Failure of passive transfer of immunity

Failure of passive transfer of immunity is recognised as the most common immune disorder in foals. As maternal immunoglobulins are not transferred to the fetus in utero, foals are born in an immunonaive state, which leaves them susceptible to infection. Variation in the reported incidence of failure of passive transfer of immunity is considered to be because of varying management practices and the availability of colostrum banks. Good management practices include close monitoring of the foal's ability to nurse, the quality of the mare's colostrum and early recognition of the immune status of the foal and whether veterinary intervention is warranted.

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Failure of passive transfer of immunity is recognised as the most common disorder in foals that affects the immune system (Nath et al, 2010). It occurs secondary to (Giguère and Polkes, 2005):

- Insufficient ingestion of colostrum or colostrum with insufficient immunoglobulin content
- Failure to absorb immunoglobulins from the gut
- Catabolism of circulating immunoglobulins in neonatal foals that are ill.

Maternal immunoglobulins are not transferred to the fetus in utero due to the diffuse epitheliochorial placenta of the mare (Jeffcoat, 1974; Tyler-McGowan et al, 1997). Foals are therefore born in an immunonaive state, which renders them susceptible to infection and subsequent death, and septicaemia has been reported in the literature as a major factor in neonatal morbidity and mortality (McGuire et al, 1977; Sturgill and Carter, 2008) with failure of passive transfer of immunity being recognised as a factor in the subsequent development of sepsis (Morris et al, 1985; Cohen, 1994; Tyler-McGowan et al, 1997). Variation in the incidence of failure of passive transfer of immunity is considered to be a result of varying management practices and the availability of colostrum banks that allow for early identification of poor quality colostrum and supplementation where necessary (Galvin and Corley, 2010).

Colostrum

The mammary glands of the mare have a small cistern (storage area) from which the foal nurses throughout the day, with the ejection of milk requiring the release of oxytocin. Healthy foals should nurse several times an hour, therefore, the newborn foal needs to be able to stand and drink as soon as possible, with most healthy foals achieving this within 2–3 hours (Shepherd, 2010). Poor suckling behaviour may be noted in foals that are weak and unable to suckle, or because the mare does not allow the foal to nurse (Nath et al, 2010). The objective assessment of foal vigour (determined by maturity, congenital defects, general health and conformation) by attendants or owners is vital, as this has been identified as a critical factor in the development of failure of passive transfer of immunity (Clabough et al, 1991).

In the first 1–3 hours after birth, the intake of colostrum by the foal should be monitored, as the average 50 kg foal should ingest 5–12% of their bodyweight (Bedenice, 2023). Colostrum is the first form of milk produced by the mare in the last few weeks of pregnancy under the influence of oestrogen and progesterone (LeBlanc, 2001). Good quality colostrum is essential for the establishment of passive immunity, and the subsequent development of the immune system in foals (Schneider and Wehrend, 2019). Colostrum is rich in nutrients such as essential amino acids, lipases, proteinases and antioxidants (Reiter and Reed, 2023). Colostrum has (Barreto et al, 2020):

- A dry matter of 29% (higher than milk, which has 14%)
- Fat levels which are approximately 20% higher than milk fat
- A high protein content (10%, on average), of which 80% is composed of immunoglobulins.

Immunoglobulins, or antibodies, are Y-shaped glycoproteins produced by plasma cells that participate in the humoral immune response against pathogens such as bacteria, viruses and fungi, and there are five different types found in placental mammals – immunoglobulin M, immunoglobulin G, immunoglobulin A, immunoglobulin E and immunuglobulin D (Justiz-Valliant et al, 2023). Immunoglobulin G and A are both found in equine colostrum, with immunoglobulin G found in greater amounts than immunoglobulin A (Reiter and Reed, 2023). The transfer of immunoglobulin G from the maternal circulation to the colostrum begins two weeks before parturition, with colostrum immunoglobulin concentrations decreasing approximately 12 hours after the birth of the foal (Pasquini et al, 2005). Good quality colostrum contains a mean of 70 g/L immunoglobulin G at foaling, falling rapidly after 2–3 hours to below 5 g/L at 24 hours (Perkins and Wagner, 2015). Factors that can affect the quality of the colostrum include (Vaala, 2007; Salamon et al, 2009):

- Poor maternal immune or nutritional status
- Premature lactation
- Placentitis
- Premature placental separation
- Advanced maternal age
- Maiden pregnancies
- Breed
- Ingestion of endophyte-contaminated fescue grass or hay.

A 2020 study by Barreto et al reported that breed influences the percentage of protein found in colostrum, with their results suggesting that the colostrum of Quarter Horse mares may contain more protein and be less dense in energy when compared to breeds reported in other studies.

The absorption of colostral proteins and macromolecules is completed non-selectively by specialised cells in the small intestine, with maximal absorption taking place soon after birth and rapidly decreasing to less than 1% by 20 hours after birth (Jeffcott, 1971; Jeffcott, 1974). During the first 4 weeks of life (as the foal grows), maternally derived serum immunoglobulin declines rapidly as immunoglobulin G is catabolised and diluted in the increasing plasma volume and the foal begins to produce its own immunoglobulin (LeBlanc, 2001).

Neonatal foal management and colostrum assessment

Good management practices associated with foaling, such as observation of the birth, early identification of factors associated with the nursing ability of foals and the evaluation of the quality of the colostrum produced by mares, should aid with the prevention and early recognition of failure of passive transfer of immunity (Nath et al, 2010). Detecting failure of passive transfer of immunity is an important part in the initial clinical examination of the neonatal foal to reduce morbidity and mortality, and assessing the quality of colostrum from the mare can be useful to identify foals who are at a higher risk of developing failure of passive transfer of immunity (Rampacci et al, 2023). It has been reported in the literature that 67% of foals receiving low quality, and 45% of foals receiving mediocre quality colostrum have failure of passive transfer of immunity (Trundell, 2022).

A radial immunodiffusion assay can provide a quantitative measurement of immunoglobulin G levels in colostrum. However, this test cannot be performed easily on the farm, is expensive and the results are not known for approximately 24 hours (Dascanio and McCue, 2014). Visually, good quality colostrum is thick, sticky in texture and yellow in colour, although colour is not a reliable indicator of quality (Chavatte et al, 1998). Assessment of the quality of colostrum can be more reliably based on its biophysical properties such as density, refractive index, relative density and viscosity (Schneider and Wehrend, 2019). Density of equine colostrum should be 1060 g/L, and the refractive index (or relative density) measured with a refractometer (*Table 1*) has been proven to correlate with immunoglobulin G (Schneider and Wehrend, 2019). The use of a digital or handheld (Brix) refractometer, which measures the concentration of dissolved solids in a solution (Dascanio and McCue, 2014), provides a cheap and rapid means of qualitatively measuring colostral immunoglobulin G concentration, and can be utilised easily as a screening tool by owners and breeders (Elsohaby et al, 2019). Low levels of immunoglobulin G will have a lower amount of light scatter (low reading); whereas high colostral immunoglobulin G will cause more light scatter (high reading) (Trundell, 2022).

It is recommended that serum from the neonatal foal should be tested at 8–12 hours old to determine whether sufficient colostral immunoglobulin G has been absorbed (Korosue et al, 2012). Failure of the foal to ingest or absorb a sufficient amount of colostral immunoglobulin G results in complete failure of passive transfer immunity or partial failure of passive transfer immunity (Liepman et al, 2015; Ujvari et al, 2017). Failure of passive transfer immunity has been defined as a serum immunoglobulin G concentration of <200 mg/dL at 24–48 hours after birth (Claybough et al, 1991), and more recently, <400 mg/dL at 24 hours of age (Sellon, 2006; Nath et al, 2010; Korosue et al, 2012). By using a single cut off value, Liepman et al (2015) found an increased likelihood of death if the concentration of protein was <8 g/L.

When selecting the most appropriate test to use it is important to consider overall accuracy, time necessary to perform the test, simplicity of the testing procedure, and cost (Sellon, 2006). The single radial immunodiffusion test is considered to be the most accurate (gold standard) test for quantitative measurement of immunoglobulin G concentration in foals (Ujvari et al, 2017). However, results of single radial immunodiffusion tests are generally not available for 24 hours, and the test is expensive (Korosue et al, 2012). A study by Davis and Giguère (2005) reported that there is also a need for universal reference standards among manufacturers of radial immunodiffusion assays. Other rapid, inexpensive point-of-care tests for clinical use are available, including an enzyme-linked immunosorbent assay test, zinc sulphate turbidity test, glutaraldehyde coagulation tests and latex agglutination tests, which have been shown to have acceptable sensitivity and specificity; however, they provide semi-quantitative results and are subject to interpretation error (Ujvari et al, 2017). The zinc sulphate turbidity test is a relatively accurate, inexpensive test, with results available within an hour and can be used 12 hours after birth; however, the reaction of the test is temperature-dependant and false positives can result if the test is performed outside of the recommended temperature of the solution (between 30–37°C (Pompermayer et al, 2019)). The SNAP® Foal IgG test is a rapid (results within 10 minutes), inexpensive, enzyme-linked immunosorbent assay test, designed to use 'stall-side' with whole blood or plasma that is easy to use. However, results of a study by Metzger et al (2006) reported that whilst the test has good sensitivity, it has moderate-to-poor specificity for the detection of failure of passive transfer of immunity in hospitalised foals, and that specificity of the test is affected by sepsis score and bacteraemia. This may lead

Table 1. The relationship between colostrum quality, immunoglobulin G concentration measured by radial immunodiffusion assay and refractometry (Brix) score (Adapted from Dascanio and McCue, 2014).

Colostrum quality	Immunoglobulin G concentration (mg/dl)	Brix score (%)
Very good	>8000	>30
Good	5000–8000	20–30
Fair	2800–5000	15–20
Poor	<2800	<15

KEY POINTS

- Failure of passive transfer of immunity is recognised as the most common disorder of foals to affect the immune system.
- Good quality colostrum is essential for the establishment of passive immunity, and the subsequent development of the immune system in foals.
- Various factors can affect the quality of the colostrum, including poor maternal immune or nutritional status, premature lactation, advanced maternal age and maiden pregnancies.
- Detecting failure of passive transfer of immunity is an important part in the initial clinical examination of the neonatal foal to reduce morbidity and mortality, and assessing the quality of colostrum from the mare can be useful to identify foals who are at a higher risk of developing failure of passive transfer of immunity.
- The use of a digital or handheld (Brix) refractometer, which measures the concentration of dissolved solids in a solution, provides a cheap and rapid means of qualitatively measuring colostral IgG concentration, and can be utilised easily as a screening tool by owners and breeders.
- A colostrum bank, or storage on farm, is the best (and cheapest) management method that can be implemented during the foaling season.

to over-diagnosis of failure of passive transfer of immunity in sick, hospitalised foals, particularly when the serum immunoglobulin G concentration of 800 mg/dL is used as the cut-off value, which is common in referral hospitals. Therefore, the context of where these tests are used should be considered.

Treatment

A colostrum bank, or storage on farm, is the best (and cheapest) management method that can be implemented during the foaling season. High quality colostrum can be frozen for later administration to foals that are at risk of failure of passive transfer of immunity (Stoneham et al, 1991). It is important that records of the source of colostrum are kept, as well as the date the colostrum was sourced, to avoid prolonged storage of colostrum (>2 years) (Nath et al, 2010). If low immunoglobulin G levels are recorded between 8–12 hours of birth, banked (fresh or frozen) colostrum can be administered via nasogastric tube as the intestinal mucosa is still able to absorb the immunoglobulins (Trundell, 2022). Serum immunoglobulin G testing should be repeated 12–24 hours post-treatment. If frozen colostrum is used, it should be slowly thawed in lukewarm water, as excessively hot water (or the use of a microwave) will denature the colostral immunoglobulins.

If low immunoglobulin G levels are recorded after 24 hours of birth, the intestinal mucosa will no longer be able to absorb the immunoglobulins, and immunoglobulin G will need to be administered parenterally (Trundell, 2022). Foals with immunoglobulin G concentrations of <400 mg/dL should receive plasma (Sellon, 2000), and intravenous administration of plasma is recommended to increase a foal's serum immunoglobulin G concentration to 800 mg/dL (Nath et al, 2010). Plasma should ideally be collected from hyperimmunised animals, to ensure the quality of immunoglobulin G, and commercial frozen plasma is available (Trundell, 2022). Initial infusion rates should be slow, and the foal should be closely monitored for adverse reactions, which can include (Sellon, 2006):

- Muscle fasciculations
- Piloerection
- Increased heart or respiratory rates
- Fever
- Respiratory distress
- Abdominal pain
- Blanching of mucous membranes
- Collapse.

If any significant changes are observed, the transfusion should be stopped.

Conclusions

Failure of passive transfer of immunity is a common condition that is seen in neonatal foals, and the best approach to management is through prevention and early recognition of the problem. A thorough history of the mare should be kept, and owners and breeders should be educated about the importance of colostrum. Monitoring of the foal by trained attendants should be in place to ensure that foals stand and suckle vigorously within a few hours of birth. Assessment of the quality of colostrum of the mare should be undertaken, and a Brix refractometer provides the owner or breeder with an easy and inexpensive means of doing this. Breeders should consider establishing a colostrum bank for supplementing foals that are unable to suckle, and serum immunoglobulin G testing of foals should be undertaken to establish the immune status of the foal and whether treatment is necessary either with oral colostrum or intravenous plasma. EQ

Conflict of interest

The author declares that there are no conflicts of interest.

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