FORMATION OF ANTIGENIC PROPERTIES OF KIDNEY TISSUE IN HUMAN EMBRYOGENESIS

R. F. Averkina and O. E. Vyazov

UDC 612.64'46.017.1

The tissues of the metanephros of human embryos between the ages of 6 and 10 weeks contain antigens similar to those of the blood serum and other organs (liver, heart, lung, spleen), as well as common organ antigens not identical with blood serum proteins. Antigens of narrower specificity appear later: a common renal-hepatic antigen after the 11th-13th week of development, and a specific renal antigen after the 18th week.

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An understanding of the principles governing the formation of the antigenic structure of different organs in human embryogenesis is important for the solution of many theoretical and practical problems (elucidation of the role of immunologic factors in morphogenetic processes, the study of problems connected with transplantation of organs and tissues, the investigation of forms of pathological pregnancy linked with immunologic incompatibility of mother and fetus, and so on).

The object of this investigation was to study the dynamics of formation of antigenic properties of human kidney tissue during embryogenesis, because the few references to this subject in the literature [5-7] do not provide a clear understanding of its nature.

TABLE 1. Formation of Antigenic Structure of Human Kidney Tissue during Embryogenesis

Extracts from metanephros tissue	Precipitation band*							
	№ 1	№ 2	№ 3	№ 4	№ 5	№ 6	№ 7	№ 8
Human embryos and fetuses . .	±	+	±	+	+	±	+	+
Precipitation band								
6 weeks	0	0	0	+	0	+	0	+
7 »	0	0	0	+	0	+	0	+
8 »	0	0	0	+	0	+	0	+
9 »	0	0	0	+	0	+	0	+
10 »	0	+	0	+	0	+	0	+
11 »	0	+	0	+	±	+	0	+
12 »	0	+	0	+	±	+	0	+
13 »	0	+	0	+	+	+	0	+
14 »	0	+	0	+	+	+	0	+
18 »	0	+	0	+	+	+	+	+

* Bands counted from well containing extracts. Tests carried out 7-11 times with each extract and serum. +) Positive reaction; ±) weakly positive, precipitation band not formed in all tests; 0) absence of precipitation band.

EXPERIMENTAL METHOD

Antisera against adult human kidney tissues and saline extracts of adult human kidney tissues from human embryos and fetuses of 6, 7, 8, 9, 10, 11, 12, 13, 14, and 18 weeks of development were used in the investigation. The material was obtained from the No. 46 Hospital of the Leningrad District of Moscow after operation for the termination of pregnancy. The age of the embryos, determined clinically, was further confirmed (where possible) by reference to the table given in Patten's book [9], in which the age of human embryos is determined from the sitting height and the crown-heel length. The kidneys (metanephros) were removed, arranged in order of times of development, and kept in a frozen state at −4° until a sufficient weight had been collected for the experiment. Saline extracts were prepared in proportions of 10 mg tissue to 0.1 ml physiological saline. The agar-diffusion reaction was the principal test used.

EXPERIMENTAL RESULTS

To determine at what stages of human development water-soluble antigens characteristic of the human kidney appear in the metanephros, experiments were carried out initially with whole kidney antisera. Merging of the precipitation bands formed by the antiserum and extracts from embryonic tissues with the precipitation bands obtained with the same serum and adult human kidney extract demonstrated their identity. Each antigen detected in the human kidney

Laboratory of Immunology of Embryogenesis, Institute of Experimental Biology, Academy of Medical Sciences of the USSR, Moscow (Presented by Academician N. N. Zhukov-Verezhnikov, Academy of Medical Sciences of the USSR.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 68, No. 7, pp. 94-97, July, 1969. Original article submitted May 22, 1968.

TABLE 2. Detection of Various Antigens in Extracts from Metanephros of Human Embryos and Fetuses

Kidney antisera	Antigens detected	Extracts from metanephros tissue of human embryos and fetuses (aged in weeks)									Extracts from metanephros tissue of adult human
		6-7	8	9	10	11	12	13	14	18	
Absorbed by human blood serum	Common to kidney	+	+	+	+	+	+	+	+	+	+
By human blood serum and mixture of extracts from heart, lung, and spleen	Common to kidney and liver	0	0	0	0	0	0	+	+	+	+
By blood serum and mixture of extracts from liver, heart, lung, and spleen	Specific renal	0	0	0	0	0	0	0	0	+	+

Fig. 1. Agar diffusion reaction with unabsorbed kidney antiserum (in central well). 1 and 2) Extract of adult human kidney; 3 and 4) (A) extract from metanephros of 8-week embryo; 5 and 6)(A) extract of metanephros of 7-week embryo. Three precipitation bands merging with certain precipitation bands (Nos. 4, 6, and 8) formed between the central well and 1-2, can be seen between the central well and 3-6; 3 and 4) (B) extract from metanephros of 14-week embryo treated with antiserum against human blood serum; 5 and 6) (B) the same extract, untreated. Four precipitation bands can be seen between the central well and 5-6, and two bands between the central well and 3-4, merging with the precipitation bands (Nos. 4, 5, 6, and 8) formed with extract of human kidney tissue; 3-6) (C) extract from metanephros of 18-week embryo treated with antisera against human blood serum and against human heart tissue. Two precipitation bands merging with precipitation bands No. 5 and 7, formed with human kidney tissue extract, can be seen between the central well and 3-6.

extract was studied and its properties determined relative to its organ specificity in previous experiments [1].

As Table 1 and Fig. 1 show, of the 8 antigens detected in adult kidney extract, 3 were found in extracts of the metanephros of embryos aged 6, 7, and 8 weeks of development. Two of these antigens (Nos. 4 and 6) were identical with antigens of other organs (liver, heart, lung, spleen), and the third antigen (No. 8) was identical not only with antigens of many organs, but also with serum proteins. An antigen (No. 2) identical with an antigen of the blood serum and several organs was found in extracts from the metanephros of human embryos at 9 and 10 weeks of development. An antigen (No. 5) identical with liver antigen was detected in extracts from the metanephros of the embryos starting with the 11th week of development, and more clearly after the 13th week. One further precipitation band was formed with extract from the metanephros of an 18-week fetus, which was obtained also with extract from adult human kidney only.

To increase the accuracy of these findings, analogous experiments were performed in which absorbed kidney antisera were used.

As Table 2 and Fig. 2 show, the results of these additional experiments confirmed the previous findings and showed that common organ antigens are present in extracts from the metanephros of human embryos at 7-18 weeks of development, because the test was positive with these extracts and kidney antisera absorbed by human blood serum. A kidney antigen, identical with liver antigen, was detected in the metanephros after the 13th week of development. A specific renal antigen did not appear in the metanephros until the 18th week of development. Adult human kidney contains at least 2 or 3 such antigens.

Similar results relating to the order of appearance of the various common organ and specific antigens were obtained by the study of the formation of antigenic properties of the mesonephros tissues during embryogenesis of the frog, tissues of the meso- and metanephros tissues during embryogenesis of the chick [3], and also tissues of the crystalline lens of the frog [8], chick [2], and mouse [4].

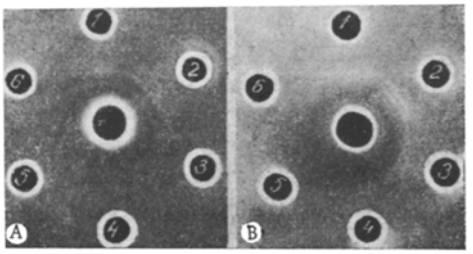

Fig. 2. Agar diffusion reaction with kidney antiserum (in central well) absorbed by blood serum and by extracts of heart, lung, spleen, liver. 1, 2) Extract from adult human kidney; 3, 4) (A) extract from metanephros of 14-week embryo; 3, 4) (B) extract from metanephores of 18-week embryo; 5, 6) mixture of blood serum and extracts of human heart, lung, spleen, liver; 2 precipitation bands can be seen between the central well and 1-2; 3, 4) (A) no precipitation bands; 3, 4) (B) one precipitation band formed.

These results thus show that during development of amphibians, birds, and mammals, water-soluble antigens of the kidney and lens tissues can be found at earlier stages than antigens common only to a limited number of organs (for example, to the kidney and liver). Specific organ antigens are found at still later stages of development. These results are in agreement with the morphological data on the basis of which Karl Baer formulated his law of embryonic identity. According to one of the propositions of this law, "From the more common form the less common is formed, and so on until eventually the most special is formed."

It can thus be concluded from these results that this law governing the process of differentiation of tissues (organs) in embryogenesis also applies at the molecular level.

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