Effect of gold thioglucose-induced obesity on adipose tissue weight and cellularity in male and female mice suckled in large and small litters: investigations into sex differences and site differences

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1. Over- or undernutrition of newborn mice was caused by suckling in litters consisting initially of four or eighteen pups. After weaning, mice were fed *ad lib.* At 13 weeks some mice received gold thioglucose (GTG, 600 mg/kg, intraperitoneally) to induce hyperphagia, and all were killed at 39 weeks.

2. Mice suckled in small litters were heavier, with more body fat and protein. GTG treatment induced rapid weight gain and treated mice from large litters were heavier than untreated mice from small litters. However, the effect of litter size was not totally removed since GTG-treated small-litter mice were heavier than GTG-treated large-litter mice and had more fat, although body protein was not different.

3. Fat distribution between the depots was related to total body fatness and not to the treatment.

4. In male mice, preweaning undernutrition resulted in smaller fat depots containing smaller cells. GTG treatment of large-litter mice restored both to the levels found in small-litter mice: the depots of the latter mice were not significantly different after treatment.

5. In female mice, preweaning undernutrition resulted not only in smaller depots and cells but also fewer cells in all depots except mesenteric. GTG-treatment caused larger depots and cells in all mice with no difference in cell size whether mice were from large or small litters. The number of cells in the perirenal and mesenteric depots was greater in GTG-treated mice and was the same whether mice were from large or small litters.

6. We conclude that the level of preweaning nutrition does not affect the ability of adipose tissue to develop subsequently through hypertrophy or hyperplasia of the adipocytes or both, given a sufficient energy surplus consisting of normal pelleted feed, low in lipid.

Preweaning undernutrition in rats, brought about by suckling in large litters, results in slow subsequent growth during *ad lib.* feeding and a permanently lowered body-weight (Widdowson & McCance, 1960). The low adipose-tissue mass in rats undernourished early in life is caused by the presence of fewer and smaller adipocytes up to 20 weeks of age (Knittle & Hirsch, 1968). However, if the rats are kept to greater ages, the adipocytes may reach normal size, although their number remains depressed (Faust *et al.* 1980). Feeding these animals a high-fat diet increases the number of recognizable cells in certain depots to that observed in depots from animals suckled in small litters, but the latter also develop more cells when given the high-fat diet so that the difference in cellularity produced by the level of preweaning nutrition still exists. It is not clear whether such a result stems from an inability of the fat cells to increase in number to the same extent in the animals undernourished early, or whether their energy intake when on the high-fat diet responds proportionately to their body size so that the stimulus for adipocyte development is less. Furthermore, the hyperplasia induced in this way may result from a specific effect of fat in the diet.

We therefore wished to determine if greater increases in energy intake could totally remove the effect of preweaning undernutrition. Damage to the ventro-medial hypothalamus (VMH) in growing rats is well known to result in hyperphagia, increased energetic efficency and the development of obesity but does not cause hyperplasia of the epididymal or retroperitoneal fat depots (Hirsch & Han, 1969; Johnson *et al.* 1971). However, gold thioglucose (GTG)-induced obesity (Brecher & Waxler, 1949) in mice results in hyperplasia, at least in certain fat depots (Johnson & Hirsch, 1972; Wise, 1975; Rakow, 1977). Since

the effects of different levels of preweaning nutrition in mice resemble those in rats (Parkes, 1926; Widdowson & McCance, 1960; Martin, 1974) we have used GTG to induce obesity in mice suckled in large (LL) and small (SL) litters. The mice were treated with GTG at 13 weeks of age so that the effects of preweaning undernutrition were well established and the normal perinatal hyperplasia in adipose tissue had essentially ceased (Johnson & Hirsch, 1972; Greenwood & Hirsch, 1974). Both male and female mice were investigated since females are reported to develop a greater obesity after treatment with GTG (Sanders *et al.* 1973).

EXPERIMENTAL

Animals

Female CFLP mice from our own colony, which had bred once successfully, were randomly paired with males in individual cages. When two litters, totalling at least twenty-two mice, were born in the same night, the largest litter was split so that four pups remained with their mother (SL) and the rest were marked and fostered on the other dam who was allowed to keep enough of her own pups to make a litter of eighteen (LL). The mice were weaned at 21 d but the progeny were discarded if more than seven mice in large litters had died during the suckling period. Mice were fed *ad lib.* on Oxoid breeding diet and were weighed weekly. At 13 weeks, mice within each litter of similar sex and weight were selected and all except one in each of these selected groups were treated with GTG, 600 mg/kg, intraperitoneally. At 39 weeks of age, the surviving GTG-treated mice which had shown a good response with rapid initial weight gain and steady subsequent growth were starved for 24 h together with their controls. They were then bled from the orbital sinus while under diethyl ether anaesthesia, and were killed by cervical dislocation.

Carcass analysis

The inguinal subcutaneous, perigenital (epididymal or parametrial), perirenal (including the retroperitoneal) and mesenteric fat depots were removed and weighed. The stomach and intestines were removed, washed free of contents, blotted dry and returned to the residual carcass. Three samples were taken from each depot for determination of adipocyte size; one from near each end of the depot and one from the centre. There were no significant differences between the mean cell size of the three samples so the results were pooled. The water content of the weighed residue of the fat depots and the residual carcass were determined by freeze-drying and lipid was then extracted with diethyl ether and weighed after evaporation of the solvent. The whole dry defatted carcass was digested and the nitrogen content determined by the Kjeldahl method. Adipocyte size was determined by the microscopic method of Sjostrom *et al.* (1971). To avoid subjective selection of cells to be sized, all cells greater than 18 μm in diameter touching or intersecting the graticule centre line were sized. The diameters of 100 cells were determined, approximately thirty-three from each sample, and the volume was calculated for each cell. Adipocyte numbers were determined by dividing the total volume of the 100 measured cells into the volume of depot fat, assuming a density of 0·91 g/ml for the extracted fat. This procedure avoids problems of asymmetry in the frequency distribution of adipocyte volumes.

Statistics

Results are presented as means with their standard errors. The significance of differences between means was determined by analysis of variance or Student's t test. $P < 0{\cdot}05$ was considered significant. Correlation coefficients and regression constants were determined by simple linear regression.

RESULTS

Body-weight and composition

Mice suckled in small litters of four (SL) were significantly heavier ($P < 0{\cdot}001$) than mice suckled in large litters of eighteen (LL) at 3 weeks of age. The weight difference increased up to 39 weeks (Figs. 1 and 2) when male and female SL mice were 31 and 36% heavier than the respective LL mice. Total carcass fat, protein and water were all significantly higher in SL mice (Table 1) but the greater effect of litter size on body-weight of female mice stemmed mainly from differences in body fat. Whereas male SL mice contained 61% more fat, female SL mice contained 117% more than the respective LL mice at 39 weeks.

Mice treated with GTG lost weight for 2 d; they then gained weight rapidly for approximately 3 weeks and then more slowly at a similar rate to that of untreated SL mice (Figs. 1 and 2). GTG treatment diminished the weight difference between animals suckled in LL and SL but did not remove it (Table 1). However, differences in carcass protein content and the proportions of carcass fat, protein and water were removed. Female mice gained more weight after GTG treatment than male mice mainly through a greater deposition of fat.

Adipose depot lipid, adipocyte volume and number

The sizes of the dissected depots, expressed as weight of lipid, are shown in Figs. 3 and 4. The lipid content ranged generally from 810 to 910 g/kg except for the depots from LL females. The depots of these mice contained 753, 833, 785 and 652 g lipid/kg for the subcutaneous, parametrial, perirenal and mesenteric depots respectively: these values were significantly lower ($P < 0{\cdot}01$) than in all other treatments, between which there were no consistent differences. Mice suckled in LL had smaller depots than mice suckled in SL but the differences were not significant for the epididymal fat pads. The extent of the differences varied with depot and sex. In SL males the proportions of the subcutaneous, perigenital, perirenal and mesenteric depots were 1·30, 1·25, 1·73 and 2·09 times their respective weights in LL males, and in SL females were 1·99, 2·73, 2·91 and 2·63 times their respective weights in LL females.

Male SL mice treated with GTG had three depots slightly larger than in untreated mice although the difference was not significant: paradoxically, the epididymal fat pad was significantly smaller than in untreated mice. Treatment of LL mice with GTG abolished the effect on fat depot size of preweaning undernutrition and their depots did not differ significantly from those of SL male mice. The effect of GTG was much greater in female mice. The depots from treated female SL mice were all significantly larger than in untreated mice. GTG treatment of LL mice not only restored the size of the subcutaneous and parametrial depots to that of SL mice but caused the perirenal and mesenteric depots to become much larger than those in SL mice. However, only the subcutaneous depots of LL GTG-treated mice reached the same size as the depots in GTG-treated SL females.

In male mice the differences in depot sizes between mice suckled in LL or SL resulted from differences in the size of the adipocytes and not through differences in their number (Fig. 3). However, the small epididymal fat pads of GTG-treated SL mice had significantly fewer adipocytes, which were smaller, but not significantly so, than those in untreated SL males. In females, the small depots of LL mice, compared with SL mice, resulted from both significantly smaller cells and, with the exception of the mesenteric depot, significantly fewer cells. GTG-treated female mice had larger cells in all depots compared with untreated mice from the same sized litter, whereas cell number was only higher in the perirenal and mesenteric depots for mice in litters of four and eighteen and for the latter in the parametrial depot.

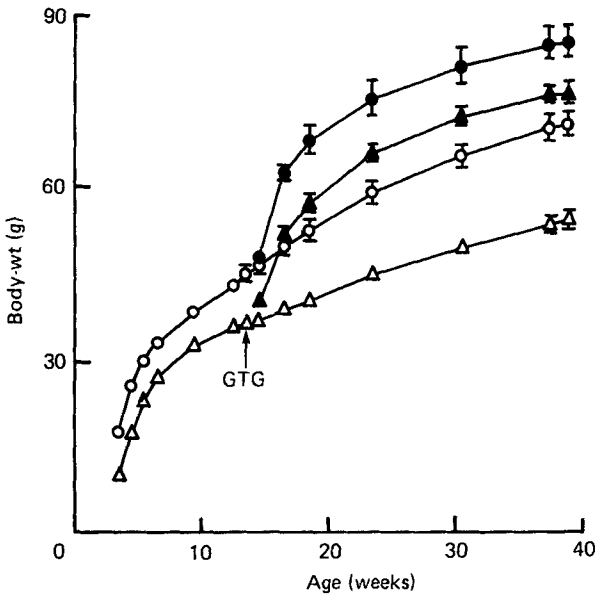

Fig. 1. Postweaning weight gain (g) of male mice suckled in large litters (LL) (△), or small litters (SL) (○), and after treatment with gold thioglucose (GTG) at 13 weeks, LL GTG (▲); SL GTG (●). Results are means with their standard errors represented by vertical bars for SL twelve mice, LL fourteen mice, SL GTG eight mice, LL GTG thirteen mice.

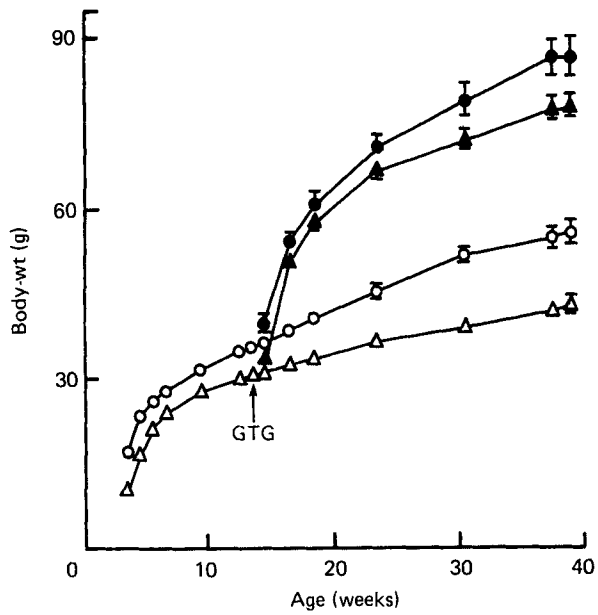

Fig. 2. Postweaning weight gain (g) of female mice suckled in large litters (LL) (△), or small litters (SL) (○), and after treatment with gold thioglucose (GTG) at 13 weeks, LL GTG, (▲); SL GTG, (●). Results are means with their standard errors represented by vertical bars for SL fifteen mice, LL sixteen mice, SL GTG ten mice, LL GTG eighteen mice.

Table 1. *Body-weight and carcass composition of 39-week-old mice from small litters (SL), large litters (LL), small litters treated with gold thioglucose (GTG) (SL GTG) and large litters treated with GTG (LL GTG)*

(Mean values with their standard errors)

	SL		LL		SL GTG		LL GTG	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
			Male mice					
No. of animals...	12		14		8		13	
Live wt*(g)	64·6^{b}	1·9	49·2^{a}	1·6	77·9^{c}	2·6	69·5^{b}	1·5
Carcass wt (g)	60·4^{b}	1·8	45·6^{a}	1·6	72·3^{c}	2·6	65·6^{b}	1·4
Carcass fat (g)	23·7^{b}	1·3	14·7^{a}	1·3	30·5^{c}	1·9	29·6^{c}	1·5
Carcass protein (g)	8·5^{b}	0·2	7·3^{a}	0·1	9·0^{b}	0·4	8·6^{b}	0·2
Carcass water	25·1^{b}	0·4	21·2^{a}	0·3	28·7^{c}	0·7	24·5^{b}	0·5
			Female mice					
No. of animals...	15		16		10		18	
Live wt* (g)	51·7^{b}	2·0	38·1^{a}	1·6	81·6^{d}	3·0	72·1^{c}	1·7
Carcass wt (g)	47·5^{b}	1·9	34·8^{a}	1·5	76·1^{d}	3·1	67·2^{c}	1·6
Carcass fat (g)	18·3^{b}	1·7	8·6^{a}	1·3	41·6^{d}	2·7	34·5^{c}	1·3
Carcass protein (g)	6·6^{b}	0·1	5·9^{a}	0·2	7·7^{c}	0·3	7·2^{c}	0·1
Carcass water (g)	20·6^{b}	0·5	18·2^{a}	0·3	23·7^{c}	0·5	22·3^{c}	0·5

$^{a, b, c}$ Within rows, treatment means followed by different superscript letters differed significantly ($P < 0·05$).
* After 24 h without food.

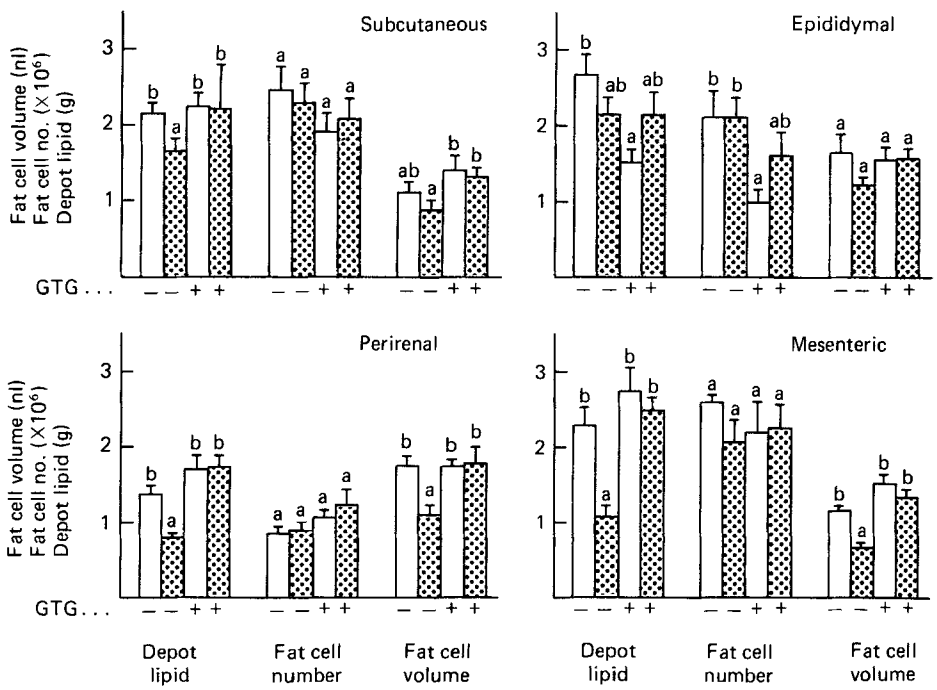

Fig. 3. Adipose depot lipid content, adipocyte number and size in 39-week-old male mice suckled in large (LL) or small (SL) litters, with (+) or without (−) treatment with gold thioglucose (GTG) at 13 weeks. Results are means with their standard errors represented by vertical bars for SL mice (□), and for LL mice (▨). Treatment means with different superscript letters differed significantly ($P < 0·05$).

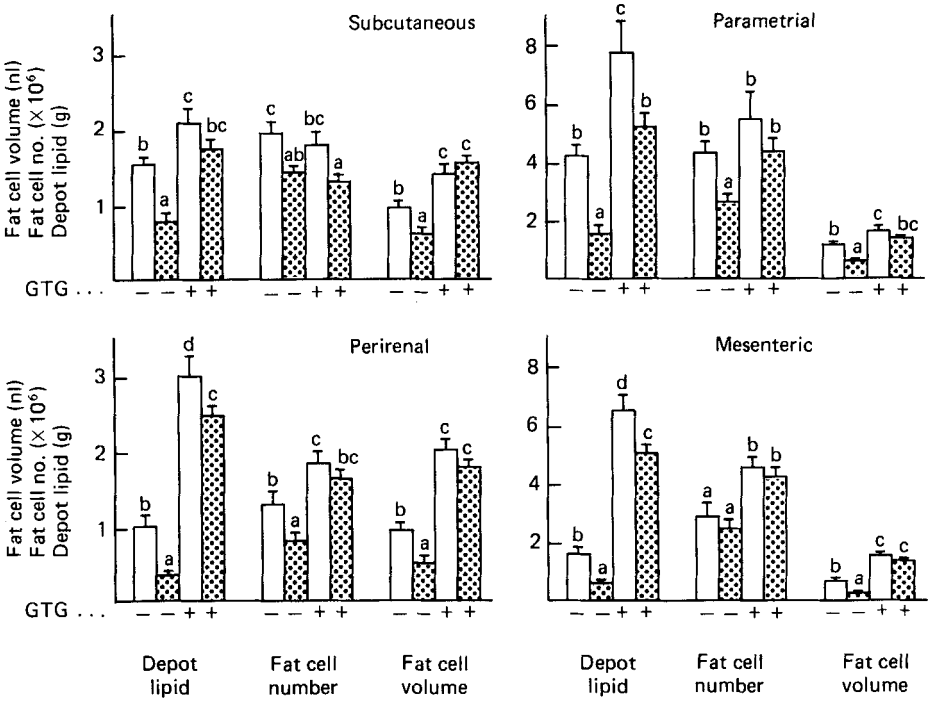

Fig. 4. Adipose depot lipid content, adipocyte number and size in 39-week-old female mice suckled in large (LL) or small (SL) litters, with (+) or without (−) treatment with gold thioglucose (GTG) at 13 weeks. Results are means with their standard errors represented by vertical bars for SL mice (□), and for LL mice (▨). Treatment means with different superscript letters differ significantly ($P < 0.05$).

Table 2. *Correlation coefficients and regression constants for all treatments combined: N, cell number (× 10⁶) on depot lipid (g); V, cell volume (nl) on depot lipid (g); L, depot lipid (% of total body lipid) on total body lipid (g)*

(Regression equation $y = a + bx$)

Depot		Male mice				Female mice			
		r	*a*	*b*	SE†	*r*	*a*	*b*	SE†
Subcutaneous	N	0·29	1·26	0·45	0·23	0·32*	1·17	0·27	0·11
	V	0·41**	0·41	0·38	0·13	0·70***	0·30	0·55	0·07
	L	0·56***	12·59	−0·15	0·03	−0·61***	9·29	−0·10	0·02
Genital	N	0·69***	0·16	0·74	0·12	0·78***	1·52	0·57	0·06
	V	0·22	1·18	0·15	0·10	0·68***	0·59	0·13	0·02
	L	−0·61***	18·83	−0·37	0·07	0·07	16·77	0·03	0·05
Perirenal	N	0·49**	0·43	0·43	0·12	0·66***	0·75	0·37	0·06
	V	0·46**	0·89	0·50	0·15	0·85***	0·41	0·52	0·04
	L	0·43**	3·80	0·06	0·02	0·83***	2·90	0·12	0·01
Mesenteric	N	0·53***	0·99	0·60	0·14	0·62***	2·17	0·40	0·07
	V	0·43**	0·67	0·23	0·07	0·84***	0·29	0·20	0·02
	L	0·52***	5·08	0·14	0·03	0·86***	3·31	0·30	0·02

*$P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
† Standard error of slope, *b*.

Table 3. *Depot lipid as a percentage of total body lipid for mice from small litters (SL), large litters (LL), small litters treated with gold thioglucose (GTG) (SL GTG) and large litters treated with GTG (LL GTG)*

(Mean values with their standard errors)

	SL		LL		SL GTG		LL GTG	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
			Male mice					
No. of animals...	12		14		8		13	
Subcutaneous	$9{\cdot}2^{b}$	0·5	$11{\cdot}0^{c}$	0·5	$7{\cdot}4^{a}$	0·4	$7{\cdot}5^{a}$	0·5
Epididymal	$11{\cdot}6^{c}$	1·2	$14{\cdot}4^{c}$	0·7	$4{\cdot}4^{a}$	0·7	$7{\cdot}3^{b}$	1·0
Perirenal	$5{\cdot}4^{a}$	0·3	$4{\cdot}9^{a}$	0·3	$5{\cdot}5^{a}$	0·4	$5{\cdot}7^{a}$	0·4
Mesenteric	$9{\cdot}8^{b}$	0·6	$6{\cdot}9^{a}$	0·6	$8{\cdot}9^{b}$	0·6	$8{\cdot}3^{ab}$	0·4
			Female mice					
No. of animals...	15		16		10		18	
Subcutaneous	$8{\cdot}6^{b}$	0·5	$8{\cdot}3^{b}$	0·4	$5{\cdot}0^{a}$	0·3	$5{\cdot}0^{a}$	0·3
Parametrial	$23{\cdot}2^{b}$	1·1	$15{\cdot}2^{a}$	1·3	$17{\cdot}9^{a}$	2·1	$14{\cdot}6^{a}$	1·2
Perirenal	$5{\cdot}4^{b}$	0·3	$3{\cdot}5^{a}$	0·3	$7{\cdot}8^{c}$	0·5	$7{\cdot}1^{c}$	0·3
Mesenteric	$7{\cdot}9^{b}$	0·7	$5{\cdot}8^{a}$	0·6	$15{\cdot}5^{c}$	0·7	$14{\cdot}5^{c}$	0·7

[a, b, c] Within rows, treatment means with different superscript letters differed significantly ($P < 0{\cdot}05$).

Differences in the size of depots (measured as lipid) from male mice within treatments were poorly correlated with adipocyte volume and only reached significance ($P < 0{\cdot}05$) for the mesenteric depot of SL GTG-treated mice and the perirenal depot of LL mice. Significant correlations between depot size and adipocyte number occurred in the perirenal and mesenteric depots of SL GTG-treated mice, the epididymal depot of LL mice, the epididymal and mesenteric depots of LL GTG-treated mice and the epididymal and mesenteric depots of SL male mice. However, when all treatments were analysed together, there were highly significant correlations between depot size and cell number for all depots except the subcutaneous depot in male mice (Table 2). The overall correlations between depot size and cell volume were also significant except for the epididymal fat pad.

In females, differences in depot size for mice of the same treatment resulted from differences in adipocyte volume or number, according to the particular treatment. Depot size was best correlated with adipocyte volume in the SL mice and with cell number in the LL GTG-treated mice. For LL mice, the size of the parametrial and perirenal depots was correlated with cell number. In the SL GTG-treated mice there were only two significant correlations for depot size: with cell number in the parametrial depot and with cell volume in the perirenal fat pad. Over all treatments, however, depot size was very highly correlated with both adipocyte size and number except for the cell number in the subcutaneous depot which was significant only at the $P < 0{\cdot}05$ level (Table 2).

Adipose tissue distribution

In male mice, preweaning undernutrition resulted in the subcutaneous and epididymal depots containing a higher proportion of the body lipid and the perirenal and mesenteric depots containing a lower proportion than in well-nourished SL mice (Table 3). In female LL mice the proportion of body lipid was lower in all four depots although the difference was small and not significant for the subcutaneous depot. The increased lipid deposition in GTG-treated mice resulted in a different distribution of body lipid. Male SL GTG-treated

mice had similar proportions of body lipid in the perirenal and mesenteric depots but lower proportions in the subcutaneous and epididymal depots compared with untreated mice. Although treated female SL mice also had lower proportions of body lipid in the subcutaneous and parametrial depots, the proportions in the perirenal and mesenteric depots were higher than in untreated mice. Treatment of male LL mice with GTG resulted in a lipid distribution similar to that in SL GTG-treated males except for the epididymal fat pad which formed a higher proportion. In female LL GTG-treated mice, the parametrial depot formed a lower proportion of the body lipid compared with SL GTG-treated females, although the difference was not significant, while the proportions in the other three depots were similar. Overall, therefore, only the epididymal depot contained different proportions of the total body lipid after GTG treatment as a result of preweaning undernutrition.

There were good correlations between the proportion of body fat in a depot and the total body fat when mice in all treatment groups were considered together (Table 2). The overall regressions were significant for all depots except the parametrial suggesting that, irrespective of the treatment used to obtain differences in fatness, the relation between total body fat and its distribution between the depots was normal. The proportion of body lipid present in the perirenal and mesenteric depots increased with increasing total body lipid whereas the proportion in the subcutaneous depot decreased in both male and female mice. The proportion, in the epididymal fat pad also decreased and the relation was highly significant despite the marked effect of preweaning nutrition on distribution. The proportion of the body lipid in the parametrial depot was not significantly related to total body lipid when all animals were considered together. However, if the treatments with and without GTG were considered separately there were significant increases ($P < 0{\cdot}05$ and $P < 0{\cdot}001$ respectively) in the proportion of body lipid present in this depot with increased total body lipid within treatments. Without GTG the regression was: intercept 12·1, slope 0·517, r 0·646, n 31, $P < 0{\cdot}001$; and with GTG: intercept 2·1, slope 0·368, r 0·469, n 28, $P < 0{\cdot}01$.

DISCUSSION

The overall results from the present study show that the differences in body size and composition induced by suckling mice in litters of four or eighteen, which persist to 39 weeks, can be reversed by making the latter hyperphagic with GTG at 13 weeks of age. However, there is a residual effect of litter size in that the GTG-treated SL mice are significantly heavier than the GTG-treated LL mice, similar to the residual effect of preweaning nutrition seen in rats induced to overeat on a high-fat diet (Faust *et al.* 1980). In male mice, this difference arose from a lower water content in LL GTG-treated mice, although it was not significant, and a difference in the unmeasured component of the carcass, presumably mainly mineral, which was 3·8 g in the SL GTG-treated mice and 2·6 g in the LL GTG-treated mice. The weight and proportion of body lipid were not different between these treatments and this dissimilarity with the studies on rats may be related to the failure of differences in preweaning nutrition to alter the number of fat cells present. In females, the difference in weight between SL GTG-treated and LL GTG-treated mice was caused by the greater carcass lipid of the former. At the cellular level, this difference was due to the presence of more cells in all the depots studied, significantly so in the subcutaneous depot, but cell volumes were not significantly different in any depot.

The absence of a lower cell number in LL compared with SL males was unexpected but may be a breed effect similar to that observed by Martin (1974) and Eisen & Leatherwood (1978). The undernutrition in the present study was effective with differences in weight between litters at 10 weeks of 18% compared with 13% and 8% in other studies (Martin, 1974; Eisen & Leatherwood, 1978). It seems unlikely that cell number was low in our mice

at 12–13 weeks of age and that it subsequently increased since the cell number appears to be constant after this age, at least in the epididymal fat pad of normal mice (Johnson & Hirsch, 1972; Greenwood & Hirsch, 1974), and litter size does not appear to affect the age at which the number reaches a plateau (Eisen & Leatherwood, 1978). However, one explanation for the fewer fat cells in the epididymal fat pads of GTG-treated mice is that cell number was still increasing at 13 weeks of age, and may have been impeded by the GTG treatment. A similar effect occurred in the epididymal fat pad of VMH-lesioned rats (Hirsch & Han, 1969).

It is not clear why the adipose tissue of female mice should be more affected by preweaning nutrition and there are no previous reports of comparative studies of male and female mice. Although adipose tissue forms a greater proportion of the body in females, the SL female mice were only 15% heavier than the LL females at 13 weeks whereas SL males were 23% heavier than LL males. However, Cryer & Jones (1980) observed a greater effect of litter size on the fat content and adipocyte cell number of female rats compared with male rats. The effect of GTG was much greater in the female mice as expected (Sanders *et al.* 1973). Adipocyte volumes within each depot were not significantly different for GTG-treated mice from LL and SL, similar to the results with male rats from litters of four or twenty induced to overeat on a high-fat diet (Faust *et al.* 1980). The increases in cell number after GTG treatment suggested that the degree of energy excess can increase adipocyte number as effectively as high dietary lipid. The hyperplastic response of the parametrial and perirenal depots to GTG treatment in female mice resembles that observed by Lemonnier (1972) with a high-fat diet.

The growth of adipose tissue is believed to occur through an initial increase in the cell number in the early postnatal period followed by an increase in size of the cells produced (Greenwood & Hirsch, 1974). Our results support the hypothesis that the production of new cells in the adult is stimulated when the existing cells reach a maximum size (Faust *et al.* 1978). In female LL GTG-treated mice, sizes of all four depots were significantly correlated with cell number, suggesting that maximum cell size is well controlled. However, in SL GTG-treated mice, which had cells of similar size to those of LL GTG-treated mice, cell number was significantly correlated with depot size only in the paremetrial depot in which the cell number was unchanged by GTG treatment. Such differences emphasize the individuality in the response of depots. It seems feasible that the differences in cell replication during the suckling period between litters of four and eighteen may be the cause. In mice well-nourished in litters of four, sufficient preadipocytes may have been deposited to allow for the growth induced by GTG, and the increased cell number which we have recorded merely represents the filling of these cells.

Liebelt *et al.* (1965) reported that the growth of individual depots relative to total body fat was unaffected by GTG treatment and our results confirm this even with the added complication of litter size. The order of development of the depots was subcutaneous, perigenital, perirenal and mesenteric for both male and female mice. This is similar to that in rats (Bailey *et al.* 1980) but differs from mice in which the allometric coefficient was determined from 5 to 15 weeks of age (Allen & McCarthy, 1980). The similar distributions of body lipid in SL GTG-treated and LL GTG-treated females indicate that factors other than the ability of the adipose tissue to grow are responsible for the differences in body lipid content between these groups. Our results confirm the great capacity of the adipose tissue to respond in a co-ordinated manner to wide differences in rates and quantity of lipid deposition irrespective of whether such growth is occurring through increase in cell size or number.

We conclude that preweaning undernutrition in mice does not permanently restrict the ability of their adipose tissues to grow through hypertrophy and probably hyperplasia in

the presence of energy excess provided by a normal pelleted diet. The final difference in total body lipid after treatment with GTG between LL and SL female mice resulted from small and mostly non-significant differences in both cell size and number within the individual depots. Furthermore, the proportional increase in depot lipid and adipocyte size and number after GTG treatment was much greater for mice from LL. Thus it was unlikely that either cell size or number was limiting food intake and the difference probably resulted from the failure of GTG to induce the same degree of energy excess in both groups of mice.

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