

creted during such a brief anoxia period is insufficient to account for the greatly increased blood pressure response to anoxia. This reaction is, therefore, under the conditions of our experiments exclusively or almost completely due to increased sympathetic discharges and not to humoral factors.

It is interesting to note that our results as to the relation of sympathetic discharges to the secretion of adrenin are similar to those of Heymans⁶ and Nowak⁷ who studied the significance of adrenin secretion for the blood pressure response in carotid sinus reflexes. They found that the rise of blood pressure following a decrease of the pressure in the carotid sinus was quantitatively unaltered by the elimination of the adrenals although it is known that under these conditions the adrenin secretion increases (Heymans,⁸ and others).

Summary. The blood pressure rise which increases in response to the inhalation of 6% oxygen when the blood sugar falls during the course of insulin hypoglycemia is not influenced by bilateral ligation of the adrenals. It is, therefore, concluded that under the conditions of our experiments an increased secretion of adrenin does not account for the greatly increased blood pressure response. The latter seems to be due to increased sympathetic discharges only.

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Concentration and Possible Significance of Histaminase in the Human Placenta.

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Occasional reports have appeared which indicate the presence of histamine and its precursors in the placenta.¹⁻⁴ This seems logical because of the amount of degenerating tissue present in the placenta during the later months of pregnancy. Since histamine may be

⁶ Heymans, C., *Compt. Rend. Soc. Biol.*, 1933, **114**, 148.

⁷ Nowak, St., *Compt. Rend.*, 1934, **115**, 1731.

⁸ Heymans, C., *Arch. internat. Pharm. Therap.*, 1929, **35**, 269.

¹ Harding, V. J., and Fort, C. A., *J. Biol. Chem.*, 1918, **35**, 29.

² Bartholomew, R. A., and Kracke, R. R., *Am. J. Obst. and Gynec.*, 1932, **24**, 797.

³ Bartholomew, R. A., and Parker, F., *Am. J. Obst. and Gynec.*, 1934, **27**, 67.

⁴ Hofbauer, J., *Am. J. Obst. and Gynec.*, 1926, **12**, 159.

formed in amounts theoretically capable of stimulating a sensitive uterus, it seemed consistent to assume that the placenta might contain appreciable amounts of the enzyme histaminase for the purpose of inactivating histamine and thereby rendering it inert as an oxytocic. When histaminase was found⁵ to be present in the human placenta in extremely variable amounts the question arose whether the enzyme content of the organ might be related to the efficiency of uterine contractions. The study was then extended, and at the conclusion of the analyses for histaminase the clinical labor histories were examined and correlated.

One hundred eighty-two placentae were used in this study. Each placenta was weighed immediately after delivery, multiple incisions were made, and the organ was then placed in acetone. From this point the preparation and assay of histaminase were conducted according to the method of Best and McHenry.⁶ The placentae were thoroughly ground and mixed before aliquots were taken for the preparation of the powders. All assays were made in duplicate. The original incubation of each placenta was conducted using 1000 mg of powder to 1 mg of ergamine acid phosphate. If inactivation occurred in both flasks, a second incubation was started using 750 mg of placenta powder to 1 mg of ergamine. If this amount was sufficient to completely inactivate the contained histamine, the amount of powder was then reduced to 500 mg, 250 mg, and so on, with reductions of 50 mg at each subsequent assay, until no inactivation occurred. The number of units of histaminase present in 1000 mg of placenta powder was then computed, and the approximate amount in the entire placenta determined. In this way it is possible to determine the approximate number of units of histaminase in a given placenta and the values obtained, though not entirely precise, are sufficiently accurate for purposes of comparison.

In Table I a *normal labor* was considered as one in which uterine contractions were of average or better than average efficiency, and in which the duration fell within the limits of error for the particular group of patients presented. In those patients in whom labor was "*induced*," one or more of the following methods was used: castor oil, enemata, quinine, and stripping or rupture of the membranes. In women who were given a *test of labor*, strong uterine contractions were allowed to progress until the obstetrician was convinced that there was disproportion sufficient to preclude delivery from below.

⁵ Danforth, D. N., and Gorham, F., *Am. J. Physiol.*, 1937, **119**, 294.

⁶ Best, C. H., and McHenry, E. W., *J. Physiol.*, 1930, **70**, 349.

TABLE I.

Labor history	No. of specimens	Avg No. of units of histaminase per entire placenta
Normal	71	Less than 31 $\pm$ 1.0
Shorter than normal, not induced	32	" " 31 $\pm$ 2.4
Induced, good response	31	" " 32 $\pm$ 3.6
Longer than normal, the contractions good	24	" " 25 $\pm$ 1.1
Caesarian section following test of labor	8	" " 26 $\pm$ 0.7
Caesarian section before onset of labor	5	More than 43 $\pm$ 2.7
Longer than normal, sluggish contractions	9	" " 45 $\pm$ 1.5
*Uterine inertia	2	110 and 198
Total specimens	182	

*These 2 specimens were obtained from women who were past term and in whom labor had started spontaneously and had continued with very poor contractions for 40 and 44 hours respectively. Dilatation of the cervix did not occur. Labor was terminated at the end of this time by Caesarian section.

When computed statistically many of the differences cited are shown to be barely significant. Because of the rather obvious grouping, however, there appears to be some correlation between the efficiency of uterine contractions during parturition and the amount of histaminase in the placenta. In those women in whom contractions were poor, excessive amounts of histaminase were found; where contractions were strong and allowed to proceed for longer than the normal time the placentae were relatively poorer in histaminase.

These findings may be interpreted in several ways. *First*, one may assume that the efficiency of the laboring uterus is inversely proportional to and dependent upon the histamine-destroying power of the uterus. As this histamine-destroying power is lost, labor may proceed unimpeded. This hypothesis would indicate that the presence of histamine is an essential for the maintenance of normal parturition, and might even point to this factor as the etiologic agent in the spontaneous onset of labor. Since histamine is known to be oxytocic and since its liberation by degenerating tissue is quite probable, such a hypothesis is not irrational. However, there are several reasons why this theory is probably untenable. Marcou⁷ has found that the blood histamine level declines steadily in the few days before labor, and does not return to normal until after delivery. If the placentae were a source of histamine in amounts sufficient to precipitate labor, one might expect a rise in the blood level before parturition. Further, we⁸ have been unable to initiate premature labor in guinea pigs and rabbits by the administration of histamine in physiologic doses. An-

⁷ Marcou, L., and Atanasiu-Vergu, *Bull. l'Acad. Med. de Roumaie*, 1937, **3**, 1.

⁸ Ivy, A. C., and Danforth, D. N., unpublished data.

other objection is that this theory does not consider those autacoids, especially estrin and progestin, which have been shown to play a major rôle in changes in uterine motility.

Second, the inverse relationship of placental histaminase to efficiency of labor pains may be due to the unknown factor or factors which initiate and promote the continuance of labor. That is, the observed changes may be an effect and not a cause.

Third, and most likely, the histaminase content of the placenta is in no way *directly* related to uterine contractions, but may be thought of rather as an index of the amount of active, functioning parenchymatous tissue in the placenta. If this interpretation is accepted, then the rôle of the placenta in the onset and maintenance of parturition becomes more apparent, and physiologic senescence is indicated as a salient, if not causal, factor in the onset and maintenance of labor.

Summary. Although the amount of histaminase in the placenta shows some correlation with the efficiency of uterine contractions, the evidence is not sufficiently definite to warrant such a conclusion.

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The Relation of Bile and Pancreatic Juice to Duodenal Ulcer in Dogs.

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Among the numerous investigators who have worked with complete external biliary fistulas in dogs, the majority¹⁻⁶ have reported a high incidence of duodenal ulcer. Puestow⁷ makes no mention of ulceration in a series of dogs with a segment of the duodenum containing the orifice of the common duct exteriorized, but he is quoted by Blanck⁵ as having stated that several of his animals died rather

¹ Berg, Johnston and Jobling *Proc. Soc. Exp. Biol. and Med.*, 1927, **25**, 334.

² Berg and Jobling, *Arch. Surg.*, 1930, **20**, 997.

³ Kim and Ivy, *J. A. M. A.*, 1931, **97**, 1511.

⁴ Hawkins and Whipple, *J. Exp. Med.*, 1935, **62**, 599.

⁵ Blanck, *Surg. Gyn. and Obst.*, 1935, **61**, 480.

⁶ Hanke, *Arch. f. klin. chir.*, 1937, **187**, 675.

⁷ Puestow, *Arch. Surg.*, 1931, **23**, 1013.