ACID-BASE BALANCE OF THE URINE IN PREGNANT RABBITS WITH NORMAL AND PATHOLOGICAL FETAL DEVELOPMENT

M. G. Nemets

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Investigations conducted in the author's laboratory have shown that the provision of conditions for normal intrauterine development is regulated by means of dominant mechanism in the central nervous system, described as the gestation dominant. Inhibition of the gestation dominant leads to pathological types of intrauterine development, including physiological immaturity of the newborn animal [1-3, 5, 6]. Under the influence of the gestation dominant formed in the mother, a group of physiological transformations takes place. The most important of these are, first, gravidic changes in the uterus, and second, metabolic changes. Special investigations have shown that the latter group include disturbances of acid-base balance (an increase in the blood pH). When the gestation dominant in pregnant animals is inhibited, an uncompensated acidosis develops. In connection with the discovery of these changes in the acid-base balance it is important to analyze the state of the acid-base in the urine during normal pregnancy and during inhibition of the gestation dominant.

The object of the present investigation was to study the titratable acidity and alkalinity, the ammonia concentration, and the pH of the urine. From the results of titration the acid-base coefficient of the urine was calculated by dividing the titratable alkalinity.

EXPERIMENTAL METHOD

Chinchilla rabbits were kept in specially built metabolism cages for collecting the urine. After micturition,the urine of these rabbits passed through the perforated floor and then through a metal grating and filter paper, where it was purified and filtered, and it was collected in a receiver containing xylol to act as preservative and to prevent fermentation of the urea [7]. For the analyses 24 h samples of urine were collected (for 2 days) and their volume was measured and recorded. Samples of 10 ml were taken from the total volume of the 24 h urine for titration. Acidity was titrated with 0.1 N NaOH solution using phenolphthalein in a 0.5% solution in water and alcohol as indicator [4]. Before titration neutral potassium oxalate was added to the urine to prevent decomposition of the ammonium salts. The alkalinity was titrated with 0.1 N HCl solution using methyl orange in a 1% aqueous solution as indicator.

Ammonia in the urine was determined by Conway's micromethod [2] modified for a photoelectric colorimeter. The calibration scale was plotted for ammonium sulfate. Each ammonia determination was carried out on not less than three samples of two successive 24 h volumes of urine. The results were analyzed only if identical values were obtained with the different samples. The pH of the urine was measured by means of a potentiometer using the LP-5 system.

Investigations of the gestation dominant and of its inhibition have led to the introduction of a special method of analysis [2, 5, 6], and this was used in the present investigation. It is described below. The parameters for investigation were determined in rabbits before pregnancy, then in pregnancy terminating by birth of physiologically mature newborn offspring and, finally, during pregnancy terminating spontaneously by stillbirth, or by birth of living but physiologically immature newborn offspring. Later, in a special series of experiments, stillbirths and birth of physiologically immature offspring were reproduced experimentally by inhibition of the gestation dominant, which was done by means of a technique of formation of experimental neurosis used in the author's laboratory and described previously [2, 5,6]. After birth of the offspring of these females the physiological state of the living offspring was investigated in the neonatal

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Titratable Acidity (T. A.), Titratable Alkalinity (T. Alk.), Acid Base Coefficient (A. B. C.), and Urine Ammonia Concentration in Nonpregnant and Pregnant Rabbits (M ± m)

Group of animals	Period of pregnancy	$\frac{\text{T. A.}}{\text{T. Alk.}}$ in mg%	Differences between means	P*	A. B. C.	Ammonia (in mg%)
Nonpregnant rabbits (70)†		$\frac{107\pm8,0}{440\pm22}$			0,26	6,2±0,7
Pregnant rabbits, giving birth to physiologically mature offspring (27)	I third	$\frac{48\pm6,8}{450\pm28,0}$	$\frac{59}{10}$	<0,05 >0,05	0,10	6,0±0,5
	II third	$\frac{53\pm5,6}{570\pm35,0}$	$\frac{54}{130}$	<0,05 <0,05	0,09	6,5±0,6
	III third	$\frac{55\pm6,0}{580\pm30,0}$	$\frac{52}{140}$	<0,05 <0,05	0,09	6,0±0,5
Pregnant rabbits giving birth to dead and physiologically immature offspring (27)	I third	$\frac{106\pm14,0}{324\pm25,0}$	$\frac{58}{126}$	<0,05 <0,05	0,32	6,1±0,6
	II third	$\frac{102\pm14,0}{280\pm35,0}$	$\frac{49}{290}$	<0,05 <0,05	0,36	5,9±0,4
	III third	$\frac{185\pm29,0}{300\pm29,0}$	$\frac{130}{180}$	<0,05 <0,05	0,62	6,5±0,5

*P is calculated for rabbits with normal pregnancy relative to nonpregnant animals, and for rabbits with pathological pregnancy relative to animals with normal pregnancy.

†The number of animals in the group is shown in parenthesis.

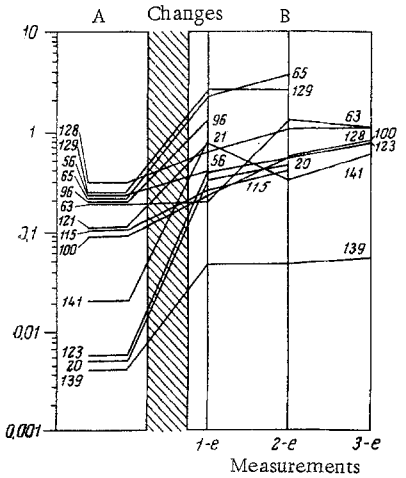

Fig. 1. Acid-base coefficient in pregnant rabbits before (A) and after (B) experimental neurosis. The values are plotted in a logarithmic scale along the ordinate.

period and during subsequent postnatal ontogenesis until sexual maturity. The diagnosis of physiological maturity or immaturity was made on the basis of the results of this investigation.

EXPERIMENTAL RESULTS

The results obtained are given in the table. The titratable acidity of the urine during normal pregnancy was practically identical in all three periods (thirds) of pregnancy, but was much lower (approximately by half) than before pregnancy. The titratable alkalinity of the urine during normal pregnancy was higher than in the nonpregnant state, starting with the 2nd third (by about 30%). These changes are reflected in the acid-base coefficient, which fell significantly throughout pregnancy (by 2.6 times in the 1st third and by 2.9 times in the next). No significant differences were found in the excretion of ammonia in the urine either in the course of pregnancy or when this index was compared in the pregnant and nonpregnant rabbits.

During pregnancy terminating by stillbrith and by birth of physiologically immature offspring, compared with normal pregnancy, a significant increase was found in the mean titratable acidity of the urine (particularly marked during the last third)

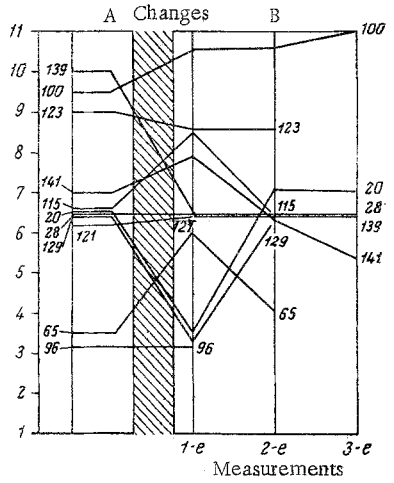

Fig. 2. Concentration of ammonia (in mg%, ordinate) in the urine of pregnant rabbits before (A) and after (B) experimental neurosis.

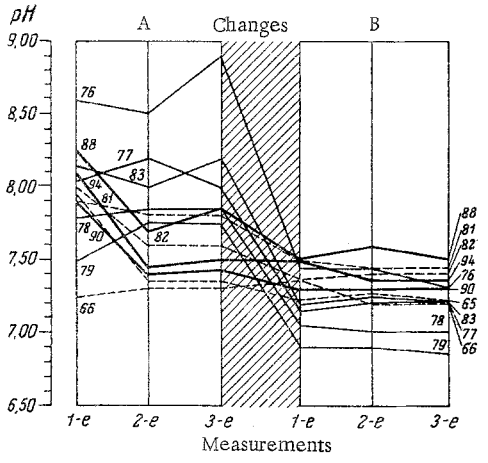

Fig. 3. pH of urine in the last 10 days of pregnancy and 40-60 days after parturition (B). Legend: ——birth of physiologically mature, ----- birth of physiologically immature and dead fetuses, ——experimental neurosis.

associated with a decrease in the titratable alkalinity. This led to a considerable increase in the acid-base coefficient of the urine (by about 7 times in the last third of pregnancy). The excretion of ammonia in the urine in this group of pregnant animals was essentially indistinguishable from that in the proceding group throughout the course of pregnancy.

The results of the experiments on the pregnant rabbits with experimental neurosis in the pregnant females the acid-base coefficient of urine rose sharply as a result of an increase in the titratable acidity and a decrease in the titratable acidity and a decrease in the titratable alkalinity. The increase in this coefficient was so large, that in some experiments it actually exceeded unity. The excretion of ammonia in the urine showed no consistent changes in these circumstances.

In a special series of experiments carried out along the same lines as the previous series, the pH of the urine was determined during pregnancy and in nonpregnant rabbits. The distinguishing feature of these observations was that the pregnant and nonpregnant states were compared in the same rabbit by carrying out the investigation before and after parturition—on the 40th-60th day, i.e., after the end of lactation. It is clear from Fig. 2 that in the pregnant animals giving birth to physiologically mature offspring the pH of the urine during pregnancy before parturition was higher than after parturition. During pregnancy terminating by stillbirth or by the birth of physiologically immature offspring, this difference was less marked or absent altogether. After the creation of an experimental neurosis in the pregnant females, the pH of the urine fell (Fig. 3).

Normal pregnancy is thus characterized by a decrease in the titratable acidity, an increase in the titratable alkalinity, a sharp decrease in the acid-base coefficient, and an increase in the pH of the urine. During a disturbance of intrauterine development, the opposite changes are observed. No consistent changes were found in the excretion of ammonia with the urine of the pregnant rabbits, whether in normal conditions or during acidosis characterizing inhibition of the gestation dominant. The fact that the excretion of ammonia with the urine of the rabbits is unchanged both when the acid-base balance is displaced to the alkaline side in normal pregnancy and during acidosis in the case of a pathological pregnancy, suggests that these herbivorous animals lack a well-developed homeostatic ammonia-forming mechanism of the kidneys. This evidently largely explains the tendency toward the development of uncompensated acidosis by rabbits when pregnancy is disturbed. The absence of the ammonia-forming homeostatic mechanism, and also of other protective mechanisms during pregnancy, distinguishes this species of animal from man because of its greater predisposition toward inhibition of the gestation dominant by the action of stress factors [2, 3, 6].

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