

**MAMMARY DEVELOPMENT IN MICE:  
EFFECTS OF HEMIHYSTERECTOMY IN PREGNANCY AND OF  
LITTER SIZE *POST PARTUM***

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SUMMARY

1. Mice were hemihysterectomized on day 8 of pregnancy to reduce the number of foeto-placental units.

2. Fetal mortality was not affected by hemihysterectomy; mean single-pup weight at birth was increased when compared with sham-operated controls.

3. Pregnant sham-operated and hemihysterectomized animals were killed on days 13 and 18 of gestation, and their mammary glands were analysed for total DNA ( $\text{DNA}_t$ ) and RNA ( $\text{RNA}_t$ ). Both were significantly lower in the hemihysterectomized group on day 18, but not on day 13.

4. Milk yield was assessed, by daily weighing of the litter, in groups of sham-operated and hemihysterectomized lactating animals suckling nine pups each. There was no difference in yield between the two groups.

5. One group of sham-operated mice suckling nine pups, one of hemihysterectomized mice suckling nine pups and one of hemihysterectomized mice suckling four pups were killed on day 5 of lactation for mammary gland analysis. There was no significant difference in mammary weight or  $\text{DNA}_t$  between the sham-operated and hemihysterectomized animals suckling nine pups, although  $\text{RNA}_t$  was still reduced in the latter. Mammary weight,  $\text{DNA}_t$  and  $\text{RNA}_t$  were all significantly lower in the hemihysterectomized group suckling four pups than in either of the other two groups.

6. It is concluded that the less well developed mammary glands of mice which give birth to small litters are capable of compensatory growth during the first few days of lactation if a sufficiently strong suckling stimulus is given.

7. It is suggested that control of mammary development by the fetus during gestation and by the suckling young during early lactation are both mechanisms designed to ensure that milk yield is appropriate to the needs of the young.

INTRODUCTION

Except in species which have been specifically bred for increased milk production, a 'successful' lactation is one which is nutritionally appropriate to the needs of the young. Thus it could be seen as advantageous, in evolutionary terms, for the number and weight of the young to exert some control over mammary development. In the mouse, mammary growth does not cease at parturition but continues for the first five

days of lactation (Knight & Peaker, 1982). Thus there is scope for an influence of the fetuses *in utero* on mammogenesis during gestation and also for an effect of the suckling young on growth *post partum*. The importance of the placenta(e) in mammogenesis has long been recognized (Selye, Collip & Thomson, 1934; Newton & Lits, 1938), and relationships between the number of fetuses carried and mammary growth and/or milk yield have been demonstrated in a number of polytocous species (goat: Hayden, Thomas & Forsyth, 1979; sheep: Rattray, Garrett, East & Hinman, 1974; guinea-pig: Davis, Mephram & Lock, 1979). The DNA content of lactating mammary glands of rats is also directly related to the number of young suckled (Tucker, 1966). There is an apparent dichotomy of opinion concerning fetal effects in mice, for although a clear relationship has been established between fetal number and mammary development during gestation (Nagasawa & Yanai, 1971), there is apparently little or no correlation between the number of fetuses carried and milk yield (Nagai, 1978; Eisen, Nagai, Bakker & Hayes, 1980). The work described here was designed to resolve this problem, and to investigate ways in which the young might control their own destiny by influencing mammary development.

#### METHODS

*Animals.* Mice derived from Tuck's no. 1 strain (A. Tuck & Son, Battlesbridge, Essex) were kept at 21 °C with a daily photoperiod of 14 h (0500–1900) and fed a rodent breeding diet (Oxoid Ltd., Basingstoke, Hants.) *ad libitum*. Mating dates were established from the appearance of vaginal plugs; the day on which a plug was observed was designated day 1 of pregnancy and the day following parturition (20 d *post coitum*) was called day 1 of lactation. Average litter size for the colony was  $11.6 \pm 0.27$  (s.e. of mean).

*Surgical procedure.* Mice were used on day 8 of pregnancy. They were anaesthetized with pentobarbitone sodium (Sagatal; May & Baker Ltd., Dagenham, England; 6 mg/100 g body weight i.p.). A small mid-line skin incision was made in the inguinal region, through which the peritoneum was opened. Both uterine horns were exposed and the fetuses counted, and those mice in which one horn contained either five or six fetuses were selected for hemihysterectomy. The contralateral horn was removed after ligation of blood vessels, leaving the one horn containing five or six fetuses (hemihysterectomized animals). Those animals in which neither horn contained five or six fetuses were sham-operated controls, i.e. neither horn was removed. The peritoneum and skin were then closed in layers using continuous sutures.

This particular procedure was adopted to ensure that two distinct sets of experimental animals were created, in one of which each animal had approximately half the number of fetuses possessed by each animal in the other set. Alternative techniques, such as the tying of one oviduct prior to conception, have in the past resulted in a spread of fetal number between individuals which makes evaluation of the effect of the fetus much more difficult (see for example Kensinger, Collier & Bazer, 1980).

*Experimental design.* Groups of six hemihysterectomized and sham-operated animals were killed on days 13 and 18 of pregnancy. The number and weight of fetuses were recorded and all mammary tissue was removed, blotted dry, weighed, frozen in liquid nitrogen and stored at -15 °C until analysed.

Milk yield was studied in sham-operated and hemihysterectomized animals. The size of the litter was adjusted to nine on day 1 of lactation by removal or addition of pups of the same age, as appropriate. Mother and young were then weighed each day between 0900 and 1030 h until day 15 of lactation.

Three groups of mice were killed on day 5 of lactation for mammary gland analysis. The first of these consisted of sham-operated animals suckling nine pups (sham-operated, normal litter size), the second of operated animals suckling nine pups (hemihysterectomized, normal litter size) and the third of operated animals suckling four pups (hemihysterectomized, small litter size).

*Determination of nucleic acids.* Nucleic acids were extracted from the mammary tissue using a modification of the Schmidt-Thannhauser technique (Munro & Fleck, 1966). DNA concentration was determined by the diphenylamine method of Burton (1956) and RNA concentration was measured spectrophotometrically.

## RESULTS

### *Mammary gland weight and nucleic acid content*

Hemihysterectomy on day 8 of gestation had no effect on mammary gland wet weight later in gestation (day 13 or 18) (Table 1). On day 5 of lactation mammary weight was significantly ( $P < 0.01$ ) lower in hemihysterectomized animals suckling four young than in sham-operated or hemihysterectomized animals suckling nine young, and there was no difference between the latter two groups. Mammary wet weight of sham-operated animals increased from day 13 to day 18 of gestation, and from day 18 of gestation to day 5 of lactation.

The concentration of DNA ([DNA]) in mammary tissue of hemihysterectomized animals was slightly but significantly ( $P < 0.05$ ) reduced on day 13 of gestation and considerably ( $P < 0.01$ ) reduced on day 18 (Table 2). There were no differences in [DNA] between any of the groups killed on day 5 of lactation. Total mammary DNA content ( $\text{DNA}_t$ ) was reduced in hemihysterectomized animals on day 18 of gestation but not on day 13, and was also reduced in lactating hemihysterectomized animals suckling four pups when compared to the other two lactating groups.  $\text{DNA}_t$  of sham-operated animals more than doubled between days 13 and 18 of gestation and increased further by day 5 of lactation.

RNA concentration ([RNA]) and total content ( $\text{RNA}_t$ ) were reduced in hemihysterectomized animals on day 18 of gestation, but not on day 13. On day 5 of lactation there was no difference in [RNA] between the sham-operated and hemihysterectomized animals suckling nine pups, although  $\text{RNA}_t$  was slightly reduced in the latter. Both [RNA] and  $\text{RNA}_t$  were markedly reduced in the hemihysterectomized lactating animals with small litters.  $\text{RNA}_t$  increased approximately 2.5-fold between days 13 and 18 of gestation and a further fivefold between day 18 of gestation and day 5 of lactation in sham-operated animals. The RNA-DNA ratio (a measure of potential synthetic capacity per cell) remained at around 1 during gestation and then rose to 4.4 on day 5 of lactation. This increase was significantly less in hemihysterectomized animals suckling four pups than in the other two lactating groups (Table 2).

Table 3 gives the percentage changes in mammary weight,  $\text{DNA}_t$ ,  $\text{RNA}_t$  and RNA-DNA ratio between hemihysterectomized and sham-operated animals killed on day 18 of gestation and the three groups killed on day 5 of lactation. When compared to sham-operated values, the hemihysterectomized group suckling nine pups showed slightly more weight increase, twice the increase in  $\text{DNA}_t$ , one-and-a-half times the increase in  $\text{RNA}_t$  and roughly the same increase in the RNA-DNA ratio. In the hemihysterectomized group suckling four pups mammary  $\text{DNA}_t$  increased by about the same amount as the sham-operated controls while the other three variables increased considerably less than in the sham-operated group.

TABLE 1. Body weight and mammary gland weight of hemihysterectomized (HHX) and sham-operated (Sham) mice on days 13 and 18 of gestation and day 5 of lactation

	Day 13 of gestation		Day 18 of gestation		Day 5 of lactation	
	Sham	HHX	Sham	HHX	Sham, normal litter size	HHX, normal litter size
Number of animals	6	6	6	6	6	6
Body weight (g)	39.96 ± 0.94	37.84 ± 1.11 n.s.	55.27 ± 3.05 <i>P</i> < 0.001*	45.24 ± 2.59 <i>P</i> < 0.05	46.67 ± 0.91 <i>P</i> < 0.05†	42.30 ± 1.09 <i>P</i> < 0.05
Conceptus weight (g)	4.43 ± 0.24	1.59 ± 0.11 <i>P</i> < 0.01	16.47 ± 1.49 <i>P</i> < 0.01*	7.79 ± 1.23 <i>P</i> < 0.01	—	—
Body weight minus conceptus weight	35.54 ± 0.77	36.25 ± 1.15 n.s.	38.80 ± 1.99 n.s.*	37.45 ± 1.49 n.s.	46.67 ± 0.91 <i>P</i> < 0.01†	42.30 ± 1.09 <i>P</i> < 0.05
Body weight minus conceptus weight minus mammary gland weight	33.96 ± 0.68	34.71 ± 1.00 n.s.	36.39 ± 1.75 n.s.*	35.18 ± 1.46 n.s.	42.34 ± 0.75 <i>P</i> < 0.05†	39.70 ± 1.07 n.s.
Mammary weight: total (g)	1.58 ± 0.11	1.54 ± 0.20 n.s.	2.41 ± 0.08 <i>P</i> < 0.001*	2.27 ± 0.11 n.s.	4.32 ± 0.36 <i>P</i> < 0.01†	2.63 ± 0.14 <i>P</i> < 0.01
Mammary weight (g/100 g body weight)	4.42 ± 0.25	4.21 ± 0.25 n.s.	6.26 ± 0.25 <i>P</i> < 0.01*	6.09 ± 0.34 n.s.	9.24 ± 0.67 <i>P</i> < 0.01†	6.22 ± 0.35 <i>P</i> < 0.01

Values are mean ± s.e. of mean. n.s., non significant; \*, *P* vs. sham on day 13 of gestation; †, *P* vs. sham on day 18 of gestation; remainder, *P* vs. sham at same stage.

TABLE 2. Concentrations and total contents of nucleic acids in mammary tissue of hemihysterectomized (HHX) and sham-operated (Sham) mice on days 13 and 18 of gestation and day 5 of lactation

	Day 13 of gestation			Day 18 of gestation			Day 5 of lactation			
	Sham		HHX	Sham		HHX	Sham, normal litter		HHX, normal litter	HHX, small litter
	6		6	6		6	size	size	size	
Number of animals	6		6	6		6	6	6	6	
DNA concentration ([DNA]; mg g <sup>-1</sup> )	2.62 ± 0.13	2.32 ± 0.03 <i>P</i> < 0.05	3.77 ± 0.20 <i>P</i> < 0.001*	2.66 ± 0.24 <i>P</i> < 0.01	3.37 ± 0.17 n.s.†	2.92 ± 0.15 n.s.	3.54 ± 0.25 n.s.	2.92 ± 0.15 n.s.	3.54 ± 0.25 n.s.	
Total DNA content (DNA <sub>t</sub> ; mg)	4.09 ± 0.26	3.60 ± 0.49 n.s.	9.08 ± 0.44 <i>P</i> < 0.001*	5.96 ± 0.48 <i>P</i> < 0.001	14.29 ± 0.65 <i>P</i> < 0.001†	12.68 ± 0.96 n.s.	9.13 ± 0.19 <i>P</i> < 0.001	12.68 ± 0.96 n.s.	9.13 ± 0.19 <i>P</i> < 0.001	
RNA concentration ([RNA]; mg g <sup>-1</sup> )	3.04 ± 0.35	3.48 ± 0.39 n.s.	4.96 ± 0.22 <i>P</i> < 0.001*	3.57 ± 0.42 <i>P</i> < 0.05	15.02 ± 1.02 <i>P</i> < 0.001†	13.15 ± 0.62 n.s.	10.80 ± 0.56 <i>P</i> < 0.01	13.15 ± 0.62 n.s.	10.80 ± 0.56 <i>P</i> < 0.01	
Total RNA content (RNA <sub>t</sub> ; mg)	4.70 ± 0.46	5.23 ± 0.72 n.s.	11.93 ± 0.54 <i>P</i> < 0.001*	7.88 ± 0.56 <i>P</i> < 0.001	63.23 ± 2.40 <i>P</i> < 0.001†	56.38 ± 1.42 <i>P</i> < 0.05	28.24 ± 1.69 <i>P</i> < 0.001	56.38 ± 1.42 <i>P</i> < 0.05	28.24 ± 1.69 <i>P</i> < 0.001	
RNA-DNA ratio	1.17 ± 0.15	1.50 ± 0.17 n.s.	1.33 ± 0.10 n.s.*	1.34 ± 0.09 n.s.	4.43 ± 0.11 <i>P</i> < 0.001†	4.53 ± 0.25 n.s.	3.08 ± 0.24 <i>P</i> < 0.001	4.53 ± 0.25 n.s.	3.08 ± 0.24 <i>P</i> < 0.001	

Values are mean ± s.e. of mean. n.s., non significant; \*, *P* vs. sham on day 13 of gestation; †, *P* vs. sham on day 18 of gestation; remainder, *P* vs. sham at same stage.

TABLE 3. Percentage increase in mammary gland weight and nucleic acid content between day 18 of gestation and day 5 of lactation in hemihysterectomized (HHX) and sham-operated (Sham) mice, and the effect of litter size

Percentage increase between day 18 of gestation and day 5 of lactation in	Sham, normal litter size (%)	HHX, normal litter size (%)	HHX, small litter size (%)
Mammary gland weight	79	92	16
DNA <sub>t</sub>	57	113	53
RNA <sub>t</sub>	430	615	258
RNA-DNA ratio	233	238	130

### *Fetal weight and viability*

The over-all means for the number of fetuses remaining after hemihysterectomy or sham-operation on day 8 of pregnancy were  $5.12 \pm 0.17$  ( $n = 30$ ) and  $14.87 \pm 0.45$  ( $n = 24$ ) respectively. Values for some of the individual groups are given in Table 4. By day 13 of gestation the number of fetuses remaining alive was reduced by 7.9% in the sham-operated animals and by 10.3% in the hemihysterectomized group; by day 18 these figures had increased to 19.8% and 18.9% but there were further increases before term. There was considerable variability in both the proportion of animals that lost fetuses and in the number of fetuses lost per animal; hence standard errors are not given for the over-all percentage mortality. Nevertheless, it is apparent that roughly half of the loss occurred between days 8 and 13 of gestation, and half between days 13 and 18 with no further loss thereafter. Percentage mortality was not increased in the hemihysterectomized groups as compared to the sham-operated controls. Fetal and pup weights were also recorded. On day 13 of gestation there was no difference in mean single-fetus weight between the two groups, on day 18 the fetuses of the hemihysterectomized animals were non-significantly heavier and on day 1 of lactation the difference in pup weight was significant ( $2.04 \pm 0.05$  g compared with  $1.72 \pm 0.02$  g,  $P < 0.001$ ; Table 4).

### *Litter weight*

The total weight of the litter of hemihysterectomized animals was significantly higher on day 1 of lactation ( $16.60 \pm 0.37$  g compared with  $15.11 \pm 0.22$  g,  $P < 0.05$ ) because four or five of the nine pups were their own, which were heavier at birth than pups of sham-operated animals (see above). Thereafter there were no differences in litter weight between the two groups on any day, or in total weight gain over the 15 d weighing period ( $54.00 \pm 1.22$  g and  $53.08 \pm 3.57$  g in sham-operated and hemihysterectomized animals, respectively).

Results for the three groups killed on day 5 of lactation are shown in Table 5. Again, there was no difference in litter weight gain over the 5 d period between sham-operated and hemihysterectomized animals suckling nine pups. Over-all the small litters of the hemihysterectomized group suckling four pups were not as heavy and gained less weight, although when expressed on an individual pup basis they were heavier and gained more than either of the nine-pup litter groups.

TABLE 4. Fetal mortality in hemihysterectomized (HHX) and sham-operated (Sham) pregnant mice

	Day 13 of gestation		Day 18 of gestation		Day 1 of lactation†	
	Sham	HHX	Sham	HHX	Sham	HHX
Number of animals	6	6	6	6	6	6
Number of fetuses remaining after operation on day 8 of gestation	14.66 ± 0.56	4.83 ± 0.31 <i>P</i> < 0.001	14.50 ± 0.76 n.s.*	5.50 ± 0.56 <i>P</i> < 0.001	15.50 ± 0.76 n.s.†	5.17 ± 0.31 <i>P</i> < 0.001
Number of fetuses or young surviving	13.50 ± 0.92	4.33 ± 0.42 <i>P</i> < 0.001	11.67 ± 0.95 n.s.*	4.50 ± 0.72 <i>P</i> < 0.001	12.30 ± 1.17 n.s.†	4.50 ± 0.34 <i>P</i> < 0.001
Percentage mortality	7.9	10.3	19.5	18.2	20.6	13.0
Number of mice losing fetuses	4	2	6	4	5	3
Range of number of fetuses lost	0-3	0-2	2-5	0-3	0-5	0-2
Weight of individual fetuses or young	0.075 ± 0.004	0.073 ± 0.008 n.s.	1.00 ± 0.04 <i>P</i> < 0.001*	1.23 ± 0.12 n.s.	1.72 ± 0.02 <i>P</i> < 0.01†	2.04 ± 0.05 <i>P</i> < 0.001

† Data from sham-operated, normal litter and hemihysterectomized, small litter groups killed on day 5 of lactation. Values are mean ± s.e. of mean. n.s., non significant; \*, *P* vs sham on day 13 of gestation; †, *P* vs sham on day 18 of gestation; remainder, *P* vs sham at same stage.

TABLE 5. Weight gain of nine pup and four pup litters of hemihysterectomized (HHX) and sham-operated (Sham) mice between days 1 and 5 of lactation

	Sham normal litter	HHX normal litter	HHX small litter
Number of animals	6	6	6
Number of young born	12.3 ± 1.17	4.33 ± 0.71 <i>P</i> < 0.001	4.5 ± 0.34 <i>P</i> < 0.001
Number of young suckled*	9	9	4
Individual weight of young† on day 1 of lactation	1.72 ± 0.02	1.78 ± 0.05 n.s.	2.04 ± 0.05 <i>P</i> < 0.001
Individual weight of young on day 5 of lactation	3.37 ± 0.13	3.25 ± 0.13 n.s.	4.39 ± 0.17 <i>P</i> < 0.001
Total litter weight, day 1 of lactation	15.42 ± 0.20	16.08 ± 0.47 n.s.	8.00 ± 0.20 <i>P</i> < 0.001
Total litter weight, day 5 of lactation	30.42 ± 1.16	29.25 ± 1.19 n.s.	17.58 ± 0.70 <i>P</i> < 0.001
Litter weight gain, day 1 to day 5	15.00 ± 1.11	13.17 ± 1.01 n.s.	9.42 ± 0.52 <i>P</i> < 0.01
Individual pup weight gain, day 1 to day 5	1.66 ± 0.12	1.45 ± 0.12 n.s.	2.35 ± 0.13 <i>P</i> < 0.01

\* Adjusted on day 1 of lactation. † Following litter adjustment. Values are mean ± s.e. of mean. n.s., non significant; *P* vs. sham, normal litter.

### Body weight

When corrected for conceptus weight (which was obviously greater in the sham-operated controls than in the hemihysterectomized animals) body weight did not differ between sham-operated and hemihysterectomized animals at either stage of gestation (Table 1). On day 5 of lactation, hemihysterectomized animals suckling four pups were significantly (*P* < 0.05) lighter than either of the groups suckling nine pups. Part of this difference was due to variation in mammary weight, although after correction for this the former group still tended to be lighter. The body weight of sham-operated animals was increased significantly on day 5 of lactation compared to day 18 of gestation.

### DISCUSSION

The immediate effect of hemihysterectomy was to reduce the number of fetoplacental units by more than 50% (14.87–5.12). This procedure had no effect on subsequent fetal mortality but produced fetuses which were individually heavier at birth than those of sham-operated animals (Table 4). There was a significant deleterious effect on mammary development, since mammary nucleic acid content was reduced at the end of gestation (Table 2). DNA<sub>t</sub> and RNA<sub>t</sub> were both decreased by roughly equal amounts, hence the RNA–DNA ratio did not change. [DNA] and [RNA] were also both decreased, whereas mammary weight was not noticeably affected. This suggests that the glands of the hemihysterectomized animals were more fatty and contained larger but fewer epithelial cells at the end of gestation than those of the sham-operated controls. These results support the findings of Nagasawa & Yanai (1971) who obtained a significant positive correlation between mammary



development during gestation and the number of fetuses carried in mice. Similar conclusions have been drawn for sheep (Ratray *et al.* 1974), goats (Hayden *et al.* 1979) and guinea-pigs (Davis *et al.* 1979), and in the latter two cases a positive correlation was also found between fetal number and subsequent milk yield. Thus there is considerable evidence for an effect of the fetuses on mammary growth during gestation in a number of species.

How is this achieved? Mammary growth is stimulated by combinations of steroids (oestrogens, progesterone and corticosteroids) and polypeptide hormones (prolactin, growth hormone and placental lactogen) (see Cowie, Forsyth & Hart, 1980). Production of placental lactogen by the placenta(e) appears in many species to be of prime importance for mammogenesis particularly during the latter two-thirds of gestation when circulating prolactin and growth hormone concentrations are low in most species. Thus it may be possible for the fetuses to exert control over mammary development by regulating placental lactogen production. If one assumes that secretion is proportional to placental mass which in turn is proportional to fetal number and/or mass, then it follows that more or heavier fetuses will be associated with increased placental lactogen production. There is some evidence for this in goats (Hayden *et al.* 1979; Hayden, Thomas, Smith & Forsyth, 1980), sheep (Taylor, Jenkin, Robinson, Thorburn, Friesen & Chan, 1980) and mice (Markoff & Talamantes, 1981) although other studies have failed to detect correlations between the hormone's concentration and placental mass (see Cowie *et al.* 1980). It is most unlikely that secretion of the hormone is simply a function of placental mass in all species, although other controlling factors are, as yet, unknown. In the rat for instance a minimum of only three fetoplacental units is necessary for ensuring maximum mammary development (Anderson, 1975). If mammogenesis is driven by placental lactogen secretion in this species (the rôle of prolactin, particularly with relation to self-licking of nipples by pregnant rats, has still to be assessed (Roth & Rosenblatt, 1968), then it follows that either placental lactogen secretion is maximal with only three placentae or else the gland is incapable of responding to any extra hormone.

Hemihysterectomy had no effect on litter weight gain in groups of mice suckling nine pups (Table 5), indicating that milk yield was not influenced by the number of fetuses carried. Skjervold (1977) claimed that 10–15% of the variation in milk yield that he observed between different strains of mice cross-fostering identical litters was due to differences in the number of fetuses, while Nagai (1978) determined a figure of 1–7% and Eisen *et al.* (1980) considered that the fetal effect was insignificant when variation between strains in maternal body weight was taken into account. Bateman (1957) also found no correlation between fetal number and milk yield, using a large number of mice of one strain.

Since in the present experiment mammary development was reduced in dams carrying a small number of fetuses, why was milk yield not also decreased? It is known that mammary growth continues into lactation in mice (Knight & Peaker, 1982). Glands of hemihysterectomized and sham-operated animals were, therefore, compared on day 5 of lactation (Table 2) and it was found that growth had not only continued but had indeed been stimulated in the hemihysterectomized animals suckling nine pups, but not in those suckling four, when compared to sham-operated animals suckling nine pups (Table 3). This compensatory growth was most apparent

in terms of DNA<sub>t</sub>, indicating that cell hyperplasia was largely responsible for the increased growth rate. Since RNA<sub>t</sub> also increased, the ratio of RNA to DNA increased by a similar amount between day 18 of gestation and day 5 of lactation in sham-operated and hemihysterectomized animals with normal litter sizes. Compensatory growth did not occur in the hemihysterectomized animals suckling four pups, although their glands did continue to grow during early lactation, at the same rate as sham-operated controls when compared on a DNA<sub>t</sub> basis but at a slower rate in terms of RNA<sub>t</sub> (Tables 2 and 3).

Correlations between the number of suckling young and mammary DNA<sub>t</sub> during lactation have been demonstrated before (Tucker, 1966; Moon, 1969), although no attempt was made to differentiate between stimulation of growth by large litters and partial involution of glands suckled by small litters. In this case growth continued but at a slower rate; hence the possibility that the results were affected by involution caused by the reduced suckling stimulus can be ruled out.

The results demonstrate that the young of mice are capable of influencing mammary development both *pre partum* and *post partum*. The mechanisms by which this is achieved are unknown, but probably involve placental lactogen secretion and suckling-induced prolactin secretion, respectively. The suckling stimulus may have been slightly higher in hemihysterectomized animals with nine pups than in the sham-operated animals, since their pups were a little heavier. However, it is unlikely that such a small difference, which was in any case only apparent on day 1 of lactation, could have stimulated prolactin secretion sufficiently to account for the rather large difference in growth rates (that of the hemihysterectomized animals was twice that of the sham-operated animals in terms of DNA<sub>t</sub>). Hence an additional control mechanism, responding to actual gland size, could be envisaged, and a likely candidate is local control at the intramammary level, as suggested by Knight & Peaker (1982).

If it is accepted that fetoplacental control of mammary growth is a mechanism by which mammary development, and hence milk yield, is optimized to the future requirements of the young, then it follows that the extension of the young's influence to early lactation could be a continuing mechanism to ensure that yield is matched to demand. In this respect it is interesting to note that wild house mice have communal nests (Matthews, 1952) and that, by analogy with domesticated forms (Lane-Petter, 1976), they suckle the young of other females in the nest as well as their own. Therefore, effective litter size may be adjusted naturally *post partum* in such animals. In other words the normal physiological altruism of lactation directed to the feeding of the mother's own young may be extended to those of her kin in such communally-nesting small rodents; *post partum* control of mammary development could be a mechanism of particular importance in such species.

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