fifty mice on the D_{55} diet were allowed access to *ad libitum* food ($D_{55}N$) for 2 weeks before males were reintroduced and of these, 49 became pregnant and littered.

Fifty-one mice remained on the restricted diet ($D_{55}R$); 14 females became pregnant and littered, 19 resorbed their foetuses, and 18 mice had not littered when all mice on full feed had completed their pregnancies. The litter size was significantly smaller for the $D_{55}R$ group (3·1) than for the $D_{55}N$ group (10·2) (l.s.d.= 6·8; $P = 0{\cdot}01$; d.f.= 61). The rehabilitated females had heavier pups (1·9 g) than the underfed females (1·6 g) (l.s.d.= 0·2; $P = 0{\cdot}01$; d.f.= 61), but the sex ratio (0·47) did not differ between the two groups.

Discussion

Inhibition and lengthening of the oestrous cycle due to undernutrition have been reported in the mouse (Ball *et al.* 1947) and rat (Cooper and Haynes 1967). In the present work severe underfeeding of mice (D_{55}) resulted in the lengthening of the oestrous cycle compared to *ad libitum* feeding, 85% and 70% dietary levels. The average oestrous cycle length (about 7 days) during the pretreatment period in this experiment was longer than that usually accepted for the mouse (4–6 days) under controlled lighting and in the presence of the male (Asdell 1964). Whitten (1959) showed that the cycles became more irregular in female mice caged in groups, and the increase in the cycle length in the present experiment was possibly due to this effect as the experimental animals were housed in groups of five mice per cage. Severe dietary restriction (D_{55}) for a period of 60 days decreased the incidence of oestrus in a number of mice which showed persistent vaginal dioestrus for most of the period of restriction.

In the work reported here *ad libitum* feeding for 2 weeks before the introduction of males and the subsequent *ad libitum* feeding until delivery showed that the litter size, pup birth weight and sex ratio of the previously underfed mice did not differ from that of control mice.

Carr *et al.* (1949) reported anoestrus in C_3H strain female mice as a result of 50% dietary restriction. When these mice were given fresh pituitary implants they showed positive vaginal smears; caloric supplement with dextrose after 14 months and *ad libitum* feeding for 1 week after 21 months dietary restriction also resulted in positive smears in all mice.

The reproductive performance of restricted mice upon rehabilitation as determined by litter size, birth weight and sex ratio was similar to that of control mice, whilst the control mice had a longer prenatal period. However, Lamond and Bindon (1969) reported that mice in which growth had been restricted during adult life and which were subsequently allowed *ad libitum* feeding, on the average produced 2–3 more pups than normal colony mice, or mice which had been restricted and then allowed only a moderate rate of growth.

Dietary restriction at the levels and for the period studied in the present experiments did not have any significant effect on the ovulation rate of mice. The ovulation rate increased with parity, being greater for the third pregnancy than for the first and second pregnancies which did not differ significantly. Lamond and Bindon (1969) reported that the previous nutritional history of mice affected the response to induced ovulation by gonadotrophins. Pregnant mare serum gonadotrophin

(PMSG) did not stimulate significant follicular development in mice which were losing weight, but if they were fed above normal quantities of food PMSG-injected mice produced more ova than unrestricted mice given the same ration.

Hypophysectomized mice fed a restricted diet produced fewer ova when injected with gonadotrophins than those on *ad libitum* food intake but in another experiment none of the mice in the restricted group ovulated (Fielden and Brumby 1962).

Mice which were fed 85% and 70% of *ad libitum* food intake had the same implantation rate as those fed *ad libitum*, whereas those on 55% food intake had significantly lower implantation rates. It seems that to have a detrimental effect on implantation in the mouse, dietary restriction should be in excess of 30% of *ad libitum* food intake.

It has been shown that a 48-h fast in mice from the end of the 3rd day post-coitum results in a high incidence of degenerating embryos on days 6 and 7, and of failure to implant (McClure 1966). Complete fasting of female mice for 48 h during the 4th and 5th days after mating caused the total destruction of the embryos in all of the tested mice. The effect became less pronounced as the fasting period was moved to either side of the 4th and 5th days, that is the period of implantation and the early development of decidua (McClure 1966).

The effect of dietary levels on embryonic survival in mice was studied by counting the number of viable foetuses in the uteri on day 16 of gestation. The number of live embryos on this day was lower for the mice on all the restricted dietary levels compared to those on *ad libitum* food intake.

The fact that of the D_{55} mice that had finished their second pregnancy only two had copulatory plugs showed that mating behaviour of mice on the D_{55} diet was reduced to a very low level. The only mouse that was used to estimate LES must have had a deep copulatory plug which had gone unnoticed. This mouse continued pregnancy till the physical signs of gestation, mainly enlargement of the abdominal area, confirmed its pregnancy. The comparison of the LES of D_{55} mice with other groups for the third pregnancy is difficult as this was based on only one record, compared to 11–12 records for other groups.

Dietary restriction of 15% did not affect the littering ability of mice, and restriction of 30% did not affect the first pregnancy. The mice on 30% dietary restriction showed a high resorption rate (about 20%) during their second and third gestations. Almost all the mice on D_{100}, D_{85}, and D_{70} dietary levels and 62% of the D_{55} mice produced their first litter.

The resorption rate of the D_{55} mice was high during the first (30%), second (33%), and third (26%) pregnancies. Only 67% of the D_{55} mice completed their second pregnancies and of those only two became pregnant and completed their third litters. As these results show, the littering and resorption rates are not affected until the food intake is reduced more than 15% of the *ad libitum* intake, and these functions are affected more adversely with successive pregnancies when restriction is more than 30%.

The litter size of mice in the present experiment decreased with increased dietary restriction, and likewise mice which were underfed only during pregnancy had a smaller litter size than the 100% group (Smart and Silence 1977) but there were no significant differences between individual groups (60, 50 and 40%). Mice which were fed 85% of *ad libitum* food intake produced young as heavy as fully fed mice but restriction at 30 and 45% affected the birth weight, both levels having the same effect. Similarly, Smart and Silence (1977) reported smaller birth weights for pups from mice underfed during pregnancy only, but Wodzicka-Tomaszewska *et al.*

(1974) found no difference in the litter size and birth weight when mice were underfed for 18 days before mating.

Those females which did not litter at all, or did not complete their second or third pregnancies, recovered after a short period of full feeding and showed a far better reproductive performance than their counterparts on restricted diets. All of the D_{70} females and 98% of D_{55} mice which subsequently received *ad libitum* food intake became pregnant and littered; the litter size and birth weight of these mice were greater than those of females which remained on restricted food intake, but the sex ratio was not affected by the level of food intake. The littering rate improved with full feeding for a period of 2 weeks and the litter size and birth weight were almost the same as those of mice on full feed. These findings are in agreement with those in the rat (Chow 1964; Widdowson and Cowen 1972).

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