

DIFFERENCES BETWEEN THE β -FETO-PROTEIN
OF DIFFERENT INDIVIDUALS

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In recent years individual differences have been discovered between the serum proteins of different people. It has been shown by electrophoretic separation [7, 18, 20, 22] that differences occur in the electrophoretic mobility of the protein of the α_2 -globulin fraction (haptoglobin); two types of this protein have been identified and a detailed study has been made of the inheritance of both types of haptoglobin [8, 14]. Recently a variant of haptoglobin has been discovered which differs immunologically from the types of this protein hitherto known. This haptoglobin has been found in the serum of three brother siblings [2].

Chemical investigations have shown the presence of identical N-terminal amino acids in the two different types of haptoglobin, but a difference in their secondary structure was found [21]. Besides haptoglobin, human blood serum also contains other proteins exhibiting individual variation, for example γ -globulin [11], transferrin [3, 10, 17], factor Gc [13-16], and β -lipoprotein [1, 4].

The study of individual differences in the serum proteins is interesting from various points of view; investigations in the field of the immunology of pregnancy are particularly important. Interest in this problem is justified by the existence of the incompatibility between mother and fetus based on the system of Rhesus antigens, discovered many years ago and subsequently intensively studied.

In this connection considerable importance is attached to the investigation of individual differences in the embryonic proteins. These proteins, which are not found in the adult, have been described by several authors [5, 6, 9, 12, 19].

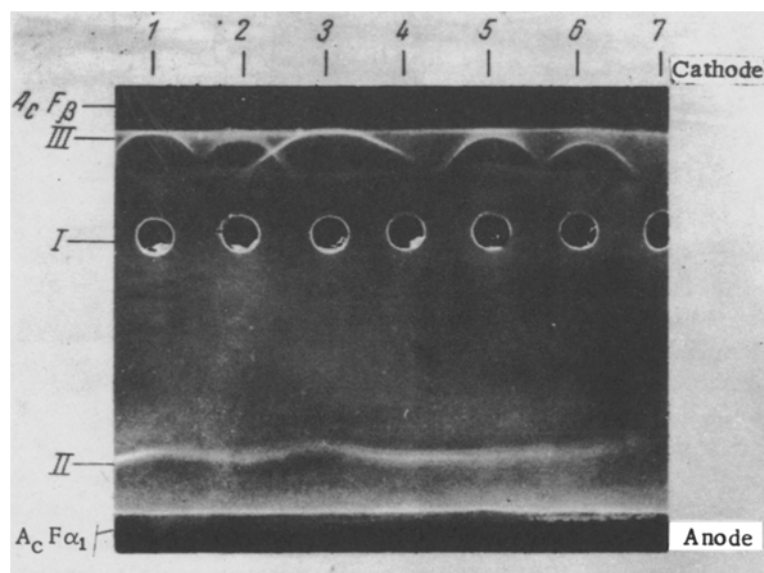
In the present investigation an attempt was made to compare α_1 -fetoprotein and β -fetoprotein immunochemically.

EXPERIMENTAL METHOD

Blood serum was obtained from 30 human fetuses at times between the 9th and 40th weeks of pregnancy. Electrophoresis of the serum of these fetuses was performed in a 1% agar gel with 0.005 M veronal buffer at pH 8.6, with a potential gradient of 5 V/cm for 1 h. The start wells were arranged crosswise in a row 8 mm apart. At the end of electrophoresis a transverse gutter was cut out of the agar, the same for all the test samples, at a distance of 5 mm on the anode side of the albumin region, and a similar gutter was cut out 5 mm on the cathode side of the β -globulin region.

The albumin zone was identified by using albumin stained with Evans blue as label. For this purpose serum with added dye was poured into one of the start wells. The β -globulin zone was identified by hemoglobin, added to the same start well.

Into the first gutter was poured antiserum against α -fetoprotein, obtained from a rabbit immunized with serum from embryos obtained between the 18th and 20th weeks of pregnancy, and exhausted with serum of full-term



Electrophoresis of serum of fetuses. I) Start wells; II) region between albumin and α_1 -globulin; III) region of β -globulins. AcF α_1) Gutter with antiserum against α_1 -fetoprotein; AcF β) gutter with antiserum against β -fetoprotein. 1, 2, 5, 6 - sera of D. twins. In the region of the β -globulins an intersection with the precipitation line of the usual variant F β can be seen (3); 4-7 - sera of adults. The α_1 -fetoprotein gives a confluent line with all fetuses.

fetuses. Into the second gutter was poured antiserum against β -fetoprotein, obtained from a rabbit immunized with the serum of a full-term newborn infant, exhausted with the serum of an adult human.

EXPERIMENTAL RESULTS

After immunization a wavy precipitation line appeared in the region of the α_1 -globulin zone, common to all sera. A confluent line was obtained in all 30 fetuses investigated (see figure). In the region of the β -globulin zone a common precipitation line for all the sera also was formed. In this case, however, we obtained an arc interrupted at both ends, and crossing lines derived from neighboring test samples.

This serum, possessing a β -fetoprotein differing immunologically from the rest, belonged to a premature fetus (33rd week of pregnancy, twins, boy and girl). We investigated the serum of both twins. The serum of the second fetus possessed a β -fetoprotein likewise not identical with the β -fetoprotein usually found; the β -fetoproteins of both twins were the same. We called this variant of β -fetoprotein F β_D , the index D standing for the initial letter of the child's surname.

Hence the α_1 -fetoprotein in our investigations was identical in all the fetuses, while the β -fetoprotein (F β) was not identical in one case.

In subsequent investigations the distribution of F was studied among full-term and premature fetuses. The existence of a variant F β not identical with the F β widely occurring in human fetuses indicates the possibility of immunological conflicts, and, in particular, the possibility of sensitization of the mother by this unusual protein.

A case has already been described in which sensitization by serum proteins of a different group developed after repeated transfusions of human plasma to a human recipient. Sensitization by fetoproteins has not yet been reported clinically, although as investigations in this direction proceed, such cases will probably come to light. These facts are of fundamental importance in relation to certain pathological problems (toxemias of pregnancy, spontaneous abortion).

SUMMARY

With the aid of electrophoresis in agar gel with subsequent diffusion immuno-manifestation a study was made of the degree of immunological similarity between the fetoproteins in the serum of individual human fetuses. Alpha-feto-protein was identical in all of the fetuses investigated, whereas beta-feto-protein differed in one case; a cross with a common precipitation line. This serum belonged to one of the two premature 33-week-old twins (a boy and a girl). In the serum of the second twin beta-feto-protein was identical to that of the first and also gave a cross phenomenon with all the rest. The mentioned protein was absent from the sera of adults.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.