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THE INFLUENCE OF THE GROWTH RATE ON THE OVARIN RESPONSIBILITY TO EXOGENOUS GONADOTROPIN IN THE IMMATURE RAT

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It is known that the variation of nutrition during the suckling period affected the subsequent growth of young rats and that the sexual maturation of these young rats was more closely related to body weight than to chronological age (2–7). It has also been reported that members of small litters of rats grow faster and mature earlier than members of large litters. However, the relation of altered growth rate to the development of the endocrine system concerned with the sexual maturation has not been fully confirmed. Especially, little is known about the development of the ovarian function before puberty. In the present investigation, therefore, the development of the ovarian function was examined in relation to the responsibility of the ovary to exogenous gonadotropin.

Materials and Methods

Female rats of the Wister strain were used in this inverstigation. They were fed on a dry pellet diet containing 20% crude protein and water ad lib. All rats were maintained in a room at a temperature of 25°C with constant periods of light (from 6 A.M. to 6 P.M.) and darkness. The rats were divided into two groups according to the litter size—a large group of sucklings 17–20 and a control group of 8.

In large group, two or three litters born on the same day were mixed and 17–20 sucklings were returned to one mother on the next day after parturition. The sucklings were allowed to suckle for 21 days. In control, each rat was reared normally in litters of 8 sucklings for 21 days. After weaning, the rats of both groups were fed on a dry pellet diet and water ad lib. The body weight, and vaginal opening were examined in some of the rats in both groups.

As an index of the responsibility of the ovarian function in the immature rats, the occurrence of ovulation by treatment of gonadotropin was examined. The methods for determining the rate of ovulation in the present work was essentially the same as the superovulation technique reported by Zarrow and Wison(9).

Gonadotropin used in this investigation were PMS (Serotropin from Teikoku-Zoki Co.) and HCG (Puberogen from Tomoda-Seiyaku Co.). The immature rats were treated with 30 IU of PMS followed by the injection of 10 IU of HCG in a volume of 0.1 ml of 0.85% saline 56 hours after the PMS injection. The first injection of PMS in immature rats was treated from 19 to 31 days after parturition. The animals were killed at 18 to 20 hours after the final injection and the oviduct was removed. The number of tubal ova was counted under a dissecting microscope.

The age of the animal recorded in these experiments was the age at the time of the initial injection of PMS.

Results

The influence of the growth rate on vaginal opening

The effects of the number of sucklings during 21 days on the subsequent weight increase of growing animals until the 6th week is illustrated in Fugure 1. Mean body weight at weaning was 45.6 g in control and 27.5 g in the large group. The value in control was a mutch for "optimal growth" which earlier workers have got

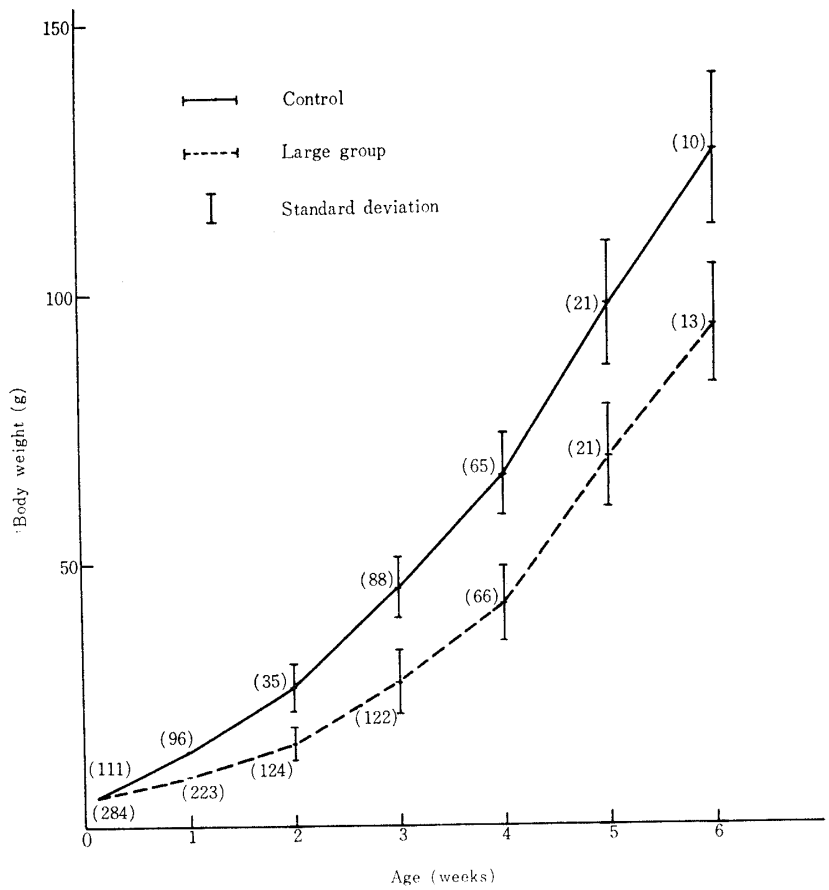

Fig. 1. Growth curve of rat in both groups. Number of rats are indicated in parentheses.

Table. 1. The age (days) and the body weight (g) at vaginal opening in immature rats. Values indicate mean ± S.D.

Litter size	No. of rats	Age of vaginal opfning	Body wt. at vaginal opening
Control (8)	10	35.8±2.9	100.6±11.4
Large group (17-20)	13	41.4±2.5	95.5±10.3

in infantile rats from reduced litters (3 sucklings) during suckling (2, 3, 5). The retarded growth at each week in the large group was the same as the results of their investigations. Vaginal opening, occurred at 35.8 days in the control and at 41.4 days in the remainder (Table 1). The mean body weight at vaginal opening was 100.6 g and 95.5 g respectively in each group. Although there was a significant difference in the day at vaginal opening ($P<0.01$), no difference was observed about the body weight between both groups. It seem that the vaginal opening depends on body weight rather than on chlonorogical age in case of altering the milk supply during suckling as previously described (2, 3, 5).

The relation between age and ovulation rate

The ovulation was not observed until 21 days and then was recorded at almost 100% each day thereafter in control (Table 2). In the group with large litters, the first observation of ova in the oviduct was made at 23th day and attained a level of almost 100% at each subsequent day except 27th day. The onset of

Table 2. Effect of gonadotropin treatment on the ovulation in each age (days) of immature rats

	Age (days)	19	21	23	25	27	29	31
Control	No. of rats	5	14	12	8	7	8	7
	Body wt. (g)	36.0± 7.3	45.5± 7.7	49.6± 5.4	46.4± 4.8	61.6± 2.7	77.8± 6.9	76.4± 4.5
	Ovarian wt. (mg)	34.1±16.7	86.5±31.9	13.9±36.6	121.5 ±23.4	81.4± 5.2	113.0 ±15.4	85.4±14.1
	Ovulation ratio	0/50	6/14	11/12	8/8	7/7	8/8	7/7
	No. of ova	0	5.0±7.6	11.5±10.8	25.9±24.8	46.0± 5.9	46.9±11.9	32.3±13.8
Large group	No. of rats		16	20	21	17	10	8
	Body wt. (g)		27.9± 2.9	32.9±10.7	41.6± 9.6	39.6± 9.6	46.2±)4.5	48.0± 4.4
	Ovarian wt. (mg)		43.9±19.5	91.6±39.5	108.4 ±37.0	167.5 ±48.1	132.1 ±31.2	76.1±15.6
	Ovulation ratio		0/16	13/20	18/21	12/17	10/10	8/8
	No. of ova		0	9.5±7.7	29.7±20.9	13.2± 7.5	34.7±16.2	21.0± 9.9

Values indicate mean ± S.D. in body weight, ovarian weight and number of ova.

ovulation in the large group was slightly slower than in the control group. The difference was significant between the groups (P<0.05).

The relation between body weight and ovulation rate

The body weight in Table 3 is that at the time of the initial injection of gonodotropin. The ovulation was not yet observed at the period of 20–30 g in control. The first ovulation in control occurred at the period of 30–40 g showing 11% positive. In the large group, on the other hand, ovulation had already started at the period of 20–30 g indicating 23% positive followed by 76%, 93% at 30–40 g, 40–50 g respectively. Therefore, the onset of ovulation in the large group was at a fairly lower body weight than control. There was a significant difference in the ovulation rate at the period of 30–40 g in the two groups (P<0.01). The difference was also recognized at the period mixed with 20–30 g and 30–40 g (P<0.05).

The relation between age and ovarian weight

In both groups, the rapid increase in ovarian weight was observed just before the initiation of ovulation. The maximum value of ovarian weight was found to be delayed 4 to 6 days in the large group as compared with the control. However, the highest value of ovarian weight did not differ in the two groups (Table 2).

The relation between body weight and ovarian weight

The ovarian weight was found to be heavier with smaller body weights in the large group compared with the control. The results in this section showed a similar tendency to the result obtained in the relation between body weight and ovulation rate. A significant difference in the ovarian weight between the two groups was observed at the period of 20–30 g, 30–40 g body weight respectively (P<0.01).

Table 3. The relationship between body weight and ovulation of immature rats treated with gonadotropins

	Body wt. (g)	20-30	30-40	40-50	50-60	60-70	70-80
Control	No. of rats	7	9	14	13	7	11
	Ovarian wt. (mg)	11.3± 4.2	17.1± 4.4	115.2 ±44.1	125.3 ±32.3	88.3±12.3	96.2±22.7
	Ovulation ratio	0	1/9	9/14	11/13	7/7	10/10
Large group	No. of rats	27	17	28	20		
	Ovarian wt. (mg)	56.0±27.3	105.3 ±32.7	119.8 ±50.6	115.5 ±41.5		
	Ovulation ratio	5/27	13/17	26/28	17/20		

Values indicate Mean ± S.D.

The relation between number of tubal ova and growth rate

The number of ova was only dealt with in rats where the ovulation was recognized. When the number of ova obtained from the 23th to 31th day was compared in the two groups, there was a significant smaller value in the large group ($P<0.01$). The mean number of ova was 21.8 in the large group and 30.5 in control.

Discussion

The vaginal opening in immature rats was observed on different days in both groups. It occurred at virtually identical body weight. These results seem to confirm that the vaginal opening depends on body weight rather than on chronological age and they are in accord with the reports of previous workers (2, 3, 5).

Folowing treatment with gonodotropin, the onset of ovulation in immature rats was observed at 21 days of age in control and 23 days of age in the large group. Zarrow and Wilson have reported that none of the rats treated with gonodotropin at 15–16 days of age ovulated and twenty percent ovulated at 17–18 days of age. The failure of the present investigation to obtain ovulation at 17–18 days of age is probably due to the difference of litter size. The initial ovulation in rats treated with gonodotropin was delayed 2 days in the large group as compared with control. Thereafter, about one hundred percent of the immature rats ovulated in both groups. On the other hand, the onset of induced ovulation in the large group was at a fairly lower body weight than control. However, there was still a significant difference in body weight within each age and this large standard deviation in each age indicates that other factors were probably present. Therefore the onset of ovulation in rats treated with gonadotropin seems to be influenced both by age and by body weight, and to be not related mainly to body weight as the occurrence of vaginal opening.

The average number of ova released in immature rats from 23 to 31 days of age by injection of gonadotropin was clearly smaller in the large group than in control.

The depression of the hypophysial function has been shown in rats[8] and pig[1] when they were fed under the undernutrition during growing phase. However, there is few evidence concerning the responsibility on gonad to gonadotrophin.

The decrease of ova count in the large group seems that the retarted state of somatic development in a large litter somehow alters the sensitivity of the ovary to gonadotropin.

Summary

The growth rate of young rats was modified by variation in litter size during suckling and the effect of growth rate on the maturation of ovarian function was studied. The responsibility of ovary to exogenous gonadotropin was examined as a maturation of ovarian function.

The onset of induced ovulation in immature rats treated with gonadotropin was delayed 2 days in the large group (17–20 sucklings) as compared with control (8 sucklings). However, the onset of induced ovulation in large group was at a fairly lower body weight than in control. The average number of ova released in the immature rats from 23 to 31 days of age was clearly smaller in the large group compared to the control.

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