109. Ontogenetic Development of Blood Group Substances in Embryos and Newborns. II. M-N Type Substances

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Introduction

Wiener (1938) discovered an antigen in the blood cells of the anthropoid ape, which is similar to the M antigen in the human blood cells and found further that when the rabbits are immunized against the blood cells of the apes, the anti-M antibody is formed in some rabbits but not in others. Wiener explained this as due to individual differences in the rabbits. Dahr and Lindau (1938) discovered the existence of various M antigens in the blood cells of the lower monkeys, which are quantitatively different from the human M-substance. In Japan, S. Hayashida (1944) found that the M-substance in the blood cells of Formosan monkeys is simpler in structure than that of men and designating this as M2-type, he discovered that there are, in the human M-substance, two types, one, the M1 and the other, the M2 which is more complex in structure than M2.

The M and N antigens in the human foetuses have been studied by Akune (1931), Hashimoto (1933), and Doki. We reinvestigated the results of Doki, and made further studies on the ontogenetic development of the partial antigens (M1 and M2) of the M antigen. Some of the interesting results which we have obtained from these studies shall be communicated here.

Experimental

Method of preparation of partial antibodies

A) Anti-M partial antibodies

1) Anti-M1 agglutinin

5 cc of the saline suspension of the human OM-type blood cells in the concentration of 10% injected into the conch vein of the rabbit from six to seven times at intervals of three days. The animals were sacrificed seven days after the last injection and the serum was taken. It was then inactivated by heating at 56°C for thirty minutes and after addition of carbonic acid in the concentration of 0.5%, it was kept in an ice-box. At the time of the experiment, the serum was treated with the ON-type human blood cells to remove
the heteroagglutinin and it was then treated further with Formosan monkey blood cells (M₂), whereby the anti-M₂ agglutinin was absorbed away, leaving a pure anti-M₁ agglutinin.

2) Anti-M₂ agglutinin

A rabbit was immunized with 10% saline suspension of Formosan monkey blood cells. The procedure was exactly the same as the previous cases. After the serum was obtained and kept under refrigeration, it was, at each experiment, treated with the human ON blood cells to remove the heteroagglutinin. It was further treated with blood cells of ON-type taken from foetuses of 5-6 months; thereby agglutinins of non-specific nature that exist both in Formosan monkeys and foetal blood cells were removed.

B) Anti-N agglutinin

Here also the procedure which is exactly the same as in other experiments was used. A pure anti-N agglutinin was prepared from the serum of rabbits immunized against ON-type human blood cells by absorbing it with human blood cells of OM-type.

Experimental Results

1. The M-type substance

As indicated in Table I, the development of M₁-type substance is poor at an early foetal period, showing the value of 19.2 at the second month. Whereas the strength of M₂-type substance is striking, reaching as high as 453.1 at the second month. M₁ part develops rapidly till about fifth month of gestation (69.4) and then slowly until parturition when the value reaches 91.1. It continues to develop further thereafter and reaches the adult level at about 5-6 years of age. In contrast to this, M₂ part, which is strikingly well developed at very early stage of gestation, declines gradually after the second month reaching the value of 291.7 at the fifth month. Due to a gradual and further decline, the value drops to 136.1 at the time of parturition and finally to the adult value of 101.6 after birth. It is interesting that the development is entirely different in M₁ and M₂. What have
been just discussed are presented in Fig. 1.

2. The N-type substance

As shown in Table I, similar to M1-type substance, N-type substance shows the value of 18.5 at the second month of gestation, but it develops strikingly fast thereafter till the fifth month, reaching the value of 59.7. Its development continues gradually until parturition and reaches the adult level. Fig. 1 shows the manner of development of this substance.

Summary and Conclusion

From the results of our studies presented thus far in details, we may tabulate the essential facts and draw our conclusion. With regard to M- and N-type substances, the following points should be noted:

1) The M- and N-substances are definitely recognized, as in the case of A·B·O group substances, at the second foetal month.

2) The M1-type substance is only weakly developed at earlier embryonic stages, but its development gradually progresses with time of gestation.

3) The M2-type substance shows a type of development entirely different from the M1-type substance. This substance is already highly developed at the earliest period of gestation and gradually regresses thereafter reaching very closely the adult level at parturition. The regression continues further after birth.
On the basis of these results obtained from our studies of the ontogenetic development of the various blood type substances, we may conclude that many of the blood type substances are undifferentiated at the early period of foetal life, but they differentiate gradually with time of gestation, showing further development in some and regression in others, and finally reach in all cases the characteristic adult level of men.

References