

Hemolytic Disease of the Newborn in Domestic Animals and its Prevention

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Hemolytic disease of the newborn is caused by the immunization of a mother against blood group antigens possessed by her foetus but not by herself. In man, the antibody produced in the serum of the mother can reach the foetus in utero and exert a destructive effect on its red blood cells. However, in horses and pigs the antibody can not reach the foetus in utero and so the disease is not initiated before birth. The newborn in these species are born healthy. But after suckling the colostrum in which the antibodies are concentrated, the newborn suffers from hemolytic disease. The ingested antibodies in colostrum is absorbed from the intestine and the animals begin to suffer from an acute hemolytic anemia accompanied, in sever cases, by hemoglobinuria and death.

The present paper deals with this disease from the serological point of view, the cause and fluctuation of antibody making, its absorption in foetus, its appearance and how it can be prevented in Japan.

A) The disease in foals

1. Horse blood groups related with hemolytic disease

Horse blood groups have been classified by three agglutinogens (Pf₁, Pf₂ and Pf₃) and two hemolysinogens (U₁ and U₂) by Dr. Hosoda et al (1942, 1959). Five specific reagents for blood typing are available in Japan. All the reagents were prepared by immunizing rabbits with horse red cells. The blood factors U₁ and U₂ are detected

by hemolytic tests and Pf₁, Pf₂ and Pf₃ by agglutination tests. Factors U₁ and Pf₁ were always associated with each other throughout our experimental data. The genetic studies indicate that there are at least three independent blood group systems in the horse. The alleles which determine factors U₁ and U₂ behave as co-dominants. Factors Pf₂ and Pf₃ behave as dominant genes, each of which is a recessive alleles that determine the absence of the factor. In all three loci, U₁, U₂ and Pf₃ appear to be genetically independent.

The studies on the role of the blood groups in inducing the hemolytic disease of foals indicated that the difference of the blood groups divided by these five factors between dams and their offsprings or their stallions did not cause the appearance of the disease. Some dams which we examined had typical antibodies in natural, but no hemolytic symptom appeared in their offsprings. However, there were always atypical antibodies, which were detected by anti-gamma globulin sensitization tests (Coombs test), in the sera of the dams which gestated foals suffering from hemolytic disease. This fact suggested that the atypical antibodies are important to development of the disease. Atypical antibodies were also classified into three factors, H₁, H₂ and H₃. It is necessary to develop the disease for the offsprings have at least one of the blood factors detected by the atypical antibodies and the dams have the corresponding antibody. Average frequencies of the blood group factors are shown in Table 1.

Table 1. Frequency of blood group antigens in two breeds

| Breeds | No. | Blood group antigens (%) | | | | | | | |
|-------------|-----|--------------------------|-----------------|-----------------|----------------|----------------|----------------|----------------|----------------|
| | | Pf ₁ | Pf ₂ | Pf ₃ | U ₁ | U ₂ | H ₁ | H ₂ | H ₃ |
| Light breed | 103 | 91.2 | 0.97 | 98.1 | 98.1 | 1.9 | 67.0 | 80.6 | 86.4 |
| Half breed | 64 | 75.0 | 23.4 | 92.2 | 64.1 | 18.7 | 20.3 | 96.8 | 75.0 |
| Total | 167 | 85.0 | 9.6 | 95.8 | 85.0 | 8.4 | 49.1 | 86.8 | 82.0 |

2. Production and Fluctuation of Type-Specific Atypical Antibodies

For the occurrence of hemolytic disease the existence of atypical antibodies in the serum of dams has been always shown. Why are atypical antibodies produced so high as to evoke the disease? The reason has not yet been fully understood. Bruner et al (1948) stated that natural immunization of a dam seems to result from the conception of the foetus possessing different blood group antigens from that of its mother. However our data showed that there were some cases in which antibodies existed in some stallions and fillies other than dams. The following hypothesis on the origin of antibodies in the mare sera are proposed from our experiments.

- (1) Sensitization of mares through placenta by different blood group antigenic substances of foetus.
- (2) Iso-immunization of transfusion of incompatible blood.
- (3) Injection of vaccins which contain blood type specific substances.
- (4) Genetical characters of dam in the production of antibodies.

The fluctuation of the atypical antibodies in naturally sensitized mares is somewhat different in each case. In some cases high titer of the antibodies is maintained throughout the year. In others, low titer is seen for a short period of a week or two weeks before and after parturition.

The antibodies in the serum of a mare are concentrated in the colostrum, in which the titer is usually higher than that in the serum. After suckling, the antibodies in the colostrum decrease sharply and reach to 1:8 of the original level on the fourth day after parturition.

On the other hand, the antibodies do not

exist in the serum of foals before nursing. As soon as the foals begin to nurse, the antibodies are detected in the serum.

3. Prevention and treatment of hemolytic disease

Hemolytic disease results from the antigen-antibody reaction. Therefore, to prevent the developing of the disease, the following three ways are recommended.

- (1) Exhaust the antibodies in colostrum by artificial hand suckling or suckling by another foal over 5 days old before nursing the foal.
- (2) Use artificial calf milk for about 3 days.
- (3) Nurse with milk from other dam for 3 days.

When the colostrum is already intaken by the foal and the symptoms has appeared, bleed the animal immediately followed by transfusion of the blood from other horses than its own dam and repeat the treatment several times.

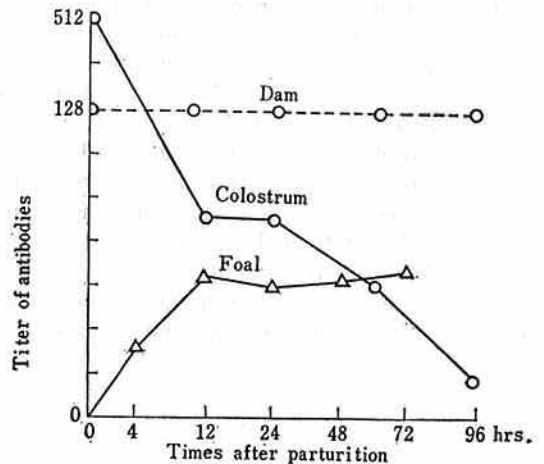


Fig. 1 Fluctuation of Type-specific atypical antibodies in the serum and colostrum after parturition

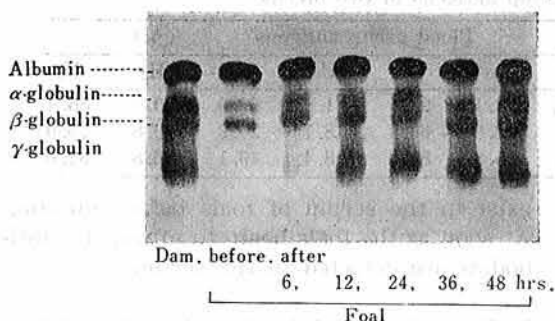


Fig. 2 Electrophoresis of the sera of foal before and after nursing

B) The disease in piglets

The first case of hemolytic disease in piglets that occurred in Japan was reported in 1966, and thereafter much attention has been focused on this disease.

The report described the five full-sib sows, four of which bore at least an affected litter from mating of Berkshire and Landrace breed, and one of which farrowed a normal one.

Serological finding showed that strong reactive agglutinating against the bore's red cells always existed in the serum of the sows which farrowed piglets suffering from the hemolytic disease, but they did not exist at a high level in the serum of normal sows.

The appearance of clinical signs seem to depend upon the titer of antibodies in the sows. In sever cases all the piglets died within 10 hours after suckling, and in mild cases some died within 3 days and other survived with only slight anemia.

The animals are healthy at birth. The three significant signs that may develop in hemolytic disease are pallor, lassitude and jaundice. The last of these may never appear if the piglets died quickly.

Typical hematological change in the blood of four piglets affected by the disease are

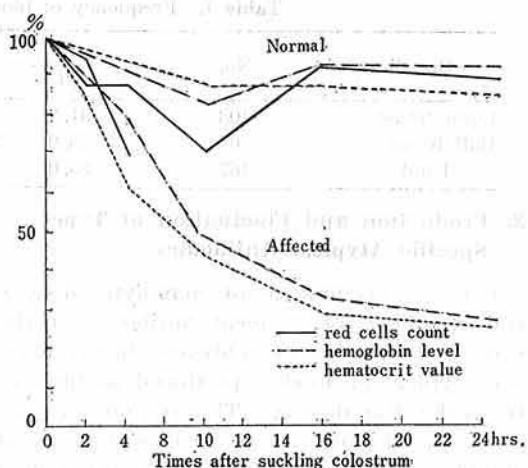


Fig. 3 Hematological changes in the blood of piglets affected hemolytic disease

shown in Fig. 3. The hemoglobin level, red cells counts and hematocrit values fell abruptly when compared with a normal decline of these. In severe cases the red cells agglutinated strongly so that the counting of red cells even 4 hours after suckling was impossible. Photographs show the direct agglutination of red cells of the piglets at successive time intervals after suckling. A test as to whether agglutination, with the aid of slight centrifugation, can be found or not seems to be a useful and simple diagnosis of this disease, which distinguish it from other diseases.

One of the possibilities of iso-immunization of sows will be brought about by crystal violet swine fever vaccine, which contains red blood cells antigens. However the apparently low incidence of the disease suggests that some other reasons may play a part in the appearance of this disease. Frequency of the appearance of this disease and the blood group factors responsible for the disease are under investigation.