PATTERN DIFFERENCES IN_ THE LACTATIONAL FUNCTION OF TWO INBRED STRAINS OF MICE

著者	MITSUMOTO Takatsugu
journal or publication title	Tohoku journal of agricultural research
volume	11
number	1
page range	53-61
year	1960-05-31
URL	http://hdl.handle.net/10097/29302

PATTERN DIFFERENCES IN THE LACTATIONAL FUNCTION OF TWO INBRED STRAINS OF MICE

By

Takatsugu MITSUMOTO

Department of Animal Husbandry, Faculty of Agriculture,
Tohoku University, Sendai, Japan

(*Received February 5, 1960*)

Introduction

Generally, in mammals, it has been accepted that the maternal influences, which affect considerably the growth of the young from implanted time to the weaning period, may be divided into the environment in intrauterine (prenatal) and the lactational performance, which involve both quantitative and qualitative effects (postnatal). So far as the lactational effect is concerned, its performance may directly correlate with the growth rate and the viability of suckling youngs and indirectly influence the vitality (growth and maturation adequate for reproduction) after weaning. Accordingly, lactational performance are of considerable importance to the economic character of farm animals, especially for milking pattern which closely correlate with the milk yields of dairy cattle (3, 4, 17, 23).

On the other hand, with regards to the lactational capacity of laboratory animals, many workers have demonstrated by the mammary response of animal treated with hormone (10, 16), by the weights of mammary glands and the histological appearances in it and by the *in vitro* tissue slices technique that various metabolic activities of mammary tissue correlate with the physiological state of the glands (8, 9, 10, 11, 18, 19, 20, 22, 24).

Moreover, the preweaning weights of suckling youngs and the suckling activity of youngs have been discussed in relation to the measurement of lactation by Enzmann (6), Mayer (13), Bateman (1, 2), Dikkshit and Tasker (5), Nagai and Yamada (15) and Mori *et al.* (14).

In the present paper, the pattern differences of the lactational function of mice are described and it is briefly discussed how the differences in lactational pattern affect the growth of suckling youngs.

Materials and Methods

Animals. The used animals consisted of dd-, ss-strains and dsF_1 mice. The last were produced by crossing dd females with ss males. Both the parent stocks had been bred to the eighteenth by the successive brother-sister matings in the Laboratory of Animal Breeding and each strain has its own characteristic pattern of reproduction and of other aspects of physiology (12). Each mouse was fed daily with about 10 g. of the cooked feed prepared in the author's laboratory. The primiparous lactation mice weighing 24–27 g. at the age of 100–110 days were housed in individual wooden cages provided with straw cut for bedding, under room conditions. Shortly after birth each litter was adjusted to six youngs and, whenever possible, they were equally distributed as to sex. The following procedure was on each of the days 5, 10, 15 and 20 postpartum, and each group contained from four to six animals. They were killed by decapitation without injure the cervical mammary glands, the litters being allowed to suckle the dams up to the time of autopsy.

Reciprocal fostering. Animals, which were bred from between two strains on the same day, were exchanged to foster the litters of them after each litter was adjusted to six youngs, and the growth of the litters fostered to 30 days postpartum were observed.

Preparation of slices. The whole mammary gland were carefully cut off, weighed and placed in ice-cold 1.15 per cent Potassium Chloride solution. A part of the abdominal and inguinal mammary glands were preserved for histological examination. The thoracic, abdominal and inguinal mammary glands, which were available for the slices, were cut approximately at 0.3 mm. thick by means of the slicer. The slices were washed in cold 1.15 per cent Potassium Chloride solution.

Manometric methods. The oxygen consumption ($-Q_{O_2}$) was measured by ordinary manometric flasks of Warburg. Batches of mice mamary gland slices weighing approximately 110 mg. were incubated at 37.0°C in 2.2 *ml.* of the Ringer-phosphate buffer of Krebs (PH 7.4) up to one hour. Subchamber of flasks contained 0.2 *ml.* of 2N Potassium Hydroxide solution to occlude Carbon Dioxide. In all experiments with the substrate, 0.3 per cent Glucose was used (8). Determination in the duplicate without the substrate was also performed on slices from animals in each group. The gas phase was 100 per cent Oxygen and were gassed for 10 min. before the taps were closed.

Estimation of dry matter. Aliquots of slices were dried at 110°C for 24 hrs. and the percentage of dry matter in it was calculated.

Statistical methods. For all groups the means and their standard error were calculated, except for the growth of the reciprocally fostered litters. Differences between groups were examined by the 't' test after testing the homogeneity of populations by the 'F' test (25).

Results

Litter weights at various stages of lactation. The litter weights of the animals tested at various stages of lactation are shown in Table 1. At birth, the litter sizes of dsF_1 are significantly higher than those of dd and ss, but the litter weights between them are not-significant. It is seen from Table 1 that the litter weights of dd and dsF_1 are significantly higher than those of ss, while no significant differences between dd and dsF_1 at various stages are found.

Table 1. Means of litter weights at various stages of lactation.

	dd		ss		dsF_1	
At birth No. of animals	5		5		5	
Litter sizes	6.0 ± 0.44^{1}		6.6 ± 0.71^{7}		8.4 ± 0.50^{13}	
Litter weights	8.9 ± 0.61		9.6 ± 0.42		10.6 ± 0.66	
Stage of lactation	No. of animals	Litter weights (g.)	No. of animals	Litter weights (g.)	No. of animals	Litter weights (g.)
0	5	8.3 ± 0.30^{2}	5	7.6 ± 0.15^{8}	5	7.6 ± 0.28
5	5	16.6 ± 0.73^{3}	4	11.2 ± 1.11^{9}	5	16.5 ± 1.02^{14}
10	5	27.1 ± 1.11^{4}	5	21.7 ± 1.12^{10}	5	25.4 ± 0.98^{15}
15	6	32.1 ± 1.56^{5}	4	27.7 ± 1.17^{11}	5	31.1 ± 0.91^{16}
20	5	37.3 ± 1.29^{6}	5	31.7 ± 2.22^{12}	5	35.2 ± 1.42^{17}

Means with standard error.
Significance of differences between strains and between various stages.

1—13*	5—11*	11—16†
2— 8†	6—12†	12—17†
3— 9*	9—14*	7—13†
4—10*	10—15*	

* : Significant at 0.05 level of probability.
† : $0.10>P>0.05$ at level of probability.

Weights of mammary gland at various stages of lactation. As will be seen in Tables 2 and 5, the weights of the whole mammary gland of ss gradually increased to 20 days and also those of dd and dsF_1 gradually increased to 15 days, thereafter becoming markedly reduced at the 20 days of lactation. Obviously significant differences are for the values between dd and ss at the 20 days of lactation, but not for the values between them at other stages. The results, which are detailed in Tables 2 and 5, indicate apparently the pattern differences between two strains of the gross mammary gland weights at stages of lactation.

Table 2. Mean weights of whole mammary gland at various stages of lactation.

	dd		ss		dsF_1	
Stage of lactation	No. of animals	Weight of whole mammary gland (mg.)	No. of animals	Weight of whole mammary gland (mg.)	No. of animals	Weight of whole mammary gland (mg.)
5	5	1718±135[1]	4	1634±122[5]	5	1890± 83[7]
10	5	2097±126[2]	5	1832±102	5	2249±159[8]
15	6	2227±123[3]	4	2114± 96	5	2346± 91[9]
20	5	1256±106[4]	5	2245±242[6]	5	1366± 57[10]

Means with standard error.
Significance of differences between strains and between various stages.

1—3**	5— 6†	7— 9**
1—4*	4— 6***	7—10*
2—4**	6—10***	9—10**
3—4**	7— 8†	8—10*

*** : Highly significant at 0.005 level of probability.
** : Significant at 0.01 level of probability.
* : Significant at 0.0 5 level ef probability.
† : 0.10>P>0.05 at level of probability.

Oxygen consumption at various stages of lactation. The dry matter content of slices and oxygen consumption of mammary gland slices are given in Table 3, however, those of dsF_1 were not measured in the present experiments. The dry matter content of slices of dd are gradually reduced with the proceeding of lactation, while that of ss are gradually increased. Table 5 show that the pattern difference between the dry matter content of two strains are significant. These patterns may correlate with the lactogenic activity in mammary glands.

The results show some indications that the oxygen consumption on a dry matter basis of dd in early stages of lactation are higher than that at the last stage, i. e. gradually reduced towards the last stage of lactation, but the values of ss are apparently constant. The means of dd are slightly higher than those of ss at all stages. Only a difference between the endogeneous value of dd at 10 days of lactation and that of ss at the same stage are significant.

With respects to the differential value (i. e. subtract endogeneous value from substrated value), the oxygen consumption in the presence of Glucose are fairly high in comparison with the endogeneous value at all experiments. It is noted that its values of dd are markedly low at 10 and 20 days of lactation, while that of ss are constant though it tended to be highest at 10 and 15 days of lactation.

As to the oxygen consumption converted to whole mammary gland,

Table 3. Oxygen consumption of mammary gland slices at various stages of lactation.

Strains	Stage of lactation	No. of animals	% Dry matter of tissue slices	$-Q_{O_2}$ μl./slice 100mg./hr. no substrate A	$-Q_{O_2}$ μl./slice 100mg./hr. 0.3% glucose B	$-Q_{O_2}$ μl/mg. Dry matter/hr. no substrate	$-Q_{O_2}$ μl/mg. Dry matter/hr. 0.3% glucose	B−A	$-Q_{O_2}$ μl/hr. Converted to whole mammary gland no substrate	$-Q_{O_2}$ μl/hr. Converted to whole mammary gland 0.3% glucose
dd	5	5	37.95±1.80[1]	93.73±15.36	141.35±13.30[10]	2.46±0.34	3.73±0.33[15]	47.42±9.82[17]	1537±165[21]	2399±239[29]
	10	5	33.01±1.60	101.34± 6.08[7]	118.81±12.04	3.09±0.18[12]	3.61±0.34	17.46±6.82[18]	2115±156[22]	2468±231[30]
	15	6	31.74±1.03[2]	64.12± 6.53[8]	110.46± 4.65	2.04±0.26[13]	3.50±0.69	46.34±8.52[19]	1402±112[23]	2457±149[31]
	20	5	30.45±1.89[3]	79.55± 8.92	99.88± 7.43[11]	2.60±0.32	3.30±0.80[16]	20.34±9.03[20]	1028±185[24]	1274±171[32]
ss	5	4	32.45±2.34[4]	73.09± 9.22	102.97±15.97	2.31±0.36	3.28±0.21	32.38± 8.96	1194±185[25]	1669±275[33]
	10	5	35.74±2.01	63.68±12.00[9]	101.81± 8.82	1.77±0.29[14]	2.84±0.84	38.18± 7.66	1153±204[26]	1857±152[34]
	15	4	32.53±0.88[5]	65.82± 6.62	106.90±11.27	2.02±0.19	3.28±0.11	41.08± 4.93	1369± 83[27]	2220±152[35]
	20	5	40.79±2.64[6]	87.68± 9.08	122.04±11.75	2.18±0.24	3.02±0.10	34.35±10.77	1908±136[28]	2679±280[36]

Means with standard error.

Significance of differences between strains and between various stages.

1—2*	5— 6*	12—13**	18—19*	22—23**	24—28**	29—32***	30—34†
1—3*	7— 8†	12—14***	19—20*	22—24**	25—28*	30—32***	32—36***
3—6**	8— 9*	15—16*	17—20*	23—24†	26—28*	31—32***	33—36**
4—6*	10—11*	17—18*	21—22†	22—26**	27—28*	29—33†	34—36*

*** : Highly significant at 0.005 level of probability.
** : Significant at 0.01 level of probability.
* : Significant at 0.05 level of probability.
† : 0.10>P>0.05 at level of probability.

Table 4. Reciprocal fostering.
A. Growth of reciprocal fostered litters between two strains.

Dam Litter		At birth	Days after parturition 0	5	10	15	20	25	30
dd → ss	Litter sizes	8	6	6	6	6	6	6	6
	Litter weights	10.3	8.3	17.5	29.5	36.5	41.2	49.7	59.7
ss → dd	Litter sizes	6	6	6	6	6	6	6	6
	Litter weights	8.3	8.3	15.5	23.0	32.0	43.0	60.1	70.4
dd → ss	Litter sizes	6	6	6	6	6	6	6	6
	Litter weights	7.1	7.1	16.3	27.9	36.3	41.4	46.6	59.0
ss → dd	Litter sizes	6	6	5	4	4	4	4	4
	Litter weights	7.9	7.9	13.0	20.0	26.0	35.3	45.6	55.2
dd → ss	Litter sizes	8	6	6	6	6	6	6	6
	Litter weights	10.0	7.5	16.4	27.8	37.8	43.5	49.4	68.2
ss → dd	Litter sizes	5	6	5	5	5	5	5	5
	Litter weights	5.5	7.0	14.3	23.4	32.2	40.4	50.7	74.5
dd → ss	Means of litter weights		7.4	16.7	28.4	36.9	42.0	48.6	62.3
ss → dd	Means of litter weights		7.4	14.3	22.1	30.1	39.6	52.1	66.7

Table 4. B Oxygen consumption and weights of mammary gland of dams, which were fostered litters exchanged, at 20 day postpartum.

Dam Litter	Weights of whole mammary gland (g)	% Dry matter of tissue slices	$-Q_{O_2}$ $\mu l.$/100mg./hr. slice		$-Q_{O_2}$ $\mu l.$/mg.Dry matter/hr.		$-Q^{O_2}$ $\mu l.$/hr. Converted to whole Mammary gland	
			no substrate	0.3% glucose	no substrate	0.3% glucose	no substrate	0.3% glucose
dd → ss	1214	34.0	94.55	106.01	2.78	3.12	1115	1287
ss → dd	1806	35.0	49.85	127.76	1.42	3.65	900	2307
dd → ss	1654	34.7	42.00	87.07	1.21	2.51	695	1440
ss → dd	2228	34.2	67.46	114.46	1.97	3.35	1503	2550
dd → ss	2095	34.3	100.14	140.57	2.92	4.10	2098	2745
ss → dd	2378	36.1	87.20	139.09	2.42	3.85	2074	3308
	Means	Means	Means	Means	Means	Means	Means	Means
dd → ss	1654	34.3	78.89	111.22	2.30	3.24	1303	1824
ss → dd	2137	35.1	68.17	127.10	1.93	3.62	1492	2732

Tables 3 and 5 show that the pattern differences between the values of two strains at stages of lactation are obviously significant both endogeneous and substrate, i. e. the value of dd at early stages of lactation are higher than that of ss, however, the value of ss at the last stage of lactation are obviously higher than that of dd at the same stage.

Reciprocal fostering. The results are detailed in Tables 4 A and B. Table 4 A shows that the growth of litters of ss, which were nursed by dams of dd, are fairly high at early stages of lactation and low at the last stages, but the growth of litters of dd, which were nursed by dams of ss, give contrary pattern as compared with that of the formers. Table 4 B shows some indications that the results obtained by reciprocal fostering approximately agree with that of the spontaneous conditions at the same stages of lactation. It is suggested that the pattern differences in lactational function may be unable to alter with ease by different suckling stimuli and also may be a part of the dams' own characters on these two strains.

Discussion

It has been recently discussed by Bateman (1, 2) and Nagai *et al* (15) from the standpoint of improving the lactational performance in mice, on the relationship between the lactational performance and the growth of suckling youngs. They estimated that the lactational effects contributed to the variation in weights of suckling youngs from 30 to 70 per cent at 12 days of age. Enzmann (6) reported that the milk-production curve of mice rises from parturition until about the tenth day and afterwards declines until the completion of weaning. Batemann (2) observed that the maximum amount of milk in mice is available when the litter is born. From the aformentioned papers and authors as well as unpublished data, it was suggested that the pattern difference of lactation may exist between strains of mice. In this experiment, therefore, the pattern differences between strains in mice were estimated. It is suggested that the lactational pattern affects the growth of suckling youngs.

The oxygen consumption was measured so as to determine the activity of secreting tissue and converted it to compensate the number of secreting cells to the whole mammary gland, because the manifestation of lactational performance are ultimately controlled by the number of secreting cells and their activities in mammary glands though it may correlate with the activity in other endocrine glands. To estimate the lactational activity in the gland, it might be also possible to use the lactose synthesis, DNA content and stagnant milk in mammary gland slices.

Although the results obviously show pattern differences between two strains (Tables 3 and 5), the pattern may be partially controlled by the dams own genotype and or suckling stimuli of her youngs. The suckling stimuli of newborns fostered from other dams at the weaning period are capable to prevent the involution of mammary glands (21). Therefore, reciprocal fostering

Table 5. Analysis of variance of various characters at stages of lactation.

Source of variation	d.f.	Mean squares		
		Weight of whole mammary gland	Percentage of dry matter	Oxygen consumption coverted to whole mammary gland
Strain	1	167269	46.88	7919
Stage	3	470525**	83.65**	36039
Interaction	3	825693***	100.86**	1466582***
Error	31	95595	17.06	158396

*** : Highly significant at 0.005 level of probability.
** : Significant at 0.01 level of probability.

was undertaken between two strains to determine the factor which mostly affect the lactational pattern. The growth of reciprocal fostered litters are performed nearly with a contrary pattern as compared with those of natural conditions. Further, from Table 4 A, it may be assumed that dams of ss tend to adjust the sizes of youngs fostered by themselves at early stages, in which the capacity of lactation is low. Accordingly, it might be clear that the growth of litter is affected by lactational pattern of each strains. Tables 4 A and B suggested that these lactational patterns may be characteristic of dams genotype. This was also suggested by the trends in weights of the whole mammary gland of dsF_1 during lactation.

From these attemps, it may be suggested that not only the high and low capacity in milk yields, but also the lactational pattern are of considerable importance as to the breeding problems in mice.

Summary

The pattern differences lactational function of mice were studied and it was briefly discussed how the differences in lactational pattern affect the growth of suckling youngs. The oxygen consumption was measured in mammary gland slices and converted to the whole mammary gland.

The lactational pattern differences between two strains were highly significant ($P<0.005$), i.e. the values of dd at early stages of lactation were higher than those of ss, on the contrary the value of ss at the last stage of lactation was obviously higher than that of dd at the same stage.

Reciprocal fostering suggested that the growth of suckling youngs were markedly affected by the lactational pattern of each strains and further the lactational pattern may be characteristic of the genotype in the strain.

Acknowledgment

The author wishes to express his gratitude to Prof. Dr. S. Nishida for his valuable suggestions and constant guidance during the course of the present work and to Prof. Dr. G. Umezu for his valuable advice. Special thanks are due to Assistant Mr. A. Shibata for much help in the manometric technique and helpful suggestions. He is indebted to Dr. Y. Yamada, National Institute of Genetics, Mishima, for his kindness in reading the manuscript.

References

1) Bateman, N. (1954). Physiol. Zoöl., **27**, 163.
2) Bateman, N. (1957). J. Agric. Sci., **49**, 60.
3) Bussert, K. (1957). Züchtgsk., **29**, 173.
4) Cersovsky, H. (1957). Z. Tierzücht, **6**, 1.
5) Dikkshit, P. K. and A. D. Tasker (1956). Proc. Soc. Exp. Biol., **93**, 235.
6) Enzmann, E. V. (1933). Anat. Rec., **56**, 345.
7) Falconer, D. S. (1947). J. Agric. Sci., **37**, 224.
8) Folly, S. J. and T. H. French (1949). Biochem. J., **45**, 117.
9) Folly, S. J. and T. H. French (1949). Biochem. J., **45**, 270.
10) Folly, S. J. (1956). The Physiology and Biochemistry of Lactation, Edinburgh.
11) Goto, I. (1958). Jap. J. Zootech. Sci., **29**, 261. (in Japanese with English summary).
12) Ishigaki, S. (1959). Essays in Commemoration of the 10th Anniversary. p. 64. Labs. Anim. Breed., Tohoku Univ. (in Japanese).
13) Mayer, D. T. (1935). J. Nutrition, **10**, 343.
14) Mori, A., M, Takeda, S. Ishigaki and S. Nishida (1959). Jap. J. Zootech. Sci., **30**, (Supp.). Abstr. 72.
15) Nagai, J. and J. Yamada (1958). Jap. J. Zootech. Sci., **29**, 231. (in Japanese with English summary).
16) Nagai, J. (1959). Jap. J. Breed., **9**, 154.
17) Naito, M. (1956). The Progress in Animal Husbandry. p. 62. Yôkendô. Tôkyo. (in Japanese).
18) Naito, M. (1958). J. Dairy Rec., **25**, 17.
19) Naito, M. (1958). J. Dairy Rec., **25**, 392.
20) Oshima, M. and T. Goto (1955). Jap. J. Animal Reprod., **1**, 65.
21) Oshima, M. and T. Goto (1956). Jap. J. Animal Reprod., **2**, 15.
22) Ôta, K. (1959). Jap. J. Zootech. Sci., **30**, 177. (in Japanese with English summary).
23) Sanders, H. G. (1930). J. Agric. Sci., **20**, 145.
24) Shimizu, H., Y. Shoda, K. Kretani and S. Ugami (1957). Jap. J. Zootech. Sci., **28**, 239. (in Japanese with English summary).
25) Snedecor, G. W. (1946). Statistical methods. Iowa State College Press. Ames.