

HISTAMINE LEVELS IN THE BLOOD OF PREGNANT MARES*

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The problem of histamine metabolism has long been the subject of research. The excretion of histamine during pregnancy has been studied in cats, mice, hamsters, and many other animals, and also in human beings. However, few papers have been published on the levels of histamine in the blood of pregnant animals. In this paper the variation in blood histamine levels in pregnant mares from the first month of pregnancy until term is reported.

Materials and Methods

Six pregnant mares of the PSI strain plus two controls were studied.

The method followed was that of Gaddum modified by Code (1937). Blood was collected in syringes containing heparin and put into flasks also containing heparin. Proteins were precipitated with 10% (w/v) trichloroacetic acid and, after standing for $\frac{1}{2}$ –1 hr, filtered by suction. This was repeated three times. To the filtrate was added concentrated HCl and this solution was boiled for 90 min in a reflux air condenser, water being added to prevent desiccation. Then twice-distilled ethanol was added and the residue dried *in vacuo* on a hot water-bath. This dried residue was suspended in distilled water and filtered. This was repeated twice. The filtrate was neutralized with 0.2N NaOH and tested on a guinea-pig intestine against a standard histamine solution (1 mg/1 ml Tyrode's solution).

Results

Figure 1 shows a typical assay of an extract of pregnant mare's blood. Further details of the assay are given in the legend to the figure. Figure 2 shows the variations in blood histamine levels during pregnancy. It is seen that there is already an increase in histamine concentration in the first two months of pregnancy which is significantly different from control values at $P = 0.02$. There is a sharp decrease (to control levels) in the third and fourth months, and a slight (not significant) rise in the fifth and sixth months. However, there is a significant increase in blood histamine level in the seventh and eighth months ($P < 0.01$) and also in the ninth and tenth months of pregnancy ($P = 0.05$).

Discussion

These results agree with those reported by Kahlson and Rosengren (1968) for other species, namely that there is an increase in histamine concentration in the blood in the last third or last quarter of pregnancy. However, as we do not have data on histamine levels in mare's blood immediately after birth, we are unable to compare such levels with those of other species.

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It has already been shown by Kameswaran and West (1962), Lilja and Svensson (1967), and Kahlson and Rosengren (1968) that there is an increase in urinary excretion of histamine in the rat during the last third of pregnancy, and that this increase is maintained until the 20th day when there is a sharp drop at the time

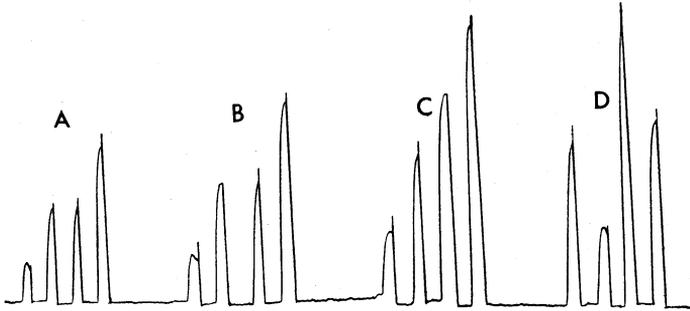


Fig. 1.—Typical assay of extract of pregnant mare's blood. Reference to each group of peaks A–D shows how the activity of such extracts compare with the activity of standard histamine solutions when tested on guinea-pig intestine. Groups A and B (from left to right): 0.5, 1 ml blood extract; 0.05, 0.1 μg histamine. Group C (from left to right): 0.5 ml blood extract; 0.05 μg histamine; 1 ml blood extract; 0.1 μg histamine. Group D (from left to right): 0.05 μg histamine; 0.5 ml blood extract; 0.1 μg histamine; 1 ml blood extract.

of birth of the young. As well as this increase in urinary excretion in the rat Kahlson and Rosengren and co-workers (1958, 1960, 1968) also reported similar increases for the mouse and the hamster during pregnancy. However, Rosengren (1963, 1965)

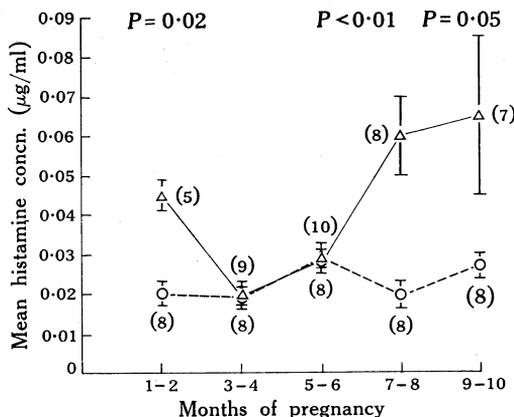


Fig. 2.—Changes in blood histamine levels during pregnancy. Δ Pregnant animals. \circ Control animals. Vertical lines indicate standard errors. Numbers in parentheses indicate the number of determinations. Significance of differences (from analysis of variance) of values for 1–2, 7–8, and 9–10 months of pregnancy are indicated.

pointed out that the mouse differed from other species studied in that there was an increase in urinary histamine excretion from the very first day of pregnancy, whereas with the hamster the increase in histamine excretion is confined to the last third of pregnancy.

The abovementioned authors suggested that this increase in histamine concentration in body fluids was due to an increase in histamine formation in the tissues, and not to an increased liberation of pre-formed histamine. The histamine-forming capacity of these tissues seems to be related to the general process of growth, since histamine formation is found to be associated with foetal, regenerative, and reparative processes (cf. Grahn *et al.* 1969).

Kameswaran and West (1962), Rosengren (1963, 1965), Maudsley (1964), Lilja and Svensson (1967), and Kahlson and Rosengren (1968) all suggest that the increased histamine production is mainly of foetal origin. However, the main site of production varies and, depending upon the species, may be the foetal liver, the foetal skin, the placenta, or even the kidneys and stomach of the mother.

Kobayashi (1964) reported increased diamine oxidase levels in rat plasma during pregnancy which decreased in the last 6 days of gestation. This would favor longer biological existence of circulating histamine of foetal origin in the mother.

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