PROBLEM OF THE IMMUNOLOGICAL INTERRELATIONS OF THE MOTHER AND HUMAN FETUS

COMMUNICATION I. THE ISOSEROLOGICAL FEATURES OF RETROPLACENTAL BLOOD OF WOMEN IN CHILDBIRTH AND THE UMBILICAL BLOOD OF THE NEWLY BORN

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Despite the great importance of the problem of the mutual immunobiological relations between the organism of the mother and fetus this problem has been insufficiently studied.

It is known that hemolytic disease of the newborn and certain other pathological forms in pregnancy are connected with Rhesus factor incompatability of the blood of the mother and the fetus.

As regards the group antigenic differences of the mother and fetus and their significance for the normal development of the latter this question has not yet been conclusively solved [1, 2, 3, 6, 8, 9, 10, 11, 13, 15].

In any event while the group differences of the mother and fetus may be the cause of the disease in the baby organism this happens very seldom. It has been established that in 90 per cent of the cases hemolytic disease of new born is etiologically associated with the Rhesus factor.

The hypothesis has been advanced that the absence of the harmful influence of the group incompatability of the mother and fetus is to be explained by the existence of definite defense factors; however the mechanism of action of the latter is still not clear.

In view of the theoretical and also practical interest, the question of the immunobiological mutual relations of the mother and human fetus requires further investigation.

Part of the object of our work included study of the isoserological properties of the blood of the lying-in woman and the newborn in relation to blood group.

EXPERIMENTAL METHODS

The investigation was concerned with the retroplacental blood of the lying-in woman and the umbilical blood of the newborn.

Determination of the group adherence of the erythrocytes of the investigated blood was effected by the generally accepted methods: hemagglutination reaction with standard blood sera I ($O\alpha\beta$), II ($A\beta$) and III($B\alpha$) groups on a slide and also in test tubes with preliminary single washing of the erythrocytes with physiological saline (by centrifugalization).

The prescence and titer of the isoagglutinins of the investigated blood was determined by means of the standard erythrocytes of groups A and B, taken from the same persons. The tested sera were estimated in test tubes by the method of centrifugalisation.*

EXPERIMENTAL RESULTS

204 blood samples of women in confinement and the same number of blood specimens of the newborn were studied. It was established that the group correlations of the blood in the new born were analogous to the correlations in lying-in women and in line with the generally known data in determination of blood groups among the adult population.

Upon comparison of the blood groups of the 204 women in confinement and the blood groups of the newborn, it was shown that the blood in 142 cases (69.6%) belonged to the same group and 62 cases (30.4%) to different ones.

It is important to note that in all 62 cases when the blood group of the mother and child was different, pregnancy proceeded normally and terminated with at term birth of healthy children. This fact gives grounds for assuming that the organism of the mother and fetus possesses a sufficiently effective defense mechanism protecting them from mutual damage in cases of group incompatability.

Of particular interest is investigation of the blood sera of pregnant women and the newborn for isoantibody prescence and titer.

The results of the corresponding investigation, set out in Table 1, show that the height of the titer of α and β isoantibodies in the blood of the women in confinement has a definite relationship to the character of the group blood relations of the mother and child.

In cases where the blood group of mother and child were compatible the highest titer of the isoagglutinins was found in the majority of maternal blood samples.

Thus, of 61 samples of sera containing α agglutinins, the latter were found at a titer of 1:128-1:512 in 49 (80.3%). Only in one case were α antibodies found at a low (1:2) titer.

Of 102 samples of sera containing β agglutinins the latter were at a high titer (1:128-1:512)in 66 cases (64.7%) and at a low titer (1:2) only in 4 (3.8%) cases.

As regards serologically incompatible pregnancy, on the other hand, a high titer of isoantibodies in the retroplacental blood was found considerably less often - α in 10%, β in 27.2% of the cases; in the majority of sera the hemagglutinins were at a minimally low titer (α in 25%, β in 54.5% of the cases).

It is necessary to emphasize that the fall in the isoantibody titer in the retroplacental blood seen in "divergent group" pregnancy only affected those which could be combined with the hemagglutinins in the blood and tissues of the fetus. For example, in the blood groups: mother - $O\alpha\beta$, child - $A\beta$ - in the maternal blood the titer of α agglutinins fell; β agglutinins in such a case were found at an unchanged high titer; in the blood groups: mother - $O\alpha\beta$, child - $B\alpha$ only the titer of β agglutinins fell; in the maternal groups $A\beta$ or $B\alpha$, child $O\alpha\beta$ the isoantibodies in the maternal retroplacental blood were at a high titer.

The reasons for the decrease in the isoantibody titer in the maternal retroplacental blood in "divergent group" pregnancy are not known; one may only suppose that in a given case there takes place coupling of the antibodies indicated by the identical hemagglutinins in the fetal blood.

In the study of the umbilical blood of new born the following special features were discerned.

Of 128 blood samples of children of the I ($O\alpha\beta$), II ($A\beta$) and III ($B\alpha$) groups, isoantibodies were found in 78 samples, i. e. in 60.9% of the cases. In 50 sera (39.1% of the cases) isoagglutinins were not identified in the blood of the newborn.

The titer of the isoantibodies in the blood of the newborn was considerably lower than in the blood of adult persons and in the majority of sera did not exceed 1:4 - 1:8. In certain cases the titer of these isoantibodies was sufficiently high: 1:64, 1:128 and even 1:256.

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* A detailed description of the method is contained in a monograph by P. N. Kosyakov "Antigenic Substances of the Organism and their Significance in Biology and Medicine," (in Russian). Moscow, 1954.

The most interesting feature noted in the investigation of the umbilical blood of the newborn was the dependence of the presence and titer of the isoantibodies on the group blood correlation of the mother and baby (Table 2).

It is clear from Table 2 that with serologically compatible correlations of mother and child, the isoantibodies in the serum of the umbilical blood were found in over 70 per cent of the cases.

Thus, α agglutinins were found in 36 serum samples from 49 subjects, i.e. 73.5%; β agglutinins were seen in 59 serum samples from 84 subjects, i.e. 71.5% of the cases.

When the blood of mother and child was serologically incompatible, α agglutinins were found only in one case out of 16; β agglutinins in 3 sera from 12 subjects.

In the majority of serum samples from the umbilical blood of the new born in "divergent group" pregnancy, isoagglutinins were not found: α in 93.8% of the cases, β in 75% of the cases.

As our investigations showed the titer of isoantibodies in the umbilical blood of the new born, also had a law-governed relationship to the character of the group correlations of the blood of mother and child. The greatest height – 1:64, 1:128, 1:256 of titers of isoagglutinins in the umbilical blood was reached in cases when the blood of mother and child was of the same group; in cases of serological incompatability, isoantibodies were not present in the majority of blood samples of the new born while in certain cases they were found at a titer not exceeding 1:2.

It is important to note that in the latter cases (with incompatible blood groups) we did not find, or found only at an extremely low titer, those isoagglutinins which in the given group combination might have been bound by the hemagglutinins in the blood of the mother.

Our findings, establishing the dependence of presence of isoantibodies in the blood of the new born on the character of the group correlations of the blood of mother and child, concur with the observations of other investigators [3, 12].

Many authors [3, 4, 7, 8, 14] hold the view that in the blood of the newborn natural hemagglutinins are still not present and the isoantibodies found in the umbilical blood are maternal.

The results of our investigation refute this opinion advanced in the literature. Thus, in the blood groups: child – O$\alpha\beta$, mother – Bα in 2 cases both α and β agglutinins were discerned in the blood of the new born; in the correlations of the blood groups of the child – Bα, mother – Aβ there were only α agglutinins in the umbilical blood of the new born. The cases indicated by us demonstrate that the isoagglutinins found in the umbilical blood of the new born are antibodies peculiar to and belonging to the child and not passed to the fetus from the maternal blood.

TABLE 1

Dependence of Titer of Isoantibodies in the Retroplacental Blood of Woman in Confinement on Character of Group Correlations.

Group co-relations of blood of mother and child	Serum of woman in confinement		Isoantibodies found at titer			
			to 1:2		From 1:126 to 1:512	
			Number of sera samples			
	Total samples investigated	Isoantibodies	In absolute numbers	In %	In absolute numbers	In %
Serologically compatible	61	α	1	1.6	49	80.3
	120	β	4	3.8	66	64.7
Serologically incompatible	20	α	5	25.0	2	10
	11	β	6	54.5	3	27.2

TABLE 2

Dependence of Presence of Isoantibodies in Umbilical Blood of Newborn on Character of Group Correlations.

Group correlations of blood of mother and child	Serum of woman in confinement		Isoantibodies found at titer			
			to 1:2		From 1:126 to 1:512	
			Number of sera samples			
	Total samples investigated	Isoantibodies	In absolute numbers	In %	In absolute numbers	In %
Serologically compatible	49	α	36	73.5	13	26.5
	84	β	59	71.5	25	28.5
Serologically incompatible	16	α	1	6.2	15	93.8
	12	β	3	25.0	9	75

Further investigations are necessary on the question of the mechanism effecting the change noted by us in titer of isoantibodies in the retroplacental blood of the women in confinement and the umbilical blood of the new born when they are serologically imcompatible.

The fall in the titer of the corresponding isoantibodies taking place in serologically incompatible pregnancy and also the disappearance from the blood of the fetus of hemagglutinins which in combining with the group antigens of the maternal blood may lead to disease of their organisms, may be considered as one of the defense mechanisms ensuring the normal course of pregnancy and development of a healthy baby.

There are grounds for assuming that this fall in the titer of the isoantibodies is due to combining (neutralization) of these antibodies by the corresponding group antigens.

We further believe that the process of combination of the maternal isoagglutinins by the group antigens identical to the hemagglutinins of the fetal blood and the isoantibodies of the fetus by group antigens of maternal blood develops not in the maternal organism nor that of the fetus but in the tissues of the placenta and possibly in the amniotic fluid.

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