NOTE

Parathyroid Hormone Concentrations in Maternal and Fetal Blood and in Amniotic Fluid from Pregnant Rats

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ABSTRACT. Changes of parathyroid hormone (PTH) concentrations in maternal and fetal blood and in amniotic fluid throughout rat pregnancy were determined by radioimmunoassay. PTH levels in maternal blood increased during the last quarter of gestation, and seemed to play a significant role for maintaining maternal blood ionic calcium at a constant level. PTH levels in fetal blood and amniotic fluid remained mostly undetectable (less than 100 pg/ml).—KEY WORDS: parathyroid hormone, pregnant rat.

Calcium transfer from the mother to the fetuses during pregnancy results in decreased total calcium concentrations in maternal blood [11, 12] accompanied by increased maternal absorption [6, 9] and resorption [9] of calcium. Maternal hyperparathyroidism has been accepted in the human [2, 15] and cattle [1], and parathyroid hormone (PTH) is considered to play an important role in the calcium metabolism during pregnancy. In the previous study, ionic calcium in maternal and fetal blood of rats was found to be maintained at a constant level and the constant calcium levels in maternal and fetal blood seemed to be related to amniotic calcium [8]. Blood PTH levels, however, have never been quantitated in pregnant rats to our knowledge. The objectives of this study are to characterize the changes of PTH concentrations in maternal and fetal blood and in amniotic fluid throughout rat pregnancy and to correlate identified changes of PTH with the calcium levels in maternal and fetal blood.

The Wistar rats bred in our laboratory were used. They received a commercial chow (Nippon Formula Feed Manufacturing Co., Japan) and tap water ad libitum. Female rats, 10 to 12 weeks of age (weighing nearly 210 g) were caged overnight with males for mating and were examined for the presence of sperms in the vaginal smear on the following morning. The day of detection of sperms was defined as "day 0" of gestation. The delivery took place on day 21 of gestation in most rats. Maternal and fetal blood and amniotic fluid were obtained by the method previously published [8]. Some fetal blood samples taken during early stages were pooled by several litters to make 200 µl plasma for a PTH determination.

PTH in each sample was measured in duplicate by double antibody radioimmunoassay (RIA), using RIA kit (Eiken I.C.L., Japan) [10]. Dose response was confirmed in some of the samples, and the dilution curve was shown to be parallel to a standard one. The minimum detectable concentration of PTH was 100 pg/ml.

Blood PTH concentrations in 101 pregnant and 9 non-pregnant female rats are illustrated in Fig. 1 (a). The mean value was 516 pg/ml for non-pregnant females. No significant changes were noted in maternal blood PTH level from days 0 to 15 of gestation, with somewhat higher levels on days 8 and 9 and
lower levels from days 12 to 15. PTH concentration began to rise on day 16 and reached the peak level of 715 pg/ml on day 19. Thereafter, it fell to 614 pg/ml on day 21. These results are compatible with previous findings that PTH levels are higher during late pregnancy of the human [2, 15] and cattle [1] and that the parathyroid glands of pregnant rats on day 21 weigh heavier than those of non-pregnant rats [17]. A decrease in blood ionic calcium would easily explain the elevation of maternal blood PTH during the last quarter of gestation, since this represents an established stimulus of PTH secretion [13]. However, the previous report has revealed that ionic calcium in maternal blood is maintained at a fairly constant level throughout the pregnancy [8]. Therefore, it might be supposed that a transient decrease in the blood ionic calcium due to the increased calcium demands of the growing fetuses facilitates PTH secretion, and the elevated PTH secretion then rises the decreased blood ionic calcium, as hypothesized by Cushard et al. [2]. This process, which seems to repeat itself, probably maintains the PTH level height. An inexplicable fall of PTH was noted on day 21 of gestation, and this might result in the decrease in maternal total calcium levels [8].

PTH concentrations in fetal blood from days 15 to 21 are shown in Fig. 1 (b). PTH was measurable in only 7 out of 44 samples. The PTH measured on days 15, 16 and 17 is possibly of maternal origin, transferred through the placenta, since fetal PTH secretion seems to be insignificant as early as day 15 or 16 [7, 14, 20], and since PTH declined from higher levels on day 15 to an undetectable value on day 18. The placental transfer of
PTH in early stage must be investigated, though it is not occurred on day 21 [5]. The physiological significance of PTH measured in the fetal blood for the regulation of fetal calcium metabolism is not known from the present study. PTH was detectable in none of the fetal blood samples on days 18, 19 and 20, and in only 2 out of the 8 samples on day 21. These results are different from those previously described by Thomas et al. [21], who measured PTH only in fetal blood, not in maternal blood, to show that PTH decreased from 875 pg/ml on day 19 to 213 pg/ml on day 20 and then increased on day 21 in fetal rat. The parathyroid glands of the human and ovine fetuses are generally recognized to have the potential secretory ability [16, 19]. Their secretory activity, however, seems to be depressed by some mechanism(s) under normal physiological condition, since PTH levels in human cord blood were extremely low [3, 15]. In rats, the fetal parathyroid glands on day 21 of fetal age have been suggested to be functional, because the enlargement of the fetal parathyroids occurs owing to maternal hypocalcemia [18] and because anti-PTH serum administered to fetuses decreases total calcium in their blood [4]. The undetectable lower levels of fetal blood PTH revealed in this study, indicating undeveloped or depressed function of the fetal glands, might favor fetal bone formation. The PTH level tended to elevate on day 21, and this is probably due to the increased secretory activity of the fetal gland towards the neonatal life.

In amniotic fluid, PTH concentrations were undetectable or very low throughout pregnancy (Fig. 1 (c)). PTH levels in amniotic fluid on days 20 and 21 showed a rising tendency. This is probably because the amniotic fluid is concentrated by severe decrease in total volume of amniotic fluid during the last two days. PTH detected in amniotic fluid was thought to be of fetal origin.

REFERENCES
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正常妊娠ラットの母体血、胎仔血および羊水中PTH値について（短報）：原田郁子・小野憲一郎・長谷川彰彦・友田 勇（東京大学農学部家畜内科学教室）——Wistarラットの妊娠時期を追って、母体血、胎仔血および羊水中のPTH値をラジオイムノアッセイ法により測定した。母体血のPTH値は妊娠末期に上昇し、イオン化カルシウム値の一定値維持に重要な役割を果たしていると思われた。胎仔血および羊水中のPTH値は大部分が測定感度以下であった。