The results thus suggest that frequency facilitation is accompanied by two processes: an increase in the reserves of accessible mediator and an increase in the probability of liberation of the acetylcholine quantum. The increase in P is due to summation of the second component of facilitation whereas the increase in n is due to superposition of the first component, which follows a more protracted course during repetitive stimulation. The increase in n is evidently a process of mobilization of the mediator and is linked with preparation of acetylcholine quanta for liberation, whereas the increase in P is associated with activation of the secretion mechanism on account of an increased rate of Ca^{++} inflow into the nerve ending.

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BIORHYTHM OF THE PARTIAL PRESSURE OF OXYGEN IN UTERINE AND FETAL TISSUES

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It has long been known that the body exhibits great resistance to hypoxia and anoxia during antenatal and early postnatal periods of development [6, 9, 11, 12, 16]. The cause of this phenomenon has not yet been explained. Some workers attribute the increased tolerance to differences in the energy metabolism of newborn infants, to which an important relative contribution is made by anaerobic glycolysis [15, 18]. Other workers consider that neonatal tissues have a low level of oxidative metabolism [17]. The glycogen content in the heart and liver of newborn infants also is known to be 10 times higher than in the adult [5, 14]. However, the mechanism of stimulation of reactions which readjust the metabolism of the fetus in order to maintain its viability under conditions of oxygen lack has never been explained. Now, after much research, it has been shown that preliminary training under conditions of moderate hypoxia increases the resistance of the body to more severe hypoxia and to various other pathogenic factors [3, 4, 7, 8, 10]. The resistance of the body has been shown to be increased irrespective of the conditions of creation of hypoxia, i.e., it is independent of whether the hypoxic state is continuous for a certain period of time or whether it is induced by repeated short exposures to oxygen insufficiency [1].

The uterus in sexually mature animals is known to exhibit continuous contractile activity. During pregnancy considerable contractile activity of the uterus, both isotonic and isometric, also is observed [2]. There are data in the literature on the partial pressure of oxygen (pO_2) in the tissues of the uterus and fetus, which show that pO_2 falls during each contraction, even if only for short duration [13]. The biological significance of the

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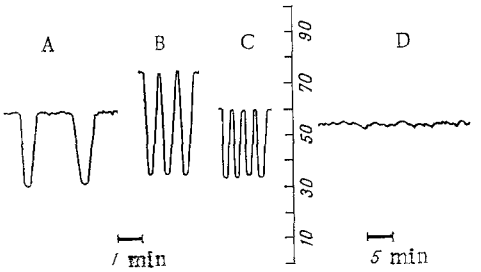

Fig. 1. Values of pO_2 in tissues of uterus, intrauterine fetus, and intestine of rats (in hPa). A) In nonpregnant uterus; B) in uterus at 3rd-5th days of pregnancy; C) in tissues of intrauterine fetus, at the 13th-14th days; D) in wall of small intestine.

periodic fall in pO_2 in uterine and fetal tissues during contractions has not hitherto been discussed.

In the investigation described below changes in pO_2 of the uterus and fetus were compared with values of pO_2 in the tissues of smooth-muscle organs exhibiting continuous involuntary contractile activity (intestine).

EXPERIMENTAL METHOD AND RESULTS

The experimental animals were 77 mature Wistar rats, anesthetized with pentobarbital sodium (35 mg/kg). The value of pO_2 was determined in the tissues of the uterus, the intrauterine fetus, and the maternal intestine by a polarographic method, using a copper amalgam and cadmium electrode pair. Values of pO_2 were recorded on PO-4 (Denmark) and LP-7e (Czechoslovakia) polarographs. In some experiments pO_2 in the uterine wall and intestine was determined synchronously, and at the same time in the myometrium of different parts of the uterus.

It was shown polarographically that the pO_2 level in the myometrium of the rats fluctuated rhythmically during spontaneous contractions of the nonpregnant uterus from 59.7 ± 2.2 to 30.9 ± 1.8 hPa, i.e., it was reduced by 51.7%. The time from the fall in pO_2 from its maximal to its minimal value and to complete recovery of its initial level (which we called the "hypoxic cycle") averaged 45.9 ± 2.9 sec. The mean frequency of the hypoxic cycles was 0.63 ± 0.07 cycle/min (Fig. 1).

On the 3rd-5th days of pregnancy the pO_2 level in the uterine tissues fluctuated rhythmically between 75.4 ± 3.9 and 33.1 ± 2.9 hPa. The hypoxic cycle averaged 28.4 ± 2.3 sec and the frequency of the cycles was 1.47 ± 0.14 cycle/min. Comparison of these results with those obtained in the nonpregnant uterus shows that the maximal values of pO_2 were 26.3% higher, and that a rhythmic fall to 43.9% was observed 2.3 times more often. The pattern of rhythmic fluctuation of pO_2 in the tissues of the 13-14-day fetus was similar. The maximal value of pO_2 averaged 60.1 ± 3.6 hPa and the minimal 32 ± 5.2 hPa, i.e., the decrease amounted to 53.4%. Hypoxic cycles in the fetal tissues were observed 2.9 times more often than in the uterus of the nonpregnant rats, with a frequency of 1.98 ± 0.3 cycle/min. The duration of the hypoxic cycle was shorter than in the uterus of nonpregnant rats, namely 19.8 ± 1.9 sec. If the duration of the reduced pO_2 in the myometrium of nonpregnant rats and of the fetus was analyzed over a period of 1 min, its mean value in the uterus was 28.9 sec and in the fetal tissues 39.2 sec, i.e., the fetus was in state of moderate hypoxia for well over half the time. When pO_2 was recorded in the wall of the small intestine its level remained stable throughout the period of investigation (up to 30 min), despite clear peristaltic activity, with a mean level of 54.5 ± 2.2 hPa (Fig. 1).

The rhythmic decrease in pO_2 discovered in the uterine and fetal tissues, giving rise to periodic hypoxia, may evidently be a physiological stimulator of metabolic reactions leading to increased resistance of the fetus to hypoxia. It is also possible that the periodic fall in pO_2 in the uterine tissues may be a genetically determined physiological mechanism, acting outside and also during pregnancy, aimed at increasing the nonspecific resistance of the uterus and fetus to various pathogenic factors. Since the functional activity of the

pregnant uterus is accompanied by a rhythmic fall in the oxygen concentration in its tissues and also, as we know, by significant general hemodynamic changes in the body, it can be tentatively suggested that the pO_2 biorhythm in the uterine tissues during pregnancy may be a factor increasing the nonspecific resistance of the mother. Since a biorhythm of pO_2 fluctuations also is observed in the nonpregnant uterus, the possibility cannot be ruled out that a similar mechanism of active increase in resistance may occur outside pregnancy also.

The presence of an active biorhythm of adaptation peculiar to women (as opposed to men) may perhaps be connected with the greater viability (including a longer life span) of women and their increased functional resistance to various unfavorable influences.

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