

# EXPERIMENTAL INVESTIGATION OF KANAMYCIN CIRCULATION BETWEEN MOTHER AND FETUS

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UDC 612.649:612.388]:615.332  
(Kanamycin)

Kanamycin passes through the placenta of albino rats in comparatively small amounts. The permeability of the placenta is practically the same on the 16th and 20th days of pregnancy. The kanamycin concentration in the tissue juice or blood serum of the fetuses reaches a maximum 2-3 h after administration of various doses of the antibiotic, its level being 7-21 and 28-31% respectively of the concentration in the maternal blood serum. The kanamycin concentration in the tissue juice and serum of the fetuses 6 h after administration is 1.4-3.4 times higher than its concentration in the maternal blood serum.

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The placental barrier is permeable to some degree to all antibiotics used in medical practice [1, 4-14]. Since kanamycin, a tuberculostatic preparation of the 2nd order, may be given to pregnant women with tuberculosis for long periods, it seemed advisable to study the permeability of the placental barrier for this antibiotic.

## EXPERIMENTAL METHOD

Permeability of the placental barrier to kanamycin was investigated in 82 female albino rats on the 16th (at the end of the period of placentation) and 20th days of pregnancy (at the end of development of the mature placenta). Kanamycin sulfate was injected subcutaneously into the pregnant rats in a single dose of 150 mg/kg (expressed as base) 30 min and 1, 2, 3, and 6 h before sacrifice. To study the relationship between permeability of the placenta and dose of antibiotics, kanamycin was injected into the pregnant rats subcutaneously in doses of 15, 45, 150, and 400 mg/kg 3 h before sacrifice. The kanamycin concentration in the blood serum of the pregnant rats and 20-day fetuses and also in the tissue juices of 16- and 20-day fetuses was determined by the agar diffusion method at pH 7.8-8.0. The test organism was *Bacillus subtilis* L<sub>2</sub> (spores).

## EXPERIMENTAL RESULTS

As Table 1 shows, after injection of kanamycin into pregnant rats in a dose of 150 mg/kg, the concentration of the antibiotic in the maternal serum reached a maximum after 30 min, and in the tissue juices and blood serum of the 16- and 20-day fetuses, after 2-3 h. The maximal kanamycin concentration in the blood serum of the 20-day fetuses and in the tissue juices of the 16- and 20-day fetuses was 3, 7, and 15 times respectively less than that in the blood serum of the pregnant rats at this period. The concentration of the antibiotic in the fetal tissue juices and blood serum 6 h after injection of this dose was 1.4-3.4 times greater than its concentration in the maternal blood serum. The kanamycin concentration in the serum of 20-day fetuses in the first 6 h of observation was approximately twice that in the tissue juices. The degree of permeability of the placenta to kanamycin was practically the same on the 16th and 20th days of pregnancy.

The study of the relationship between placental permeability and dose of kanamycin at the period of maximal concentration of the antibiotic in the fetus showed that if kanamycin was given to pregnant rats in a therapeutic dose (15 mg/kg) practically no antibiotic could be detected in the tissue juices of the fetus. The kanamycin concentration in the blood serum of 20-day fetuses was only 13% of its concentration in the maternal blood serum. With an increase in dose of the antibiotic to 45, 150, and 400 mg/kg its concentra-

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Department of Chemotherapy, Institute for the Search for New Antibiotics, Academy of Medical Sciences of the USSR, Moscow (Presented by Active Member of the Academy of Medical Sciences of the USSR Z. V. Ermol'eva). Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 66, No. 9, pp. 59-62, September, 1968. Original article submitted June 6, 1967.

TABLE 1. Dynamics of Kanamycin Concentration in Blood Serum of Pregnant Rats and Fetuses and in Tissue Juices of Homogenized Fetuses after Subcutaneous Injection on 16th Day of Pregnancy in a Dose of 150 mg/kg

Time when animal sacrificed after beginning of pregnancy (in days)	Material tested	Concentration of kanamycin (in $\mu\text{g/ml}$ ) at times after injection given below				
		1/2 h	1 h	2 h	3 h	4 h
16	Maternal blood serum	$327.0 \pm 36.30$ (226.8-428.6)	$237.6 \pm 36.60$ $143.5 \pm 331.7$	$93.3 \pm 18.00$ (37.0-139.5)	$33.7 \pm 8.10$ (11.2-56.2)	$2.5 \pm 0.52$ (1.0-3.9)
	Fetal tissue juices	$1.9 \pm 0.44$ (0.35-3.07)	$4.2 \pm 0.76$ (2.25-6.14)	$6.2 \pm 0.59$ (4.63-7.67)	$4.5 \pm 0.83$ (2.15-6.75)	$4.2 \pm 0.71$ (2.25-6.19)
20	Maternal blood serum	$276.0 \pm 28.5$ (197.0-355.0)	$244.5 \pm 29.40$ (168.7-319.9)	$134.9 \pm 14.4$ (97.9-171.9)	$44.5 \pm 10.4$ (19.01-19.97)	$1.3 \pm 0.21$ (0.59-1.93)
	Fetal tissue juices	$1.0 \pm 0.36$ (0.04-2.04)	$2.7 \pm 0.62$ (1.14-4.35)	$5.6 \pm 0.54$ (4.24-7.02)	$6.1 \pm 0.78$ (4.18-8.00)	$1.8 \pm 0.31$ (0.99-2.71)
	Fetal blood serum	$2.8 \pm 0.52$ (1.35-4.25)	$5.9 \pm 1.29$ (2.68-9.22)	$10.9 \pm 1.40$ (6.30-14.50)	$14.0 \pm 2.70$ (7.06-20.94)	$4.4 \pm 0.74$ (2.34-6.46)

Note. Here and in Table 2 results of statistical analysis of data of 5-8 determinations are given. Confidence limits for  $P = 0.05$  are given in parentheses [2].

TABLE 2. Kanamycin Concentration in Blood Serum of Pregnant Rats and Fetuses and Also in Tissue Juices of Fetuses 3 h after Subcutaneous Injection on 16th and 20th Days of Pregnancy in Doses of 15, 45, 150, and 400 mg/kg

Time when animal sacrificed after beginning of pregnancy (in days)	Material tested	Dose 15 mg/kg				Dose 45 mg/kg				Dose 150 mg/kg				Dose 400 mg/kg			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
16	Maternal blood serum	$1.36 \pm 0.4$ (0.38-2.34)				$3.70 \pm 0.81$ (1.45-5.95)				$33.72 \pm 8.10$ (11.20-56.24)							
	Fetal tissue juices	Traces				$0.78 \pm 0.09$ (0.52-1.04)				$4.45 \pm 0.83$ (2.15-6.75)							
20	Maternal blood serum	$1.09 \pm 0.3$ (0.67-1.51)	100			$7.14 \pm 0.60$ (5.2-8.97)				$44.49 \pm 10.4$ (19.01-69.97)							
	Fetal tissue juices	0				$0.47 \pm 0.1$ (0.17-0.76)				$6.09 \pm 0.78$ (4.18-8.00)							
	Fetal blood serum	$0.14 \pm 0.03$ (0.07-0.21)	13			$1.97 \pm 0.16$ (1.53-2.41)				$14.0 \pm 2.7$ (7.06-20.94)							

Note. 1) Kanamycin concentration in  $\mu\text{g/ml}$ , 2) in percent of concentration of antibiotic in maternal blood serum.

tion in the maternal blood serum on the 20th day of pregnancy increased by 7, 44, and 170 times, and in the fetal blood serum by 13, 100, and 290 times respectively. With an increase in dose of kanamycin, the permeability of the placenta thus increased to a greater degree than the concentration of the antibiotic rose in the maternal blood serum (Table 2).

Kanamycin thus passes through the placental barrier in small quantities, and its toxicity for the fetus can thus be considered to be lower than for the mother.

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