Introduction
Tests for diagnosis of or potential for developing conditions due to antibody mediated destruction of red blood cells (erythrocytes) in horses are of three types. The first is used to determine the blood type of a horse; the second is used to determine whether anti-erythrocyte antibody is present in serum or colostrum; and the third is used to determine if antibody is attached to the red blood cells (Coombs’ test). The results of blood typing, antierythrocyte antibody and Coombs’ testing in horses provides information useful in the diagnosis, management or prevention of antibody-associated adverse reactions on red blood cells. Antibodies to red blood cells (often referred to as antierythrocyte antibodies) can be transferred to another horse through either colostrum (as from dam to foal) or through transfusion, or they may develop to a horse’s own red blood cells. When antierythrocyte antibodies are transferred from a mare to its foal, a syndrome called neonatal isoerythrolysis (NI) may develop. Antierythrocyte antibodies transferred through transfusion may cause several types of adverse reactions, called transfusion reactions. When a horse develops antibodies to its own erythrocytes autoimmune hemolytic anemia (AIHA) may occur.
Neonatal Isoerythrolysis (NI) in Horse Foals

Neonatal isoerythrolysis is a disease of newborn horse foals and mule foals that occurs within the first week of life. (See below for information on the condition in newborn mules.) It is caused when the mare produces antibodies against the foal’s red blood cells and transfers those antibodies to the foal through colostrum during the early stages of lactation and nursing. This syndrome may occur when the blood type of the mare is different than that of the stallion and the foal inherits the sensitizing red blood cell type from the stallion. Mares that are negative for red blood cell factors have the potential to develop antibodies against those factors. Mares only become sensitized as a result of exposure to blood of a fetus with incompatible blood type as a result of placentitis, difficult parturition, or from exposure to blood containing the foreign blood factors from a previous blood transfusion. Horses have 8 different blood group systems, each of which has different factors. Some of the factors are more commonly associated with NI (e.g. factors Aa, Qa and Qb). There are several other, but less common, factors (Ua, Ka, Qc, Pa, Pb, Ab) that can also cause NI. However, for unknown reasons, only a small number of mares that are negative for a factor develop these antibodies. Generally, a mare does not develop sufficient amount of antibodies to cause NI in its foal during the first pregnancy from breeding to a stallion that has a factor for which the mare is negative. However, in rare cases a mare may produce sufficient antibody during a first pregnancy and can cause NI in her foal. Increased risk of developing NI occurs with subsequent pregnancies due to breeding to that stallion or another stallion with the same red blood cell factor. After ingestion of colostrum containing antibodies to red cell factors, the antibodies are absorbed into the foal’s blood. This is unlike the situation in humans where the antibodies (which most frequently are anti-Rh antibodies) cross the placenta during late pregnancy. The antibodies attach to the factors (antigens) on the foal’s red blood cells, and through a series of reactions, cause the foal’s red blood cells to rupture (erythrocyte lysis, which describes the syndrome’s medical name, neonatal isoerythrolysis).

Neonatal Isoerythrolysis (NI) in Newborn Mules

Neonatal isoerythrolysis is not a common condition in horse foals, although, when it does occur, it is a severe, life threatening condition. In contrast, the reported incidence of NI in newborn mules is about 10%, which is much higher than the incidence in horses. In many mule pregnancies, the mare develop antierythrocyte antibodies. It is probable that this occurs because there are many differences in blood group factors between horses and donkeys. In mules and donkeys the specific red blood cell factors have not been identified, therefore blood typing is not available. It is likely with every donkey/horse breeding that there is the potential for NI. Mules suffering from NI frequently manifest thrombocytopenia (low platelet count) as well as anemia,
presumably because of the presence of anti-platelet antibody as well as anti-red cell antibody. Alloimmune thrombocytopenia (platelet destruction due to anti-platelet antibody) may occur without NI as well.

**Determining the Potential for Developing NI**

A mare that has produced a foal that developed NI is likely to produce others. The risk of producing another NI foal is greater if the mare is bred to the same stallion or a stallion with the same inciting blood type as that of the original stallion. Mares that have previously produced a NI foal are excellent candidates for antierythrocyte antibody screening in subsequent pregnancies. Mares that are either factor Aa, Qa, or Qb negative, are also good candidates for antibody screening. In addition, mares bred to a donkey are at risk of producing a NI newborn, and they are also excellent candidates for antierythrocyte antibody screening.

**Prevention of NI**

There are two ways to prevent NI. One method is to withhold colostrum from the foal of a mare that has antibodies to red cell factors of her foal. The foal should be muzzled and the mare’s milk emptied for 24-48 hours under the advisement of a veterinarian. An alternate source of colostrum should be administered to the foal. The other method is to breed mares only to stallions that have red cell factors that she also has or have red cell factors to which she is unlikely to develop antibodies. Certainly, if the mare is already pregnant, only the first method is feasible. In this situation, the mare’s serum should be tested for antierythrocyte antibodies 2 to 3 weeks before she is scheduled to foal. The results of this testing provides information that can used to predict the possibility that a foal will develop NI. The antibody screen tests for antibodies to 31 red cell factors. Antierythrocyte antibody testing is performed using a panel of red blood cells from 11 horses and one donkey. In addition, if the stallion or jack’s red blood cells are available, crossmatching with the mare’s serum is also performed at no extra charge.

**Blood typing** of the mare and potential stallions can provide information that is useful for preventing NI. For mares that have had a foal that developed NI, this information can be used to select a sire that is negative for the blood group factor to which she has antibodies. Currently, the following blood factors are determined. A (a,b,c,f,g), Ca, D (a,g,k), Ka, P (a,b), Q (a,b,c), Ua, V and W.

**Diagnosis of NI**

Clinical signs of red blood cell lysis in the affected foal usually occur within 6-72 hours after birth. The major clinical signs are lethargy, elevated pulse (heart rate), increased
respiratory rate, anemia and jaundice. If mild, the foal may recover without treatment, however the disease may progress to severe anemia and organ dysfunction leading to death.

Diagnosis is confirmed by demonstrating antibody on the surface of the foal’s red cells by performing a Coombs’ test (EDTA sample). Diagnosis is supported by demonstrating anti-red cell antibodies in the colostrum or serum of the mare.

**Samples for testing**

For NI antibody screen of the mare, 2 ml of serum is required. Allow the blood from a 10 ml red top tube to clot for 30 minutes, spin and separate the serum into another tube. If the mare has had a previous NI foal, please send a whole blood (EDTA) tube as well.

For blood typing of the mare or stallion, whole blood either in EDTA (purple top) or ACD (yellow top) is necessary. To crossmatch an antibody screened mare with the stallion, an EDTA or ACD tube of the stallion’s whole blood and serum from mare’s blood are needed. For Coombs’ testing of the foal, EDTA whole blood sample is required.

The samples should be stored in a refrigerator until they are ready to be shipped. If only serum is shipped, no ice pack is required. For a blood type (whole blood in EDTA or ACD), send with an ice pack. Protect the samples from direct contact with the ice pack. It is best to ship the samples Federal Express or 2 day air.

**Send the samples to:**

Hematology Laboratory  
Room 1012, Veterinary Medical Teaching Hospital  
One Garrod Drive  
University of California, Davis  
Davis, CA 95616
**Contact information:** 530-752-1303  
530-754-9007 FAX  
E-mail:  

**Samples from outside the USA:** Contact the hematology laboratory to receive a copy of the import permit or [download permit](#)

**Cost:**  
$60 for antibody screens (NI)  
$50 for blood typing  
Please include a check payable to VMTH with the submission of the sample and form. If you choose to pay by Visa or Mastercard, please complete the required information on the sample submission form.

**Submission Form**  
*Please fill in required information and a form will be FAXed and mailed.*

**Reporting of Results**  
Generally testing is performed within a few days of receiving the sample. Results will be transmitted through FAX or phoned.

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