How to Evaluate the Icteric Foal: Differential Diagnosis and Management Strategies (21-Nov-2003)

W. Vaala

B. W. Furlong and Associates, Oldwick, NJ, USA.

Abstract

Therapy and prognosis for the icteric foal depends on the cause of icterus. Jaundice is caused by hyperbilirubinemia resulting from hemolytic disease or hepatobiliary disease. The most common cause of hemolytic disease is neonatal isoerythrolysis (NI). Severe cases of NI require transfusions with whole blood, packed red cells, or artificial hemoglobin. Other less common causes of hemolysis include disseminated intravascular coagulation (DIC), bacterial toxin-induced hemolysis, and incompatible blood or plasma transfusions. Hepatobiliary disease in newborn foals may be caused by hepatocellular necrosis associated with Equine Herpes Virus 1 (EHV-1) infection, bacterial hepatitis secondary to sepsis, or hepatic dysfunction after peripartum asphyxia. Causes of primary liver disease in older foals include necrotizing hepatitis caused by Clostridium piliformis infection (Tyzzer's disease) and cholangiohepatitis caused by biliary stasis associated with gastroduodenal ulcer disease. Liver disease caused by EHV-1 infection and Tyzzer's disease is generally fatal.

1. Introduction

Icterus in the foal is caused by hyperbilirubinemia resulting from hemolytic disease (increased bilirubin production) or hepatobiliary disease (decreased bilirubin clearance). The most common cause of hemolysis in the newborn foal is neonatal isoerythrolysis (NI) caused by absorption of colostral antibodies directed against surface antigens on the foal's red blood cells. Other causes of hemolysis in the foal include disseminated intravascular coagulation (DIC) associated with sepsis, bacterial toxin-induced red cell destruction, and incompatible blood transfusions. Hepatobiliary disease in the newborn foal may be caused by hepatocellular necrosis associated with Equine Herpes Virus 1 (EHV-1) infection, bacterial hepatitis secondary to septicemia, or hepatic dysfunction after peripartum asphyxia. Causes of primary liver disease in older foals include necrotizing hepatitis caused by Clostridium piliformis infection (Tyzzer's disease) and cholangiohepatitis caused by biliary stasis associated with gastroduodenal ulcer disease. A rare and fatal form of liver disease and hepatoencephalopathy, reported in Morgan weanlings, is caused by an inherited disorder resulting in hyperammonemia. Icterus caused by hemolysis is accompanied by anemia and hemoglobinuria. Icterus caused by liver disease is associated with increased concentrations of serum enzymes that are elevated during hepatocellular injury (aspartate transferase, lactate dehydrogenase, sorbitol dehydrogenase) or cholestasis (alkaline phosphatase, gamma glutamyl transferase). If hepatic dysfunction is severe, other biochemical markers of liver failure may be observed. The cause of neonatal icterus can be determined after considering the history of periparturient events, the age of onset of jaundice, pertinent physical examination findings, and selected laboratory tests.

2. Neonatal Isoerythrolysis

If icterus develops in an older foal after ingestion of colostrum from a multiparous mare that is negative for the Aa or Qa alloantigen, then NI should be considered. Typically, an affected foal is healthy at birth and nurses normally. Within 24 - 72 h, the foal develops progressive icterus, hemoglobinuria, anemia, weakness, tachypnea, and tachycardia. Affected foals die of anemic hypoxia. The cause of this condition is the foal's ingestion of colostral antibody directed against surface antigens on the foal's red blood cells (RBCs), which results in hemolysis or accelerated removal of circulating RBCs and leads to varying degrees of anemia and accompanying icterus. Clinical signs of NI relate to the severity and rapidity of the onset of anemia. Signs occur only after colostrum has been
ingested and sufficient amounts of offending antibody have been absorbed. This results in RBC destruction. Antibody absorption is usually complete 4 - 5 h after a meal of colostrum is ingested. In severe cases, profound hemolysis develops and results in a short, rapidly fatal clinical course that may be only hours in duration. These foals show pallor of mucous membranes, weakness, tachypnea, tachycardia, and acute collapse and may die. Seizures and other central nervous system (CNS) signs may develop as a result of brain hypoxia. Foals with milder forms of NI develop hemolysis within hours to days after delivery. As hemolysis progresses, foals develop icterus, lethargy, weakness, loss of nursing vigor, tachypnea, tachycardia, and pigmenturia. A low grade fever may be associated with hemolysis.

Pigmenturia and anemia in the absence of blood loss are the hallmarks of intravascular hemolysis. A diagnosis of NI is supported by an incompatible minor agglutination cross match between foal and mare (foal's RBCs and mare's serum); a positive hemolytic cross match between foal and mare requiring the addition of rabbit complement; a positive Coombs test to detect anti-RBC globulins; low or decreasing packed cell volume (PCV) with a stable or normal total protein (TP) concentration, indicating intravascular RBC destruction rather than blood loss; and indirect hyperbilirubinemia compatible with hemolysis and hemoglobinuria. Secondary complications include metabolic acidosis, azotemia, and hypoglycemia. During the regenerative phase of anemia, a neutrophilic leukocytosis with a left shift may develop, which has been attributed to generalized bone marrow stimulation.

NI is the result of RBC destruction by alloantibodies. These alloantibodies are produced by the mare as a result of alloimmunization by foreign erythrocyte antigenic factors of the foal which were inherited from the stallion and not possessed by the mare. Although there are 32 blood group antigens known for horses, Aa and Qa are the antigens most commonly associated with the disease. Theoretically, antibodies can be stimulated to every RBC antigen, but antibodies to most antigens either do not occur naturally or are not important clinically. The incidence of NI is relatively low and varies between breeds. The prevalence of NI causing antibodies is 2% in Standardbred mares and 1% in Thoroughbred mares. Mares that lack Aa and Qa antigens are at risk to produce NI-causing antibodies. The inheritability of different blood group factors also varies. Therefore, the risk of a mare producing a NI foal depends on the following variables: (1) if the mare is negative for Aa or Qa, (2) if the stallion is positive for Aa or Qa, (3) the likelihood that the foal will inherit the Aa or Qa antigen from the stallion and (4) the likelihood that the mare will produce antibodies against the Aa or Qa antigen. For example, 2% of Thoroughbred mares lack the Aa antigen and are at risk to produce antibodies against that antigen. However, only 50% of Thoroughbred mares "at risk" actually make antibodies. The likelihood that foals from these mares will inherit the Aa factor from a Thoroughbred stallion is 85%. Therefore, there are not many thoroughbred mares at risk of having a NI foal caused by antibodies to the Aa antigen. Sixteen percent of thoroughbred mares are positive for Qa. Only 3% of these mares make anti-Qa antibody. The foal has a 60% chance of inheriting the Qa antigen. Among Standardbreds, only 22% of pacer mares are negative for Aa, and only 17% of those mares produce anti-Aa antibodies.

Other blood groups that have been associated with rare cases of NI include Ab, Pa, Dc, and Ua. The C system contains only two alleles: Ca and C- (null). Almost every horse that is Ca negative (C-/C-) produces anti-Ca antibody. These antibodies are not associated with NI, but they can cause problems in the diagnosis of NI with non-specific tests. Anti-Ca antibody seems to play a protective role in mares at risk to produce anti-Aa or -Qa antibody. The presence of anti-Ca antibody in these mares seems to suppress production of harmful antibodies. Anti-Ca antibodies are believed to destroy fetal RBCs before the mare has a chance to mount an immune response.

A mare not possessing Aa antigen may produce antibodies to Aa if her foal inherits that antigen from the stallion. Typically, the mare does not produce the offending antibodies during the first pregnancy; therefore, the first foal remains unaffected. At parturition, some of the foal's RBCs leak into the mare's circulation and stimulate a primary immune response. Maximum antibody response to the foal's RBCs occurs in the mare approximately 9 days post-partum. In subsequent pregnancies, there must be maternal exposure to small amounts of offending fetal RBC antigens. Sources of exposure may include uterine trauma during previous pregnancies, uterine disease during the current gestation, and transplacental hemorrhage. This results in leakage of fetal red cells into the mares circulation during late gestation and subsequently, stimulation of a secondary immune response, resulting in increased maternal antibody production and increased sequestration of offending antibody into the colostrum. Therefore, the ideal time to test a pregnant mare to determine if she is producing anti-RBC antibodies is during the last 3 - 5 wk of pregnancy. Hemolytic tests used to screen late pregnant mares for rising antibody titers against Aa and Qa are considered positive if hemolysis occurs at dilutions above 1:16. If antibodies are detected at dilutions between 1:2 and 1:16, the mare should be retested to see if her titer is increasing. A rising titer suggests that she is carrying a foal with an offending blood type and that the mare is producing anti-foal RBC antibodies. Her foal should be prevented from nursing her colostrum, the mare should be stripped of her colostrum, the colostrum should be discarded, and the foal should receive colostrum from a mare with no history of having NI foals.

If the mare's anti-RBC titer has not been tested before foaling, then, at the time of foaling, a cross match between the foal's RBCs and mare's colostrum can be performed using the Jaundice Foal Agglutination test (JFA) [1]. Dilutions of the mare's colostrum and foal's RBCs are tested for agglutination. Tubes containing diluted colostrum and foal blood are centrifuged at low speeds for several minutes. The reaction is measured as agglutination. The use of the centrifuge causes offending colostral antibodies to agglutinate the RBCs. The titer is defined as the highest dilution that gives strong (+3) agglutination.
Positive reactions at 1:16 or greater in horses and 1:64 or greater in mules are considered significant. The JFA test may miss antibodies against Ab and Ca, and R and S blood group factors. It is important to use pre-suckle foal blood, because after ingestion of the antibody, the foal's cells may become coated with antibody and auto-agglutinate in the JFA test. If clinical signs of NI are detected when the foal is still < 24-h old, then further nursing from the mare should be prevented, and the mare should be stripped of all remaining colostrum. The foal can be physically separated from the mare or muzzled. Muzzling the foal is usually the less stressful alternative. An alternate source of colostrum should be obtained. I prefer to wait until the foal is at least 36-h old before allowing nursing to resume. Mildly affected foals should receive enforced stall rest. If metabolic acidosis or azotemia develops, then IV fluids are indicated. Tachypneic foals may benefit from intransanal oxygen to help fully saturate RBC hemoglobin. Rapidly developing hemolysis may predispose to brain hypoxia and the onset of seizures or other CNS signs (e.g., head tilt). Foals with seizures should receive anticonvulsants (diazepam 5 - 10 mg, IV, or phenobarbital 3 - 9 mg/kg, given slowly, IV).

If the foal's PCV is < 15% or decreasing rapidly, then a whole blood transfusion is required. The donor red cells must be compatible with the mare's serum/colostral antibodies, because those are the offending antibodies circulating in the foal. The most unsatisfactory donor is the stallion. The ideal red cell donor is the mare because her red cells will not react with her own compatible with the mare's serum/colostral antibodies, because those are the offending antibodies circulating in the foal. The most unsatisfactory donor is the stallion. The ideal red cell donor is the mare because her red cells will not react with her own antibodies. However, only washed red cells from the mare are safe to administer. Whole maternal blood transfusions will contain not only beneficial red cells but more of the offending antibodies as well. The mares red cells must be washed at least twice to remove serum antibodies. As much as 5 - 8 l of whole blood can be collected from a 1000 - 1200 lb mare. Blood can be collected in acid citrate dextrose (ACD) or sodium citrate anticoagulant. The red cells are allowed to separate to the bottom of the bottle or bag over 1 - 2 h. The plasma is removed, and an equal volume of 0.9% saline is added, the suspension is gently mixed. The cells are allowed to separate a second time (this second sedimentation is time-consuming and requires many hours) or preferably, can be centrifuged in a large volume centrifuge. A nearby hospital may be willing to provide this service. The saline supernatant is removed, and the red cells are resuspended in an equal volume of 0.9% saline. The washed cells are administered using a blood administration venoset equipped with a filter. An Aa and Qa negative donor, free of Aa and Qa antibody, is a valuable addition to any practice, because this horse can serve as a suitable whole blood donor for most NI foals.

Severe NI cases may require multiple transfusions. If volume overload becomes a limiting factor, an exchange transfusion may be necessary. The new product Oxyglobin [a] Solution represents an alternative solution for some NI foals. This is a hemoglobin-based, oxygen-carrying solution that contains polymerized bovine hemoglobin in a modified Lactated Ringers Solution. Oxyglobin Solution increases plasma and total hemoglobin concentration and thus, increases arterial oxygen content. Oxyglobin solution also increases oncotic pressure. The suggested dose is 10 - 30 ml/kg, administered at a maximum rate of 10 ml/kg/h. Overdosage or excessive rate of administration may result in cardiorespiratory compromise and hypertension [2,3]. The product has a 2-yr shelf life and does not require cross-matching. A major consideration is the cost factor. A lower dose (3 - 5 ml/kg) can be tried and may provide sufficient clinical improvement without unreasonable expense.

The effect of severe hyperbilirubinemia on brain development in the foal is not known. In infants, unconjugated bilirubin levels >18 mg/dl have been associated with an increased incidence of kernicterus or bilirubin encephalopathy (i.e., yellow staining of the brain) and CNS toxicity. Unconjugated bilirubin has the ability to enter brain cells and cause neuronal death. Signs of bilirubin encephalopathy in the newborn include progressive lethargy, rigidity and opisthotonus, high-pitched cry, fever, and convulsions. A similar condition has been documented in foals [4]. Factors that increase the risk of kernicterus include hypoxia, hypoglycemia, acidosis, concurrent bacterial infection, moderate to severe hemolysis, and administration of drugs that compete with unconjugated bilirubin for transport proteins (e.g., sulphonamides). Severe hyperbilirubinemia requires exchange transfusion. Phototherapy with ultraviolet (UV) light (e.g., special blue fluorescent lights are optimal, but cool white and blue lamps can be used) can be used to convert unconjugated bilirubin into a more polarized photo-isomer, which cannot be taken up as readily by neurons. Phenobarbital administration helps stimulate synthesis of hepatic glucuronyl transferase responsible for conjugating bilirubin. Hypoxia and acidosis should be corrected. Enteric reabsorption of unconjugated bilirubin can be decreased with frequent milk feeds and administration of activated charcoal. Most foals with uncomplicated cases of NI recover uneventfully. The prognosis for intact neurological survival decreases if the foal experiences severe, acute hemolysis accompanied by seizures or severe metabolic acidosis. Prevention of NI should be the focus of future breedings [5]. Blood typing can be used to identify mares "at risk" for having NI foals and to select a "compatible" stallion. Most cases of NI occur when a mare that lacks either the blood group antigen Aa or Qa is bred to a stallion that possesses the corresponding factor, either Aa or Qa. Interpreting a blood type report can be confusing, because there is often more information provided than is required to make decisions about breeding. A blood type report usually contains two sections: blood group markers and biochemical or electrophoretic markers. Only the blood group markers are important to assess the risk of breeding two individuals. The A and Q systems are the most important. In the blood group marker section, the A system will be identified by an uppercase "A". There will also be lowercase letters (from a to g), a minus sign, or a combination of lowercase letters and minus signs. If an "a" is listed for the A blood group, the factor Aa was detected. If a minus sign is listed under the "a" in the list of factors, then the horse is "Aa negative". The Q system
will be identified in a similar fashion with an uppercase Q and lowercase letters (a - c) or a minus sign. It is important to determine if the horse is positive or negative for factor Qa. A mare is at risk of producing a NI foal if she is negative for Aa, Qa, or both and is bred to a stallion that is positive for the corresponding factor. Sample blood group results:

<table>
<thead>
<tr>
<th>Sample Blood Group Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mare 1</strong></td>
</tr>
<tr>
<td>A: a b c d e f g</td>
</tr>
<tr>
<td>Q: a b c</td>
</tr>
<tr>
<td>Mare is Aa negative and Qa positive</td>
</tr>
<tr>
<td><strong>Stallion 1</strong></td>
</tr>
<tr>
<td>A: a b c d e f g</td>
</tr>
<tr>
<td>Q: a b c</td>
</tr>
<tr>
<td>Stallion is Aa and Qa positive</td>
</tr>
<tr>
<td><strong>Stallion 2</strong></td>
</tr>
<tr>
<td>A: a b c d e f g</td>
</tr>
<tr>
<td>Q: a b c</td>
</tr>
<tr>
<td>Stallion is Aa negative and Qa negative</td>
</tr>
</tbody>
</table>

Stallion 1 is not compatible with Mare 1, because he has factor Aa, and Mare 1 lacks Aa. If the foal inherits the stallion's blood type at that allele, then the mare is at risk for producing anti-Aa antibodies. Stallion 2 would be compatible, because he is negative for Aa. If Stallion 2 and Mare 1 are bred, there is no risk that the foal would be Aa positive because both mare and stallion are negative for that factor. The Qa factor is not a risk factor, because the mare is Qa positive and is not at risk for producing anti-Qa antibodies, regardless of the stallion's blood type.

Prevention of NI can be accomplished by identifying a mare at risk to produce a NI foal, identifying a compatible stallion, and/or performing a JFA test on the foal's pre-suckle blood and mare's colostrum. After a mare has had a NI foal, she is at increased risk to have another affected foal.

3. EHV-1

Pronounced jaundice accompanied by severely injected mucous membranes in a newborn foal immediately after delivery and before colostrum ingestion is most likely caused by EHV-1 infection. The clinical picture usually associated with EHV-1 infection includes abortion storms and/or the delivery of rapidly fading, premature foals. However, EHV-1 infection has also been associated with full-term deliveries of infected foals and abortion in individual mares on a breeding farm. Neonatal EHV-1 infection is almost always fatal and is associated with hepatic necrosis and severe interstitial pneumonia. Virus-infected foals are usually born weak, and they succumb to progressive respiratory distress and multi-organ failure. It is often difficult to distinguish EHV-1 infection from severe bacterial septicemia. Some foals may have concurrent infections with both virus and bacteria.

EHV-1 produces a leukocyte-associated viremia, which results in either transplacental infection of the fetus and/or virus replication within endometrial and placental endothelial cells. Abortion or premature delivery is caused by infection of the fetus and/or virus-induced vasculitis and thrombosis of placental and endometrial vessels. Affected foals may be the product of a premature delivery or term pregnancy. Because EHV-1 induced parturition is often precipitous, the mare often lacks adequate udder development at the time of delivery, regardless of the length of gestation. The placenta is often grossly normal. There may be a farm history of multiple abortions and/or early neonatal deaths, or EHV-1 infection may only affect a single broodmare. Delivery is often normal but occasionally can be complicated with premature placental separation.

Clinical signs of EHV-1 infection in the newborn foal include severely injected, icteric mucous membranes and sclera, depression, generalized weakness, progressive respiratory distress, and septic shock associated with multi-organ system failure. Signs of icterus are usually apparent immediately after delivery. Even the hooves may appear yellow. The presence of severe injection with concurrent icterus should increase the index of suspicion for EHV-1 infection. Many affected foals may be the product of a precipitous delivery and shortened gestation length, and they may show signs of prematurity.

Blood work often reveals a severe leukopenia and a more dramatic lymphopenia (lymphocytes < 500 - 1000 µm) accompanied by hypoglycemia, indirect hyperbilirubinemia, and a variable increase in hepatocellular enzymes (e.g., aspartate aminotransferase [AST] and sorbitol dehydrogenase [SDH] ) [6]. Arterial blood gas analysis reveals hypoxemia, progressive hypercapnia, and respiratory acidosis. Some virus-infected neonates may have concurrent bacteremia. Buffy coat samples can be submitted for virus culture. Thoracic radiographs reveal diffuse interstitial pneumonia. Arterial blood gas analysis demonstrates severe and progressive hypoxemia, hypercapnia, and mixed metabolic/respiratory acidosis.

If EHV-1 infection is suspected, anti-viral medications can be instituted using oral acyclovir. Oral bioavailability of acyclovir is relatively poor (15 - 30%). The drug is distributed throughout tissues, but then it crosses the placenta and concentrates in milk. Doses of acyclovir used in foals vary with ranges of 8 - 16 mg/kg, PO, q 8 h. There is little information in the literature to document the effects of acyclovir on EHV-1. Aggressive therapy for acute sepsis should also be initiated with IV fluids, hyperimmune plasma, broad spectrum, bactericidal antibiotics, and respiratory support. Prognosis for survival is grave.

The most common necropsy findings in EHV-1 infected neonates include hepatic and lymphoid necrosis, pulmonary atelectasis and edema, pneumonia, and bronchiolitis. EHV-1 infection can be confirmed by identification of viral intranuclear
inclusion bodies in various tissues including the liver, lymphoid tissue, lungs, adrenal glands, and ileum. EHV-1 virus has been isolated from the lung, liver, brain, buffy coat samples, and amniotic fluid. To confirm suspected EHV-1 infection, sections of liver, lung, and adrenal gland should be submitted for immunoperoxidase staining and fluorescent antibody staining. The mare of the infected foal should be kept isolated from other broodmares for at least 2 wk, because virus shedding from the urogenital and respiratory tracts may persist for a variable time period.

4. Tyzzer's Disease
Acute onset of icterus, profound depression, and collapse in an older foal between the ages of 7 - 42 days is most compatible with acute bacterial hepatitis and liver failure caused by Bacillus piliformis, now renamed Clostridium piliformis (e.g., Tyzzer's disease). The incidence is sporadic with only one foal on a farm usually affected, although outbreaks among foals have been reported [8]. Route of infection is presumed to be oral ingestion of the organism from contaminated soil or the feces of an infected horse, possibly the mare. Clinical signs include acute onset of severe depression and weakness accompanied by intense icterus, mucous membrane hyperemia and injection, anorexia, hypotension, diarrhea, and signs of septic shock. Terminal foals become moribund and may seize uncontrollably. Laboratory findings include markedly elevated levels of AST (>10,000 IU/L) and SDH, hyperbilirubinemia (both direct and indirect bilirubin), profound hypoglycemia, and severe metabolic acidosis. Supportive therapy for fulminating liver failure can be instituted but is almost always unrewarding. Treatment includes shock doses of IV crystalloid fluids (20 - 50 ml/kg), hypertonic glucose infusions, IV colloid administration (e.g., Hetastarch 10 - 20 ml/kg/h), IV hyperimmune plasma incubated with 100 units of heparin added/l, intranasal oxygen, anticonvulsants (phenobarbital, 3 - 10 mg/kg, given slowly, IV; avoid diazepam), IV pressor support (e.g., dopamine 2 - 10 µg/kg/min, dobutamine 2 - 15 µg/kg/min), pentoxyfylline (8.4 mg/kg, orally, q 8 - 12 h), and broad-spectrum antibiotics (K penicillin: 15000 - 44000 IU/kg, IV, q 6 h; gentamicin: 6.6 mg/kg, IV, q 24 h; metronidazole: 15 mg/kg, orally, q 8 h or 10 mg/kg, IV, q 8 h). Oral administration of neomycin (4 - 8 mg/kg, q 8 h) may help decrease enteric ammonia production. Be aware that correction of acidosis can increase the amount of ionized ammonia and exacerbate CNS signs. Maintain adequate serum concentrations of potassium to help reduce hyperammonemia. The prognosis for survival is grave. Diagnosis is based on fecal polymerase chain reaction (PCR) testing for C. piliformis and/or histopathology of the liver. Post-mortem findings include gross icterus, petechiae, pulmonary hemorrhage, and multifocal white spots in the liver. Microscopic examination of the liver reveals focal area of coagulation necrosis with neutrophil infiltration and large bacilli within the cytoplasm of hepatocytes. The organism is most easily seen with a Warthin-Starry silver stain.

5. Other Causes of Icterus
Less intense icterus in the newborn may be caused by hepatic dysfunction associated with generalized septicemia and bacterial hepatitis. In this group of foals, jaundice may be caused by biliary stasis, secondary bacterial hepatitis, or hemolysis associated with DIC. Pre-partum events associated with neonatal sepsis include vaginal discharge and precocious lactation suggestive of placentitis. Clinical signs of sepsis in the foal include injected mucous membranes, progressive weakness, and depression accompanied by leukopenia, hemoconcentration, and metabolic acidosis. Hypoxic-ischemic liver damage should be considered in foals showing other signs of hypoxic ischemic encephalopathy (HIE) such as stupor, abnormal mentation, and seizures. Such foals may be the product of deliveries complicated by dystocia and/or placental disease and dysfunction, including premature placental separation, placentitis, and placental edema. Liver disease associated with hypoxic liver disease usually resolves with successful management of the primary problem. A rare form of liver disease and hepatencephalopathy (HE) has been reported in Morgan weanlings and is associated with abnormal behavior, unthriftiness, and poor growth after weaning. Affected foals display signs of dementia and depression characteristic of HE [9]. Serum chemistries reveal an abnormal amino acid profile in the urine and serum characteristics of the inherited disorder in humans described as hyperornithinemia, hyperammonemia, and homocitrullinuria (HHH) syndrome. This disorder is thought to be caused by a defective mitochondrial transporter protein, which results in a deficiency of ornithine, a requirement for the completion of urea synthesis. Ornithine deficiency results in an increase in blood ammonia and ornithine concentrations. It has been seen among groups of related Morgan weanlings. There is no treatment.

6. Summary
A grave prognosis for survival is often associated with icterus. Additionally, it is accompanied by intense mucous membrane injection and laboratory evidence of severe hepatocellular disease, regardless of the age of onset of clinical jaundice.

Footnotes
References


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