

Sepsis, Failure of Passive Transfer, and Fluid Therapy in Calves.¹

Amanda M. House, Max Irsik, Jan K. Shearer²

Septicemia and Neonatal Infection

Infection and septicemia are significant causes of morbidity and mortality in newborn animals. Calves require adequate colostrum for passive antibody protection, because maternal immunity is not transferred through the placenta. The amount of exposure to the infecting agent and the neonate's ability to modulate the infection through the immune system both affect the occurrence of septicemia. Septicemia is defined as the acute invasion of the systemic circulation (the blood stream) by pathogenic bacteria, which may cause sepsis or septic shock with localization in various body systems or organs. The most common cause of septicemia is failure of passive transfer (FPT).

Possible routes of infection for septicemia:

Possible routes of infection for bacterial invasion include ingestion, inhalation, umbilical infection, and in utero infection. As a result, infection of the umbilical stump, pneumonia, and diarrhea are common visible signs.

Most common bacterial causes of Septicemia in Calves:

E. coli – most common

Salmonella spp

Listeria monocytogenes

Pasturella spp

Streptococcus spp

Leptospira spp

Actinobacillus spp

Clinical Signs of Septicemia:

Weakness/recumbency/depression

Absent or decreased suckle reflex

Dehydration

Fever or hypothermia (normal temperature does not rule out sepsis)

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 2. Amanda M. House, assistant professor; Max Irsik, assistant professor; Jan K. Shearer, professor; College of Veterinary Medicine, Large Animal Clinical Sciences, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, 32611.

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Hyperemic mucous membranes, +/- petechiae (pinpoint hemorrhages on the gums)

Signs of localizing infection such as diarrhea, meningitis (infection of the nervous system), hypopyon (infection in the eye), pneumonia, swollen joints or umbilicus

Diarrhea is a common localizing sign of sepsis in calves and other newborn animals

Acute death

Diagnosis:

Definitive diagnosis is accomplished with blood culture of the etiologic agent. The veterinarian must obtain a sterile blood sample and submit it to the lab. However, evidence of localizing infection (such as diarrhea, pneumonia, etc.) is suggestive, especially if FPT is present.

Clinical Pathology:

When evaluating the white blood cell count, a decrease or increase in white blood cells may be present depending upon the progress of the infection or septicemia. Plasma fibrinogen concentration (which is an indicator of systemic inflammation) may be increased. Changes in the serum chemistry profile will vary depending on degree of dehydration and the presence or absence of diarrhea. A decrease in total protein (total protein < 5.5 g/dl) is suggestive of failure of passive transfer, however, it is important to remember that dehydration may falsely elevate the total protein. A decrease in blood glucose may also be present in calves not nursing adequately, and is a common finding in septicemia.

Treatment:

Supportive care with intravenous and/or oral fluids, colostrum or plasma and antibiotics. Localizing signs of diarrhea, pneumonia, or other abnormalities will direct additional therapy (eg. Oxygen supplementation, anticonvulsants if seizing, etc).

Failure of Passive Transfer

Newborn calves rely on antibodies present in colostrum for protection against common environmental pathogens. Adequate passive antibody transfer should be the cornerstone of all neonatal preventive health programs. Neonates are immunocompetent at birth, but endogenous antibody production does not reach protective levels until 1 month of age, and maximum levels until at least 2-3 months of age. Failure of passive transfer alone is not a disease; however, it predisposes neonates to infection and septicemia if not immediately identified and corrected.

Normal Immunoglobulins and Passive Transfer

The primary immunoglobulin in colostrum is IgG. Other proteins, fat, vitamins, and minerals contained in colostrum are also important energy and nutrient sources for the newborn calf. Immunoglobulins are transferred into the colostrum beginning 4-6 weeks prior to expected delivery of the calf. This results in higher IgG concentrations in colostrum than in maternal serum. Ideally, colostrum should be consumed by the calf in the first 6-8 hours of life. Immunoglobulins ingested in colostrum are transferred across the small intestine and transported via the lymphatic system to the blood. Immunoglobulin absorption has reached maximum levels at 12-24 hours in newborns, and the ability to absorb immunoglobulins begins to decline at 8-12 hours of age. Gut closure and the complete loss of ability to absorb immunoglobulins occurs by 24 hours of age.

Studies suggest that calves (average 45 kg) need at least 100 g of IgG in colostrum for adequate passive transfer. The amount of immunoglobulin in colostrum is affected by (1) the volume of colostrum fed and (2) the concentration of immunoglobulins in the colostrum (in other words, the quality of the colostrum). The efficiency of absorption by the calf's GI tract is the third factor affecting adequate passive transfer. Historically, a minimum of 2 liters of colostrum is recommended to be fed in the first few hours of life. An additional 2 liters fed by 12 hours of age ensures the best protection. Immunoglobulin

levels in colostrum can be estimated by measuring the specific gravity of the colostrum with a colostrometer. A specific gravity of 1.050 is associated with high quality colostrum, but false positives can occur. Measurement of the colostrum specific gravity should not be a substitute for measuring the IgG levels in the calf.

Routes of colostrum ingestion:

1. Natural suckling – more common in beef breeds of cattle where the calf is not removed from the cow immediately after birth.
2. Bottle feeding – more common in dairy breeds, because most calves are removed immediately following parturition from the cow. Administer minimum of 2 Liters by 6 hours of age, and ideally another 2 L by 12 hours old.
3. Esophageal feeder – also more common in dairy calves, single larger volumes of 3-4 liters per 45 kg weight are often administered. Compared to bottle feeding, this method typically results in the lowest number of calves with failure of passive transfer, because of the larger volume and subsequent concentration of IgG received immediately after birth.

Assessment of Passive Transfer

Ideally, all calves should be assessed for passive transfer within 12-24 hours of birth, and at least once within the first few days of life. IgG is detectable in serum 2 hours following a colostrum feeding, and therefore sampling at 8-12 hours of age will give a good indication if early nursing has occurred in calves that are not bottle fed. Peak serum immunoglobulin concentration is not seen until approximately 32 hours of age, due to ongoing transport of immunoglobulins across the intestinal wall. Several tests are available for assessment of adequate colostrum consumption (hence adequate passive transfer). The only tests that directly measure the IgG concentration are the radial immunodiffusion and enzyme-linked immunosorbent assay (ELISA). The gold standard test is radial immunodiffusion, and adequate levels of IgG are considered to be 1,000 mg/dl (10 mg/ml) or higher. In veterinary practice, the most practical routine tests for assessment of

passive transfer are the ELISA, sodium sulfite turbidity test, and measurement of serum total protein.

Tests for Adequate Passive Transfer:

1. Radial Immunodiffusion (RID): Used most commonly in research studies and as the gold standard. Takes longer to perform than desirable (at least 24 hours), and is not a chute or stall side assay. Normal result is 1,000 mg/dl or higher.
2. Enzyme-linked Immunosorbent Assay (ELISA): This is a chute or pen side assay with similar accuracy to the RID. The test is reasonably accurate and is relatively cost effective. Whole blood or plasma may be utilized.
3. Sodium Sulfite Turbidity Test: This is a good, rapid, and accurate stall side assessment of IgG. Historically, this test was performed as a 3 step test with 14%, 16%, and 18% sodium sulfite solutions. The test solutions cause precipitation of high molecular weight proteins (immunoglobulins). Precipitation of the immunoglobulins results in a turbid solution, which is how the test is read out. Studies evaluating this test in calves have shown that the test is most reliable as a single dilution procedure using an 18% test solution, with turbidity indicating adequate colostrum consumption.
4. Zinc Sulfate Turbidity Test: This test follows the same basic principle as for the Sodium Sulfite Turbidity Test. Different problems with the blood (such as red cell destruction or lysis) can interfere with the results of this test, so it is less frequently used.
5. Serum Total Protein: Serum total protein measured by a refractometer gives an excellent indirect measurement of IgG in calves. Dehydration will cause false positives in affected calves. A value of 5.5 g/dl or higher is associated with adequate passive transfer, and is probably the best evaluation for sick calves. Serum total protein of 5.2 g/dl or higher is associated with adequate passive transfer, and is likely the best cut-off for healthy, well-hydrated calves.

6. Serum Gamma-Glutamyltransferase (GGT)
Activity: GGT is a liver enzyme in large animals. The GGT concentration is high in the colostrum of ruminants, and serum GGT of calves that have been fed colostrum are 60-160 times greater than normal adult serum activity and correlate moderately with serum IgG concentrations. Assessing GGT has no advantage over other methods of assessing IgG concentration, and its use as a sole indicator of passive transfer is discouraged.

7. Whole-Blood Glutaraldehyde Coagulation Test:
This test utilizes the fact that uncharged amino groups on proteins will form cross-linkages with aldehyde groups forming a visible clot. Clot formation is due to "gelation" of gamma globulins (antobodies), however increased fibrinogen concentration will result in clot formation in a whole blood sample. This test is generally not recommend to use in calves.

Treatment of Failure of Passive Transfer

Although calves with FPT have an increased risk of developing septicemia and infections, not every calf with untreated FPT will become ill. Calves in a clean environment with reduced bacterial exposure will have improved survival. The decision to treat a calf with FPT on the farm will be affected by economic and environmental factors, as well as the calf's clinical condition and value to the owner.

Treatment of FPT within the first 12 hours of life can be most cost effectively done with colostrum (2-4 liters) orally. Many cases are discovered after gut closure has occurred, and treatment with commercially available plasma (20 ml/kg IV) or a whole blood transfusion (1-3 liters) from the dam is most effective. Whole blood transfusion reactions are rarely reported in calves, and cross-matching is not routinely done due to the large number of blood types in cattle.

High quality colostrum from a cow is the best way to treat failure of passive transfer in the first 12 hours of the calf's life. Colostrum replacers can also be utilized. Colostrum replacers are not the same as colostrum supplements. The colostrum replacers are bovine serum based products that contain at least 100

g of IgG per liter plus fat, protein, vitamins, and minerals. They are generally better than using poor quality colostrum. Examples of colostrum replacers include Acquire® (manufactured by American Protein Corp., Inc), and Land O' Lakes® Colostrum Replacer. Replacers are labeled for use when colostrum is not available. Colostrum supplements alone cannot raise the calf's IgG above 10 mg/ml. They should be used in addition to low or medium quality colostrum, but not as a replacement for colostrum.

Fluid Therapy in Calves

Dehydration is a common cause of death in calves with diarrhea and contributes to mortality in cases of septicemia and septic shock. Practical and cost effective fluid therapy for calves can be a challenge. Assessment of the calf's clinical condition and percent dehydration is a critical first step in determining the appropriate fluid choice. Fluid and electrolyte losses in diarrhea can require intravenous fluid rates of 80 mls/kg/per hour (that is over 3 liters per hour in a 40 kg (88lb) calf).

Important Calculations for Fluid Therapy

Maintenance fluid requirement for adult cattle:
50 mls/kg/day (25 liters in an 1100 pound cow)

Maintenance fluid requirement for newborn calf:
3-4 liters in a 40 kg calf

Calculation of replacement fluids in dehydration:

Replacement fluid (L) = % dehydration x body weight (kg)

For example, a calf (assume 40 kg) that is weak and estimated to be 10% dehydrated would require $.10 \times 40 = 4$ Liters of replacement fluids in addition to maintenance

Oral Fluid Therapy in Calves

Oral electrolyte solutions can be life saving and cost effective in calves with dehydration and diarrhea. The primary contraindication for oral fluid therapy is ileus (stasis) of the gastrointestinal tract. A general recommendation for oral fluid therapy is to

calculate the calf's total maintenance and replacement fluid requirement over 24 hours and administer it divided into equal doses orally every 2-4 hours. Rate of administration can be via a nipple bottle or by orogastric intubation (using an esophageal feeder or similar).

Selection of an appropriate oral electrolyte solution depends on the severity of electrolyte derangements and degree of systemic acidosis (evaluated by looking at blood pH and TCO₂ or bicarbonate). Since acidosis is common in diarrheic calves, several oral alkalinizing agents are available commercially and contain bicarbonate or other metabolizable bases (such as citrate or acetate). Although many products are available on the market for oral electrolyte supplementation, they are not all approved for use in calves with diarrhea. It is important to remember that nutritional support in the form of cow's milk or milk replacer may be required for thin or severely diarrheic calves.

Intravenous Fluid Therapy in Calves

Intravenous fluid therapy is practical in hospitalized calves, but can be more challenging on the farm. While constant rate infusions are ideal for continuous rate of solutions, especially those containing bicarbonate, bolus fluid infusions have also been utilized. The total fluid requirement accounting for maintenance and losses should be calculated for 24 hours and divided over fluid boluses every 4-6 hours, depending on what is practical. Balanced polyionic crystalloid fluids containing electrolytes are ideal for replacement needs. The profound acidosis that may accompany diarrhea should ideally be evaluated with blood pH, bicarbonate, and/or TCO₂ levels. Alkalinizing fluids such as isotonic bicarbonate solutions (1-4 L IV slowly) are typically required for profoundly diarrheic calves. Intravenous fluid therapy is not required in all cases of neonatal infections and suspected septicemia. The calf's clinical hydration and serum chemistry profile results should be taken into consideration when deciding on the most appropriate form of fluid therapy.

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