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An Irregular Agglutinin and Erythroblastosis Fetalis* (Hemolytic Disease of the Newborn).

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The importance of iso-immunization, *i.e.*, immunization within the same species, in the etiology of erythroblastosis fetalis has been demonstrated.[1-7] Race and co-workers[8] state that in one of 10 pregnancies, the mother is Rh-negative and the baby Rh-positive and that in one of 5 pregnancies, the mother possesses an agglutinin for the agglutinogens A or B which are present in the blood of her fetus. Despite this statement, the incidence of clinical erythroblastosis fetalis is much less than would be expected if circulating agglutinins were capable of passing the placental barrier in all cases of iso-immunization.

In support of the theory of iso-immunization, Levine and co-workers[5] estimated that more than 90% of the mothers of erythroblastotic babies were Rh-negative in contrast to the 15% of Rh-negative individuals in a random sample of the population. The observation that 10% of women bearing children afflicted with erythroblastosis fetalis were Rh-positive suggested that factors other than Rh were involved in the etiology of this condition. Javert[7] reported a case of erythroblastosis fetalis in which the mother was Rh-positive and the father Rh-negative. An atypical agglutinogen was present in the erythrocytes of the father and of the affected fourth-born child, and absent from the cells of the mother. The specific agglutinin was present in the mother's serum. Levine tested the blood of the first-born child and found it to be Rh-positive, and lacking the agglutinogen for the atypical agglutinin present in the mother's serum. This agglutinin was designated anti-Hr by Levine.[7] Wiener[9] stated that the serum Levine termed anti-Hr agglutinated all Rh-negative and those of the Rh-positive erythrocytes which were not agglutinated by a special variety of anti-Rh serum which detected only 70% Rh-positives in a random sample-group. Therefore, he considered this reaction to be analogous to that observed in some individuals of the sub-group A_1, in whose serum the erythrocytes of group O and sub-group A_2 are agglutinated.

Race and co-workers[8] found six of a series of 50 mothers bearing erythroblastotic infants to be Rh-positive. The husbands of only 2 of these 6 subjects were available for examination, and these were found to be Rh-negative. In another observation these authors examined the fathers of 2 erythroblastotic children, borne by Rh-positive mothers, and found one father to be Rh-negative and the other to be Rh-positive. As stated by Race: "In this last case the serum of the mother (group O Rh-positive) contained a very powerful antibody more active at 37° C than at room temperature. This serum gave clear-cut positive reactions with the red cells of 80% of a large number of unselected group O persons, including her erythroblastotic child (group O Rh-positive). When tested against group O Rh-negative

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1 Levine, P., Katzin, E. M., and Burnham, L., *J. A. M. A.*, 1941, **116**, 825.

2 Levine, P., and Polayes, S. H., *Ann. Int. Med.*, 1941, **14**, 1903.

3 Burnham, L., *Am. J. Obs. and Gyn.*, 1941, **42**, 389.

4 Levine, P., Vogel, P., Katzin, E. M., and Burnham, L., *Science*, 1941, **94**, 371.

5 Levine, P., Burnham, L., Katzin, E. M., and Vogel, P., *Am. J. Obs. and Gyn.*, 1941, **42**, 925.

6 Levine, P., *Am. J. Clin. Path.*, 1941, **11**, 898.

7 Javert, C. T., *Am. J. Obs. and Gyn.*, 1942, **43**, 921.

8 Race, R. R., Taylor, G. L., Cappell, D. F., and McFarlane, M. N., *Brit. Med. J.*, 1943, **2**, 289.

9 Wiener, A. S., *Blood Groups and Transfusions*, 1943, Ed. 3, C. C. Thomas, Springfield, Illinois.

bloods it was found to agglutinate strongly a series of 50 consecutive samples. After removal of the anti-A and anti-B iso-antibodies the serum still agglutinated the husband's cells (group A_1 Rh-positive). This antibody is not specific for any of the blood-cell antigens A, B, O, M, N, P, Rh, but it is suspected that it is similar to the irregular agglutinin found by Levine, Javert, and Katzin (see Levine, 1941†) in the blood of an Rh-positive mother with Rh-negative husband and an erythroblastotic child, and named by them "anti-Hr."

Gallagher and co-workers[10] observed that 9 of 21 mothers, who bore infants presenting jaundice, were Rh-positive. Potter and co-workers[11] reported an instance of erythroblastosis fetalis which occurred in a child borne of Rh-negative parents.

We take this opportunity to report our findings of an irregular agglutinin of high titer in the serum of a woman who gave birth to an erythroblastotic infant.

Case. B.B. A multiparous white woman, aged 26 years (Wassermann and Kahn tests negative) gave the following obstetric history: a spontaneous miscarriage at one month (January, 1939) and 3 induced abortions, the first at 1½ months (April, 1939), the second at one month (July, 1939), and the third at one month (February, 1941). Following curettage she was given two 500 cc transfusions of citrated whole blood (Rh factor unknown) without reaction. On January 30, 1942, she gave birth to an apparently normal full-term, living female child, who on the tenth postnatal day was found to have a hemoglobin content of 45%. No nucleated red blood corpuscles were seen. A diagnosis of anemia of the newborn was made. On 9/27/43 she delivered a living female child, weight 3480 g. The baby was weak and markedly jaundiced. The blood count showed 81% nucleated red cells and a diagnosis of erythroblastosis fetalis was made. The infant was placed in an oxygen tent and received 3 transfusions, totalling 200 cc of compatible Rh-negative blood. It died 9/29/43.

Determinations of the Rh factor were made following the birth of this child. The mother was found to belong to group A_1B, type N, Rh-positive, and the father to group O, type N, Rh-negative. The surviving child, as well as the erythroblastotic child, belonged to group B, Rh-positive. An irregular agglutinin of high titer (1:64) active at 37°C and not identifiable by the A, B, O, M, N, P, or Rh agglutinogen, was present in the serum of the mother. When tested against a series of 50 samples of blood, it agglutinated 16 samples of Rh-negative cells more strongly than the 34 Rh-positive cells. The agglutinogen counterpart of this agglutinin was present in the red blood corpuscles of her husband and of the 2 children, but was absent from her own cells. The immunization of the mother may have been produced by the aborted fetuses which could have possessed the specific agglutinogens present in the erythrocytes of the husband and/or which conceivably might also have been present in the blood which the mother received by transfusion.

Summary. An irregular agglutinin found in the serum of an Rh-positive mother of an erythroblastotic child sired by an Rh-negative father is described in this communication. This agglutinin differs‡ from that designated as anti-Hr by Levine, because it agglutinated all Rh-positive as well as Rh-negative blood samples.

† Levine, P. (1941) in *Year-book of Pathology and Immunology*, p. 509, Chicago.

[10] Gallagher, F. W., Danis, P. G., and Jones, L. R., *J. Ped.*, 1943, **22**, 171.

[11] Potter, E. L., Davidsohn, I., and Crunden, A. B., *Am. J. Obs. and Gyn.*, 1943, **45**, 254.

‡ In the case reported by Race, both parents were Rh-positive.