

MICROBIOLOGY AND IMMUNITY

ACQUIRED TOLERANCE TO FOREIGN SERUM IN RATS

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It has been established by the work of numerous authors that the introduction of a foreign antigen into an animal in the embryonic stage of development depresses the ability of the animal to produce antibodies to this antigen in postnatal life. Owen [7] first observed such acquired tolerance to blood of a foreign group in binovular twin calves, and Dunsford and Bowley [3] in binovular human twins. In both cases exchange of blood was established in the embryonic stage through the communication of the placental blood vessels. Billingham, Brent and Medawar [2] and Gashek [1] were able to establish tolerance experimentally in birds and mammals to normal tissues and blood of animals of other lines and furthermore to establish skin transplantation and blood transfusion between such animals. The antigens were suspensions of organs from animals from the donor line and they were injected into the recipient during the embryonic stage. The attempts of Gashek and Simonson [8] to build up in birds and mammals tolerance to normal tissue from another species have not yet been successful.

Successful transplantation of a tumor from animals of one species into animals of another species by the aid of the technic of preliminary injection of a suspension of normal tissues from the donors into the embryos of the recipients was achieved by Koprovsky [6] and Wallace [9].

The results obtained oblige one to suppose that the placenta menon described possesses broad biological characteristics and extends to many other antigens.

Hanau and Oyama [5] and Dixon and Maurer [4] were able to lower the ability of rabbits to produce antibodies to bovine serum albumin by injecting the newborn animals. Such lowered immunological activity persisted even after all the antigen had disappeared from the organism.

In our own experiments we attempted to produce tolerance in rats to horse serum by injecting it into the embryos on the 17th - 18th day of development (period of gestation in the rat: 21 - 22 days).

METHODS AND RESULTS

We anesthetized pregnant rats with ether and cut through the skin of the abdomen, the muscle layer and the peritoneum along the midline. Through the wall of the uterus and the embryonic membrane we injected each embryo either intramuscularly or subcutaneously with 0.03 - 0.04 ml of horse serum. We used a 1 ml syringe and a No. 25 needle. In all 10 rats were operated on. Of the progeny it was possible to save 11 young from three rats (Nos. 9, 19 and 7).

On attaining a weight of 200 g (2-2½ month of age) all the experimental animals and 9 control (unoperated) rats of the same weight and degree of maturity were immunized intravenously with normal horse serum in increasing doses: 0.1, 0.2, 0.3, 0.4 and 0.5 ml. We made the injections every other day.

Precipitin Reaction with Sera of Experimental and Control Rats

	Animals	No. young	Dilution of Antigen				
			1:10	1:50	1:100	1:150	1:200
Experimental	Young of Rat No. 19	59	+	±	—	—	—
		64	+	±	—	—	—
	Young of Rat No. 7	60	+	—	—	—	—
		61	+	—	—	—	—
		62	—	—	—	—	—
		63	++	—	—	—	—
Controls	Not previously injected with antigen	82	+++	+++	++	+	++
		83	+++	++	+++	+	++
		84	—	++	++	+	++
		85	++	+	+	++	+
		47	++	++	++	+	+
		48	++	+	+	+	+
		49	+++	++	+	—	—

Note. All rat sera diluted 1:2.

About 7 days after the last injection blood was taken from all the rats.

Antibody to horse serum present in the sera was checked by the precipitin reaction (see Table).

In the offspring of one of the operated rats (No. 9) the ability to produce precipitins against horse serum compared to the controls, was not reduced, which is possibly connected with technical errors in the injection of serum into the embryos. The progeny of the other two rats (Nos. 7 and 19) showed definite lowering of the precipitin titer as compared with the controls. To one of the offspring (No. 62) there may be ascribed complete tolerance to the injected antigen: precipitation is absent with a 1:10 dilution of horse serum just as with further dilutions.

Thus the results obtained confirm the principle established by other authors. A foreign antigen, injected into an organism during embryonic life, when the reticuloendothelial system is not capable of manufacturing antibodies, ceases to be an antigen for this organism. The mechanism of this phenomenon is so far not clear, and the solution of the present question demands systematic investigations along various lines.

SUMMARY

Introduction of normal horse serum into rat embryos resulted in marked depression of antibody formation to this antigen in the adult animals.

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