Foal with Overo lethal white syndrome born to a registered quarter horse mare

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Abstract — A 16-hour-old white foal, born to a registered quarter horse mare, was examined for signs of colic. The foal had Overo lethal white syndrome, which causes ileocolonic aganglionosis. This was confirmed by DNA testing. Since there is no treatment for Overo lethal white syndrome, the foal was euthanized.

Résumé — Poulain né d'une jument Quarter horse enregistrée et présentant le syndrome létal de l'Ovéro blanc. Un poulain âgé de 16 heures, né d'une jument Quarter horse enregistrée, a été examiné pour des signes de coliques. Le poulain avait le syndrome létal de l'Ovéro blanc, confirmé par test d'ADN, syndrome accompagné d'une aganglionie iléocolique. Comme il n'y a pas de traitement pour le syndrome létal de l'Ovéro blanc, le poulain a été euthanasié.

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A 14-year-old, pregnant mare with American Quarter Horse Association registration papers was purchased at auction in March 2000, with the knowledge that she had been bred to a paint stallion. The mare was registered as solid chestnut with a star, strip and snip, a dark spot above her nostrils, a white spot in the right nostril, and no other white markings. The mare's sire, a registered American paint horse, was sorrel with an Overo pattern.

Gestation and parturition were uneventful, and the filly foal suckled spontaneously within 2 h of birth. The mare quickly accepted the foal, which was very mobile and inquisitive in the paddock. The only unusual observations were the distinctively white coat of the foal and failure to pass the meconium (Figure 1). Within 12 to 16 h of birth, the foal started to show signs of colic.

When examined on day 1, the foal appeared very uncomfortable, alternating between standing, lying down, and rolling on its back. It was completely white with blue irides. The pupillary light reflex and menace response were present. Oral mucous membranes and capillary refill time were normal, but the heart rate was slightly elevated (110–120 beats/min). There was a mild increase in lung sounds in the cranioventral lung fields. All joints, the umbilicus, and the rectal temperature (38°C) were normal. The most significant finding was the lack of borborygmi on ascultation of the abdomen. Feces were present deep within the rectum. The clinical findings suggested a meconium impaction or, more likely, Overo lethal white syndrome (OLWS).

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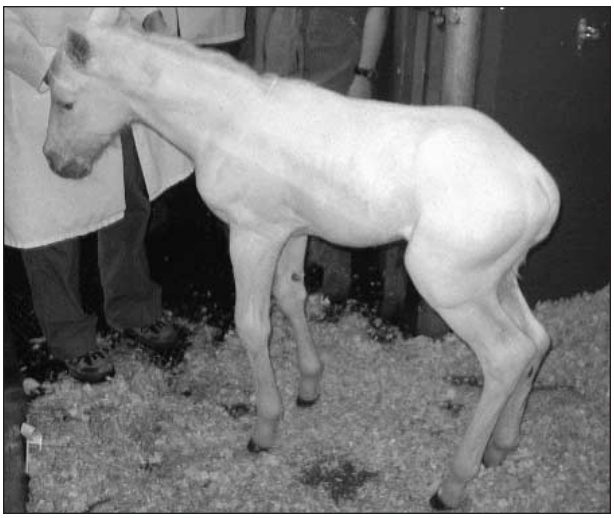

Figure 1. Overo lethal white foal born to a registered Quarter horse mare.

As supportive therapy, 120 mL of mineral oil was administered as an enema to assist with the passage of the meconium plug, and flunixin meglumine (Cronyxn; Vetrepharm, Belleville, Ontario), 150 mg, IV, was given to relieve abdominal pain. Response to the analgesia was marked and the foal became recumbent.

On day 2, the foal continued to show signs of colic. Euthanasia was recommended, and blood samples were taken from the mare and foal to confirm the diagnosis of OLWS. The foal was euthanized and a postmortem was performed. On gross examination, the foal lacked pigmentation and the abdomen was grossly distended. The lungs were mildly edematous, but the liver, spleen, kidneys, and adrenal glands appeared normal. The peritoneal cavity contained serosanguinous brown fluid, suspected to have leaked from the intestines ante- and

postmortem. There was no evidence of an intestinal accident and no strictures were identified along the length of the intestine. The serosal surface of the small colon and rectum was pale. Most of the intestinal tract was gas filled, and the caudal aspect of the large intestine was distended with particulate matter. Samples (skin, liver, lung, intestine, heart, spleen, kidney, and eye) were collected into 10% buffered formalin and submitted for histopathologic examination. Histologically, no melanin was seen in the skin and there were few active hair follicles. Many follicles were devoid of hair or were in catagen phase (transition between active and resting hair growth). The liver and lungs were mildly congested. In a few areas of the lung, aspirated squamous epithelial cells and a light mononuclear cell infiltrate were seen. The colon was normal, except for the absence of ganglion cells, which was compatible with ileocolonic aganglionosis, as seen in OLWS (2).

Blood samples from the mare and foal were submitted for DNA analysis (Minnesota Veterinary Diagnostic Laboratory, College of Veterinary Medicine, University of Minnesota, St. Paul, Minnesota, USA), which confirmed that the mare was heterozygous and that the foal was homozygous for the OLW gene.

Overo lethal white syndrome occurs in newborn foals that receive a copy of the mutated OLW gene from each parent. Horses with white Overo patterning are more likely carriers of the gene than solid-colored horses (2). The mutated gene alters neural crest cell migration or survival, which affects the progenitor cells for melanocytes and intestinal ganglia. Affected foals suffer from aganglionosis of the submucosal and myenteric ganglia of the distal part of the small intestine and of the large intestine, resulting in intestinal immotility and colic (2). Phenotypically, the altered gene causes lack of skin pigmentation and white coat color. The Overo coat pattern is described as white markings on the lateral and ventral aspects of the neck and torso, whereas a pattern with more white on the dorsal cervical and lumbar regions and the legs is called tobiano (3). The Overo coat pattern is seen in the American paint horse, American miniature horse, half-Arabian, Thoroughbred, and crop-out (unregistered because of excessive white marking) quarter horse (QH).

The lethal OLWS gene is an autosomal dominant with variable expression. Heterozygotes demonstrate assorted white coat patterns, and, on very rare occasions, may be solid-colored; for example, if the dominant lethal gene is not being expressed or has spontaneously mutated. Additional studies are necessary to explain the sporadic occurrence of Overo foals from nonspotted QH parents. Two carriers of the mutated gene must be mated to produce a homozygous lethal white foal. According to Mendelian genetics, an Overo × Overo mating would be expected to produce 25% solid-colored foals, and 50% Overo foals, and 25% OLW foals (1).

Stud book records and observation of born foals show that the probability of producing an OLWS offspring is less than 25%. Possible factors contributing to this unexpectedly low frequency may include failure to report OLW foals to breed registrations, early embryonic loss of homozygote foals, or the relative proportion of carriers in the breeding population (1).

Understanding the inheritance of the lethal gene is important for economic reasons, as paints are desirable in western horse shows, and it would be an advantage to be able identify horses carrying the Overo gene (3). Inaccurate data on the risk of OLWS may deter people from using breeding stock with Overo blood lines. With accurate genetic information, breeders could avoid the psychological and economic losses associated with the Overo lethal gene by testing breeding stock for carrier status and breeding known Overos only to proven non-Overos.

As there is no treatment for OLWS, testing is essential to prevent its occurrence (1). Before DNA testing was available, carriers were identified phenotypically by the proportion of white in the coat: the more white, the greater risk of being a carrier. Although this technique identified most carriers, it was inaccurate. A DNA-based test that identifies horses that are heterozygous for the Overo lethal white gene has been developed. The allele-specific polymerase chain reaction test locates and amplifies the specific mutated site in the endothelin receptor B gene (EDNRB gene). This site has been identified in humans with Hirschsprung disease, in whom similar gastrointestinal effects from a mutation of the EDNRB gene are seen. Sequencing of the DNA of the EDNRB gene revealed a dinucleotide thymine-cytosine to adenine-guanine mutation. This results in substitution of the amino acid isoleucine for lysine in the first transmembrane domain of the EDNRB protein (termed Ile118Lys mutation) (4). The EDNRB protein is responsible for regulation of embryonic neural crest cells that develop into ganglia and melanocytes. Foals homozygous for the Ile118Lys mutation in the EDNRB gene have only 20% of the functional protein ability of control horses (5). Innervation to the intestine is impaired, causing fatal constipation. Heterozygotes commonly have the Overo coat pattern without intestinal abnormalities. In a study to determine the phenotype of heterozygotes, > 95% were Overo and < 1% were solid colored (2). Variation in the expression of the Overo pattern and inability to predict the exact genotype from the phenotype are due to augmentation of the white coloring by other genes. In order to explain the sporadic occurrence of an OLW foal from a solid-colored QH, further research is required to understand this multifactorial inheritance pattern. The association between coat color spotting, intestinal aganglionosis, and mutations of the EDNRB gene has been studied in mouse models (6,7). It is possible that the EDNRB gene in the QH spontaneously mutates or mutates at a higher rate than in rodents (2).

Proper sampling is important for DNA analysis. Blood or hair samples can be used, but there are difficulties in obtaining DNA from blood, and the blood must be unclotted, kept refrigerated, and delivered to the laboratory within 24 h. Hair samples must include the roots and 15 to 20 hairs, and can be collected from the mane or tail, and require no specific packaging (Minnesota Veterinary Diagnostic Laboratory, University of Minnesota, personal communication).

This case demonstrates the classic clinical and pathological presentation of an OLW foal with unusual

parental lineage. The QH mare represents the small proportion of solid-colored heterozygotes.

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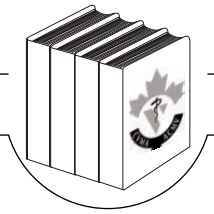
BOOK REVIEW



COMPTE RENDU DE LIVRE

World Health Organization. ***Foodborne Disease: A Focus for Health Education.*** World Health Organization, Geneva, 2001, 198 pp, ISBN 92-4-156196-3, US$55.80.

Health education on the prevention of foodborne disease is of the utmost importance. You are not convinced? Would you change your mind if you discovered that foodborne diseases caused by bacteria, parasites, viruses, toxins, and chemical residues are much more prevalent than you had realized? What if you were told, for example, that every year, 8% to 10% of the population is affected by a foodborne disease? Now, what if you were to learn that, over the last 30 years, the frequency of foodborne diseases has increased by over 300%? That type of information, along with precise statistics on foodborne diseases, costs of foodborne diseases, economic implications and various factors affecting prevalence rates of foodborne diseases, is given in *Foodborne Diseases: a Focus for Health Education.* But this book gives you much more than that. Contrary to the false belief that foodborne diseases are only mild gastroenteritis, you will find that many foodborne diseases could also result in serious acute complications, such as haemolytic uremic syndrome, or chronic sequellae, such as chronic arthritis, Guillain-Barré syndrome, etc.

The 3 basic lines of defense against foodborne diseases are explained: namely, the increase of hygiene of raw foodstuff in agriculture and aquaculture; the application of food processing technologies to control contaminants at the processing level; and, the most critical, the education of consumers and food handlers. Multiple examples of the behaviors (socio-economics, cultural, etc.) that influence foodborne diseases are also provided. The authors then explain the Hazard Analysis: Critical Control Point (HACCP) concept as an internationally accepted tool to manage food safety hazards.

The book highlights the fact that food safety is the shared responsibility of all stakeholders, including policy-makers, food producers, food processors, food handlers, and consumers. These various groups need to be educated to their respective roles in the prevention of foodborne diseases. To be successful in reducing foodborne diseases, it is not sufficient to have a pathogen reduction policy and to perform inspections. Any country wishing to decrease foodborne diseases needs to develop and implement a food safety education program. This is a key component of a farm to fork implementation of HACCP-based systems, and it is an integral part of risk management. A lot of material has already been developed, and this volume provides many useful references to the existing material that could be used as a starting point for food safety educators.

Key elements for setting up a food safety education program on a national basis or for a specific segment of the population are explained. The book also provides criteria that could be used to evaluate the food safety education programs, based on practical international experience. At the end of the volume, a table of characteristics, transmission, and preventive measures is given for major foodborne diseases. A table on issues to risk communication is also provided.

The conclusion of the book states, "It is hoped that this book will make a positive contribution to the quest for increased health education in food safety." That would be indeed my personal conclusion after having read the book, which is a must for any person involved in food safety education or, even, in food safety risk communication.

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