

# Biogenetic amines in placental tissue. Relation to the contractile activity of the human uterus

## *Preliminary communication*

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*Summary:* *Object:* To examine the distribution of mast cells in human placental tissue and to analyse the interactions between mast cell mediators (histamine and serotonin (5-HT)) and contractile activity of the uterus during delivery.

*Design:* 34 placentas were examined. Histamine and serotonin levels in placental samples were estimated using fluorimetric method. Distribution of mast cells were analysed immunohistochemically on the same material.

*Setting:* Dept. of Pathophysiology, Medical Academy, Warsaw, Poland. (\*) Laboratory of Developmental Neuropathology, Centre of Experimental and Clinical Medicine, Polish Academy of Sciences, Warsaw. (\*\*) Clinic of Obstetrics and Gynecology, Second Medical Faculty, Medical Academy, Warsaw.

*Subjects:* 34 women, whose pregnancies ended in time and in preterm delivery, with normal, abnormal or without contractile activity of the uterus (elective cesarean section).

*Main outcome measurements:* Comparative charts of histamine levels in placental samples in relation to term and course of the labour.

*Results:* Concentration of histamine in placental cuts obtained from maternal surface of the placenta was significantly higher in the case of delivery without contractile activity of the uterus (elective cesarean section). Immunohistochemical identification of mast cells proved, that in regions located close to fetal surface of the placenta and in connective tissue foci, mast cells were most numerous.

*Conclusions:* It is postulated that the simultaneous release of mast cell mediators (especially histamine) in placental tissue could be an important factor for evoking contractile activity of the human uterus, initiating labour. Further investigations should give answers on the points of these dependences.

*Key words:* Placenta; Mast cells; Histamine; Contractile activity; Delivery;

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## INTRODUCTION

The mechanisms inducing contractions of the human myometrium during pregnancy, in result evoking delivery, are still well known (2, 3, 11, 13, 15). There are many theories on the release of labour (5, 11, 17). The most general seems to be of conception of multifactorial grounds in

induction contractile activity of the uterus during delivery. There are several factors affecting the gravida and the fetus during pregnancy (see figure 1). Among the placental factors, responsible for induction of labour, the role of biogenic amines (histamine and serotonin (5-HT)) in placental tissue is still widely discussed. At present, it has been suggested that placental population of mast cells might be involved in the mechanisms that control myometrium contractility. It has been proved, that mast cell mediators (histamine 5-HT) contract myometrial smooth muscle cells (<sup>4, 5, 12, 13</sup>). In pregnancy the contractile response of these amines is upregulated (increased sensitivity). Concentrations of histamine in blood serum automatically increase as pregnancy progresses, especially during the second half. Some hours after labour the histamine level in blood serum rapidly decreases. That change might be caused by a massive release of this amine during the process of parturition (<sup>12, 13</sup>).

The human placenta is a relatively rich source of histamine (<sup>10</sup>). Placental histamine derives mainly from mast cells. The distribution of mast cell in the placenta was examined in our investigation. It is very important to remember, that, different from the mast cell in the majority of experimental animals, human mast cells do not contain serotonin (5-HT). Serotonin in human placental tissue derives on the whole from circulation (<sup>3, 8, 9</sup>). In our preliminary examination the correlation between biogenic amines (histamine and 5-HT) levels in placental samples and contractile activity of the human uterus was analysed.

Table 1. — *Main factors affecting gravida and the fetus responsible for initiation uterine contractions.*

A) Maternal
B) Fetal
C) Placental
D) Uterinal
E) External (environmental).

SUBJECTS AND METHODS

Placentas were obtained from 34 women whose pregnancies differed in many respects (pregnancy duration, course of pregnancy and labour, method of delivery (spontaneous labour, cesarean section). Four homogeneous groups were formed as well as possible (see tab. 2).

#### SUBJECTS AND METHODS

Each of the placentas were carefully weighed, placento/fetal index was estimated, using planimetric methods placental volume and exchange area were calculated. Five specimens were exci-

Table 2. — *Four homogeneous groups. The cardinal criterion - the mode of delivery.*

Group	Characteristic	Number
1)	full-term pregnancy with contractile activity of the uterus	12
2)	pregnancy ending before term with contractile activity of the uterus	6
3)	cesarean section, full-term pregnancy with contractile activity of the uterus	10
4)	elective cesarean section, full-term pregnancy without contractile activity of the uterus	6

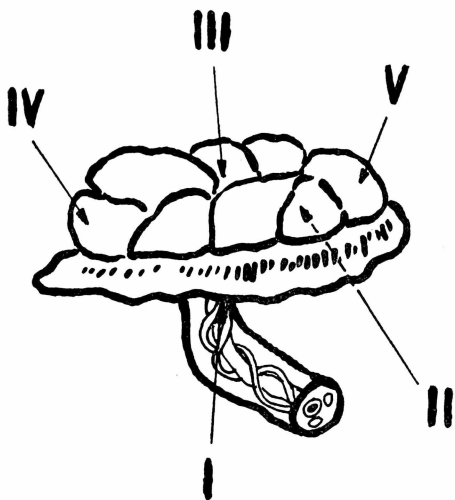


Fig. 1. — Location of samples collected from placental tissue. I, II: cuts obtained from fetal surface; III, IV, V: cuts from maternal surface.

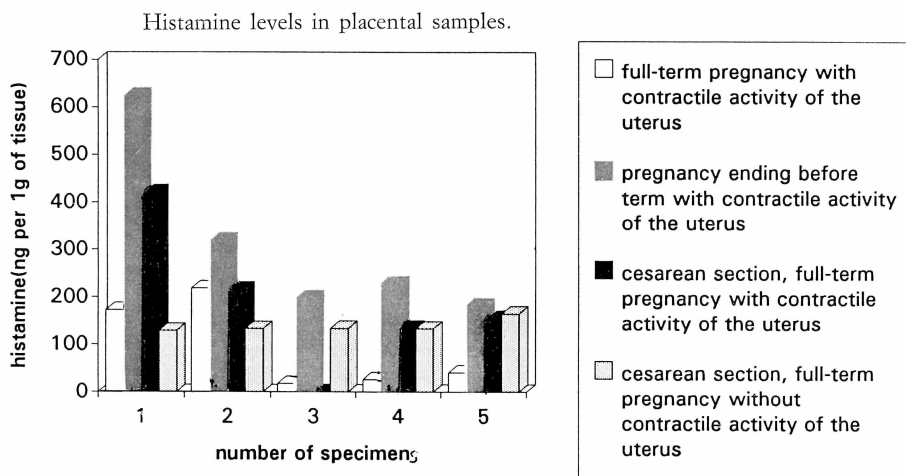


Fig. 2. — Summarized chart — in order: samples from group 1, 2, 3 and 4 (see also legend).

sed: 2 from the region contiguous to fetal surface of the placenta (the first — from place of umbilical cord insertion, the next — from peripheral region), and 3 from the region contiguous to maternal surface (the first one — from the central part the next two — from peripheral regions of the placental maternal surface (see figure 1). The samples obtained after delivery were at once frozen in carbon dioxide snow.

After homogenization histamine and 5-HT concentration were determined fluorometrically. Simultaneously, other samples were fixed in for-

malin and paraffined or frozen before straining with Toluidine blue and with thionine. Mast cells in sections were also marked by tryptase and chymase antibodies (immunohistochemically).

## RESULTS AND DISCUSSION

The estimated histamine levels are presented on the summarized chart (figure 2). Because of non-conclusive results we gave up presentation serotonin (5-HT) in this

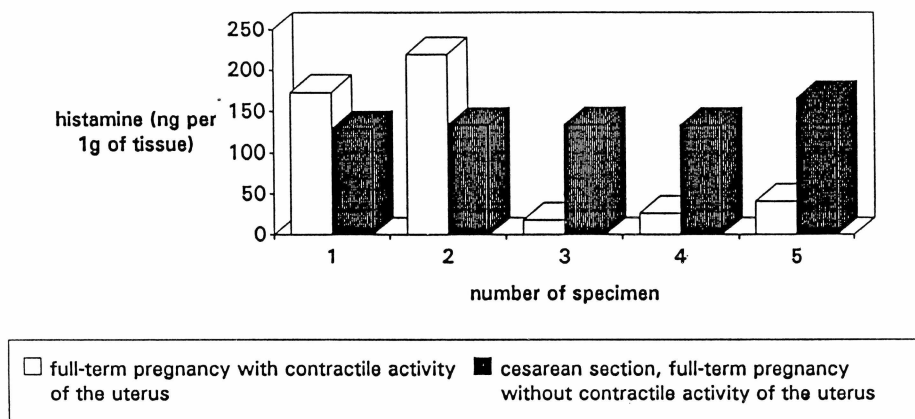


Fig. 3. — The correlation between histamine level in placental tissue and contractile activity of the human uterus.

preliminary communication. We hope that a larger number of samples will make it possible to draw conclusions in the future.

In placentas obtained from labour with normal contractile activity of the uterus histamine concentrations in samples from maternal surface were always lower, than in cuts adjacent to the fetal surface of the placenta. In material obtained after elective cesarean sections (without contractile activity), histamine levels in all of the placental samples (both from fetal and maternal surfaces) were essentially similar. Comparison of results from group number 1 and group number 4 reflects differences distinctly (see figure 3). We have to mention that these groups are as homogeneous as possible. All pregnancies ended at term, medium weight of the placentas oscillated from 635 to 660 g, exchange area and placento/fetal indices were similar. In all cases the sex of healthy children was the same (female). All women in labour were nulliparas.

In placentas from group number 3 (cesarean section, full-term pregnancy with contractile activity of the uterus) histamine levels in successive placental cuts resembled group number 1 (fullterm pregnancy with contractile activity).

Placentas obtained in result immature labour from 2nd group. Labour contractions began suddenly in healthy pregnant women (2 patients with spontaneous abortion in anamnesis), and tocolytic treatment was ineffective. Proportions of histamine concentrations in placental cuts resembling situation observed in normal labour, but levels of the amine were considerably higher in group number 2.

The immunocytochemical method revealed mast cells in all placentas. The use of specific antibodies (anti-tryptase, anti-chymase) allowed us to visualise bigger numbers of mast cells, than traditional histological staining. Immunoreactive cells corresponding to mast cells were present in great numbers particularly in regions lo-

cated close to the fetal surface of the placenta and in connective tissue foci.

Our preliminary results indicate, that the role of placental mast cells and histamine in physiological and pathological induction of labour is significant. Further investigations (more placentas examined) will allow us to present the data and results statistically. The basic question is the essence of placental histamine influence on uterine contractile activity (does histamine exerts this effect directly or indirectly?). Otherwise: whether histamine penetrates to the myometrium, or not. The mast cell population of the uterus and its role must be mentioned during the considerations. In any case, placental histamine is used during contractions of the uterus. Greater numbers of mast cells located immunohistochemically than in traditional histological staining proved partial degranulation of placental mast cells. We hope, that the continuation of our studies will make it possible to explain some of problems mentioned.

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