

## OVARIAN FOLLICULAR DEVELOPMENT AND GONADOTROPHIN LEVELS DURING PREPUBERTAL LIFE IN THREE STRAINS OF RAT WITH DIFFERENT SENSITIVITY TO FSH

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Females of three strains of *Wistar* rats (03, 04 and 12) bred in our laboratory show significantly different responses to exogenous FSH, in the Steelman-Pohley assay (04 > 03 > 12). The fertility and some ovarian parameters of these strains have been reported previously (MAULEON and PELLELIER, 1964; MAULEON, 1972; LAND *et al.*, 1974). The present study was undertaken to explain the differences in sensitivity to FSH. Strain 03 is considered as the reference strain as its fertility is comparable with that of other *Wistar* rats.

### MATERIALS AND METHODS

Ovarian follicular population and atresia were studied quantitatively following the techniques described by de REVIERS (1974).

Pituitary FSH and LH contents were measured respectively by the STEELMAN and POHLEY (1953) and PARLOW (1961) assays. Plasma FSH and LH levels were measured by the NIAMDD radioimmunoassay in groups of 5 to 8 females from different litters. Radioimmunoassay of oestrogen was performed according to the method described by TERQUI and DELOUIS (1975).

### QUANTITATIVE STUDY OF GROWING FOLLICLES

Follicular development was studied quantitatively to test the hypothesis that interstrain differences in sensitivity to FSH were due to differences in the number of ovarian follicles. Ovaries were studied at 12, 20 and 32 days after birth as these are important times in ovarian development in strain 03 (de REVIERS and MAULEON, 1976). In this strain there are many small and medium-sized follicles at day 12

(429) ; at day 20, the number reaches a maximum (843 per ovary) ; by day 32, the number is much smaller (325).

In the three strains, the ovarian follicular population has the same pattern of development (fig. 1). However, there are fewer developing follicles in strain 12 than in the two other strains. At day 20, their number is 633 per ovary in strain 04 but only 328 in strain 12. No antral follicles are found in strain 12 at this age whereas there are twice as many in strain 04 as in 03. By day 32, the number of follicles is similar in the three strains.

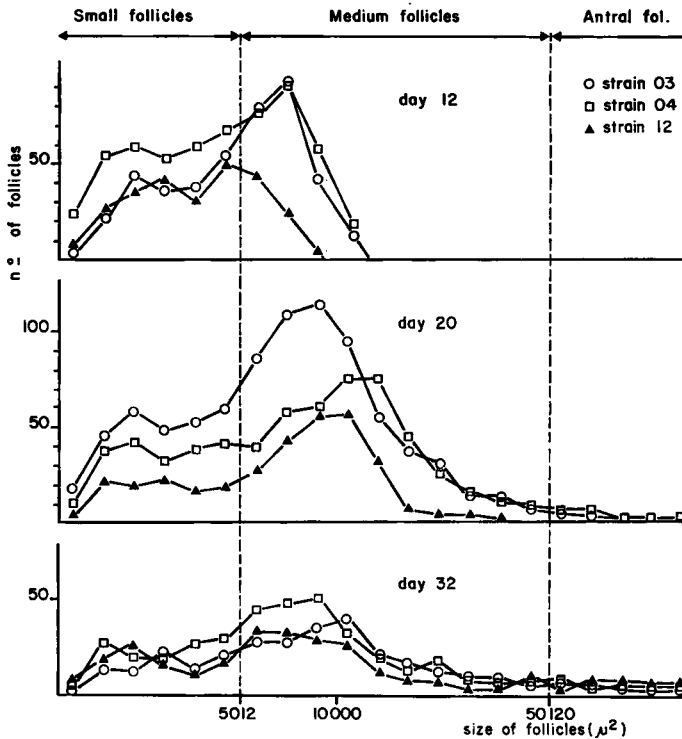


FIG. 1. — Changes with age of normal follicle population in ovaries of three strains of rats

At birth, the number of oocytes is larger in strain 12 than in strain 03 ( $04 > 12 > 03$ ) (LAND *et al.*, 1974). The small number of follicles which develop in strain 12 could be due to atresia or to inadequate stimulation by gonadotrophic hormones.

#### FOLLICULAR ATRESIA

The ratio of the total volume occupied by normal and by atretic follicles was calculated. At day 20, this ratio is nearly the same in the ovaries of the three strains of rat but it is lower at day 24 and 32 in strain 12 than in the two other strains. Thus, during this period, atresia is more marked in strain 12. But this does not explain the low number of normal follicles found at day 20.

PITUITARY FSH AND LH

The pituitary FSH and LH levels were measured at days 12, 16, 20, 24, 28 and 32. The pattern of change in pituitary gonadotrophin content is the same in all three strains (fig. 2). FSH peaks at day 20 whereas the LH peak occurs at day 24. However, the actual levels of the two hormones are different. The FSH peak level is highest in strain 04 (04 > 12 > 03) and the LH peak is highest in strain 12 (12 > 04 > 03).

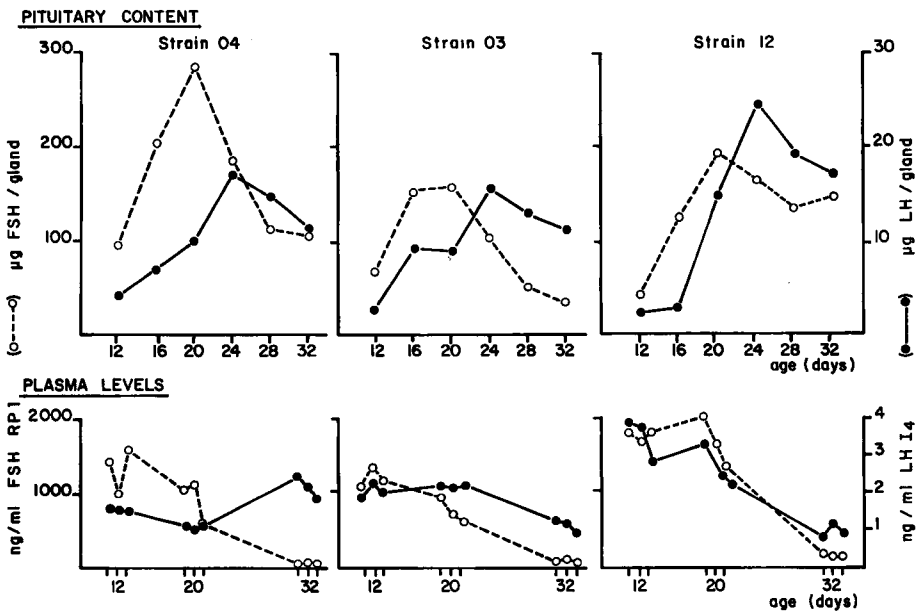


FIG. 2. — Pituitary contents, plasma FSH and LH levels in female rats of three strains during prepubertal life

PLASMA LEVELS OF FSH, LH AND TOTAL OESTROGEN

Radioimmunoassays of plasma FSH and LH were performed on days 11, 12 and 13, 19, 20 and 21 and 31, 32 and 33 (fig. 2). FSH levels are very high at 12 and 20 days in all three strains and low at day 32. However, FSH levels are higher in strain 12 (12 > 04 > 03), the difference between strains 12 and 03 being statistically significant ( $P < 0.01$ ). LH levels are higher in strain 12 (12 > 03 > 04) ( $P < 0.05$  strain 12 vs 04) at days 12 and 20.

Total oestrogen levels were measured at the same times. The levels are extremely high at day 12 (2 231, 1 598 and 2 146 pg estrone/ml respectively in strains 03, 04 and 12) and day 20 (3 263, 2 859 and 3 359 pg estrone/ml) and low at day 32. Due to large individual variation the differences between strains are not significant.

## DISCUSSION

Though the onset of puberty (vaginal opening) occurs later in rats of strain 12 than in the two other strains (40-45 days *vs* 32-38 days) it seems that FSH and LH levels change in the same way in the three strains. As a matter of fact the peak levels of FSH and LH in the pituitary occur at the same time and the highest plasma levels occur at comparable times. These findings suggest that the general pattern of hypophyseal and ovarian development is similar in the three strains. However, the levels of gonadotrophic hormones are different and this may be responsible for the differences in ovarian follicular population.

High plasma levels of FSH and LH in strain 12 are not associated with an unusual degree of follicular development. Moreover, MAULEON (1972) has shown that at the 25th day of postnatal life, the number of primordial follicles starting development is lower in strain 12 than in strain 03 (4 p. 100 *vs* 11 p. 100). Thus, these high levels of FSH and LH seem to exert an inhibitory effect on follicular growth and to favour atresia. In the 04 strain, a high FSH level stimulates follicular growth and antral formation. However, the hormonal balance (low level of LH) does not seem suitable for initiation of follicular growth. This would explain the small proportion of growing follicles in strain 04 (6.3 p. 100 *vs* 11.0 p. 100 in strain 03) (MAULEON, 1972). But, as the number of primordial follicles is higher in the 04 than in the 03 strain (6931 *vs* 4151), the absolute number of follicles starting to grow is similar.

We cannot exclude the possibility that the observed differences in sensitivity to FSH in the Steelman Pohley assay might be due to differences in the FSH receptors. Further work is needed to elucidate these interstrain differences in FSH sensitivity.

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## RÉSUMÉ

DÉVELOPPEMENT DE LA POPULATION FOLLICULAIRE OVARIENNE  
ET NIVEAUX D'HORMONES GONADOTROPES CHEZ DES RATTES IMPUBÈRES  
APPARTENANT A TROIS SOUCHES DE SENSIBILITÉ A FSH DIFFÉRENTE

La population folliculaire ovarienne, les niveaux hypophysaires et plasmatiques de FSH et LH ont été mesurés chez des rattes âgées de 12, 20 et 32 jours ; ces rattes appartiennent à trois souches (03, 04 et 12) dont la sensibilité ovarienne à FSH exogène est différente (04 > 03 > 12). La souche 03 est considérée comme souche de référence car sa fertilité est normale.

A 12 et 20 jours d'âge, le nombre total des follicules ovariens est plus faible chez les rattes de la souche 12 ; le nombre des follicules à antrum trouvé à 20 jours est plus grand chez les rattes de la souche 04. L'atrésie folliculaire est peu différente entre souches.

Le pic de FSH hypophysaire à 20 jours est plus élevé dans la souche 04 ( $04 > 12 > 03$ ) et celui de LH à 24 jours est plus élevé dans la souche 12 ( $12 > 04 > 03$ ).

Chez les rattes de la souche 12, aux âges étudiés, les niveaux plasmatiques sont plus élevés en FSH ( $12 > 04 > 03$ ) et en LH ( $12 > 03 > 04$ ).

Entre la naissance et la puberté, la fonction hypophysaire et la population ovarienne évoluent aux mêmes moments dans les trois souches : ce sont les niveaux des hormones gonadotropes et le nombre des follicules en croissance qui diffèrent. Les hauts niveaux de FSH et de LH trouvés dans la souche 12 semblent être défavorables à l'initiation de la croissance folliculaire tandis que le niveau élevé en FSH de la souche 04 favorise surtout l'apparition de l'antrum.

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