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Research Article

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Potassium Deficiency in the Pregnant Dog *

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Stewart and Welt (1) reported that the induction of potassium depletion in pregnant rats did not result in a fetal potassium deficit. Two alternative hypotheses were offered to explain the sparing of the fetus. First, there might be some form of active transport resulting in the transfer of potassium from mother to fetus. Second, the usual gradient for potassium between extracellular and cellular fluid might be so much greater in the fetus that the concentration of potassium in fetal plasma is lowered, thus establishing a downhill chemical gradient from maternal arterial to fetal plasma. In the first instance, there should be an uphill chemical concentration gradient for potassium between the maternal and fetal circulations; in the second circumstance, one would anticipate the reverse. Either of these explanations could have been valid in the earlier study (1) and not been detected, since total fetal carcass was analyzed, and small but significant changes in the extracellular concentration of potassium would have been masked.

This study was therefore undertaken in dogs to examine the relationship between the concentrations of potassium in maternal and fetal serum shortly before term in animals that were ingesting either a normal diet or one that was complete except for the omission of potassium.

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Materials and Methods

Female beagle dogs ranging in weight from 7 to 9 kg were mated on 3 consecutive days with a male of the same strain, approximately 7 to 10 days after the initiation of the oestrual period. On the second day of breeding, a sample of venous blood and a muscle biopsy were obtained to estimate the concentrations of electrolytes in serum and muscle before pregnancy. The control animals were provided with a diet recommended by Albritton (2) that contained all the nutritional components in adequate quantities. The animals in the experimental group received the same diet but with the omission of potassium beginning on the first day after mating.

Approximately 3 to 4 days before the expected date of whelping, the pregnancies were terminated by Caesarean section with sodium pentobarbital as the general anesthetic. Prior to the section, a Cournand needle was placed in a maternal femoral artery. In the first studies the animals were permitted to breathe naturally. Because of the possibility that hypoxia might develop, the remainder of the studies were performed using an endotracheal tube and a pump-respirator employing room air or oxygen. There were no apparent differences among the two groups of animals.

After the uterus was exposed, each amniotic sac was visualized by separate transverse incisions. The amniotic membrane was opened; the fetus was extracted and wrapped in a warm, wet cloth to prevent vasoconstriction of the umbilical vessels. Blood samples were then obtained simultaneously from the umbilical artery and vein and from the maternal femoral artery. Muscle tissue was taken from the mother, and the puppies were used for total carcass analysis.

Sodium and potassium analyses were made with a standard internal flame photometer, chloride with a Cotlove chloridometer (3), and total CO_2 content by the method of Van Slyke and Neill (4). The muscle tissue and carcass were prepared as described previously (5).

The statistical analyses employed the following equation when differences between maternal femoral arterial and umbilical vein blood were evaluated:

$$t = \frac{\bar{d}}{\sqrt{\left(\Sigma\left(\frac{d_i^2}{n_i}\right) - \frac{\Sigma d^2}{n_i}\right)\left(\frac{1}{n_i} \times \frac{1}{B-1}\right)}},$$

where t refers to the t test, $\bar{d}$ represents the mean of all the differences, d_i represents the sum of the differences between the fetuses and a single bitch, n_i represents the number of

TABLE I

Analyses of maternal serum and muscle

Group	Serum				Muscle				
	K	Na	Cl	CO_2	K	Na	Cl	Na_i*	H_2O
	mmoles/L				*mmoles/100 g FFDS*†				*g*
Control, prepregnant (5)‡	4.3	150	112.6	25	35.4§	15	11	1.7	335
Control, at term (5)	4.1	146	112	21	39.5	13	9.8	1.6	344
Experimental, prepregnant (6)	4.1§	145	111	23.7‖	36.1§	15.3‖	11.3	2.0§	350¶
Experimental, at term (6)	2.7	145	113	20.3	28.4	20	9.3	9.2	329

* Na_i = intracellular sodium.
† FFDS = fat-free dry solids.
‡ Numbers in parentheses refer to the number of animals in the group.
§ Statistically significant at p = <0.01. The designation of statistical significance refers to paired groups.
‖ Statistically significant at p = <0.05.
¶ Statistically significant at p = <0.02.

observations of differences between fetus and bitch, and *B* represents the number of bitches.[1]

In other instances the *t* was computed by the standard formula for pooled variance.

Results

The prepregnant and at-term values for the control bitches were not different from each other, except that the muscle potassium content was higher at term (Table I). In contrast, the experimental bitches had the classical chemical hallmarks of potassium depletion—hypokalemia, a depressed content of muscle potassium, and an increase in calculated intracellular sodium. Table II shows the significant difference in the concentrations of potassium between the maternal arterial and the fetal umbilical vein blood, a difference even among the control animals but markedly exaggerated in the case of the potassium-depleted bitches. In this latter instance the mean concentration of potassium in umbilical vein serum was twice that of the mean value for the maternal arterial serum. These data are also presented in Figures 1 and 2.

Among other significant dissimilarities, there are clear differences between the concentrations of chloride in the serum of umbilical blood and the maternal arterial serum. In this instance, however, the concentration gradient is from the maternal to the fetal circulation. The magnitude of the difference in the concentrations of chloride is not, however, greater in the control than in the potassium-depleted group. The total CO_2 con-

[1] The authors are indebted to Dr. J. E. Grizzle of the Department of Biostatistics, School of Public Health, University of North Carolina, for this formula. It permits a more rigid analysis of the data; since the number of fetuses per bitch was different, the formula permits an evaluation of the variance due to the bitches.

TABLE II

Maternal and fetal serum electrolyte concentrations

Group	Specimen	Serum			
		K	Na	Cl	CO_2
		mmoles/L			
Control*	Maternal femoral artery	4.1†	146	112†	21
	Umbilical vein	5.3	147	106	25‡
	Umbilical artery	5.1	149	107	28.5
Experimental*	Maternal femoral artery	2.7†	145	113*	20.3‡
	Umbilical vein	5.4§	144	108.5	24.5
	Umbilical artery	5.9	145	108.5	26

* See Figures 1 and 2.
† Statistically significant at p = <0.01. Statistical comparisons are between maternal femoral arterial and umbilical vein sera in the appropriate groups, unless a different pairing is indicated.
‡ Statistically significant at p = <0.02.
§ Statistically significant at p = <0.05.

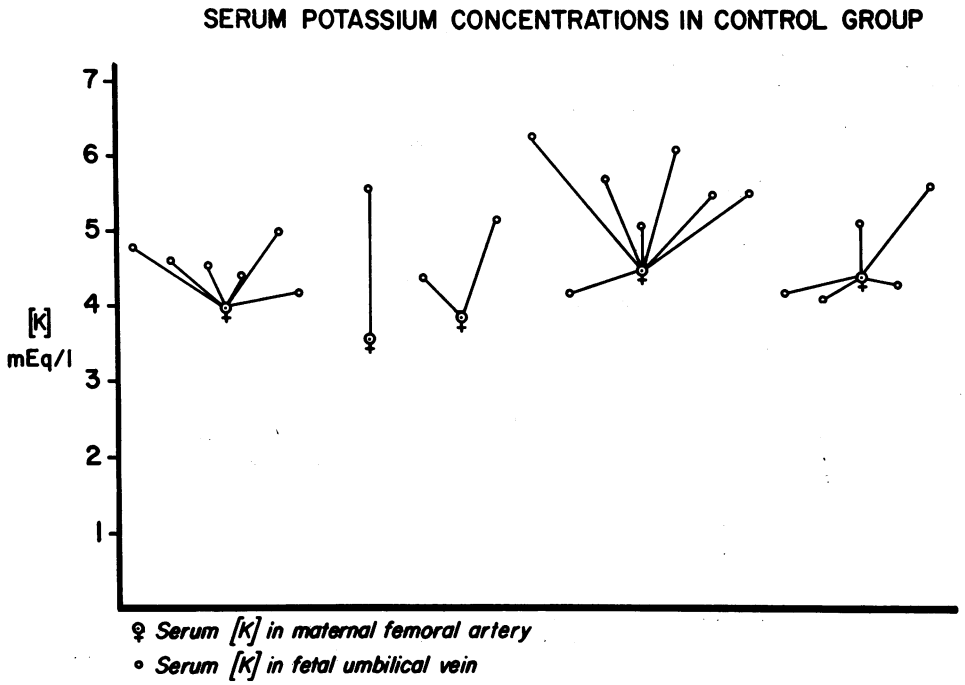

FIG. 1. CONCENTRATIONS OF POTASSIUM IN SERUM OF THE MATERNAL FEMORAL ARTERY AND OF THE FETAL UMBILICAL VEIN AMONG THE CONTROL BITCHES AND THEIR PUPPIES.

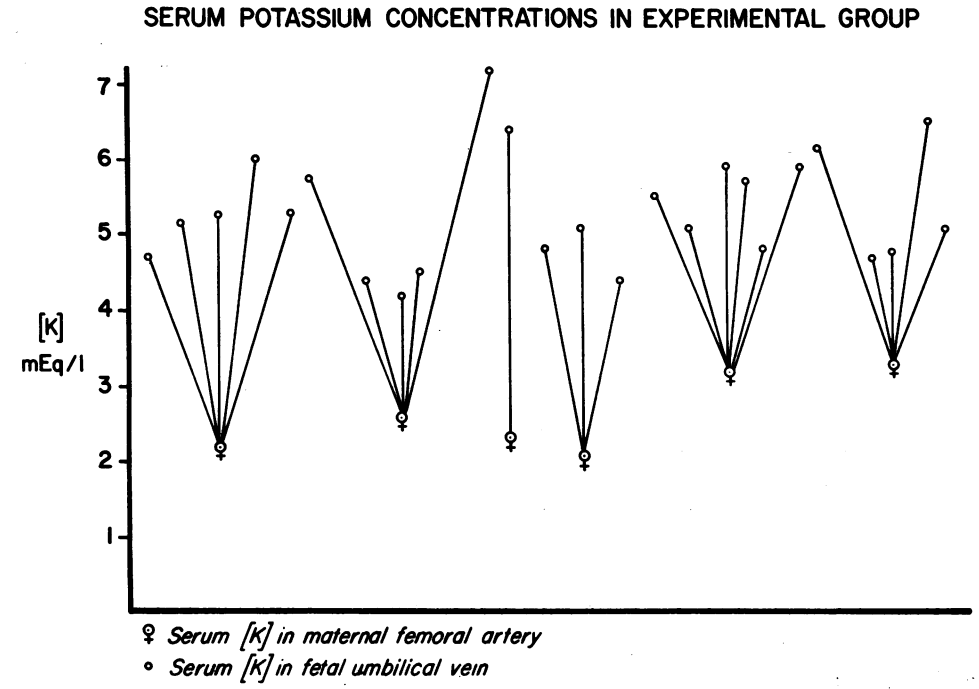

FIG. 2. CONCENTRATIONS OF POTASSIUM IN SERUM OF THE MATERNAL FEMORAL ARTERY AND OF THE FETAL UMBILICAL VEIN AMONG THE POTASSIUM-DEPLETED BITCHES AND THEIR PUPPIES.

TABLE III

Potassium content of fetal carcass, fetal dry weight, and litter size

Group	Fetal carcass K		Fetal dry wt	Litter size
	mmoles/100 g FFDS	*mmoles/ carcass*	*g*	*no.*
Control (5)*	35.8	9.5	27	4.4
Experimental (6)	35.6	9.4	26.4	4.2

* Numbers in parentheses refer to the number of animals in the group.

tent of umbilical serum is higher than that of the maternal serum in the experimental but not in the control group.

There are also a few differences between umbilical vein and umbilical artery. In the experimental group there is a higher concentration of potassium in the umbilical artery, but this is of borderline significance; in the control group there is a higher total CO_2 content in the umbilical artery.

There are no differences in the potassium content of the fetuses when expressed in terms of unit weight of fat-free dry carcass solids or total carcass, nor is there a difference in the dry weight of the fetuses, nor in the size of the litters (Table III).

Discussion

The canine fetus is clearly spared the potassium depletion induced in the mother. In addition, there is an uphill chemical concentration gradient for potassium between the maternal and fetal side of the placental circulation; that this gradient can be of striking proportions is seen in the dogs that were deficient in potassium. These data strongly suggest the interposition for this ion of some form of active transport involving unknown components of the placental structure. The gradient of the difference in the levels of chloride between these two circulations is in an opposite direction. The magnitude of the difference is, however, the same in the experimental as in the control group, despite the marked difference in potassium concentrations in the former, suggesting that these two gradients of opposite direction and charge are not directly interrelated.

Conceivably, the higher concentration of potassium in the umbilical vein than in the maternal arterial serum is a consequence of hypoxia of the placenta and a movement of cellular potassium to an extracellular position. To circumvent this possibility, adequate respiration was assured with a pump-respirator in the majority of the experiments. Furthermore, if there had been any significant hypoxia of placental tissue, it should have been even more striking in the fetal tissue and been reflected in more significant changes in potassium and CO_2 content between umbilical vein and umbilical arterial blood. In fact, in the control group there was a small though significant change in total CO_2 content, and in the experimental group there was only a borderline difference in the level of potassium in the two sera. These alterations do not support the suggestion that hypoxia was responsible for the higher levels of potassium in the umbilical vein blood.

There are, of course, other examples of active transport of materials between the maternal and fetal circulations. Among these are sugars, amino acids, iron, and water-soluble vitamins. These are all discussed in an excellent review of this problem (6), but in no instance has a specific mechanism been isolated and studied.

Summary

Potassium depletion was readily induced in pregnant bitches by feeding a diet deficient in this cation. This deficit of potassium did not interfere with the pregnancy in terms of size of litter or the viability and weight of the fetuses. There was no evidence that the fetuses of potassium-deficient bitches were depleted of this ion. There was a significant uphill chemical concentration gradient for potassium across the placentae of both control and experimental animals from mother to fetus. This was most striking in the case of the potassium-depleted bitches. There was a downhill chemical concentration gradient for chloride from maternal serum to fetal serum that was of the same magnitude in both groups of animals. The results of this study strongly suggest the probability of an active mechanism for the transport of potassium from mother to fetus.

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