

Do Heterologous Proteins Pass from Mother to Fetus in Cow, Cat and Guinea Pig? (27998)

ABRAHAM C. KULANGARA* AND A. M. SCHECHTMAN† (Introduced by J. D. Ebert)

Department of Zoology, University of California, Los Angeles

There is increasing evidence for the passage of serum albumin as well as gamma globulin from the maternal circulation into that of the fetus in some mammals. However, evidence for the passage of albumin is limited to species that are known to pass antibodies to the young before birth. Thus, human and bovine serum albumins injected intravenously into pregnant rabbits are found in the fetal blood and in the contents of exocoelom, amnion, allantois and stomach (1). In the guinea pig, the principal serum proteins of the mother are reported to pass during the last week of gestation (2). In the macaque, homologous albumin and gamma globulin are said to pass, although there is no evidence for the passage of alpha and beta globulins (3). In cattle and horses, little or no antibody is passed *in utero*; and in the dog and cat small amounts are passed, most of the antibody being passed *via* the colostrum and milk (4). The question therefore arises whether any serum protein other than antibody may be transmitted *in utero* in mammals which do not readily transmit antibody protein. Heterologous serum proteins were used in an attempt to answer this question, and the results are reported here.

Materials and methods. Cows in advanced pregnancy were injected with human serum albumin (HA); pregnant cats were injected with this protein and with bovine serum albumin (BA) and human gamma globulin (HGG) as well. The serum and other fluids of the fetuses or newborn were examined for presence of the injected proteins. The fluids were titrated by the interfacial precipitin ring test using specific antisera. The sensitivities of the antisera used differed widely, hence, similar titers indicate the presence of quite different amounts of the 3 proteins. Precautions to prevent contamination of fetal

samples with maternal fluids were similar to those used earlier (1). Since antibodies and homologous serum albumin are known to be transferred across the guinea pig placenta mainly before birth, tests for transfer of heterologous serum proteins were performed in that species as a general test of the adequacy of the technic.

Results. Four pregnant cows, 500-550 kg body weight, were given HA as indicated in Table I. The calves were separated from mothers immediately after birth and before nursing. Shortly after calving, samples of maternal blood, calf blood, and colostrum were taken. The colostrum was diluted with an equal volume of saline and then centrifuged. The supernatant solution and the sera from the blood samples were titrated with antiserum (Table I).

With the quantities of protein injected, there appears to be no perceptible passage across the placenta into the fetus. Among the cows given intravenous injection, minimum concentration of HA in maternal serum was about 0.5 mg/ml. Such maternal titers or even lower ones in the pregnant rabbit, are regularly associated with the presence of HA in the fetal serum and in other fetal compartments (1,5).

To provide maximal protein concentration in the immediate vicinity of the conceptus, HA was injected into the uterine lumen in one cow (8034-Guernsey, Table I). An insemination tube was passed beyond the cervix by guiding its tip with the hand inserted into the rectum. A polyethylene tube, connected to a syringe, was then passed through the insemination tube and 120 ml of solution containing 16.8 g of HA was injected. Seventy hours later, although the maternal serum showed a definite titer, there was no trace of the protein in the calf's serum. It would appear, therefore, that the bovine fetal membranes near term present a true barrier to passage of HA from mother to fetus.

* Present address: Dept. of Embryology, Carnegie Institution of Washington, Baltimore, Md.

† Deceased.

TABLE I. Injection of Human Albumin into Pregnant Cows.

Cow No.	HA injected (g)	Sampling time (hr after inj of mother)	Reciprocal of titer in		
			Maternal serum	Calf serum	Colostrum
7718-Holstein	44.1	18	2 ¹¹	neg	2 ⁴ -2 ⁵
5181-Guernsey	27.4	63	2 ⁸	"	
5138 "	49.0	96	2 ⁹	"	neg
8034 "	16.8	70	2	"	"

All cows were given intravenous injections, except cow 8034, which was given intrauterine injection. Sensitivity of antiserum was 2¹⁰ or 1 μ g/ml.

Whether this is also true at earlier stages of gestation is not clear.

Pregnant cats (3-4 kg body weight), in the last few weeks of gestation, also were injected intravenously with the proteins (Table II). The fetuses were removed under anesthesia on the day after injection and samples of blood and the fluids from various fetal compartments were obtained.

Only a small amount of HGG passes from the mother to the circulation of the cat fetus; even relatively large doses of HGG (cat no. 5, Table II) fail to raise the low fetal serum titers significantly. In contrast to the fetal rabbit(5), no HGG was detected in

any other fetal compartment, with perhaps the exception of the stomach of cat no. 4.

However, all the fetuses from 2 cats injected with serum albumin, whether bovine or human, showed high titers in the blood and other fluids. It is noteworthy that cat no. 2 expelled the first fetus 7 hours after injection and the titer of the serum of this fetus was 1/8192. Thus, heterologous serum albumins seem to pass in large amounts from mother to cat fetus, although only much smaller quantities of gamma globulin do so.

Eleven pregnant guinea pigs (0.7-1.4 kg body weight) were given different doses of HA, BA, and HGG intravenously, and the

TABLE II. Injection of Proteins into Pregnant Cats.

No.	Protein dose (mg/kg)	Time (hr)*	Reciprocal of titer in					
			Maternal serum	Fetal serum	Exocoelomic fluid	Amniotic fluid	Stomach content	Allant. fluid
1	HA	62.5	19	2 ¹³	2 ¹²	2 ⁸	2 ³	
				2 ¹¹		2 ⁵		
				2 ¹¹		2 ⁵		
				2 ¹²		2 ⁵	2	
2	BA	200	7-20	2 ¹⁸	2 ¹³			
				2 ¹³				
				2 ¹³				
				2 ¹³			2 ⁹	
				2 ¹³	2 ⁷	2 ⁹	2 ⁹	
3	HGG	78	18	2 ⁷	2 ²	neg	neg	
				2 ²	"	"	neg	1
				2 ²	"	"	"	neg
				2	"	"	"	neg
4	HGG	115	19	2 ⁷	2	neg	2 ³	neg
				2 ³	1	1	2 ²	2
				2	neg	1		
5	HGG	260	22	2 ¹¹	2 ²	neg	neg	
				2 ³	neg	"	"	
				2 ³	"	"	"	

* Time between injection and sampling. Cat No. 2 began expelling fetuses 7 hr after injection. The last fetus had been delivered by next morning, hence 7-20 hr is recorded in this column. Urine of this cat showed a titer of 1/4 for BA.

Sensitivities of antisera used: anti-HA : 2¹⁰ or 1.0 μ g/ml
 anti-BA : 2¹³ or 0.125 μ g/ml
 anti-HGG : 2⁹ or 2.0 μ g/ml

TABLE III. Injection of Proteins into Pregnant Guinea Pigs.

No.	Injected protein dose (mg/kg)	Time (hr)*	Reciprocal of titer in—			
			Maternal serum	Fetal serum	Exocoelomic fluid	Amniotic fluid
1	HA	62.5	2 ⁴	1 neg 1 neg		1
2	HA	125	2 ¹¹		1 1	neg " "
3	HA	250	2 ¹³	2 ⁵	2 ²	" "
4	BA	125	2 ¹⁵	2 ¹¹ 2 ¹¹ 2 ¹⁰		2 2 2 2 2 ² 2 ²
5	BA	250	2 ¹⁵			2 ² 2
6	HGG	62.5	2 ⁷	2 ⁴		neg
7	HGG	125	2 ⁹		neg	" "

* Time between injection and sampling.

Guinea pigs No. 1 and 6 were in last week of pregnancy; the others were 4-5 weeks pregnant.

Uterine fluid of guinea pig No. 3 was tested for HA; titer was 2⁹.

Sensitivities of antisera used for titration given in footnote to Table 2.

fetuses were sampled the next day. The titers from one animal for each dose are given in Table III. Significant passage of HA seems to occur only at a maternal dose above 62.5 mg/kg. Even after correcting for the difference in antiserum sensitivities, the titers suggest that BA passes more readily into the fetal circulation than HA. All 3 proteins were found in high titers in the fetal serum; only traces of them were found in other fetal fluids.

Summary. Human albumin was injected into pregnant cows, and human albumin, bovine albumin, and human gamma globulin were injected into pregnant cats and guinea pigs. Subsequently, the blood and other fluids were obtained from the fetus or newborn and titrated with specific antisera against the 3 proteins. In cows near term no human albumin passed to the fetus. In cats both human and bovine albumins passed in large amounts into fetal blood and into the fluids of exocoelom, amnion, and stom-

ach; but human gamma globulin passed to fetal serum in only small amounts and was virtually absent in the other fetal fluids. In guinea pigs, all 3 proteins were found in high titers in the fetal serum, but only traces of them were found in other fetal fluids.

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