ABDOMINAL DISTENTION IN THE ADULT HORSE

BASICS

DEFINITION

Process by which the abdomen becomes enlarged, changing its normal contour and shape.

PATHOPHYSIOLOGY

The accumulation of fluid, gas, or ingesta in the peritoneal cavity, presence of abdominal masses, increased size of abdominal organs, or abdominal wall abnormalities such as edema may result in the distention and/or change in shape of the abdominal contour.

SYSTEMS AFFECTED

• GI—any condition, physical or functional, resulting in the vascular or nonvascular obstruction of the GI transit may lead to accumulation of gas and ingesta, resulting in abdominal distention
• Cardiovascular—secondary to GI obstruction, fluid sequestration and accumulation may lead to a hypovolemic shock. Vascular compromise of the GI tract leads to decreased GI protection, access of bacteria and/or toxins to the systemic circulation, and extravasation of a transudate/exudate into the peritoneal cavity. Intra-abdominal blood loss (hemoperitoneum) may occur from trauma or rupture of mesenteric or other (i.e. uterine, renal, ovarian) vessels due to increased traction or trauma (e.g. during foaling), from any other abdominal viscera (e.g. rupture of the spleen, liver, or ovarian follicle or cyst), or ascites secondary to heart failure. Electrolyte abnormalities from endotoxic shock or uroperitoneum may lead to secondary arrythmias and death. Alterations in oncotic or hydrostatic pressure may also lead to edema on the peritoneal cavity or intramurally in the intestinal wall
• Respiratory—abdominal distention may lead to increased pressure of the diaphragm, resulting in a shallow and fast respiratory pattern associated with atelectasis and hypoventilation due to failure of the alveoli to open. Occasionally rupture of the diaphragm resulting in internal entrapment and obstruction of the GI tract may be the initiating cause. In this case the presence of abdominal viscera in the thorax prevents the lungs from fully expanding, compounding the effects that pain and distention may have on the respiratory system
• Musculoskeletal/nervous/ophthalmic/skin—these systems may be injured through self-inflicted trauma secondary to abdominal pain. In cases of abdominal wall hernias, produced by trauma or lack of muscular tone with an eventual muscle rupture in older horses, the GI tract may become incarcerated, leading to its obstruction and potentially its vascular compromise, further promoting abdominal distention. Lack of condition and fitness may over time lead to loss of abdominal muscular tone
• Reproductive—advanced pregnancy, either single or twin, will result in a marked change in the abdominal contour. Occasionally uterine torsion may be responsible for altered abdominal contour. Hydrops and ruptured of the prepubic tendon can be seen in pregnant mares and will manifest as change in the abdominal contour

SIGNALMENT

• All horses without exception may develop abdominal distention
• Pregnant mares may develop hydrops (any time during pregnancy), uterine torsion (mid-term), uroperitoneum (postpartum), or rupture of the mesocolon (postpartum), leading to hemoperitoneum and large colon torsion (peripartum)
• Rupture of the prepubic tendon occurs in older, sedentary mares in late pregnancy
• Miniature horses are predisposed to development of fecaliths, enteroliths, and small colon impactions
• Older horses are predisposed to pedunculating lipomas causing intestinal obstruction and are overrepresented in the incidence of tumors leading to hemoperitoneum, such as mesotheliomas, splenic hemangiosarcomas, and renal carcinomas
• Geographic distribution is important to consider the incidence of selected conditions such as ileal hypertrophy (southeast USA), enteroliths (south USA), and sand impactions (south USA)
• Uroperitoneum occurs mostly in male horses as a result of a ruptured bladder or urethra

SIGNS

Historical Findings

The clinical progression should help differentiate between vascular and nonvascular GI obstructions and other non-GI causes of distention.

Physical Examination Findings

A careful evaluation of clinical progression, historical facts, and of the horse including all systems may provide the information to determine the nature of the distention. Rectal examination, although practical, inexpensive, and quick, may not give a complete picture of the entire abdomen and may become less important if access to a good US machine and technique are possible.

CAUSES

Accumulation of Gas

• Functional obstruction—primary or secondary ileus. Primary ileus due to increased sympathetic drive. Secondary ileus due to pain (visceral or musculoskeletal), ischemic necrosis (e.g. verminous arteritis) post surgery, electrolyte abnormalities (e.g. endurance horses), dehydration, inflammation of the bowel (enteritis) or abdominal cavity (peritonitis), and sedative or anesthetic drugs (e.g. α_2 agents, opioids)
• Physical obstruction: either vascular (large colon volvulus, mesenteric root volvulus, strangulating lipoma) or nonvascular (impaction, enteroliths, nephrosplenic entrapment)
• Cecal tympany from abnormal cecal motility patterns
• Excessive feed stuff fermentation—grain overload
• Free gas within the abdominal cavity secondary to trauma or anaerobic infections
• Colitis

Accumulation of Fluid

• Hemoperitoneum—ruptured viscera, vessel, ovarian cyst/follicle or tumor
• Uroperitoneum—ruptured bladder secondary to trauma, or obstructive urolithiasis
• Hydrops amnion or allantois
• Ascites—peritonitis, neoplasia, hypoproteinemia, right-sided heart failure
• Colitis or enteritis—secretory process leading to accumulation of fluid in lumen of large colon or small intestine
• Cecal impaction with fluid due to abnormal motility patterns
• Pyometra/mucometra

Solid Mass

• Abscess
• Neoplasia—lymphosarcoma, squamous cell carcinoma, mammary adenocarcinoma, mesothelioma, hemangiosarcoma, renal carcinoma, ovarian granulosa cell tumor

Body Wall Abnormality

• Hernia
• Prepubic tendon rupture

RISK FACTORS

• Cribbing predisposes horses to tympany of the colon and epiploic foramen entrapment
• Gastric ulcers predispose horses to gastric rupture
• Sudden exposure to large amounts of carbohydrate-rich feed or diets consisting of increased proportions of highly fermentable feedstuff (especially whole-grain corn) and decreased amounts of roughage can predispose to gastric, cecal, large colon tympany, and large colon displacement or volvulus
• Colonic impactions often occur in horses that are old or debilitated or that have poor dentition or in horses eating a diet with a large amount of fiber or following water deprivation
• Sudden change in physical activity or sudden stall rest imposed by another injury may lead to cecal or large colon impaction
• Sudden change of diet, even hay batch, has been associated with colic and abdominal gas distention
• Enterolithiasis occurs frequently in the states of California, Florida, and Indiana

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ABDOMINAL DISTENTION IN THE ADULT HORSE (CONTINUED)

• Sand impactions are seen frequently in the southern and coastal states
• Ileal hypertrophy has been associated with ingestion of Bermuda grass hay
• Periparturient mares are at increased risk of large colon volvulus, particularly if it has happened before
• Miniature horses are predisposed to small colon impactions
• Overconditioned and old horses are predisposed to strangulating lipomas

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

Other conditions with the appearance of abdominal distention include:
• Marked subcutaneous edema along the ventral abdomen and thorax
• Pregnancy—diagnosis may be made via rectal palpation with or without ultrasonography
• "Hay belly"—may be diagnosed on history (malnourished, old, or nonfit horses or severely parasitized horses, diets high in poor quality roughage) and by fecal examination
• Pendulous abdomen secondary to pituitary adenoma and Cushing disease—usually accompanied by other distinctive signs, such as abnormal haircoat and failure to shed winter coat
• Extreme obesity—ribs not palpable, fat deposits evident along crest of neck, over tail-head, etc.
• Subcutaneous emphysema from penetrating chest wound, ruptured trachea, or subcutaneous anaerobic infection—characteristic crepitus noticed on palpation of the skin

Differentiating Causes

Signalment, history, physical examination, laboratory work, rectal palpation, and US examination findings often provide sufficient information to permit a tentative diagnosis. Some conditions are associated with characteristic findings:
• GI gas accumulation (bloat)—reduced GI sounds may be heard, and increased gaseous distention may be identified on percussion as a hyperresonant sound colloquially termed "ping"; depending on the inciting cause and the degree of distention present, various degrees of abdominal pain are present. Hypermotile sounds can also be auscultated in cases of spasmodic colic, which can be associated with an excessive amount of gas being produced
• Ascites from right-sided heart failure—tricuspid insufficiency results in findings including heart murmur, exercise intolerance, jugular distention and pulse, and edema of the ventral abdomen, pectoral muscles, and distal limbs
• Ascites from intra-abdominal mesothelioma—because this tumor originates from the fluid-producing cells of the peritoneum, several liters of peritoneal fluid may be produced within a 24 h period; ascites may be more dramatic than is noted with other conditions
• Body wall defect from prepubic tendon rupture—one of the only causes of unilateral abdominal distention in the horse; also results in cranioventral positioning of the mammary gland, cranial tilting of the pelvis, and severe ventral abdominal swelling
• Presence of diarrhea may point towards colitis or enteritis. Evaluation of nasogastric reflux may be useful in this situation

CBC/BIOCHEMISTRY/URINALYSIS

Results are dependent on the cause. It is important to asses PCV, TP, and WBC, including a differential evaluation of WBC.

OTHER LABORATORY TESTS

• Abdominocentesis should be performed carefully in pregnant mares with intestinal distention, where the bowel may be torn easily by inadvertent penetration with a needle or teat cannula despite proper restraint.
  ◦ Abdominal lactate content when compared with systemic circulating lactate may offer valuable information toward the diagnosis of a vascular obstruction
  ◦ WBC count, TP level, and specific gravity of the peritoneal fluid should be measured, and the fluid should be assessed cytologically for evidence of degenerate neutrophils, neoplastic cells, bacteria, or plant material
  ◦ Other parameters such as Cr may also be measured in cases where uroperitoneum is suspected. In cases of uroperitoneum, Cr in the peritoneal fluid exceeds serum Cr levels by a ratio of > 2:1
  ◦ An increase in WBC count and TP levels and the appearance of degenerate neutrophils are indicative of increasing inflammation within the abdomen
  ◦ With hemoperitoneum, free-flowing blood may be evident from the needle or teat cannula during the centesis procedure. This should not be mistaken for puncture of the spleen during the procedure, in which case the PCV of the obtained sample is higher than the circulating blood

IMAGING

• Abdominal radiography may help to diagnose gas accumulation within bowel segments in small horses and ponies. Enteroliths or sand impactions may be evident in adult horses in the mid- to ventral abdomen on the lateral view
• US of the abdomen can be useful in skilled hands and can be used to identify the location, amount, character, and echogenicity of peritoneal fluid and abdominal viscera, particularly thickness of the intestinal wall. It can also provide information on the condition of the heart, liver, spleen, kidney, and bladder, and can help identify the presence of intra-abdominal adhesions or masses

OTHER DIAGNOSTIC PROCEDURES

• Laparoscopy allows visualization of the abdominal cavity in the standing horse, and can be used to provide a definitive diagnosis of the cause of abdominal distention. It can be used in selected cases (i.e. peritonitis, ruptured bladder) to direct appropriate therapy and treatment. In the presence of GI distention the ability to identify the nature of the obstruction may be compromised
• Exploratory laparotomy through a flank incision in the standing horse is very limiting and should only be performed in selected cases as a therapeutic intervention if a confirmed diagnosis such as nephrosplenic entrapment or uterine torsion has been made
• Exploratory laparotomy through a ventral midline incision in the anesthetized horse should not be delayed unnecessarily as it may be a life-saving diagnostic and therapeutic tool if used appropriately

TREATMENT

• Specific treatment is largely dependent on the cause of abdominal distention. Cardiovascular stabilization through rehydration and correction of electrolyte and acid–base abnormalities should be initiated prior to treatment of the primary disease process
• In horses with severe gaseous distention, trocarization of the cecum and/or large colon may be necessary to improve ventilation and comfort. Although the complications of this procedure are reportedly very low, it is associated with peritonitis and any horse that is trocarized should be treated preemptively with anti-inflammatory drugs and broad-spectrum antibiotic therapy to reduce and minimize the inherent risk of peritonitis
• Mares with hydrops or rupture of the prepubic tendon may require induction of parturition. Horses with abdominal distention should be confined to a stall and monitored continuously until a diagnosis has been made and appropriate treatment initiated
• Feed should be withheld from horses showing any signs of abdominal discomfort
• Prompt and adequate referral to a hospital facility may be required in cases requiring surgical intervention or prolonged nursing care

(CONTINUED) ABDOMINAL DISTENTION IN THE ADULT HORSE

MEDICATIONS

Drug therapy is dictated by the inciting cause.

FOLLOW-UP

Plans for monitoring are based on cause and treatment.

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

- Termination of pregnancy may be indicated in mares with hydrops or nonresolving uterine torsion
- Induction of parturition may be necessary in mares close to term that have experienced rupture of the prepubic tendon. These mares should be monitored carefully and parturition attended as they may require assistance with delivery due to their inability to perform effective abdominal press for fetal expulsion

SYNONYMS

Bloat

SEE ALSO

- Acute adult abdominal pain—acute colic
- Colic, chronic/recurrent
- Oral stereotypic behavior

ABBREVIATIONS

- Cr = creatinine
- GI = gastrointestinal
- PCV = packed cell volume
- TP = total protein
- US = ultrasonography, ultrasound
- WBC = white blood cell

Suggested Reading

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Author Antonio M. Cruz
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa

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ABDOMINAL HERNIA IN ADULT HORSES

BASICS

OVERVIEW

Abdominal hernia is an exteriorization of internal organs through a defect or an anatomic opening in the abdominal wall. In adult horses, abdominal hernias include ventral, incisional, and acquired inguinal hernia.

SIGNALMENT

Ventral Hernia

Common in older, late-term pregnant mares. Draft breeds are predisposed.

Incisional Hernia

Complication of ventral midline celiotomy in 6–18% of horses.

Acquired Inguinal Hernia

- Refers to the passage of intestine (small intestine most commonly) and/or omentum through the vaginal ring into the inguinal canal and in the scrotum
- Particularly in the stallion
- Standardbred, draft breeds, Tennessee Walking, and Andalusian horses are predisposed

SIGNS

Ventral Hernia

Painful swelling is associated with a body wall defect.

Incisional Hernia

Incisional edema and swelling. Discharge from the incision and increase in drainage of peritoneal fluid are commonly observed prior to dehiscence.

Acquired Inguinal Hernia

Colic signs depending on degree of intestinal strangulation and scrotal swelling. The testis is usually cool due to vascular compromise.

CAUSES AND RISK FACTORS

Ventral Hernia

In pregnant mares, old broodmares, and twin gestation. Associated with trauma, hydrops (allantois and amnion).

Incisional Hernia

Incisional infection, edema and drainage, postoperative pain, re-laparotomy, and suture material and suture patterns. Older and heavy horses, type of incision, degree of surgical trauma, length of surgery, and difficulties during recovery. No stent bandage during recovery.

Acquired Inguinal Hernia

Often in stallions after copulation or strenuous exercise. Large vaginal rings may predispose to herniation.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Ventral Hernia

Prepubic tendon rupture (pelvis tilted cranioventrally, cranioventral displacement of the udder).

Incisional Hernia

Postoperative wound infection, severe peri-incisional edema, seroma, and sinus formation are easily differentiated from incisional hernias with the abdominal wall being intact on palpation and US examination.

Acquired Inguinal Hernia

Torsion of the spermatic cord, orchitis, testicular vasculature thrombosis, hydrocele, hematocele, and testicular neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

Unremarkable in absence of secondary intestinal strangulation.

IMAGING

Abdominal US

US is used to confirm herniation, to evaluate the extent of the abdominal wall defect, and to identify hernia contents.

OTHER DIAGNOSTIC PROCEDURES

External Palpation

To define the hernia ring and contents. To differentiate between reducible and nonreducible hernias. Palpation of inguinal regions and scrotum is mandatory in stallions with signs of colic.

Rectal Palpation

Rectal palpation of stallions with inguinal hernia reveals presence of distended intestine (small intestine most commonly) entering the vaginal ring.

TREATMENT

Ventral Hernia and Incisional Hernia

Small hernias are treated initially conservatively by supporting the ventral abdominal wall, decreasing the amount of local inflammation and edema, and preventing enlargement of the hernia. Rest, low-bulk diet, and monitoring for signs of intestinal obstruction. Anecdotal reports of incisional hernia healing using postsurgical commercially available abdominal bandage. Ventral or incisional hernia may resolve with conservative treatment, but surgical closure of the abdominal defect 8–12 weeks after its occurrence is usually required. In a recent report, herniorrhaphy was performed within 21 days for treating external traumatic abdominal hernias in horses and mules. Application of a mesh is based on the size of the wall defect and the surgeon's preference. Horses with acute severe incisional dehiscence (eventration) are emergency surgical candidates.

Acquired Inguinal Hernia

Treatment is usually surgical by performing a ventral midline celiotomy, resecting the nonviable small intestine, and castrating the horse. During the early phase, it may be possible to reduce the hernia using external inguinal/scrotal massages under general anesthesia in dorsal recumbency or using traction per rectum.

MEDICATIONS

DRUG(S) OF CHOICE

Ventral and Incisional Hernia

Anti-inflammatories to decrease inflammation and antibiotics to resolve infection to allow fibrous tissue to form at the hernial ring prior to herniorrhaphy.

FOLLOW-UP

- The prognosis for ventral hernia is guarded. Incisional and inguinal hernias warrant a favorable prognosis
- From 3 to 5 months of rest is required after surgical correction of both ventral and incisional hernias

ABBREVIATIONS

- US = ultrasonography, ultrasound

Suggested Reading

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Author Albert Sole-Guitart
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa

Client Education Handout available online

ABDOMINOCENTESIS—INCREASED PERITONEAL FLUID

BASICS

DEFINITION

• Procedure for sampling peritoneal fluid by collection through the abdominal wall
• Abdominocentesis is usually performed at the most dependent part of the abdominal wall. The site is clipped and prepared aseptically. Either a needle or a blunt-tipped cannula can be used to enter the abdominal cavity. Using a needle is usually faster and is associated with less bleeding from vessels in the skin; the cannula is less likely to result in inadvertent enterocentesis or laceration of the intestinal wall. When using a cannula, the site is first infused with local anesthesia and a small skin incision is made
• Transabdominal ultrasound may be used to locate fluid pockets
• Peritoneal fluid is collected into EDTA-containing tubes for assessment of the total nucleated cell count and cytology, and into a sterile clot tube for bacterial culture or biochemical tests
• Equine abdominal fluid normally appears clear and colorless to slightly yellow and does not clot
• Total protein commonly is assessed by refractometer and normally is < 2.5 g/dL
• The nucleated cells may be counted by hemocytometer or by using some hematology analyzers. The nucleated cell count in fluid from normal horses is < 5000 cells/μL, with a predominance of nondegenerative neutrophils (22–98%) and large mononuclear cells (1–68%), which include mesothelial cells and macrophages. Small lymphocytes may constitute 0–36% of the total cell count and eosinophils up to 7%; mast cells and basophils are rarely seen. Normally, few erythrocytes are present
• Biochemical measurements in addition to total protein may include lactate as an indicator of intestinal ischemia or hypoperfusion, glucose as an indicator of septic peritonitis and creatinine, and/or potassium to aid in diagnosis of uroabdomen

PATHOPHYSIOLOGY

• Normal peritoneal fluid is a dialysate of plasma; many of the low-molecular-weight substances in blood are present in the peritoneal fluid at similar concentrations
• High-molecular-weight molecules (e.g. proteins) normally are not present in abdominal fluid
• Cells in normal peritoneal fluid include mesothelial cells that line the abdominal cavity and cover visceral surfaces, and small numbers of cells from the blood and lymphatics
• Fluid circulates constantly through the abdominal cavity and is drained via lymphatic vessels. When fluid production exceeds drainage, effusion develops. This may occur with some systemic disorders (e.g. cardiovascular disease) or with local disorders of abdominal organs or mesothelium. Changes in peritoneal fluid protein, cell numbers, and cell types may reflect those disorders
• During inadequate intestinal perfusion and ischemia, anaerobic glycolysis can result in increased peritoneal fluid lactate concentration. A peritoneal fluid lactate concentration that is higher than the serum concentration provides evidence of intra-abdominal infection or ischemia
• When infection is present in the abdomen, the peritoneal fluid glucose concentration is usually < 30 mg/dL, as glucose is actively consumed by bacteria. It is also reported that a difference of > 50 mg/dL between the serum and peritoneal fluid is highly diagnostic for infection in the abdomen. The glucose measurement might be most useful when timely cytologic examination is not available
• A localized process in the abdomen, such as a walled-off abscess or a tumor, may not be reflected in a peritoneal fluid sample
• Repeated sampling of peritoneal fluid is necessary, in some cases, to follow the course of a disease or to monitor therapy, whether it is medical or surgical

SYSTEMS AFFECTED

• GI
• Hepatobiliary
• Hemic/lymphatic/immune
• Renal/urologic
• Cardiovascular
• Reproductive

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Any breed, age, or sex.

SIGNS

• Colic
• Chronic weight loss
• Abdominal distention
• Diarrhea
• Pyrexia

CAUSES

• Peritonitis caused by compromised gut wall
• Hemorrhage (hemoabdomen)
• Intra-abdominal neoplasia
• Intestinal parasitism and secondary thromboembolism
• Inflammation of abdominal organs
• Compromised venous return due to intestinal displacement, distention, etc.
• Breeding and foaling injuries
• Bile or urine leakage
• Postsurgical inflammation or other complications
• Abdominal abscess
• Decreased oncotic pressure
• Congestive heart failure

RISK FACTORS

• Abdominal surgery
• Pregnancy
• Hypoalbuminemia

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Peritonitis

Peritonitis may be caused by a number of conditions, including a displaced or strangulated bowel, bowel necrosis, obstruction, bowel rupture, abscess, or thromboembolism.
• The fluid is an exudate with an increased nucleated cell count and a predominance of neutrophils
• The total protein usually is > 2.5 g/dL due to the presence of inflammatory proteins
• Bacteria are present in septic peritonitis and may be intracellular or extracellular. Degenerative changes in neutrophils are usually seen and the glucose concentration of the fluid is decreased
• With gut rupture, cells often are degenerate and mixed bacterial types, ciliated protozoa, and plant material may be seen
• Postsurgical peritonitis also produces an exudate with increased cell numbers and total protein within 24 h and lasting up to 2 weeks. Neutrophils generally are not degenerate and no bacteria are seen. Increased RBC numbers may be seen

Hemorrhage

• With a splenic tap, the PCV is higher in abdominal fluid than in blood, and small lymphocyte numbers may be increased
• With hemorrhage into the abdomen, the PCV of fluid is lower than that of blood. Platelets are absent, and erythrophagocytosis or macrophages containing hemoglobin-breakdown pigments may be seen
• With blood contamination at the time of sampling, fluid initially may look clear, with bloody streaks appearing during sampling. Phagocytosis of RBCs is not seen, and platelets may be present

Neoplasia

A diagnosis may be established on finding neoplastic cells in fluid but absence of neoplastic cells does not rule out neoplasia, because tumor cells may not exfoliate into fluid.

Parasitism

Migration of parasitic larvae may be associated with increased eosinophils, but this does not occur often and is not diagnostic for parasitism.

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ABDOMINOCENTESIS—INCREASED PERITONEAL FLUID (CONTINUED)

Uroabdomen
• Typically, peritoneal fluid creatinine and potassium concentrations are increased compared with serum concentrations
• Hyperkalemia, marked hyponatremia, and hypochloremia are typical but are not present in all cases

Ascites
• A transudate with low cell numbers and low protein content may be present with hypoalbuminemia or lymphatic or vascular obstruction or stasis
• Serum biochemical profile and history contribute to this diagnosis

Congestive Heart Failure
Increased hydrostatic pressure within vessels may result in a modified transudate with a higher cell count and protein level than a transudate, but these values may be normal for equine abdominal fluid.

CBC/BIOCHEMISTRY/URINALYSIS
• Inflammatory causes of abdominal effusion may be associated with leukocytosis or hyperfibrinogenemia if disease is systemic
• Left shift or toxic changes in neutrophils indicate systemic inflammation
• Serum biochemistries help in assessing causes of transudate, e.g. panhypoproteinemia is consistent with GI protein loss; elevated liver enzymes suggest hepatic disease
• Serum electrolyte concentrations and comparison of serum and fluid creatinine concentrations aid in diagnosis of uroperitoneum

OTHER LABORATORY TESTS
Bacterial culture is helpful in some cases, such as abdominal abscess.

IMAGING
Ultrasonography
• May be useful in identifying a subjective increase in peritoneal fluid, hemoabdomen, GI distention or wall thickening, intussusception, masses, adhesions, abnormal liver/spleen/kidney, and enteroliths
• Ultrasonographic location of peritoneal fluid might help in performing abdominocentesis

Abdominal Radiography
In adult horses, may aid in establishing the diagnosis of diaphragmatic hernia, sand enteropathy, and enteroliths.

OTHER DIAGNOSTIC PROCEDURES
• Palpation per rectum might aid in the diagnosis of GI abnormalities or abdominal effusion
• Laparoscopy may be used to establish the diagnosis in cases of chronic colic or weight loss
• Gastroscopy can be useful in establishing the diagnosis of gastric ulcers, impaction, and neoplasia
• Exploratory laparotomy is necessary for definitive diagnosis in some cases

PATHOLOGIC FINDINGS
As described.

TREATMENT
Directed at the underlying cause.

MEDICATIONS
Based on the underlying cause.

FOLLOW-UP

PATIENT MONITORING
No specific monitoring procedures are indicated following an uncomplicated abdominocentesis.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
• Subcutaneous swelling at the site may be more commonly observed when a blunt cannula is used for the procedure
• Accidental enterocentesis is rarely associated with clinical disease but causes an increased nucleated cell count in abdominal fluid within 4 h. When the gut is tapped, there will be few, if any, cells, large numbers of bacteria, and plant material on cytologic examination. Also, the physical condition of the horse is relatively normal compared with one with a gut rupture
• Puncture of a compromised intestinal wall could cause leakage and rapid development of severe peritonitis. Sand impaction is associated with increased risk of intestinal puncture
• Accidental amniocentesis may occur in pregnant mares. This has not been reported to be associated with any specific sequelae

EXPECTED COURSE AND PROGNOSIS
Dependent on the underlying cause.

MISCELLANEOUS

AGE-RELATED FACTORS
Foals normally have peritoneal fluid protein concentrations similar to those of adults, but total nucleated cell counts (< 1500 cells/μL) that are lower than those of adults.

PREGNANCY/FERTILITY/BREEDING
There are no significant differences between fluid from mares that are pregnant or have recently foaled and fluid from nonperipartum mares.

SYNONYMS
• Abdominal paracentesis
• Belly tap
• Intraperitoneal tap

SEE ALSO
• Abdominal distention in the adult horse
• Acute adult abdominal pain—acute colic
• Peritonitis

ABBREVIATIONS
• GI = gastrointestinal
• PCV = packed cell volume
• RBC = red blood cell

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Author Susan J. Tornquist
Consulting Editor Sandra D. Taylor

ABNORMAL ESTRUS INTERVALS

BASICS

DEFINITION

• Estrus—period of sexual receptivity of the mare for the stallion
• Abnormal estrus interval—mare displays sexual behavior for longer or shorter periods than normal
• Abnormal interovulatory intervals result from altered estrus or diestrus lengths

PATHOPHYSIOLOGY

Mares are seasonally polyestrous with the ovulatory period in spring/summer:
• Average estrous cycle is 21 days
• Estrus length averages 5–7 days
• Diestrus length more consistently 14–15 days

Key Hormonal Events in the Equine Estrous Cycle

• FSH causes follicular growth
• Follicular estradiol (E_2) stimulates increased GnRH pulse frequency and LH secretion
• LH surge causes ovulation
• Progesterone (P_4) (CL origin) rises from basal levels (<1 ng/mL) at ovulation to > 4 ng/mL by 4–5 days post ovulation
• A second FSH surge in diestrus initiates another follicular wave
• Endometrial $PGF_{2\alpha}$ is released 14–15 days post ovulation, causing luteolysis and a decline in P4 levels

Sexual Behavior

• Absence of P_4 allows onset of estrus behavior even if E_2 is present in small quantities
• Conditions that eliminate P_4 and/or > E_2 concentrations are likely to induce estrus behavior (including bilateral ovariectomy)

SYSTEMS AFFECTED

• Reproductive
• Behavioral
• Endocrine

SIGNALMENT

• Mares of any age/breed
• Ponies have longer estrous cycles (average 24 days) than mares

SIGNS

Historical Findings

• Chief complaints—infertility, failure to show estrus, prolonged estrus, split estrus, or frequent estrus behavior
• Reproductive history—review breeding/teasing records, previous foaling data, urogenital infections/treatments, pharmaceutical interventions
• Seasonal influences—review time of year, individual variation (onset/duration/termination of cyclicity)
• Have clients log behaviors in a journal for persistent estrus cases to identify patterns

Physical Examination Findings

• Poor body condition/malnutrition or metabolic disease (pituitary pars intermedia dysfunction) may contribute to abnormal cyclicity
• Poor perineal conformation can result in pneumovagina, ascending infections, and/or urine pooling, anestrus/infertility
• Clitoral enlargement may relate to drug history (anabolic steroids) or intersex conditions
• TRP and US are essential for evaluation. Rule out pregnancy. Assess uterine size/tone, ovarian size/shape/location, and cervical relaxation. Serial TRP may be needed to completely define status
• Vaginal speculum examination to identify inflammation, urine pooling, cervical competency, conformational abnormalities

CAUSES

Shortened Estrus Duration

• Split heats often observed during transition periods (seasonality)
• Silent heat—mare with normal cyclic ovarian activity but minimal or no overt sexual receptivity
• Often behavior-based problem—nervousness, foal-at-side, maiden mare; possibly previous anabolic steroid use

Lengthened Estrus Duration

• May appear as persistent estrus behavior or split heats
• Persistent estrus behavior due to cystitis, vaginitis, urine pooling, ovarian neoplasia (GTCT), chromosomal abnormalities
• Split heats often observed during transition periods (seasonality)
• Up to 30% of bilaterally ovariectomized mares may show persistent estrus

Shortened Interestrus Interval

Premature luteolysis:
1. endometritis
2. endotoxemia (i.e. colic, colitis, laminitis)
3. iatrogenic due to intrauterine infusions, biopsy, administration of $PGF_{2\alpha}$

Lengthened Interestrus Interval

• Prolonged CL function—diestrus ovulation, persistent CL (due to idiopathic/spontaneous or uteropathic (pyometra) causes), pregnancy, early embryonic death after maternal recognition of pregnancy or endometrial cup formation, oxytocin treatment, placement of intrauterine marbles, use of deslorelin implants
• Suppression of estrus behavior by treatment with altrenogest or natural P_4
• Induction of anestrus via GnRH vaccination or bilateral ovariectomy

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Conditions with Similar Symptoms

• Behavior complaints must be investigated as to the inciting cause—physiologic, pathologic, or psychologic
• All mares should be submitted for physical and urogenital examination including TRP, US, and vaginal speculum examination
• Urinalysis, uterine culture, uterine cytology, and endometrial biopsy can provide specific diagnoses for persistent estrus behavior, endometritis
• Serial examination may be required to differentiate silent heat, split heat, transitional period, prolonged CL function
• GTCT may be suspected on US; confirm with serology
• Karyotype to diagnose chromosomal disorders

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

• Serum progesterone
  ◦ Basal < 1 ng/mL (no luteal tissue present)
• GTCT panel
  ◦ Nonpregnant mare—AMH < 3.8 ng/mL, inhibin < 0.7 ng/mL, testosterone 20–45 pg/mL
  ◦ GTCT if AMH > 8.0 ng/mL, inhibin > 0.7 ng/mL, testosterone > 100 pg/mL
• Karyotype

IMAGING

• Transrectal US of reproductive tract
• Hysteroscopy to diagnose uterine abnormalities

OTHER DIAGNOSTIC PROCEDURES

N/A

TREATMENT

• Serial monitoring of the mare's reproductive tract by TRP and US
• For persistent estrus:
  ◦ Treat underlying endometritis, cystitis, vaginitis, urine pooling
  ◦ Correct poor perineal conformation (Caslick's vulvoplasty, Gadd procedure, Pouret procedure)
• For prolonged diestrus:
  ◦ Rule out pregnancy
  ◦ Treat pyometra or other uterine disease, if present

A

ABNORMAL ESTRUS INTERVALS (CONTINUED)

- ◦ $PGF_{2\alpha}$ treatment
- ◦ Remove marble or deslorelin implant

• For anestrus:
- ◦ Identify if mare is cyclic or truly anestrus
- ◦ If cyclic, modify teasing/breeding management schemes. Breed based on TRP and US, if possible
- ◦ Ovariectomy if GTCT diagnosed
- ◦ If anestrus during the breeding season, identify and treat inciting cause, if possible
- ◦ Consider artificial lighting schemes or pharmaceuticals to advance the vernal transition period in broodmares

MEDICATIONS

DRUG(S) OF CHOICE

• To induce luteolysis—$PGF_{2\alpha}$ (dinoprost tromethamine, Lutalyse (Pfizer) 10 mg IM) or analogs

• To induce ovulation in estrus—deslorelin 1.8 mg IM: ovulation within 48 h if follicle(s) > 30 mm; hCG 2500 IU IV: ovulation within 48 h if follicle(s) > 35 mm

• To hasten vernal transition:
- ◦ Altrenogest (0.044 mg/kg PO daily ≥ 15 days) if follicles > 20 mm are present and mare is exhibiting behavioral estrus. $PGF_{2\alpha}$ is given on day 15
- ◦ Combination P_4/E_2 treatments followed by $PGF_{2\alpha}$ are also used
- ◦ Dopamine antagonists—domperidone 1.1 mg/kg PO daily or sulpiride 1.0 mg/kg or 200 mg/mare IM daily; often used in combination with artificial photoperiod
- ◦ FSH—used experimentally

• To suppress estrus:
- ◦ Oxytocin 60 IU IM daily 7–14 days post ovulation or for 29 days at any time during the cycle
- ◦ Altrenogest 0.044 mg/kg PO daily
- ◦ Natural P_4—available in several injectable formulations (short- or long-acting)

CONTRAINDICATIONS

$PGF_{2\alpha}$ and analogs—contraindicated with equine asthma/bronchoconstrictive disease.

PRECAUTIONS

• Horses
- ◦ $PGF_{2\alpha}$ causes sweating/colic-like symptoms due to stimulation of smooth muscle. Symptomatic treatment if not resolved in 1–2 h
- ◦ Antibodies to hCG can develop:
  - ■ Limit use to < 2 or 3 times per breeding season
  - ■ Half-life of antibodies is 1 to several months
- ◦ Deslorelin implants are associated with prolonged interovulatory periods in nonpregnant mares, if not removed soon after ovulation has been confirmed. Not available in the USA
- ◦ Progesterone supplementation may be contraindicated in mares with a history of uterine infection

• Humans
- ◦ $PGF_{2\alpha}$ should not be handled by pregnant women or persons with asthma/bronchial disease
- ◦ Altrenogest should not be handled by pregnant women or persons with thrombophlebitis, thromboembolic disorders, cerebrovascular/coronary artery disease, breast cancer, estrogen-dependent neoplasia, undiagnosed vaginal bleeding, or tumors that developed with use of oral contraceptives or estrogen-containing products

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

Cloprostenol sodium (Estrumate (Schering-Plough Animal Health) 250 µg/mL IM) is a $PGF_{2\alpha}$ analog. This product is used in similar fashion to dinoprost tromethamine and has been associated with fewer side effects. While it is not currently approved for use in horses, it is in broad use in the absence of an alternative.

FOLLOW-UP

PATIENT MONITORING

The mare should be examined serially until normal cyclicity or pregnancy is determined.

POSSIBLE COMPLICATIONS

Undesirable behavior, infertility, prolonged nonpregnant intervals.

MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

$PGF_{2\alpha}$ administration to pregnant mares can cause luteolysis and abortion. Definitively rule out pregnancy before administering this drug or its analogs.

SYNONYMS

• Persistent estrus
• Prolonged CL function

SEE ALSO

• Aggression
• Anestrus
• Clitoral enlargement
• Disorders of sexual development
• Early embryonic death
• Endometritis
• Large ovary syndrome
• Ovulation failure
• Pneumovagina/pneumouterus
• Prolonged diestrus
• Pyometra
• Urine pooling/urovagina
• Vaginitis and vaginal discharge
• Vulvar conformation

ABBREVIATIONS

• AMH = anti-Müllerian hormone
• CL = corpus luteum
• E_2 = estradiol
• FSH = follicle-stimulating hormone
• GnRH = gonadotropin-releasing hormone
• GTCT = granulosa–theca cell tumor
• hCG = human chorionic gonadotropin
• LH = luteinizing hormone
• P_4 = progesterone
• $PGF_{2\alpha}$ = prostaglandin $F_{2\alpha}$
• TRP = transrectal palpation
• US = ultrasonography, ultrasound

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Author Lisa K. Pearson
Consulting Editor Carla L. Carleton
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ABNORMAL SCROTAL ENLARGEMENT

BASICS

DEFINITION
Clinically visible increased scrotal size due a process involving the scrotum or its content (testes, epididymides, blood supply). The enlargement may be bilateral or unilateral. Clinic and systemic signs are variable and depend on the cause.

PATHOPHYSIOLOGY
- The equine scrotum and associated contents are relatively well protected. The scrotum is almost symmetrical and covered with a think pliable skin with freely movable content
- Scrotal enlargement may appear acutely or progressively
- Acute scrotal enlargement is more common and often due to trauma (breeding accident, jumping), spermatic cord torsion, inguinal/scrotal herniation, or inflammatory processes (epididymitis, orchitis)
- Trauma can result in scrotal hemorrhage, edema, rupture of the tunica albuginea, hematocele
- Progressive enlargement of the scrotum is often due to vascular abnormalities or poor thermoregulation (poor lymphatic drainage, edema, hydrocele) or neoplasia
- Scrotal enlargement may be observed following abdominal surgery

SYSTEMS AFFECTED
Reproductive

GENETICS
N/A

INCIDENCE/PREVALENCE
Scrotal enlargement due to trauma is the most common presentation in breeding stallions.

SIGNALMENT
- Intact male horses
- Inguinal hernia is a common cause of scrotal enlargement in foals

SIGNS
Historical Findings
- Gross changes in the size of the scrotum (usually acute)
- Pain (generally colic-like symptoms)
- Reluctance to breed, jump, or walk
- Extreme environmental temperatures (hot or cold)

Physical Examination Findings
- Increased scrotal size (unilateral or bilateral)
- Abnormal testicular position
- Abnormal scrotal temperature (too warm or cold)
- Edema/engorgement of scrotum and/or contents
- Scrotal lesions (laceration, abscesses, neoplasia)
- Pain may be elicited on palpation (spermatic cord torsion, epididymitis, orchitis, rupture)
- Derangements in systemic parameters (elevated heart rate, respiratory rate, inappetence, CBC abnormalities)
- Any combination of abnormalities may be present and not all signs are present in every animal

CAUSES
- 3 most common:
  - Trauma; may include testicular hematoma/rupture
  - Inguinal/scrotal hernia
  - Torsion of the spermatic cord, also known as testicular torsion
- Inflammatory/infectious causes:
  - EIA
  - EVA/equine arteritis virus
  - Orchitis/epididymitis
- Neoplasia:
  - Primary scrotal—melanoma, sarcoid
  - Testicular neoplasia—seminoma, teratoma, interstitial cell tumor, Sertoli cell tumor
- Noninflammatory scrotal edema
- Hydrocele/hematocele
- Varicocele

RISK FACTORS
- Breeding activity
- Large internal inguinal rings
- Systemic illness
- Extremes of ambient temperature (hot or cold)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Differentiating Causes
- Duration of problem
  - Acute—traumatic injury, torsion of spermatic cord, herniation, infection
  - Chronic—neoplasia, temperature-induced hydrocele/edema, varicocele, infection
- History of recent breeding, semen collection, and/or trauma
- Palpation of the caudal ligament of the epididymis (attaches epididymal tail to caudal testis and aids in the determination of testicular orientation)
- Palpation of the inguinal rings
- US (see Imaging)

CBC/BIOCHEMISTRY/URINALYSIS
- Inflammatory or stress leukocyte response
- Increased fibrinogen
- Results of serum biochemistry profile and urinalysis are usually normal

OTHER LABORATORY TESTS
- EVA
  - Serum neutralization or complement fixation
  - Acute and convalescent serum samples
  - If stallion is seropositive, carrier state is determined with virus isolation
  - Virus isolation from serum and/or seminal plasma
  - Semen is the best sample for diagnosis (freeze portion of ejaculate and send to approved laboratory along with serum samples)
  - *Send samples to an approved laboratory*
- EIA
  - Agar gel immunodiffusion or ELISA, the Coggins test

IMAGING—SCROTAL US
Examination of scrotal contents may reveal:
- Bowel with inguinal/scrotal herniation
- Rupture of the testis/tunica albuginea
  - Accumulation of hypoechoic fluid in scrotum with loss of discrete hyperechoic tunica albuginea around testicular parenchyma
  - Hypoechoic appearance of contents will gradually contain echogenic densities with the formation of fibrin clots
- Engorgement of the pampiniform plexus and/or testicular congestion with torsion of the spermatic cord
  - Doppler can verify loss of blood flow to the testis
- Hypoechoic dilation of venous plexus of spermatic cord with varicocele
- Hypoechoic accumulation of fluid within the vaginal cavity with hydrocele
- Loss of homogeneity in testicular parenchyma with neoplasia
  - May see areas of increased or decreased echogenicity or be variable throughout

OTHER DIAGNOSTIC PROCEDURES
- Needle aspirate and cytology—to differentiate hydrocele from recent hemorrhage
- Neoplasia—diagnosed using fine needle aspirate and/or biopsy

PATHOLOGIC FINDINGS
Dependent on etiology.

TREATMENT
- Treatment is directed at the cause of scrotal enlargement
- Management of inflammation is a primary concern with abnormal scrotal enlargement
- Sexual rest is indicated for all causes of scrotal enlargement

APPROPRIATE HEALTH CARE
- Acute scrotal enlargement warrants hospitalization for treatment and care
- Chronic scrotal enlargement may or may not warrant hospitalization; etiology dependent

NURSING CARE
- Cold therapy (cold packs, ice water baths, water hose/hydrotherapy) for acute scrotal trauma is implemented only in the absence of testicular rupture
  - Testicular tunics *must* be intact
  - Cold therapy sessions should not exceed 20 min and can be repeated every 2 h

ABNORMAL SCROTAL ENLARGEMENT (CONTINUED)

• Scrotal massage with emollient salve—useful to reduce scrotal edema and ischemic injury
• Fluid removal should be considered with a hydrocele
  ◦ Use only an aseptically placed needle or an IV catheter
  ◦ Excess fluid accumulation may cause thermal damage to the testes, acts as an insulator
• Administration of IV fluids is dependent on the systemic status of the horse

ACTIVITY
The need to restrict activity depends on the etiology of scrotal enlargement.

DIET
Diet modification is necessary only with secondary ileus or as a preoperative consideration.

CLIENT EDUCATION
• Fertility may be irreversibly impaired with acute scrotal trauma
• Semen evaluation should be performed 90 days after nonsurgical resolution of scrotal enlargement
• Compensatory semen production may occur in the remaining testis of a horse undergoing hemicastration
• Following removal of a neoplasia, examine carefully for evidence of metastatic tumor growth (serial examinations)

SURGICAL CONSIDERATIONS
• Hemicastration is the treatment of choice for:
  ◦ Torsion of the spermatic cord, if the duration of vascular compromise has caused irreversible damage and/or gonadal necrosis
  ◦ Unilateral inguinal/scrotal herniation
  ◦ Testicular rupture
  ◦ Unilateral neoplasia
  ◦ Varicocele
  ◦ Nonresponsive hydrocele/hematocele
• Primary repair of scrotal laceration is required to protect scrotal contents
  ◦ Repair generally fails due to extensive scrotal edema associated with traumatic injury

MEDICATIONS

DRUG(S) OF CHOICE
• Anti-inflammatory therapy (phenylbutazone 2–4 mg/kg PO or IV BID or flunixin meglumine 1 mg/kg IV BID) is indicated in all cases
• Diuretics (furosemide 0.5–1 mg/kg IV) may be useful in managing scrotal edema
• Antibiotic therapy should be considered in cases of scrotal laceration or scrotal hemorrhage
• Tetanus toxoid should be administered for scrotal trauma or prior to surgery

CONTRAINDICATIONS
N/A

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
Semen collection and evaluation 90 days after complete resolution of cause and/or surgery.

PREVENTION/AVOIDANCE
Adequate management of breeding to avoid trauma.

POSSIBLE COMPLICATIONS
• Infertility
• Endotoxemia
• Laminitis
• Scrotal adhesions
• Death

EXPECTED COURSE AND PROGNOSIS
• Prognosis for survival and fertility are good in unilateral cases of trauma or spermatic cord torsion if managed quickly and correctly
• Recurrent severe hematocele; hydrocele may result in testicular degeneration and loss of fertility

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

SEE ALSO
Abnormal testicular size

ABBREVIATIONS
• EIA = equine infectious anemia
• ELISA = enzyme-linked immunosorbent assay
• EVA = equine viral arteritis
• US = ultrasonography, ultrasound

Suggested Reading

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Author Ahmed Tibary
Consulting Editor Carla L. Carleton
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ABNORMAL TESTICULAR SIZE

BASICS

DEFINITION
Any significant deviation (increase or decrease) in the size of the testes. This may be unilateral or bilateral.

PATHOPHYSIOLOGY
- The testes and epididymides are positioned in a horizontal orientation and are freely movable within the scrotum
- Changes in testicular size are often first noticed as a variation in scrotal size
- Abnormal testicular size may be congenital or acquired
- Testicular hypoplasia is the most common congenital abnormality
  - It may be associated with incomplete or delayed testicular descent (cryptorchidism)
  - Hypoplastic testes are hard, dense, and have poor or arrested spermatogenic activity
- Acquired abnormal testicular size can be acute or progressive
- *Acute enlargement* of a testis occurs after trauma, torsion of the spermatic cord, or orchitis/epididymitis. Testicular neoplasia may be seen in some cases of acute enlargement
- Progressive enlargement of the testis is often due to *testicular neoplasia*
  - Seminoma, teratoma, Sertoli cell tumor, interstitial cell tumor
  - Of these, seminoma is the most frequently reported testicular tumor of the stallion
  - Most equine testicular tumors arise from germ cells, including seminomas and teratomas
  - The effect of neoplasia on testicular size (increase or decrease) may be insidious
- Reduction of testicular size, *testicular atrophy*, is often a consequence of testicular degeneration
- *Testicular degeneration* may arise from thermal injury, infection, trauma, vascular insult, hormonal disturbances, toxins, and age. Spermatogenesis is severely affected. Reduction or loss of fertility depends on the degree of compromise of spermatogenesis and whether the affection is bilateral or unilateral

SYSTEMS AFFECTED
- Reproductive
- Other systems (respiratory, gastrointestinal, lymphatic) may be affected subsequent to metastasis of primary testicular neoplasia

GENETICS
Cryptorchidism and testicular hypoplasia are suspected to have genetic components.

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
- Intact male horses
- Any age

SIGNS
Historical Findings
- Recent history of breeding or semen collection
- Gross changes in the size of a testis
- Reduced fertility
- Pain (generally colic-like symptoms)
- Reluctance to breed, jump, or walk

Physical Examination Findings
- Increased or decreased scrotal size
- Increased or decreased testicular size
- Abnormal testicular texture (too soft or too firm)
- Abnormal testicular position
- Abnormal scrotal temperature (too warm or too cold)
- Edema/engorged scrotum and/or contents
- Derangements in systemic parameters (elevated heart rate, respiratory rate, inappetence, CBC abnormalities)

CAUSES
- Common causes of decreased testicular size
  - Cryptorchidism
  - Testicular degeneration, atrophy
- Common causes of increased testicular size
  - Trauma (testicular hematoma, rupture)
- Other causes of increased testicular size
  - Neoplasia (primarily seminoma)
  - Orchitis/epididymitis (bacterial infection, EIA, EVA, *Strongylus edentatus* infection, autoimmune)

RISK FACTORS
- Breeding activity
- Systemic illness
- Temperature extremes
- Anabolic steroid use

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Differentiating Similar Signs
- Scrotal enlargement due to scrotal hydrocele/hematocele and scrotal or inguinal hernia may be confused with testicular enlargement
- US examination and measurement of the testes is the best means of differentiating the pathologies

Differentiating Causes
- Duration of problem
  - *Acute*—traumatic injury, infection
  - *Chronic*—cryptorchidism, neoplasia, infection, testicular degeneration/hypoplasia
- History of recent breeding and/or trauma
- Palpation of the caudal ligament of the epididymis (attaches epididymal tail to caudal testis and aids in the determination of testicular orientation)
- Testicular hypoplasia is usually congenital, while testicular degeneration is acquired
- US (see Imaging)

CBC/BIOCHEMISTRY/URINALYSIS
- Inflammatory or stress leukocyte response
- Eosinophilia may be an indicator of a parasitic infection
- Increased fibrinogen in peripheral blood
- Serum biochemistry profile and urinalysis are usually normal

OTHER LABORATORY TESTS
- EVA
  - Serum neutralization or complement fixation
  - Requires acute and convalescent serum samples
  - If stallion is seropositive, carrier state is determined with virus isolation
  - Semen is best sample for diagnosis (freeze portion of ejaculate and send to approved laboratory with serum samples)
  - *Send samples to an approved laboratory*
- EIA
  - Agar gel immunodiffusion or ELISA, the Coggins test
- Testicular degeneration
  - Endocrine profile (luteinizing hormone, FSH, testosterone, estrogens) from pooled samples obtained hourly for a minimum of 4 samples (due to pulsatile release of hormones)
  - Abnormal elevation of FSH and low total estrogen concentration are indicative of testicular degeneration

IMAGING—SCROTAL/TESTICULAR US
Testicular parenchyma should appear uniformly echogenic. Aberrations that may be identified by US include:
- Rupture of the testis/tunica albuginea
  - Hypoechoic fluid accumulates in the scrotum with loss of discrete hyperechoic tunica albuginea around testicular parenchyma
  - Hypoechoic appearance of contents will gradually be replaced with echogenic densities as fibrin clots form
- Engorgement of the pampiniform plexus and/or testicular congestion with torsion of the spermatic cord
  - Doppler can verify loss of blood flow to the testis
- Loss of homogeneity in testicular parenchyma with neoplasia
  - Neoplasia results in heterogeneity (usually a circumscribed area) in testicular parenchyma
  - May see areas of increased or decreased echogenicity or be variable throughout

OTHER DIAGNOSTIC PROCEDURES
- Needle aspirate and cytology—diagnose and/or differentiate recent hemorrhage or neoplasia
- Testicular biopsy (histopathology)—diagnose and/or differentiate neoplasia and testicular degeneration/hypoplasia

ABNORMAL TESTICULAR SIZE (CONTINUED)

• Semen evaluation is useful in the diagnosis of testicular degeneration or hypoplasia:
  ◦ Oligospermia
  ◦ Azoospermia
  ◦ Presence of round spermatids (spheroids)

PATHOLOGIC FINDINGS
• Testicular hypoplasia—round, small diameter seminiferous tubules, spermatogenic arrest
• Testicular degeneration—large, collapsed seminiferous tubules, vacuolization, poor or incomplete spermatogenesis
• Testicular neoplasia—depends on neoplasm

TREATMENT

Treatment is directed at the cause of testicular abnormality.

APPROPRIATE HEALTH CARE
Inpatient versus Outpatient
• Most causes of testicular enlargement require hospitalization for treatment/resolution
• Horses with testicular degeneration that are not systemically ill may be managed on the farm
• Horses with hypoplastic testes can be managed on an outpatient basis

NURSING CARE
• Cold therapy (cold packs, ice water baths, water hose/hydrotherapy) is indicated for acute orchitis/epididymitis
• Cold therapy sessions should not exceed 20 min and can be repeated every 2 h
• Sexual rest is indicated in most cases until resolution of the problem
• Administration of IV fluids is dependent on the systemic status of the horse

ACTIVITY
Restriction depends on the cause of the testicular aberration.

DIET
Modification is necessary only with cases of secondary ileus or as a preoperative consideration.

CLIENT EDUCATION
• Fertility may permanently be lowered
• Testicular degeneration results in various degrees of reduction in ejaculate quality
• Testicular hypoplasia is a permanent condition
• Horses with neoplasia should be examined carefully for evidence of metastatic tumor growth
• Compensatory sperm production may occur in the remaining testis of a horse undergoing hemicastration
• Serial semen evaluations are beneficial to monitor the fertility status of horses following testicular insult and treatment
  ◦ Semen should be evaluated 75–90 days after complete resolution of testicular insult

SURGICAL CONSIDERATIONS
Hemicastration is the treatment of choice for:
• Torsion of the spermatic cord, if the duration of vascular compromise has caused irreversible damage and/or gonadal necrosis
• Testicular rupture
• Unilateral neoplasia or any condition causing irreparable damage to testis/es

MEDICATIONS

DRUG(S) OF CHOICE
• Anti-inflammatory therapy (phenylbutazone 2–4 mg/kg PO or IV BID or flunixin meglumine 1 mg/kg IV BID) is indicated in most cases
• Antibiotic therapy should be considered in cases of orchitis/epididymitis and testicular trauma
• Tetanus toxoid should be administered after testicular trauma and/or prior to surgery
• Antiparasitic therapy for *Strongylus edentatus* infection (ivermectin 0.2 mg/kg PO every 30 days until resolution of lesions)

CONTRAINDICATIONS
N/A

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
Semen collection and evaluation 90 days after complete resolution of testicular problem and/or surgery.

POSSIBLE COMPLICATIONS
• Infertility/subfertility
• Endotoxemia
• Laminitis
• Scrotal adhesions
• Death

EXPECTED COURSE AND PROGNOSIS
Dependent on etiology.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Cryptorchidism is commonly associated with testicular hypoplasia
• Male equine hybrids (mules or hinnies) often have hypoplastic testes

AGE-RELATED FACTORS
• Prepubertal testes are small and can be misdiagnosed as pathologically hypoplastic
• Testicular growth increases rapidly from 12 to 24 months of age in horses
• Testes may take 4–5 years to reach full size and maturity

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

SEE ALSO
• Abnormal scrotal enlargement
• Cryptorchidism

ABBREVIATIONS
• EIA = equine infectious anemia
• ELISA = enzyme-linked immunosorbent assay
• EVA = equine viral arteritis
• FSH = follicle-stimulating hormone
• US = ultrasonography, ultrasound

Suggested Reading

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Author Ahmed Tibary
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ABORTION, SPONTANEOUS, INFECTIOUS

BASICS

DEFINITION

Fetal loss after 40 days of gestation (term *stillbirth* may apply >300 days) involving maternal, placental, and/or fetal invasion by microorganisms.

PATHOPHYSIOLOGY

• Approximately 5–15% of abortions are infectious. • Abortion *storms* can occur, especially with EHV or MRLS when caterpillar populations are greatly increased. • Can involve viruses, bacteria, rickettsia, protozoa, fungi, or, with MRLS, ingestion of ETC. Some of the specific microorganisms associated with spontaneous, infectious equine abortions are listed below

Viruses

• EHV-1 (1P and 1B strains); EHV-4; rarely EHV-2. EHV abortions generally occur late in gestation; >7 months. • EVA (>3 months of gestation). • Equine infectious anemia (direct causal relationship not yet established). • Vesivirus: recent correlation between its antibodies and equine abortions

Bacteria

• Placentitis and possible, subsequent fetal infection by *Streptococcus* spp., *Actinobacillus* spp., *Escherichia coli, Pseudomonas* spp., *Klebsiella* spp., *Staphylococcus* spp., nocardioform actinomycetes, such as *Amycolatopsis* spp., *Cellulosimicrobium* spp., *Crossiella* spp., and *Rhodococcus* spp., *Taylorella equigenitalis* (rare, reportable), and *Leptospira* serovars. • Endotoxemia causes release of prostaglandin F2 alpha (especially <80 days of gestation (day 60 in many mares)); may be factor later in gestation, if repeated exposure. • MRLS is closely associated with ETC, or, potentially, other species of caterpillars, the setae of which cause microscopic bowel puncture and subsequent bacteremic spread to the fetus and/or placenta; species of *Actinobacillus* and nonhemolytic *Streptococcus* are cultured approximately 65% of the time

Rickettsiae

Ehrlichia risticii (Potomac horse fever).

Fungi

Placentitis caused by *Aspergillus* spp., *Candida* spp., or *Histoplasma capsulatum.*

Protozoa

Sarcocystis neurona or, possibly, *Neospora* spp. in aborted fetuses from EPM-affected mares.

MRLS

1. A major concern in years when caterpillar populations are greatly increased; the geographic distribution, financial impact, and unusual pathogenesis of this syndrome make it a topic worthy of separate discussion.
2. Early (≈40–150 days of gestation) and late (>269 days of gestation) abortion syndromes.
3. Associated with greatly increased populations of ETCs.
4. Oral exposure to ETC setae in conjunction with MRLS; currently theorized to be associated with microscopic bowel puncture and bacteremic spread to fetus and/or placenta

Depending on the specific infectious cause, the pathophysiologic mechanisms of spontaneous infectious abortions can involve the following sequence of events: • Fetal death by microorganisms. • Fetal expulsion after placental infection, insufficiency, or separation. • Premature parturition induced by microbial toxins, fetal *stress*, or a combination of mechanisms. • Final result—fetal death followed by absorption, maceration, or autolysis; fetal death during the stress of delivery (*stillbirth*) or birth of a live fetus incapable of extrauterine survival. • Some have suggested a caterpillar toxin-associated cause for the 2001–2002 outbreak of MRLS in central Kentucky and surrounding areas. • It is currently thought ingestion of ETC by pregnant mares is associated with penetration of intestinal mucosa by bacteria-contaminated, barbed caterpillar setae and their fragments. These migrate in blood vessels as septic setal emboli, deposited in vascular, immunologically susceptible targets, such as the early and late-term fetus and placenta

SYSTEMS AFFECTED

• Reproductive. • Other organ systems can be affected if there is maternal systemic disease

SIGNS

Historical Findings

One or more of the following: • Vaginal discharge, which can potentially be mucopurulent, hemorrhagic, or serosanguineous. • Premature udder development with dripping milk. • Anorexia or colic; GI disease. • Failure to deliver on expected due date. • *Recent* (1–16 weeks before presentation) systemic infectious disease or, similarly, recent introduction of infected *carrier* horses to the premises. • Other, recently aborting mares. • Inadequate EHV-1 prophylaxis. • History of placentitis. • Previous history of dystocia, especially with perineal and/or cervical trauma. • Previous endometrial biopsy with moderate/severe endometritis or fibrosis. • None or excessive abdominal distention consistent with gestation length. • Behavioral estrus in a pregnant mare, which might be normal, depending on gestation length, time of year, gestation length at time of loss. • Climatic and environmental conditions favoring increased populations of ETC (*Malacosoma americanum*) or, possibly, other caterpillar species with setae and development of MRLS in early and late pregnant mares. • Possibly geographic location if suspect MRLS and nocardioform placentitis

Physical Examination Findings

• Early pregnancy loss is frequently unobserved and is described as *asymptomatic*. • Unless complications occur, abortion may occur rapidly, with the sole sign being a relatively normal, previously pregnant mare later found open. • Signs range from none to multisystemic and life-threatening disease, especially if dystocia occurs during delivery or if maternal organs are infected. • Depending on microorganisms involved, multiple animals can be affected. • Most *symptomatic* spontaneous infectious abortions occur during the second half of gestation; characterized by one or more of the following findings on physical examination: ◦ Fetal parts/placental structures protruding through vulvar lips; abdominal straining or discomfort. ◦ Premature placental separation (*red bag*). ◦ Vulvar discharge (variable appearance), premature udder development, dripping milk. ◦ A previously documented pregnancy is not detected at the next examination. ◦ Evidence of fetal death by TRP, transrectal or transabdominal US. ◦ Anorexia, fever, signs of concurrent systemic disease, especially with endotoxemia, dystocia, RFM. ◦ Evidence of placental separation or echogenic allantoic fluid, especially in association with MRLS, as observed using transrectal or transabdominal US

RISK FACTORS

• Pregnant mares intermixed with young horses or horses in training are susceptible to EHV-1, EVA, or *E. risticii*. • Immunologically naive mares brought to premises with enzootic EHV-1, EVA, *E. risticii,* or *Leptospira* infections. • Pregnant mares traveling to horse shows or competitions. • Poor perineal conformation or dystocia with perineal lacerations or cervical trauma predisposes mares to ascending bacterial or fungal placentitis and, possibly, subsequent fetal infection. • Concurrent maternal GI disease or EPM. • Large numbers of ETCs in pastures with pregnant mares. • Geographic location with respect to MRLS and nocardioform placentitis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other Causes of Abortion

• Abortion, spontaneous, noninfectious. • Twinning. • Fetal abnormalities/teratogenesis. • Umbilical cord abnormalities with excessive twisting and thrombosis. • Placental pathology. • Maternal malnutrition or other noninfectious systemic disease. • Old mare, history of early embryonic death or abortion. • Old mare, poor endometrial biopsy. • Maternal exposure to: ◦ Endophyte-infected tall fescue pasture, exposure to ergotized grasses, small cereal

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ABORTION, SPONTANEOUS, INFECTIOUS (CONTINUED)

grains during last month of gestation; little or no mammary development (agalactia, if term is reached). ◦ Phytoestrogens. ◦ Other xenobiotics. • Iatrogenic or inappropriately timed induction of labor

Other Causes of Labor or Abdominal Discomfort

• Normal parturition. • Dystocia unassociated with abortion. • Prepartum uterine artery rupture. • Colic associated with uterine torsion. • Discomfort associated with hydrops of fetal membranes or prepubic tendon rupture. • Colic unassociated with reproductive disease

Other Causes of Vulvar Discharge

• Normal parturition. • Dystocia unassociated with abortion. • Normal estrus. • Endometritis. • Metritis or partial RFM. • Mucometra or pyometra

IMAGING

Transrectal and transabdominal US can evaluate fetal viability, placentitis, and alterations in appearance of amniotic and/or allantoic fluids, as well as other gestational abnormalities.

OTHER DIAGNOSTIC PROCEDURES

• Except for placentitis, abortions secondary to endotoxemia, and fetal expulsion associated with dystocia, most abortions are *asymptomatic*. The expelled fetus and fetal membranes vary in condition from intact to autolytic in appearance. • Definitive diagnosis of equine abortion in ≈50–60% of all cases. • Excluding twins and EHV-1, the diagnostic rate may only be 30%, especially if limited samples are submitted and are accompanied by moderate to severe fetal and placental autolysis with environmental contamination. • Laboratory testing to determine the cause of a spontaneous, potentially infectious abortion includes the following procedures: ◦ CBC, serum biochemistry for inflammatory or stress leukocyte response, or evidence of other organ system involvement. ◦ Suspected endotoxemia—maternal P_4 assay is indicated if the pregnancy is at risk prior to determining an infectious cause of an impending abortion. ELISA or RIA analyses for P_4 may be useful at <80 days of gestation (normal levels vary from >1 to >4 ng/mL, depending on reference laboratory). At >100 days, RIA detects both P_4 (very low > day 150) and cross-reacting 5α-pregnanes of uterofetoplacental origin. Acceptable levels of 5α-pregnanes vary with stage of gestation and the laboratory used. ◦ To aid in establishing a diagnosis of abortions caused by placentitis, a maternal uterine swab/uterine lavage sample or, as advocated by some, a uterine biopsy can provide samples for culture and cytology (swab or lavage) or histopathology (biopsy). ◦ Analyses for other maternal hormones can be performed. ◦ Maternal serologic testing can be useful in diagnosing infectious abortions (diagnostic for abortions by *Leptospira* serovars; confirms EVA abortion). Serum samples should be collected in all cases of abortion in which cause is unknown (a paired sample collected 21 days later might be indicated). • The following samples should be collected from the fetus and the fetal membranes for histopathologic and cytologic evaluations, as well as microbiologic, serologic, and molecular testing procedures: ◦ Fresh/chilled fetal thoracic or abdominal fluid and serum from the fetal heart or cord blood. ◦ Fetal stomach contents. ◦ 10% neutral-buffered formalin-fixed and chilled/frozen fetal membranes (chorioallantois or allantochorion; amnion or allantoamnion), as well as fixed and chilled/frozen samples of fetal heart, lung, thymus, liver, kidney, lymph nodes, spleen, adrenal, skeletal muscle, and brain. ◦ Stained cytologic smears collected from fetal membranes

PATHOLOGIC FINDINGS

Viruses

• EHV ◦ Gross pleural effusion, ascites, fetal icterus, pulmonary congestion, and edema; 1 mm, yellowish-white spots on enlarged liver; relatively fresh fetus. ◦ Histopathologic findings for EHV-1 and -4 include areas of necrosis, prominent, eosinophilic, intranuclear inclusion bodies in lymphoid tissue, liver, adrenal cortex, lung, as well as a hyperplastic, necrotizing bronchiolitis. ◦ Fluorescent antibody staining of fetal tissues. ◦ Virus isolation from aborted fetus. ◦ PCR can be used for EHV-1/EHV-4, as well as, possibly, other viruses and microorganisms listed below, depending on the diagnostic laboratory. • EVA ◦ Few gross lesions. ◦ Autolyzed fetus. ◦ Placental/fetal vascular lesions. • Vesivirus ◦ Nonspecific lesions

Bacteria and Fungi

• Fetal infection and placentitis ◦ Gross pleural effusion, ascites with enlarged liver; rare plaques of mycotic dermatitis; placental edema and thickening with fibronecrotic exudate on the chorionic surface, especially at the *cervical star* in fungal infections. ◦ Histopathologic evidence of inflammatory disease; autolysis may make interpretation difficult. • Leptospirosis ◦ Gross fetal icterus and autolysis. ◦ Nonspecific histologic changes; mild, diffuse placentitis

Endotoxemia

Fetus minimally autolyzed.

Rickettsiae

• *Ehrlichia risticii* ◦ Gross placentitis. ◦ Typical histopathologic findings include colitis, periportal hepatitis, lymphoid hyperplasia, and necrosis

Protozoa

There are reports of *Sarcocystis neurona*-associated abortions in EPM-positive mares.

MRLS

Histopathologic findings similar to bacterial infections.

TREATMENT

APPROPRIATE HEALTH CARE

• Except late-gestational placentitis (>270 days) and endotoxemia, no therapy indicated to preserve fetal viability with spontaneous, infectious abortion. • For mares that abort, there is only *prophylactic* therapy for metritis or endometritis. • Therapy is generally limited to intrauterine lavage with or without antibacterial therapy but might include a systemic component consisting of antibiotics, NSAIDs, and/or IV fluids, especially if septicemia, endotoxemia, and/or laminitis are suspected. • Preexisting GI disease and complications, such as laminitis, may warrant hospitalization and intensive care

NURSING CARE

Most affected horses require limited nursing care, except in instances of endotoxemia and Gram-negative septicemia, dystocia, RFM, metritis, laminitis.

ACTIVITY

There should be paddock exercise to permit observation, but this recommendation is subject to change if the mare exhibits clinical signs of laminitis.

DIET

Feed and water intake, as well defecation and urination, should be monitored, but no particular dietary changes should take place in the absence of GI disease or laminitis.

CLIENT EDUCATION

Inform owners of: • Availability of vaccines to prevent some types of viral abortion. • Increased risk for abortion in mares with a previous history of dystocia (especially those mares with perineal or cervical trauma) or placentitis. • Possible complications of abortion

SURGICAL CONSIDERATIONS

Indicated in instances of dystocia or GI disease requiring surgical intervention or repair of previous perineal lacerations, cervical trauma, or other structural abnormalities.

MEDICATIONS

DRUG(S) OF CHOICE

• Altrenogest administered 0.044–0.088 mg/kg PO daily can be started later during gestation, continued longer, or used only for short periods of time, depending on serum P_4 levels during the first 80 days of gestation, clinical circumstances, risk factors, clinician preference. Note that serum levels reflect only endogenous P_4, not

exogenous, oral product. • If near term, altrenogest frequently is discontinued 7–14 days before the foaling date unless indicated otherwise by fetal maturity/viability, or actual gestational age is in question

PRECAUTIONS, POSSIBLE INTERACTIONS

• Altrenogest is only used to prevent abortion in cases of endotoxemia or placentitis (>270 days of gestation) if the fetus is viable. • Altrenogest is absorbed through skin; wear gloves and wash hands

ALTERNATIVE DRUGS

• Injectable P_4 (150–500 mg oil base) IM. • Newer, repository forms of P_4 are occasionally introduced; however, some evidence of efficacy should be provided prior to use

FOLLOW-UP

PATIENT MONITORING

• 7–10 days post abortion, TRP and US to monitor uterine involution. • Observation for signs of systemic disease, laminitis. • Assess genital tract health using vaginal speculum, hysteroscopy, uterine culture and cytology, and/or endometrial biopsy. • Base treatment on results of these testing procedures. Uterine culture <14 days postpartum or post abortion can be affected by contamination at the time of parturition (abortion)

PREVENTION/AVOIDANCE

Vaccines

• A killed-virus EHV-1 vaccine at 5, 7, and 9 months of gestation (some recommend vaccination at 3 months of gestation, as well); approved for abortion prevention in pregnant mares; 2 month interval due to short-lived vaccinal immunity. • Other EHV vaccines, including combinations of EHV-1 and -4, have been used off-label for abortion prevention, with some anecdotal reports of their efficacy for this purpose. • EVA vaccine not specifically labeled for abortion prevention; a modified live vaccine only to be administered to open mares 3 weeks before anticipated exposure to infected semen or in enzootic conditions. First-time vaccinated mares should be isolated for 3 weeks after exposure to infected semen. Note that some countries forbid importation of horses with titers to EVA

Additional Prophylactic Steps

• Segregate pregnant mares from horses susceptible/exposed to infections. • Isolate immunologically naive individuals until immunity to enzootic infections is established and/or enhanced. Depending on infectious agent, protection may only be accomplished postpartum. • Limit transport of pregnant mares to exhibitions or competitions. • Careful observation of pregnant mares and monitor mammary development. • Use appropriate biosecurity protocols and isolate aborting mares, with proper disposal of contaminated fetal tissues. • Proper diagnostics to identify an infectious cause of abortion. • Correct structural abnormalities, such as poor perineal conformation, perineal lacerations, or cervical trauma, in order to prevent ascending placentitis. • Manage preexisting endometritis before next breeding. • Prevent pregnant mare exposure to ETCs until 7–8 weeks after ETC death. • Insecticides to control ETCs; consider toxicity of insecticide

POSSIBLE COMPLICATIONS

• Abortion in late pregnancy can be associated with dystocia and other potentially life-threatening conditions. • Future fertility and reproductive value can be impaired by dystocia, RFM, endometritis, laminitis, septicemia, trauma to genital tract

EXPECTED COURSE AND PROGNOSIS

• Most patients recover with appropriate treatment. • Complications can involve significant impact on mare's survivability and future fertility. • Prognosis is guarded for pregnancy maintenance with endotoxemia and placentitis. • Mares with placentitis, especially those with predisposing structural abnormalities, are more susceptible to future recurrence of this type of abortion

MISCELLANEOUS

SYNONYMS

• Abortion. • Spontaneous abortion. • Infectious abortion. • Bacterial abortion. • Viral abortion. • Fungal abortion. • Mycotic abortion. • Protozoal abortion. • Rickettsial abortion

SEE ALSO

• Abortion, spontaneous, noninfectious
• Contagious equine metritis (CEM)
• Dystocia
• Endometrial biopsy
• Endometritis
• Fetal stress/distress/viability
• High-risk pregnancy
• Placental insufficiency
• Placentitis
• Premature placental separation
• Retained fetal membranes

ABBREVIATIONS

• EHV = equine herpesvirus
• ELISA = enzyme-linked immunosorbent assay
• EPM = equine protozoal encephalomyelitis
• ETC = eastern tent caterpillar
• EVA = equine viral arteritis
• GI = gastrointestinal
• MRLS = mare reproductive loss syndrome
• NSAID = nonsteroidal anti-inflammatory drug
• P_4 = progesterone
• PCR = polymerase chain reaction
• RFM = retained fetal membranes/placenta
• RIA = radioimmunoassay
• TRP = transrectal palpation
• US = ultrasonography, ultrasound

Suggested Reading

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Author Tim J. Evans
Consulting Editor Carla L. Carleton

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ABORTION, SPONTANEOUS, NONINFECTIOUS

BASICS

DEFINITION

Fetal loss >40 days (term *stillbirth* may apply >300 days) due to noninfectious conditions.

PATHOPHYSIOLOGY

Approximately 85–95% of abortions are noninfectious in nature. Some of the specific causes of spontaneous, noninfectious equine abortions are as follows.

- *Twin pregnancies* that persist >40 days, ≈70% end in abortion/stillbirth
- *Luteal insufficiency/early CL regression*
  - Anecdotal—decreased levels of luteal progesterone at <80 days of gestation
- *Placental abnormalities*
  - Umbilical cord torsion, as evidenced by vascular compromise, e.g. cord thrombus, can be associated with abortion
  - Torsion of the amnion
  - Long umbilical cord/cervical pole ischemia disorder
  - Confirmed body pregnancy
  - Placental separation
  - Villous atrophy, hypoplasia, or placental insufficiency (can also be associated with prolonged gestation)
  - Hydrops
  - Various placental abnormalities reported with foals resulting from SCNT
- *Fetal abnormalities*
  - Developmental abnormalities, such as hydrocephalus or anencephaly
  - Fetal trauma
  - Chromosomal abnormalities
- *Maternal abnormalities*
  - Concurrent maternal disease, such as PPID and EMS/IR
  - Trauma
  - Malnutrition/starvation; selenium deficiency
  - Anecdotal—severe maternal anxiety/stress and/or pain, such as severe laminitis
  - Moderate to severe endometritis and/or endometrial periglandular fibrosis
  - Lymphatic cysts—anecdotal
  - Chromosomal abnormalities
- *Xenobiotics*
  - Ergopeptine alkaloids associated with fescue toxicosis or ergotism can be associated with placental thickening and abortion, although prolonged gestation is more common
  - Phytoestrogens—anecdotal abortions early in spring
  - Xenobiotics causing maternal disease, such as cardiac glycosides, taxine alkaloids, carbamates, organophosphates
  - Originally proposed with mare reproductive loss syndrome, but *penetrating septic septal emboli* now suspected
  - Equine protozoal encephalomyelitis therapies during pregnancy
- Repeated large doses of corticosteroids during late gestation*Iatrogenic causes*
  - Prostaglandin F2 alpha to terminate a pregnancy
  - Procedures mistakenly done on a pregnant mare, such as artificial insemination, intrauterine infusions, samples taken for cytology, culture, or biopsy
  - Possible mechanisms can involve the sequence of events below:
    - Fetal death/premature parturition—some intrinsic structural or functional defect or exposure to xenobiotics
    - Fetal expulsion <80 days of gestation after CL loss, a result of endometritis or other factors
    - Fetal death/expulsion by placental insufficiency or separation
    - Fetal *stress*, dead twin fetus, maternal *stress*, or combination
    - Fetal reabsorption, maceration, mummification, autolysis, death during delivery (stillbirth) or delivery of live fetus incapable of extrauterine survival

SYSTEMS AFFECTED

- Reproductive
- Other organ systems can be affected if there is maternal systemic disease

SIGNS

Historical Findings

One or more of the following:

- Signs consistent with labor at an unexpected stage of gestation
- Dystocia, birth of nonviable foal
- Previous history of abortion, dystocia, or birth of a nonviable foal
- Vaginal discharge, which is generally mucoid, hemorrhagic, or serosanguineous
- Premature udder development; dripping milk
- Anorexia or colic
- *Recent* systemic disease
- Moderate/severe endometritis and/or endometrial periglandular fibrosis
- None/excessive abdominal distention consistent with stage of gestation
- Behavioral estrus in pregnant mare, which might be normal for stage of gestation and is dependent on time of year and stage of pregnancy when pregnancy is lost

Physical Examination Findings

- Depends on the cause, time of fetal death, stage of gestation, duration of the condition, and whether pregnancy ended in dystocia or with RFM
- Abortion usually occurs rapidly and is unobserved
- Signs range from none to multisystemic and life-threatening disease
- Most *symptomatic* spontaneous noninfectious abortions occur during the second half of gestation, characterized by one or more of the following physical examination findings:
  - Fetal/placental structures protruding through vulval lips; abdominal straining or discomfort
  - Premature placental separation (*red bag*)
  - Vulval discharge (variable appearance), premature udder development, dripping milk
  - Previously diagnosed pregnancy absent at next examination; fetal death determined by TRP or transrectal/transabdominal US
  - Twin fetuses
  - Placental separation or hydrops of fetal membranes
  - Signs of concurrent, systemic disease, dystocia, or RFM
- Note that signs are extremely variable. Mares pregnant at early check can remain *asymptomatic* but abort. Abortion can be unobserved early in gestation, may be rapid without signs

RISK FACTORS

- Often nonspecific
- See Pathophysiology

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other Causes of Abortion

- Infectious, spontaneous abortion
- Placentitis

Other Causes of Signs of Labor or Abdominal Discomfort

- Normal parturition
- Dystocia unassociated with abortion
- Prepartum uterine artery rupture
- Colic associated with uterine torsion
- Discomfort associated with hydrops of fetal membranes or prepubic tendon rupture
- Colic unassociated with reproductive disease

Other Causes of Vulval Discharge

- Normal parturition
- Dystocia not associated with abortion
- Normal estrus
- Endometritis, metritis, or RFM, mucometra or pyometra

DIAGNOSTIC PROCEDURES

- *Asymptomatic* unless—placentitis, secondary to endotoxemia, fetal expulsion associated with twins or dystocia
- Definitive causative diagnosis of equine abortion occurs in ≈50–60% of all cases
- Excluding twins and equine herpesvirus 1, the diagnostic rate may be only 30%
- Note that unless the cause of the abortion is obvious, such as twins or iatrogenic, must rule out infectious causes, especially if multiple mares are affected or at risk:
  - CBC, serum biochemistry
  - Maternal P_4 may be useful at <80 days of gestation
  - Maternal estrogen concentrations
  - Decreased maternal relaxin concentration associated with abnormal placental function

(CONTINUED)

ABORTION, SPONTANEOUS, NONINFECTIOUS

- ◦ Decreased maternal prolactin secretion during late gestation—associated with fescue toxicosis and ergotism
- ◦ Anecdotal reports of lower triiodothyronine/thyroxine levels with history of conception failure, early embryonic death, or abortion. The significance of low T_4 levels is unknown and somewhat controversial
- ◦ Test for PPID and EMS/IR
- ◦ Cytogenetic studies—useful if maternal or fetal chromosomal abnormalities are suspected
- ◦ Endometrial biopsy to assess endometrial inflammation and/or fibrosis
- ◦ Vaginal speculum examination and hysteroscopy if structural cervical or uterine abnormalities are suspected
- ◦ Xenobiotics—narrow testing to one or several potential xenobiotics in maternal and fetal samples. Might be very expensive, and unproductive. Feed or environmental analyses, for ergopeptine alkaloids, phytoestrogens, heavy metals, or fescue endophyte
- ◦ Imaging with transrectal and transabdominal US can be used to evaluate fetal viability, placentitis, and alterations in appearance of amniotic and/or allantoic fluids, as well as other gestational abnormalities, such as hydrops
- ◦ Collect samples for histopathology, cytology, microbiology, serology, and molecular testing procedures:
  - ■ If available, fresh/chilled fetal thoracic or abdominal fluid and serum from the fetal heart or cord blood
  - ■ Fetal stomach content
  - ■ 10% formalin-fixed and chilled/frozen samples of fetal membranes fetal viscera

PATHOLOGIC FINDINGS

- Macroscopic and histological evidence of physical causes (see Pathophysiology)
- Twins—avillous chorionic membrane at point of contact between the fetal membranes
- Umbilical cord torsion should be confirmed by evidence of vascular compromise
- Villous atrophy or hypoplasia might suggest endometrial periglandular fibrosis and/or lymphatic cysts
- Placental edema, gross and histopathological, is consistent with equine fescue toxicosis
- Various placental abnormalities reported with foals resulting from SCNT cloning procedures

TREATMENT

APPROPRIATE HEALTH CARE

- Except in cases of late-gestational placentitis (>270 days) and endotoxemia, no therapy indicated to preserve fetal viability with spontaneous, infectious abortion
- For mares that abort, there is only *prophylactic* therapy for metritis or endometritis. Therapy is generally limited to intrauterine lavage, with or without antibacterial therapy
- Preexisting GI disease and complications, such as laminitis, might warrant hospitalization and intensive care

NURSING CARE

Most affected horses require limited nursing care, except in instances of complications, e.g. septicemia, dystocia, RFM, metritis, and laminitis.

ACTIVITY

There should be paddock exercise to permit observation; recommendation subject to change if the mare exhibits clinical signs of laminitis.

DIET

Monitor feed and water intake, defecation, and urination; no particular dietary changes in the absence of GI disease or laminitis.

CLIENT EDUCATION

- The increased survivability of twin foals has led some breeders and, even, veterinarians to be less concerned about twin pregnancies. However, the risk of abortion, dystocia, and neonatal complications associated with twins still warrants prevention and/or management and discussion of the inherent risks related to pregnancy ending in abortion or complicated delivery
- Periglandular fibrosis is irreversible
- Older mares or mares with preexisting systemic disease might be at increased risk of spontaneous abortion
- Embryo transfer—especially mares with a history of abortion or those with severe endometrial periglandular fibrosis or severe structural abnormalities
- Risks associated with ingestion of endophyte-infected fescue and/or ergotized grasses and grains
- Inform owners of the possible complications of abortion

SURGICAL CONSIDERATIONS

- Dystocia or GI disease requiring surgical intervention
- Reduction of twin pregnancies can involve surgical approaches for selected fetal decapitation or other means for elimination of one twin
- Hysteroscopic removal of lymphatic cysts to prevent future abortions

MEDICATIONS

DRUG(S) OF CHOICE

- Altrenogest administered 0.044–0.088 mg/kg PO daily can be started later during gestation, continued longer, or used only for short periods of time, depending on serum P_4 levels during first 80 days of gestation, clinical circumstances, risk factors, clinician preference. Note that serum levels reflect only endogenous P_4, not exogenous, oral product
- If near term, altrenogest frequently is discontinued 7–14 days before foaling date, unless indicated otherwise by fetal maturity/viability, or actual gestational age is in question

PRECAUTIONS, POSSIBLE INTERACTIONS

- Altrenogest is only used to prevent abortion in cases of endotoxemia or placentitis (>270 days of gestation) if fetus is viable
- Altrenogest is absorbed through skin; wear gloves and wash hands

ALTERNATIVE DRUGS

- Injectable P_4 (150–500 mg oil base) IM
- Newer, repository forms of P_4 are occasionally introduced; however, some evidence of efficacy should be provided prior to use
- Medications for preexisting maternal disease

FOLLOW-UP

PATIENT MONITORING

- At 7–10 days post abortion monitor uterine involution
- Observe for any signs of systemic disease and laminitis
- Assess genital tract health— ± vaginal speculum, hysteroscopy, uterine culture and cytology, endometrial biopsy
- Base treatment on clinical results of these procedures
- Uterine culture <14 days postpartum or post abortion is affected by contamination at the time of parturition (abortion)

PREVENTION/AVOIDANCE

- Early recognition of at-risk mares
- Record double ovulations
- Early twin diagnosis (<25 days, as early as day 14 or 15)
- Selective embryonic/fetal reduction involving transrectal, transvaginal, or transabdominal US or, potentially, surgery and induced death of one fetus
- Manage preexisting endometritis before next breeding to minimize inflammation
- Careful observation of pregnant mares, monitor mammary gland development
- Remove mares from fescue pasture during last third of gestation (minimum 30 days)
- Domperidone (1.1 mg/kg PO daily) at earliest signs of equine fescue toxicosis or 10–14 days prior to due date; continue until parturition and development of normal mammary gland
- Injection with fluphenazine (25 mg IM in pony mares) on day 320 of gestation has been suggested for prophylaxis of fescue toxicosis

ABORTION, SPONTANEOUS, NONINFECTIOUS (CONTINUED)

• Careful use of medications in pregnant mares
• Avoid exposure to known toxicants

POSSIBLE COMPLICATIONS

• Dystocia, other potentially life-threatening conditions
• Future fertility and reproductive value can be impaired by dystocia, RFM, endometritis, laminitis, septicemia, trauma to genital tract
• Potential complications associated with twin reduction increase the later in gestation they are attempted

EXPECTED COURSE AND PROGNOSIS

• Most patients recover with appropriate treatment
• Complications can involve significant impact on mare's survivability and future fertility
• Guarded prognosis for pregnancy maintenance with severe endometritis and endometrial periglandular fibrosis

MISCELLANEOUS

SYNONYMS

• Abortion
• Spontaneous abortion
• Noninfectious abortion
• Twin abortion

SEE ALSO

• Abortion, spontaneous, infectious
• Dystocia
• Endometrial biopsy
• Endometritis
• Fetal stress/distress/viability
• High-risk pregnancy
• Placental insufficiency
• Placentitis
• Premature placental separation

ABBREVIATIONS

• CL = corpus luteum
• EMS = equine metabolic syndrome
• GI = gastrointestinal
• IR = insulin dysregulation
• P_4 = progesterone
• PPID = pituitary pars intermedia dysfunction
• RFM = retained fetal membranes/placenta
• SCNT = somatic cell nuclear transfer
• TRP = transrectal palpation
• US = ultrasonography, ultrasound

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Author Tim J. Evans
Consulting Editor Carla L. Carleton

ACER RUBRUM (RED MAPLE) TOXICOSIS

BASICS

OVERVIEW

• Results from the ingestion of wilted or dried *Acer rubrum* (red maple) leaves
• Most frequently reported in the eastern half of North America
• The specific toxin has not been identified. Pyrogallol and gallic acid, metabolites formed from intestinal bacterial metabolism of tannic acid found in wilted or dry leaves, have been suggested
• Clinical findings are consistent with oxidative injury to red blood cells, resulting in the formation of methemoglobin, Heinz bodies, and hemolytic anemia
• Affected organ systems include:
  ◦ Cardiovascular—tachycardia secondary to anemia
  ◦ Hemic—methemoglobinemia, hemolytic anemia, and Heinz bodies
  ◦ Renal—pigmenturia, hematuria, and proteinuria; renal failure secondary to hemoglobin deposition in the kidney
  ◦ Reproductive—abortion secondary to fetal hypoxia
  ◦ Respiratory—polypnea secondary to anemia

SIGNALMENT

No breed, gender, or age predilections.

SIGNS

• Acute death can result from rapid formation of methemoglobin. Alternatively, hemolytic crisis can develop over several days as the hemolysis and methemoglobinemia progressively worsen
• Lethargy, weakness, anorexia, and perhaps colic or fever. Yellow or brown mucous membranes, red or brown urine, tachycardia, polypnea, and dehydration

CAUSES AND RISK FACTORS

In summer and fall months after an event that results in leaf wilting such as tree pruning, fallen branches after a storm, or autumn leaves falling.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• All causes of hemolytic anemia
• Hemolytic anemia accompanied by Heinz bodies and/or methemoglobinemia indicates oxidant toxicosis. The most common causes in horses are onions, red maple, and phenothiazine anthelmintics, which can only be differentiated by a history of ingestion

CBC/BIOCHEMISTRY/URINALYSIS

• Interpretation may be difficult due to hemolysis
• Decreased packed cell volume, hemoglobin, and erythrocyte count confirm anemia, whereas increased mean corpuscular hemoglobin concentration and mean corpuscular hemoglobin support intravascular hemolysis with hemoglobinemia
• Heinz bodies are not present in all cases. They may be seen on routinely stained blood smears but are more apparent in new methylene blue-stained smears
• Serum bilirubin, especially unconjugated bilirubin, is increased because of hemolytic anemia and inappetence
• Urinalysis results include proteinuria and hemoglobinuria, with few or no intact erythrocytes
• Increased albumin and total protein result from dehydration
• Blood urea nitrogen and creatinine increase if a pigment nephropathy develops and causes acute renal failure
• Elevated liver enzymes and creatine phosphokinase may occur, probably secondary to cell damage caused by anemia-induced hypoxia
• Eccentrocytes and ghost cells have been reported

OTHER LABORATORY TESTS

The percentage of methemoglobin in the blood often is elevated.

PATHOLOGIC FINDINGS

• Gross findings include generalized icterus, enlarged spleen, and discolored kidneys. Petechiae and ecchymoses may be present
• Histopathologic findings include erythrophagocytosis by macrophages, renal pigment casts and sloughed epithelial cells, splenic and hepatic hemosiderin, and centrilobular hepatic lipidosis. Pulmonary thrombosis possible

TREATMENT

• Inpatient or outpatient according to severity
• IV fluids to maintain renal perfusion
• Blood transfusion with severe anemia
• Continuous nasal oxygen administration may be helpful

MEDICATIONS

DRUG(S) OF CHOICE

Ascorbic acid has been used for its antioxidant effects (30–50 mg/kg every 12 h added to IV fluids).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Do not treat methemoglobinemia with methylene blue because of its poor efficacy and it may increase Heinz body formation
• NSAIDs to control pain but can compromise renal function

FOLLOW-UP

PATIENT MONITORING

Monitor methemoglobinemia and anemia to adjust therapy.

PREVENTION/AVOIDANCE

Remove fallen branches immediately after storms or pruning.

EXPECTED COURSE AND PROGNOSIS

• Prognosis depends on the quantity of leaves ingested
• Death is attributed to severe methemoglobinemia, anemia, or to renal failure

MISCELLANEOUS

ASSOCIATED CONDITIONS

Laminitis can occur during or after the course of the disease.

PREGNANCY/FERTILITY/BREEDING

Anemia and methemoglobinemia can result in fetal hypoxia, followed by abortion.

ABBREVIATIONS

NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Author Scott L. Radke
Consulting Editors Wilson K. Rumbeiha and Steve Ensley
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A

ACIDOSIS, METABOLIC

BASICS

DEFINITION

• A disruption of acid–base homeostasis producing increased H^+ concentration, which is reflected by acidemia (decreased blood pH) and low plasma HCO_3^- concentration
• Normal plasma HCO_3^- concentration is ≅24 mEq/L
• Normal blood pH ranges from 7.35 to 7.45

PATHOPHYSIOLOGY

• H^+ is regulated by intracellular and extracellular buffering, respiratory buffering (i.e. variation of CO_2 levels via changes in ventilation), and regulation of HCO_3^- via renal excretion of H^+
• Renal H^+ excretion is accomplished by direct secretion of limited amounts of H^+, increased generation of ammonium ions, and titration to phosphates and urates (titratable acidity)
• Resorption of HCO_3^- occurs when H^+ is secreted, 90% in the proximal tubule and the remainder in the distal nephron
• Buffering of H^+ occurs rapidly and is accomplished by proteins, phosphates, and HCO_3^-
• The most important buffer is HCO_3^-
• Respiratory compensation responds within minutes
• Definitive regulation of H^+ and HCO_3^- concentrations is accomplished by the kidney
• Renal processing of acidosis begins within hours but may take days to normalize pH
• Inability to excrete H^+, loss of HCO_3^-, increased production of H^+, and accumulation of acids are the major mechanisms producing metabolic acidosis
• Hyperproteinemia (i.e. weak acids) and overhydration (i.e. dilutional acidosis) also produce metabolic acidosis via alteration of the balance between strong cations and anions

SYSTEMS AFFECTED

Respiratory

• Chemoreceptors sense low pH in blood or CSF and stimulate hyperventilation to increase elimination of CO_2 and increase pH
• Decreased respiratory muscle strength can lead to hypoventilation and worsening acidosis

Cardiovascular

• Hyperkalemia secondary to acidemia may cause arrhythmias and decreased cardiac contractility
• Vasodilation of arterioles; constriction of veins
• Vascular effects may be offset by catecholamine effects

Neuroendocrine

• CNS depression
• CSF acidosis in acute situations

Renal

The kidney responds to low arterial pH by increasing H^+ excretion and generating increased concentrations of HCO_3^- to bring the systemic pH back to normal.

Metabolic

• Decreased affinity for O_2—hemoglobin binding, enhancing release of O_2 to tissues
• Increased protein catabolism
• Increased ionized Ca^{2+} concentration

GENETICS

Fanconi syndrome may be heritable in Quarter Horses.

SIGNALMENT

Any breed, age, or sex.

SIGNS

• Dependent on the underlying cause
• Weakness, depression, and tachypnea are clinical signs of metabolic acidosis

CAUSES

• Loss of HCO_3^- from the GI tract (e.g. colitis)
• RTA results in HCO_3^- loss both directly and indirectly, depending on the type of tubular dysfunction
• Aminoaciduria, lactic aciduria, and glucosuria is suggestive of Fanconi syndrome
• Renal failure results in an inability to excrete H^+ and accumulation of uremic acids
• Lactic acidosis can result from anaerobic metabolism, which occurs secondary to decreased tissue perfusion. Hypovolemia from severe dehydration (e.g. diarrhea, sweating, decreased intake), fluid sequestration (e.g. ascites, pleural effusion, internal diarrhea), or hemorrhage leads to decreased tissue perfusion. SIRS produces acidosis via several mechanisms, including hypotension (decreased tissue perfusion), decreased cardiac contractility, tissue ischemia, fluid shifts, hypoxemia, and hepatic damage
• Chronic causes of hypoxemia produce lactic acidosis
• Grain overload produces metabolic acidosis via production of lactic acid, fluid sequestration in the GI tract, and secretion into the GI tract
• High-intensity anaerobic exercise and rhabdomyolysis results in production of lactate, which can result in transient metabolic acidosis
• Malignant hyperthermia is uncommon but has occurred in anesthetized horses and results in severe lactic acidosis
• Acute or endstage hepatic failure may result in metabolic acidosis due to failure of the liver to metabolize lactic acid
• Asphyxia at parturition may decrease perfusion, which can result in lactic acidosis
• Ingestion of exogenous acids (e.g. salicylates, ethylene or propylene glycol) is uncommon
• Proteins are weak acids; conditions producing significant hyperproteinemia (e.g. chronic infection, immune-mediated disease, plasma cell myeloma, lymphoma) produce metabolic acidosis
• Total parenteral nutrition can lead to metabolic acidosis when cationic (e.g. lysine, arginine) or sulfur-containing amino acids are metabolized as H^+ is formed

RISK FACTORS

• Patients with chronic renal failure or chronic hypoxemia (e.g. severe equine asthma) may be at greater risk for acidosis with progression of their primary problem
• Horses on acetazolamide for hyperkalemic periodic paralysis may develop acidosis more readily, as acetazolamide is a carbonic anhydrase inhibitor that causes increased HCO_3^- excretion
• Highly anionic diets can induce metabolic acidosis in equids

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Some causes of metabolic acidosis can be identified on physical examination (e.g. diarrhea, hypovolemia, colic with ischemic lesions)
• Decreased HCO_3^- concentrations are also seen in conditions with chronic respiratory alkalosis; PCO_2 is low if compensation is occurring, but pH will be normal or mildly increased

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

• Excessive anticoagulant may falsely decrease results via dilution
• Excessive Na^+ heparin (acidic) may falsely decrease HCO_3^- concentrations

Disorders That May Alter Laboratory Results

With poor peripheral perfusion, results of blood gas analysis on samples taken from peripheral vessels may not reflect the overall systemic condition. Appropriate reference ranges must be used (venous vs. arterial).

CBC/BIOCHEMISTRY/URINALYSIS

• Measurement of serum electrolytes and protein concentrations is important to determine the cause and to guide treatment
• Calculation of the AG may be useful, especially in mixed acid–base disorders
• Proportionate changes in Na^+ and Cl^- concentrations occur with alterations of fluid balance
• Normal Na^+ concentrations with hypochloremia or hyperchloremia indicate acid–base imbalance
• Albumin/protein concentrations are not considered when calculating the AG; however, because proteins are weak acids, hyperproteinemia (e.g. dehydration, chronic inflammation, neoplasia) can contribute to metabolic acidosis
• Urinalysis and fractional excretion of electrolytes, in combination with serum creatinine and blood urea nitrogen

concentrations, are useful in cases of renal dysfunction

Horses with Hyperchloremia and Normal AG

• Loss of HCO_3^-—diarrhea, type 2 RTA, and primary respiratory alkalosis; however, severely affected colitis patients often are acidotic and low in Na^+, K^+, Cl^-, and HCO_3^- because of water intake after isotonic fluid loss
• Salt poisoning
• Cl^- retention—renal failure, type 1 or 4 RTA, and acetazolamide therapy

Horses with Increased AG

Accumulation of unmeasured anions, such as:
• Lactate—hypovolemia, hypotension from SIRS, hypoxemia, third space fluid loss, anaerobic exercise, rhabdomyolysis, liver failure, malignant hyperthermia
• Phosphates, sulfates, and organic acids—renal failure, toxic ingestion

OTHER LABORATORY TESTS

Total CO_2

• Closely approximates HCO_3^- concentration because most CO_2 is carried in the blood as HCO_3^-
• Respiratory alkalosis also decreases TCO_2; differentiation can only be made with blood gas analysis
• Analyze rapidly with minimal room-air exposure as CO_2 will decrease

Blood Gas Analysis

• Needed to determine primary change in blood pH
• Decreased blood pH indicates acidemia. A concurrent decrease in HCO_3^- indicates primary metabolic acidemia. An accompanying decrease in PCO_2 indicates respiratory compensation
• Decreased HCO_3^- with increased blood pH indicates compensation for a respiratory alkalosis
• Determine if hypoxemia is contributing to lactic acidemia
• Blood gas parameters must be assessed against appropriate reference ranges for the sample taken
• Blood lactate—elevation indicates contribution to metabolic acidemia

IMAGING

Ultrasonography can be useful in evaluating colitis, ascites, and pleural effusion, as well as cardiac, renal, and hepatic architecture.

PATHOLOGIC FINDINGS

Dependent on the underlying cause.

TREATMENT

Directed at the primary cause.

MEDICATIONS

DRUG(S) OF CHOICE

• Isotonic fluid therapy is usually sufficient to correct lactic acidosis from hypovolemia in mild cases
• With severe hypovolemia, therapy may include hypertonic saline, colloids, or blood transfusion followed by crystalloid fluid administration
• Alkalinizing therapy is reserved for patients with a pH < 7.2 that persists following rehydration
• $NaHCO_3^-$ is most frequently utilized
• $NaHCO_3^-$ deficit (mEq) is calculated as follows—base deficit × body weight (kg) × 0.3 (extracellular fluid space (0.5 in foals))
• A negative BE, or 24 minus HCO_3^-, can be used for the base deficit
• In acute cases, half the deficit can be given over 30 min, in fluids, or as a 5% solution to adults
• Isotonic HCO_3^- (1.3%) is a good choice in neonates or severely affected adults
• Correction to a pH > 7.2 and BE ≥ −5 is usually adequate

PRECAUTIONS

• Use HCO_3^- therapy cautiously in patients with respiratory compromise, because the CO_2 that is generated may not be eliminated, causing a further decrease in pH
• Na^+ load may affect blood volume in neonates and patients with compromised renal, neurologic, or cardiac function
• Rebound alkalosis or cerebral acidosis is reported from overdose or rapid administration of HCO_3^- since both CO_2 and H_2CO_3 cross the blood–brain barrier

POSSIBLE INTERACTIONS

HCO_3^- cannot be mixed with Ca^{2+}.

ALTERNATIVE DRUGS

Oral rehydration solutions (4–8 L PO every 2 h in adults without ileus).

FOLLOW-UP

PATIENT MONITORING

Serial blood gas analysis to evaluate efficacy of therapy.

POSSIBLE COMPLICATIONS

• Hyperkalemia
• Cardiac arrhythmias, hypotension
• Severe, untreated metabolic acidosis with a pH < 7.0 may result in death

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Hyperchloremia
• Hyperkalemia
• Respiratory alkalosis

AGE-RELATED FACTORS

• Asphyxia during parturition in neonates
• Conditions associated with premature neonates

PREGNANCY/FERTILITY/BREEDING

Metabolic acidosis may decrease uterine blood flow and result in placental insufficiency.

SEE ALSO

• Chloride, hyperchloremia
• *Clostridium difficile* infection
• Diarrhea, neonate
• Hypoxemia
• Idiopathic colitis
• Potassium, hyperkalemia
• Potomac horse fever (PHF)
• Septicemia, neonate

ABBREVIATIONS

• AG = anion gap
• BE = base excess
• CNS = central nervous system
• CSF = cerebrospinal fluid
• GI = gastrointestinal
• PCO_2 = partial pressure of carbon dioxide
• RTA = renal tubular acidosis
• SIRS = systemic inflammatory response syndrome
• TCO_2 = total carbon dioxide

Suggested Reading

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Author Sara L. Connolly
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A

ACIDOSIS, RESPIRATORY

BASICS

DEFINITION
• Increase in blood PCO_2
• Homeostatic mechanisms maintain normal blood concentrations within a narrow range
• Arterial concentrations in the range 35–42 mmHg
• Venous concentrations in the range 43–49 mmHg

PATHOPHYSIOLOGY
• CO_2 is formed in all tissues during metabolic energy production and diffuses passively out of cells and into the blood in gaseous form
• Most of this CO_2 (65–70%) combines with water almost instantaneously to form carbonic acid, which then dissociates into HCO_3^- and H +
• Most CO_2 is transported in the blood as HCO_3^-. Some is bound to proteins, especially deoxygenated hemoglobin, and a small amount is dissolved directly into plasma
• In the lungs, the reverse occurs, and CO_2 passively diffuses out of capillaries into the alveoli
• These 3 forms of CO_2 exist in equilibrium in the blood, but PCO_2 as measured by blood gases depends on the dissolved portion
• The chemical components of the carbonic acid equilibrium are:

$$CO_2 + H_2O = H_2CO_3 = H^+ + HCO_3^-$$

• Alveolar CO_2 then is removed mechanically by ventilation as air moves in and out of the lungs
• Hypercapnia is present only when tissue production exceeds the capacity of normal lungs to eliminate CO_2 or when components of the respiratory system are abnormal
• Respiratory acidosis results from disease or alteration of the respiratory center in the brain, peripheral chemoreceptors that control respiration, mechanical components of respiration (chest wall, respiratory muscles), or the respiratory tract (airways, alveoli, pulmonary vasculature, lung parenchyma). This can result in hypoventilation, diffusion impairment, or V/Q mismatching
• Because CO_2 diffuses across alveolar membranes in direct proportion to ventilation, hypoventilation leads to increased blood CO_2 concentration
• Diffusion impairment (e.g. pneumonia) rarely results in hypercapnia given that CO_2 diffuses very readily across alveolar membranes
• Increased blood CO_2 concentration develops as a compensatory response of the lungs to metabolic alkalosis

SYSTEMS AFFECTED
Respiratory

GENETICS
N/A

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
• Any breed, age or sex
• Neonatal foals with perinatal asphyxia
• Anesthetized patients develop some degree of hypercapnia when breathing spontaneously
• Because of their size, equids are predisposed to hypoventilation under anesthesia

SIGNS
Historical Findings
• Neonatal foals born from a dam with dystocia
• Respiratory noise may be heard, especially with exercise, in cases of upper airway obstruction

Physical Examination Findings
• None if minute ventilation is increased via increased tidal volume; if not, tachypnea may be present
• Decreased respiratory rate or an apneustic breathing pattern may be present in neonatal foals with perinatal asphyxia
• Decrease or absence of airway sounds may be found at auscultation in cases with damage or disease of the chest wall or thorax
• Abnormal sounds may be present with pulmonary disease

CAUSES
• Upper airway obstruction leading to hypoventilation. Specific causes—nasal edema, cyst, mass, or infection of the paranasal sinuses, laryngeal or pharyngeal paralysis or inflammation, soft palate displacement, pharyngeal or epiglottal cysts, and tracheal masses or collapse
• Hypoxia to the respiratory center of the brainstem in foals with perinatal asphyxia can cause hypoventilation
• Injury or disease of the thorax, diaphragm, or pleura may restrict movement of the chest wall or respiratory muscles. Tension pneumothorax may rapidly lead to death
• Large volumes of pleural or peritoneal fluid, as well as severe GI distention, may restrict diaphragmatic movement, leading to hypoventilation
• Paresis or paralysis of the respiratory muscles can be seen with neurologic diseases such as botulism, tetanus, encephalitis, or head trauma
• Respiratory muscle damage caused by box elder seeds (i.e. seasonal pasture myopathy)
• Severe pneumonia, pulmonary edema, or acute respiratory distress syndrome can cause diffusion impairment
• Premature foals with significant atelectasis (diffusion impairment) and weak thoracic muscles (hypoventilation)
• Hypoventilation caused by muscle relaxation and decreased sensitivity of the respiratory center to CO_2 occurs in all anesthetized horses. Heavy sedation also may produce temporary hypercapnia via muscle relaxation and respiratory center insensitivity
• Pregnant animals are more prone to hypoventilation under general anesthesia because of abdominal distention from the pregnant uterus
• Defective cellular metabolism of muscle is seen with malignant hyperthermia. This syndrome is very rare but has been seen in horses with inhalant anesthesia or succinyl choline administration. Abnormal metabolic processes in muscle cells are triggered, resulting in tremendous production of heat and CO_2, such that elimination mechanisms are overwhelmed and respiratory acidosis results
• Anaerobic exercise produces temporary respiratory acidosis because ventilation is limited when chest wall movement is linked to stride at high speeds

RISK FACTORS
• General anesthesia, heavy sedation
• Pregnancy
• Prolonged recumbency
• History of malignant hyperthermia in related individuals
• Prematurity, dystocia, asphyxia or sepsis, persistent fetal circulation, or pulmonary hypertension in neonates

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Physiologic states or disease processes that present with tachypnea (e.g. fever, hyperthermia, excitement, anxiety, painful conditions, hypoxemia, metabolic acidosis, and CNS derangements)
• Under anesthesia, tachypnea also may result from a light plane of anesthesia, hypoxemia, metabolic acidosis, or faulty anesthetic rebreathing systems
• Compensatory hypercapnia secondary to metabolic alkalosis caused by upper GI obstruction, early large colon impaction or simple obstruction, or supplementation with HCO_3^- or other alkalinizing agent. pH in these cases is often still higher than normal because compensatory hypoventilation is limited once hypoxemia develops

LABORATORY FINDINGS
Drugs That May Alter Laboratory Results
N/A

Disorders That May Alter Laboratory Results
• With poor peripheral perfusion, results of blood gas analysis on samples taken from peripheral vessels may not reflect the overall

systemic condition. Appropriate reference ranges must be used (venous vs. arterial)
• Prolonged exposure to room air may alter PCO_2 concentrations, because the sample equilibrates with the air
• Cellular metabolism of red blood cells continues after sampling; if not measured quickly, PCO_2 concentrations may be falsely elevated

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
• Arterial blood gas analysis is necessary to evaluate adequacy of ventilation and gas exchange and to document hypercapnia
• Handheld analyzers are available and easy to use, and some require only small amounts of whole blood. Otherwise, pre-heparinized syringes are preferred or use syringes heparinized before sampling
• Perform sampling anaerobically. Immediately evacuate any air bubbles, and cap the needle with a rubber stopper
• Perform analysis within 15–20 min. If not possible, samples can be stored on ice, and results may be valid for 3–4 h when glass syringes or dedicated arterial blood gas syringes are used

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
• Capnography or capnometry to measure CO_2 indirectly from expired gases
• Samples of end-tidal gases reflect arterial PCO_2 concentrations, because this gas is essentially alveolar gas
• Continuous monitoring of anesthetized or ventilated patients
• V/Q mismatch is always present in anesthetized or recumbent patients, and end-tidal CO_2 concentrations may underestimate arterial concentrations by ≅10–15 mmHg

TREATMENT
• Emergency therapy occasionally may be necessary for upper airway obstructions (e.g. passage of a nasotracheal tube or tracheotomy). Stridor is usually present in affected horses
• Definitive therapy for hypercapnia involves resolution of the primary disease process affecting ventilation, diffusion, or gas exchange
• Avoid excessive anesthetic depth. If depth is adequate, controlled ventilation is necessary when hypoventilation persists and $PaCO_2$ is > 60 mmHg
• In neonates, postural therapy and coupage may improve gas exchange
• With botulism or severe lung disease, treat hypercapnia with controlled ventilation

MEDICATIONS
DRUG(S) OF CHOICE
Caffeine
Respiratory stimulant (10 mg/kg PO loading dose followed by 2.5 mg/kg PO every 12 h) for foals with perinatal asphyxia that do not have ileus.

Doxapram
• Respiratory stimulant (0.2–0.5 mg/kg IV or an infusion of 0.01–0.05 mg/kg/min) in foals with perinatal asphyxia or muscular weakness
• Anesthetized patients who are breathing poorly may respond temporarily to its effects, but controlled ventilation, decreasing depth, and anesthetic reversal are more specific and appropriate therapies
• Not indicated for healthy patients being weaned from controlled ventilation

CONTRAINDICATIONS
• Controlled ventilation may cause barotrauma in foals with meconium aspiration
• Partial obstruction of the small airways may lead to air trapping in alveoli, which may rupture

PRECAUTIONS
• Monitor ventilated patients continuously for airway obstruction caused by accumulation of secretions, kinking of tubing, hoses, etc.
• Oxygen toxicity can develop with inspired PO_2 > 50% or if PaO_2 > 100 mmHg is maintained for prolonged periods (10–12 h).

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP
PATIENT MONITORING
Use serial arterial blood gas analyses or capnometry to assess adequacy of ventilation and monitor progress, especially during weaning from ventilation.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
• Respiratory acidosis lowers systemic pH and may affect ionization of protein-bound drugs
• Acidosis decreases heart contractility and may cause or contribute to CNS depression
• Hypercapnia and resultant acidosis predispose patients to cardiac arrhythmias, especially under general anesthesia
• The $PaCO_2$ concentration greatly affects cerebral blood flow and cerebrospinal fluid pressure
• Severe or prolonged hypercapnia may contribute to brain damage or herniation in cases of head trauma

EXPECTED COURSE AND PROGNOSIS
Dependent on the underlying cause.

MISCELLANEOUS
ASSOCIATED CONDITIONS
Disorders that result in metabolic alkalosis.

AGE-RELATED FACTORS
Neonates with perinatal asphyxia or prematurity.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
See Risk Factors.

SYNONYMS
• Hypercapnia
• Hypercarbia

SEE ALSO
• Botulism
• Neonatal maladjustment syndrome

ABBREVIATIONS
• CNS = central nervous system
• GI = gastrointestinal
• $PaCO_2$ = partial pressure of carbon dioxide in arterial blood
• PaO_2 = partial pressure of oxygen in arterial blood
• PCO_2 = partial pressure of carbon dioxide
• PO_2 = partial pressure of oxygen
• V/Q = ventilation/perfusion

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Author Sara L. Connolly
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A

ACTINOBACILLOSIS

BASICS

OVERVIEW

• Acute rapidly progressive septicemia due to *Actinobacillus equuli* or *Actinobacillus suis*-like organisms in neonatal foals. Also known as "sleepy foal disease"
• *A. equuli*—Gram-negative coccobacillary to rod-shaped pleomorphic organism
• Normal inhabitant of the mucous membranes of the alimentary tract
• Fetal infection may follow transplacental infection
• Kidneys are a frequent site of neonatal infection
• Can have characteristic lesions including embolic nephritis, embolic pneumonia, lymphoid necrosis, multifocal hepatic necrosis, and septic arthritis. Subsp. *haemolyticus* appears to prefer the respiratory tract
• Adult infection frequently endogenous. Fecal contamination or spread from oral mucous membranes. Soft tissue abscesses, respiratory infections, and rarely conjunctival, urinary tract, joint, guttural pouch, skin, and genital tract infections

SIGNALMENT

• Foals < 2 days of age
• Adults—any age

SIGNS

Foals

• Acute onset, depression, diarrhea, recumbency, distended painful joints, sudden death
• Fever may not be present, hypothermia. May progress rapidly to septic shock
• Bone and joint infections may not be obvious for days to weeks and may be unaccompanied by signs of systemic disease

Adults

• Depends on affected organ system. Systemic actinobacillosis—rare and associated with underlying disease or another predisposing factor
• Primary peritonitis

CAUSES AND RISK FACTORS

Foals

• Commonly associated with failure of transfer of passive immunity
• Perinatal stress, prematurity, and/or unsanitary environmental conditions
• Portals of entry include respiratory tract, gastrointestinal tract, placenta, and umbilical remnant

Adults

• Pneumonia and pleuropneumonia secondary to viral infection or stressful events
• Trauma predisposes to abscess formation

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Foals

• Other causes of bacterial, viral, and fungal neonatal sepsis
• Equine herpesvirus type 1, equine viral arteritis
• Perinatal hypoxic–ischemic anoxic or inflammatory insults

Adults

• Other causes of fever or peritonitis
• Other bacterial, viral, or fungal pneumonia or pleuropneumonia
• Other causes of respiratory distress, fever, coughing, and nasal discharge—sinusitis, guttural pouch empyema, heaves (recurrent airway obstruction), inflammatory airway disease, interstitial pneumonia, mycoplasma infections, neoplasia, dysphagia

CBC/BIOCHEMISTRY/URINALYSIS

Foals

• Leukocytosis or leukopenia
• Hyperfibrinogenemia at birth possible with in utero infections. Increases in fibrinogen and SAA common
• Increased creatinine and/or blood urea nitrogen with renal involvement
• Metabolic acidosis, hypoxemia, and hypercapnia may be observed in foals in septic shock
• Hypoglycemia may be present
• Frequent complete or partial failure of passive transfer (serum IgG <800 mg/dL)
• Urinalysis may be abnormal with renal involvement

Adults

• Leukocytosis and hyperfibrinogenemia possible
• Anemia of chronic disease in longstanding infection
• Other abnormalities depend on body system involved

IMAGING

Foals

• Radiographs—thorax, joints
• Ultrasonography—umbilicus, kidneys
• Computed tomography—pulmonary disease in neonatal foals

Adults

Radiographic and ultrasonographic evaluation of affected body system.

OTHER DIAGNOSTIC PROCEDURES

Foals

• Blood culture
• Synovial bacterial culture
• Kidneys—multifocal microabscesses at postmortem examination

Adults

• Culture/cytology of affected body system
• Normal inhabitant of equine gastrointestinal mucosa so results should be interpreted cautiously

TREATMENT

Foals

• Hospitalization
• Intranasal oxygen supplementation
• Early antimicrobial therapy

MEDICATIONS

DRUG(S) OF CHOICE

Foals

• Isotonic polyionic balanced fluids
• IV plasma based on IgG concentrations
• IV dextrose or parenteral nutrition
• Broad-spectrum antimicrobial therapy, gentamicin 12 mg/kg IV SID or amikacin 25–30 mg/kg IV SID and potassium penicillin 20 000 IU/kg IV QID or ceftiofur sodium 5–10 mg/kg IV BID–QID. Monitor plasma creatinine concentration. Therapeutic drug monitoring desirable
• Systemic inflammatory response syndrome or multiorgan dysfunction syndrome—intensive fluid management and inopressor therapy
• Severe respiratory disturbance—assisted ventilation
• Regional limb perfusion and/or direct instillation with antimicrobials for septic joints

Adults

Antimicrobial therapy based on culture/sensitivity.

MISCELLANEOUS

• Continue treatment until clinical signs have resolved and white blood count, differential, and fibrinogen/SAA concentration are within normal limits for 48 h
• Commonly isolated from foals lost to mare reproductive loss syndrome and adult horses affected by pericarditis during the same time period

ABBREVIATIONS

• IgG = immunoglobulin G
• SAA = serum amyloid A

Suggested Reading

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Author Pamela A. Wilkins
Consulting Editor Ashley G. Boyle

ACUTE ADULT ABDOMINAL PAIN—ACUTE COLIC

BASICS

DEFINITION

Signs are associated with discomfort originating within the abdominal cavity. May develop acutely or gradually. Considered chronic when persisting for more than 3–4 days.

PATHOPHYSIOLOGY

• Most acute abdominal pain originates from the GI tract but may also arise from other systems
• In the intestinal tract, pain may originate from increased intramural tension, tension on a mesentery, ischemia, inflammation, smooth muscle spasms, or a combination of any of these
• Causes can be divided into strangulating and nonstrangulating lesions.
Nonstrangulating lesions include intraluminal lesions, extraluminal lesions, mural lesions, as well as spasmodic colic, intestinal displacement, ileus, and inflammatory bowel disease. Strangulating lesions, such as torsions and incarcerations, are usually associated with a compromise of local blood supply followed by intestinal necrosis. The necrosis may lead to cardiovascular shock

SYSTEMS AFFECTED

• Cardiovascular—dehydration and endotoxemia may lead to shock and result in organ failure
• GI—the large colon and the distal part of the small intestine are commonly involved
• Other systems can be involved (e.g. urinary system, reproductive tract, hepatobiliary, peritoneum and pleura)

SIGNALMENT

Nonspecific. There may be an age, breed, or sex predisposition for a specific problem.

SIGNS

General Comments

May be subtle and easily missed initially. As the disease progresses, changes in clinical parameters, rectal examination findings, transabdominal ultrasound findings, and laboratory data allow a more accurate localization.

Historical Findings

• Abdominal pain can appear acutely or following an episode of anorexia, depression, and/or decreased fecal output. Recent history of change in the exercise, diet, or availability of drinking water may also be present
• Mild abdominal pain—decrease in appetite and/or fecal output, mild depression, yawning, extended neck and rolling of the upper lip, teeth grinding, muscle fasciculation
• Moderate abdominal pain—frequent lying down, pawing, flank watching, groaning, posture for urinating with small quantities of urine passed, kicking the abdomen, attempts to roll
• Severe abdominal pain—walking in a tight circle, constantly getting up and down, rolling, traumatizing self and handlers, sweating, labored breathing

Physical Examination Findings

Depending on the stage of the disease signs may vary in severity:
• General findings—abdominal distention, sweating, increased respiratory rate, changes in body temperature, abnormal quality and quantity of feces
• Cardiovascular findings—tacky mucous membranes, increased capillary refill time, increased heart rate, dehydration, cold extremities. In endotoxemic shock, the cause of pain is likely due to a strangulating lesion or to a severe inflammatory process (colitis, peritonitis)
• GI findings—increase, decrease, or absence in gut motility, gas-filled resonant viscus on percussion, presence of net gastric reflux on passage of the nasogastric tube. Possible gastric reflux in stomach and small intestinal lesions. Abnormalities on rectal examination—gaseous distention of viscus by gas, liquid, or food; displacement of viscus; thickening of the intestinal wall; presence of tight bands, uterine or renal abnormalities

CAUSES

GI

• Nonstrangulated obstructive lesions:
  ◦ Gastric—ulcers, distention, impaction, rupture, tumor. Small intestine—enterocolitis, ascarid impaction, ileal impaction, ileal hypertrophy, stricture, adhesions. Large colon—ulceration, colitis, impaction, gas distention, mild displacement, left dorsal and right displacement, enterolith, sand impactions. Cecum—impaction, gas distention. Small colon—impaction, enterolith
• Strangulating obstructive lesions:
  ◦ Small intestine—incarceration into a space/rent in the mesentery/inguinal ring/gastrosplenic ligament/epiploic foramen, strangulation by lipoma, volvulus. Large colon—volvulus, incarceration, thromboembolic infarction. Cecum—intussusception, thromboembolic infarction, torsion. Small colon—strangulating lipoma, submucosal hematoma, thromboembolic infarction

Others

• Reproductive—uterine torsion, laceration, abortion, parturition, testicular torsion, hematoma in the broad ligament, trauma
• Renal/urologic—renal/ureteral/bladder/urethral calculi, cystitis, renal inflammatory processes
• Hepatobiliary—hepatitis, hepatobiliary calculi

RISK FACTORS

• No access to water
• Sudden change in diet
• Poor enteric parasite control
• Pregnancy
• Previous abdominal surgery
• Congenital abnormalities
• Certain medication

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of pain that might mimic pain originating from the abdominal cavity include myositis, pleuropneumonia, hemorrhagic shock, rabies, and musculoskeletal injuries.

CBC/BIOCHEMISTRY/URINALYSIS

• Increase in packed cell volume and total protein with dehydration
• Possible hypoproteinemia secondary to GI protein loss
• Leukopenia in acute inflammation and endotoxemia or leukocytosis in chronic inflammation
• Metabolic acidosis and production of lactic acid in cardiovascular shock. Metabolic alkalosis and loss of chloride when large amount of gastric reflux is present. Increased lactate concentration in presence of endotoxemia, tissue hypoxia, liver disease
• Hypokalemia and hypocalcemia, especially if anorexia is present and in lactating mare
• Hypochloremia and hyponatremia (colitis)
• Alkaline phosphatase may be increased
• Azotemia in severe dehydration or acute renal failure

OTHER LABORATORY TESTS

Abdominal Paracentesis

• Normal fluid has a pale, clear yellow color
• Increase of the protein level and WBCs is indicative of primary peritonitis or secondary to morphologic change of the viscera
• Foul-smelling reddish-brown fluid with an increase in the RBCs, WBCs, and protein is indicative of necrotic bowel. Presence of plant materials suggests intestinal rupture
• Lactate concentration > 1 mmol/L may indicate intestinal ischemia

Urinalysis

A change in specific gravity, increase in leukocyte content, RBCs, and pH may be noticed in cases with renal disease.

IMAGING

Radiographs

May be useful in sand impactions or enteroliths in adults. In foals for localization of gas, fluid distention, impaction, or congenital abnormality (atresia coli).

ACUTE ADULT ABDOMINAL PAIN—ACUTE COLIC (CONTINUED)

Ultrasonography

• Evaluation of—amount and characteristics of abdominal fluid; motility, wall thickness, and diameter of small intestine and its location; motility and wall thickness of the large intestine; nephrosplenic space for presence of intestine; intussusceptions, abscesses, or mass
• Also useful in evaluating the stomach, kidneys, liver, spleen, uterus, etc.

Endoscopy

Gastroscopy—evaluation of the stomach for ulcers, impaction or tumor.
Cystoscopy—evaluation of the urethra, bladder, and opening of the ureters for inflammation or calculi.

OTHER DIAGNOSTIC PROCEDURES

Exploratory laparotomy/laparoscopy.

TREATMENT

• Horses should be taken off feed until diagnosis/resolution of the underlying problem
• The history, physical examination, and laboratory results will help differentiate between medical or surgical condition
• Reasons for exploratory laparotomy—moderate to severe abdominal pain, unresponsiveness to medical treatment, progressive increase in heart rate or heart rates above 60–70/min, cardiovascular compromise or deterioration, presence of moderate to severe gas distention or displacement of the large colon, gas distention of small intestine, gastric reflux, abnormal paracentesis findings
• Supportive treatment for medical and surgical cases includes pain management, IV fluids, gastric decompression if necessary, electrolyte replenishment, and control of the abdominal pain

MEDICATIONS

DRUG(S) OF CHOICE

• Analgesics—control the abdominal pain
  ◦ NSAIDs initially—flunixin meglumine (0.5–1.1 mg/kg IV, IM every 8 h), α_2-blockers such as xylazine (0.25–0.5 mg/kg IV or IM), detomidine (5–10 µg/kg IV or IM), or romifidine (0.02–0.05 mg/kg IV or IM)
  ◦ Narcotic analgesic butorphanol (0.02–0.075 mg/kg IV) in conjunction with the α_2-blockers
• Spasmolytics (indicated in spasmodic colic)—*N*-butylscopolammonium bromide (0.3 mg/kg)
• Laxatives—mainly used for impactions:
  ◦ Mineral oil—10 mL/kg via nasogastric tube
  ◦ Osmotic laxative—disodium (0.5 g/kg) or magnesium sulfate (0.5–1 g/kg) in 4 L of warm water via nasogastric tube ideally followed by oral or IV fluid therapy. Dioctyl sodium sulfosuccinate (10–30 mg/kg of a 10% solution). Water, via an indwelling nasogastric tube, if there is no gastric reflux
• Parenteral fluid treatments—in cases of dehydration or moderate to severe impaction problems, IV fluid (100–150 mL/kg/day). If cardiovascular shock is present, hypertonic saline (2 L of 7% NaCl in an adult horse) prior to balanced electrolyte solutions may be given. Correction of electrolyte imbalances, especially hypokalemia and hypocalcemia, which are important for intestinal motility. Moderate to severe sodium bicarbonate deficit may be corrected as well as low plasma protein level (< 40 g/L)
• Treatment of endotoxemia—flunixin meglumine 0.25 mg/kg every 6 h
• Intestinal motility stimulants (see chapter Ileus)
• Antimicrobial therapy if peritonitis is suspected or surgery is performed

CONTRAINDICATIONS

Acepromazine is contraindicated due to its peripheral vasodilatory effect.

PRECAUTIONS

Repeat use of α_2-blockers and butorphanol causes prolonged ileus. Repeat dose of NSAIDs, especially in presence of dehydration, can result in gastric or large colon ulceration as well as renal damage.

FOLLOW-UP

PATIENT MONITORING

Monitor closely for deterioration of clinical signs and cardiovascular status until resolution of the abdominal pain. Following resolution of these signs, reintroduction to feed should be done gradually.

POSSIBLE COMPLICATIONS

• Endotoxemia
• Laminitis
• Circulatory shock
• Adhesions
• GI rupture
• Peritonitis

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Older horses are more predisposed to strangulated lipoma and epiploic foramen entrapment; younger horses are more predisposed to ulcer problems, intussusception, and ascarid impactions.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Mares in late gestation or in the postpartum period are predisposed to large colon torsion. Parturition can present clinical signs similar to a GI accident.

SYNONYMS

Colic

ABBREVIATIONS

• GI = gastrointestinal
• NSAID = nonsteroidal anti-inflammatory drug
• RBC = red blood cell
• WBC = white blood cell

Suggested Reading

Hackett ES. Specific causes of colic. In: Southwood LL, ed. Practical Guide to Equine Colic. Ames, IA: Wiley Blackwell, 2013:204–230.
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Author Nathalie Coté
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa

ACUTE EPIGLOTTIDITIS

BASICS

OVERVIEW
Epiglottiditis is a nonspecific inflammatory disease of the epiglottis.

SIGNALMENT
• Primarily racehorses (2–10 years) in active race training
• Occasionally seen in older horses (15–30 years) with inflammatory disease or neoplasia
• No known breed or sex predilection
• May be associated with epiglottic abscess or epiglottic chondritis

SIGNS
• Chief complaints—abnormal respiratory tract noise and exercise intolerance
• Coughing (eating) is fairly common
• Some horses act mildly pained when swallowing

CAUSES AND RISK FACTORS
• Cause—suspect viral or subepiglottic trauma or surgical trauma
• Repeated, strenuous exercise may induce inflammatory changes on the subepiglottic mucosal surface
• Inhaled particulate activities, bacterial or viral infections
• May be secondary to surgical trauma

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• The diagnosis is established based on endoscopy of the upper respiratory tract
• Occasionally, the endoscopic appearance of a swollen epiglottis is misinterpreted as epiglottic entrapment by the aryepiglottic folds
• May be associated with epiglottic abscess or chondritis

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
Imaging is not usually performed.

OTHER DIAGNOSTIC PROCEDURES
• During endoscopy, the epiglottis may appear swollen and discolored (reddish-purplish), primarily along the lateral margins and ventral (lingual) mucosal surfaces. Epiglottis may appear more rounded and bulbous. The ventral mucosal surfaces often are ulcerated, and in more chronic cases granulation tissue surrounded by fibrous connective tissue is seen
• If ulceration is seen at the rostral tip or dorsal surface of the epiglottic cartilage one should suspect associated epiglottic chondritis and abscessation
• Horses with epiglottiditis often intermittently or persistently displace the soft palate dorsally
• The caudal free margin of the soft palate may have a variable amount of inflammation, ulceration, or thickening

TREATMENT

• Outpatient (stall-side) basis
• Discontinue exercise for a minimum of 7–21 days, depending on the extent of the problem
• If swallowing is difficult or stimulates coughing, hay may need to be eliminated completely or partially from the diet

MEDICATIONS

DRUG(S) OF CHOICE
• Horses are initially treated with phenylbutazone (4.4 mg/kg IV) or flunixin meglumine (1.1 mg/kg IV) and dexamethasone (0.044 mg/kg IV). Spray 20 mL of a pharyngeal spray (140 mL of DMSO, 140 mL of glycerin, 266 mL of distilled water, and 14 mL of dexamethasone 4 mg/mL and often an antibiotic such as nitrofurazone) into the pharynx twice daily for 7–14 days through a 10 F catheter introduced via the nasal passages
• Antimicrobial therapy may be indicated if infection is suspected—procaine penicillin G (IM), trimethoprim–sulfamethoxazole (PO), ceftiofur (IM, IV) at usual recommended dosages for 5–7 days

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
No contraindications.

FOLLOW-UP

PATIENT MONITORING
Substantial improvement of the epiglottis and adjacent tissue and in pharyngeal function usually is seen at follow-up endoscopy after about 1 week of therapy. Continue rest and therapy until healing is judged complete (repeated endoscopy performed at 1 week intervals).

PREVENTION/AVOIDANCE
Horses with more chronic-appearing inflammation or with associated epiglottic abscess and/or chondritis may require more protracted therapy (2–4 weeks), and complete resolution of thickening and cartilage deformity may not occur. Occasionally, epiglottic entrapment may develop.

POSSIBLE COMPLICATIONS
Healing may result in fibrosis or cicatrix on the lingual epiglottic surface sufficient to interfere with normal soft palate function. Endoscopy may reveal intermittent or persistent dorsal displacement of the soft palate, which may need surgical treatment.

EXPECTED COURSE AND PROGNOSIS
Epiglottiditis is a serious, potentially career-limiting or -ending problem in racehorses. Prognosis depends primarily on severity of the condition during the initial examination and the degree of involvement and resulting deformity of the epiglottic cartilage. Resolution of acute inflammation results in complete return to normal exercise tolerance.

MISCELLANEOUS

SEE ALSO
• Dorsal displacement of the soft palate (DDSP)
• Inspiratory dyspnea

ABBREVIATIONS
DMSO = dimethylsulfoxide

Suggested Reading

Hawkins JF, Tulleners EP. Epiglottitis in horses: 20 cases (1988–1993). J Am Vet Med Assoc 1994;205:1577–1580.
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Ortved KF, Cheetham J, Mitchell LM, Ducharme NG. Successful treatment of persistent dorsal displacement of the soft palate and evaluation of laryngohyoid position in 15 racehorses. Equine Vet J 2010;42:23–29.

Author Norm G. Ducharme
Consulting Editors Daniel Jean and Mathilde Leclère

A

ACUTE HEPATITIS IN ADULT HORSES (THEILER DISEASE)

BASICS

OVERVIEW

The clinical disease (acute hepatitis, Theiler disease, serum hepatitis) is characterized by fulminant hepatic failure and encephalopathy in adult horses. There appear to be 3 separate epidemiologic diseases with identical clinical, clinicopathologic, and pathologic findings:

- Acute, often fulminant hepatitis in horses that have received equine-origin blood products approximately 4–10 weeks earlier and less severe to subclinical disease in other horses receiving the same product
- Acute, sometimes fulminant hepatitis occurring in a horse that was in contact with a blood product-inoculated Theiler disease horse, but that did not itself receive the equine-origin blood product
- Acute, fulminant hepatitis in horses (often broodmares on pasture in the fall) with no known equine-origin blood product administration. This last syndrome can occur as farm outbreaks

SIGNALMENT

Adult horses, particularly those with a history of receiving equine-origin serum (especially tetanus antitoxin) or plasma approximately 4–10 weeks earlier. May also be horses without recent history of equine blood product administration (nonbiologic origin acute hepatitis).

SIGNS

- Usually sudden in onset and rapidly progressive, with death occurring 2–6 days later in some cases
- Horses are often icteric and pass dark urine owing to the presence of bilirubin
- Many have signs of hepatic encephalopathy including acute blindness and aimless wandering around the stall or paddock
- Frequent yawning has been reported. Other neurologic signs may range from mild to severe depression or coma to maniacal behavior or seizures
- Hemolysis and hemoglobinuria may be present, are poor prognostic indicators, and are thought to be the result of damage to the red blood cells passing through the damaged sinusoids, oxidative damage resulting from liver failure, or release of large amounts of copper or iron from the diseased liver
- Some horses may have signs of photosensitivity and abdominal pain

CAUSES AND RISK FACTORS

- Most commonly associated with administration of an equine-origin blood product 4–10 weeks before the onset of signs. Some epidemiologic evidence suggests that some cases may result from an infectious agent
- Currently, there are at least 4 viruses that can establish chronic/persistent infection in horses and are being studied for their possible association with liver disease. NPHV (also called equine hepacivirus [EHCV]), TDAV, and EPgV are from the family Flaviviridae, genus *Hepacivirus*, which also includes the human hepatitis C virus. The fourth virus, EqPV-H, is in the family Parvoviridae, genus unclassified

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute onset of icterus in adult horses has multiple causes—prehepatic, hepatic, or posthepatic; serum biochemistries and CBC assist in differentiating these causes:
  - Prehepatic—red maple or wild onion toxicity, equine infectious anemia, immune-mediated hemolytic anemia poisoning
  - Hepatic—anorexia, Theiler disease, *Clostridium novyi,* bacterial cholangiohepatitis, hepatotoxicity
  - Posthepatic—cholelithiasis and other causes of biliary obstruction
- Signs of HE can be very similar to those of several acute neurologic diseases—rabies, Eastern equine encephalomyelitis, Western equine encephalitis, and acute protozoal myeloencephalitis. Icterus and serum biochemical changes help in differentiating these problems
- Hematuria, hemoglobinuria, myoglobinuria, and bilirubinuria may cause pigmenturia; urinalysis and serum biochemistries aid in differentiation. Urine from horses with hepatic failure will have green-colored bubbles (bilirubinuria) when shaken and this can serve as a useful point-of-care test to differentiate liver failure and HE from other causes of encephalopathy including encephalitides

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—usually normal, a small number of horses may have thrombocytopenia likely associated with disseminated intravascular coagulation
- Biochemistry—typical of acute, severe liver disease predominantly affecting hepatocellular function
- Marked increase in aspartate aminotransferase (often nearly 2000 IU/L; >4000 IU/L seems to be associated with a poor prognosis)
- Marked elevations in SDH and GLDH
- Moderate increases in biliary-derived enzymes (GGT usually increased to 100–300 IU/L). GGT continues to increase during initial recovery due to bile duct hyperplasia and this should not be interpreted as a poor prognostic indicator. GGT may remain elevated, although progressively decreasing values, for ≥2 weeks after clinical recovery
- Both conjugated and unconjugated bilirubin are increased with conjugating often constituting less than 20% of total bilirubin
- Increased anion gap
- Mild hyperglycemia, rarely hypoglycemia
- Urinalysis—bilirubinuria and hemoglobinuria. The latter is a poor prognostic indicator

OTHER LABORATORY TESTS

- Prolongation of prothrombin time and partial thromboplastin time
- Hyperlactatemia
- Hyperammonemia
- Elevated bile acids
- Equine hepatitis virus PCR panel is available for research and informational purposes. Panel includes PCR testing for TDAV, NPHV, EPgV, and EqPV-H. (Note that there is no evidence for EqPeg causing liver disease in horses and testing may not be warranted.) Submit serum, fresh or formalin-fixed paraffin-embedded liver, or equine biologic products to the Cornell University Animal Health Diagnostic Center

IMAGING

Ultrasonography may suggest the liver is smaller and more hypoechoic than normal. May appear otherwise unremarkable.

OTHER DIAGNOSTIC PROCEDURES

Liver biopsy is not indicated in horses with "classic" signs of Theiler disease as histologic data will likely not change therapy.

PATHOLOGIC FINDINGS

- The liver is almost always smaller than normal. In 13 cases of Theiler disease, liver weight in comparison with body weight was 1%. In healthy control horses, liver weight was 1.6% of body weight, suggesting a 40% decrease in hepatic size following disease
- Histologically, affected livers show severe centrilobular or massive liver necrosis/apoptosis with portal areas less severely affected but with a mononuclear cell infiltration and slight to moderate bile duct proliferation, with or without fibrosis. Vasculitis has occasionally been reported. Alzheimer type II astrocytes are present in the brain in virtually all of the cases

TREATMENT

- Goals of therapy are to treat or prevent HE, provide supportive care including IV fluids, nutritional support, and antioxidant, anti-inflammatory, and antibiotic therapies
- Restrict activity, and avoid sunlight
- In cases with HE, house the horse in a quiet place, preferably padded to prevent injury
- Fluid therapy—correct deficits using hypertonic saline (7.5%, 4 mL/kg) or balanced isotonic crystalloid fluid preferably with an acetate rather than a lactate buffer at

(CONTINUED) ACUTE HEPATITIS IN ADULT HORSES (THEILER DISEASE)

20–30 mL/kg for the first hours with 50 g dextrose and 20 mEq KCl added to each liter. Continue at maintenance rate in patients that are not eating and drinking. Multiple B vitamins can be added to the fluids
• Nutritional support—if the horse is still eating, a high-carbohydrate, low-protein diet is recommended. Highly palatable grass hay (fed at approximately 1.5% of body weight per day) along with small amounts of high glycemic feeds at <1.0 g/kg/day should be offered in 4–6 meals per day. The protein should be high in BCAAs. Sorghum or soaked beet pulp have high concentrations of BCAAs. Commercial BCAA pastes can be administered in patients that are not eating

MEDICATIONS

DRUG(S) OF CHOICE

• Control of HE includes decreasing GI-derived neurotoxins (predominantly ammonia), decreasing cerebral edema, correcting glucose, electrolyte, and acid–base abnormalities, and maintaining perfusion and oxygenation to the brain and other vital organs. Ideally, all sedation should be avoided, but to prevent injury detomidine (5–10 µg/kg IV) can be used. If more long-term sedation is required, gabapentin (5–12 mg/kg PO every 12 h) or pregabalin (2–4 mg/kg PO every 12 h) could be considered. Conversely, in horses with profound coma, sarmazenil (0.04 mg/kg IV) or flumazenil (0.01–0.02 mg/kg IV) may be useful GABA receptor antagonists
• Metronidazole (15 mg/kg PO every 12 h), Neomycin (10–20 mg/kg PO every 8 h) and/or lactulose (0.3–0.5 mL/kg PO or per rectum every 8 h) may help reduce ammonia production and absorption from the GI tract
• Anti-inflammatory treatment—pentoxifylline (7.5 mg/kg PO or IV (compounded) every 8–12 h) to reduce systemic inflammation
• Antimicrobial therapy—bactericidal antibiotic (e.g. ceftiofur) to prevent bacterial translocation from GI tract to blood
• Antioxidant therapy—acetylcysteine by slow IV administration (up to 100 mg/kg) diluted in 5% dextrose. *S*-adenosyl methionine (10–15 mg/kg PO) to provide antioxidant effect

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Neomycin should not be given for more than 24–36 h; it may induce severe diarrhea
• Avoid overly sedating horses with HE as excessive lowering of the head in the standing horse may induce cerebral edema
• Ideally, all oral medications should be given by dose syringe rather than nasogastric tube as nasal bleeding resulting from passage of a stomach tube can result in ingestion of considerable amounts of blood protein, which would likely increase blood ammonia production
• Because the liver metabolizes many drugs, their duration of action may be increased in acute hepatic disease

FOLLOW-UP

PATIENT MONITORING

Monitor liver enzymes and bilirubin every 2–3 days. Maintain adequate serum potassium levels to reduce hyperammonemia.

EXPECTED COURSE AND PROGNOSIS

• Horses with severe HE have a poor prognosis. Horses that continue to eat for 3 days and have supportive treatments may fully recover
• Decline in serum SDH and GLDH after 2–3 days of treatment along with concurrent improvement in clinical signs suggests a favorable prognosis
• There are no proven long-term consequences in horses that recover

MISCELLANEOUS

ABBREVIATIONS

• BCAA = branched-chain amino acid
• EPgV = equine pegivirus
• EqPV-H = equine parvovirus
• GI = gastrointestinal
• GGT = γ-glutamyltransferase
• GLDH = glutamate dehydrogenase
• HE = hepatic encephalopathy
• NPHV = nonprimate hepacivirus
• PCR = polymerase chain reaction
• SDH = sorbitol dehydrogenase (IDH)
• TDAV = Theiler disease-associated virus

Suggested Reading

Chandriani S, Skewes-Cox P, Zhong W, et al. Identification of a previously undescribed divergent virus from the Flaviviridae family in an outbreak of equine serum hepatitis. Proc Natl Acad Sci USA 2013;110(15):E1407–1415.
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Authors Kathleen R. Mullen and Thomas J. Divers
Consulting Editors Michel Lévy and Heidi Banse
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Client Education Handout available online

A

ACUTE KIDNEY INJURY (AKI) AND ACUTE RENAL FAILURE (ARF)

BASICS

DEFINITION
Both AKI and ARF are a consequence of an abrupt, sustained decrease in GFR, resulting in azotemia and disturbances in fluid, electrolyte, and acid–base homeostasis. The term AKI has been introduced to increase awareness of subclinical renal damage that may accompany many disease processes.

PATHOPHYSIOLOGY
• Most commonly due to combined hemodynamic and nephrotoxic insults
• Perpetuated by decreased GFR in damaged glomeruli and tubular obstruction with desquamated tubular epithelial cells and debris

SYSTEMS AFFECTED
• Renal/urologic—injury/failure
• Endocrine/metabolic—disturbances in electrolyte and acid–base homeostasis
• GI—inappetence, possible diarrhea, and increased risk of ulcers
• Nervous/neuromuscular—occasional ataxia or encephalopathy in severe cases
• Hemic/lymphatic/immune—altered hemostasis, increased susceptibility to infection
• Musculoskeletal—acute laminitis in severe cases

GENETICS
N/A

INCIDENCE/PREVALENCE
• Low for ARF
• AKI may be a common secondary problem with many disease processes

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Breed Predilections
None

Mean Age and Range
Foals <30 days of age (especially when receiving nephrotoxic medications, or affected with hypoxic–ischemic multiorgan damage or septicemia) may be at greater risk, but all ages can be affected.

Predominant Sex
None

SIGNS
Historical Findings
Horse are often presented for concurrent medical problems.

Physical Examination Findings
• Lethargy, anorexia, dehydration, edema, ulcers, or uremic odor in the oral cavity
• Severity of lethargy and anorexia often are greater than would be expected for the primary disease process
• Oliguria/anuria
• Rectal examination may reveal an enlarged, painful left kidney
• Markedly azotemic patients may have neurologic deficits—ataxia, hypermetria, and mental obtundation

CAUSES
• Hemorrhagic, hypovolemic, or endotoxic shock
• Pigmenturia
• Vasculitis
• Disseminated intravascular coagulation
• Use of nephrotoxic medications—aminoglycosides; NSAIDs
• Other nephrotoxins include heavy metals (e.g. mercury [in counterirritants or blisters], lead, cadmium), vitamins D and K3, and high doses of oxytetracycline, especially when administered to neonates
• In occasional cases, infectious agents—*Actinobacillus equuli* in neonates; *Leptospira* spp. in all age groups

RISK FACTORS
• Renal hypoperfusion
• Exposure to nephrotoxins or nephrotoxic drugs, particularly in patients with dehydration
• Colic, diarrhea, pleuritis, peritonitis, prolonged exercise, rhabdomyolysis, hemolysis, or septicemia/endotoxemia

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Uroperitoneum
• Obstruction of lower urinary tract
• Chronic kidney disease
• Heart failure
• Gastric ulcers

CBC/BIOCHEMISTRY/URINALYSIS
• Normal to high PCV, variable leukogram, CBC changes reflect underlying primary disease process
• AKI may be reflected by minor increases in Cr (0.3 mg/dL or a 50% increase) that often do not exceed the upper limit of the reference range
• ARF is characterized by progressive increases in BUN (50–150 mg/dL; 18–54 mmol/L) and Cr (2.0–20 mg/dL; 177–1768 µmol/L)
• Variable hyponatremia, hypochloremia, hyperkalemia, hypocalcemia, and hyperphosphatemia
• Mild to moderate metabolic acidosis, severity varying with the underlying disease process; development of renal tubular acidosis may complicate recovery
• Mild to moderate hyperglycemia and hyperlactatemia
• Urine specific gravity—may remain high (>1.035) with AKI, low (<1.020) with ARF; best assessed during initial patient evaluation (before rehydration)
• ARF may be accompanied by mild to moderate proteinuria, glucosuria, pigmenturia, and increased RBCs and casts on sediment examination
• Urine pH—normal to acidic, especially with concurrent depletion of body potassium stores
• Myoglobinuria or hemoglobinuria/hematuria

OTHER LABORATORY TESTS
• Increased fractional clearances (i.e. excretions) of sodium and phosphorus; decreased clearance of potassium
• Enzymuria—urinary GGT:Cr ratio >25
• Rising titers to *Leptospira* spp. may be found in horses with ARF attributable to leptospirosis

IMAGING
Transabdominal/Transrectal Ultrasonography
• Kidneys may be enlarged (diameter >8 cm; length >15 cm), with increased echogenicity of renal cortices
• Rarely subcapsular/perirenal edema or hemorrhage
• Variable dilation of renal pelves
• Nephrolithiasis/ureterolithiasis would indicate underlying chronic kidney disease and possible "acute-on-chronic" exacerbation of renal failure

OTHER DIAGNOSTIC PROCEDURES
• Percutaneous renal biopsy with routine histopathologic, immunohistochemical, and electron microscopic evaluation of the sample may provide information regarding cause, severity, and prognosis. Proceed with caution, however, because life-threatening hemorrhage can be a complication
• CVP >8–10 mmHg indicates fluid overload

PATHOLOGIC FINDINGS
• Gross—enlargement of kidneys due to nephrosis and subcapsular and interstitial edema, causing tissue to bulge onto cut surfaces
• Histopathologic—glomeruli may be congested and have a cellular infiltrate; tubules have denuded or flattened epithelium and varying amounts of accumulated eosinophilic debris

TREATMENT

APPROPRIATE HEALTH CARE
Properly recognize and treat all underlying primary disease processes, usually on an inpatient basis for continuous fluid therapy.

NURSING CARE
Fluid Therapy
• After initial measurement of body weight, judiciously correct estimated dehydration with normal (0.9%) saline or another potassium-poor electrolyte solution over 12–24 h

(CONTINUED) ACUTE KIDNEY INJURY (AKI) AND ACUTE RENAL FAILURE (ARF)

• Avoid overzealous fluid replacement (more than twice maintenance rate) unless a higher fluid administration rate is needed for primary disease process
• Fluids may be supplemented with calcium gluconate or sodium bicarbonate if hyperkalemia or acidosis requires specific correction
• Additional fluid replacement is no longer necessary once appetite and drinking return to normal (i.e. there is no benefit to continuing fluid therapy until Cr returns to a normal value)

Oral Electrolyte Supplementation

• Sodium chloride (30 g) can be administered in concentrate feed or as an oral slurry/paste every 6–12 h to encourage increased drinking and urine output
• Potassium chloride can be supplemented in nonhyperkalemic patients with total body potassium depletion—common with anorexia of ≥ 2 days

ACTIVITY
Stall rest, with limited hand-walking or small paddock for grazing grass if appetite is poor.

DIET
Encourage intake by offering a variety of concentrate feeds, bran mash, and hay types.

CLIENT EDUCATION
None

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
• Judicious fluid therapy is the mainstay of treatment—see Nursing Care
• Furosemide—for oliguria/anuria (i.e. lack of urination during first 6 h of fluid therapy or urine output <0.5 mL/kg/h); this diuretic may be administered twice (1–2 mg/kg IV or IM) at 1 h intervals; if effective, urination should be observed within 1 h after the second dose; if ineffective, consider a furosemide constant rate infusion; if ineffective, discontinue treatment
• *Routine use of mannitol and dopamine in patients with ARF is no longer recommended*

CONTRAINDICATIONS
Avoid all nephrotoxic medications—gentamicin, tetracyclines, and NSAIDs.

PRECAUTIONS
• As little as 40 mL/kg of IV fluids (20 L per 500 kg horse) may produce increases in CVP and significant pulmonary edema in oliguric/anuric patients
• Furosemide—at repeated dosages can result in electrolyte derangements
• Reassess dosage schedule of drugs eliminated by urinary excretion

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
Consider peritoneal dialysis or hemodialysis (foals only) in refractory cases.

FOLLOW-UP

PATIENT MONITORING
• Assess clinical status (emphasizing hydration), urine output, and body weight at least twice daily during the initial 24 h of treatment and at least daily thereafter
• Monitor for subcutaneous and pulmonary edema—increased respiratory rate and effort as evidence of overhydration
• Assess azotemia and electrolyte and acid–basis status at least daily for the initial 3 days of treatment
• Consider placing a central venous line to maintain CVP <8 cmH_2O in more critical patients and neonates

PREVENTION/AVOIDANCE
• Anticipate compromised renal function in patients with other diseases or undergoing prolonged anesthesia and surgery; institute appropriate treatment to minimize dehydration and potential renal damage
• Ensure adequate hydration status in patients receiving nephrotoxic medications, especially when combined (i.e. aminoglycosides and NSAIDs or tetracyclines)
• Avoid concurrent use of multiple anti-inflammatory drugs—NSAIDs

POSSIBLE COMPLICATIONS
• Pulmonary and peripheral edema; conjunctival edema may be dramatic
• Severe hyperkalemia accompanied by cardiac arrhythmias and death
• Laminitis—often rapidly progressive and refractory to supportive care
• Signs of neurologic impairment—ataxia; mental obtundation
• GI ulceration or bleeding
• Coagulopathy
• Sepsis

EXPECTED COURSE AND PROGNOSIS
• Prognosis for recovery varies with the underlying primary disease process
• ARF may complicate recovery, prolong hospitalization and treatment, and increase cost
• Prognosis for recovery from AKI/ARF usually is favorable if azotemia decreases by 25–50% after the initial 24 h of treatment; extent of recovery of renal function in patients with ARF may require 3–6 weeks to fully assess
• Guarded prognosis for patients with Cr >10 mg/dL at initial evaluation and when azotemia remains unchanged after the initial 24 h of treatment
• Poor prognosis for patients that have persistent anuria (>24 h), that have increased magnitude of azotemia after the initial 24 h of treatment, that rapidly develop edema, or that remain oliguric >72 h

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Neonates, especially premature or dysmature foals, may have markedly elevated Cr concentrations (approaching 25 mg/dL) due to placental insufficiency; this azotemia typically resolves in 2–3 days and should not be confused with ARF or uroperitoneum.

ZOONOTIC POTENTIAL
Leptospirosis has infectious and zoonotic potential; avoid direct contact with infective urine.

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
• Acute nephrosis
• Acute tubular necrosis
• Vasomotor nephropathy

SEE ALSO
• Anuria/oliguria
• Chronic kidney disease (CKD)
• Pigmenturia (hematuria, hemoglobinuria, and myoglobinuria)

ABBREVIATIONS
• AKI = acute kidney injury
• ARF = acute renal failure
• BUN = blood urea nitrogen
• Cr = creatinine
• CVP = central venous pressure
• GFR = glomerular filtration rate
• GGT = γ-glutamyltransferase
• GI = gastrointestinal
• NSAID = nonsteroidal anti-inflammatory drug
• PCV = packed cell volume
• RBC = red blood cell

Suggested Reading

McLeland S. Diseases of the equine urinary system. Vet Clin NA: Equine Pract 2015;31(2):377–387.
Tyner GA, Nolen-Walston RD, Hall T, et al. A multicenter retrospective study of 151 renal biopsies in horses. J Vet Intern Med 2011;25:532–539.

Author Harold C. Schott II
Consulting Editor Valérie Picandet

A

ACUTE-PHASE RESPONSE

BASICS

OVERVIEW

• The APR is a highly conserved, nonspecific, innate response to damage- or danger-associated signals. APR enhances the body's response to infection and/or inflammation and aids in the restoration of homeostasis
• The physiology of the APR:
  ◦ Activation of inflammatory response initiated by innate recognition of DAMPs (DNA, etc.) and/or PAMPs (endotoxin, lipoteichoic acids, etc.) by pattern recognition receptors
    ▪ May also occur secondary to physiologic stress and neural inputs
  ◦ Inflammatory activation results in increased production of proinflammatory mediators, particularly cytokines such as IL-6, IL-1, and tumor necrosis factor
  ◦ IL-6 is primarily responsible for altering the hepatic production of APPs, resulting in:
    ▪ Increased production of positive APPs (FIB, SAA, CRP, Hp, ceruloplasmin, hepcidin, α_1-antitrypsin, etc.)
    ▪ Decreased production of negative APPs (albumin, transferrin)
  ◦ Extrahepatic production of some APPs may occur (SAA, Hp)
• APPs have numerous roles in the response to infection or injury:
  ◦ Minimize ongoing tissue damage, interfere with the growth and reproduction of pathogenic organisms, facilitate wound repair and tissue healing, enhance phagocytosis
• APPs are divided into 3 groups:
  ◦ Major APPs have very low plasma concentrations in normal animals and increase more than 100-fold during APR (SAA)
  ◦ Moderate APPs are present at measurable levels in normal animals but increase 5–10-fold during APR (Hp)
  ◦ Minor APPs increase gradually to ~2 × resting concentrations (FIB)
• Substantial interest exists in the utility of APPs as indicators of occult infection, injury, or inflammation
  ◦ Monitoring APPs over time may aid in assessing response to treatment
  ◦ APPs may have utility as prognostic markers in a number of diseases or conditions

SIGNALMENT

• No specific signalment, as this is an innate response that occurs in any individual at any stage of the life cycle
• Monitoring the APR may have utility in monitoring disease status and response to treatment, or in a herd situation by enabling the early identification of individuals with an occult inflammatory stimulus

SIGNS

• Activation of APR may be accompanied by physical changes consistent with systemic inflammation (fever, decreased appetite, lethargy, depression, and cachexia)
• Other signs are typically referable to the primary disease process, rather than the APR itself

CAUSES AND RISK FACTORS

Based upon the primary disease process.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Because the APR is nonspecific it may be difficult to differentiate between initiating pathologies
• The pattern of the response may be the same regardless of initiating stimulus

CBC/BIOCHEMISTRY/URINALYSIS

• CBC changes in association with the APR include leukocytosis and anemia of inflammation
• Biochemistry changes include decreases in serum albumin, calcium, and iron concentrations

OTHER LABORATORY TESTS

Abnormalities of coagulation may be present.

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

• Increased APPs should initiate an investigation aimed at identifying the underlying etiology
• The failure of one or more APPs to decline over time may indicate the need for patient reevaluation
• Increasing APPs during treatment may indicate worsening of the patient's condition, requiring reevaluation of the patient

TREATMENT

Treatment should be directed towards resolution of the primary disease process and controlling the inflammatory response.

MEDICATIONS

DRUG(S) OF CHOICE

No specific treatment.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

FOLLOW-UP

PATIENT MONITORING

• Serial monitoring of APPs such as FIB, SAA, and Hp has demonstrated utility in detecting occult disease conditions and monitoring the response to treatment
• APR has proven less useful in prognostication

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

• Increased positive APP levels are expected while the primary inflammatory stimulus is present
• The rate at which APP levels return to normal is variable, with major APPs such as SAA decreasing rapidly and minor APPs such as FIB returning more slowly to normal

MISCELLANEOUS

SEE ALSO

Anemia, chronic disease

ABBREVIATIONS

• APP = acute phase protein
• APR = acute phase response
• CRP = C-reactive protein
• DAMP = damage-associated molecular pattern
• FIB = fibrinogen
• Hp = haptoglobin
• IL = interleukin
• PAMP = pathogen-associated molecular pattern
• SAA = serum amyloid A

Suggested Reading

Crisman MV, Scarratt WK, Zimmerman KL. Blood proteins and inflammation in the horse. Vet Clin North Am Equine Pract 2008;24:285–297, vi.
Schrödl W, Buchler R, Wendler S, et al. Acute phase proteins as promising biomarkers: perspectives and limitations for human and veterinary medicine. Proteomics Clin Appl 2016;10(11):1077–1092.

Author Harold C. McKenzie
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson

BASICS

OVERVIEW
• Fatal respiratory disease in Arabian foals with SCID
• May be a severe pathogen in Fell Pony foals affected by "Fell Pony syndrome"
• Other breeds may be affected as foals, but seldom succumb
• Approximately 25% of affected foals also have diarrhea
• A role for adenovirus in adult respiratory disease has been suggested

SIGNALMENT
• Usually older than 8–10 weeks when clinical signs become present unless FTPI is present
• Primarily Arabians; other breeds affected sporadically (Fell Ponies)
• SCID-affected foals are frequently clinically normal at birth

SIGNS
• Identical to other causes of foal pneumonia—fever, tachypnea, dyspnea, depression, and abnormalities on thoracic auscultation
• Mild to moderate diarrhea may also be present (EAdV-2 strains)

CAUSES AND RISK FACTORS
• Foals with SCID have a defect in lymphoid stem cells that may result from altered purine metabolism. The absence of an adaptive immune response causes these foals to be susceptible to even minor pathogens, such as adenovirus
• Owing to maternally derived immunity reaching a nadir at 1–2 months of age, these foals become unable to mount an appropriate immune response and deteriorate
• Foals that are immunosuppressed for other reasons, such as Fell Pony syndrome
• Adenovirus (EAdV-1) may predispose foals to bacterial pneumonia and may play a significant role in the pathogenesis of bacterial pneumonia in non-SCID foals
• Antigenically distinct adenovirus, EAdV-2, has been identified in non-SCID foals with diarrhea, usually associated with concurrent rotavirus infection. The role of EAdV-2 in foal diarrhea is not clear

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Other viral and bacterial causes of pneumonia in immunocompromised foals:
• Equine herpesvirus type 1
• Equine influenza virus
• Equine arteritis virus
• *Streptococcus equi* var. *zooepidemicus*
• *Actinobacillus equuli*
• *Pasteurella* spp.
• *Klebsiella pneumoniae*
• *Salmonella* spp.
• *Bordetella bronchiseptica*
• *Rhodococcus equi*
• Other causes of diarrhea in foals—bacterial, viral, and parasitic

CBC/BIOCHEMISTRY/URINALYSIS
Antemortem diagnosis of SCID is supported by finding appropriate clinical signs in an Arabian foal of the appropriate age with persistent severe lymphopenia (≤500 cells/μL) and the absence of IgM on SRID (see Other Laboratory Tests).

OTHER LABORATORY TESTS
• Antibody titers—SCID foals do not demonstrate a 4-fold rise; non-SCID-affected foals develop a rise in 10 days
• Virus isolation/PCR—may be isolated/identified from normal and infected foals
• Histopathology—intranuclear inclusions can be detected in tissues. Antemortem—may demonstrate intranuclear inclusions in conjunctival and nasal epithelial cells. Postmortem—gross and histologic evidence of lymphoid hypoplasia of the thymus, spleen, and lymph nodes
• SRID—precolostral testing of SCID foals demonstrates an absence of IgM, but, as IgM is absorbed by the foal from colostrum, foals with adequate transfer of maternal antibody cannot be tested until IgM levels have waned, usually at ≥3 weeks of age
• Fell Pony syndrome—measurement of IgM after 4 weeks of age (concentration will be decreased) and demonstration of B-cell lymphopenia

IMAGING
• Radiographs—pneumonia
• Ultrasonography—lymphoid tissues may be suggestive of, but not diagnostic for, SCID

TREATMENT
• No specific treatment
• Non-SCID foals—supportive, with broad-spectrum antibiotics
• SCID and Fell Pony foals—treatment is not productive. Experimental treatment in SCID foals with bone marrow stem cell transplants

MEDICATIONS

DRUG(S) OF CHOICE
• Non-SCID foals—treat concurrent bacterial infection based on culture and sensitivity
• Foals with adenovirus associated with rotavirus—supportive therapy

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

CLIENT EDUCATION
• SCID prevention—genetic testing for identification of carriers and removal from breeding programs
• Approximately 1 of 4 foals from the mating of 2 heterozygotes results in a SCID foal
• Arabian foals from parents of unknown SCID status—test at birth for IgM levels (presuckle) and lymphocyte count
• Fell Pony syndrome—recommendations not yet established. Future availability of testing for mutation in the sodium/myoinositol cotransporter gene possible

MISCELLANEOUS

ABBREVIATIONS
• EAdV = equine adenovirus type
• FTPI = failure of transfer of passive immunity
• Ig = immunoglobulin
• PCR = polymerase chain reaction
• SCID = severe combined immunodeficiency syndrome
• SRID = serial radial immunodiffusion

Suggested Reading

Fox-Clipsham LY, Carter SD, Goodhead I, et al. Identification of a mutation associated with fatal foal immunodeficiency syndrome in the Fell and Dales pony. PLoS Genet 2011;7:e1002133.

Thomas GW, Bell SC, Carter SD. Immunoglobulin and peripheral B-lymphocyte concentrations in Fell Pony foal syndrome. Equine Vet J 2005;37:48–52.

Author Pamela A. Wilkins
Consulting Editor Ashley G. Boyle

A

ADRENAL INSUFFICIENCY

BASICS

OVERVIEW

• Synonymous with hypoadrenocorticism and "adrenal exhaustion"
• Characterized by glucocorticoid (i.e. cortisol) and/or mineralocorticoid (i.e. aldosterone) deficiency caused by adrenal cortex destruction (primary AI), ACTH deficiency (secondary AI), or suppression of the HPA axis by exogenous steroid or ACTH administration
• May be permanent, complete AI ("Addison disease," rare), or transient, "relative" AI secondary to concurrent critical illness (RAI/CIRCI)

Systems Affected

• Endocrine
• Cardiovascular
• Renal
• Musculoskeletal
• Gastrointestinal
• Behavioral
• Immune

SIGNALMENT

Any age, sex, and breed. RAI/CIRCI is most common in neonatal foals, especially premature foals.

SIGNS

• Acute RAI/CIRCI—signs of septic shock, including fever or hypothermia, hyperemic mucous membranes, weakness, hypotension, hemoconcentration, cardiovascular collapse, and death
• Chronic cases—depression, anorexia, weight loss, poor hair coat, exercise intolerance, polyuria/polydipsia, mild abdominal pain, salt craving, and diarrhea

CAUSES AND RISK FACTORS

• Chronic administration of glucocorticoids, exogenous ACTH, or anabolic steroids
• HPA axis immaturity attributable to prematurity in neonatal foals
• HPA axis suppression and/or adrenal hemorrhage and necrosis subsequent to systemic inflammatory response or sepsis/septic shock

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Renal failure, colitis, primary cardiovascular disease.

CBC/BIOCHEMISTRY/URINALYSIS

• Acute RAI/CIRCI—hemoconcentration, leukopenia (neutropenia), and hypoglycemia. If mineralocorticoid secretion is also affected, hyponatremia, hypochloremia, hyperkalemia, and decreased sodium–potassium ratio (reference range >27) may be seen, but this is uncommon
• Chronic cases—mineralocorticoid secretion is generally maintained, so serum electrolytes are usually within normal limits

OTHER LABORATORY TESTS

• Measure baseline plasma ACTH and cortisol concentrations. AI should be considered in ill or stressed animals with ACTH and cortisol concentrations below reference intervals, though this is not a sensitive test for AI
• ACTH stimulation testing—administer synthetic ACTH (1 μg/kg IV or IM, 100 μg IV for a neonatal foal). Measure serum cortisol before and 90–120 min after ACTH. An increase <2–4-fold is consistent with AI
• With insufficient aldosterone secretion, fractional excretion of sodium (reference range <1%) is increased despite a normal or low serum sodium concentration

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

N/A

TREATMENT

• Complete rest and avoidance of stress, particularly surgery, infection, and trauma
• Fluid, dextrose, and electrolyte support
• Treat the underlying primary cause
• If mineralocorticoid insufficiency, provide sodium supplementation (e.g. salt) and avoid potassium supplementation

MEDICATIONS

DRUG(S) OF CHOICE

• Glucocorticoid and, if necessary, mineralocorticoid replacement at physiologic doses equivalent to daily corticosteroid production rates
• For acute RAI/CIRCI in foals, low-dose hydrocortisone (1.3 mg/kg/day IV divided every 4–6 h) is recommended. This dose may also be effective in adult horses with RAI/CIRCI and acute AI, though it has not been well studied to date
• Avoid long-term or high-dose steroid supplementation as this can prolong HPA axis suppression. In acute RAI/CIRCI, a tapering course of hydrocortisone over 3–7 days is recommended
• For longer term therapy in adult horses with chronic AI, the maintenance dose of prednisolone is approximately 25 mg/day. However, exposure to stress dramatically increases corticosteroid requirements. During periods of stress, increase the dose by 2–10-fold and divide into 2 or 3 daily doses
• Mineralocorticoid replacement with fludrocortisone may be considered

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

FOLLOW-UP

PATIENT MONITORING

• Monitor electrolytes, renal function, acid–base balance, blood glucose, and blood pressure
• Once the animal is stable, HPA axis recovery can be documented by repeating ACTH stimulation test

PREVENTION/AVOIDANCE

Avoid excessive use of exogenous glucocorticoids, ACTH, and anabolic steroids.

POSSIBLE COMPLICATIONS

Excessive glucocorticoid administration, especially with long-acting forms (e.g. triamcinolone), increases susceptibility to infections and may induce insulin dysregulation, which could increase the risk of laminitis.

EXPECTED COURSE AND PROGNOSIS

N/A

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

• AI = adrenal insufficiency
• ACTH = adrenocorticotropin hormone
• CIRCI = critical illness-related corticosteroid insufficiency
• HPA = hypothalamic–pituitary–adrenal
• RAI = relative adrenal insufficiency

Suggested Reading

Hart KA. Adrenal glands. In: Smith BP, ed. Large Animal Internal Medicine, 5e. St. Louis, MO: Elsevier Mosby, 2015:1228–1233.

Author Kelsey A. Hart
Consulting Editor Michel Lévy and Heidi Banse
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Client Education Handout available online

AFLATOXICOSIS

BASICS

OVERVIEW
• Intoxication by aflatoxins
• Diffuse liver disease is its hallmark with acute and chronic forms dictated by dose and duration of exposure
• Ingestion of aflatoxin-contaminated cereal grains, especially corn. Cereal-based pelleted feed can also be a source
• Drought conditions favor aflatoxin production on grains. Aflatoxin production by contaminating fungi is more likely in warm (>25°C) and humid (97–99% relative humidity) conditions
• Outbreaks of aflatoxicosis in horses are rarely reported and have been linked to the ingestion of aflatoxin-contaminated feed in the range of 58.4–200 μg/kg

SIGNALMENT
Younger horses are more susceptible.

SIGNS
• Clinical signs of aflatoxicosis in horses are principally referable to hepatocellular necrosis and may include inappetence, lethargy, fever, jaundice, weakness, weight loss, reduced growth, tremors, ataxia, and even death
• Experimental ponies given single lethal doses of aflatoxin (2 mg/kg) developed fever, elevated heart and respiratory rates, tenesmus, bloody feces, and tetanic convulsions with death occurring 3–32 days after dosing. Ponies administered high oral doses of aflatoxin (400 μg/kg for 5 days) were lethargic, anorectic, and slightly icteric on the 5th day. Signs of hepatic encephalopathy occur when blood ammonia levels are sufficiently elevated
• Chronic low-level exposure may present as an ill-defined loss of condition or mild diarrhea

CAUSES AND RISK FACTORS
The most likely contaminated diets are corn-based, while less likely exposure comes from diets containing peanut and cottonseed meals.

DIAGNOSIS

• Signs and lesions of aflatoxicosis reflect liver disease. None are pathognomonic for either acute or chronic aflatoxin poisoning
• Diagnosis of aflatoxicosis is supported by laboratory demonstration of aflatoxin concentrations in feed
• Demonstration of aflatoxins in liver (postmortem) or stomach contents may also be supportive of the diagnosis
• Hepatic biopsy—evidence of centrilobular necrosis in acute cases; periportal fibrosis, biliary hyperplasia, and Kupffer cell hemosiderosis may be evident in chronic cases
• Overt liver failure is a rare manifestation of aflatoxicosis in horses
• Elevated serum liver enzymes

DIFFERENTIAL DIAGNOSIS
Any causes of liver diseases.

CBC/BIOCHEMISTRY/URINALYSIS
• White blood cell counts, especially lymphocytes, are decreased and blood glucose may be decreased. Total serum/plasma lipid and cholesterol concentrations may be elevated
• Elevations of prothrombin time, serum/plasma aspartate aminotransferase, alkaline phosphatase, γ-glutamyltransferase, and bile acids are consistent with the severe liver necrosis and biliary hyperplasia seen postmortem

OTHER LABORATORY TESTS
• Chemical analysis of feed samples is necessary to confirm the presence of aflatoxin. The inability to obtain samples contemporary with the time of exposure might preclude detection of aflatoxin levels consistent with chronic intoxication
• Feed concentrations of aflatoxin necessary to induce acute intoxication typically exceed the FDA cut-off for safe aflatoxin levels (>20 μg/kg) in feed intended for horses
• Chemical analysis of gastric contents and tissues (postmortem) for aflatoxins may help support the diagnosis

IMAGING
Ultrasonographic images of aflatoxin-affected hepatic parenchyma have not been reported. Logically, generalized parenchymal hyperechogenicity might be identified in chronic cases (consequence of fibrosis).

OTHER DIAGNOSTIC PROCEDURES
• Necropsy findings include fatty liver, hemorrhagic enteritis, and pale swollen kidneys
• Histologic changes in the liver include fatty degeneration, centrilobular necrosis, periportal fibrosis, and bile duct hyperplasia

TREATMENT

Specific antidotes are unavailable. Removal of aflatoxin-contaminated feed should be undertaken. Symptomatic and supportive treatment for hepatic disease should be undertaken (Carlson 2015).

MEDICATIONS

DRUG(S) AND FLUIDS
Dextrose 5% should be given slowly IV to hypoglycemic animals. Balanced electrolyte solutions are given for maintenance.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Drugs subject to hepatic clearance should be given cautiously.

FOLLOW-UP

PATIENT MONITORING
Liver enzymes should be monitored to evaluate liver status.

PREVENTION/AVOIDANCE
Test grain/feeds before feeding.

EXPECTED COURSE AND PROGNOSIS
Survival of acute intoxication does not guarantee complete recovery. Ponies have died from liver failure up to 30 days following a single toxic dose of aflatoxin.

MISCELLANEOUS

ABBREVIATIONS
FDA = United States Food and Drug Administration

Suggested Reading

Caloni F, Cortinovis C. Toxicological effects of aflatoxins in horses. Vet J 2011;188(3):270–273.
Carlson KL. Hepatic diseases in the horse. In: Sprayberry KA, Robinson NE, eds. Robinson's Current Therapy in Equine Medicine, 7e. St. Louis, MO: WB Saunders, 2015:287–293.

Authors Stan W. Casteel and Philip J. Johnson
Consulting Editors Wilson K. Rumbeiha and Steve Ensley

A

AFRICAN HORSE SICKNESS

BASICS

OVERVIEW
• Infectious disease affecting the cardiovascular and respiratory systems, characterized by fever and edema
• Not reported in the USA. Most commonly found on the African continent, with recent outbreaks investigated in South Africa, Zimbabwe, and Mozambique. India, Turkey, Iraq, Syria, Lebanon, Jordan, and Spain have reported outbreaks in the past
• Geographic range of the disease is limited by that of its principal vector, *Culicoides* spp. The disease is most prevalent in low-lying, moist, warm areas

SIGNALMENT
• All breeds of horses as well as other equids, such as donkeys and mules. Donkeys and zebras are more resistant than horses and infections may be subclinical
• There is no apparent breed, age, or sex predilection
• Dogs fed uncooked infected horse meat have developed AHS

SIGNS
• Fever (but not accompanied by inappetence)
• Pulmonary edema with coughing, frothy nasal discharge, dyspnea
• Subcutaneous edema of head and neck, edema of supraorbital fossa
• Colic

CAUSES AND RISK FACTORS
• Caused by the AHS virus, a viscerotropic RNA virus of the genus *Orbivirus*
• Transmitted by arthropod vectors, primarily *Culicoides* spp., but also mosquitos and ticks,
• Not transmitted with direct contact between equids
• Spread of the disease to uninfected countries can occur through travel of infected horses or movement of infected insect vectors in aircraft or heavy wind
• Virus affects vascular endothelium, resulting in the clinical sign of edema that predominates
• Disease occurs seasonally, during warm wet periods

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Equine infectious anemia, equine viral arteritis, purpura haemorrhagica, equine anaplasmosis, and equine piroplasmosis may have similar clinical presentation to AHS and may require laboratory testing to differentiate it
• Index of suspicion for AHS should be raised when there is a history of travel to countries known to harbor the disease
• Congestive heart failure may result in pulmonary and subcutaneous edema, but heart murmurs and/or venous distention should be present, and fever may not be present

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
• Definitive diagnosis depends on identification of virus by PCR or virus isolation from whole blood or tissues (spleen, lung, lymph node), or antibodies to AHS virus in serum
• In the USA, if AHS is suspected, the federal area veterinarian in charge should be notified immediately so that appropriate samples can be forwarded for testing

IMAGING
• Thoracic radiography may reveal evidence of pulmonary edema
• Thoracic ultrasonography may reveal pleural effusion or pericardial effusion

PATHOLOGIC FINDINGS
• Pulmonary edema, with frothy fluid in the bronchi and trachea
• Pleural effusion
• Pericardial effusion
• Yellow gelatinous edema fluid in the musculature of the neck and jugular groove
• Petechial hemorrhages on endocardium, epicardium, and oral mucous membranes and tongue

TREATMENT

There is no specific treatment for AHS. Supportive nursing care and symptomatic treatment may improve outcome in some cases, but usually the course of the disease is not altered by treatment.

MEDICATIONS

DRUG(S) OF CHOICE
N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

PREVENTION/AVOIDANCE
• Vaccination is effective. However, nine serotypes of the virus exist, and vaccination with one strain does not result in immunity to heterologous strains, so polyvalent strains of vaccine should be used
• Vaccination should be combined with other measures aimed at limiting exposure to insect vectors, such as fly-proof stabling, pasturing only during daylight, use of insect repellents, and keeping horses on high ground away from low-lying, swampy, insect-infested areas
• Countries free of the disease restrict importation of horses from countries known to harbor the disease, or impose quarantine of at least 60 days in insect-proof housing. Zebras and donkeys, because of inapparent infection, are particularly dangerous

EXPECTED COURSE AND PROGNOSIS
• Mortality in horses generally is high, up to 90%. In mules and donkeys, mortality may be lower (50%)
• The incubation period ranges from 7 to 14 days. Once clinical signs are observed, the clinical progression is rapid. Death usually occurs within 4–5 days after the onset of fever
• Survivors do not harbor the virus. Survivors have life-long immunity to the homologous strain

MISCELLANEOUS

ZOONOTIC POTENTIAL
The disease does not affect humans.

ABBREVIATIONS
• AHS = African horse sickness
• PCR = polymerase chain reaction

Suggested Reading

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OIE—World Organisation for Animal Health. Information on aquatic and terrestrial animal diseases. http://www.oie.int/en/animal-health-in-the-world/animal-diseases

Author Raymond W. Sweeney
Consulting Editor Ashley G. Boyle

BASICS

DEFINITION
• Agalactia—failure of the mammary gland to secrete colostrum or milk after foaling
• Hypogalactia—also referred to as dysgalactia is subnormal milk production

PATHOPHYSIOLOGY
• Estrogens (equilin, equilenin, and estradiol-17β from the fetoplacental unit) in late gestation induce mammary duct development
• Progestagen (5β-pregnane) stimulates lobuloalveolar growth
• Lactogenesis is triggered by a decrease of progestagen and increase of prolactin in the last few days of pregnancy
• After initiation of lactation, prolactin is not required for maintenance
• Colostrogenesis is initiated a few days prior to parturition. Lactation peaks 30–60 days postpartum
• Milk production is 2.5–4% of body weight and requires nutritional demands of the dam are met
• Agalactia/hypogalactia may be caused by alterations of hormonal events (low prolactin level), defects in the mammary tissue itself (mammary disease), poor nutritional status, or presence of systemic illness or disease

SYSTEMS AFFECTED
• Reproductive
• Endocrine/metabolic

GENETICS
Milk production is likely determined by genetics.

INCIDENCE/PREVALENCE
Agalactia or dysgalactia is commonly seen in equine practice when predisposing factors are present.

GEOGRAPHIC DISTRIBUTION
• Fescue toxicosis—tall fescue infected by the fungus *Neotyphodium coenophialum* in central and southeast USA
• Black oat infected by *Claviceps purpurea* in Brazil
• Rye grass infected by *Neotyphodium lolii* in Argentina

SIGNALMENT
Mares of any breed or age may be affected.

SIGNS
Historical Findings
• Grazing endophyte-infected tall fescue or ergot-infected feeds prepartum
• Prolonged gestation, history of placentitis, dystocia, thickened fetal membranes, retained fetal membranes, and *red bag* (premature placental separation)
• Previous history—agalactia/hypogalactia or mammary gland disease
• Clinical evidence of systemic disease; known exposure to infectious disease

Physical Examination Findings
• Weak, septicemic foal—FTPI and/or inadequate nutrition
• Flaccid udder and secretion of a clear or thick, yellow-tinged fluid from the teats
• Mastitis—swollen, painful udder, warm to the touch, secretion of grossly or microscopically abnormal milk
• Distinct, palpable masses with mammary abscessation or neoplasia

CAUSES
Endocrinologic Disorders
• Ergot alkaloids (fescue toxicosis) depress prolactin secretion (dopamine DA_2 receptor agonists and serotonin antagonists)
• Abortion/premature birth affects normal progesterone, estrogen, and prolactin fluctuations necessary for lactation onset

Mammary Gland Disease
• Inflammation and/or infection
• Abscessation or fibrosis
• Neoplasia
• Trauma

Systemic Disease
• Any debilitating systemic disease or stress-producing disorder
• Malnutrition/nutritional deficiency

Others
• Poor nutrition
• Obesity

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Differentiating Similar Signs
• Differentiate agalactia/hypogalactia from behavioral nursing problems:
  ◦ Mare anxiety, pain, udder edema
  ◦ Direct examination of udder and secretions
  ◦ Observe interaction between mare and foal as its attempts to nurse
• Failure of milk letdown can occur in mares:
  ◦ Oxytocin stimulates milk letdown, *not* milk secretion

DIFFERENTIATING CAUSES
• Indicators of fescue syndrome:
  ◦ History of fescue ingestion
  ◦ Prolonged gestation
  ◦ Dystocia
  ◦ Retained fetal membranes, thickened fetal membranes
  ◦ Weak, dysmature foal; mare with agalactia
• Full physical examination to differentiate mastitis, mammary fibrosis, neoplasia, abscessation, traumatic injury, systemic illness

OTHER LABORATORY TESTS
Serum prolactin levels are decreased in fescue-induced agalactia.

OTHER DIAGNOSTIC PROCEDURES
• If mastitis is suspected
  ◦ Cytology or culture of udder secretion
• If neoplasia is suspected
  ◦ Fine needle aspirate—cytology
  ◦ Biopsy—histopathology

TREATMENT

APPROPRIATE HEALTH CARE
• Promote lactation using selective D_2 dopamine receptor antagonists
• Mastitis
  ◦ Local or systemic antibiotics based on culture/sensitivity
  ◦ Frequent stripping of mammary gland
  ◦ Heat packs or hydrotherapy
  ◦ Correct nutritional deficiencies

NURSING CARE
• Foals at risk of FTPI need oral administration of colostrum from another mare
• Foals with FTPI need supportive treatment and IV administration of hyperimmune plasma

ACTIVITY
N/A

DIET
Supplementation of mare feed to meet lactation demand.

CLIENT EDUCATION
• Management of mares at risk of agalactia (remove from infected pastures)
• Close monitoring of periparturient mares for mammary gland development or overt edema
• Test colostrum quality upon parturition
• Observe foal nursing behavior

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE FOR FESCUE TOXICITY
• Domperidone (1.1 mg/kg PO daily)
  ◦ Selective DA_2 dopamine receptor antagonist; reverses effects of fescue ingestion
  ◦ Treat for minimum of 15 days prepartum; discontinue when/if lactation is observed at foaling
  ◦ If the mare is agalactic at foaling and has not been treated prior to parturition, initiate treatment at foaling and continue for 5 days or until lactation ensues
• Thyrotropin-releasing hormone—2.0 mg, SC, BID, 5 days, begin day 1 postpartum
  ◦ Increases serum prolactin, due to its action as a prolactin-releasing factor

AGALACTIA/HYPOGALACTIA (CONTINUED)

CONTRAINDICATIONS
• Perphenazine, dopamine receptor antagonist; published, but:
  ◦ Severe side effects in horses preclude its use
  ◦ Sweating, colic, hyperesthesia, ataxia, posterior paresis
• Metoclopramide is used to treat agalactia of unknown origin
  ◦ Significant risk for developing severe central nervous system side effects in horses
  ◦ Its use is contraindicated

PRECAUTIONS
• Remove pregnant mares from endophyte-infected fescue pastures/hay minimum 30 days, preferably 60–90 days, prepartum
• If removal is not possible, treat with domperidone during last 2–4 weeks of gestation

ALTERNATIVE DRUGS
• Acepromazine maleate (20 mg IM TID)
  ◦ Some dopamine antagonistic properties; tried as agalactia treatment
    ■ At least one report of it having no effect on lactation
  ◦ Sedation is the primary side effect
• Reserpine (0.5–2.0 mg IM every 48 h or 0.01 mg/kg PO every 24 h)
  ◦ Depletes serotonin, dopamine, and norepinephrine in the brain and other tissues
  ◦ Gastrointestinal motility is greatly increased and can cause profuse diarrhea
  ◦ Sedation—a common side effect
  ◦ Not FDA approved for agalactia
• Sulpiride (3.3 mg/kg PO daily)
  ◦ Dopamine antagonist to treat agalactia; less effective than domperidone
  ◦ Not FDA approved for agalactia

FOLLOW-UP

PATIENT MONITORING
• If effective, most treatments stimulate milk production in 2–5 days
• In absence of other systemic signs, agalactia is not life-threatening
• Foals need intensive medical and nutritional management with prolonged agalactia

MISCELLANEOUS

ASSOCIATED CONDITIONS
Mare
Prolonged gestation, abortion, dystocia, uterine rupture, thickened placental membranes, red bag, retained fetal membranes, infertility, prolonged luteal function, early embryonic death, weak and dysmature foals.

Neonate
• FTPI
• Malnutrition
• Starvation

SEE ALSO
• Dystocia
• Failure of transfer of passive immunity (FTPI)
• Fescue toxicosis
• Mastitis
• Prolonged pregnancy
• Retained fetal membranes

ABBREVIATIONS
• FDA = United States Food and Drug Administration
• FTPI = failure of transfer of passive immunity

Suggested Reading

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Author Ahmed Tibary
Consulting Editor Carla L. Carleton
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BASICS

DEFINITION
• Behaviors that do, or attempt to do, injury to another with the apparent motivation of causing harm
• Agonistic behaviors include threats, offensive aggressive behaviors, defensive behaviors, and submissive behaviors
• Aggression occurs in specific contexts or circumstances and is influenced by numerous variables, including internal states, external stimuli, learned experiences, etc
• It can be classified in numerous overlapping categories, e.g. according to the target, function, motivation, whether offensive or defensive

PATHOPHYSIOLOGY
• Aggression usually is a normal, species-typical behavior but can be triggered by anxiety, fear, and underlying pathophysiologic conditions that result in pain or endocrine and CNS abnormalities. Underlying conditions may be acute or chronic as well as intermittent. Consequently, corresponding aggression may vary in intensity and frequency
• "Grouchiness" or "irritability" may be related to low or moderate levels of pain
• Endocrine and gonad abnormalities, e.g., hypertestosteronism and ovarian and ovarian tumors in mares, retained testicles in males
• CNS disorders, e.g., encephalopathies, rabies, irritating or ablative lesions
• Low serum serotonin levels have been associated with aggressive behavior, stress, and illness

SYSTEMS AFFECTED
• Many physiologic and behavioral systems can be affected
• Musculoskeletal, skin, ophthalmic injuries may be incurred due to aggressive behaviors
• Reproductive behaviors may be interrupted
  ◦ Horses may exhibit aggression towards members of the same sex to disrupt courtship and copulation. Some breeding stallions managed "in-hand" are aggressive to the mare and handlers
  ◦ Some mares are aggressive towards their foals. In free-ranging situations the foal may not survive; in a controlled environment, successful intervention is possible. Some mares aggressively defend their foals against other animals, including people
• Aggressive outbursts can severely affect the human-animal bond and consequently impair a horse's welfare
• Frequent or prolonged states of aggression can result in chronic stress and result in changes in the hypothalamic–pituitary–cortical continuum. Chronic stress can affect immune function, body maintenance
• Interference with learning and performance

GENETICS
Genetics has been shown to influence specific types of aggressive behaviors in many species, but the mechanisms are unknown.

INCIDENCE/PREVALENCE
Unknown

GEOGRAPHIC DISTRIBUTION
Unknown

SIGNALMENT
Breed Predilections
Aggressive protection of foals is reported more often in Arabian mares.

Mean Age and Range
• Any age
• Playful aggression is most common in young horses and colts
• Intraspecific, intermale aggression is more common and intense in mature males

Predominant Sex
• Intact males are more likely to show aggression to other horses and people
• Self-mutilation is most likely to be exhibited by isolated stallions and geldings

SIGNS
General Comments
Aggressive behaviors range from mild threats to intense injurious acts.
• Mild forms include laying back of ears, lowering and extending head, nodding or swinging of head and neck, shifting of hindquarters toward another sometimes with mild pushing
• Moderate aggression adds threats to bite, strike or kick, tail switching, sometimes slight hopping motions with rear quarters, head and body bumping, harsh vocal squeals. There is an apparent restraint in intensity and effort
• High levels of aggression include serious efforts to bite, strike, or kick, severe bites, and attempts to knock opponent off balance. Rearing and striking with forelegs (boxing)
• Play aggression includes components of above but of low intensity, usually not causing any or serious harm between unshod horses
• Defensive behaviors include moving away and/or shifting rear quarters toward aggressor
• Offensive behaviors usually involve a head-on approach and threat
• Submissive behaviors include deferring to more dominant animal and "snapping" (jaw-waving, teeth-clamping, or *unterlegenheitgebärde*). Sometimes a slight sucking sound occurs. The ears are usually in a somewhat horizontal position
• Mares with elevated testosterone levels may show "stallion-like" behaviors, e.g. mounting other mares, vocalizing like a stallion, herding other mares, and aggression to other horses

Historical Findings
• Ask questions to identify exactly what behaviors are occurring. Determine when, where, how often they occur, when did they start and how did they progress, the targets of the aggression; the situations that tend to make it worse and situations when it does *not* occur; and what has been done thus far to deal with the problem. These answers form the basis for diagnosis, treatment, and risk assessment
• Aggressiveness associated with endocrine abnormalities is generally of gradual onset

Physical Examination Findings
• Examine carefully for pain. Chronic vertebral problems are often overlooked as a source of pain and aggression or grouchiness in riding horses
• Reproductive tract abnormalities, including retained testicles. Mares may have ovarian abnormalities, enlarged clitoris, blind vaginal sac, "cresty neck"

CAUSES
• Pain
• Fear/defense
• Play aggression usually is inhibited and causes few serious injuries among unshod horses of similar ages and weight; however, play can cause serious injury to people
• Protective—occurs in defense of other animals or people with whom the aggressor has a relationship and that are perceived to be under threat
• Dominance—hierarchies exist in groups of horses and are usually initially established via aggression, threats, and reciprocal deference. Once hierarchies are established and there is sufficient opportunity for the subordinate horse to defer, high levels of aggression rarely occur
• Resource guarding—food, preferred pasture partners, water, shelter, etc. Usually directed toward other horses but can be directed toward people
• Redirected—occurs during conflict situations in which a horse attacks another animal or person when access to the original target is blocked
• Redirected aggression occurs when a horse is motivated to be aggressive but is either physically or psychologically prevented from aggressing the eliciting stimuli and, instead, redirects the aggression to another target
• Infanticide—stallions may kill foals that are not theirs or are not recognized as theirs
• Sex related—occurs as part of courtship, copulation, or intrasexual competition
• Endocrine abnormalities
• CNS abnormalities such as encephalitis. Rabies may be manifested as "dumb," "furious," "paralytic," or any combination as well as other pathologic signs. These horses may be violent and, in attempts to control them, handlers are exposed to saliva and biting

RISK FACTORS
• Inappropriate use of punishment and mismanagement

A

AGGRESSION (CONTINUED)

• Small enclosures and poorly designed enclosures that prevent escape or deferral to threats
• Inadequate designs of water and feeding sites that result in fighting over access to resources
• Indiscriminate hand feeding treats can lead to "nipping"
• Adjacent stabling of horses that exhibit aggression toward each other
• Insufficient exercise
• Foals reared in isolation from other horses may not develop adequate social skills and may develop inappropriately rough play aggression with people

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Rule out pathologic conditions, before establishing solely a nonmedical behavioral diagnosis
• Aberrant, intense, steadily increasing aggressiveness or "grouchiness" warrants comprehensive medical workup
• Nonmedical diagnoses are based on circumstances and behavioral signs exhibited and ruling out medical causes
• Be aware that residual aggressive behaviors can persist after successful treatment of medical problems and management changes. Behavior modification may also be necessary

CBC/BIOCHEMISTRY/URINALYSIS
Dependent on clinical signs.

OTHER LABORATORY TESTS
• Dependent on clinical signs
• Testosterone, estrogen, and inhibin assays may be indicated
• Karyotyping of mares exhibiting stallion-like behaviors

IMAGING
Radiographs, endoscopic examinations, transrectal ultrasonography of reproductive organs.

OTHER DIAGNOSTIC PROCEDURES
• Rectal palpation
• Vaginal examination
• Lameness examination
• Visual recordings of the behavior to study and to monitor occurrence and intensity of the behavior

PATHOLOGIC FINDINGS
Dependent on etiology of aggression.

TREATMENT

AIMS
• Identify underlying reason for aggression and contributing factors
• Correct medical causes
• Specific treatments vary with the kind of aggression
• Most treatments of nonmedical conditions involve changing handling techniques, physical or social environments, and/or using behavior modification techniques to change the motivational state of the animal
• Behavior modification must be done precisely if it is to be safe and effective. Even stallions that are "unruly" when bred "in-hand" can be successfully retained using positive and negative reinforcement with very little or no punishment. It should always be remembered that the use of aversive stimuli comes with the risk of causing anxiety, fear, and aggression. Referral to an experienced and competent veterinary behaviorist, applied animal behaviorist, or trainer is often necessary to help the client implement the plan
• Assess the risks of treating and keeping a horse exhibiting aggression

APPROPRIATE HEALTH CARE
N/A

NURSING CARE
N/A

ACTIVITY
• Prevent or control access to targets of aggression
• Increase appropriate and safe types of exercise

DIET
Reduction of energy and protein intake is reported to reduce activity level and aggressiveness. However, numerous interventions (generally increased exercise and changes in environment) are usually also implemented simultaneously and it is difficult to assess the effect of the diet.

CLIENT EDUCATION
• Advise owner of risks involved with keeping the animal when considering treatment. Aggressive animals can deliver serious injury or cause death, and keeping an aggressive animal may place the client at risk of criminal and civil legal actions
• Advise owner that, even if underlying medical reasons are alleviated, there may be residual behavior patterns that require behavior modification and/or training

SURGICAL CONSIDERATIONS
• Removal of abnormal gonads in mares (ovarian tumors, aberrant testicular tissue) has a good prognosis
• Castration of stallions and colts usually reduces, but does not always eliminate, aggressive behaviors directed towards other horses and people. Age and experience of horse prior to castration are reported to be unrelated to effectiveness of castration
• Castration has been reported to completely improve self-mutilation in only 3 of 10 self-mutilating stallions

MEDICATIONS

DRUG(S) OF CHOICE
• No drug is approved by the FDA for the treatment of aggressive behaviors in horses
• Pain medications may help to reduce or eliminate pain-elicited aggression
• Anxiolytics or antidepressants may help with fear-motivated aggression
• Naturally occurring and synthetic progestins can inhibit aggression in domestic and wild equids. In larger doses progestins can reduce arousal and can be sedating

CONTRAINDICATIONS
• Benzodiazepines may increase aggressive behaviors
• Use of commercial synthetic progestins can affect testosterone levels, sperm production, and testicular morphology. There are few reported studies on the consequences of long-term use of exogenous progestins in horses
• Synthetic progestins are not disallowed when used to regulate the estrus cycle of performance mares. The drugs however are usually banned for use in other performance horses

PRECAUTIONS
• Inform clients that use of psychoactive drugs and progestins for aggression problems constitutes off-label and experimental use
• Inform clients regarding possible benefits, dangers, and side effects
• Obtain written informed consent before prescribing off-label medication

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
• Contact clients on a regular basis to check compliance with recommendations and to provide additional support
• Behavioral problems generally require intensive follow-up

PREVENTION/AVOIDANCE
• Avoid inappropriate use of punishment
• Rear foals with other horses. Ideally foals should remain with mother for 6 months and allowed access to other foals and (appropriate) horses as much as possible and for as long as possible
• Sufficient exercise and opportunities for appropriate play
• Adequate space to defer to dominant horses
• Strategic placement of critical resources, e.g. food, water, shelter, to alleviate competition

• Ground work that results in the horse consistently and quickly yielding to the requests of the handler. Most easily accomplished with naive and young horses
• If the aggression is not pathophysiologic, at the first indication there might be an aggressive behavior problem advise clients to seek help from qualified, accomplished professionals who address such behaviors

POSSIBLE COMPLICATIONS
See Client Education.

EXPECTED COURSE AND PROGNOSIS
• Ovariectomies usually resolve aggressive and stallion-like behaviors of mares related to ovarian pathologies
• Removal of normal or retained testicles in males generally results in reduction of aggressive and typically masculine behaviors. Approximately one-third retain some aggressive behaviors to other horses and interest in mares. From 5% to 17% retain some aggressiveness toward people
• Successful treatment of nonmedical causes of aggression is dependent on many variables

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

SEE ALSO
• Excessive maternal behavior/foal stealing
• Fear
• Learning, training, and behavior problems
• Maternal foal rejection
• Self-mutilation
• Stallion sexual behavior problems

ABBREVIATIONS
• CNS = central nervous system
• FDA = United States Food and Drug Administration

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Author Victoria L. Voith
Consulting Editor Victoria L. Voith
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ALKALINE PHOSPHATASE (ALP)

BASICS

DEFINITION

• Serum ALP concentration is mainly used as a marker for cholestasis. Although nonhepatic tissues may contribute to serum ALP concentration, the potential for significant contribution other than from bone is limited
• Reference intervals vary depending on the assay substrate employed; thus, comparisons across laboratories may not be valid

PATHOPHYSIOLOGY

• 2 genes produce distinct ALP isoenzymes—intestinal ALP and tissue-unspecific ALP
• Intestinal ALP is expressed only in the intestine and the tissue-unspecific ALP elsewhere; however, the equine kidney expresses both
• Post-translational modification (especially glycosylation) produces tissue-specific isoforms of ALP (e.g. bone, liver) and affects circulating half-life
• High tissue concentrations occur in kidney, intestine, liver, and bone; lower concentrations occur in placenta and other tissues
• Although intestine and kidney have much higher tissue concentrations than liver and bone, renal ALP is not released into blood, and intestinal ALP has a very short half-life of ≅8 min. Thus, serum concentrations consist mostly of liver and, to a lesser extent, bone ALP
• Liver ALP activity is greatest on the biliary canalicular membrane of hepatocytes. Increased blood activity results from increased synthesis (i.e. induction) or membrane release. The mechanism of release into the blood is proposed to involve membrane solubilization by bile salts, release of membrane fragments, or biliary regurgitation. A serum phospholipase contributes to cleavage of the enzyme from the membrane
• Cholestasis leads to increased serum ALP concentrations. Hepatocellular injury alone has little effect. Bile duct ligation leads to nearly 3-fold elevations within 10 days
• Serum ALP concentration rises with biliary hyperplasia, as seen with GGT
• Because increased ALP often involves enzyme induction, serum ALP increases in acute obstructive icterus may lag behind other markers such as conjugated bilirubin and bile salts

SYSTEMS AFFECTED

• Hepatobiliary—increases are associated with cholestasis
• Musculoskeletal—increases are associated with increased osteoblastic activity
• GI—severe GI disease can be associated with mild increases, the source of which is often unclear
• Reproductive—placental increases during pregnancy. Semen ALP comes mainly from the epididymis and testes. High semen ALP and few/no sperm confirms decreased sperm production versus ejaculatory failure or blockage

SIGNALMENT

• Neonates and foals—activity at days 1–3 of age is up to 20-fold above that of adults. Values decrease to < 5- to 10-fold by 2 weeks, and then taper to adult concentrations by 6 months to 1 year
• Pregnancy—equivocal impact on serum ALP concentration; some diseases associated with cholestasis and increased ALP are more common in pregnant mares (e.g. hyperlipemia, Theiler's disease)
• Ponies and donkeys—particularly susceptible to hyperlipemia and hepatic lipidosis

SIGNS

General Comments

Signs result from the underlying disease process.

Historical Findings

• Owners may report icterus, dark urine, anorexia, weight loss, lethargy, and behavioral changes associated with hepatic disease in conditions associated with cholestasis
• Abdominal pain (colic) may occur with acute hepatopathies or biliary obstructions

Physical Examination Findings

• Icterus
• Increased heart and respiratory rates, fever, photosensitization, weight loss, or obesity vary with the nature and severity of the underlying disease process

CAUSES

Hepatobiliary System

• Metabolic—secondary to severe anemia, hyperlipemia, or fasting (< 50% increase within 2–3 days, nonpathologic)
• Immune-mediated, infectious—chronic active hepatitis, Theiler's disease (i.e. serum hepatitis), amyloidosis, endotoxemia, viral (e.g. EIA, equine viral arteritis, equine herpesvirus in perinatal foals), bacterial (e.g. Tyzzer's disease, salmonellosis), fungal, protozoal (piroplasmosis), and parasitic (e.g. liver flukes, larval migrans)
• Nutritional—hepatic lipidosis
• Degenerative—cirrhosis; cholelithiasis
• Toxic—pyrrolizidine alkaloid-containing plants (e.g. *Senecio*, *Crotalaria*), alsike clover, aflatoxin, rubratoxin; chemical toxins (e.g. arsenic, chlorinated hydrocarbons, phenol, paraquat) primarily cause hepatocellular injury; cholestasis secondary to hepatocellular swelling or progression to a chronic hepatopathy may increase serum ALP concentration; some anesthetics (e.g. halothane) are associated with mild, transient increases
• Anomaly—biliary atresia; portovascular shunt
• Neoplastic—rare

Musculoskeletal System

• Rapid bone growth—juveniles
• Severe bony lesions

GI System

GI disease—enteritis, colitis, intestinal displacement.

Reproductive System

Pregnancy increases placental ALP, with mild increases in total serum ALP concentration possible.

Hematopoietic System

• Severe anemia (e.g. acute EIA, red maple leaf toxicity, onion toxicity, postparturient hemorrhage) leads to hypoxic injury and hepatocellular swelling, with subsequent cholestasis
• Hepatic lymphoma, leukemias, etc.

RISK FACTORS

Those associated with any disease leading to cholestasis.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Increases caused by bone ALP mostly seen in growing animals. In adults, increased bone ALP likely involves lameness or obvious bony lesions. Increases from bone ALP are relatively mild
• Highest elevations generally associated with longstanding conditions involving severe cholestasis
• Concurrent obesity and high enzyme concentrations suggest hyperlipemia/lipidosis, whereas anorexia and weight loss are typical of most other differentials

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

• Arsenate, beryllium, cyanide, fluoride, manganese, phosphate, sulfhydryl compounds, and zinc may cause falsely low values
• Complexing anticoagulants (e.g. citrate, EDTA, oxalate) inhibit ALP and should not be used for sample collection

Disorders That May Alter Laboratory Results

• Extreme icterus, severe lipemia, and marked hemolysis may affect values
• Activity tends to increase with storage

Valid if Run in a Human Laboratory?

• Valid, but concentrations vary with the methodology used
• Equine reference intervals should be generated in-house or based on literature values using the same methodology

(CONTINUED)

ALKALINE PHOSPHATASE (ALP)

CBC/BIOCHEMISTRY/URINALYSIS

• No routine laboratory tests provide a causative or specific diagnosis for ALP increases
• Most suggest a process (e.g. injury, cholestasis, insufficiency, inflammatory) rather than a cause

Erythrocytes

• Nonregenerative anemia may be seen with liver disease
• Microcytosis is associated with portosystemic shunts
• Acanthocytes, schistocytes (hepatic microvascular disease) are associated with decreased RBC survival
• Severe hemolytic anemia can cause hypoxic injury leading to hepatocellular swelling and secondary cholestasis

Leukocytes

• Neutrophilia or neutropenia and monocytosis may occur with inflammatory liver disease
• Evidence of antigenic stimulation (e.g. lymphocytosis, reactive lymphoid cells) may be seen

Glucose

Postprandial hyperglycemia or fasting hypoglycemia may occur with hepatic insufficiency/shunts.

Albumin

• Decreased production with hepatic insufficiency may decrease serum concentrations; usually a late event
• Albumin is a negative acute-phase reactant; mild decreases may occur with inflammation

Blood Urea Nitrogen

Decreased concentrations (especially relative to creatinine) occur with hepatic insufficiency/shunts due to decreased conversion of ammonia to urea.

GGT

Increases with either injury or cholestasis.

Bilirubin

• Conjugated—increases with cholestasis
• Unconjugated—increases with increased RBC destruction or decreased hepatic uptake as with fasting or decreased function

Triglycerides

Increased with hyperlipemia.

Urinalysis

• Bilirubinuria indicates cholestasis
• Ammonia urates may be observed with hepatic insufficiency/shunt

OTHER LABORATORY TESTS

Bile Acids

• Sensitive indicator of hepatic disease but not specific for the type of process
• Assesses enterohepatic circulation, adequate hepatocellular perfusion, and hepatobiliary function
• More sensitive than ALP for cholestasis

Ammonia

Serum concentrations correlate inversely with hepatic functional mass.

Clearance Tests (Sulfobromophthalein, Indocyanine Green)

• Prolonged clearance intervals with decreased functional mass or cholestasis
• Accelerated clearance (possibly masking insufficiency) with hypoalbuminemia

Coagulation Tests

Prothrombin time; activated partial thromboplastin time; may be prolonged with hepatic insufficiency/shunting.

IMAGING

Ultrasonography—useful for assessing liver size, shape, position, and parenchymal texture.

OTHER DIAGNOSTIC PROCEDURES

Aspiration cytology or biopsy for microbiologic testing, cytologic imprints, and histopathologic evaluation.

TREATMENT

• Decision regarding outpatient versus inpatient treatment depends on the severity of disease, intensity of supportive care required, need for isolation of infectious conditions, etc.
• Avoid negative energy balance, especially in ponies and donkeys, to avoid/treat hyperlipemia and hepatic lipidosis
• A high-carbohydrate, low-protein diet reduces ammonia production
• Specific therapy depends on the underlying cause

MEDICATIONS

DRUG(S) OF CHOICE

Liver disease:
• Fluid and nutritional support may be needed
• Anorexic and hypoglycemic cases may benefit from IV 5% dextrose (2 mL/kg/h); otherwise, fluid support depends on specific electrolyte and acid–base abnormalities
• Lactulose (333 mg/kg PO every 8 h) by nasogastric tube is suggested to combat GI ammonia production/absorption but may cause diarrhea

CONTRAINDICATIONS

Dependent on the underlying cause.

PRECAUTIONS

• Dependent on the underlying cause
• With suspected hepatic insufficiency, assess coagulation profiles before invasive procedures

POSSIBLE INTERACTIONS

Dependent on the underlying cause.

ALTERNATIVE DRUGS

Dependent on the underlying cause.

FOLLOW-UP

PATIENT MONITORING

Serial chemistries can help to establish a prognosis by characterizing disease progression and identifying evidence of improvement.

PREVENTION/AVOIDANCE

Dependent on the underlying cause.

POSSIBLE COMPLICATIONS

Dependent on the underlying cause.

EXPECTED COURSE AND PROGNOSIS

• Dependent on the underlying cause
• Hypoglycemia or ALP > 900 IU/L with liver disease carries a guarded prognosis

MISCELLANEOUS

ASSOCIATED CONDITIONS

Dependent on the underlying cause.

AGE-RELATED FACTORS

See Signalment.

ZOONOTIC POTENTIAL

Dependent on the underlying cause.

PREGNANCY/FERTILITY/BREEDING

See Signalment.

SYNONYMS

N/A

SEE ALSO

See Causes.

ABBREVIATIONS

• ALP = alkaline phosphatase
• EIA = equine infectious anemia
• GGT = γ-glutamyltransferase
• GI = gastrointestinal
• RBC = red blood cell

Suggested Reading

Helene A, Perron MF, Sandersen C, et al. Prognostic value of clinical signs and blood parameters in equids suffering from hepatic diseases. J Equine Vet Sci 2005;25:18–25.
Smith GW, Davis JL. Diseases of the hepatobiliary system. In: Smith B, ed. Large Animal Internal Medicine, 5e. St. Louis, MO: Elsevier Mosby, 2015:843–872.

Author John A. Christian
Consulting Editor Sandra D. Taylor

A

ALKALOSIS, METABOLIC

BASICS

OVERVIEW

• A disruption of acid–base homeostasis producing decreased H^+ concentration, which is reflected by alkalemia (increased blood pH) and high plasma HCO_3^-
• Normal plasma HCO_3^- concentration is ≅24 mEq/L
• Normal blood pH ranges from 7.35 to 7.45
• Hypoventilation should increase CO_2 concentrations to lower pH; however, respiratory compensation is limited once hypoxemia develops

Pathophysiology

• The kidney normally is capable of responding to a high pH by excreting HCO_3^- into the urine. Metabolic alkalosis persists only when renal excretion of HCO_3^- is impaired or reabsorption is enhanced
• Excessive loss of H^+, retention of HCO_3^-, and contraction of extracellular fluid volume without loss of HCO_3^- (i.e. contraction alkalosis) are the common mechanisms that initiate metabolic alkalosis

Systems Affected

• Respiratory
  ◦ Chemoreceptors sense high pH in blood or cerebrospinal fluid and depress ventilation to decrease removal of CO_2
• Cardiovascular
  ◦ Cardiac arrhythmias
  ◦ Arteriolar vasoconstriction
  ◦ Decreased coronary and cerebral blood flow caused by vasoconstriction
• Metabolic
  ◦ Increased affinity of O_2–hemoglobin binding, which inhibits release of O_2 to the tissues
  ◦ Decreased ionized Ca^{2+} concentration
• Renal
  ◦ The kidney responds to high pH by excreting HCO_3^-

SIGNALMENT

• Any breed, age, or sex
• Horses used for endurance exercise

SIGNS

Historical Findings

Recent participation in endurance event.

Physical Examination Findings

Dependent on the underlying cause.

CAUSES AND RISK FACTORS

• Gastrointestinal loss of H^+ and Cl^- is seen with gastric reflux that occurs with anterior enteritis and ileus
• Salivary loss of Cl^- (e.g. ptyalism, dysphagia, esophageal trauma/obstruction)
• Cl^- loss is seen with excessive sweating (e.g. endurance event) and diuretic therapy (furosemide). Equine sweat contains large amounts of Cl^- and K^+; fluid loss can be extreme with moderate intensity exercise, especially in warm, humid conditions
• K^+ depletion is associated with anorexia, renal failure, and diuretic therapy (acetazolamide)
• Iatrogenic HCO_3^- therapy in racehorses
• Hypoalbuminemia since proteins are weak acids

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

N/A

CBC/BIOCHEMISTRY/URINALYSIS

• Measurements of serum electrolytes, protein concentrations, and chemistries are important to determine the cause and to guide treatment
• Normal or elevated Na^+ concentrations with hypochloremia are suggestive of metabolic alkalosis
• K^+ and Cl^- are decreased in horses that sweat excessively; K^+ may be low because of the primary cause or as a response to the extracellular shift of H^+
• Ionized Ca^{2+} is decreased
• Mg^{2+} may be decreased, especially with sweat loss
• Urinalysis may reveal decreased urine pH

OTHER LABORATORY TESTS

• Many laboratories measure TCO_2, which closely approximates HCO_3^-
• TCO_2 must be analyzed rapidly and with minimal room-air exposure within the sample tube
• Increased blood pH indicates alkalemia. A concurrent increase in blood HCO_3^- concentration indicates metabolic alkalemia. An accompanying increase in PCO_2 concentration indicates respiratory compensation
• Increased HCO_3^- concentration with decreased blood pH indicates compensation for a respiratory acidosis
• The exacerbation of severe asthma is often associated with increased blood pH, increased PCO_2 concentration, and increased HCO_3^- concentration, suggesting excess compensation for a respiratory acidosis
• Blood gas parameters must be assessed against appropriate reference ranges for the sample taken

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

N/A

TREATMENT

Directed at the primary cause.

MEDICATIONS

DRUG(S) OF CHOICE

• Replacement of fluid losses with isotonic fluids may be sufficient to restore acid–base status in mild cases
• Address specific electrolyte losses
• Large volumes may be needed in some endurance athletes with excessive fluid losses from sweating or hyperthermia
• With hypochloremia, give fluids containing Cl^-, or the alkalosis will not be corrected even if hydration is restored
• 0.9% saline or isotonic crystalloids with added Ca^{2+} and KCl are the fluids of choice
• With excessive K^+ loss, IV supplementation is necessary if the horse remains anorexic

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Any alkalinizing therapy (e.g. lactated Ringer's solution) can worsen the alkalosis.

FOLLOW-UP

PATIENT MONITORING

Serial blood gas analysis and measurement of electrolytes are important in evaluating efficacy of therapy.

POSSIBLE COMPLICATIONS

• Hypokalemia
• Hypocalcemia

EXPECTED COURSE AND PROGNOSIS

Dependent on the underlying cause.

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Hypochloremia
• Hypokalemia
• Respiratory acidosis

SEE ALSO

• Chloride, hypochloremia
• Hyperthermia
• Potassium, hypokalemia

ABBREVIATIONS

• PCO_2 = partial pressure of carbon dioxide
• TCO_2 = total carbon dioxide

Suggested Reading

Hinchcliff KW, ed. Fluids and electrolytes in athletic horses. Vet Clin North Am Equine Pract 1998;14(1):1–225.

Author Sara L. Connolly
Consulting Editor Sandra D. Taylor
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BASICS

OVERVIEW

- Decrease in blood PCO_2 concentration
- Arterial concentrations in range 35-42 mmHg
- Venous concentrations in range 43-49 mmHg

Pathophysiology

- CO_2 is formed in all tissues during metabolic energy production and diffuses passively out of cells and into the blood in gaseous form
- Most (65–70%) CO_2 combines with water almost instantaneously to form carbonic acid, which then dissociates into HCO_3^- and H^+. Therefore, most CO_2 is transported in the blood as HCO_3^-, with some bound to proteins and a small amount dissolved directly into plasma
- In the lungs, the reverse occurs, and CO_2 passively diffuses out of capillaries into the alveoli
- These 3 forms of CO_2 exist in equilibrium in the blood, but PCO_2 as measured by blood gases depends on the dissolved portion
- Alveolar CO_2 is then removed mechanically by ventilation as air moves in and out of the lungs
- Respiratory alkalosis occurs with hyperventilation or when tissue production of CO_2 drops but ventilation remains unchanged

Systems Affected

- Brain (hypocapnia decreases cerebral blood flow)
- Alterations in pH affect acid–base balance, protein binding, and electrolyte levels directly in the blood and via effects on the kidney
- The kidney responds to high pH by generating more H^+ and excreting more HCO_3^-. It also reabsorbs Cl^- to maintain electroneutrality. Alkalosis decreases serum K^+ and ionized Ca^{2+} concentrations
- Severe alkalemia can cause venoconstriction and predispose to arrhythmias

SIGNALMENT

Any breed, age, or sex.

SIGNS

Tachypnea

CAUSES AND RISK FACTORS

Acute—Hyperventilation

- Exercise, fever, hyperthermia, pain, anxiety, excitement, or fear
- Stimulation of medullary respiratory center (e.g. central nervous system disorder, septicemia, acidosis, endotoxemia)
- Tissue hypoxia from anemia, hypovolemia, or hypoxemia

Chronic

- Chronic respiratory disease or chronic, painful conditions (e.g. laminitis)
- Overventilation with mechanical ventilators produces low PCO_2 concentrations in anesthetized patients and sick neonates
- Prolonged general anesthesia may lower tissue CO_2 production and produce respiratory alkalosis
- Compensatory response to primary metabolic acidosis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any condition that causes tachypnea
- Chronic respiratory alkalosis results in compensatory metabolic acidosis, in which HCO_3^- is low and pH should be normal, because compensation is very effective in this circumstance
- Primary acute metabolic acidosis; often, pH remains low in severe cases, because respiratory compensation rarely is complete

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

- With poor peripheral perfusion, results of blood gas analysis on samples taken from peripheral arteries may not reflect the overall systemic condition
- Prolonged exposure to room air may alter PCO_2 concentrations because the sample equilibrates with the air

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

- Blood gas analysis. Abnormalities that indicate a primary respiratory alkalemia are elevated pH and decreased PCO_2. A concurrent decrease in HCO_3^- indicates metabolic compensation
- Venous samples may be adequate to identify the condition, but arterial samples are necessary to evaluate adequacy of pulmonary function as a cause. Samples must be evaluated against appropriate reference values
- Handheld analyzers require only small amounts of whole blood. Otherwise, use heparinized syringes
- Perform sampling anaerobically. Immediately evacuate any air bubbles and cap the needle with a rubber stopper
- Perform analysis within 15–20 min. If not possible, samples collected in syringes designed for arterial blood collection can be stored on ice, and results will be valid for 3–4 h

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

- Capnography or capnometry to measure CO_2 indirectly from expired gases
- Samples of end-tidal gases reflect arterial PCO_2 concentrations
- Continuous monitoring of anesthetized or ventilated patients
- V/Q mismatch is always present in anesthetized or recumbent patients, and end-tidal CO_2 concentrations may underestimate arterial concentrations by ≅10–15 mmHg

TREATMENT

Treat underlying cause.

MEDICATIONS

DRUG(S) OF CHOICE

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

FOLLOW-UP

PATIENT MONITORING

Repeat blood gas analysis following resolution of clinical signs and/or treatment.

POSSIBLE COMPLICATIONS

Severe alkalemia can result in neurologic signs, muscular excitability, and cardiac arrhythmias.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Disorders that result in metabolic acidosis.

PREGNANCY/FERTILITY/BREEDING

Late-term pregnant mares might hyperventilate because of decreased lung volume caused by abdominal distention.

SYNONYMS

- Hypocapnia
- Hypocarbia

SEE ALSO

- Acidosis, metabolic
- Chloride, hyperchloremia
- Potassium, hypokalemia

ABBREVIATIONS

- PCO_2 = partial pressure of carbon dioxide
- V/Q = ventilation–perfusion ratio

Suggested Reading

Viu J, Armengou L, Ríos J, et al. Acid base imbalances in ill neonatal foals and their association with survival. Equine Vet J 2017;49(1):51–57.

Author Sara L. Connolly
Consulting Editor Sandra D. Taylor
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A

ALOPECIA

BASICS

DEFINITION
• Alopecia is characterized by an absolute decrease in the number of hairs per given area of body surface or hairs that are shorter than normal even though their number is within normal limits. Simply stated, it is a loss or lack of the hair from skin areas where it is normally present
• Alopecia may be congenital or acquired
• Congenital alopecia is rare in horses and represents changes in hair follicle quantity or quality
• Common etiologies of acquired alopecia are adnexal destruction or atrophy secondary to infection, physical trauma, immune-mediated reactions, nutritional supplements and deficiencies, toxicities, physiologic stressors, hypersensitivities, neoplasia, and various miscellaneous causes. Acquired alopecia can be subdivided into infectious and noninfectious causes

PATHOPHYSIOLOGY
• Acquired alopecia represents a disruption in the growth of the hair follicle with or without damage to the hair bulb, follicular wall, and/or hair shaft. The animal is born with a normal hair coat, has or had normal hair follicles at one time, and is or was capable of producing structurally normal hairs
• Congenital alopecia is the result of abnormal morphogenesis or lack of adnexal structures (therefore hair) in regions of the body where they normally are expected. Animals with congenital hypotrichosis may be born with varying degrees of hypotrichosis or a complete haircoat; however, if born with a complete haircoat a rapid onset of progressive permanent alopecia within the first few months of life ensues

SYSTEMS AFFECTED
Skin/exocrine

GENETICS
Congenital alopecia does not necessarily imply a genetic basis, although in most cases the disease is based on genetic abnormalities and thus is hereditary. The exact mode of inheritance is unknown.

INCIDENCE/PREVALENCE
True incidence is unknown.

GEOGRAPHIC DISTRIBUTION
Presumably worldwide.

SIGNALMENT
• Congenital hypotrichosis has been documented in certain Arabian lines and a blue roan Percheron
• Appaloosas with foundation bloodlines have hair dystrophy/thinning of the long mane and tail hair
• Acquired alopecia can occur in all breeds
• Appaloosas and Quarter Horses are predisposed to alopecia areata
• Both sexes are affected equally

SIGNS
General Comments
• May be an acute onset or slowly progressive
• Multifocal patches of circular alopecia are most commonly associated with bacterial folliculitis, dermatophytosis, or dermatophilosis
• Large diffuse areas of alopecia may indicate an immune-mediated etiology or congenital abnormality
• Congenital hypotrichosis may be regional, multifocal, or generalized. It might become clinically apparent only weeks after birth and usually does not continually progress with age

CAUSES
• Noncicatricial alopecia (nonscarring causes)
  ◦ Mild to moderate inflammation of the hair follicle (folliculitis and furunculosis)
  ◦ Defects in the hair shaft
  ◦ Hair follicle dystrophies
  ◦ Altered hair follicle function
  ◦ Trauma (self-induced from pruritus)
• Cicatricial alopecia (scarring causes)
  ◦ Physical, chemical, or thermal injury
  ◦ Severe furunculosis
  ◦ Neoplasia
  ◦ Severe inflammatory disease such as in cutaneous onchocerciasis

Congenital Causes
• Congenital hypothyroidism may be a cause of congenital hypotrichosis and alopecia
• Trichorrhexis nodosa is a hair shaft defect that may be hereditary or acquired
• Congenital hypotrichosis
• Epidermolysis bullosa
• Mane and tail dystrophy
• Follicular dysgenesis

Acquired Causes
Infectious
• Bacterial
  ◦ The most common bacterial infection is dermatophilosis. Folliculitis and furunculosis due to *Staphylococcus* spp. (common) and *Corynebacterium pseudotuberculosis* (uncommon). Other bacterial causes are abscesses due to *Fusiformis* and *Streptococcus* spp.
• Fungal
  ◦ Dermatophytosis due to *Microsporum gypseum*, *M. equinum* or *M. canis* or *Trichophyton equinum* var. *equinum* cause alopecia. Other fungal causes are mycetoma and subcutaneous mycosis such as phycomycosis and pythiosis
  ◦ Brittle tail syndrome caused by the contagious, keratolytic fungus *Equicapillimyces hongkongensis* is a newly described condition causing weakening and breakage only of the tail hairs
  ◦ Piedra is a rare fungal infection caused by *Trichosporon beigelii* that causes white nodules on the hair shafts that cause breakage of the shafts. The mane, tail, and distal limbs are most commonly affected
• Parasitic
  ◦ Follicular parasitic infections of the follicle that result in alopecia are rare and include *Demodex equi* and *Pelodera strongyloides*. Other more common parasitic infections that cause alopecia are *Culicoides*, onchocerciasis, lice, ticks, oxyuriasis and mites (*Sarcoptes* spp., *Chorioptes* spp., *Psoroptes* spp., and Trombiculidae)
• Viral
  ◦ Viral papillomas—congenital, cutaneous, or pinnal

Noninfectious
• Immune mediated
  ◦ Cell-mediated autoimmune disease directed toward the hair follicle and adnexa
    ▪ Alopecia areata
    ▪ Hair follicle dystrophy—possible variant of alopecia areata
    ▪ Sebaceous adenitis—rare, case reports in 2006 and 2013
  ◦ Drug eruptions
  ◦ Pemphigus foliaceus
  ◦ Systemic lupus erythematosus
  ◦ Sarcoidosis
• Physical
  ◦ Burns from chemicals, hot, cold, or ropes
  ◦ Scalding from exudate, urine, or feces
  ◦ Tail and mane rubbing as stable vice
• Neoplasia
  ◦ Sarcoids
  ◦ Squamous cell carcinoma
• Miscellaneous
  ◦ Symmetrical atrophy of hair follicles secondary to endocrine disorders is extremely rare to nonexistent
  ◦ Anagen and telogen effluvium
  ◦ Anhidrosis
  ◦ Iodism
  ◦ Selenium, mimosine, or mercury toxicities
  ◦ Copper deficiency

RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Accurate diagnosis of alopecia requires a careful history and physical examination
• Key points in the history include recognition of breed predispositions for congenital alopecia; the duration and progression of lesions; the presence or absence of pruritus or evidence of contagion
• On physical examination, the distribution of lesions should be noted (focal, multifocal, generalized, or symmetrical), and the hairs examined to determine if they are being shed from the hair follicle or broken off. Signs of secondary infections or ectoparasites should be noted. The degree of crusts, scale, and exudate help prioritize the differentials

- Patchy, localized to multifocal
  - Bacterial folliculitis and furunculosis
  - Dermatophytosis
  - Dermatophilosis
  - Linear alopecia
  - Alopecia areata—results from selective and reversible damage to anagen hair follicles. Initial lesions may be focal or multifocal, well-circumscribed alopecia that progresses to diffuse alopecia. The mane, tail, and face are often involved and hoof dystrophies can occur. The alopecic skin has minimal or no visible inflammation. Prognosis varies, some cases spontaneously resolve, some respond to immunosuppressive doses of steroids, while others have no hair regrowth
- Generalized, symmetrical, and large patchy multifocal
  - Normal shed—"physiologic telogen effluvium"
  - Telogen effluvium—a reaction pattern characterized by widespread alopecia in response to severe metabolic stress. Serious illness, high fever, pregnancy, and adverse reaction to supplements are all potential inducers of telogen effluvium. Rapid premature cessation of anagen growth leads to abrupt synchronization of the follicular cycle such that hair follicles proceed in unison through catagen and telogen. This leads to hair loss of variable severity when old telogen hairs are forced out by new, synchronous anagen hairs. Hair loss usually occurs within 3–4 weeks after the insult but may occur up to 2 months later. Alopecia resolves spontaneously if the initiating factor is no longer present, and new anagen hairs grow
  - Anagen effluvium—a reaction pattern characterized by shedding during anagen arrest. Severe stresses such as high-dose cytotoxic therapy or infectious or metabolic disease halt anagen hair growth and result in hair loss within days to weeks of the insult. The hairs are lost due to structural weakness or dysplastic changes damaging the hair shaft

CBC/BIOCHEMISTRY/URINALYSIS
Useful to rule out metabolic causes.

OTHER LABORATORY TESTS
N/A

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
- Cytology should be obtained from pustules, papules, erosions, or ulcers. Neutrophilic exudate with intra- and/or extracellular cocci representative of a secondary folliculitis are easily identified if cytology is sampled from ruptured pustules or impression smears made from the underside of crusts or a fresh erosion or ulcer. Impression smears from the surface of lesions often do *not* show bacteria, but rather numbers of shed keratinocytes
- Direct hair examination (trichography)—hairs will have either anagen or telogen roots. Telogen hairs have uniform shaft diameters and slightly rough-surfaced, tapered, spear-shaped angular non-pigmented roots. Anagen hairs have rounded, smooth pigmented bulbs that bend. Distal ends of hair shafts may appear fractured from self-induced trauma. No normal animal should have all of its hairs in telogen but rather should have an admixture of anagen and telogen. Anagen defluxion reveals fragmented hair shafts with the absence of roots. Animals with alopecia areata may have short hairs with fractured distal ends and shafts that taper towards the proximal end (exclamation point hairs)
- Perform skin scrapings to rule out ectoparasites
- Perform bacterial and dermatophyte test medium cultures to determine bacterial species and susceptibility and/or dermatophyte infections
- Perform skin biopsies if the tests listed above do not identify or suggest an underlying cause. A biopsy evaluates hair follicles, adnexal structures, inflammation, and anagen/telogen ratios. Biopsies may reveal evidence for bacterial, parasitic, or fungal causes of alopecia but should *not* be considered as the definitive test for determination of alopecia caused by infectious agents. If cytologic identification reveals evidence of folliculitis, treat the patient with appropriate antimicrobials, parasiticides, or antifungals for a minimum of 3 weeks. If no improvement in the degree of alopecia is noted, obtain a biopsy for histopathology, preferably while the patient is still receiving treatment. Often biopsies submitted from patients with moderate to severe bacterial folliculitis make it difficult to determine and may mask the primary cause of alopecia. Submit biopsies from affected and nonaffected sites
- Definitive diagnosis of alopecia areata requires histologic confirmation. Multiple biopsies need to be collected as pathognomonic lesions can be sparse. Biopsy from newly developed areas of alopecia, rather than older lesions

PATHOLOGIC FINDINGS
- Biopsies of telogen effluvium are misleading, as they will demonstrate most follicles in the active growing (anagen) phase. Often the hair cycle has returned to normal by the time the decision to biopsy has been made
- Anagen effluvium findings include apoptosis and fragmented cell nuclei in the keratinocytes of the hair matrix of anagen follicles, as well as eosinophilic dysplastic hair shafts within the pilar canal
- Alopecia areata has 2 major histologic features. The first is hair follicle miniaturization and the second feature is lymphocytic bulbitis. The lymphocytic bulbitis involves anagen follicles and is best found in recently developed areas of alopecia. A lymphocytic mural folliculitis affecting the follicular isthmus is possible. The bulbitis may be very difficult to demonstrate especially in chronic lesions where the inflammation may be nonexistent. Chronic lesions only exhibit small telogen follicles lacking hair shafts that may be somewhat atrophic
- Histologic findings of alopecia secondary to infectious organisms are covered in the appropriate dermatology sections

TREATMENT
The clinical approach to alopecia is to identify the cause and, if the etiology is something that may benefit from pharmaceutical treatment, then therapy may resolve the clinical signs.

APPROPRIATE HEALTH CARE
Relevance equated to etiology; most require outpatient medical management.

NURSING CARE
Relevance equated to etiology.

ACTIVITY
Patients with multifocal to generalized hypotrichosis may be more susceptible to hypothermia and solar dermatoses.

DIET
Telogen effluvium has been associated with the administration of a feed supplement.

CLIENT EDUCATION
Relevance equated to etiology.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS
DRUG(S) OF CHOICE
- Varies with cause
- Dermatophytosis—lime sulfur or enilconazole, miconazole/chlorhexidine rinses; systemic griseofulvin
- Dermatophilosis—topical antimicrobial therapy
- Bacterial folliculitis—systemic and topical antimicrobial therapy
- Pemphigus foliaceus—immunosuppressive therapy
- There are no hair growth-promoting pharmaceuticals for horses

CONTRAINDICATIONS
N/A

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
None

ALTERNATIVE DRUGS
None

ALOPECIA (CONTINUED)

FOLLOW-UP

PATIENT MONITORING
Varies with cause.

PREVENTION/AVOIDANCE
- Varies with cause
- Patients with documented congenital alopecia and their parents should not be used for breeding

POSSIBLE COMPLICATIONS
N/A

EXPECTED COURSE AND PROGNOSIS
- Prognosis is based on whether the alopecia is classified as noncicatricial or cicatricial
- Cicatricial alopecia is characterized by permanent destruction of the hair follicles and regrowth of hair will not occur
- In noncicatricial alopecia, future hair growth will occur if the causative factors are eliminated or corrected
- Telogen and post-anagen effluvium resolve upon identification and elimination of cause

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
Dermatophytosis and dermatophilosis are zoonotic.

PREGNANCY/FERTILITY/BREEDING
- Postpartum telogen effluvium is thought to be due to the physiologic stress of pregnancy and lactation
- Avoid the use of griseofulvin to treat dermatophytosis in pregnant mares
- Mares that receive iodine-deficient diets give birth to weak or dead foals with no haircoat

SYNONYMS
- Alopecia = hypotrichosis
- Anagen effluvium = anagen defluxion or defluvium
- Telogen effluvium = telogen defluxion or defluvium

SEE ALSO
- Dermatophilosis
- Pemphigus foliaceus
- Sarcoid

Suggested Reading

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Author David Senter
Consulting Editor Gwendolen Lorch
Acknowledgment The author acknowledges the prior contribution of Gwendolen Lorch.

AMITRAZ TOXICOSIS

BASICS

OVERVIEW

• Amitraz, a formamide acaricide, is widely used for the control of mites and ticks in veterinary medicine
• Not approved for use in horses but intentional or accidental exposures have occurred
• Clinical signs are referable to the CNS or GI system
• Acts on α_2-adrenergic receptors in the CNS and on both α_1- and α_2-adrenergic receptors in the periphery. It is also believed to inhibit monaminoxidase, block prostaglandin E_2 synthesis, and cause a local anesthetic effect
• High doses cause depression while low doses result in hyperreactivity to external stimuli. Aggressive behavior possible
• Reduces smooth muscle activity in the GI tract
• Depresses respiratory rate centrally, probably by inhibiting respiratory neurons located in the ventral portion of the brain. α_2-Adrenergic agonists can accentuate amitraz-induced respiratory depression
• Inhibits antidiuretic hormone and thus may promote diuresis
• Induces hyperglycemia and hypoinsulinemia by inhibiting insulin secretion mediated by α_2-adrenergic receptors located within the pancreatic islets
• More slowly metabolized in ponies than in sheep, which may explain higher toxicity in equines

SIGNALMENT

N/A

SIGNS

Depression, ataxia, muscular incoordination, and impaction colic, which may persist for days. Facial swelling, tachypnea, and tachycardia have also been reported.

CAUSES AND RISK FACTORS

• Deliberate or accidental exposure for parasite control
• May be deliberately administered IV to alter performance in athletic horses due to its sedative/tranquilizing effects
• When in stored solutions, may break down to the highly toxic *N*-3,5-dimethylphenyl-*N*-methyl formadine derivative to more easily induce toxicosis
• No demonstrable adverse effects in a chronic low-dose toxicity study in horses

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Signs of colic can be due to many other disorders
• Signs of depression and ataxia can be due to viral encephalomyelitis, hepatoencephalopathy, meningitis, or brain abscess or tumor

CBC/BIOCHEMISTRY/URINALYSIS

• With acute intoxication, total protein and packed cell volume may increase due to dehydration and a mild acidosis may be seen
• Hyperglycemia and hypoinsulinemia result from inhibition of insulin release

OTHER LABORATORY TESTS

Drug-testing laboratories have methods for the detection of amitraz and its major metabolite in performance horses.

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

Experimental amitraz-treated horses had fecalith obstruction in the proximal small colon aboral to marked colonic impaction.

TREATMENT

• If dermal exposure to amitraz occurs, horses should be immediately bathed with soap and water to reduce further absorption
• If ingested, activated charcoal (1–4 g/kg PO in water slurry (1 g in 5 mL of water)) can be administered via nasogastric tube to reduce absorption
• Mineral oil per nasogastric tube may be used to manage feed impaction
• Oxygen and mechanical ventilation may be necessary if respiratory depression is severe
• IV or fluid therapy or fluids via nasogastric tube may be beneficial

MEDICATIONS

DRUG(S) OF CHOICE

• The α_2-adrenergic antagonists yohimbine and atipamezole are used for treatment of amitraz intoxication in dogs and cats, but their use has not been documented in horses
• Yohimbine has a high affinity for the α_2-adrenergic receptors α_2A, α_2B, and α_2C and a low affinity for the α_2D receptor. Yohimbine reverses amitraz-induced sedation in horses. A suggested dose for horses is 0.15 mg/kg IV slowly
• Atipamezole is a potent and selective α_2-adrenergic antagonist, is considered a new generation of α_2-adrenergic antagonists owing to its high selectivity for α_2-adrenergic receptors, like α_2A, α_2B, and α_2C receptors, and has a 100 times higher affinity for the α_2D receptor than yohimbine. Atipamezole is more efficacious in reversing amitraz toxicity in cats than yohimbine. A suggested dose for horses is 0.1 mg/kg IV
• Analgesics such as NSAIDs may be used to control GI pain

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Atropine is contraindicated due to the known sensitivity of horses to the anticholinergic effects on GI motility
• Adverse drug interactions are possible with xylazine, benzodiazepines, and macrocyclic lactones (e.g. ivermectin)

FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

The impaction colic effects of amitraz toxicosis may persist for days, but the prognosis is good with supportive treatment. Once the impaction resolves, some horses may experience diarrhea transiently.

MISCELLANEOUS

ABBREVIATIONS

• CNS = central nervous system
• GI = gastrointestinal
• NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Auer D, Seawright AA, Pollitt CC, et al. Illness in horses following spraying with amitraz. Aust Vet J 1984;61:257–259.
Queiroz-Neto A, Zamur G, Goncalves SC, et al. Characterization of the antinociceptive and sedative effect of amitraz in horses. J Vet Pharmacol Ther 1998;21:400–405.

Author Patricia M. Dowling
Consulting Editors Wilson K. Rumbeiha and Steve Ensley

A

AMMONIA, HYPERAMMONEMIA

BASICS

DEFINITION

• Free ammonia (NH_3) is a nonprotein nitrogen compound that can permeate cells and result in hyperammonemia. At physiologic pH, almost all blood ammonia is the ammonium ion (NH_4^+), which is less permeable for cells. In order to eliminate waste nitrogen as ammonia, mammals convert it to an excretable form—urea. To a lesser extent, ammonia is eliminated by conversion to glutamine
• Reference intervals for plasma ammonia concentrations are dependent on the type of assay and reported units. Hyperammonemia occurs when concentrations exceed the established laboratory reference intervals

PATHOPHYSIOLOGY

• The major source of blood ammonia is derived primarily from dietary nitrogen via the GI tract bacterial proteases, ureases, and amine oxidases
• Ammonia also may be derived from catabolism of glutamine and protein, and skeletal muscle exertion
• Ammonia is delivered to the liver via the portal vein or hepatic artery, where functional hepatocytes remove ammonia to form urea by means of the Krebs–Henseleit urea cycle
• Often, 70% of the liver mass has inadequate function before serum hyperammonemia is detected. If functional liver mass is inadequate, ammonia is not converted to urea, and plasma ammonia concentration increases. Urea concentrations also rise when glomerular filtration is inadequate. Acid–base status affects the absorption of ammonia
• As blood pH increases, free ammonia (NH_3) increases and can permeate cells via nonionic diffusion to produce toxicity. Ammonia is one of the compounds responsible for clinical signs of hepatic encephalopathy
• Hyperammonemia has a toxic effect on neuron cell membranes by inhibition of ATP and alteration of the tricarboxylic acid cycle; both lead to neuronal cell energy depletion
• Other neurotoxins in hepatic encephalopathy are the result of—alterations in monoamine neurotransmitters due to altered aromatic amino acids, increased activity of GABA, glutamate receptor alterations, and increased endogenous benzodiazepine-like substances. Additionally, GI-derived neurotoxins are implicated, such as mercaptans, short-chain fatty acids, and phenols

SYSTEMS AFFECTED

• Nervous—ammonia is neurotoxic and the brain is affected by high plasma concentrations
• The degree of hyperammonemia does not necessarily correlate with the severity of hepatic encephalopathy signs since other compounds are involved. Ammonia interferes with the blood–brain barrier, cerebral blood flow, cellular excitability, neurotransmitter metabolism, and ratios of neurotransmitter precursor amino acids
• Degenerative changes of the neurons and supporting cells have been observed in chronically affected animals

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

• Portacaval shunts have been reported in foals (rare)
• Ponies/donkeys (hepatic lipidosis)

SIGNS

General Comments

• Clinical signs of hyperammonemia are primarily those of hepatic encephalopathy, although this is not the only substance responsible for clinical signs
• Signs may be sporadic, progressive, and worsen after feeding

Historical Findings

Ptyalism, behavior changes, visual deficits (blindness), compulsive circling, pacing, anxiety, head pressing, stupor, coma, unusual positions/posture, sudden falling to the ground, violent thrashing.

Physical Examination Findings

Stunted growth, loss of body condition, poor hair coat, mentation changes and aberrant behavior. Similar findings as discussed in liver disease (e.g. icterus) may be observed, especially in horses with acute hepatitis. In animals affected chronically, neuronal degeneration occurs and signs become persistent.

CAUSES

• Liver disease resulting in inadequate functional mass. Hepatic encephalopathy is a prominent clinical feature of hepatic failure in the horse, and is associated with hepatitis and hepatic cirrhosis. Abnormalities of the urea cycle, abnormal portal blood flow, or any disorder that results in markedly impaired liver function can cause hyperammonemia
• Decreased functional hepatic mass can result from toxins such as pyrrolizidine alkaloids, excess iron, blue-green algae, mycotoxins, urea poisoning, ammonium salt fertilizers, and other hepatotoxic drugs or chemicals; infectious diseases such as Tyzzer's disease due to *Clostridium piliforme* in foals, virus-associated Theiler's disease; and syndromes including hyperlipidemia in ponies and occasionally in horses, with associated hepatic dysfunction
• Portosystemic shunts; acquired or congenital
• Intestinal hyperammonemia in the absence of liver disease is thought to occur when intestinal disease induces increased ammonia production by microflora and a concurrent increase in GI permeability

RISK FACTORS

• Horses in areas with hepatotoxic plants or toxins
• Administration of equine-derived biologics (e.g. plasma, tetanus anti-toxin)
• Feedstuffs contaminated with high levels of urea, nitrogen, ammonium salts, or mycotoxins
• Anorexia in overconditioned horses

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Primary neurologic diseases such as inflammatory, degenerative, infectious, or neoplastic CNS diseases. Rabies should be a differential diagnosis for abnormal behavior
• Behavior-based problems
• Possible intestinal bacterial overgrowth resulting in transient hyperammonemia (proposed)
• Differentiation consists of evaluating the history, signalment, and results of serum biochemistry, hematology, urinalysis, and hepatic biopsy

CBC/BIOCHEMISTRY/URINALYSIS

• CBC—microcytosis may occur in animals with portosystemic shunts, but may be difficult to determine in the horse; red blood cell histograms may be useful
• Ammonia is labile in blood samples, limiting the diagnostic use
• Biochemistry—liver enzymes may be normal in animals with portosystemic shunts, but bile acid concentrations and ammonia concentrations will be elevated. Usually, other biochemical abnormalities are present, indicating hepatic dysfunction if the liver disease is severe enough to produce hepatic encephalopathy. Finding elevated liver enzymes (sorbitol dehydrogenase, glutamate dehydrogenase, alkaline phosphatase, γ-glutamyltransferase, or aspartate aminotransferase) and hyperbilirubinemia, hypoglycemia (not common), hyper- or hypocholesterolemia, or low blood urea nitrogen suggestive of end-stage hepatic failure support a diagnosis of liver disease
• Urinalysis—ammonium biurate crystals and low urine specific gravity due to underlying liver disease in some animals

OTHER LABORATORY TESTS

• Measurement of serum bile acid concentrations has largely replaced ammonia assays due to convenience of sampling. Of note, generally bile acid samples in horses are obtained at one time point and postprandial bile acid measurements are not performed,

since horses have continuous bile acid secretion due to the lack of a gallbladder and a weak common bile duct sphincter
• Coagulation factor production may be decreased in liver failure, resulting in prolonged prothrombin time and partial thromboplastin time

IMAGING
Ultrasonographic evaluation of the liver and portal vessels is advised.

OTHER DIAGNOSTIC PROCEDURES
Hepatic biopsy can determine lesions leading to inadequate functional hepatic mass, such as fibrosis, dysplasia, or microvascular shunts. Prior coagulation assessment is advised.

PATHOLOGIC FINDINGS
• Decreased functional hepatic mass; decreased liver size; microhepatica
• Portosystemic shunt
• Degenerative changes of the neurons and supporting cells have been observed in chronically affected animals
• Lesions of cutaneous photosensitivity/dermatitis in some cases of hepatic failure

TREATMENT

APPROPRIATE HEALTH CARE
• Prevent signs associated with hepatic encephalopathy
• Fluid administration is needed to correct dehydration and maintain tissue perfusion. It is important to maintain normal plasma potassium concentrations because low plasma potassium may increase the intracellular movement of ammonia

NURSING CARE
See Appropriate Health Care.

ACTIVITY
Restrict activity.

DIET
Feed a very low protein diet, or fast the patient initially, and then institute a protein-restricted diet when the patient is stable.

CLIENT EDUCATION
Discussion of the prognosis.

SURGICAL CONSIDERATIONS
Correction of hepatic shunts.

MEDICATIONS

DRUG(S) OF CHOICE
• Lactulose is an acidifying agent used to decrease ammonia absorption from the intestine and lower plasma ammonia concentration in equine hyperammonemia. Lactulose acts as a cathartic laxative and maintains ammonia in its nonabsorbable ammonium ion form
• Antibiotics with a broad spectrum against intestinal flora have been used orally, such as the nonabsorbable aminoglycoside neomycin; however, neomycin is contraindicated in GI obstruction and can be nephrotoxic. Metronidazole has been used in horses with acute colitis, but caution should be used with this drug because decreased hepatic clearance can result in neurologic signs

CONTRAINDICATIONS
Any drugs that affect the CNS must be used with caution because of the common association of hyperammonemia with hepatic encephalopathy and possibly impaired hepatic metabolism. Barbiturates and benzodiazepine-like drugs are of particular concern.

PRECAUTIONS
• Sodium bicarbonate in fluids should be administered slowly, because rapid correction of acidosis may favor intracellular ammonia movement
• Ammonia tolerance testing is contraindicated in animals with baseline hyperammonemia

POSSIBLE INTERACTIONS
Because of impaired hepatic metabolism, any drugs that inhibit metabolism by the liver or are metabolized by the liver should be used with caution or the dosage should be adjusted.

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
Repeated assessment of plasma ammonia can be helpful. Monitoring of serum potassium and glucose concentrations is advised in critical patients.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Inaccuracy due to the labile nature of ammonia in blood samples. Delay in processing results in falsely elevated readings of ammonia concentration.

EXPECTED COURSE AND PROGNOSIS
Guarded prognosis for most causes of hyperammonemia.

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Congenital hepatic shunts are found in young animals versus acquired shunts that may occur at various ages.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

SEE ALSO
• Bile acids
• Hepatic encephalopathy
• Icterus (prehepatic, hepatic, posthepatic)
• Toxic hepatopathy

ABBREVIATIONS
• CNS = central nervous system
• GABA = γ-aminobutyric acid
• GI = gastrointestinal

Internet Resources

Cornell University College of Veterinary Medicine, Ammonia. http://www.eclinpath.com/chemistry/liver/liver-function-tests/ammonia

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Author Claire B. Andreasen
Consulting Editor Sandra D. Taylor

AMYLASE, LIPASE, AND TRYPSIN

BASICS

OVERVIEW

• Serum amylase or lipase concentrations above laboratory reference interval in horses are suggestive of pancreatic disease
• Pancreatic disease and panniculitis (inflammation of adipose tissue) are rare in horses
• Reference range for serum activity of amylase and lipase are <35 IU/L and <87 IU/L, respectively
• Amylase and lipase are rarely measured in routine equine serum biochemical profiles
• Trypsin is released from damaged pancreatic cells

Pathophysiology

• Amylase in blood comes from a number of sources, including intestinal mucosa, liver, and pancreas
• Amylase is cleared from the blood by the kidneys, so renal dysfunction could lead to higher concentrations remaining in the blood
• Damage to pancreatic cells can cause leakage of amylase into the blood or peritoneal fluid, but this is not common in the horse
• Lipase is derived from the pancreas, gastrointestinal mucosa, and other tissues. Clinical serum assays detect all forms of lipase
• Although uncommon in the horse, damage to pancreatic cells can cause release of lipase into the blood or peritoneal cavity
• Panniculitis can result in abnormally high serum activity of amylase and lipase. This disease is often associated with pancreatitis
• Increased activity of trypsin in blood is a result of leakage from damaged pancreatic cells, usually in horses with colic

Systems Affected

Pancreas, peritoneum, peripheral adipose tissue.

SIGNALMENT

N/A

SIGNS

Varies with underlying cause:
• Pancreatitis—colic, gastric reflux, tachycardia, and signs of hypovolemic shock
• Hyperlipemia—depression, anorexia, lipemic serum
• Panniculitis—possible colic

CAUSES AND RISK FACTORS

• Proximal duodenitis-jejunitis (proximal enteritis) enteritis
• Hyperlipemia
• Glucocorticoid administration
• Heparin-induced lipoprotein lipase activity
• Obstruction to common bile and pancreatic ducts
• Renal disease
• Pancreatitis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Colic with small intestinal distention should lead a clinician to suspect inflammation and obstruction of the small intestine rather than pancreatic inflammation, although colic and ileus can be caused by peritonitis secondary to pancreatitis
• In a pony, donkey, or miniature horse, hyperlipemia should be considered

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

N/A

Disorders That May Alter Laboratory Results

• Hemolysis inhibits lipase activity
• Lipemia falsely decreases serum lipase activity measured by kinetic assays

CBC/BIOCHEMISTRY/URINALYSIS

• Peritoneal fluid amylase and lipase activities are usually less than those in blood except in pancreatitis
• GGT is concentrated in the pancreas as well as the liver, so increased serum activity could indicate pancreatitis as well as hepatitis or cholestasis, or elevations of GGT could be secondary to the proximity of the bile duct to an inflamed pancreatic duct

OTHER LABORATORY TESTS

• Serum triglyceride >500 mg/dL indicates hyperlipemia, and can interfere with insulin's ability to inhibit hormone-sensitive lipase and thus, increase lipolysis
• Nonesterified fatty acid concentrations >0.5 mEq/L could indicate hyperlipemia due to fat mobilization and can interfere with insulin's ability to inhibit hormone-sensitive lipase, thus increasing lipolysis
• Abdominocentesis to compare peritoneal fluid amylase and lipase concentrations with serum concentrations. Peritoneal fluid concentrations of amylase and lipase greater than serum concentrations suggest pancreatitis, but this also can be a nonspecific finding of peritonitis/serositis

DIAGNOSTIC PROCEDURES

Exploratory celiotomy may be indicated in cases of colic with undiagnosed causes of continued pain or indications of small intestinal obstruction. Abdominal fluid analysis should precede this invasive procedure.

TREATMENT

Dependent on the underlying cause.

MEDICATIONS

DRUG(S) OF CHOICE

Dependent on the underlying cause. There is no specific treatment for pancreatitis or panniculitis in horses.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

FOLLOW-UP

PATIENT MONITORING

• Repeat measurements of blood and peritoneal fluid amylase, lipase, and trypsin
• Observe frequently for signs of colic

POSSIBLE COMPLICATIONS

• Small intestinal obstruction, pancreatitis, and hyperlipemia can cause death
• Leakage of amylase and lipase into the peritoneal cavity can induce nonseptic peritonitis

MISCELLANEOUS

SEE ALSO

• Acute adult abdominal pain—acute colic
• Hyperlipidemia/hyperlipemia

ABBREVIATIONS

GGT = γ-glutamyltransferase

Suggested Reading

Parry BW, Crisman MV. Serum and peritoneal fluid amylase and lipase reference values in horses. Equine Vet J 1991;23: 390–391.
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Author Jenifer R. Gold
Consulting Editor Sandra D. Taylor
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ANAEROBIC BACTERIAL INFECTIONS

BASICS

DEFINITION

Caused by bacteria that live and grow in the absence of molecular oxygen. Facultative—growing with or without oxygen; obligate (discussed here)—growing without oxygen.

PATHOPHYSIOLOGY

Dermal and mucosal surfaces serve as protective barriers to infection. A breach in this protective barrier allows normal flora or commensal bacteria to gain access and potentially allows an infection to become established. Contamination of a wound or an injection site by environmental organisms may lead to infection. Anaerobic organisms establish invasion through virulence factors, and release of enzymes and toxins. Anaerobic infections develop primarily in body sites where there is low oxygen tension, a low redox potential, or both.

SYSTEMS AFFECTED

Upper Respiratory Tract

• Apical abscesses. • Sinusitis. • Pharyngeal abscesses

Lower Respiratory Tract

• Pneumonia. • Pulmonary abscesses. • Pleuropneumonia

GI

• Sialadenitis. • Peritonitis. • Abdominal abscesses. • Enteritis. • Colitis

Musculoskeletal

• Soft tissue abscesses. • Foot abscesses. • Thrush. • Canker. • Osteomyelitis. • Sequestra. • Septic arthritis. • Clostridial myonecrosis

Neuromuscular

Primarily affected by the toxins of these bacteria

Vascular

• Omphalophlebitis/omphalitis. • Thrombophlebitis

Hematopoietic

Sepsis

Reproductive

Metritis

Ophthalmic

• Ulcerative keratitis. • Stromal abscess

GEOGRAPHIC DISTRIBUTION

Worldwide distribution.

SIGNS

Variable depending on what system and organism is involved.

Upper Respiratory Tract

• Nasal discharge. • Facial swelling and crepitation. • Malodorous exudates

Lower Respiratory Tract

• Cough. • Nasal discharge. • Malodorous breath, pleural fluid. • Fever. • Inappetence. • Abnormal lung sounds. • Lethargy

GI

• Dysphagia. • Abdominal discomfort. • Fever. • Diarrhea. • Inappetence. • Reflux

Musculoskeletal

• Swollen and painful muscles or joints. • Lameness. • Fever. • Crepitation over swollen muscles

Vascular

• Swollen and painful umbilicus. • Fever. • Lethargy. • Inappetence. • Swollen, hard, painful veins

Hematopoietic

• Fever. • Depression. • Tachycardia, ± arrhythmias. • Tachypnea, ± dyspnea. • Mucous membrane alterations. • Laminitis. • Abdominal discomfort

Reproductive

• Vaginal discharge. • Fever. • Lethargy. • Endotoxemia

Ocular

• Blepharospasm. • Epiphora. • Corneal opacity

CAUSES

The most common bacterial species involved in anaerobic infections include: • *Bacteroides* spp. • *Clostridium* spp. • *Fusobacterium* spp. • *Peptostreptococcus* spp. • *Prevotella* spp. • *Eubacterium* spp.

RISK FACTORS

Concurrent diseases, wounds, corticosteroid therapy, antibiotic therapy, immunosuppression, leukopenia, tissue anoxia, prior or concurrent aerobic infections, presence of a foreign body.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Upper Respiratory Tract

• Aerobic infection (*Streptococcus* spp., *Staphylococcus* spp.). • Fungal infection (*Cryptococcus neoformans, Coccidioides immitis*). • Granuloma. • Neoplasia (anaerobes may proliferate in necrotic neoplastic tissues)

Lower Respiratory Tract

• Aerobic infection (*Streptococcus* spp., *Staphylococcus* spp., *Escherichia coli*, *Klebsiella, Pasteurella, Bordetella* spp.). • Fungal infection (*Coccidioides, Cryptococcus, Histoplasma, Aspergillus, Candida* spp.). • *Mycoplasma* infection. • Thoracic trauma. • Esophageal rupture. • Neoplasia

GI

• Peritonitis—aerobic infection (*Streptococcus* spp., *E. coli*), neoplasia. • Abdominal abscesses—aerobic infection (*Streptococcus* spp., *Rhodococcus equi, Corynebacterium pseudotuberculosis*), neoplasia, granuloma. • Enteritis/colitis—*Salmonella* spp., Potomac horse fever, idiopathic, parasitic, antibiotic associated, NSAID drug toxicity, fungal infection. • Sialadenitis—botulism, oral foreign body, dental disease

Musculoskeletal

• Aerobic infection (*Staphylococcus aureus*, *Corynebacterium pseudotuberculosis*). • Fungal infection. • Neoplasia

Vascular

Aerobic infection (*Streptococcus* spp., *E. coli, Proteus* spp.).

Hematopoietic

Aerobic infection (*Streptococcus* spp., *Staphylococcus* spp., *E. coli, Actinobacillus* spp., *Salmonella* spp., *Klebsiella* spp.).

Reproductive

• Aerobic infection (*Streptococcus zooepidemicus, E. coli, Klebsiella* spp., *Staphylococcus* spp., *Proteus* spp., *Pseudomonas* spp., *Corynebacterium* spp.). • Fungal infection (*Candida* spp.). • Neoplasia

Ocular

Other causes of ulcerative keratitis, e.g. aerobic bacteria, fungi, viruses, immune mediated.

CBC/BIOCHEMISTRY/URINALYSIS

• Inflammatory leukogram. • Hyperfibrinogenemia, increased serum amyloid A concentration. • Elevated total protein. • ± Anemia of chronic disease. • Blood chemistry is usually normal unless there is secondary systemic involvement or severe disease

OTHER LABORATORY TESTS

• Direct cytology—all aspirated fluids should be Gram stained. • Anaerobic culture—aspirates/tissue specimens must be placed in the appropriate anaerobic bacterial transport medium and stored at room temperature with minimal exposure to oxygen. • Fluorescent antibody testing. • Direct immunofluorescence testing

IMAGING

• Radiographs of the affected anatomic region revealing abscessation, fluid line, areas of consolidation, or lytic bone changes. • Sonograms of the affected anatomic region revealing gas echoes, fluid, abscessation, areas of consolidation, or masses

PATHOLOGIC FINDINGS

Lesions are characterized by necrotic, edematous, emphysematous, and hyperemic tissues. Neutrophils, monocytes, and macrophages may accumulate in the tissue architecture, with bacteria interspersed.

ANAEROBIC BACTERIAL INFECTIONS (CONTINUED)

TREATMENT

AIMS
Elimination of infection—effective antimicrobial therapy, exposure to oxygen, drainage of purulent exudates, and debridement of necrotic tissue.

APPROPRIATE HEALTH CARE
• Initial hospitalization for intensive therapy, antimicrobials, and debridement/drainage.
• Hyperbaric oxygen therapy has been anecdotally utilized in areas with extensive tissue necrosis

NURSING CARE
Care may include staged debridement, frequent hot compress therapy, and/or bandaging. Intensive care of indwelling tubes for constant drainage of body cavities may be required. Supportive care includes IV fluids and/or total/partial parenteral nutrition.

ACTIVITY
Most likely decreased or restricted and will depend on the body system affected.

CLIENT EDUCATION
Some cases may be life-threatening depending on the extent of the illness and complications may arise. In cases with severe muscle necrosis requiring debridement or fasciotomies, a cosmetic appearance may not be likely.

SURGICAL CONSIDERATIONS
Surgery may be necessary to perform fasciotomies, to debride necrotic tissue, or to graft skin on large areas that sloughed tissue during active infection. Surgery may also be required for the placement of an indwelling catheter to allow for lavage and flushing.

MEDICATIONS

DRUG(S) OF CHOICE

Penicillin
First line of defense against anaerobic infections. Excellent activity against most anaerobic infections, except beta-lactamase-producing *Bacteroides*. Preferred drug for clostridial infections. Dose 22 000–44 000 IU/kg QID IV (aqueous) or BID IM (procaine).

Ampicillin
Comparable to penicillin in its spectrum. Dose 25–100 mg/kg IV QID.

Metronidazole
Consistently effective against obligate anaerobes including *Bacteroides fragilis*; not effective against facultative anaerobes or aerobes. Rapid oral absorption (bioavailability 75–85%). Distributes well into synovial fluid, peritoneal fluid, cerebrospinal fluid, and urine; poor endometrial concentrations. Use orally in cases of diarrhea caused by *Clostridium* spp. Per rectum to horses that are anorexic or are refluxing (bioavailability 30%). Dose 15–25 mg/kg PO, IV, or per rectum QID–TID.

Tetracyclines
Can be used for anaerobic infections but penicillin-resistant *Bacteroides* spp. are demonstrating tetracycline resistance. Dose of oxytetracycline 5–7.5 mg/kg IV BID. Doxycycline is effective against most anaerobes, but, as with oxytetracycline, resistance to *Bacteroides* spp. is common. Dose 10–20 mg/kg PO BID. Higher doses have been associated with fatal colitis.

Chloramphenicol
All obligate anaerobes are susceptible. It has good tissue penetration into central nervous system, peritoneal, pleural, and synovial fluids. Absorption decreases with repeated oral administration; the result is lower concentrations with subsequent doses. Dose 45–60 mg/kg PO TID–QID.

Cephalosporins
In general, variable efficacy against most anaerobes for both ceftiofur and cefquinome.

Rifampin (rifampicin)
Usually not necessary in most anaerobic infections but it may be useful in polymicrobial infections in walled-off abscesses. Most strains of *Bacteroides* and *Clostridium* are sensitive to rifampin. Dose 5 mg/kg PO BID.

Trimethoprim–sulfonamides (TMS)
Trimethoprim and sulfa combinations are effective against some obligate anaerobes. Activity is unpredictable. Dose 30 mg/kg BID PO.

CONTRAINDICATIONS
Static drugs such as chloramphenicol are not recommended for immunocompromised patients.

PRECAUTIONS
Chloramphenicol can cause the development of aplastic anemia rarely in humans. Oral administration of metronidazole may cause anorexia but resolves when the drug is discontinued, or with mouth washes after treatments.

POSSIBLE INTERACTIONS
Chloramphenicol may affect the metabolism of other drugs.

FOLLOW-UP

PATIENT MONITORING
Response to therapy can be noted by monitoring changes in clinical signs. Hematologic and sonographic evaluations also help to establish the patient's response to therapy.

PREVENTION/AVOIDANCE
IM injections have been reported to cause severe necrotizing myonecrosis; avoid giving these injections of irritating drugs if possible or monitor injection sites closely after administration. Provide proper and immediate treatment of wounds to help prevent anaerobic infections.

POSSIBLE COMPLICATIONS
Severe infections may result in severe tissue sloughing, laminitis, endotoxemia, or death.

EXPECTED COURSE AND PROGNOSIS
Depends on the body system affected and the severity of the disease.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Depends on the body system affected and the severity of the disease.

PREGNANCY/FERTILITY/BREEDING
Infection of the reproductive tract may result in breeding and conception problems.

ZOONOTIC POTENTIAL
Bacteria can cause disease in both humans and horses, but no direct transmission is likely unless there is severe immunocompromise or contamination of an open wound.

SEE ALSO
• Botulism
• Clostridial myositis
• Tetanus

ABBREVIATIONS
• GI = gastrointestinal.
• NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Moore RM. Diagnosis and treatment of obligate anaerobic bacterial infections in horses. Compend Contin Educ Pract Vet 1993;15(7):989–994.

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Author Imogen Johns
Consulting Editor Ashley G. Boyle
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ANAPHYLAXIS

BASICS

DEFINITION
• Anaphylactic shock is an immediate (type 1) hypersensitivity reaction that is systemic and life-threatening
• Anaphylactoid reactions, which are not a hypersensitivity, may induce similar clinical signs and outcomes

PATHOPHYSIOLOGY
• Exposure to antigens (allergens) can result in synthesis of antigen-specific IgE
• IgE binds to, and sensitizes, tissue mast cells or circulating basophils
• Reexposure to antigen results in release of substances from sensitized cells that mediate type 1 hypersensitivities and, in severe cases, anaphylaxis
• Sensitization occurs ~10 days after first exposure, but can persist for years
• Anaphylactoid reactions usually involve activation of the complement system and degranulation of mast cells or basophils. These reactions do not require previous exposure and host sensitization with IgE

SYSTEMS AFFECTED
• Shock organs of the horse are the respiratory and gastrointestinal tracts
• The skin and hemic systems may also be involved

GENETICS
High levels of IgE are associated with certain ELA-DRB haplotypes.

INCIDENCE/PREVALENCE
Prevalence unknown, but 16% of blood transfusions reported allergic reactions in one study, and 6–10% of adverse drug reactions are reported to be allergic.

SIGNALMENT
There is no breed, sex, or age predilection.

SIGNS
General Comments
Mild, moderate, or severe clinical signs may occur depending on the dose and route of antigen challenge, organ system involved, and individual inflammatory responses of the patient.

Historical Findings
Possible exposure to antigens and/or agents associated with anaphylaxis.

Physical Examination Findings
• Mild cases may present with urticaria and rhinitis; moderate cases with angioedema, diarrhea, sweating, and colic; severe reactions with dyspnea and respiratory distress, tachypnea, pulmonary emphysema, coughing, hypotension, and collapse
• Pale mucous membranes, poor peripheral pulses, and cold extremities may be associated with cardiovascular collapse

CAUSES
• A wide range of antigens or agents may induce anaphylaxis or anaphylactoid reactions
• Reactions can occur at any time, including, rarely, after the first exposure to highly charged or osmotically active agents (e.g. iodinated radiocontrast medium, dextran)
• Implicated agents include insect venom, vaccines, whole blood or blood products, antimicrobials, anthelmintics, thiamine, vitamins (B, K, E/selenium), iron, copper, halothane, thiamylal, and guaifenesin, or inadvertent injection of products, e.g. milk
• The sensitizing agent is often not identified

RISK FACTORS
• Prior exposure to potential allergens
• Previous anaphylactic reactions
• Repeated parenteral administration of the same biologic preparation at high doses

DIAGNOSIS

• Diagnosis largely based on history and classical clinical presentation
• A *rule of twos* states that reactions begin from 2 min to 2 h following injection, infusion, ingestion, contact, or inhalation
• Response to treatment may support the diagnosis

DIFFERENTIAL DIAGNOSIS
• Acute pneumonia may resemble anaphylaxis, but horses are usually more toxemic and lung changes are prominent in ventral lobes compared with widespread involvement with anaphylaxis
• An inappropriate dose or route of drug administration (such as intracarotid injection) may result in collapse associated with neurologic deficits (e.g. blindness, seizures)

CBC/BIOCHEMISTRY/URINALYSIS
Hemoconcentration, leukopenia, thrombocytopenia, hyperkalemia, increases in hepatic and myocardial enzyme activities, and coagulation deficits are reported, although diagnostic relevance is uncertain.

OTHER LABORATORY TESTS
N/A

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
Provocative intradermal/conjunctival challenge testing with the suspected antigen may help confirm diagnosis, but value is questionable due to high rate of false negatives and risk of inducing anaphylaxis.

PATHOLOGIC FINDINGS
• Severe, diffuse pulmonary emphysema, and peribronchiolar edema at necropsy
• Widespread petechiae, edema, and extravasation of blood in the wall of the large bowel, subcutaneous edema, congestion of the kidney, spleen, and liver, and evidence of laminitis

TREATMENT

AIMS
Immediate steps include (1) stop exposure to trigger if possible; (2) rapid assessment of patient status; (3) secure airway and check vital parameters; and (4) perform tracheotomy if necessary (e.g. respiratory distress).

APPROPRIATE HEALTH CARE
In severe cases, early recognition of clinical signs and immediate steps are critical for patient survival.

NURSING CARE
Oxygen Therapy
• High-flow oxygen therapy is indicated during systemic anaphylaxis to help improve tissue oxygenation
• Recommended flow rates are 5–10 L/min for foals and 10–15 L/min for adults directly into the nasal passage

Fluid Therapy
• Horses that remain hypotensive following epinephrine treatment should receive fluid therapy
• Crystalloids and colloid fluids may help restore intravascular fluid volume, cardiac output, and aerobic metabolism. Careful monitoring is required to evaluate for worsening of tissue edema that accompanies anaphylaxis, especially the upper airways, lungs, and neural tissues
• Volumes of crystalloids recommended in foals is 50–80 mL/kg divided into separate bolus doses; for adults 10–20 mL/kg/h
• Hypertonic (7.2%) saline solution may also be used in adult horses exhibiting shock at 2–4 mL/kg simultaneously with crystalloid fluids
• As a general rule ~10 L of crystalloids should be provided over time for each liter of hypertonic saline

DIET
• Oral intake should be discontinued until recovery from an anaphylactic event
• Diet should be evaluated to determine if components are potential cause of anaphylactic reaction

SURGICAL CONSIDERATIONS
Nasotracheal intubation or tracheotomy if severe respiratory distress to secure the airways prior to epinephrine treatments.

MEDICATIONS

DRUG(S) OF CHOICE
• Epinephrine is the most effective treatment for systemic anaphylaxis and shock

A

ANAPHYLAXIS (CONTINUED)

• Epinephrine should be administered immediately upon recognition of signs, even if there is doubt, and simultaneously during patient assessment
• In adult horses, recommended dose is 0.01 mg/kg of a 1:1000 dilution slowly IV, or 0.02 mg/kg IM when dyspnea and hypotension are mild
• When IV access is not possible, a higher dose may be administered via the intratracheal route (20 ml/450 kg horse)
• In foals 0.01–0.02 mg/kg given slowly IV is recommended
• Additional medications may be considered for severe cases, or for localized reactions

Vasopressors

• Vasopressors should be considered for horses with persistent hypotension refractory to epinephrine and volume replacement
• Dobutamine (50 mg diluted in 500 mL of 5% dextrose solution; 100 µg/mL; using 5–10 µg/kg/min over 10–20 min), dopamine (titrated as a continuous infusion at 1–20 µg/kg/min), norepinephrine (0.1–1.5 µg/kg/min), and vasopressin (0.01–0.04 µg/kg/min as a constant infusion for refractory hypotension or 0.3–0.6 µg/kg as a single dose for cardiovascular collapse)
• Drugs should be titrated to maintain a mean arterial blood pressure > 60–70 mmHg
• Cardiac monitoring is recommended as arrhythmias may develop

Bronchodilators

• May be used in horses exhibiting bronchospasm resistant to epinephrine
• Inhalation therapy with β_2-agonists (e.g. albuterol) (every 3–4 h via an inhaler; 720 µg or 8 puffs at 90 µg/puff) or nebulization (2–5 mL of a 0.5% solution diluted in sterile saline)

Furosemide

Furosemide (1 mg/kg IV) is indicated in horses with pulmonary edema.

Antihistamines

• Antihistamines may be used to control clinical signs such as urticaria and pruritus
• If cardiovascular status of horse is stable doxylamine succinate (0.5 mg/kg slowly IV or IM), pyrilamine maleate (1.0 mg/kg slowly IV, IM, or SC), tripelennamine hydrochloride (1 mg/kg IM not IV), or hydroxyzine hydrochloride (1–1.5 mg/kg PO) may be administered every 6-12 h

Glucocorticoids

• Systemic glucocorticoids are not useful in the acute phase, but are indicated to halt progressive inflammation, prevent recurrence of anaphylaxis, and prevent late-phase or protracted reactions
• Dexamethasone (0.2–0.5 mg/kg IV) is used for treating rapidly progressing edema
• Prednisolone sodium succinate (0.25–10 mg/kg IV) is preferred for systemic reactions
• Prednisolone (0.4–1.6 mg/kg PO SID) may be used for managing persistent urticaria

CONTRAINDICATIONS

The use of equine plasma and dextrans is contraindicated in anaphylaxis treatment owing to concerns with induction of subsequent anaphylactic events.

PRECAUTIONS

• Epinephrine may increase the risk of arrhythmia
• Dobutamine potentiates hypoxemia-induced cardiac arrhythmias
• Glucocorticoid administration has been associated with laminitis
• If antihistamines are given, slow IV administration is recommended to avoid adverse effects

POSSIBLE INTERACTIONS

Antihistamines enhance the effects of epinephrine on vascular resistance and, therefore, should be used separately.

ALTERNATIVE DRUGS

N/A

FOLLOW UP

PATIENT MONITORING

Biphasic, multiphasic, or protracted anaphylactic episodes may occur after the primary event despite therapy.

PREVENTION/AVOIDANCE

• Avoidance of known allergens/antigens
• If avoidance is not possible, pretreatment with flunixin meglumine and antihistamines or corticosteroids and antihistamines may be warranted
• Allergen-specific IgE testing may aid in detecting sensitivity to agents and facilitate avoidance
• Desensitization procedures have not been well documented in horses
• In horses with suspected drug reactions avoid drugs with immunologic or biochemical similarity
• Oral therapy versus parenteral should be considered if drug is required
• Horses with known history of anaphylaxis should be monitored for 20–30 min after giving agents of unknown sensitivity
• Cross-matching prior to transfusions may decrease risk of anaphylaxis
• Adverse reactions to procaine penicillin G are less likely with avoidance of repeated injected sites, slow drug administration, and proper drug storage. Reaction is more likely due to the excitatory effects of unbound procaine than anaphylaxis

POSSIBLE COMPLICATIONS

Complications can include laminitis, purpura haemorrhagica, subcutaneous edema, hemolytic anemia, and hemorrhagic colitis.

EXPECTED COURSE AND PROGNOSIS

• Prognosis depends on type and severity of the event; speed of disease onset and recognition by owners/veterinarians; response to treatment; and development of complications
• Local reactions are rarely life-threatening and the prognosis will largely reflect response to treatment
• Severe systemic reactions carry a considerable risk of death
• The risk of death increases when recognition of a systemic response, or subsequent emergency treatment, is delayed

MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

None

SEE ALSO

Blood and plasma transfusion reactions

ABBREVIATIONS

Ig = immunoglobulin

Suggested Reading

Radcliffe RM. Anaphylaxis. In: Felippe MJB, ed. Equine Clinical Immunology. Ames, IA: Wiley Blackwell, 2016:31–38.

Author Jennifer L. Hodgson
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson

BASICS

DEFINITION
Decreased erythrocyte count or hemoglobin content as a consequence of a decrease in PCV, RBC count, or Hb concentration.

PATHOPHYSIOLOGY
- Anemia results from 1 or more of the following:
  - Blood loss (internal or external hemorrhage)
  - Increased RBC destruction (intravascular or extravascular hemolysis)
  - Decreased or ineffective RBC production
- Characterization of anemia (regenerative vs. nonregenerative) is best done by examining bone marrow aspirates. Serial monitoring of PCV and plasma TP concentration may be useful
  - Evaluation of immature RBCs and RBC indices in peripheral blood is unrewarding in horses, even during intense erythropoiesis
- The circulating RBC mass varies due to the effects of breed, age, activity, and splenic contraction, which can increase the RBCs by ~50%
- Nonregenerative anemia occurs when the rate of erythropoiesis is insufficient to replace aged RBCs, and develops slowly due to the long lifespan of equine RBCs (≈ 150 days)
- Mechanisms associated with nonregenerative anemia include:
  - Diseases interfering with erythropoiesis (↓ erythrocyte life span or ↓ erythropoietin responsiveness)
  - Deficiency or alterations in substances necessary for RBC production
  - Diseases that damage or displace bone marrow elements and affect RBC precursors and/or all marrow precursors

SYSTEMS AFFECTED
Decreased circulating RBC mass, decreased oxygen-carrying capacity, and reduced blood viscosity are the main consequences of anemia, but severity is dependent on the magnitude and rate of development of anemia.

GENETICS
Hereditary disorders of hemostasis may contribute to blood loss anemia.

INCIDENCE/PREVALENCE
Dependent upon etiology.

GEOGRAPHIC DISTRIBUTION
See Anemia, Heinz body.

SIGNALMENT
There is no breed, sex, or age predilection.

SIGNS
General Comments
Clinical signs relate to the compensatory mechanisms activated in response to anemia as well as the primary disease process (often more prominent).

Historical Findings
- Dependent upon primary disease process
- Most common presenting complaints are exercise intolerance, signs of depression, and inappetence

Physical Examination Findings
- Horses with chronic anemia may be subclinical, but exercise may induce exaggerated tachycardia, weakness, and reduced performance
- In acute or severe cases, tachycardia, tachypnea, and low-grade holosystolic heart murmur are present at rest
- Pale mucous membranes
- Other signs depend on the primary disease process and may include:
  - Icterus, fever, and pigmenturia (hemolysis)
  - Weight loss, polyuria, and polydipsia (chronic renal failure)
  - Weight loss, fever, and lethargy (chronic infectious, inflammatory, neoplastic, or immune-mediated processes)

CAUSES
Hemorrhage
External hemorrhage, epistaxis, hemothorax, hematuria, hemoperitoneum, GI hemorrhage, or coagulopathy.

Hemolysis
- Immune-mediated disease (secondary immune-mediated anemia, autoimmune hemolytic anemia or NI)
- Infectious diseases (piroplasmosis, anaplasmosis, and EIA)
- Oxidant induced (red maple, phenothiazines, and wild onions)
- Iatrogenic (hypotonic or hypertonic IV solutions)
- Other toxicities (IV DMSO, heavy metal toxicosis, bacterial toxins, snake bite)
- Miscellaneous (endstage hepatic disease, hemolytic uremic syndrome, hemangiosarcoma, and disseminated intravascular coagulation)

Nonregenerative Anemia
- Anemia of chronic disease associated with infectious, inflammatory, neoplastic, or endocrine disorders
- Iron deficiency due to chronic hemorrhage or nutritional deficiency
- Bone marrow failure (myelophthisis, myeloproliferative disease, bone marrow toxins, radiation, immune mediated)
- Miscellaneous (chronic renal disease, chronic hepatic disease, or recent hemorrhage/hemolysis)

RISK FACTORS
- Dependent on risk factors for the primary disease process
- Age (e.g. neoplasia, middle uterine artery rupture) and sex (e.g. idiopathic urethral hemorrhage in geldings)
- Any infectious or inflammatory disease
- Foals consuming incompatible colostrum are at risk for NI
- Inadequate preventative anthelmintic use or long-term high-dose NSAID administration
- Geographic location for exposure to infectious agents or toxic plants

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
- Identification of the basic mechanisms involved, using historical, clinical, hematologic, and biochemical findings
- Severe hemorrhage or hemolysis should be suspected with sudden onset of clinical signs or a history of trauma
- Chronic nonregenerative anemia secondary to infectious, inflammatory, or neoplastic conditions may be associated with fever and weight loss
- Laboratory error may result in a falsely low PCV or RBC count and falsely high MCH and MCHC

CBC/BIOCHEMISTRY/URINALYSIS
- PCV, RBC count, and (except in IV hemolysis) Hb concentrations below the lower limit of reference intervals
- Reticulocytes, nucleated RBCs, Howell–Jolly bodies, polychromasia, anisocytosis, and RBC indices are less useful for classification of anemia in horses
- A moderate increase in MCV (hemolytic anemia) and red cell distribution width (hemorrhagic anemia) may occur 2–3 weeks after onset of regenerative anemia
- Increased MCH values may indicate free Hb (hemolysis) while decreased MCH, MCHC, and mean cell volume may indicate iron deficiency anemia
- Heinz bodies may be observed with hemolytic anemia due to oxidative injury
- Rouleaux formation may complicate recognition of autoagglutination in immune-mediated hemolytic anemia
- Neoplastic cells may be observed in blood smears with myeloproliferative disorders
- Severe neutropenia and thrombocytopenia may accompany myelophthisis
- Blood loss usually results in concomitant decreases in PCV and TP
- Hemolytic anemia usually results in decreased PCV, normal TP, and marked increases in serum total direct bilirubin concentration with normal liver enzymes
- Nonregenerative anemia due to inadequate erythropoiesis may be accompanied by normal or increased TP (due to increased globulin and fibrinogen concentrations) and an inflammatory leukogram

OTHER LABORATORY TESTS
- Positive direct Coombs test is evidence for immune-mediated hemolytic anemia

ANEMIA (CONTINUED)

• Microscopic examination of blood diluted with saline (1:4) aids in differentiating autoagglutination from rouleaux formation in horses with immune-mediated hemolytic anemia
• Serum Fe concentration usually is increased, total iron-binding capacity usually decreased, and storage iron usually increased in horses with anemia of chronic disease
• Serum iron concentration, percentage saturation of transferrin, and storage iron usually are decreased, while total iron-binding capacity usually is increased in iron deficiency anemia
• Coggins or C-ELISA test for diagnosis of EIA
• Serology for *Babesia, Theileria*, or *Anaplasma phagocytophilum*
• Identification of organisms in blood smears

IMAGING
As indicated for underlying disease processes.

OTHER DIAGNOSTIC PROCEDURES
• Bone marrow aspiration and core biopsy may show increased erythropoiesis and a decreased M:E ratio in horses with regenerative anemia or may reveal decreased erythropoiesis and an increased M:E ratio with nonregenerative anemia. Infiltration with abnormal cell types may be observed in myelodysplasia or myeloproliferative disorders
• Abdominocentesis or thoracocentesis to detect internal hemorrhage
• Fecal occult blood to detect GI hemorrhage, but this test lacks sensitivity and specificity
• Endoscopy to assist in detecting respiratory or GI hemorrhage

PATHOLOGIC FINDINGS
Associated with primary disease.

TREATMENT

AIMS
Aims of therapy are identification and elimination of primary cause of anemia, nursing care, minimizing physiologic stress, ensuring adequate tissue perfusion, and administering blood transfusions if indicated.

APPROPRIATE HEALTH CARE
• Large-volume isotonic or small-volume hypertonic saline fluid therapy if there are signs of hemorrhagic shock
• Whole blood or packed RBC transfusion if PCV decreases to < 8–12%, although transfusion may be required despite higher PCV (~20%) in cases of acute blood loss
  ◦ Cross-matching is strongly recommended, particularly if the patient has received previous transfusions or has been pregnant
  ◦ If cross matching is not possible a known Aa/Qa-negative donor should be used, if available
  ◦ If a typed donor is not available then a gelding of the same breed that has never received a transfusion may be a reasonable alternative

NURSING CARE
• Close monitoring of vital signs, serial determination of PCV and TP, and adjustment of infusion rate are essential in horses receiving fluid therapy
• Monitor for renal failure induced by hemoglobinuria or hypoxia

ACTIVITY
• Horses with lethargy, intolerance to mild exercise, or a PCV < 15% should be restricted to stall rest
• Transport of severely anemic animals may cause clinical deterioration

DIET
• Ensure access to oxidative plant toxins is eliminated
• Oral iron supplementation in horses with confirmed iron deficiency anemia (rare)

CLIENT EDUCATION
Dependent upon etiology.

SURGICAL CONSIDERATIONS
May be indicated with significant uncontrolled internal hemorrhage, although this carries a high anesthetic risk. Loss of accumulated blood may be associated with clinical deterioration—consider autotransfusion.

MEDICATIONS

DRUG(S) OF CHOICE
Specific therapy of the primary disease process.

PRECAUTIONS
• Severe reactions to transfusions may occur and necessitate careful monitoring and prompt therapy
• Hypertonic saline should be used with caution in horses with uncontrolled bleeding as it may cause increased blood loss
• Parenteral administration of iron formulations is not recommended as iron deficiency is extremely rare and serious adverse reactions may occur

FOLLOW-UP

PATIENT MONITORING
Monitor PCV to assess regenerative responses. PCV should increase by an average of 0.5–1% per day within 3–5 days of an acute hemorrhagic or hemolytic episode.

PREVENTION/AVOIDANCE
Dependent upon etiology.

POSSIBLE COMPLICATIONS
Hypoxia-associated injury to numerous tissues and organ systems, or death in severe cases.

EXPECTED COURSE AND PROGNOSIS
Highly dependent upon the cause, severity, and rapidity of onset.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Dependent upon etiology.

AGE-RELATED FACTORS
Dependent upon etiology.

PREGNANCY/FERTILITY/BREEDING
For discussion of NI, see Anemia, immune mediated

SEE ALSO
• Blood and plasma transfusion reactions
• Myeloproliferative diseases

ABBREVIATIONS
• C-ELISA = competitive enzyme-linked immunosorbent assay
• DMSO = dimethylsulfoxide
• EIA = equine infectious anemia
• GI = gastrointestinal
• Hb = hemoglobin
• MCH = mean cell hemoglobin
• MCHC = mean cell hemoglobin concentration
• M:E = myeloid-to-erythroid
• NI = neonatal isoerythrolysis
• NSAID = nonsteroidal anti-inflammatory drug
• PCV = packed cell volume
• RBC = red blood cell
• TP = total protein

Suggested Reading

Satué K, Muñoz A, Gardón JC. Interpretation of alterations in the horse erythrogram. J Hematol Res 2014;1:1–10.

Author Harold C. McKenzie
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson
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ANEMIA, CHRONIC DISEASE

BASICS

OVERVIEW

• ACD is thought to be a protective response that limits the availability of iron for bacterial growth
• ACD, or "anemia of inflammatory disease," is associated with substantial, sustained activation of the immune system
• ACD typically presents as a mild to moderate, nonregenerative, normochromic, normocytic anemia
• ACD is characterized by low serum iron concentration and low to normal TIBC with normal to increased serum ferritin concentrations
• Proinflammatory cytokines induce hepcidin production by the liver
  ◦ Hepcidin regulates systemic iron homeostasis and decreases serum iron and total body iron stores
  ◦ Hepcidin reduces the function of ferroportin, the primary iron transporter molecule in duodenal enterocytes and macrophages
  ◦ This leads to impaired enteric iron absorption (enterocytes) and increased iron retention (macrophages)
  ◦ Anemia ensues due to decreased availability of iron for Hb production (*relative* iron deficiency)
• Impaired EPO responsiveness and decreased RBC survival also result from the action of proinflammatory cytokines and contribute to the development of anemia

SIGNALMENT

• Animals with chronic inflammation
• Older animals may be at increased risk, but there is no defined age, breed, or sex predilection for ACD

SIGNS

• Often subclinical, but exercise may induce exaggerated tachycardia, weakness, and reduced performance
• Pale mucous membranes, weakness, lethargy
• Fever, weight loss, or signs referable to primary disease process may be present
• Tachycardia, tachypnea, low-grade holosystolic heart murmur

CAUSES AND RISK FACTORS

Acute and chronic inflammatory conditions, such as infection, neoplasia, autoimmune disorders, or chronic kidney diseases.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Chronic anemia due to insensible blood loss (GI or urogenital)
• Iron deficiency anemia
• Anemia associated with chronic renal disease (EPO deficiency)
• Myelodysplastic or myeloproliferative disorders
• Aplastic anemia (toxins, drugs)
• Pure red cell aplasia (recombinant human EPO exposure)

CBC/BIOCHEMISTRY/URINALYSIS

• PCV, total RBC count, and Hb concentrations below the lower limit of reference intervals
• Mild to moderate normochromic, normocytic anemia that may progress to hypochromic and microcytic
• Inflammatory leukogram, increased total protein, and hyperglobulinemia may be present due to chronic antigenic stimulation

OTHER LABORATORY TESTS

Hyperfibrinogenemia and increased serum amyloid A may indicate chronic antigenic stimulation.

IMAGING

As indicated for diagnosis of primary disease.

OTHER DIAGNOSTIC PROCEDURES

• Decreased serum iron concentration (range 120–150 μg/dL)
• Normal to decreased TIBC (range 200–262 μg/dL)
• Decreased transferrin saturation (range 20–52%)
• Normal to increased serum ferritin concentration (range 152 ± 54.6 μg/dL)
• Bone marrow aspiration or core biopsy may reveal decreased erythropoiesis and increased iron storage

TREATMENT

• Directed towards resolution of the primary disease process
• Treatments that decrease the production or activity of proinflammatory cytokines may aid in decreasing hepcidin production—pentoxifylline appeared to be of benefit in some human studies
• Treatments that inhibit the activity of hepcidin show potential benefit in human patients but are not available for equine patients

MEDICATIONS

DRUG(S) OF CHOICE

• Iron supplementation has been suggested but oral administration is unlikely to be effective due to impaired GI absorption
• Parenteral iron supplementation may be of more benefit than oral supplementation but carries increased risk of iron toxicity and is not recommended
• Recombinant human EPO should not be used owing to the risk of pure red cell aplasia

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

FOLLOW-UP

PATIENT MONITORING

• Monitoring as indicated for management of primary disease process
• Serial monitoring of CBC to assess PCV and red blood cell indices (mean cell hemoglobin, mean cell hemoglobin concentration, mean cell volume, RBC distribution width) for evidence of a regenerative response

PREVENTION/AVOIDANCE

Effective treatment of primary disease, where possible, is the best form of prevention.

POSSIBLE COMPLICATIONS

• Most cases are subclinical, but affected animals may be susceptible to stress or exercise-induced tachycardia and tachypnea
• More severe consequences are rare, as the anemia is typically mild to moderate in nature

EXPECTED COURSE AND PROGNOSIS

ACD is expected to resolve in conjunction with resolution of the primary disease process.

MISCELLANEOUS

SEE ALSO

Anemia

AGE-RELATED FACTORS

N/A

ABBREVIATIONS

• ACD = anemia of chronic disease
• EPO = erythropoietin
• GI = gastrointestinal
• Hb = hemoglobin
• PCV = packed cell volume
• RBC = red blood cell
• TIBC = total iron-binding capacity

Suggested Reading

Carlson GP. Anemia of inflammatory disease. In: Smith BP, ed. Large Animal Internal Medicine, 5e. St. Louis, MO: Elsevier Mosby, 2015:1068.

Author Harold C. McKenzie
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson

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ANEMIA, HEINZ BODY

BASICS

DEFINITION
• Heinz bodies are small, round, blue-black, refractile aggregations of oxidized, precipitated hemoglobin, present near the margin of RBCs
• Heinz body anemia occurs as a result of exposure to certain oxidizing agents
• Heinz bodies damage the RBC membrane, resulting in lysis (intravascular hemolysis) and removal of the damaged RBCs from the circulation by the reticuloendothelial system (extravascular hemolysis)

PATHOPHYSIOLOGY
• Mild oxidative stress is associated with normal oxygen transport within RBCs
• There are protective enzyme systems in place to counteract the oxidative stress; however Heinz body hemolytic anemia can result if these systems are overwhelmed
• Denatured hemoglobin precipitates to form Heinz bodies, which attach to the RBC membrane and cause increased cell fragility with resultant intravascular or extravascular hemolysis
• Many oxidant toxins also oxidize ferrous iron (Fe^{2+}) in the hemoglobin molecule to the ferric form (Fe^{3+}), resulting in methemoglobin production. Methemoglobin decreases the oxygen-carrying capacity of the blood, resulting in tissue hypoxia

SYSTEMS AFFECTED
• Hemic/lymphatic/immune—regenerative anemia with bone marrow RBC hyperplasia and splenomegaly. Release of hemoglobin and other products of hemolysis may result in pyrexia
• Cardiovascular and respiratory—tachycardia and tachypnea, holosystolic heart murmur, mucous membrane pallor
• Renal/urologic—intravascular hemolysis may result in hemoglobinuria, hemoglobinuric nephropathy, and acute anuric renal failure
• Hepatobiliary—hyperbilirubinemia and icterus, hypoxic hepatocellular damage
• Gastrointestinal—hypoxic damage to intestines may result in motility disorders and colic
• Musculoskeletal—hypoxic damage to laminae may result in laminitis

GENETICS
N/A

INCIDENCE/PREVALENCE
Data currently unavailable.

GEOGRAPHIC DISTRIBUTION
Acer rubrum (red maple) is widespread throughout eastern and central North America.

SIGNALMENT
Can occur in horses of any breed, age, or sex.

SIGNS
Historical Findings
• Exercise intolerance or sudden onset of dullness, lethargy, inappetence, and/or colic are common presenting signs
• Acute, apparently unexplained death
• There may be history of access to wilted or dried leaves or bark of red maple (*A. rubrum*) or other oxidative toxins (e.g. phenothiazine, wild onions)

Physical Examination Findings
• Weakness, pale or icteric mucous membranes, tachypnea, tachycardia, and holosystolic heart murmur. Pyrexia may be associated with hemolysis
• With concurrent methemoglobinemia there may be muddy-brown, cyanotic mucous membranes, and brownish blood
• Pigmenturia/hemoglobinuria and oliguria (or polyuria) may occur due to hemoglobin-induced nephropathy
• Rectal examination may reveal an enlarged spleen
• Severely affected horses may develop ataxia, and death may occur

CAUSES
• Ingestion of wilted or dried red maple leaves or bark, wild or domestic onions, members of the Brassica family
• Phenothiazine, methylene blue, or acetylphenylhydrazine toxicities
• Reported in a case of lymphoma possibly due to failure of the reticuloendothelial system to remove Heinz bodies
• Reported with EIA

RISK FACTORS
• Exposure to toxins (e.g. wilted or dried red maple leaves (more likely in the fall), onions)
• Lymphoma
• EIA infection
• When RBCs from a Saddlebred colt with glucose-6-phosphate dehydrogenase deficiency were exposed to acetylphenylhydrazine, more and smaller Heinz bodies were produced
• Thin horses may be at greater risk of phenothiazine toxicosis
• Selenium deficiency results in decreased glutathione peroxidase (involved in RBC counteraction of oxidative stress) and, therefore, may contribute to Heinz body formation
• Equine RBCs have less developed protective mechanisms to reverse the oxidation of hemoglobin

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Causes of anemia include hemorrhage, hemolysis, and decreased RBC production
• Hemorrhage is usually easily differentiated based on history and physical examination findings. Hemorrhage is usually also associated with hypoalbuminemia as well as anemia (after the initial 12 h), which is not a feature of hemolysis
• Anemia of chronic inflammation may be associated with inflammatory, infectious, or neoplastic disorders, e.g. lymphosarcoma (usually a more complex history and other clinical signs associated with affected organ system) or purpura haemorrhagica (usually a history of respiratory disease)
• Horses with immune-mediated hemolytic anemia will be positive on flow cytometry for erythrocyte-bound immunoglobulins and may have a positive Coombs test (poor sensitivity)
• EIA cases will have a positive Coggins or C-ELISA test
• Piroplasmosis cases may have intracellular organisms on Giemsa- or new methylene blue-stained blood smears and/or be seropositive or seroconvert on convalescent titer
• Cases of anaplasmosis may have intracytoplasmic inclusion bodies in neutrophils on Giemsa-stained blood smears and/or a positive PCR result
• Envenomation and heavy metal toxicosis (e.g. chronic consumption of lead, copper, or selenium) must be differentiated based on history of exposure
• Familial methemoglobinemia has been described in Standardbreds
• Nitrate/nitrite toxicity can be differentiated based on history of exposure

CBC/BIOCHEMISTRY/URINALYSIS
• Variable anemia; PCV is often <20%
• Direct blood smears may reveal eccentrocytes, RBC fragments, and anisocytosis
• An inflammatory leukogram may be present (neutrophilia is common)
• Increased mean corpuscular hemoglobin reflects hemoglobinemia associated with intravascular hemolysis
• Biochemical abnormalities usually include increased total and indirect bilirubin, azotemia (associated with hemoglobinuric nephropathy), and increased hepatic enzyme activity (associated with hypoxic injury to the liver)
• Urinalysis may reveal bilirubinuria, hemoglobinuria (no microscopic hematuria), methemoglobinuria, and proteinuria

OTHER LABORATORY TESTS
• Heinz bodies will be visualized on crystal violet or new methylene blue-stained smears. Initially, a very high percentage of RBCs have Heinz body inclusions but later, as these are removed from the circulation, the number of affected cells decreases
• Increased RBC osmotic fragility
• Bone marrow aspiration may reveal a regenerative response with an myeloid to erythroid ratio <0.5

• Co-oximetry can be performed to ascertain methemoglobin content (normal is ≤1.77%)

IMAGING
Splenic/hepatic ultrasonography may be used to detect splenic/hepatic enlargement—may appear hyperechoic or hypoechoic with some loss of architecture due to increased fluid component.

OTHER DIAGNOSTIC PROCEDURES
A thorough diagnostic workup is indicated to ascertain underlying etiology.

PATHOLOGIC FINDINGS
• Gross—pale or icteric tissues, enlarged liver and spleen, renal congestion, possible signs of congestive heart failure
• Histopathology—renal tubular nephrosis with hemoglobin casts, centrilobular hepatic degeneration and necrosis, and phagocytized RBCs and hemosiderin in the spleen and liver

TREATMENT

APPROPRIATE HEALTH CARE
• In-hospital medical management may be necessary depending on the severity of the anemia and associated clinical signs
• Activated charcoal and mineral oil should be administered via nasogastric intubation to reduce further absorption of toxin
• IV fluid therapy with isotonic crystalloids should be initiated to improve perfusion, prevent hemoglobin-induced nephropathy, and promote diuresis (however excessive hemodilution should be avoided)
• Cross-matched blood or packed RBC transfusion should be considered if PCV decreases to <8–12%, or if there is persistent tachycardia, tachypnea, weak pulse pressure, or a poor response to isotonic fluid therapy
• Oxygen therapy is ineffective if oxygen-carrying capacity is decreased owing to methemoglobinemia

NURSING CARE
Close monitoring of vital signs, IV fluid rates (to avoid excessive hemodilution), CBC/biochemistry, urine output, and renal function is recommended.

ACTIVITY
Exercise and stress should be avoided to prevent increased oxygen demand.

DIET
Palatable and nutritious feeds should be provided to encourage voluntary intake.

CLIENT EDUCATION
Clients should be warned of the hazards of exposure to wilted red maple leaves (including red maple hybrids) and other toxins.

SURGICAL CONSIDERATIONS
Anemia and methemoglobinemia put these cases at increased anesthetic risk and therefore surgery should be postponed if possible (or blood transfusion may be required before an emergency procedure).

MEDICATIONS

DRUG(S) OF CHOICE
Treatment is largely supportive, as there is no specific therapy.

CONTRAINDICATIONS
• Methylene blue therapy may exacerbate Heinz body formation and has been associated with decreased survival
• Corticosteroid use has also been associated with decreased survival

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
Vitamin C (ascorbic acid) (30 mg/kg twice daily, diluted in IV fluids) has been used for methemoglobin-associated conditions (no proven efficacy).

FOLLOW-UP

PATIENT MONITORING
• The PCV should be monitored closely and should remain stable or slowly increase over time (reflective of bone marrow regeneration and therapeutic response)
• Renal function and urine output should also be monitored, as well as for signs of laminitis

PREVENTION/AVOIDANCE
• Limiting access to potential toxins including wilted red maple leaves and onions
• Minimizing use of phenothiazines or, if absolutely necessary, attempt to use the minimum effective dose

POSSIBLE COMPLICATIONS
• Laminitis
• Nephropathy/renal failure
• Abortion, weak foals
• Coma and death

EXPECTED COURSE AND PROGNOSIS
• Prognosis is variable depending on the severity of the anemia and whether or not there is concurrent methemoglobinemia
• Horses with red maple toxicity have a guarded to poor prognosis, with a 60% fatality rate

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Methemoglobinemia
• Pigment nephropathy

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
Pregnant mares may abort or deliver a weak foal.

SYNONYMS
• Oxidant-induced hemolysis
• Oxidative hemoglobinemia

SEE ALSO
• Anemia
• Anemia, immune mediated
• Infectious anemia (EIA)
• Methemoglobin

ABBREVIATIONS
• C-ELISA = competitive enzyme-linked immunosorbent assay
• EIA = equine infectious anemia
• PCR = polymerase chain reaction
• PCV = packed cell volume
• RBC = red blood cell

Suggested Reading

Alward A, Corriher CA, Barton MH, et al. Red maple (*Acer rubrum*) leaf toxicosis in horses: a retrospective study of 32 cases. J Vet Intern Med 2006;20:1197–1201.

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Author Rana Bozorgmanesh
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson
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ANEMIA, IMMUNE MEDIATED

BASICS

DEFINITION
IMHA is a destruction of RBCs associated with immunoglobulin and/or complement attachment to either RBC antigens or foreign antigens coating the surface of RBCs.

PATHOPHYSIOLOGY
• Can be primary or secondary (most common)
• Primary IMHA occurs when the immune system produces specific autoantibodies to normal erythrocyte antigens (includes NI, or transfusion reaction)
• Secondary IMHA most commonly occurs as a result of agents that:
  ◦ Alter the RBC membrane, exposing antigens to which the host produces antibody (e.g. infectious agents, neoplasia)
  ◦ Form immune complexes that adsorb to the RBC and fix complement (e.g. infectious agents)
  ◦ Directly bind to the RBC and act as haptens that bind antibody (e.g. drugs)
  ◦ Stimulate the immune system, resulting in production of antibodies with cross-reactivity to RBCs (e.g. infectious agents, neoplasia)
• Antibody- and/or complement-coated RBCs are removed from the circulation by extravascular hemolysis (if removed by the reticuloendothelial system) and/or intravascular hemolysis (if complement mediated)

SYSTEMS AFFECTED
• Hemic/lymphatic/immune
• Cardiovascular/respiratory
• Hepatobiliary
• Renal
• Gastrointestinal

GENETICS
Foals born to multiparous dams known to be RBC antigen Aa or Qa negative are at increased risk of developing NI.

INCIDENCE/PREVALENCE
• Unknown
• Weak anecdotal evidence suggests IMHA is a rare consequence of other disease states in adult horses
• NI is reported in foals in most countries

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Any breed, age, or sex.

SIGNS
General Comments
Signs often reflect the primary, underlying disease process such as infection or neoplasia.

Historical Findings
• History generally reflects an underlying disease process and may include chronic weight loss (e.g. neoplastic diseases) or signs of depression and inappetence (e.g. infectious diseases)
• Exercise intolerance, weakness, and lethargy
• There may be a history of exposure to blood transfusion(s) or certain drugs (typically in the previous 5–12 days)

Physical Examination Findings
• Signs of anemia—proportional to the degree of anemia
• Exercise intolerance, weakness, pale or icteric mucous membranes, fever, tachypnea, tachycardia, holosystolic heart murmur, abdominal pain, and hemoglobinuria
• Foals with NI typically present with acute-onset weakness and icterus during the first few days of life
• Severe debilitation and death may occur

CAUSES
Primary Immune Mediated
• NI
• Autoimmune hemolytic anemia
• Incompatible blood transfusion

Secondary Immune Mediated
• Infectious—e.g. acute viral infections, EIA, *Clostridium perfringens, Rhodococcus equi*, or streptococcal organisms
• Neoplastic—e.g. lymphoma
• Drug associated—e.g. penicillins, trimethoprim–sulfamethoxazole, and potentially cephalosporins, rifampin (rifampicin), chloramphenicol and various NSAIDs

RISK FACTORS
• Foals born to multiparous dams that have previously had a blood transfusion(s), or the mare is RBC antigen Aa or Qa negative, are at increased risk of developing NI
• Exposure to incompatible blood transfusion and certain drugs

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other diseases causing anemia
• Hemorrhage (acute or chronic)
• Heinz body anemia

CBC/BIOCHEMISTRY/URINALYSIS
• PCV is often <0.20 L/L (<20%)
• May have neutrophilic leukocytosis
• RBC autoagglutination:
  ◦ May be observed due to the presence of antibodies and/or complement on the surface of the RBCs
  ◦ Must be distinguished from rouleaux formation. "In saline" agglutination test can be used to differentiate—place one drop of blood on slide, add 0.9% saline as 1:4 with blood. Normal RBCs disperse evenly on the slide, while agglutination results in clumping of cells
  ◦ Spherocytes may be observed in blood smears, but are more difficult to identify in horses owing to the lack of central pallor in normal equine RBCs
• Increased mean corpuscular hemoglobin suggests intravascular hemolysis, which may also result in discolored plasma
• Increased serum total bilirubin concentration (indirect greater than direct)
• Bilirubinuria and hemoglobinuria may be observed in the rarer cases when intravascular hemolysis occurs

OTHER LABORATORY TESTS
• Positive direct antiglobulin (Coombs) test (detects presence of antibody on the surface of RBCs). False-negative results are possible, particularly if there has been prior corticosteroid therapy. False-positive results also can occur, emphasizing the need to use multiple methods to confirm the diagnosis of IMHA
• RBC osmotic fragility may be increased in IMHA, although this test can be positive with RBCs damaged by oxidant insults
• Bone marrow aspiration reveals a diffuse, regenerative erythron (myeloid to erythroid ratio is <0.5)
• Infectious causes of IMHA may have positive serology and/or evidence of hematologic parasites on direct or special stained blood smears:
  ◦ Horses with EIA will be seropositive for virus on Coggins or C-ELISA tests
  ◦ Horses with equine piroplasmosis may have organisms observed in Giemsa- or new methylene blue-stained blood smears, be seropositive or seroconvert on their convalescent titer, or be positive via PCR
  ◦ Horses with equine granulocytic ehrlichiosis may have granular inclusion bodies observed in cytoplasm of neutrophils in Giemsa-stained blood smears, be seropositive or seroconvert with acute and convalescent samples, or be positive via PCR

IMAGING
No specific imaging findings would be expected for IMHA itself—abnormalities identified are related to the original disease process.

OTHER DIAGNOSTIC PROCEDURES
A thorough diagnostic workup should be performed to rule out neoplasia and infectious causes of secondary IMHA.

PATHOLOGIC FINDINGS
• Necropsy findings may include an enlarged liver and spleen and pale or icteric tissues
• Findings referable to the initial disease process

TREATMENT

AIMS
• Treatment of IMHA involves identification and resolution (if possible) of any underlying

infection or disease, reduction of the immune response, and provision of supportive care
• Administration of any drugs should be discontinued as IMHA could be caused by an adverse drug reaction. If antimicrobial therapy is required, a molecularly dissimilar antibiotic should be used

APPROPRIATE HEALTH CARE
• Most cases of IMHA are treated in hospitals, especially if severe
• Balanced polyionic IV fluid therapy may be indicated to expand vascular volume if volume depleted, and to induce diuresis if significant hemoglobinuria is present
• Emergency medical therapy with cross-matched blood transfusion is indicated if there is evidence of tissue hypoxia (PCV < 8–12%). In foals, washed RBCs from the dam or appropriate blood-typed blood is optimal

NURSING CARE
• Serial analysis of PCV in order to monitor response to therapy should be performed
• Close monitoring of vital signs and adjustment of fluid rate is essential in horses receiving fluid therapy
• In foals with NI, provide adequate warmth and hydration, avoid stress, and confine mare and foal to restrict activity

ACTIVITY
Minimize or eliminate activity, but allow the animal access to fresh air and sunshine if possible.

DIET
• Make efforts to keep the horse eating a balanced diet, with good quality hay and grain
• Fresh water should be available ad libitum

CLIENT EDUCATION
• Clients should be made aware that horses with primary (or autoimmune) IMHA often require long-term corticosteroid therapy
• If an infectious cause is not identified, neoplasia is highly suspected, and the prognosis will be related to the neoplasia, rather than the IMHA
• Corticosteroid administration may be associated with the development of laminitis
• Clients should be educated in preventative measures for NI

SURGICAL CONSIDERATIONS
None

MEDICATIONS

DRUG(S) OF CHOICE
• In adults, corticosteroids (dexamethasone 0.1 mg/kg IV or IM every 24 h) are indicated until PCV ceases to decline. The dose may then be decreased by 0.01 mg/kg/day until the total dose is 20 mg/day (for a 500 kg horse), after which alternate-day oral prednisolone is recommended. Alternatively, oral prednisolone (1 mg/kg) may be used in place of dexamethasone at any time during therapy, although anecdotally dexamethasone is more efficacious
• From 4 to 7 days often are needed for corticosteroids to have a therapeutic effect (with stabilization of PCV) and up to 10 weeks of treatment may be necessary
• Horses without clinical signs of anemia may not need immunosuppressive therapy if the initiating cause can be effectively treated

CONTRAINDICATIONS
Corticosteroids may exacerbate underlying infectious diseases so should be used only in horses that are EIA (Coggins) negative.

PRECAUTIONS
• Cross-match before blood transfusion
• Corticosteroid therapy may predispose horses to laminitis and should be used with caution in pregnant mares

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
The immunosuppressive agent azathioprine (3 mg/kg PO once daily) has been used in horses nonresponsive to corticosteroids, or when corticosteroids were contraindicated (e.g. the development of laminitis).

FOLLOW-UP

PATIENT MONITORING
PCV should be carefully monitored during dexamethasone treatment. The frequency of dexamethasone administration can be increased to twice daily in horses initially on once a day treatment if the PCV does not stabilize within 24–48 h.

PREVENTION/AVOIDANCE
• Avoid drugs known to have caused secondary IMHA
• Provide alternate colostrum source in foals born to mares at risk of NI

POSSIBLE COMPLICATIONS
• Pigment nephropathy secondary to intravascular hemolysis
• Laminitis

EXPECTED COURSE AND PROGNOSIS
• If the primary cause can be identified and successfully treated, the prognosis for IMHA is good
• Red cell numbers recover as the immune-mediated response resolves, but may take several weeks
• Horses requiring constant corticosteroid treatment may have an incurable underlying disease such as neoplasia (e.g. lymphoma) or have true autoimmune hemolytic anemia. The prognosis for survival in these horses is poor

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Pigment nephropathy
• Laminitis

AGE-RELATED FACTORS
• All ages can be affected
• Foals with NI will develop signs within the first few days of life

PREGNANCY/FERTILITY/BREEDING
Use corticosteroids cautiously in pregnant mares.

SYNONYMS
• Autoimmune hemolytic anemia
• Immune-mediated hemolytic disease

SEE ALSO
• Anemia
• Neonatal isoerythrolysis

ABBREVIATIONS
• C-ELISA = competitive–enzyme-linked immunosorbent assay
• EIA = equine infectious anemia
• IMHA = immune-mediated hemolytic anemia
• NI = neonatal isoerythrolysis
• NSAID = nonsteroidal anti-inflammatory drug
• PCV = packed cell volume
• PCR = polymerase chain reaction
• RBC = red blood cell

Suggested Reading

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Author Imogen Johns
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson
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Client Education Handout available online

A

ANEMIA, IRON DEFICIENCY

BASICS

OVERVIEW
• Iron deficiency results from chronic external loss of blood (adult horses) or dietary deprivation (usually young foals). Unless adult horses lack access to soil, pasture, or feed, inadequate Fe intake is unlikely
• Iron deficiency impairs Hb synthesis, impairs RBC maturation, and leads to anemia
• Anemia and reduced blood Hb concentration may compromise tissue oxygen delivery

SIGNALMENT
• No breed or sex predilection
• Rapid growth of foals is associated with high Fe demands. Mare's milk has low Fe concentrations and therefore deficiency may occur in foals with limited access to pasture, Fe-rich soils, forage, or grain

SIGNS
• Clinical signs may be absent or mild due to physiologic compensation
• Lethargy and exercise intolerance may be the first signs noted
• When PCV drops below 12%, tissue hypoxia can cause tachycardia, tachypnea, and signs of depression. Pale mucous membranes will be present, and a systolic heart murmur may be noted

CAUSES AND RISK FACTORS
Risk factors for chronic hemorrhage include inadequate anthelmintic use, NSAID administration, and toxin exposure.

Chronic, Low-Grade Hemorrhage
• Severe internal or external parasitism
• Bleeding gastrointestinal, respiratory, and urogenital lesions (e.g. gastroduodenal ulcers, NSAID toxicosis, neoplasia, hemorrhagic cystitis, guttural pouch mycosis, and ethmoid hematoma)
• Coagulopathies leading to chronic blood loss (e.g. heritable coagulopathies, warfarin toxicosis, moldy sweet clover)

Diet
Inadequate dietary Fe intake (foals).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Causes of low-grade, hemolytic anemia include immune-mediated, oxidant-induced, and parasite-induced hemolysis
• Causes of decreased RBC production include anemia of chronic disease and aplastic anemia

CBC/BIOCHEMISTRY/URINALYSIS
• Initial normochromic, normocytic anemia may progress to a microcytic, hypochromic, nonregenerative anemia. Microcytosis often precedes hypochromasia
• Thrombocytosis may be observed
• Decreased plasma protein and albumin concentrations are typical with chronic hemorrhage

OTHER LABORATORY TESTS
Initial Stage
• Decreased stainable Fe in marrow macrophages
• Decreased serum ferritin concentration (reference range 152 ± 54.6 μg/dL) with serum ferritin < 45 ng/mL highly indicative of Fe deficiency

Later Stages
• Decreased serum iron concentration (reference range 120–150 μg/dL)
• Normal or increased TIBC (reference range 200–262 μg/dL)
• Decreased transferrin saturation (reference range 20–52%) with values < 16% reflecting insufficient iron available for erythropoiesis
• Decreased mean cell volume with decreased hemoglobin concentration (mean cell hemoglobin concentration)
• Serum iron, serum ferritin, and TIBC may be affected by conditions other than Fe deficiency including acute and chronic inflammation, renal disease, and corticosteroid therapy

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
• Bone marrow cytology may show predominant late rubricytes and metarubricytes, depletion of macrophage iron, and sideroblasts
• Diagnostic workup of causes of chronic hemorrhage is indicated

TREATMENT
• Horses with lethargy, intolerance to mild exercise, or a PCV < 15% should be restricted to stall rest
• Blood transfusion is rarely necessary unless PCV drops below 8% or there are clinical and laboratory signs of tissue hypoxia

MEDICATIONS

DRUG(S) OF CHOICE
• Appropriate treatment of causes of chronic blood loss
• Oral ferrous sulfate (1 g/450 kg body weight) is the safest Fe supplement
• Iron cacodylate (1 g/adult horse) may be given slowly IV, but must be used with caution owing to the possibility of anaphylaxis

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Do not use iron dextrans because of idiosyncratic reactions (anaphylaxis and sudden death)
• Iatrogenic iron overload has been reported in adult horses
• Do not give foals iron-containing products during the first 2 days of life as fatal hepatopathies may occur

FOLLOW-UP

PATIENT MONITORING
• Monitor serum iron, TIBC, and percentage saturation at ≈2 week intervals
• Discontinue iron supplementation when values for PCV, serum iron, TIBC, and % saturation return to reference ranges

PREVENTION/AVOIDANCE
Nursing foals should have access to pasture and, when appropriate, forage and grain.

POSSIBLE COMPLICATIONS
May result in death if affected animals are left untreated.

EXPECTED COURSE AND PROGNOSIS
Prolonged iron supplementation may be required.

MISCELLANEOUS

AGE-RELATED FACTORS
Foals are at increased risk owing to high iron demands and limited dietary intake.

SEE ALSO
Anemia, chronic disease

ABBREVIATIONS
• Hb = hemoglobin
• NSAID = nonsteroidal anti-inflammatory drug
• PCV = packed cell volume
• RBC = red blood cell
• TIBC = total iron-binding capacity

Suggested Reading
Satué K, Muñoz A, Gardón JC. Interpretation of alterations in the horse erythrogram. J Hematol Res 2014;1:1–10.

Author Harold C. McKenzie
Consulting Editors David Hodgson, Harold C. McKenzie, and Jennifer L. Hodgson
Acknowledgment The author and editors acknowledge the prior contribution of Nicholas Malikedes.

BASICS

DEFINITION
Failure of mare to show estrus. Can be physiologic or pathologic.

PATHOPHYSIOLOGY
Mares are seasonally polyestrus with the ovulatory period in spring/summer; primarily regulated by photoperiod:
- Increasing day length decreases melatonin secretion (pineal gland), allowing increased production and release of GnRH, stimulating gonadotropin release (FSH and LH)
  - FSH promotes folliculogenesis
  - D_2 dopamine likely regulates ovarian function locally
- When sufficient LH is produced by dominant follicle(s), ovulation occurs, initiating cyclicity
- Average estrous cycle is 21 days; defined as the interval between 2 ovulations with progesterone > 1 ng/mL. Repeatable in individual mares
- Key hormonal events of equine estrous cycle:
  - FSH causes follicular growth
  - Follicular E_2 stimulates increased GnRH pulse frequency and LH secretion
  - LH surge causes ovulation
  - P_4 (CL origin) rises from basal levels (<1 ng/mL) at ovulation to > 4 ng/mL by 4–5 days post ovulation
  - A second FSH surge in diestrus initiates another follicular wave
  - Endometrial $PGF_{2\alpha}$ is released 14–15 days post ovulation causing luteolysis and decline in P_4 levels

SYSTEMS AFFECTED
- Reproductive
- Endocrine
- Behavioral

SIGNS
Historical Findings
- Chief complaint—failure of mare to show estrus or accept stallion
- Inadequate teasing
- Seasonal influences
- Reproductive history—estrous cycle length, teasing response, prior breeding/foaling data, previous genital tract injuries/infections
- Pharmaceuticals interfering with normal estrous cycle

Physical Examination Findings
- Poor body condition/malnutrition or metabolic disease (PPID)
- Poor perineal conformation can result in pneumovagina, ascending infections and/or urine pooling, anestrus/infertility
- Clitoral enlargement may relate to drug history (anabolic steroids) or intersex conditions
- TRP and US are essential for evaluation. Rule out pregnancy. Assess uterine size/tone, ovarian size/shape/location, and cervical relaxation. Serial TRP and US may be needed to completely define status
- Vaginal speculum examination to identify inflammation, urine pooling, cervical competency, conformational abnormalities

CAUSES
Normal Physiologic
- Winter anestrus—≈30% of mares cycle year-round; most enter a period of anestrus
- 2 transitional phases occur yearly—fall transition (ovulatory to anestrus) and vernal transition (anestrus to cyclicity). Behavior and ovarian activity varies during transition
- Behavioral anestrus (silent heat)—mare has normal cycle but fails to demonstrate estrus
- Pregnancy
- Persistent endometrial cups—early embryonic death after formation of endometrial cups results in persistent CL activity
  - eCG (by endometrial cups, 35–150 days of pregnancy) is luteotropic, maintaining primary CL and formation of secondary CLs
- Postpartum anestrus—most mares reestablish cyclicity ≤ 20 days postpartum. Some fail to continue cycling after their first postpartum ovulation, due to ovarian factors, seasonal factors (foaling late in winter without artificial light supplementation), or lactational anestrus/poor body condition
- Age—puberty occurs at 12–24 months and mares > 25 years may develop ovarian senescence

Congenital Abnormalities
- Gonadal dysgenesis—no functional ovarian tissue; can result in anestrus, erratic estrus, or prolonged estrus
  - Behavioral estrus may be due to adrenal-origin steroid production and absence of progesterone
  - Typically flaccid, infantile uterus, hypoplastic endometrium, small, nonfunctional ovaries
  - Most common chromosomal defect—XO monosomy; most common intersex condition—XY sex reversal

Endocrine Disorders
- PPID—destruction of FSH/LH-secreting cells and/or overproduction of glucocorticoids
- Increased adrenal-origin androgens can suppress normal hypothalamic–pituitary–ovarian axis

Ovarian Abnormalities
- Ovarian hematoma, hemorrhagic anovulatory follicle, or ovarian abscess
- Ovarian neoplasia (most common—GTCT)

Uterine Abnormalities
Pyometra—can prevent formation and release of $PGF_{2\alpha}$, prolonging diestrus.

Iatrogenic/Pharmacologic
- GnRH vaccination—prevents ovarian activity
- Bilateral ovariectomy—although up to 30% of mares show constant estrus
- Drugs causing behavioral anestrus:
  - Anabolic steroids
  - Progesterone/progestins—inhibition of estrus behavior
  - Oxytocin treatment to prolong CL lifespan
- Placement of intrauterine marbles to prolong CL lifespan

RISK FACTORS
Foaling in late winter; poor body condition at foaling.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Differentiating Causes
- Review history/breeding/foaling records—medical/reproductive history, teasing methods
- Physical examination, serial TRP and US to determine reproductive status, cyclicity, uterine/ovarian abnormalities
- Vaginal examination

OTHER LABORATORY TESTS
- Serum progesterone
  - Basal < 1 ng/mL
- GTCT panel
  - Nonpregnant mare—AMH < 3.8 ng/mL, inhibin < 0.7 ng/mL, testosterone 20–45 pg/mL
  - GTCT if AMH > 8.0 ng/mL, inhibin > 0.7 ng/mL, testosterone 100 pg/mL
- Serum eCG—diagnosis of persistent endometrial cups
- PPID testing
- Karyotype

IMAGING
Transrectal US of reproductive tract. Hysteroscopy to diagnose uterine abnormalities.

OTHER DIAGNOSTIC PROCEDURES
Uterine cytology/culture/biopsy for diagnosis, treatment, and to monitor progression of pyometra/endometritis.

TREATMENT
- Alter management/teasing techniques to elicit a response from a mare and/or base timing of artificial insemination on TRP and US
- Advancement of the vernal transition:
  - Artificial lighting—expose mare to 14.5–16 h light/day or to additional 1–2 h light at 10 h after dusk (flash lighting). Duration of transition remains unchanged. Minimum of 60–90 days is needed to achieve cyclicity

A

ANESTRUS (CONTINUED)

- Pharmaceuticals—combinations of FSH, dopamine antagonists, and P_4/E_2

• Mare due to foal in late winter—add supplemental lighting 2 months prior to parturition to improve postpartum cyclicity and decrease potential for anestrus
• Ovarian tumors
- Removal of GTCT removes inhibin suppression of contralateral ovary, allowing cyclicity, often with longer interovulatory period. The time to cycle is affected by season:
  - If in winter, following the solstice, cyclicity resumes as day length increases
  - If in spring or summer, cyclicity may not resume until fall and significant decreases in day length
- Some mares fail to cycle again

• Pyometra/endometritis—specific intrauterine therapies based on diagnostic testing

MEDICATIONS

DRUG(S) OF CHOICE

• To induce luteolysis:
- $PGF_{2\alpha}$ (Lutalyse 10 mg IM) or analogs

• To induce ovulation in estrus:
- Deslorelin 1.8 mg IM—ovulation usually within 48 h if follicle(s) > 30 mm
- hCG 2500 IU IV—ovulation within 48 h if follicle(s) > 35 mm

• To hasten vernal transition:
- Altrenogest (0.044 mg/kg PO daily ≥ 15 days) if follicles > 20 mm are present and mare is exhibiting behavioral estrus. $PGF_{2\alpha}$ is given on day 15
- Combination P_4/E_2 treatments followed by $PGF_{2\alpha}$ are also used
- Dopamine antagonists—domperidone 1.1 mg/kg PO daily or sulpiride 1.0 mg/kg or 200 mg/mare IM daily; often used in combination with artificial photoperiod

CONTRAINDICATIONS

$PGF_{2\alpha}$ and analogs—contraindicated with equine asthma/bronchoconstrictive disease.

PRECAUTIONS

• Horses:
- $PGF_{2\alpha}$ causes sweating/colic-like symptoms due to stimulation of smooth muscle
- Symptomatic treatment is recommended if it fails to resolve in 1–2 h
- Antibodies to hCG can develop. Limit use to < 2 or 3 times per breeding season
- Deslorelin implants are associated with FSH suppression in diestrus with prolonged interovulatory period in nonpregnant mares
- Progesterone supplementation can decrease uterine clearance; use may be contraindicated in mares with a history of uterine infection

• Humans:
- $PGF_{2\alpha}$ should not be handled by pregnant women or persons with asthma/bronchial disease
- Altrenogest should not be handled by pregnant women or persons with thrombophlebitis, thromboembolic disorders, cerebrovascular/coronary artery disease, breast cancer, estrogen-dependent neoplasia, undiagnosed vaginal bleeding, or tumors that developed with use of oral contraceptives or estrogen-containing products

ALTERNATIVE DRUGS

Cloprostenol sodium (Estrumate 250 µg/mL IM) is a $PGF_{2\alpha}$ analog. This product is used in similar fashion to natural $PGF_{2\alpha}$ and has been associated with fewer side effects. Not currently approved for use in horses.

FOLLOW-UP

PATIENT MONITORING

• Serial TRP and US—establish diagnosis for etiology of anestrus
• Mares with persistent endometrial cups will return to cyclicity upon regression of endometrial cups, as eCG decreases (up to 150 days post ovulation)

POSSIBLE COMPLICATIONS

Infertility may result from intractable persistent anestrus.

MISCELLANEOUS

AGE-RELATED FACTORS

Postpartum anestrus occurs more often in old mares.

PREGNANCY/FERTILITY/BREEDING

$PGF_{2\alpha}$ administration to pregnant mares can cause luteolysis and abortion. Definitively rule out pregnancy before administering this drug or its analogs.

SYNONYMS

• Gonadal dysgenesis
• Gonadal hypoplasia
• Lactational anestrus
• Postpartum anestrus

SEE ALSO

• Abnormal estrus intervals
• Aggression
• Disorders of sexual development
• Early embryonic death
• Endometritis
• Large ovary syndrome
• Ovulation failure
• Pituitary pars intermedia dysfunction
• Prolonged diestrus
• Pyometra

ABBREVIATIONS

• AMH = anti-Müllerian hormone
• CL = corpus luteum
• E_2 = estradiol
• eCG = equine chorionic gonadotropin
• FSH = follicle-stimulating hormone
• GnRH = gonadotropin releasing hormone
• GTCT = granulosa–theca cell tumor
• hCG = human chorionic gonadotropin
• LH = luteinizing hormone
• P_4 = progesterone
• $PGF_{2\alpha}$ = prostaglandin $F_{2\alpha}$
• PPID = pituitary pars intermedia dysfunction
• TRP = transrectal palpation
• US = ultrasonography, ultrasound

Suggested Reading

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Williams GL, Thorson JF, Prezotto LD, et al. Reproductive seasonality in the mare: neuroendocrine basis and pharmacologic control. Domest Anim Endocrinol 2012;43:103–115.

Author Lisa K. Pearson
Consulting Editor Carla L. Carleton
Acknowledgment The author and editor acknowledge the prior contribution of Carole C. Miller.

BASICS

DEFINITION
ALD is an abnormal deviation from the normal axis of the limb in the frontal plane, usually accompanied by an additional degree of axial rotation. Valgus is the lateral deviation, while varus is the medial deviation of the limb to the location of the deformity. The deformity is named by the joint around which the deviation is centered.

PATHOPHYSIOLOGY
Perinatal Factors
• Flaccidity of periarticular soft tissue structures and perinatal soft tissue trauma can lead to unstable joints, resulting in abnormal loading of the articular surfaces inducing ALD
• Anything to jeopardize the intrauterine environment of the foal (i.e. placentitis, twin foal) and premature birth (<315 days) may result in incomplete ossification (carpus and tarsus) at birth

Developmental Factors
• Unbalanced nutrition (i.e. "crib feeding" leading to excessive grain intake, unbalanced trace minerals) can result in disproportionate growth at the level of the physis, causing ALD
• Frequently observed in rapidly growing foals
• Can occur days to months after birth
• Excessive exercise and trauma can result in microfractures and crushing of the growth plate leading to early closure in severe cases (i.e. Salter–Harris type V fracture)

SYSTEMS AFFECTED
Musculoskeletal—one or more joints may be involved in the front limbs and/or hindlimbs, including the fetlock, carpus, and tarsus.

GENETICS
N/A

INCIDENCE/PREVALENCE
• Most foals are born with some form of angular limb deformity; however, most cases resolve within 4 weeks without intervention
• Prevalence of thoroughbred foals with ALD requiring intervention may be as high as 4.7%

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Most commonly encountered in neonatal foals.

Breed Predilections
Observed in all breeds, most commonly Thoroughbreds, Quarter Horses, and miniature horses.

Age and Range
May either be present at birth or develop days to months following birth.

Predominant Sex
N/A

SIGNS
General Comments
• Spontaneous correction of mild ALD may occur
• Foals with ALD must be monitored closely, as there is a limited surgical window prior to various physis closures
• Some degree of carpal valgus (up to 4°) is normal in foals. This will correct as the foal grows and the chest broadens

Historical Findings
• Prematurity/dysmaturity
• Placentitis or twinning in the mare
• Witnessed or suspected trauma at the physis
• Crib-feeding practices on the farm

Physical Examination Findings
• A valgus deformity results in what is termed "splay foot," which should not be confused with outward rotation of the entire limb ("toed out")
• A varus deformity results in what is termed "pigeon toed"

CAUSES
Perinatal Factors
• Prematurity/dysmaturity
• Ligamentous laxity
• Perinatal soft tissue trauma
• Intrauterine malpositioning

Developmental Factors
• Nutritional imbalances
• External trauma to the physis
• Overload of a limb

RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Laxity of periarticular soft tissues
• Incomplete ossification/collapse of the cuboidal bones
• Diaphyseal curvature (MCIII/MTIII)

CBC/BIOCHEMISTRY/URINALYSIS
N/A

LABORATORY TESTS
N/A

IMAGING
Radiography allows for determination of the location and the degree of the deformity, as well as concurrent physitis or physeal crushing or cuboidal bone crushing. Radiographs should be centered over the joint of interest, including the mid-diaphysis of the bones proximal and distal to the deformity.

OTHER DIAGNOSTIC PROCEDURES
• Examination of the limb in both a standing and a flexed position
• Observation of the foal at a walk
• Manipulation/palpation of the limb can help determine whether the deformity is related to soft tissue laxity or bony abnormality

PATHOLOGIC FINDINGS
• Asymmetric early closure of either the medial or lateral physis due to injuries or inflammation
• Delayed ossification

TREATMENT

AIMS
A straighter limb will allow for more even load-bearing and should reduce the incidence of athletic injury.

APPROPRIATE HEALTH CARE
N/A

NURSING CARE
Splints and Casts
• The purpose is to maintain the limb in proper alignment and to facilitate adequate weight-bearing for foals with incomplete ossification of the cuboidal bones and laxity of periarticular soft tissue structures
• Problems with casts and splints in foals include osteopenia and tendon/ligament laxity. Ending the cast/splint at the level of the fetlock can help prevent these problems
• Commercial splints/braces are available and may be easier for the owner to change safely
• Splints are contraindicated if the ALD is due to radial/tibial deformity rather than incomplete ossification or laxity of periarticular structures
• Splints should be changed every 3–4 days
• Casts should be changed every 10–14 days

Corrective Shoeing
• Application of glue-on/composite materials with an extension on the medial aspect (valgus deformities) or the lateral aspect (varus deformities) may assist in correction of the deformity
• Hoof trimming may also be performed—the outside of the hoof should be lowered for valgus deformity; the inside for varus deformity. It is important to not overtrim or create an abnormal hoof shape that will further alter normal weight-bearing. Corrective shoeing/trimming should only be attempted if the physis is still open; cosmetic farrierwork on a mature animal with an angular limb deformity will result in joint pathology

ACTIVITY
Stall Rest
• Effective treatment for newborn foals, specifically for incomplete ossification and straight limbs
• Foals with ALD due to disproportionate growth at the level of the physis (>10°) and diaphyseal deformities should be stall rested for 4–6 weeks

ANGULAR LIMB DEFORMITY (CONTINUED)

• Foals with laxity of the periarticular supporting structures require supervised exercise in addition to stall rest
• It is important not to prolong stall rest beyond 4–6 weeks

DIET
Balanced nutrition is very important.

CLIENT EDUCATION
The examination of a foal for ALD should begin shortly after birth, followed by examination once a week for 4 weeks, and once monthly for 6 months.

SURGICAL CONSIDERATIONS

Growth Acceleration (Periosteal Transection and Elevation)
• Periosteal transection is performed on the concave aspect of the limb (e.g. lateral aspect of the distal radial physis for a carpal valgus deformity) in order to accelerate growth
• The timing of surgery depends on the site of abnormal growth
• The maximum effect is observed within 2 months
• Overcorrection of the deformity has not been observed
• A bandage should be maintained for 10–14 days following surgery
• Stall rest for 2–3 weeks after surgery

Growth Retardation (Transphyseal Bridging)
• Performed in foals <3 months with severe ALD or foals with significant ALD following the rapid growth phase (MCIII/MTIII and proximal phalanx = 2 months, tibia = 4 months, and radius = 6 months)
• The goal is to retard growth by bridging the convex side of the limb, allowing the shorter side of the affected limb to keep growing
• Current techniques include 1 transphyseal screw across the physis or 2 screws with a figure-of-eight cerclage wire connecting the two. The one-screw transphyseal technique may result in more acceptable cosmesis, but carries an increased risk of physitis. Surgical staple techniques and small bone plates have also been described. Periosteal transection and elevation are often performed in combination with growth retardation techniques
• A bandage should be maintained for 10–14 days
• The foal should be stall rested for 2–3 days following surgery
• Implants need to be removed as soon as the deformity has been corrected, as overcorrection can occur

Corrective Osteotomy
• Osteotomies have been performed for correction of significant ALD in foals with closed growth plates
• Current techniques—closing wedge or step osteotomy
• Maintain a bandage and splint or cast for several weeks following surgery

MEDICATIONS

DRUG(S) OF CHOICE
• For foals that require splinting or casting, conservative doses of NSAIDs may be beneficial
• For surgical cases, NSAIDs and antibiotics may be given as needed perioperatively

CONTRAINDICATIONS
N/A

PRECAUTIONS
NSAIDs can have an ulcerogenic effect on foals. Ulcer prophylaxis may include omeprazole or ranitidine during NSAID administration.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
• Foals with splints and casts should be assisted to nurse if unable to do so on their own
• Careful monitoring insures implant removal the instant correction has occurred in transphyseal bridging
• Foals with incomplete ossification should be evaluated at 2 week intervals to assess ossification progress

PREVENTION/AVOIDANCE
Balanced nutrition is very important.

POSSIBLE COMPLICATIONS
• Nonsurgical management—pressure sores, osteopenia, and tendon/ligament laxity from cast/splint application
• Surgical management—hematoma/seroma formation at surgery site, incisional infection, wound dehiscence, overcorrection
• Failure of transfer of passive immunity may result if foals are unable to nurse due to ALD following birth

EXPECTED COURSE AND PROGNOSIS
• Studies have indicated an improvement in approximately 80% of foals that have undergone a periosteal transection
• No significant difference in sales price or racing performance was seen between foals that were treated with a transphyseal screw for ALD and maternal siblings without ALD
• Foals with lameness or more than 30% collapse of the third and central tarsal bones associated with incomplete ossification have a poorer prognosis

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Timing of intervention is important.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

SEE ALSO
Flexural limb deformity

ABBREVIATIONS
• ALD = angular limb deformity
• MCIII = third metacarpal bone
• MTIII = third metatarsal bone
• NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Authors Alison K. Gardner and Shannon J. Murray
Consulting Editor Margaret C. Mudge

BASICS

OVERVIEW

• Anhidrosis (also known as dry coat disease, nonsweaters, or "dry puffers") is the inability to sweat effectively. The current theory is that overstimulation of sweat gland β_2 receptors downregulates sweating at first temporarily and then permanently
• Systems affected—skin/exocrine

SIGNALMENT

No coat color, age, or sex predilections. Warmbloods and Thoroughbreds are more commonly affected. Rare in Arabians. Up to 20% of horses may be affected when exercising in a hot, humid climate.

SIGNS

• Tachypnea at rest in warm conditions
• Extended tachypnea and hyperthermia after exercise
• Reduction or absence of sweating during or after exercise
• Brief bouts of excessive sweating may precede anhidrosis
• Dry and flaky skin with alopecia, especially on the face and neck, in chronic cases
• Lethargy and altered (decreased or increased) water intake in severe cases

CAUSES AND RISK FACTORS

• Heat-stressed horses may have increased circulating epinephrine, an adrenergic agonist, that may overstimulate the sweat gland β_2 receptors, resulting in downregulation or degradation
• Horses maintained in hot, humid climates are susceptible. Poor acclimatization after introduction from a cool climate, intense exercise during hot, humid conditions, water/salt restriction, and feeding a high-carbohydrate diet are suspected risk factors
• Treatment of foals with macrolide antibiotics causes temporary anhidrosis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Respiratory diseases that cause an increase in respiratory rate, especially heaves. Infectious diseases that cause an increase in rectal temperature.

CBC/BIOCHEMISTRY/URINALYSIS

Hyponatremia and hypochloremia in chronic severe cases. Decreased renal fractional excretion of chloride.

DIAGNOSTIC PROCEDURES

Intradermal injections, 0.1 mL/site, in the neck below the mane, of a drug with β_2-agonist activity (e.g. terbutaline sulfate, albuterol (salbutamol), epinephrine) using serial dilutions (0.001–1000 μg/mL) and a control (sterile saline)—read the results at 30 min. Sweat can be collected into absorbent pads taped over injection sites for more accurate results. Normal horses sweat in response to all dilutions. Anhidrotic horses have a decreased response to some or all.

PATHOLOGIC FINDINGS

Thickened basal laminae, thin myoepithelial and fundic epithelial cells, thickened connective tissues, and marked reduction of vesicles in the secretory cells. Luminal microvilli often are absent and the lumen of the duct is clogged with cellular debris.

TREATMENT

• Environmental management is the only reliable treatment option at present
• Horses exhibiting signs of heat stress should be immediately taken to a shaded environment, and cooled with cold water and fans
• Restrict to a stall with a fan and/or mister during hot periods of the day
• Minimize the feeding of carbohydrates
• Provide free-choice cool, fresh water and salt supplementation
• Inform clients that these horses will be prone to poor performance and will only improve once effective sweating has returned
• Discontinue use of β_2-agonists such as clenbuterol
• Keep foals that are treated with macrolides out of direct sunlight during and for a week after treatment

MEDICATIONS

DRUG(S) OF CHOICE

• Supplemental electrolytes, especially sodium salts
• Anecdotally, iodinated casein (10–15 g/day for 4–8 days) and with 1000–3000 IU PO of vitamin E (α-tocopherol) daily for 1 month, or amino acid supplements containing tyrosine

FOLLOW-UP

PATIENT MONITORING

Normally, a horse can reduce its body temperature to within normal limits approximately 30 min after exercise. Monitor respiration and rectal temperature post exercise.

PREVENTION/AVOIDANCE

• Carefully acclimatize horses to exercise in hot/humid conditions
• Keep foals treated with macrolides out of direct sunlight during and for a week after treatment
• Exercise during the cooler periods of the day
• Stall the horse in a cool environment (e.g. fan, water mister, air-conditioning) during the hotter periods of the day
• Anhidrosis is usually a lifelong problem, consider relocating the horse to a more temperate climate
• Avoid administration of β_2-agonists

POSSIBLE COMPLICATIONS

Heat stroke may occur if horses are exercised during the hotter periods of the day.

EXPECTED COURSE AND PROGNOSIS

• Most horses respond to a change in environment and begin to sweat normally after a few weeks
• Horses that have previously suffered from the disease will usually become anhidrotic if exposed to hot, humid conditions again

MISCELLANEOUS

ASSOCIATED CONDITIONS

Skin lesions—dry, flaky skin and alopecia, especially around the eyes and shoulders.

Suggested Reading

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Author Robert J. MacKay
Consulting Editors Michel Lévy and Heidi Banse

Acknowledgment The author and editors acknowledge the prior contribution of Jeremy D. Hubert and Ralph E. Beadle.

ANOREXIA AND DECREASED FOOD INTAKE

BASICS

DEFINITION

Anorexia is the loss of appetite or lack of desire for food. Some conditions may not lead to complete loss of appetite, but merely reduced food intake.

PATHOPHYSIOLOGY

Appetite Suppression

Anorexia is commonly a sign of systemic disease, including but not limited to GI disease. Reduced food intake can also be caused by various conditions affecting the lips, mouth, tongue, pharynx, esophagus, or stomach, and may include painful conditions, mechanical obstructions, or nervous or neuromuscular dysfunctions.

Anorexia appears to be the result of a modification of central regulation of feeding behavior in the hypothalamus. Many factors and substances may be involved in regulating feed intake. Anorexia associated with alterations of smell and taste has not been shown in the horse. Decreased food intake has been associated with parasitic infections, but the mechanism is unknown. Pain and depression appear to cause anorexia.

Serotonin agonists decrease food intake, apparently via central histaminergic activity. The neurotransmitter neuropeptide Y and various cytokines may cause cancer anorexia–cachexia syndrome. Primary disease conditions, such as infection, inflammation, injury, toxins, immunologic reactions, and necrosis, may cause anorexia via cytokine release. In addition, a proteoglycan has been identified on the cell membranes of animals and has been named *satiomem*. It reduces food intake and may be a satiety or anorexigenic substance.

SIGNALMENT

Signalment depends on underlying disease; any horse can be affected.

SIGNS

Signs include a general lack of interest or a lack of interest in certain types of food only.

Physical Examination Findings

- Clinical signs depend on the cause of anorexia. They are highly variable and depend on the underlying disease when due to systemic disease
- Common clinical signs in association with anorexia due to difficulty or inability of prehension, chewing, or swallowing of food include:
  - Increased salivation (ptyalism), often due to oral or dental disease or inability to swallow (CN IX, X, and XII), or intoxications
  - CN abnormalities—hypoesthesia of the face (CN V), neurogenic atrophy of the masticatory muscles (CN V, motor component), bilateral paralysis of facial muscles (CN VII)
  - Expulsion of partially chewed food ("quidding")
  - Nasal discharge containing feed material
  - Cough due to foreign material entering trachea; aspiration pneumonia can ensue
  - Oral lesions
  - Masses on the head in association with the mandibles and sinuses
  - If anorexia or decreased food intake occurs for prolonged periods of time weight loss, muscle wasting, and poor hair coat are evident. Edema can occur if hypoproteinemia due to decreased protein intake is severe
  - Slight jaundice

CAUSES

Anorexia

Anorexia can be a sign of systemic disease, commonly due to GI or abdominal disorders, including colic.

Anorexia commonly occurs after one of the following primary disease processes in any organ system—inflammation, infection (bacterial, viral, fungal, or parasitic), injury, intoxications, immunologic reactions, neoplasia, necrosis, dehydration, electrolyte imbalances, acid–base disorders, severe respiratory distress, uremia, cardiac disease, metabolic disorders, side effects of medications and pain.

Common specific causes include:

- gastric ulcers and pyloric stenosis
- primary GI colic
- peritonitis, colitis
- liver disease
- renal failure, renal tubular acidosis
- hypertriglyceridemia
- pneumonia and pleuropneumonia
- lymphoma and other malignant tumors
- neurologic disease
- cerebral disease
- laminitis
- endotoxemia, sepsis
- administration of metronidazole or valacyclovir (valaciclovir)
- prematurity and dysmaturity leading to muscle weakness in foals
- hypocalcemia, hypomagnesemia, hyponatremia
- congenital myotonia

Common causes of anorexia associated with inability to access, prehend, and swallow food include—pain (lips, tongue, mouth, teeth, mandibles, maxilla, sinuses, muscles, pharynx, esophagus, or temporomandibular joint), mechanical obstructions, and nervous dysfunction (lips, tongue, pharynx, esophagus).

Common specific causes include:

- Inability to access feed, e.g. neck pain preventing the horse from eating from the ground
- Swelling of the lips, e.g. bee stings or snake bites
- Mucosal lesions due to dental "points," virus-associated oral lesions (vesicular stomatitis), oral ulcers due to contact dermatitis, mechanical injury or phenylbutazone administration, oral lacerations, oral abscesses
- Tongue lacerations, tongue abscesses
- Neoplasia of the mouth or tongue
- Dental disease
- Postsurgical complication after head and neck surgery
- Guttural pouch disease (empyema, mycosis, neoplasia)
- Strangles
- Sinus disease (sinusitis, cysts, neoplasia)
- Neurologic disease affecting CN function, e.g. equine herpesvirus, equine protozoal myeloencephalitis, yellow star thistle poisoning, rabies, verminous encephalitis
- Tetanus, botulism, tick paralysis
- Temporomandibular joint disease
- Rhabdomyolysis affecting masseter muscles
- Mechanical obstruction in mouth, pharynx, or esophagus, e.g. foreign body, choke
- Pharyngitis
- Hyoid bone injury
- Esophageal disease (stricture, diverticulum, megaesophagus, neoplasia, choke, intramural inclusion cysts)
- Persistent right aortic arch, persistent dorsal displacement, epiglottic entrapment
- Compression of the pharynx (cysts—epiglottic, dorsal pharyngeal, aryepiglottic, soft palate, guttural pouch, or laryngeal neoplasia, strangles)
- Hyperkalemic periodic paralysis
- Muscle weakness (foals)
- Ruptured rectus capitus ventralis muscle

Unwillingness to eat can also be due to social factors such as anxiety owing to management problems (e.g. constant interruption, fear, low rank in herd).

RISK FACTORS

There are no specific risk factors for anorexia.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anorexia due to unpalatable or wrong feed materials
- Anorexia due to inability to access, prehend, and swallow food (see Causes for list of differential diagnoses)
- Anorexia due to systemic disease (see Causes for list of differential diagnoses)

CBC/BIOCHEMISTRY/URINALYSIS

- Free (unconjugated or indirect) bilirubin elevations. In cachectic animals bilirubin levels may be normal
- Hypokalemia
- Hypoproteinemia and decreased blood urea nitrogen (urea) if longstanding
- Decreased creatine kinase if associated with weight loss

(CONTINUED)

ANOREXIA AND DECREASED FOOD INTAKE

• Laboratory findings are consistent with the primary disease process (e.g. inflammation, internal organ damage) or secondary disease (e.g. aspiration pneumonia). Hematology, biochemistry (including renal and liver enzymes, albumin, globulin, triglycerides, and muscle enzymes), urinalysis, and evaluation of acute-phase proteins (fibrinogen, serum amyloid A) should be performed

OTHER LABORATORY TESTS
Based on suspected primary disease processes.

IMAGING
If the anorexia is associated with difficulties of food prehension and swallowing:
• Radiography of the head for evaluation of teeth, bones of the head, temporomandibular joint pharyngeal area, sinuses, and guttural pouches
• Radiography of the neck and thorax plus barium swallow or fluoroscopy for evaluation of the pharynx and esophagus
• Radiographs of the thorax to assess secondary complications such as aspiration pneumonia
• Ultrasonography of the tongue and pharynx
• Endoscopy of the oral cavity
• Endoscopy of the upper airways including nasal passage, pharynx, larynx, guttural pouches, and sinuses if necessary
If an underlying systemic disease is suspected:
• Abdominal and thoracic ultrasonography for primary inflammatory or neoplastic problems

OTHER DIAGNOSTIC PROCEDURES
• Examination of the food supply for evidence of contamination or spoilage
• Offering food to the patient and evaluating response, prehension, and swallowing
• Oral examination (under sedation using speculum and endoscope if available)
• Passage of a nasogastric tube to rule out a mechanical obstruction (e.g. choke)
• Neurologic examination
• Rectal examination for internal organ disease

TREATMENT
Dependent on primary disease.

ACTIVITY/DIET
Offer highly palatable and varied feed in easy to access locations in cases of anorexia. Supply feed that is easy to chew and swallow in cases of dysphagia. Force-feeding by nasogastric intubation or parenteral nutrition may be required. Activity should be limited to stall rest or hand-walking in most cases.

MEDICATIONS

DRUG(S) OF CHOICE
• Depends on primary disease process
• Oral administration of 40 g KCl once or twice daily in anorectic patients

CONTRAINDICATIONS
KCl administration may be contraindicated in patients with abnormal renal function or those suspected of having hyperkalemic periodic paralysis.

FOLLOW-UP

PATIENT MONITORING
The patient should be monitored for dehydration, electrolyte imbalance, acid–base abnormalities, and weight loss, and, in cases of dysphagia, aspiration pneumonia.

POSSIBLE COMPLICATIONS
• Dehydration
• Hypokalemia
• Hypocalcemia
• Metabolic alkalosis with salivary loss
• Weight loss
• Aspiration pneumonia with dysphagia

EXPECTED COURSE AND PROGNOSIS
Dependent on the underlying cause.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Other primary disease conditions, such as infection, inflammation, injury, toxins, immunologic reactions, and necrosis
• Cancer-related anorexia–cachexia syndrome
• Dehydration, electrolyte imbalances (hypokalemia, hypocalcemia), or acid–base disorders as a result of lack of intake of fluid and electrolytes may exacerbate the anorexia
• Salivary loss of electrolytes leads to metabolic alkalosis and hypochloremia, primarily
• Aspiration pneumonia occurs secondary to dysphagia

AGE-RELATED FACTORS
Depends on primary disease process. Foals are affected by different disease than adults.

ZOONOTIC POTENTIAL
Rabies can cause anorexia or dysphagia. Precautions should be taken while examining and treating the patient.

SYNONYMS
Decreased appetite.

SEE ALSO
• Acute kidney injury (AKI) and acute renal failure (ARF)
• Aspiration pneumonia
• Botulism
• Chronic kidney disease (CKD)
• Colic, chronic/recurrent
• Esophageal obstruction (choke)
• Gastric ulcers and erosions (equine gastric ulcer syndrome, EGUS)
• Guttural pouch empyema
• Guttural pouch mycosis
• Guttural pouch tympany
• Head trauma
• Hendra virus
• Ileus
• Lead (Pb) toxicosis
• Monensin toxicosis
• Nigropallidal encephalomalacia
• Organophosphate and carbamate toxicosis
• Peritonitis
• Rabies
• Sinusitis (paranasal)
• Snake envenomation
• *Streptococcus equi* infection
• Tetanus
• Vesicular stomatitis

ABBREVIATIONS
• CN = cranial nerve
• GI = gastrointestinal

Suggested Reading

Magdesian KG. Parenteral nutrition in the mature horse. Equine Vet Educ 2010;22:364–371.
Stratton-Phelps M. Assisted enteral feeding in adult horses. Compend Cont Educ Pract Vet 2004;26:46–49.

Author Angelika Schoster
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa

Client Education Handout available online

A

ANTHRAX

BASICS

OVERVIEW

• A fatal infectious disease that affects animals and humans caused by *Bacillus anthracis,* a Gram-positive spore-forming bacillus
• Worldwide distribution
• Mainly herbivores
• Most common form obtained after ingestion of soil, forage, or water contaminated with *B. anthracis* through wounds in the oral, pharyngeal, and GI mucosa, but the organisms may also be inhaled or inoculated by biting insects
• The organism passes to its vegetative form and produces exotoxins (lethal toxin and edema toxin) that impair phagocytosis and vascular integrity resulting in hemorrhage, edema, renal failure, shock, and almost invariably death. When *B. anthracis* is exposed to the environment, long-lasting spores (decades) are formed that are a potential source of infection for other animals

SIGNALMENT

• No gender, age, or breed predilections
• Grazing habits may affect signalment in some species

SIGNS

• Acute form—fever or hypothermia, depression, generalized muscle twitching, severe tachycardia and tachypnea, severe edema of the glottis, hypotonia of the anal sphincter, and death in less than 4 days; severe colic, bloody discharge from body orifices, and painful subcutaneous swellings
• Chronic form—pharyngeal edema, inspiratory stridor, head and neck swelling. Death up to 2 weeks after initial signs are noted
• Peracute form—death with few clinical signs, less common in horses

CAUSES AND RISK FACTORS

• Most common in tropical and subtropical climates; sporadic in temperate regions, usually in the summer
• Areas with soils high in calcium and with alkaline pH (>6.1) and with climate cycles of heavy rain and drought
• Overgrazing increases the ingestion of soil. Coarse forage causes erosions in the oral mucosa

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Lightning strike, poisoning or intoxication by plants, colic, enteritis, purpura haemorrhagica, malignant edema.

CBC/BIOCHEMISTRY/URINALYSIS

Routine laboratory findings have not been reported.

OTHER LABORATORY TESTS

Bacterial culture of blood or exudate. Results may be negative early in disease or if antibiotics have been administered. If the carcass has been opened, use lymph nodes or spleen. Cultures should only be performed in a facility capable of containment to prevent infection of laboratory personnel.

DIAGNOSTIC PROCEDURES

• Gram-positive, encapsulated, blunt-ended bacilli, occurring singly or in short chains on microscopic examination of blood smear or edema fluid. Smears become unreliable about 24 h after death
• Immunofluorescence of blood or tissue is a rapid confirmatory test for *B. anthracis* in culture
• PCR

PATHOLOGIC FINDINGS

• Because of human health risk and danger of environmental contamination, necropsy should not be performed if anthrax is suspected. Diagnosis can be made without necropsy
• Dark, nonclotting blood from orifices; absence of rigor mortis; splenomegaly; and lymphadenopathy are hallmarks of anthrax. Edema in the submucosa of the digestive tract, ventral abdomen, and chest is often observed

TREATMENT

• The high mortality, rapid course of disease, and late referral in some geographic areas usually limit the opportunity for treatment. The prognosis is poor even with treatment
• Isolate affected and in-contact animals

MEDICATIONS

DRUG(S) OF CHOICE

• Penicillin G (40 000 IU/kg IV every 4–6 h), oxytetracycline (5–11 mg/kg IV every 12 h), or enrofloxacin (7.5 mg/kg IV every 24 h). Continue treatment for at least 5 days
• Anthrax antiserum may be useful but is not available in the USA

FOLLOW-UP

• Regulatory officials should be notified when anthrax is suspected and the premises placed under quarantine
• Carcasses should not be opened. Dispose of by burning or deep (>2 m) burial with lime. The area can be disinfected with 5% aqueous lye or 10% formaldehyde. Hypochlorite (10% bleach) is sporicidal, but surfaces should be very clean before its use
• Susceptible animals should be vaccinated. Avirulent live spore vaccine. Provides immunity in 1 week. Some recommend a second vaccination in 2–4 weeks. Annual boosters are required. Severe adverse reactions have been reported. No antibiotics should be administered within 5 days before or after vaccination

MISCELLANEOUS

ZOONOTIC POTENTIAL

Severe zoonosis; gloves and mask should be worn if it is necessary to contact infected material or animals. Three presentations have been described—cutaneous (most common), pulmonary, and GI. All can progress to systemic dissemination followed by septic shock and death. Antibiotic therapy is successful if diagnosed early; commonly used antibiotics include ciprofloxacin and doxycycline.

SYNONYMS

• Charbon
• Splenic fever
• Woolsorter's disease

ABBREVIATIONS

• GI = gastrointestinal
• PCR = polymerase chain reaction

Suggested Reading

Walker RL. Anthrax. In: Smith BP, ed. Large Animal Internal Medicine, 4e. St. Louis, MO: Mosby, 2009:1180–1183.

Author Gonzalo Gajardo Aedo
Consulting Editor Ashley G. Boyle

The author and editor acknowledge the prior contribution of Laura K Reilly.

ANTICOAGULANT RODENTICIDE TOXICOSIS

BASICS

OVERVIEW

• ACRs are a commonly used class of rodenticides
• ACRs interfere with normal blood clotting and cause coagulopathy by inhibiting vitamin K epoxide reductase in liver and preventing formation of active clotting factors
• First-generation anticoagulants such as warfarin, coumafuryl, coumachlor, and coumatetralyl are short-acting, requiring multiple feedings to result in toxicosis
• Long-acting or second-generation ACRs include chlorophacinone, diphacinone, pindone, brodifacoum, bromadiolone, difethialone, difenacoum, and others. These are more toxic
• Most ACRs used today are second generation, with activity in the body lasting ~1 month or longer
• Minimum toxic dosage has not been established in horses. Coagulopathy has been reported in horses associated with a brodifacoum dosage of 0.125 mg/kg, and a diphacinone dosage of 0.2 mg/kg

SIGNALMENT

Poisoning can occur after accidental ingestion of bait or as a result of malicious intent.

SIGNS

• Hemorrhage of variable severity. Can be internal, external, or both, and can be focal or widespread
• Signs generally manifest within 2–5 days after ingestion and include pale mucous membranes, weakness, anorexia, dyspnea, tachycardia, hematomas and swellings, hematuria, bleeding from the mouth, and epistaxis
• Signs are delayed and do not occur until days after exposure, after existing clotting factors are depleted

CAUSES AND RISK FACTORS

• Careless bait placement
• Baits often contain ingredients that are attractive to horses

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Dicoumarol toxicosis
• Other causes of coagulopathy

CBC/BIOCHEMISTRY/URINALYSIS

• Anemia and hypoproteinemia suggestive of blood loss possible
• Urinalysis may show the presence of red blood cells

OTHER LABORATORY TESTS

• Prolonged PT, aPTT, and activated coagulation time. aPTT is reported to increase before PT in horses
• Chemical analysis of serum, whole blood or liver tissue (postmortem) for specific ACR compounds

IMAGING

Chest radiographs may show evidence of fluid in the chest cavity or hemorrhage within the lungs.

PATHOLOGIC FINDINGS

Hemorrhages may occur in any part of the body and may be focal or widespread.

TREATMENT

• Whole-blood or plasma transfusions to replace clotting factors if patient is actively bleeding. Whole blood is preferred with severe anemia
• Keep patient confined to stall rest
• Decontamination with AC and possibly a cathartic via nasogastric tube is appropriate if instituted soon after exposure (within several hours) and the patient is asymptomatic

MEDICATIONS

DRUG(S) OF CHOICE

• Vitamin K1 (phytonadione) 2.5 mg/kg every 24 h or divided into twice daily dosing, given PO or SC and continuing for 3–5 weeks for long-acting ACRs, or 1–2 weeks for short-acting compounds. If ACR compound is unknown, treat as for a long-acting ACR
• PO administration of vitamin K1 formulated for injection is preferable to SC injection, unless AC has been administered. Mixing vitamin K1 with a small amount of a digestible fat increases absorption. Most injectable formulations of vitamin K1 are well absorbed orally and can be administered orally until compounded vitamin K1 oral solution can be obtained
• A day or longer may be required for new clotting factor synthesis

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Do not use vitamin K3 (menadione) in horses. Vitamin K3 is ineffective and nephrotoxic
• Do not administer vitamin K1 IV as it can cause anaphylactic reaction
• NSAIDs and other drugs affecting coagulation are contraindicated

FOLLOW-UP

PATIENT MONITORING

• Continued monitoring of coagulation times and blood loss until patient is stable
• Check clotting times 2–3 days and 5 days after the last dose of vitamin K1 to determine if additional treatment is necessary

PREVENTION/AVOIDANCE

• Prevent access to rodenticide baits
• Not all rodenticides are anticoagulant compounds. Verify active ingredient if possible before treatment

POSSIBLE COMPLICATIONS

If duration of vitamin K1 therapy is too short, recurrence of coagulopathy can occur.

EXPECTED COURSE AND PROGNOSIS

• The prognosis is good if treatment is instituted before coagulopathy occurs
• The prognosis in patients with active bleeding depends on the severity and speed of hemorrhage, and the site of hemorrhage. Bleeding into the lungs, chest cavity, brain, or cranium can result in rapid death

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

• Lactating mares may excrete ACR in their milk
• Monitor foals for coagulopathy, and treat with vitamin K1 if clotting times are elevated. Alternatively, consider weaning the foal from the affected mare and providing an alternative milk supply

SEE ALSO

• Coagulation Defects Acquired
• Coagulation Defects, Inherited
• Dicoumarol (moldy sweet clover) toxicosis
• Disseminated Intravascular Coagulation

ABBREVIATIONS

• AC = activated charcoal
• ACR = anticoagulant rodenticide
• aPTT = activated partial thromboplastin time
• NSAID = nonsteroidal anti-inflammatory drug
• PT = prothrombin time

Suggested Reading

Boermans HJ, Johnstone I, Black WD, Murphy M. Clinical signs, laboratory changes and toxicokinetics of brodifacoum in the horse. Can J Vet Res 1991;55:21–27.
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Author Cynthia L. Gaskill
Consulting Editors Wilson K. Rumbeiha and Steve Ensley
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ANURIA/OLIGURIA

BASICS

DEFINITION
• *Anuria*—lack of urine production
• *Oliguria*—decreased urine production (<0.5 mL/kg/h, or <250 mL/h in a 500 kg horse)
• Anuria or oliguria may be physiologic or pathologic
• This chapter will focus on intrinsic renal failure causing anuria and oliguria

PATHOPHYSIOLOGY
N/A

SYSTEMS AFFECTED
Renal/urologic

GENETICS
N/A

INCIDENCE/PREVALENCE
Unknown

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
No age, sex, or breed predilection documented.

SIGNS
• No or insufficient urine production
• Repeated posturing to urinate, with no urine production, in case of urinary tract obstruction
• Abdominal distention in case of uroperitoneum
• Edema when persistent anuria

CAUSES
• Physiologic oliguria—hyperosmolality; any disease process leading to renal hypoperfusion (e.g. dehydration, hypotension, low cardiac output)
• Pathologic anuria/oliguria—intrinsic ARF; trauma to the lower urinary tract

RISK FACTORS
• Risk factors predisposing to ARF
• For trauma to lower urogenital tract—birth trauma (e.g. dystocia) would increase the risk of urinary tract disruption and uroperitoneum in neonates and their dams; penile trauma is more common in breeding stallions

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Pathologic Anuria/Oliguria
• Intrinsic AKI/ARF, terminal CKD, lower urinary tract disruption resulting in uroperitoneum, and urinary tract obstruction consequent to urolithiasis
• Bladder displacement
• Progressive abdominal distention should increase suspicion of uroperitoneum
• Repeated posturing to urinate, with little urine passed, supports urinary tract obstruction

CBC/BIOCHEMISTRY/URINALYSIS
• Normal to high packed cell volume in most cases; mild to moderate anemia possible with terminal CKD
• Moderate to severe increases in blood urea nitrogen (59–150 mg/dL; 18–54 mmol/L) and Cr (2.0–20 mg/dL; 177–1768 µmol/L)
• Variable hyponatremia, hypochloremia, hyperkalemia, hypocalcemia, and hyperphosphatemia—hyperkalemia and hyperphosphatemia more common with intrinsic AKI/ARF; hyperkalemia most apparent with urinary tract disruption and development of uroperitoneum
• Mild to moderate metabolic acidosis—dependent on the underlying disease process
• Mild to moderate hyperglycemia—attributed to stress
• USG—high (>1.035) with physiologic oliguria, low (<1.020) with oliguria due to intrinsic AKI/ARF; USG best assessed in urine collected during initial patient evaluation (before rehydration) or while the horse is not receiving fluids
• Oliguria with intrinsic AKI/ARF may be accompanied by mild to moderate proteinuria, glucosuria, pigmenturia, and increased numbers of red blood cells and casts on sediment examination
• Urine pH—normal to acidic, especially with concurrent depletion of body potassium stores

OTHER LABORATORY TESTS
• Fractional clearances (i.e. excretions) of electrolytes in cases of ARF/CKD
• Increased urinary γ-glutamyltransferase to Cr ratio >25 in cases of ARF
• Increased urine protein to Cr ratio in cases of CKD

IMAGING

Transabdominal and Transrectal Ultrasonography
• Kidneys may be enlarged, with loss of detail of corticomedullary junction, in intrinsic AKI/ARF
• Kidneys typically are reduced in size, with increased parenchymal echogenicity, in CKD
• Accumulation of hypoechoic fluid in the peritoneal cavity in cases of uroperitoneum
• Urinary calculi can be identified as hyperechoic structures associated with a shadow cone and distended proximal urinary tract

Urethroscopy/Cystoscopy
Endoscopy of the lower urinary tract is indicated when there is suspicion of lower urinary tract obstruction.

DIAGNOSTIC PROCEDURES
• Abdominocentesis is indicated in cases of peritoneal effusion. Peritoneal Cr concentration over twice blood concentration in cases of uroperitoneum
• Measurement of glomerular filtration rate and renal biopsies are indicated in case of CKD/chronic renal failure
• Central venous pressure/arterial pressure measurements

PATHOLOGIC FINDINGS
See specific topics.

TREATMENT

APPROPRIATE HEALTH CARE
• *Treat anuria/oliguria as a medical emergency because persistent renal hypoperfusion may lead to ischemic AKI/ARF*
• If untreated, metabolic disturbances, most notably hyperkalemia, may lead to cardiac arrhythmias and death
• Once the patient is stabilized (largely with supportive treatment in the form of IV fluid therapy), pursue further diagnostic evaluation to determine if surgical intervention (for correction of uroperitoneum or relief of obstruction) is needed
• Proper recognition and treatment of all primary disease processes, usually on an inpatient basis for continuous fluid therapy, is warranted
• Avoid nephrotoxic medications

NURSING CARE
• Fluid therapy is a large part of supportive treatment
• Peritoneal drainage and urinary catheterization to remove urine from the abdomen is part of the treatment of uroperitoneum

ACTIVITY
Stall rest.

CLIENT EDUCATION
N/A

SURGICAL CONSIDERATIONS
Surgical intervention is indicated for uroperitoneum and urolithiasis. See specific topics.

MEDICATIONS

DRUG(S) OF CHOICE
• Fluid therapy to correct renal hypoperfusion—after initial measurement of body weight, correct estimated dehydration with isotonic (0.9%) saline or another potassium-poor electrolyte solution over 12–24 h; monitor closely for subcutaneous and pulmonary edema (i.e. increased respiratory rate and effort); conjunctival edema may develop rapidly in horses with intrinsic oliguric to anuric AKI/ARF; use maintenance fluid therapy judiciously in animals that are not clinically dehydrated; if hemorrhage is contributing to hypovolemia

and renal hypoperfusion, initial treatment with hypertonic saline and/or a blood transfusion may have value
• Severe hyperkalemia (>7.0 mEq/L) or cardiac arrhythmias—treat with agents that decrease serum potassium concentration (e.g. sodium bicarbonate (1–2 mEq/kg IV over 5–15 min)), or counteract the effects of hyperkalemia on cardiac conduction (e.g. calcium gluconate (0.5 mL/kg of a 10% solution by slow IV injection))
• Furosemide—this diuretic may be administered 2 times (1–2 mg/kg IV or IM) at 1–2 h intervals; if effective, urination should be observed within 1 h after administration of the second dose; if ineffective, discontinue
• Based on recent evidence in critically ill human patients *the routine use of mannitol or dopamine in equine patients with oliguria is no longer recommended*

CONTRAINDICATIONS
Avoid all nephrotoxic medications unless specifically indicated for the underlying disease process, and then modify dosage accordingly.

PRECAUTIONS
• Monitor response to fluid therapy closely—as little as 40 mL/kg of IV fluids (20 L to a 500 kg horse) may produce pulmonary edema
• Reassess dosage schedule of drugs eliminated by urinary excretion; consider discontinuing all nephrotoxic medications (especially gentamicin, tetracycline, and NSAIDs)

POSSIBLE INTERACTIONS
Use of multiple anti-inflammatory drugs (e.g. corticosteroids and one or more NSAIDs) will have additive negative effects on renal blood flow; avoid combined administration in azotemic patients.

ALTERNATIVE DRUGS
None

FOLLOW-UP

PATIENT MONITORING
• Assess clinical status (emphasizing hydration), urine output, and body weight frequently for the first 3 days
• Assess magnitude of azotemia and electrolyte and acid–basis status at least daily for the first 3 days of treatment
• Consider placing a central venous line to maintain central venous pressure <8 cmH_2O in more critical patients and neonates

PREVENTION/AVOIDANCE
See specific topics.

POSSIBLE COMPLICATIONS
• Severe hyperkalemia accompanied by cardiac arrhythmias and death
• Pulmonary and peripheral edema; conjunctival edema may be dramatic

EXPECTED COURSE AND PROGNOSIS
Dependent on underlying cause. Poor prognosis if diuresis is not rapidly restored.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Colic; enterocolitis
• Pleuritis; peritonitis; septicemia
• Exhausted horse syndrome—multiorgan failure

AGE-RELATED FACTORS
Neonates afflicted with hypoxic–ischemic multiorgan damage or septicemia may be at increased risk of anuric/oliguric AKI/ARF.

ZOONOTIC POTENTIAL
Leptospirosis has infectious and zoonotic potential; avoid direct contact with infective urine.

PREGNANCY/FERTILITY/BREEDING
None

SYNONYMS
None

SEE ALSO
• Acute kidney injury (AKI) and acute renal failure (ARF)
• Chronic kidney disease (CKD)
• Urolithiasis
• Uroperitoneum, neonate

ABBREVIATIONS
• AKI = acute kidney injury
• ARF = acute renal failure
• CKD = chronic kidney disease
• Cr = creatinine
• NSAID = nonsteroidal anti-inflammatory drug
• USG = urinary specific gravity

Suggested Reading

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Author Harold C. Schott II
Consulting Editor Valérie Picandet

A

AORTIC REGURGITATION

BASICS

DEFINITION
Occurs when blood leaks from the aortic valve into the left ventricular outflow tract during diastole.

PATHOPHYSIOLOGY
• The aortic leaflets do not form a complete seal between the aorta and left ventricle
• During diastole, blood regurgitates into the left ventricular outflow tract, causing a left ventricular volume overload. As this volume overload worsens, stretching of the mitral annulus occurs, and MR often develops. MR compounds the severe left ventricular volume overload, and these horses often rapidly develop CHF
• Severe regurgitation results in decreased coronary artery blood flow and decreased myocardial perfusion
• Ventricular arrhythmias may develop secondary to decreased myocardial perfusion and increased myocardial oxygen demand during exercise

SYSTEMS AFFECTED
Cardiovascular

GENETICS
N/A

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Usually horses >10 years.

SIGNS
General Comments
Often an incidental finding during routine auscultation.

Historical Findings
• Poor performance
• Possibly CHF

Physical Examination Findings
• Grade 1–6/6, decrescendo or musical holodiastolic murmur with PMI in the aortic valve area radiating to the left apex and right side
• Bounding arterial pulses with moderate to severe regurgitation
• Other, less common findings—AF, ventricular premature complexes, accentuated third heart sounds, and CHF

CAUSES
• Degenerative changes of the aortic leaflets
• Aortic valve prolapse
• Nonvegetative valvulitis
• Fenestration of aortic leaflets
• Flail aortic leaflet
• Infective endocarditis
• Ventricular septal defect
• Congenital malformation
• Disease of the aortic root

RISK FACTORS
Old age.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Pulmonic regurgitation—rare; murmurs not usually detectable and should have PMI in the pulmonic valve area; differentiate echocardiographically.

CBC/BIOCHEMISTRY/URINALYSIS
May have neutrophilic leukocytosis, elevated serum amyloid A, and hyperfibrinogenemia with bacterial endocarditis.

OTHER LABORATORY TESTS
• Elevated cardiac troponin I or cardiac troponin T with concurrent myocardial disease
• Positive blood culture may be obtained with bacterial endocarditis

IMAGING
ECG
• Ventricular premature complexes may be present with severe regurgitation
• AF often develops with marked left ventricular volume overload and subsequent left atrial enlargement

Echocardiography
• Most affected horses have thickened aortic valve leaflets
• An echogenic band parallel to or a nodular thickening of the left coronary leaflet free edge are the most common findings
• Prolapse of an aortic leaflet (usually the noncoronary leaflet) into the left ventricular outflow tract frequently is detected
• Fenestration of the aortic leaflet, flail aortic leaflet, vegetations associated with infective endocarditis, or aortic root abnormalities are infrequently detected
• Left ventricle—enlarged and dilated, with a rounded apex and thinner left ventricular free wall and interventricular septum with pattern of left ventricular volume overload
• Increased septal-to-E point separation may be present
• Normal or decreased fractional shortening with left ventricular enlargement is consistent with myocardial dysfunction
• Dilatation of the aortic root occurs with longstanding regurgitation
• High-frequency vibrations on the mitral valve septal leaflet or interventricular septum usually are detected, created by turbulence in the left ventricular outflow tract
• High-frequency vibrations on the aortic leaflets usually are visualized in horses with musical holodiastolic murmurs
• Premature mitral valve closure may indicate more severe aortic insufficiency
• Decreasing aortic root diameter throughout diastole is another indication of increasing severity
• Pulsed-wave or color-flow Doppler reveals a jet or jets of regurgitation in the left ventricular outflow tract. Size of the jet at its origin and its size and extent in the left ventricle represent another means of semiquantitating its severity, as is strength of the regurgitation signal
• A steep slope and short pressure half-time of the continuous-wave Doppler spectral tracing of the regurgitation jet indicate more severe regurgitation

Thoracic Radiography
• Left-sided cardiac enlargement presents with moderate to severe regurgitation
• Pulmonary edema may be present with CHF

OTHER DIAGNOSTIC PROCEDURES
Cardiac Catheterization
• Right-sided catheterization may reveal elevated pulmonary capillary wedge pressures and pulmonary arterial pressures with severe regurgitation and concurrent MR
• Right ventricular and atrial pressures may be elevated with CHF
• Oxygen saturation of blood obtained from the right atrium, right ventricle, and pulmonary artery should be normal

Noninvasive Blood Pressure Measurement
Pulse pressure >60 mmHg—progression likely.

Exercising ECG
Should be performed in all horses with moderate to severe aortic regurgitation.

Continuous 24 h Holter Monitoring
Use if ventricular premature complexes suspected.

PATHOLOGIC FINDINGS
• Focal or diffuse thickening or distortion of one or more aortic leaflets (bands, nodules, plaques, and fenestrations) may be present
• Flail aortic leaflets, infective endocarditis, or congenital malformations of the aortic valve infrequently are detected
• Aortic root dilatation usually is present with severe, longstanding regurgitation
• Jet lesions usually are detected on the ventricular side of the mitral valve septal leaflet and, less frequently, on the interventricular septum
• Left ventricular enlargement and thinning of the left ventricular free wall and interventricular septum with significant regurgitation
• Atrial myocardial thinning with atrial dilatation has been documented in horses with AF and enlargement
• Inflammatory cell infiltrate has been detected with myocarditis and aortic regurgitation; however, most affected horses do not have significant underlying myocardial disease

TREATMENT

AIMS
• Management by intermittent monitoring in horses with aortic regurgitation that is mild or moderate in severity
• Palliative care in horses with severe aortic regurgitation

APPROPRIATE HEALTH CARE
• Most affected horses require no treatment and can be monitored on an outpatient basis
• Horses with moderate to severe regurgitation may benefit from long-term vasodilator therapy, particularly with ACE inhibitors
• Treat horses with severe regurgitation and CHF with positive inotropic drugs, vasodilators, and diuretics and monitor response to therapy

NURSING CARE
N/A

ACTIVITY
• Affected horses are safe to continue in full athletic work until the regurgitation becomes severe or ventricular arrhythmias develop
• Monitor horses with moderate to severe regurgitation by ECG during high-intensity exercise to ensure they are safe for ridden activities. These horses can be used for lower level athletic activities until they begin to develop CHF
• Horses with significant ventricular arrhythmias or pulmonary artery dilatation are no longer safe to ride

CLIENT EDUCATION
• Regularly palpate for bounding arterial pulses which indicate significant left ventricular volume overload and moderate to severe regurgitation
• Regularly monitor cardiac rhythm; any irregularities other than second-degree atrioventricular block should prompt ECG
• Carefully monitor for exercise intolerance, respiratory distress, prolonged recovery after exercise, increased resting respiratory rate or heart rate, or cough; if detected, seek a cardiac reexamination

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
• Severe regurgitation—consider benazepril (1 mg/kg PO every 12 h)
• ACE inhibitors prolong the time to valve replacement in humans with moderate to severe regurgitation
• Some horses with moderate to severe regurgitation have experienced a decrease in left ventricular chamber size with ACE inhibitors
• Treatment of affected horses in heart failure includes digoxin, diuretics, and vasodilators

CONTRAINDICATIONS
ACE inhibitors and other vasodilators must be withdrawn before competition to comply with the medication rules of the various governing bodies of equine sports.

PRECAUTIONS
ACE inhibitors can cause hypotension; thus, do not give a large dose without time to accommodate to this treatment.

ALTERNATIVE DRUGS
Other ACE inhibitors and other vasodilatory drugs should have some beneficial effect in horses with moderate to severe regurgitation, but they may be less effective than benazepril.

FOLLOW-UP

PATIENT MONITORING
• Frequently monitor arterial pulses and cardiac rhythm
• Reexamine horses with mild to moderate regurgitation by echocardiography every year
• Reexamine horses with severe regurgitation by echocardiography and with exercising ECG every 6 months to monitor progression of valvular insufficiency and determine if the horse continues to be safe to ride or drive

POSSIBLE COMPLICATIONS
Chronic regurgitation—ventricular arrhythmias; AF; MR; CHF.

EXPECTED COURSE AND PROGNOSIS
• Most affected horses have a normal performance life and life expectancy
• Progression of regurgitation associated with degenerative valve disease usually is slow. With the typical onset of regurgitation that occurs in old horses, other problems are more likely to end a horse's performance career or shorten life expectancy
• Affected horses with CHF usually have severe underlying valvular and/or myocardial disease and a guarded to grave prognosis for life. Most affected horses being treated for CHF respond to the supportive therapy and improve. This improvement usually is short lived, however, and most are euthanized within 2–6 months of initiating treatment

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Old horses are more likely to be affected.

PREGNANCY/FERTILITY/BREEDING
• Affected mares should not experience any problems with pregnancy unless the regurgitation is severe
• Treat pregnant affected mares with CHF for the underlying cardiac disease with positive inotropic drugs and diuretics; ACE inhibitors are contraindicated because of potential adverse effects on the fetus

SYNONYMS
Aortic insufficiency

SEE ALSO
• Endocarditis, infective
• Ventricular septal defect (VSD)

ABBREVIATIONS
• ACE = angiotensin-converting enzyme
• AF = atrial fibrillation
• CHF = congestive heart failure
• MR = mitral regurgitation
• PMI = point of maximal intensity

Suggested Reading

Afonso T, Giguere S, Rapoport G, et al. Pharmacodynamic evaluation of 4 angiotensin-converting enzyme inhibitors in healthy adult horses. J Vet Intern Med 2013;27:1185–1192.

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Author Virginia B. Reef
Consulting Editors Celia M. Marr and Virginia B. Reef

AORTIC RUPTURE

BASICS

DEFINITION
A defect in the wall of the aorta at the aortic root, usually in the right sinus of Valsalva or the aortic arch.

PATHOPHYSIOLOGY
• Aortic rupture can result in dissecting aneurysm, exsanguination into the thoracic cavity, cardiac tamponade from hemopericardium; a shunt between the aorta and heart if the defect is located in the aortic root; or a shunt between the aorta and pulmonary artery if the defect is located in the aortic arch
• With an aortic rupture confined to the right sinus of Valsalva, an aorticocardiac fistula is created. Blood from the aorta shunts into the right side of the heart, at either the atrial or ventricular level, depending on the site of the rupture
• Subendocardial dissection of blood into the interventricular septum is common, with subsequent rupture into the right or left ventricle (more commonly, the rupture is into the right ventricle)
• Often associated with a unifocal ventricular tachycardia that may be associated with dissection of blood into the interventricular septum
• Aortic arch rupture leads to periaortic hematoma, aortopulmonary fistulation, and pseudoaneurysm

SYSTEMS AFFECTED
Cardiovascular

INCIDENCE/PREVALENCE
Rare

SIGNALMENT
• Aortic root rupture more frequently occurs in old horses, particularly males and often during or after breeding or other exercise
• The Friesian breed is predisposed to aortic arch rupture and signs occur in young adults

SIGNS
General Comments
Often interpreted by owners as colic, because the horse appears distressed, may be looking at its flanks, and acts uncomfortable.

Historical Findings
• Acute onset of colic or distress, particularly with aortic root rupture
• Subacute or chronic low-grade colic, particularly with aortic arch rupture
• Less commonly, exercise intolerance; syncope, CHF

Physical Examination Findings
• Tachycardia
• Tachypnea
• Continuous machinery murmur—usually loudest on the right side
• Bounding arterial pulses
• Other, less common findings—jugular pulses and distention, ventricular tachycardia (unifocal), and CHF

CAUSES
• A congenital aneurysm in the wall of the aortic root, usually in the right sinus of Valsalva, predisposes to aortic root rupture
• Necrosis and degeneration of the aortic media have been associated, especially in old breeding stallions
• Aberrant parasite migration in the ascending aorta is unlikely
• Hereditary connective tissue disorders suspected to be an underlying cause in Friesians

RISK FACTORS
• Aortic aneurysm
• Aortitis
• Friesian breed

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Ventricular Septal Defect with Aortic Regurgitation
• Murmurs are systolic (band shaped and pansystolic) and diastolic (holodiastolic and decrescendo), not continuous
• Arterial pulses usually are not bounding, unless the associated aortic regurgitation is severe
• No history of acute colic or distress
• Differentiate echocardiographically

Patent Ductus Arteriosus
• No history of acute colic or distress
• No unifocal ventricular tachycardia
• Differentiate echocardiographically

CBC/BIOCHEMISTRY/URINALYSIS
Increased serum creatinine and blood urea nitrogen may occur because of impaired renal perfusion, which is associated with sustained ventricular tachycardia and blood loss.

OTHER LABORATORY TESTS
Serum cardiac troponin I can be elevated with significant myocardial cell injury.

IMAGING
ECG
Uniform ventricular tachycardia with a heart rate of >100 bpm may be present with aortic root rupture.

Echocardiography
• 2-dimensional echocardiography is diagnostic for a defect in the aortic root at the sinus of Valsalva or for a sinus of Valsalva aneurysm
• The rupture may be a small, irregular defect in the aortic wall (usually associated with the right aortic leaflet) or be visualized flailing in the right atrium or ventricle
• Anechoic to echoic fluid may be detected dissecting subendocardially into the interventricular septum, most frequently along the right ventricular side; however, dissection of blood subendocardially along the left side also occurs
• Use color-flow Doppler, pulsed-wave Doppler, or contrast echocardiography to localize the shunt associated with the aortic cardiac fistula
• Transthoracic echocardiography may demonstrate pulmonary artery dilation, displacement of the pulmonary artery, and aortopulmonary fistulation (best visualized from the left cranial window) with aortic arch rupture
• Transesophageal echocardiography is potentially useful with aortic arch rupture

Thoracic Radiography
• An enlarged cardiac silhouette should be present in horses with a large aorticocardiac shunt
• Pulmonary overcirculation and edema may be detected

OTHER DIAGNOSTIC PROCEDURES
Cardiac Catheterization
• Elevated right ventricular pressure, pulmonary arterial pressure, pulmonary capillary wedge pressure, and oxygen saturation of the blood are detected in horses with aorticocardiac fistula into the right ventricle
• With a shunt into the right atrium, right atrial pressures and oxygen saturation also are elevated

Arterial Blood Pressure
Demonstrates the wide difference between peak systolic pressure and end-diastolic pressure associated with continuous shunting of blood from the aorta into the heart.

PATHOLOGIC FINDINGS
• Postmortem examination confirms the site and extent of the rupture and the presence of aorticocardiac or aortopulmonary fistula
• Path of the dissection can be traced
• Dissecting tracts into the interventricular septum usually are lined with immature and mature fibrous tissue, and disruption of the conduction system has been detected
• Degeneration and necrosis of the aortic media have been reported in some horses with aortic rupture but not in other affected horses
• An absence of media in the right sinus of Valsalva was reported in one horse with a sinus of Valsalva (i.e. aortic root) aneurysm
• Fibrosis and scarring of the rupture site have been reported in old breeding stallions that died of unrelated causes

TREATMENT

AIMS
Palliative care.

APPROPRIATE HEALTH CARE
• Closely monitor affected horses with ventricular tachycardia if the tachycardia is uniform, the heart rate is <100 bpm, no R-on-T complexes are detected, and no clinical signs of cardiovascular collapse are observed
• If ventricular tachycardia is multiform, R-on-T complexes are detected, heart rate is >100 bpm, or with clinical signs of cardiovascular collapse, institute antiarrhythmic treatment on an inpatient basis
• If CHF also is present, institute treatment for CHF as well. Consider humane euthanasia, however, because the horse is no longer safe to use for athletic work

NURSING CARE
• Perform continuous ECG monitoring during the attempted conversion from ventricular tachycardia to sinus rhythm
• Keep horses quiet and unmoving during antiarrhythmic treatment

ACTIVITY
• Stall confinement until conversion to sinus rhythm has been successfully achieved
• Restrict athletic activity as much as possible once ventricular tachycardia has been converted

CLIENT EDUCATION
• Affected horses are not safe to ride or use for any type of athletic work because of the risk of sudden death associated with further aortic rupture or development of fatal ventricular arrhythmia
• If the horse is a breeding stallion and such continued use is desired, warn the stallion and mare handlers (and all other personnel involved) about the risk of sudden death
• Develop an emergency plan in the event the stallion becomes unsteady or unsafe to handle

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
Antiarrhythmics
• Indicated with multiform ventricular tachycardia, R-on-T complexes, heart rate >120 bpm, or clinical signs of cardiovascular collapse
• Drug selection depends on severity of ventricular tachycardia and associated clinical signs
• Lidocaine (0.25 mg/kg IV slowly, can repeat in 5–10 min) is rapid acting and has a very short duration of action. However, it also has central nervous system effects in horses and, thus, must be used carefully
• Procainamide (1 mg/kg/min IV to total dose of 20 mg/kg) and quinidine gluconate (0.5–2.2 mg/kg IV every 10 min to total dose 10 mg/kg) have been effective in converting sustained, uniform ventricular tachycardia but have a slower onset of action
• Magnesium sulfate (2.2–4.4 mg/kg IV slowly, can repeat in 5 min to total dose of 55 mg/kg) has been successful in converting sustained ventricular tachycardia and is not arrhythmogenic

CONTRAINDICATIONS
Other vasodilators or antihypertensive drugs have the potential to adversely affect the stallion's libido, breeding performance, or fertility.

PRECAUTIONS
Affected horses could experience sudden death at any time; thus, everyone working around these horses must be aware of the safety issues involved.

POSSIBLE INTERACTIONS
Any antiarrhythmic drug has the potential to cause development of a more adverse arrhythmia as well as to convert to sinus rhythm.

ALTERNATIVE DRUGS
Propranolol
• The IV form is less likely to be effective but should be considered in affected horses with refractory ventricular tachycardia
• Lowers systolic blood pressure

FOLLOW-UP

PATIENT MONITORING
• Routine monitoring of heart rate and of respiratory rate and rhythm after conversion to sinus rhythm
• Persistent tachypnea, tachycardia, or new arrhythmias indicate deterioration in clinical status
• Return of venous distention and jugular pulsations or development of ventral edema or coughing indicate the onset of CHF and worsening of ventricular volume overload

PREVENTION/AVOIDANCE
• With intact aneurysms of the sinus of Valsalva, control of systemic blood pressure may prolong the time until rupture occurs
• With degenerative changes in the aortic media, antihypertensive drugs theoretically should have some benefit. However, identification of horses at risk has not yet been accomplished

POSSIBLE COMPLICATIONS
• Deterioration of uniform ventricular tachycardia into fatal ventricular arrhythmia
• Severe, acute CHF from massive right atrial or ventricular, left atrial, and left ventricular volume overload
• Tricuspid valve rupture, leading to massive tricuspid regurgitation and CHF
• Rupture of a chorda tendinea of the tricuspid or mitral valve, leading to massive tricuspid or mitral regurgitation, respectively, and acute right- or left-sided CHF
• Sudden death

EXPECTED COURSE AND PROGNOSIS
• Prognosis for life of affected horses is grave and sudden death is possible
• Although the condition is invariably fatal, some horses can live relatively comfortably for several months after diagnosis

MISCELLANEOUS

ASSOCIATED CONDITIONS
Aortic root aneurysm.

AGE-RELATED FACTORS
Old horses are more likely to be affected with aortic root rupture, but horses as young as 4 years have been diagnosed. Aortic arch rupture typically presents in horses <4 years old.

PREGNANCY/FERTILITY/BREEDING
• Rupture of a sinus of Valsalva aneurysm has been seen in one late-gestation pregnant mare. The volume expansion of late pregnancy may predispose pregnant mares to aortic rupture at this time
• Aortic root rupture has been seen in one mare during early pregnancy. This mare experienced acute onset of ventricular tachycardia and subendocardial dissection of blood into the interventricular septum but survived to have the foal

SYNONYMS
• Aortic cardiac fistula
• Aorticocardiac fistula

SEE ALSO
Ventricular arrhythmias

ABBREVIATIONS
CHF = congestive heart failure

AORTIC RUPTURE (CONTINUED)

Suggested Reading
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Author Celia M. Marr
Consulting Editors Celia M. Marr and Virginia B. Reef
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AORTOILIAC THROMBOSIS

BASICS

OVERVIEW

Aortoiliac thrombosis occurs when a thrombus forms at the aortic quadrification and terminal portions of the aorta. Depending on its size, it may involve 1 or more of the internal and external iliac arteries. Larger thrombi may extend into the coccygeal arteries. Clinical signs relate to occlusion of these vessels and compromise to blood supply.

Systems affected

- Cardiovascular
- Musculoskeletal

SIGNALMENT

Horses of any age can be affected and there are no known breed or sex predilections.

SIGNS

- Affected horses generally present with hindlimb lameness, which is typically chronic and insidious but can be more acute and severe
- Lameness usually becomes increasingly severe with exercise
- After exercise the affected limb may be cool with reduced pulse pressure
- The thrombus may be palpable on transrectal examination
- Ejaculatory failure has been reported

CAUSES AND RISK FACTORS

Specific causes and risk factors have not been identified. Parasites are unlikely to be involved.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

There are numerous causes of hindlimb lameness. Clinical signs of aortoiliac thrombosis can be similar to those of exertional rhabdomyolysis.

LABORATORY TESTS

- Laboratory tests are not generally helpful and no link between aortoiliac thrombosis and coagulopathy has been documented
- Modest increases in serum creatine kinase and aspartate aminotransferase activity may occur and measurement of these enzymes may help rule out primary myopathy

IMAGING

- Transrectal ultrasonographic imaging will usually demonstrate the thrombus and allow the extent of blood vessel involvement to be defined; the femoral artery should also be evaluated transcutaneously
- First-pass radionucleotide imaging will also demonstrate reduction of blood flow in affected iliac arteries and scintigraphic studies are indicated in some horses presenting with hindlimb lameness to rule out other causes

TREATMENT

- Horses should be withdrawn from work and rested (stall or pasture). Some horses improve following treatment with aspirin (18 mg/kg PO every 48 h) or clopidogrel at 2 mg/kg PO every 24 hours
- Surgical thrombectomy has been successful in restoring athletic activity in approximately 65% of cases

FOLLOW-UP

PATIENT MONITORING

Transrectal ultrasonography will allow the size and extent of the thrombus to be determined.

POSSIBLE COMPLICATIONS

Platelet count should be monitored every 2–4 weeks in horses receiving long-term aspirin therapy.

EXPECTED COURSE AND PROGNOSIS

The prognosis is fair—some horses resolve completely following either medical management or surgical intervention. In others the condition is progressive and requires the horse to be retired from all forms of exercise.

Suggested Reading

Rijkenhuizen AB, Sinclair D, Jahn W. Surgical thrombectomy in horses with aortoiliac thrombosis: 17 cases. Equine Vet J 2009;41:754–758.

Warmerdam EPL. Ultrasonography of the femoral artery in 6 normal horses and three horses with thrombosis. Vet Radiol Ultrasound 1998;39:137–141.

Author Celia M. Marr
Consulting Editors Celia M. Marr and Virginia B. Reef

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ARSENIC TOXICOSIS

BASICS

OVERVIEW
• Results from excessive exposure to arsenic-containing pesticides, arsenic-contaminated soils, burn piles, and water or feed
• Ashes from chromated copper arsenate-treated lumber are high in arsenic
• Toxicity depends on the form of arsenic ingested
• Trivalent inorganic forms (e.g. arsenic trioxide; sodium, potassium, and calcium salts of arsenite) are 10-fold more toxic than inorganic pentavalent forms (e.g. sodium, potassium, and calcium salts of arsenate)
• Trivalent inorganic arsenicals inhibit cellular respiration and damage capillaries, mostly of the GI tract
• Pentavalent inorganic arsenicals uncouple oxidative phosphorylation, leading to deficits in cellular energy

SIGNALMENT
No breed, age, or sex predilections.

SIGNS
• Peracute or acute syndromes are likely
• Peracute—patient often found dead; death caused by cardiovascular collapse
• Acute—intense abdominal pain, hypersalivation, severe watery diarrhea, decreased abdominal sounds, muscle tremors, weak and rapid pulse with signs of circulatory shock, ataxia, depression, and recumbency; if the animal survives for several days, oliguria and proteinuria secondary to renal damage
• Chronic—not described in horses but should be considered in regions of high water arsenic

CAUSES AND RISK FACTORS
Accidental exposure to old arsenic-containing pesticides or arsenic-contaminated soils, ashes, water, or feed.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Lead toxicosis—evidence of neurologic dysfunction is likely; blood lead concentrations are indicative
• Mercury toxicosis
• NSAID toxicosis—history of previous prolonged use
• Cantharidin toxicosis—evidence of cystitis, history of feeding beetle-contaminated hay
• Salmonellosis
• Colitis X
• Acute cyathostomiasis
• Clostridial colitis

CBC/BIOCHEMISTRY/URINALYSIS
• Reflect circulatory shock and possible liver and kidney damage
• Hemoconcentration—elevated packed cell volume and plasma total protein
• Leukopenia with degenerative changes in peripheral blood neutrophils
• Azotemia
• Electrolytes—hypokalemia; hyponatremia; hypochloremia
• Hyperglycemia
• Hyperbilirubinemia
• Elevated lactate dehydrogenase and creatine kinase

OTHER LABORATORY TESTS
• Antemortem—measurement of arsenic in urine, whole blood, or GI contents
• Postmortem—measurement of arsenic in liver, kidney, or hair (chronic cases)
• Arsenic is rapidly excreted after exposure ceases

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
N/A

PATHOLOGIC FINDINGS
Gross
• GI hemorrhage, mucosal congestion, edema, and ulcers/erosion either localized or throughout the GI tract, which may be filled with watery, dark-green, black, or hemorrhagic ingesta and necrotic material from mucosal sloughing
• Pulmonary edema and epicardial and serosal hemorrhage
• Pale swollen kidneys

Histopathologic
Necrotizing, hemorrhagic typhlocolitis, with necrotizing vasculitis, submucosal edema, renal tubular necrosis, and hepatic fatty degeneration.

TREATMENT

• Urgent treatment is necessary
• Remove animal from known or potential source of exposure
• GI decontamination
• Treat circulatory shock, dehydration, acidosis, and colic

MEDICATIONS

DRUG(S) OF CHOICE
• Hasten elimination of absorbed arsenic with chelators
  ◦ Dimercaprol (British anti-Lewisite) is the classic arsenic chelator (loading dose of 4–5 mg/kg given by deep IM injection, followed by 2–3 mg/kg every 4 h for 24 h and then 1 mg/kg every 4 h for 2 days); adverse reactions include tremors, convulsions, and coma
  ◦ DMSA is a less toxic chelator (equine dose not established, but 10 mg/kg PO every 8 h is suggested)
• Control abdominal pain
  ◦ Flunixin meglumine (1.1 mg/kg IV or IM every 24 h for 5 days) or butorphanol tartrate (0.1 mg/kg IV every 3–4 h up to 48 h)
  ◦ Xylazine hydrochloride (0.5–1 mg/kg IV or IM) may be used in conjunction with butorphanol (0.02–0.03 mg/kg IV)
• Demulcents—mineral oil or kaolin–pectin

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Dimercaprol should not be used in patients with renal impairment
• Use NSAIDs cautiously because of possible adverse GI and renal effects

FOLLOW-UP

• Monitor renal and hepatic function
• Provide a bland diet, containing reduced amounts of high-quality protein
• Identify source of exposure and properly dispose of source
• Expected course and prognosis depend on the severity of clinical signs
• If the animal survives, recovery should be complete

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

ABBREVIATIONS
• DMSA = 2,3-dimercaptosuccinic acid, succimer
• GI = gastrointestinal
• NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Casteel SW. Metal toxicosis in horses. Vet Clin North Am Equine Pract 2001;17:517–527.
Pace LW, Turnquist SE, Casteel SW, et al. Acute arsenic toxicosis in five horses. Vet Pathol 1997;34:160–164.

Authors Arya Sobhakumari and Robert H. Poppenga
Consulting Editors Wilson K. Rumbeiha and Steve Ensley

BASICS

DEFINITION

• Intrauterine placement of extended fresh, cooled, frozen semen; aseptic technique
• Standard AI—min. 300–1000 × 10^6 PMS, fresh/cooled transported semen; 200–250 × 10^6 PMS, frozen semen; deposited into *uterine body*
• DHI for standard or lower doses—1–25 × 10^6 PMS; low volume deposited into *tip of uterine horn* (ipsilateral to DF)
• HI for LDI—1–3 × 10^6 PMS to *tip of uterine horn* (ipsilateral to DF)

PATHOPHYSIOLOGY

Advantages

• Prevent stallion overuse
• Efficient use of ejaculate—breed more mares per season (AI, 120+; live cover, 40–80)
• Wider stud use—older with problems: musculoskeletal, behavioral
• Ship semen across all borders—eliminate mare and foal transport, ↓stallion injuries; ↓trauma to mares (recent genital surgery, genital abnormalities, rejecting stallion's advance)
• Extender antibiotics prevent many infections/transmission of VD
• Assess semen before AI
• LDI—stallion with limited availability/showing, large book/short supply, subfertile/poor quality, or costly (sex-sorted)
  ◦ Divide frozen AI dose to produce more than one foal
  ◦ Stallion is dead or epididymal spermatozoa collected at the time of castration or stallion's death

SYSTEMS AFFECTED

Reproductive

SIGNALMENT

• Thoroughbreds—only live cover
• Other breed registries allow AI

SIGNS

Historical Findings

Records of prior cycles/pregnancies—predict days in heat, time of ovulation, selection of stallion, and semen to be used.

Teasing and Physical Examination Findings

• Ovulation timing is critical
  ◦ Predict by history, teasing record, previous TRP/US
  ◦ During estrus—tease daily; min. every other day
  ◦ On second day of estrus, daily or every other day TRP/US
  ◦ Perform US, as needed, to determine optimal time to breed
• TRP—DF (35 + mm), ↓uterine and cervical tone
• Follicle size/growth rate, edema of endometrial folds (peaks preovulation 72–96 h, decreased/absent 24–48 h in young, normal mares)
• DF often pear-shaped 12–24 h preovulation
  ◦ Low uterine edema plus DF (≥40 mm)—indicates ovulation is close
• Ovulation depression, corpus haemorrhagicum, corpus luteum—evidence of ovulation

DIAGNOSIS

PROCEDURAL ISSUES

Timing and Frequency of Breeding

• Semen longevity varies by stallion, preservation method
• Equine ova—short viability (8–18 h post ovulation)

Teasing and Examinations

• AI as close to ovulation as possible
• OIA—GnRH analog, hCG, or combination when DF is >35 mm induces ovulation
• US 4–6 h post AI for DUC (especially if using frozen semen) and ovulation
• Evaluate normal, fertile mares 24–48 h after AI for ovulation
• Oxytocin IM/IV 4–6 h post AI. Can be given by trained personnel to ensure uterine clearance

Fresh (Raw or Extended) Semen

• Routine breeding—every other day if not using OIA, stallion has a small book, or mare is normal
  ◦ Begin day 2 or 3 of estrus until mare teases out or when a DF follicle is detected by TRP/US
  ◦ Can use OIA
• Inseminate within 48 h preovulation (acceptable pregnancy rates)

Cooled Transported Semen

• More mare examinations; fertility of some cooled semen decreases markedly >24 h
• OIA when DF is ≥35 mm to induce ovulation; order semen
• Semen arrives 24 h after ovulatory drug administration and 12–18 h before expected ovulation
• AI ≤ 12–24 h preovulation, min. dose of 500 × 10^6 PMS for acceptable conception rates
• Semen with poor post-cooling fertility should be sent *counter to counter* (i.e. airline transport)
  ◦ Use only one AI dose if good quality semen; mare is predisposed to DUC/PMIE
  ◦ No advantage to keeping second AI dose to rebreed next day in normal mares; uterus is best incubator for sperm

Frozen Thawed Semen

• Precise timing of AI; post-thaw longevity is reduced to ≤12–24 h
• Mare management—serial, daily teasing, TRP/US
• 2 different protocols for AI depending if multiple doses or a single dose of semen; fertile mare or predisposed to DUC
• Timed AI:
  ◦ OIA when DF ≥ 35 mm
  ◦ AI at 24 h; repeat at 40 h after OIA; ensure viable sperm available during ovulatory period
  ◦ Treat mare if intrauterine fluid 4–6 h after AI
• Alternatively:
  ◦ OIA when DF ≥ 35 mm
  ◦ TRP/US—TID–QID, ensure AI very close to preovulation, or, most important, ≤6–8 h post ovulation
  ◦ Treat mare if intrauterine fluid 4–6 h after AI
• Pregnancy rate for timed AI (2 doses) is equal to a one-time AI 6–8 h post ovulation, less intensive labor, fewer mare examinations; trade-off is increased endometrial irritation
• Combined methods for AI—timed but using one dose
  ◦ OIA when DF ≥ 35 mm at 8–10 PM (preferably combination of OIA and when follicle <40 mm to have more control over induction)
  ◦ TRP/US only once or twice the next day and again at 8 AM, 34–36 h post induction to assure the presence of a DF
  ◦ TRP/US 6 h later, 40–42 h post induction; >90% of mares ovulate within this window
  ◦ If mare has ovulated, proceed to AI; if not, keep performing TRP/US every 6 h until ovulation
  ◦ This method assures AI within 2–6 h of ovulation, limiting the waste of an AI dose if ovulation does not occur
  ◦ Treat mare if DUC 4–6 h after AI

Low-Dose Insemination

• Allows use of a reduced dose of semen (fresh, cooled, frozen)
  ◦ Acceptable pregnancy with doses as low as 25 × 10^6 PMS in volumes of 20–1000 µL (1 mL)
  ◦ Deposit semen at UTJ, ipsilateral to DF
• Can be either HI or DHI
  ◦ Similar pregnancy rates when using >5 × 10^6 PMS
  ◦ HI may provide advantage when AI dose is 1–3 × 10^6 PMS
  ◦ DHI is inexpensive; requires less personnel and skills
• Mare management varies according to method of semen preservation and severity of her endometrial inflammatory reaction

General Comments

• If ovulation has not occurred within recommended times for fresh (48 h), cooled (24 h), or frozen (6–12 h) semen, rebreed
  ◦ Consider it may be an anovulatory follicle if mare is unresponsive to the OIA

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ARTIFICIAL INSEMINATION (CONTINUED)

• Older ova or semen, poor timing, percent EED increases

LABORATORY TESTS

Progesterone level of >1 ng/mL confirms ovulation.

IMAGING

US

OTHER DIAGNOSTIC PROCEDURES

Semen Analysis

• Min. parameters—volume, motility, concentration
• Morphology—optional, of particular use if stallion has fertility problems
• Small sample of cooled/frozen semen should be saved and warmed (37°C); evaluate immediately post AI
  ◦ For DHI with frozen semen—after thawing straws, remove the sealed end, place one drop of semen on a slide for evaluation pre-AI
  ◦ Pipet and stylet—completely empty straws unless purposely saving 10% of the last straw
• Slide, coverslip, pipet—prewarm to avoid cold shock
• Min. number of sperm—$300–1000 \times 10^6$ PMS (fresh/chilled); $200–250 \times 10^6$ PMS (frozen)

Stallion's Disease Status

Should be negative for equine infectious anemia, equine viral arteritis, contagious equine metritis, VD.

Mare Selection

• Her fertility matters even more if using frozen semen or its quality is poor
• Reproductive history ± normal estrous cycles, uterine cultures/cytology, DUC
• Fertility is best—normal, pluriparous/maidens; less, older pluriparous; older maiden/barren mare

Prebreeding Uterine Culture and Cytology of Mare

• All, except young maiden mares—at least one negative uterine culture and cytology prebreeding
  ◦ Avoid disease transmission to the stallion
  ◦ Early identification of possible problems
• Pregnancy rates lower, EED higher if treated for an infection in same cycle as AI

TREATMENT

Prebreeding

• Presence of ≥2 cm uterine fluid prebreeding, LRS uterine lavage up to 1 h before AI
• Use 10 IU oxytocin IV post lavage only if performed >4 h prebreeding
• Should not affect fertility

AI Technique

• Sterile, disposable equipment. Mare restrained, rectum free of manure, perineal area thoroughly cleansed (mild detergent/antiseptic solution/soap); min. three rinses to remove any residue
• Sterile sleeve; non-spermicidal lubricant applied to dorsum of gloved hand
  ◦ 50–56 cm AI pipet carried in the gloved hand for fresh and cooled semen, less frequent for frozen semen
  ◦ Index finger first passes through cervical lumen, serves as a guide by which the pipet can readily be advanced to a position no more than 2.5 cm into the uterine body
  ◦ Syringe, non-spermicidal plastic plunger, e.g. Air-Tite, containing the extended semen is attached to the pipet, semen is slowly deposited into uterus; remaining semen in the pipet is rapidly delivered by using a small bolus of air (1–3 mL) in the syringe

Fresh Extended Semen

• AI immediately after collection
• Semen mixed with appropriate extender; immediate AI; semen-to-extender ratio (1:1 or 1:2), if small ejaculate volume and high concentration or mare predisposed to PMIE

Cooled Transported Semen

• Before first shipment, perform longevity test to determine best semen extender
• Collect, dilute in extender, cool to 4–6°C for 24–48 h. With transport, can be modest decrease of fertilizing capacity (stallion dependent)
• Semen-to-extender ratio of 1:3 or 1:4 is acceptable; may be as high as 1:15 (dependent on original concentration); semen longevity optimized by extending to $25–50 \times 10^6$ spermatozoa/mL
• Ship minimum 1×10^9 PMS; approx. 50% loss in shipment; so 500×10^6 PMS remain for AI at 24 h

Frozen Thawed Semen

• Frozen semen packed in 0.5, 2.5, or 5 mL straws; stored in liquid nitrogen
• A 5 mL straw contains $600–1000 \times 10^6$ sperm cells
• Dependent on post-freeze sperm motility and AI method, 1–4 + straws may be needed
• A 0.5 mL straw contains $200–800 \times 10^6$ sperm cells
  ◦ Thawing protocols vary; reported best paired with a particular freezing method. Seek specific information regarding thawing. In absence of a recommended protocol, 37°C for 30–60 s may be an acceptable alternative
• Post thaw, semen should be in the mare within 5 min
• Methods of frozen semen AI:
  ◦ Into uterine body, regular AI pipet
  ◦ DHI—flexible pipet and stylet (0.5 mL straws, LDI flexible pipet, and inner catheter (2.5–5 mL straws))
  ◦ HI (LDI, especially when $<1–3 \times 10^6$ PMS)
• Advantages of DHI and HI over *uterine body*—reduction in sperm transport time; increased number of sperm to colonize the oviduct ipsilateral to the DF (77% vs. 54%)
• Post-AI uterine treatment, strongly recommended (high concentration of spermatozoa in thawed straw + absence of seminal plasma may induce an acute PMIE)
• No scientific evidence that reducing spermatozoa number decreases the PMIE

Procedures

• Sedation of the mare is recommended for HI but is rarely needed for DHI. Procedure should be performed quickly (≤10 min) to avoid inducing uterine trauma
• DHI—flexible 65–75 cm AI pipet through the cervix, to tip of the uterine horn ipsilateral to DF:
  ◦ Attach 3 mL syringe to the external pipet end (avoid introducing air during the procedure)
  ◦ Hold sterile pipet in a 45° curve before the procedure, the bend helps direct its tip into the desired horn
  ◦ Once through the cervix, remove the AI hand from the vagina, place it in the rectum to transrectally guide the pipet tip rostral and slightly ventral into the uterine horn, toward its tip
  ◦ Manual transrectal elevation of the uterine horn tip may help pipet passage
  ◦ Insert the 0.5 mL straw into the pipet; a flexible steel stylet pushes the straw through the pipet to the nipple at the tip; deposit the semen close to or onto the UTJ. If more than one straw is used, remove the stylet, its bulbous end grabs the straw, the next straw is then introduced
• A similar pipet, without stylet, with an inner tube, is used for AI of frozen semen from 2.5–5 mL straws. This pipet also used for AI of cooled shipped semen after centrifugation (poor quality, very dilute)
• HI—introduction of an endoscope into the mare's uterus:
  ◦ Approach and visualize the UTJ/oviductal papilla ipsilateral to DF
  ◦ Pass small catheter loaded with semen through the channel, deposit semen slowly on the UTJ
  ◦ Rapidly remove endoscope
  ◦ No significant irritation if performed in <5 min
  ◦ Volumes >1 mL tend to run down the air-distended uterine horn
• HI compared with DHI—↑expensive, ↑skill, ↑labor, ↑personnel. The method of choice if AI of $1–3 \times 10^6$ PMS

Post Breeding

• US 4–6 h after AI for DUC
  ◦ If fluid, uterine lavage (sterile saline/LRS), followed by oxytocin 4–6 h after AI
  ◦ Repeat oxytocin at 3–4 h intervals, if fluid persists; again at 12–24 h until inflammation resolves

(CONTINUED) ARTIFICIAL INSEMINATION

MEDICATIONS

DRUG(S) OF CHOICE

- OIA most effective if follicle is ≥35 mm; within 36–42 h with:
  - hCG (1500–3000 IU IV/IM; range 36–72 h)
  - GnRH analog—Sucromate (deslorelin acetate 1.8 mg IM)
  - *Compounded* GnRH analogs (deslorelin 1.5 mg IM, histrelin 1 mg IM)
  - *Compounded* GnRH analog + hCG combo (deslorelin 1.5–2 mg + hCG 1500–2500 IU IM)
- Ecbolic drugs—to treat PMIE and DUC
- Prostaglandins—misoprostol for cervical relaxation

CONTRAINDICATIONS

See chapter Endometritis.

PRECAUTIONS

See chapter Endometritis.

FOLLOW-UP

PATIENT MONITORING

- Begin teasing by 11 days post ovulation
  - Suspect endometritis if a shortened cycle; owing to endogenous prostaglandin release
- US for pregnancy 14–15 days post ovulation; rule out potential twins vs. lymphatic cyst
- Follow-up TRP/US—24–30 days (confirm embryo and heartbeat)
- Serial TRP examinations—45, 60, 90, 120 days gestation

POSSIBLE COMPLICATIONS

- Artificial vagina preparation, handling, maintenance
- Semen evaluation at collection—ship adequate AI dose and/or send correct number of semen straws
- Shipping methods—Equitainer, reusable box cooling containers, vapor tank
  - Cooled shipments—entire breeding program is at mercy of airlines/couriers
- Operator skills
  - To manipulate and place semen through the cervix, into the uterine lumen, or to the tip of the horn (proper and timely)
  - Handling storage, straw transfer from main tank, water bath, vapor shipper, thawing and evaluation of frozen semen
- Misidentification of stallions/mares

MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Cooled Semen

Per cycle pregnancy rates almost equal to on-farm fresh semen AI (60–75%) if quality is good after cooling for 24 h at 5–6°C.

Frozen Semen

- Pregnancy rates per cycle using frozen semen are 5–10% lower than cooled shipped semen for most stallions
- Spermatozoa are stressed; loss of ≅50% at freezing and thawing
- First-cycle pregnancy rates 30–45% (range 0–70%); wide range between stallions
  - Requires greatest management. Good quality of semen has positive impact on pregnancy rate
- Candidate selection for frozen semen breeding
  - Most fertile—young pluriparous mares, young maidens
  - Least fertile—old pluriparous mares, old maidens, barren mares
- Older eggs or semen due to poor timing—decreased conception rate, increased EED

SYNONYMS

Artificial breeding

SEE ALSO

- Conception failure
- Early embryonic death
- Endometritis
- Spermatogenesis and factors affecting sperm production

ABBREVIATIONS

- AI = artificial insemination
- DF = dominant follicle
- DHI = deep horn insemination
- DUC = delayed uterine clearance
- EED = early embryonic death
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- HI = hysteroscopic insemination
- LDI = low-dose AI
- LRS = lactated Ringer's solution
- OIA = ovulation induction agent
- PMIE = post-mating-induced endometritis
- PMS = progressively motile sperm
- TRP = transrectal palpation
- US = ultrasound
- UTJ = uterotubal junction
- VD = venereal disease

Author Maria E. Cadario
Consulting Editor Carla L. Carleton

A

ARYTENOID CHONDROPATHY

BASICS

DEFINITION
• A septic inflammatory process of one or both arytenoid cartilages, resulting in the formation of luminal swelling, granulomas, and deformation with enlargement
• This interferes with the ability of the affected arytenoid cartilage to fully abduct during forced inspiration and/or to resist collapsing airway pressure during inspiration. In addition "kissing lesions" on the medial surface of the opposing arytenoid cartilage may be seen

SIGNALMENT
Racehorses are more commonly affected, although it can be observed in older horses of any breed or function.

SIGNS
• Upper respiratory noise, exercise intolerance, or both
• The disease usually worsens gradually, with progressive involvement of one or both arytenoid cartilages
• Can lead to ventilation interference proportional to the loss of abductory function and the mechanical size of the granulomas or affected arytenoid cartilages. The more intense the high-intensity exercise occurs, the earlier the effect of an obstruction is detected (the horse does not "finish" or close well)
• In show horses, loss of points during competition because of upper respiratory noise may be the main concern; this upper airway noise may resemble that of horses with laryngeal hemiplegia

CAUSES
• Physical trauma to the mucosa of the arytenoid cartilage caused by air turbulence or aspiration of track surface particles during exercise or severe coughing or intubation (e.g. endotracheal, nasogastric) procedures
• Upper airway infection leading to coughing and contact ulcers on the medial surface of the arytenoid cartilage dorsal to the vocal processes. If the inflammatory condition persists and infection develops, arytenoid cartilage sepsis occurs
• In many cases, the inciting cause is never found

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Laryngeal hemiplegia
• Congenital malformation of the laryngeal cartilages (i.e. fourth branchial arch defect)

CBC/BIOCHEMISTRY/URINALYSIS
In active infection with abscessation, serum amyloid A and fibrinogen may be elevated.

OTHER LABORATORY TESTS
• Arterial blood gases during exercise
• Hypoventilation can be evaluated using arterial blood gases—typically at maximal exercise $PaCO_2$ can be >50 mmHg; PaO_2 may be <65 mmHg in affected horses

IMAGING
• Lateral radiography of the larynx may reveal enlarged laryngeal cartilages, sometimes with associated osseous metaplasia
• Ultrasonographic examination of the larynx using the mid-ventral and caudoventral windows to evaluate for abscess and the caudolateral window to assess the presence of disease in the lateral aspect of the arytenoid cartilage. MRI and CT are rarely indicated but may also reveal the extent of arytenoid cartilage involvement

OTHER DIAGNOSTIC PROCEDURES
• The diagnosis is established on the basis of videoendoscopic examination at rest:
  ◦ The body of the arytenoid is irregular and thickened
  ◦ A mass of granulation tissue may protrude from the medial surface of the arytenoid cartilage into the airway. The size or location of the protruding mass has no correlation with the amount of abduction remaining
  ◦ The corniculate process may be deformed
  ◦ Contact (i.e. "kissing") lesions may be observed on the contralateral arytenoid cartilage
• Eventually, the condition may lead to decreased or total inability of the affected arytenoid cartilage to abduct during inspiration

TREATMENT

• Medical treatment is indicated only in acute cases with mucosal ulceration and swellings
• Consider endoscopically guided excision of intralaryngeal granulations if the affected arytenoid cartilage retains sufficient abductory function for intended athletic activity
• When arytenoid abduction is severely reduced, partial arytenoidectomy (excision of the body and corniculate process of affected arytenoid cartilage) is the treatment of choice to restore exercise capacity and to reduce upper airway noise
• Permanent tracheotomy can be used in countries where athletic competition is allowed with this procedure and to salvage the animal for breeding purposes

MEDICATIONS

DRUG(S) OF CHOICE
• Acute case—broad-spectrum antibiotics and NSAIDs
• Chronic case—none, other than routine perioperative antimicrobial and anti-inflammatory agents
• Use of nasopharyngeal spray, consisting of various anti-inflammatory and antimicrobial agents (140 mL DMSO, 140 mL glycerin, 266 mL distilled water, and 14 mL dexamethasone 4 mg/mL and often an antibiotic such as nitrofurazone—makes 560 mL, enough for 2 weeks) can be applied (20 mL BID) using a soft rubber feeding tube
• If the airway is significantly compromised, a temporary tracheotomy may be needed until the swelling resolves

FOLLOW-UP

PATIENT MONITORING
• Videoendoscopy of the upper airway 2–6 weeks after surgery to monitor patient response
• Final response to treatment or continuation of monitoring of affected horses is made on the basis of evaluating exercise tolerance and upper respiratory noise
• Laser resection of the unsupported ipsilateral aryepiglottic fold might be needed to improve airway patency

POSSIBLE COMPLICATIONS
• Horses undergoing removal of the corniculate and body of the arytenoid cartilage have a slightly increased risk of tracheal aspiration of feed during deglutition. In addition, these procedures do not fully restore the airway diameter, so a mild degree of airway obstruction persists, which may interfere with performance or result in upper airway noise during exercise. Postsurgery dynamic endoscopy is indicated if results are not satisfactory to identify if a soft tissue resection of collapsing tissue is needed
• Bilateral arytenoidectomy increases the risk for tracheal aspiration of feed during deglutition and for glottic stenosis because of webbing at the resection site

EXPECTED COURSE AND PROGNOSIS
• Horses with acute swelling of the arytenoid cartilage may respond favorably to NSAIDs, topical anti-inflammatory agents, and antibiotics
• Untreated horses exhibit a progressive increase in exercise intolerance and upper respiratory noise

• Horses with focal elevated granulations on the medial surface of the arytenoid cartilage that maintain abductory function may respond to simple "lumpectomy"; recurrence of granuloma is seen in approximately 20–30% of horses
• Horses with generalized involvement of an arytenoid cartilage and without surgical treatment often develop contralateral contact or "kissing" lesions
• Horses with unilateral lesions treated surgically have a fair prognosis (60%) for elimination or significant reduction of exercise intolerance; however, the prognosis is guarded (20%) in horses with bilateral lesions

MISCELLANEOUS

SEE ALSO

• Dynamic collapse of the upper airways
• Laryngeal hemiparesis/hemiplegia (recurrent laryngeal neuropathy)

ABBREVIATIONS

• CT = computed tomography
• DMSO = dimethylsulfoxide
• MRI = magnetic resonance imaging
• NSAID = nonsteroidal anti-inflammatory drug
• $PaCO_2$ = partial pressure of carbon dioxide in arterial blood
• PaO_2 = partial pressure of oxygen in arterial blood

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Author Norm G. Ducharme
Consulting Editors Daniel Jean and Mathilde Leclère

A

ASCARID INFESTATION

BASICS

DEFINITION
Roundworm infestation caused by *Parascaris equorum*.

PATHOPHYSIOLOGY
• Direct life cycle—fecal–oral route. • Adult horses, especially brood mares, and older foals—main reservoir of infection (eggs). • Eggs accumulate in the environment (highly resistant), sticking to different surfaces, including the mare's mammary gland. • After ingestion—embryonated eggs hatch in the host's small intestine, larvae migrate through the intestinal wall to the liver and lungs, larvae travel up the bronchial tree, are swallowed, and develop into 10–50 cm long mature adult ascarids in the duodenum and proximal jejunum. Prepatent period, 10–12 weeks. • SIO—associated with a large burden of parasites

SYSTEMS AFFECTED
• Gastrointestinal—colic, enteritis, maldigestion, and malabsorption.
• Hepatobiliary—migrating larvae resulting in temporary liver damage.
• Respiratory—tracheobronchitis

INCIDENCE/PREVALENCE
• Prevalence—31–61%. • Infection prevalence—up to 100% in tested farms and in 80% of foals. • Colic due to SIO—0.5% (25/5134 cases of colic)

GEOGRAPHIC DISTRIBUTION
Worldwide

SIGNALMENT
• Any ages—primarily foals. • Adult horses—debilitated and immunocompromised

SIGNS
• Ascarid infestation—lethargy, weakness, decreased weight gain, dull hair coat, and "pot-bellied" appearance. • Mild to moderate colic—intestinal phase of the infection.
• SIO—severe colic, can be complicated with volvulus or intussusception.
• Peritonitis—perforation of the intestine.
• Coughing and mucopurulent nasal discharge with or without systemic illness—larval migration through the lungs

CAUSES
N/A

RISK FACTORS
• All foals are at risk. • Breeding farms—large yearly population of young horses grazing on same pasture. • Ascarid impaction and SIO—usually 24 h after anthelmintic therapy (72% of the cases)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other causes of delayed growth.
• SIO—small intestine strangulating lesion

CBC/BIOCHEMISTRY/URINALYSIS
• Eosinophilia—during larval migration, 10–40 days post infection. • Leukopenia and mild anemia. • Hypoproteinemia—severe infestation

OTHER LABORATORY TESTS
N/A

IMAGING
Transabdominal ultrasonography—adult ascarids within the intestinal lumen or in the peritoneal cavity (perforation).

OTHER DIAGNOSTIC PROCEDURES
• Fecal flotation. • Eosinophils in tracheal wash—verminous lung disease

PATHOLOGIC FINDINGS
Adult forms in the intestinal lumen or free in the abdominal cavity (intestinal perforation).

TREATMENT

APPROPRIATE HEALTH CARE
Treatment indicated when fecal egg counts >100 eggs per gram.

CLIENT EDUCATION
Severe parasite burdens suspected—benzimidazoles are recommended. Avoid anthelmintics that result in paralysis of the parasites (e.g. pyrantel pamoate, piperazine, organophosphates, ivermectin).

SURGICAL CONSIDERATIONS
For removal of dead parasites and correction of secondary complications (intussusceptions and intestinal volvulus).

MEDICATIONS

DRUG(S) OF CHOICE
• Anthelmintics—do not eliminate migrating larvae. Preventative therapy should be given until 1 year of age. • Broodmares—deworm at monthly intervals in the last trimester of pregnancy. Reduce environmental contamination. • Fenbendazole—10 mg/kg every 24 h PO for 5 consecutive days (varies in effectiveness against ascarids).
• Moxidectin—0.4 mg/kg PO and ivermectin 0.2 mg/kg PO. Advocated to be 100% efficient in eliminating ascarid infection in horses. Resistance to these and other macrocyclic lactone anthelmintics has been identified in Europe and North America

CONTRAINDICATIONS
See Client Education.

FOLLOW-UP

PATIENT MONITORING
Fecal floatation—conducted in 10% or more of foals every 4–6 months. If >10% of foals are positive indicates failure of the anthelmintic therapy or of the prevention and control strategies.

PREVENTION/AVOIDANCE
• Contaminated facilities—disinfection with a 5% phenolic compound. • Grazing of broodmares, foals, and weanlings on heavily contaminated pastures should be avoided.
• *P. equorum* eggs—remain viable in the environment for years. • Frequent removal of manure from stalls and pastures

POSSIBLE COMPLICATIONS
Toxicosis—overdose of anthelmintic.

EXPECTED COURSE AND PROGNOSIS
• Prognosis—favorable in uncomplicated cases (delay in growth is common).
• SIO—short-term (discharge from hospital) and long-term (>1 year) survival 64% and 27%, respectively. • Formation of adhesions—associated with nonsurvival

MISCELLANEOUS

ASSOCIATED CONDITIONS
• SIO. • Peritonitis

AGE-RELATED FACTORS
Primarily in foals.

ZOONOTIC POTENTIAL
Human infection—extremely rare.

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

ABBREVIATIONS
SIO = small intestine obstruction

Suggested Reading

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Author Diego Gomez-Nieto
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa
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ASPARTATE AMINOTRANSFERASE (AST)

BASICS

DEFINITION
• Catalyzes the transamination of L-aspartate and 2-oxoglutarate to oxaloacetate and glutamate. Requires pyridoxal 5′-phosphate as a cofactor
• AST is present in cytoplasm and in larger amounts in the mitochondria
• AST is present in skeletal muscle, cardiac muscle cells, hepatocytes, and erythrocytes
• Reported normal AST activity in horses varies from 48 to 456 IU/L

PATHOPHYSIOLOGY
• Increases in AST activity are typically indicative of hepatocellular and/or striated muscle injury; however, increases occur with hemolysis because of the high AST content in erythrocytes
• The degree of elevation of AST concentrations is proportional to the number of hepatocytes affected
• The magnitude of AST elevation with skeletal muscle injury is not necessarily proportional to the extent of tissue injury
• Increases above the reference range can occur with IM injections, recumbency, trauma, and long trailer rides
• AST is a sensitive indicator of hepatocellular and striated muscle injury; however, because it is present in many tissues, AST lacks specificity. Other biochemical parameters need to be examined concurrently with AST to localize the source of the increase (i.e. SDH for liver and CK for muscle)
• After tissue injury, AST activity increases slower and remains increased longer than SDH or CK
• Increased SDH concentration, with normal or increased AST concentration, indicates acute or ongoing hepatocellular injury. If serial serum biochemistry analyses reveal continuously or progressively increased activities of both enzymes, ongoing hepatocellular injury is likely. During treatment of hepatic disease, enzymes can be used to monitor progress and cessation of the insult. If, after documentation of recent hepatocellular injury, serial serum biochemistry analyses reveal increased AST and progressively decreasing or normal SDH activity, cessation of the original insult is likely. Because AST has a longer half-life, AST may increase even after cessation of original insult, and the activity may remain increased for weeks
• A similar interpretative approach is used when determining if muscle injury is present. Muscle and hepatocellular injury can occur concurrently, and increases in AST, CK, and SDH concentrations may be seen together

SYSTEMS AFFECTED
• Musculoskeletal
• Hepatobiliary
• Cardiovascular (myocardium)
• Hemic (erythrocytes)

GENETICS
• PSSM type 1—Quarter Horses, Paints, and draft horses are predisposed
• PSSM type 2—Quarter Horses and Warmbloods are predisposed

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
• See Genetics
• Any breed, age, or sex

SIGNS
Historical Findings
• Dependent on the underlying cause
• Strenuous exercise or overtraining

Physical Examination Findings
• Dependent on the underlying cause
• Muscle disorders—reluctance or inability to move, stiffness, and recumbency
• Liver disorders—icterus, neurologic deficits, discolored urine, anorexia, colic, weight loss, photosensitization, and fever
• Clinical signs due to hepatic failure generally do not appear until 75% of the hepatic functional mass is lost

CAUSES
• Degenerative conditions—chronic active hepatitis, rhabdomyolysis, and cholelithiasis
• Anomaly, congenital or hereditary diseases—polysaccharide storage myopathy (PSSM), glycogen branching enzyme deficiency; biliary atresia
• Metabolic diseases—shock, hypovolemia, hypoxia caused by severe gastrointestinal disease, severe anemia, or general anesthesia
• Neoplastic or nutritional diseases—neoplasia, hepatic lipidosis, and vitamin E/selenium deficiency
• Infectious and immune-mediated diseases—hepatitis of various causes (e.g. viral, bacterial, protozoal, fungal, parasitic), Theiler's disease, amyloidosis, sepsis, endotoxemia, and immune-mediated myositis
• Toxic or trauma—pyrrolizidine alkaloid-containing plants, cottonseed, castor bean, oak, alsike clover, fungal toxins (e.g. aflatoxins, cyclopiazonic acid, fumonisin, phalloidin [mushrooms]), and chemical compounds/elements, such as ethanol, chlorinated hydrocarbons, carbon tetrachloride, monensin, copper, iron, and petroleum

RISK FACTORS
Dependent on the underlying cause.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
See Causes.

CBC/BIOCHEMISTRY/URINALYSIS
CBC
• Erythrocytes—liver disease may cause nonregenerative anemia of chronic inflammation. Hemolytic anemia may increase serum AST activity, and anemia from any cause can cause hypoxic liver or muscle damage
• Leukocytes—leukocytosis or leukopenia may be seen with inflammatory diseases; morphologic changes of the leukocytes (e.g. neutrophil toxicity) also may be seen
• Platelets—quantitative decreases and increases may be seen with a variety of systemic diseases that may affect the liver or striated muscle

Biochemistry
• Glucose—decreased in endstage liver disease
• Blood urea nitrogen—increased in severe rhabdomyolysis from secondary renal injury (i.e. pigment nephropathy); decreased in liver insufficiency and endstage liver disease from decreased conversion of ammonia to urea
• Albumin—rarely decreased in endstage liver disease from decreased production
• Globulin—increased in endstage liver disease and with chronic antigenic stimulation
• SDH—increased with acute and ongoing hepatocellular injury
• Alkaline phosphatase—increased with cholestatic disease
• γ-Glutamyltransferase—increased with cholestatic disease
• CK—increased with acute or ongoing muscle injury
• Conjugated bilirubin—increased with cholestatic disease
• Unconjugated bilirubin—increased with anorexia and prehepatic cholestasis (e.g. massive in vivo hemolysis)
• Triglycerides—increases may be associated with hepatic lipidosis
• In vitro hemolysis falsely increases AST. Prolonged in vitro exposure of serum to erythrocytes falsely increases AST activity even before visible signs of hemolysis are present. To avoid this confounding factor, prompt separation of serum from the cellular components of blood is strongly recommended
• If laboratory analysis will not occur within 1–2 days, freeze the serum sample

Urinalysis
Bilirubinuria—conjugated bilirubin, detected by the commonly used dipstick and diazo tablet methods, indicates cholestatic disease.

A

ASPARTATE AMINOTRANSFERASE (AST) (CONTINUED)

OTHER LABORATORY TESTS

SBAs

• Bile acids will increase in the circulation prior to total bilirubin in cases of liver disease. In the horse, SBAs are not affected by short-term fasting (<3 days). Postprandial increases are also not seen because of the lack of a gallbladder. SBAs are a good adjunct test when abnormal liver enzymes are detected. An increase in SBAs indicates liver dysfunction
• Congenital abnormalities of the portal circulation cause SBAs to bypass the liver, which results in increases in circulation. In contrast, total bilirubin will not be increased as a result of the shunt, but may be increased due to fasting

Plasma Ammonia Concentration

• Increases indicate hepatic insufficiency/decreased functional mass
• Plasma ammonia measurement requires special handling, which limits its general availability
• Consult reference laboratory for specific sample submission requirements

Coagulation Tests and Plasma Fibrinogen Concentration

• The liver manufactures many of the coagulation factors; therefore, significant decreases in liver function may lead to deficiencies in these factors and to coagulation abnormalities
• APTT and PT—decreased APTT and PT are seen when <30% of the activity of the factors is present

Cardiac Troponin I

Elevations indicate myocarditis.

Toxicology

Analysis of tissue biopsy, feed, ingesta, serum/plasma, or other body fluids may indicate presence of a toxin.

IMAGING

Transabdominal Ultrasonography

• Evaluate size, echogenicity, shape, and position of liver
• Useful for guidance when obtaining liver biopsy for cytology, histopathology, and microbiology
• Helpful in the evaluation of muscle and tendon injuries

OTHER DIAGNOSTIC PROCEDURES

Liver or muscle biopsy for cytology (impression smear) and histopathology.

PATHOLOGIC FINDINGS

Dependent on the underlying cause.

TREATMENT

Dependent on the underlying cause.

MEDICATIONS

DRUG(S) OF CHOICE

Dependent on the underlying cause.

CONTRAINDICATIONS

With suspected hepatic insufficiency, assess the relative safety/risk of performing invasive procedures (e.g. fine needle aspiration, tissue biopsy, laparoscopy, surgery) in light of coagulation panel results.

PRECAUTIONS

Dependent on the underlying cause.

POSSIBLE INTERACTIONS

Dependent on the underlying cause.

ALTERNATIVE DRUGS

Dependent on the underlying cause.

FOLLOW-UP

PATIENT MONITORING

Serial serum biochemistry analyses to monitor progression or improvement of the disease.

PREVENTION/AVOIDANCE

Dependent on the underlying cause.

POSSIBLE COMPLICATIONS

Dependent on the underlying cause.

EXPECTED COURSE AND PROGNOSIS

Dependent on the underlying cause.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Dependent on the underlying cause.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Dependent on the underlying cause.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Previously known as glutamate oxaloacetate transaminase (SGOT).

SEE ALSO

Ammonia, hyperammonemia

ABBREVIATIONS

• APTT = activated partial thromboplastin time
• AST = aspartate aminotransferase
• CK = creatine kinase
• PT = prothrombin time
• SBA = serum bile acid
• SDH = sorbitol dehydrogenase

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Author Jenifer R. Gold
Consulting Editor Sandra D. Taylor
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BASICS

OVERVIEW
• May develop after inhalation of foreign material and bacteria into the lower respiratory tract
• Causes include dysphagia, obstructive esophageal disorders, GI reflux, and accidental inhalation of foreign material (nasogastric intubation)

SIGNALMENT
Foals appear more prone to GI reflux and subsequent aspiration pneumonia.

SIGNS
Historical Findings
• Dysphagia, ptyalism, or discharge of food, water, or milk from the nostrils
• Recent history of drenching or nasogastric intubation

Physical Examination Findings
• Clinical signs—fever, depression, anorexia, cough, nasal discharge (may be serohemorrhagic), tachypnea, and dyspnea
• Foul-smelling breath or nasal discharge suggests strongly anaerobic infection
• Abnormal lung sounds (auscultation)

CAUSES AND RISK FACTORS
Dysphagia
• Neurologic diseases affecting cranial nerves IX and X—guttural pouch diseases, botulism, lead toxicity, and viral encephalitis
• Primary myopathies of pharyngeal and laryngeal muscles—white muscle disease and hyperkalemic periodic paralysis
• Pharyngeal obstruction—strangles, pharyngeal abscess, neoplasia, foreign body, dorsal displacement of soft palate
• Congenital—cleft palate and hypoplasia of the soft palate
• Iatrogenic causes—pharyngeal and laryngeal surgery

Esophageal Disorders
• Esophageal obstruction
• Esophageal diverticulum
• Esophageal fistula
• Megaesophagus

GI Reflux
Gastric outflow obstruction (foals).

Accidental Inhalation of a Foreign Body
Administration of fluids by drenching or nasogastric tube.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Acute bronchopneumonia
• Pleuropneumonia
• Interstitial pneumonia
• Respiratory distress syndrome

CBC/BIOCHEMISTRY/URINALYSIS
• Hyperfibrinogenemia, hyperglobulinemia, and anemia are common with chronic pneumonia
• Elevated white blood cell count with neutrophilia may be observed

OTHER LABORATORY TESTS
• Increased blood and tissue concentrations of lead (lead toxicity)
• Decreased whole-blood selenium concentration and glutathione peroxidase activity with increased serum creatine kinase and aspartate aminotransferase (white muscle disease)
• Hyperkalemic periodic paralysis—genetic testing or finding hyperkalemia during clinical episodes

IMAGING
• Thoracic radiography commonly reveals ventral patchy opacity obscuring the cardiac silhouette
• Contrast radiography may help to identify esophageal diseases
• Thoracic ultrasonography may detect pleural effusion

OTHER DIAGNOSTIC PROCEDURES
• Tracheobronchial aspiration and/or thoracocentesis for cytology, Gram stain, and culture (both aerobic and anaerobic)
• Endoscopy of the respiratory and upper GI tracts may help to identify the primary cause

PATHOLOGIC FINDINGS
• Lung consolidation (ventral part)
• Acute cases—hemorrhagic and edematous areas
• Chronic cases—lungs with necrotic and purulent materials
• Pleural space—fibrinous exudate and adhesions

TREATMENT

• Restore airway patency, drain pleural effusion, etc.
• Nasal oxygen (6–10 L/min) if PaO_2 <60 mmHg
• Thoracocentesis or indwelling chest tubes can achieve drainage; a one-way valve prevents pneumothorax
• Treat primary disease
• Stall rest
• Dysphagic horses may be fed with a nasogastric tube
• Fluid therapy as needed

MEDICATIONS

DRUG(S) OF CHOICE
• Systemic administration of broad-spectrum antimicrobials. Preferred combinations include sodium or potassium penicillin (22 000–40 000 IU/kg IV every 6 h), aminoglycoside (gentamicin (6.6–8.8 mg/kg IV every 24 h) or amikacin (15–20 mg/kg IV or IM every 24 h) for foals), and metronidazole (15–25 mg/kg IV or PO every 6–8 h)
• Other antimicrobial options include procaine penicillin G (22 000 IU/kg IM every 12 h), trimethoprim–sulfamethoxazole (30 mg/kg PO every 12 h), ceftiofur (1–5 mg/kg IV or IM every 12 h), or chloramphenicol (20–50 mg/kg PO every 6–8 h for adults and foals >1 week)
• NSAIDs—flunixin meglumine (1.1 mg/kg PO or IV every 12–24 h) or phenylbutazone (2.2–4.4 mg/kg PO or IV every 12 h)

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Use aminoglycosides and NSAIDs with caution in horses with renal dysfunction and/or dehydration.

FOLLOW-UP

PATIENT MONITORING
Follow progress of pulmonary lesions by radiography/ultrasonography.

PREVENTION/AVOIDANCE
Prevent or avoid exposure to primary causes.

POSSIBLE COMPLICATIONS
• Pleuritis, lung abscess
• Thrombophlebitis
• Laminitis
• Disseminated intravascular coagulation
• Septicemia

EXPECTED COURSE AND PROGNOSIS
• Prolonged treatment is often needed
• Prognosis is guarded

MISCELLANEOUS

SEE ALSO
• Hemorrhagic nasal discharge
• Pleuropneumonia
• Respiratory distress syndrome in foals

ABBREVIATIONS
• GI = gastrointestinal
• NSAID = nonsteroidal anti-inflammatory drug
• PaO_2 = partial pressure of oxygen in arterial blood

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Author Daniel Jean
Consulting Editors Daniel Jean and Mathilde Leclère
Acknowledgment The editors acknowledge the prior contribution of Laurent Couëtil.

ATHEROMA OF THE FALSE NOSTRIL

BASICS

OVERVIEW
• Epidermal inclusion cyst, epidermoid cyst, or infundibular follicular cyst of the false nostril (nasal diverticulum)
• The term "atheroma" is likely a misnomer as the term refers to a sebaceous cyst
• Often present at birth and becomes apparent with age as the cyst enlarges
• Usually a cosmetic issue only

SIGNALMENT
• Can be noticed at any age
• Usually becomes apparent between weaning and 3 years of age
• No known sex or breed predilections

SIGNS
• Soft to firm, spherical swelling covered by normal skin in the caudal dorsal to lateral aspect of the false nostril in the area of the nasomaxillary notch
• Typically unilateral, but can be bilateral
• Not painful on palpation
• Size increases with age and can reach up to 5 cm
• Usually not associated with respiratory compromise

CAUSES AND RISK FACTORS
• Congenitally aberrant epithelial tissue between the skin and mucous membrane of the false nostril
• Can slowly enlarge due to progressive exfoliation of keratinized material within the cyst

DIAGNOSIS

Characteristic location and physical features of the swelling.

DIFFERENTIAL DIAGNOSIS
• An abscess can be ruled out as there is no heat or pain associated with the cyst
• Cysts could become inflamed if keratinized material leaks into the surrounding tissue

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
• Aspirated fluid is white to gray, milky to creamy in appearance, and odorless
• Cytologically the cyst fluid contains keratinized and nonkeratinized squamous epithelial cells
• Trichrome staining reveals squamous epithelial cells and keratinous debris
• Histologically the cyst lining comprises varying thickness of stratified squamous epithelium

IMAGING
Ultrasonographic findings consistent with cystic structure, usually unilocular, mostly homogeneous echogenicity.

OTHER DIAGNOSTIC PROCEDURES
• Palpation
• Ultrasonographic evaluation
• Centesis
• Histologic evaluation

TREATMENT

• None required/indicated. Usually not removed unless for cosmetic reasons or for airway noise or impairment from large swelling size
• If removed surgically, it is imperative to remove the entire cyst lining to prevent recurrence
• Total surgical removal can be done under general anesthesia or standing with sedation and local anesthesia of the infraorbital nerve
• The cyst can be approached surgically through the skin over the dorsum of the swelling. The cyst then is dissected in its entirety, and the wound is closed
• Another option is to open the cyst ventrally into the false nostril, drain the contents, and remove the lining using a burr instrument. In this technique, the wound is left open to heal by second intention
• Intralesional injection of neutral-buffered 10% formalin after aspirating the cyst content has been reported. Injection of formalin until leakage around the needle is seen (2–4.5 mL). There is transient swelling within 24 h of injecting the formalin. Desiccation of the cyst occurs after a few weeks

MEDICATIONS

DRUG(S) OF CHOICE
Draining and cauterizing or sclerosing the cyst has been done using tincture of iodine, silver nitrate, or both followed by packing; this requires daily treatment and carries a high risk of recurrence.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Transient swelling if chemical ablation is used.

FOLLOW-UP

Usual precautions for tetanus prophylaxis and asepsis of the surgical site.

POSSIBLE COMPLICATIONS
• A cyst may become abscessed if infection is introduced during centesis
• Transient swelling after surgery
• Recurrence if lining not removed
• Infection at surgery site
• Scar formation
• White hair at surgery site

EXPECTED COURSE AND PROGNOSIS
Favorable prognosis for both leaving the cyst untouched and for surgical removal if needed.

MISCELLANEOUS

ASSOCIATED CONDITIONS
In addition to false nostril cysts, other congenital cutaneous cysts reported in horses are dentigerous cysts and, very rarely, dermoid cysts.

AGE-RELATED FACTORS
May increase in size with age.

ZOONOTIC POTENTIAL
None

PREGNANCY/FERTILITY/BREEDING
N/A

SEE ALSO
N/A

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Author Mathilde Leclère
Consulting Editors Mathilde Leclère and Daniel Jean
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BASICS

DEFINITION
AD is defined as a multifactorial disease in which a genetic predisposition leads to the development of a cutaneous IgE- and cell-mediated hypersensitivity, most commonly against environmental allergens, and, upon exposure to that allergen, to clinical signs in the patient.

PATHOPHYSIOLOGY
The pathophysiology of equine atopy is not well elucidated. In human and canine AD, deviations in T-cell development have been detected. Allergen-specific IgE has been identified in atopic horses and CD4+ CD25+ regulatory cells in horses with IH. Whether the exact pathomechanism is similar to dogs and humans, with an initial development of Th2 cells secreting IL-4, IL-5, and IL-13 leading to a switch to IgE production and cellular and humoral hyperreactivity against specific antigens, remains to be elucidated.

SYSTEMS AFFECTED
Skin/Respiratory
The skin is only one of the organs that can be affected. There is evidence that equine asthma (heaves, recurrent airway obstruction) may also be due to a type I hypersensitivity to airborne allergens in some patients.

GENETICS
The genetic basis of equine AD is largely unknown. Based on anecdotal reports and one study, Arabians seem to be predisposed, but the number of affected horses was small and no further genetic studies were reported.

INCIDENCE/PREVALENCE
After IH, AD it is the second most common hypersensitivity in the horse.

GEOGRAPHIC DISTRIBUTION
Worldwide

SIGNALMENT
• No age or gender predisposition has been identified
• In most animals, the first clinical sign is pruritus, often affecting the head and legs
• Initial pruritus may only be seasonal
• With time, pruritus becomes more severe, more generalized, and year round

SIGNS
• AD may present as a pruritus with no primary lesions or perhaps mild erythema, or with pruritus leading to secondary lesions such as alopecia, excoriations, and crusting
• It may also present as urticaria
• Secondary surface infections may cause a bacterial folliculitis, which may be clinically mistaken for dermatophytosis

CAUSES
• The most common environmental allergens causing equine AD are storage mites, mold spores, and pollens
• Depending on the geographic location and the exact type of allergen, mold spores and pollens may have a strict seasonal occurrence or may be perennial
• Many horses have concurrent IH

RISK FACTORS
Concurrent pruritic dermatosis, such as IH or ectoparasitic disease (summation effect).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
The list of differential diagnoses varies with the predominant site of pruritus (Table 1. As there is no reliable test differentiating AD from other hypersensitivities, ectoparasites, or other differential diagnoses, those diseases must be ruled out before AD can be confirmed.

CBC/BIOCHEMISTRY/URINALYSIS
Hemogram may reveal an eosinophilia but this is nonspecific for AD as ecto- and endoparasite burdens or IH may show this change.

OTHER LABORATORY TESTS
• A number of tests are used to identify the offending allergens in AD
• An ELISA that uses the Fc-epsilon receptor on the immunoglobulin IgE as the detection platform to identify serum IgE compared better in one study than a radioallergosorbent test and a polyclonal antibody-based ELISA

Table 1

Differential diagnoses for AD

Body location	*Differential diagnoses*
Face	CAFR and IH, trombiculosis, *Dermanyssus gallinae*
Ears	CAFR and IH, *Psoroptes*
Neck	CAFR and IH
Mane	CAFR and IH, pediculosis, *Psoroptes*
Legs, pastern	CAFR, IH, and contact hypersensitivity, trombiculosis, *Dermanyssus gallinae, Chorioptes*
Dorsum	CAFR and IH, pediculosis
Ventrum	CAFR and IH, contact hypersensitivity, trombiculosis, *Dermanyssus gallinae*

• Histamine-releasing assays may be useful but are not commercially available
• None of these tests reliably differentiates AD from other skin disease and, thus, cannot be used to establish a diagnosis
• These tests serve as a guide to choosing offending allergens used in ASIT, together with the history of the patient including possible seasonality and/or specific locations

IMAGING
• Skin—N/A
• Respiratory signs—thoracic radiographs

OTHER DIAGNOSTIC PROCEDURES
• Intradermal skin tests detect the level of allergen-specific IgE in the skin directed to a panel of allergens that are region specific and thought to be clinically relevant
• Knowledge of predominant allergens and their seasonality in the area of one's practice is essential when interpreting results of allergy tests
• False-positive reactions or results that indicate subclinical sensitization may occur with both serum and intradermal testing in the horse. Several studies with control groups of healthy nonallergic horses had immediate or late-phase IDT reactions, although horses with AD, urticaria, and severe asthma showed a higher number of positive reactions. As such, IDT results cannot differentiate a hypersensitivity from another pruritic skin disease, but rather act only as a guide to choose offending allergens for ASIT
• Surface cytology from erosions or ulcers shows a neutrophilic exudate with intra- and/or extracellular cocci representative of a secondary bacterial folliculitis
• Perform skin scrapings to rule out ectoparasites
• Perform dermatophyte cultures to help rule out secondary dermatophytosis

PATHOLOGIC FINDINGS
Skin biopsies submitted for histopathology from horses with AD typically reveal edema with a superficial to deep, perivascular to interstitial, eosinophilic dermatitis and possible epidermitis pointing to hypersensitivities or ectoparasites and are not diagnostic for environmental allergy. Biopsies may be useful to rule out differential diagnoses.

TREATMENT

APPROPRIATE HEALTH CARE
• Identification and avoidance of the offending allergen is the best strategy for horses with AD
• In rare cases, changing the type of stabling, paddock, or feeding habits will lead to clinical remission

A

ATOPIC DERMATITIS (CONTINUED)

• In the majority of cases, the etiologic allergens will either be ubiquitous or not identified and therefore unavoidable

NURSING CARE
N/A

ACTIVITY
• Horses with mild AD may be worked normally with appropriate symptomatic therapy. Severely pruritic horses may not be able to perform
• Use of some antipruritic medications are illegal in competing horses

DIET
A diet high in polyunsaturated fatty acids or supplementation of such fatty acids as cold-pressed linseed or flax seed oil has been recommended. One small randomized, placebo-controlled, double-blind cross-over trial showed a reduction in the intradermal skin test response to *Culicoides* in AD horses after 42 days of supplementation with flaxseed.

CLIENT EDUCATION
• Clients rarely appreciate learning that their horse has a chronic skin disease that requires ongoing, long-term management. The need for a thorough workup to confirm a diagnosis of AD (by exclusion) is step 1. Client acceptance of long-term therapy is step 2
• Owners need to decide if they will limit treatment to symptomatic therapy or if they will choose ASIT, which is the only specific treatment available and currently the only chance of "cure"
• As they are active participants in the treatment regime, owners also need to understand how to assess response to therapy, be aware of signs of adverse effects, and when to consult the veterinarian for a needed change in treatment

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
• Treatment of choice for horses with AD is ASIT. ASIT is an extract containing offending allergens that is given subcutaneously at regular intervals
• Base the selection of allergens for inclusion in ASIT on test results, the history of the patient, and local exposure to regional allergens
• Tailor the amount and the frequency of administration of ASIT to the patient's response. For example, pruritus directly after the injection prompts a decrease in the amount or strength of ASIT, whereas increased pruritus at the end of the treatment interval before the next injection is due suggests a need to increase ASIT frequency of administration

CONTRAINDICATIONS
None

PRECAUTIONS
One possible (albeit very rare) adverse effect of ASIT is anaphylaxis. This can have particularly dramatic consequences in horses with concurrent severe asthma. In such patients, injection of the allergen extract should be preceded by 2 h by administration of an antihistamine (see Alternative Drugs) and epinephrine should be available. Monitor the horse closely for the first hour after immunotherapy injection.

POSSIBLE INTERACTIONS
None

ALTERNATIVE DRUGS
• There are a number of drugs used for symptomatic therapy, as an alternative or concurrent treatment to ASIT
• The most frequently used drugs for allergic horses are glucocorticoids. They inhibit a wide array of inflammatory mediators and cells and thus have a high efficacy in the treatment of equine pruritus. Prednisolone is preferred. It is initially given at 0.5–1 mg/kg/day and tapered after 7–14 days to the lowest possible dose every 48 h. Recent well-conducted studies have not found an association between prednisolone administration and laminitis. An alternative to prednisolone is dexamethasone, which is given initially at 0.05–0.1 mg/kg/day for a few days and then tapered to 0.01 mg/kg every third day or less, if possible
• Antihistamines are used for long- or short-term control of pruritus
• Pharmacokinetic data for many antihistamines in the horse are unknown
• Antihistamines used in the horse and their doses are listed in Table 2 Assess efficacy after 2 weeks of therapy
• Polyunsaturated omega 3 and 6 fatty acids act most likely through their influence on the immune response as well as the epidermal barrier. Their effect on horses with AD is not as clear as the one seen on canine AD. Studies have shown variable results with commercial products, flax seed, or linseed oil. If fatty acid supplementation is beneficial, improvement may occur within 4–8 weeks after commencement

Table 2

Antihistamines and their dose recommended for equine dermatitis

Antihistamine	*Dose*
Cetirizine	0.2–0.4 mg/kg every 12 h
Hydroxyzine	1 mg/kg every 8–12 h
Amitriptyline	1 mg/kg every 12 h
Chlorpheniramine (chlorphenamine)	0.25 mg/kg every 12 h
Diphenhydramine	1 mg/kg every 8–12 h
Doxepin	0.5 mg/kg every 12 h

FOLLOW-UP

PATIENT MONITORING
Severity of patient's disease will dictate the need for monitoring. Patients with severe uncontrolled pruritus should be assessed frequently to ensure secondary infections are managed and controlled.

PREVENTION/AVOIDANCE
• Prevention may be possible if the horse is relocated to a different ecologically diverse geographic location
• Avoidance of allergens is not always possible or practical, especially as many patients have multiple allergens contributing to their disease

POSSIBLE COMPLICATIONS
• Change in allergen exposure or load precipitating disease flare or recurrence of previously controlled AD
• Secondary bacterial infections
• Adverse effects to symptomatic medications

EXPECTED COURSE AND PROGNOSIS
AD is a chronic skin disease and spontaneous remission is rare. Therapies should be continued long term. Prognosis is good to fair with appropriate management.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Severe equine asthma
• Allergic conjunctivitis
• IH

AGE-RELATED FACTORS
Severity worsens with age.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
Long-term use of corticosteroids is contraindicated during pregnancy.

SYNONYMS
Equine atopy.

SEE ALSO
• Ectoparasites
• Heaves (severe equine asthma, RAO)
• Insect hypersensitivity
• Urticaria

ABBREVIATIONS
• AD = atopic dermatitis
• ASIT = allergen-specific immunotherapy
• CAFR = cutaneous adverse food reaction
• ELISA = enzyme-linked immunosorbent assay
• IDT = intradermal dilutional test

(CONTINUED) ATOPIC DERMATITIS

- Ig = immunoglobulin
- IH = insect bite hypersensitivity
- IL = interleukin
- Th2 = T-helper cell 2

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Author Ralf Mueller
Consulting Editor Gwendolen Lorch
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Client Education Handout available online

A

ATRIAL FIBRILLATION

BASICS

DEFINITION
• An irregularly irregular cardiac rhythm, with variable intensity heart sounds and pulses and inconsistent diastolic intervals
• Can be paroxysmal (resolving spontaneously within 48 h of onset), persistent, or permanent

PATHOPHYSIOLOGY
• A critical atrial mass must be present for AF to occur
• Predisposing factors—large atrial mass, atrial remodeling and fibrosis, high vagal tone, shortened and nonhomogeneous effective refractory period, potassium depletion, atrial premature complexes, bradycardia, predisposing arrhythmias (atrial tachycardia or atrial flutter), and rapid atrial pacing
• Produces no change in cardiac output at rest in the absence of significant underlying cardiac disease
• During high-intensity exercise, produces a significant increase in exercising HR (often 40–60 bpm higher than when in NSR) and subsequent fall in cardiac output and exercise capacity
• Present in many horses with CHF but is not the cause of CHF

SYSTEMS AFFECTED
Cardiovascular

SIGNALMENT
Higher incidence in Standardbred, draft, and Warmblood horses.

SIGNS
General Comments
Exercise intolerance in high performance animals; often an incidental finding in horses performing only light work.

Historical Findings
• Exercise intolerance
• Exercise-induced pulmonary hemorrhage—often profuse
• Weakness or collapse

Physical Examination Findings
• Irregularly irregular heart rhythm
• Variable intensity heart sounds and arterial pulses
• Absent fourth heart sound
• Cardiac murmurs with predisposing cardiac disease

CAUSES
• Normal horses have sufficient atrial mass and high vagal tone to develop AF without evident underlying heart disease—"lone" AF
• Diseases causing atrial enlargement further predispose horses to AF

RISK FACTORS
• AV valve insufficiency
• CHF
• Electrolyte disturbances

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Second-degree AV block—regular rhythm is interrupted by pauses containing fourth heart sound
• Atrial tachycardia with second-degree AV block—rhythm usually is regularly irregular; fourth heart sounds are present
• Atrial flutter—rhythm usually irregularly irregular; need ECG to differentiate
• NSR with multifocal ventricular premature complexes—need ECG to differentiate

CBC/BIOCHEMISTRY/URINALYSIS
Low plasma potassium or urinary fractional excretion of potassium may be present.

OTHER LABORATORY TESTS
Elevated cardiac troponin I or cardiac troponin T possible but usually within the normal range.

IMAGING
ECG
• No P waves, replaced by baseline "f" waves (Figure 1)
• The "f" waves may be coarse or fine and may occur 300–500 times per minute
• Irregular R–R interval
• Some variation in the amplitude of QRS and T complexes usually is present, but these complexes are otherwise normal in appearance

Echocardiography
• Many have little or no discernible underlying cardiac disease; therefore, the echocardiogram is normal
• Some have low shortening fraction (24–32%). This should return to normal within several days of conversion to normal NSR
• Mild left atrial enlargement occasionally occurs with permanent AF
• Atrial enlargement due to AV valve insufficiency, underlying myocardial disease, or congenital defects may be present

OTHER DIAGNOSTIC PROCEDURES
Continuous 24 h Holter Monitoring
• Use with suspected paroxysmal AF to identify underlying arrhythmias
• Use with persistent AF to determine if other concurrent arrhythmias are present

Exercise ECG
Use to detect exercise-induced arrhythmias and conduction abnormalities and to determine horse and rider safety and exercise limitations if the AF is not or cannot be converted.

PATHOLOGIC FINDINGS
• Grossly and histopathologically normal heart in horses with no underlying cardiac disease
• Focal or diffuse atrial fibrosis may be present in horses with longstanding AF
• Myocarditis, myocardial necrosis, and fatty infiltration have been documented in affected horses
• Both atrial and ventricular enlargement in horses with significant AV valvular disease

TREATMENT

AIMS
• Restoration of NSR and athletic performance in horses with no, minimal, or mild underlying heart disease
• Assessment of rider/driver/handler safety if cardioversion is not successful or not desired; rate control if indicated
• Palliative care for horses with AF in conjunction with CHF

APPROPRIATE HEALTH CARE
• Monitor horses for 24–48 h to determine if the condition will spontaneously resolve (i.e. paroxysmal)
• In horses with AF and CHF, institute treatment for CHF—using digoxin

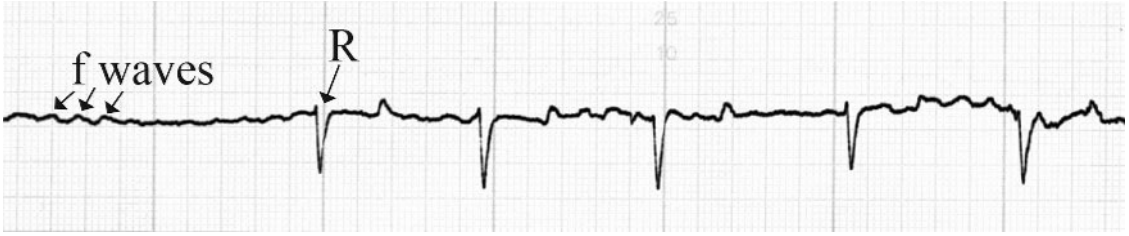

Figure 1.

Base–apex lead 25 mm/s, 5 mm = 1 mV.

(CONTINUED)

ATRIAL FIBRILLATION

(0.0022 mg/kg IV every 12 h or 0.011 mg/kg PO every 12 h), furosemide (1–2 mg/kg IV every 8 h, not PO), or torsemide (0.5–1 mg/kg PO every 12 h) and ACE inhibitor (benazepril at 1 mg/kg PO every 12 h), if indicated
• If AF is persistent, CHF is not present, and exercise intolerance is present, pharmacologic cardioversion or TVEC should be considered

NURSING CARE

• Perform continuous ECG throughout attempted conversion to NSR
• Keep horses quiet during pharmacologic cardioversion

ACTIVITY

• Horses with AF should not perform high-intensity exercise
• Horses with AF can usually perform successfully in lower level athletic work, as broodmares, and as breeding stallions
• An exercising ECG is indicated to ensure safety of horse and rider for intended use if cardioversion is not successful or not elected

DIET

• Oral potassium supplementation may be indicated with low plasma potassium, or low urinary fractional excretion of potassium or with excessive sweating
• Potassium chloride salt can be added to the feed (1 tablespoon every 12 h, gradually increasing to 28 g (1 oz) every 12 h)

CLIENT EDUCATION

• Discuss treatment-associated risks with owners—see Possible Complications
• Discuss predisposing factors to minimize the likelihood of recurrence

SURGICAL CONSIDERATIONS

• TVEC under general anesthesia is usually successful (success rate similar to quinidine)
• This utilizes a biphasic current delivered between electrodes placed in the right atrium and left pulmonary artery using pressure waveforms, echocardiography, and radiography or robotic fluoroscopy to guide and confirm electrode placement

MEDICATIONS

DRUG(S) OF CHOICE

The drug of choice for conversion is quinidine sulfate or gluconate.

Quinidine Gluconate

• Indicated with AF of duration ≤2 weeks and no underlying cardiac disease
• Administered in boluses of 0.5–1 mg/kg every 5–10 min to a total dose of 12 mg/kg

Quinidine Sulfate

• Indicated in horses with persistent AF
• Administered via nasogastric intubation at 22 mg/kg every 2 h to a total of 4–6 treatments, then every 6 h until the horse shows signs of toxicity or has converted to NSR

CONTRAINDICATIONS

• Do not administer quinidine sulfate or gluconate to horses with AF and CHF
• Horses with a resting HR of >60 bpm and/or grade 3/6 or louder systolic murmurs are likely to have CHF
• TVEC may be preferable in horses with wide QRS morphology with increased ventricular response rate

PRECAUTIONS

Quinidine is associated with the following complications.

Cardiovascular

• Prolonged QRS duration—indicates quinidine toxicity
• Prolonged QT interval—increases risk of ventricular arrhythmias
• Rapid supraventricular tachycardia—treat aggressively with digoxin to slow HR
  ◦ Digoxin is recommended in conjunction with quinidine in horses with myocardial dysfunction or rapid HR during quinidine treatment
  ◦ If HR exceeds 100 bpm, consider digoxin—0.011 mg/kg PO or 0.0022 mg/kg IV
  ◦ If HR exceeds 150 bpm, consider digoxin (0.0022 mg/kg IV) and sodium bicarbonate (1 mEq/kg IV)
  ◦ Detomidine or diltiazem may also be used to control rate with close monitoring of blood pressure
  ◦ If a horse receiving quinidine only on day 1 does not convert, consider adding digoxin orally on day 2
  ◦ Base subsequent digoxin administration during quinidine treatment on serum digoxin concentration and need to control HR or to improve myocardial contractility
• Ventricular arrhythmias do not require treatment if ventricular rhythm is slow (<120 bpm), uniform, and no R-on-T is detected
  ◦ If treatment indicated use magnesium sulfate—2–5 mg/kg bolus IV every 5 min to 50 mg/kg total
• Hypotension—monitor and treat, if severe, with IV fluids to effect and, if necessary, phenylephrine (0.1–0.2 µg/kg/min IV to effect)
• Sudden death—try to prevent with continuous ECG monitoring and treatment of any concerning arrhythmias that occur

Gastrointestinal

• Flatulence—resolves on return of quinidine plasma concentrations to negligible levels
• Oral ulcerations—prevent by administering quinidine via nasogastric tube
• Diarrhea—resolves on return of quinidine plasma concentrations to negligible levels
• Colic—associated with increasing number of doses; treat with analgesics as needed

Respiratory

Upper respiratory tract obstruction—indicates quinidine toxicity; treat with passage of a nasotracheal tube to relieve the upper airway obstruction; administer corticosteroids and antihistamines; emergency tracheotomy, if necessary.

Dermatologic

Urticaria—treat with corticosteroids and antihistamines.

Reproductive

Paraphimosis—resolves on return of plasma quinidine concentration to negligible levels.

Musculoskeletal

Laminitis—if the horse is uncomfortable, administer analgesics.

Neurologic

• Indicates quinidine toxicity
• Ataxia—resolves on return of plasma quinidine concentration to negligible levels
• Convulsions—administer anticonvulsants
• Bizarre behavior—resolves on return of plasma quinidine concentration to negligible levels

PATIENT MONITORING DURING TREATMENT WITH QUINIDINE

• Perform continuous ECG during treatment, because antiarrhythmic drugs are also arrhythmogenic
• Measure QRS and QT duration before each dose; discontinue treatment if QRS or QT duration ≥25% of the pretreatment value
• Discontinue treatment if rapid supraventricular tachycardia, ventricular arrhythmias, diarrhea, colic, ataxia, convulsions, bizarre behavior, urticaria, upper respiratory tract obstruction, or laminitis occurs

POSSIBLE INTERACTIONS

Quinidine results in increased steady-state digoxin concentration, causing potential digoxin toxicity.

ALTERNATIVE DRUGS

• IV amiodarone has been successful but has a lower cardioversion rate
• Flecainide has been associated with fatal ventricular arrhythmias and is not recommended

FOLLOW-UP

PATIENT MONITORING FOLLOWING CONVERSION

• Following conversion, perform 24 h Holter ECG. If atrial ectopy is found, rest and corticosteroid therapy may be indicated
• Evaluate left atrial contractile function; if absent or decreased, rest for 4 weeks and reevaluate
• Regularly monitor cardiac rhythm; any irregularities or poor performance should prompt reexamination

ATRIAL FIBRILLATION (CONTINUED)

• If in permanent AF, informed adult rider should monitor exercising HR with HR monitor
• Retire horse if exercising HR >220 bpm or ventricular arrhythmias or conduction abnormalities are induced by exercise or sympathetic nervous system stimulation

PREVENTION/AVOIDANCE

• Discontinue administration of furosemide and bicarbonate milkshakes
• Administer potassium or other electrolyte supplementation, if indicated
• Consider administration of ACE inhibitor to minimize atrial remodeling and fibrosis
• Consider administration of vitamin C
• Avoid thyroid hormone supplementation
• See chapter Supraventricular arrhythmias

POSSIBLE COMPLICATIONS

• If AF is not or cannot be treated, clinical signs will persist
• Some horses with AF also have exercise-induced aberrant conduction, ventricular arrhythmias or R-on-T complexes; if AF is not or cannot be converted and the horse is to continue to be used for ridden exercise, exercising ECG is indicated to ensure horse and rider safety—see chapter Ventricular arrhythmias

EXPECTED COURSE AND PROGNOSIS

• Most horses with little or no underlying cardiac disease convert to NSR with quinidine or TVEC cardioversion
• Recurrences occur in ≅15% of horses with a suspected duration of ≤4 months
• Recurrences occur in ≅45% of horses with a duration of AF of >4 months
• Recurrence is most likely during the first year after conversion but can occur at any time
• Recurrence likely in horses with left atrial enlargement or mitral regurgitation
• Prognosis for return to the previous level of athletic performance is excellent in converted horses without significant underlying cardiovascular disease
• Horses with permanent AF that do not convert to NSR with treatment or that are not candidates for conversion usually have a normal life expectancy and can be safely used for lower level athletic performance, as long as their exercising HR is <220 bpm and there is no aberrant conduction, ventricular arrhythmias, or R-on-T complexes
• With significant valvular insufficiency, severity of the valvular heart disease and its progression determine the horse's useful performance life and life expectancy
• Horses with CHF usually have severe underlying valvular heart or myocardial disease and have a guarded to grave prognosis for life
• Most affected horses treated for CHF respond to the supportive therapy and improve for a short time but are euthanized within 2–6 months of initiating treatment

MISCELLANEOUS

ASSOCIATED CONDITIONS

Any cardiac disease resulting in atrial enlargement predisposes to AF.

AGE-RELATED FACTORS

Older horses are more likely to have significant underlying cardiac disease, with valvular insufficiency and atrial enlargement and are not usually candidates for conversion.

PREGNANCY/FERTILITY/BREEDING

• Affected pregnant mares without underlying cardiac disease and CHF should not experience any problems
• Affected pregnant mares with CHF—treat for the underlying cardiac disease with digoxin and furosemide. Although not studied in the horse, ACE inhibitors are contraindicated in pregnant mares due to the risk of birth defects documented in other species

SYNONYMS

A fib, AF

SEE ALSO

• Mitral regurgitation
• Myocardial disease
• Supraventricular arrhythmias
• Tricuspid regurgitation
• Ventricular arrhythmias

ABBREVIATIONS

• ACE = angiotensin-converting enzyme
• AF = atrial fibrillation
• AV = atrioventricular
• CHF = congestive heart failure
• HR = heart rate
• NSR = normal sinus rhythm
• TVEC = transvenous electrical cardioversion

Suggested Reading

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Author Virginia B. Reef
Consulting Editor Celia M. Marr and Virginia B. Reef

ATRIAL SEPTAL DEFECT

BASICS

DEFINITION

• A congenital defect (i.e. hole) in the interatrial septum that creates a communication between the right and left atria
• Can be located in the atrial septum immediately adjacent to the ventricular septum (i.e. atrium primum defect), in the area of the foramen ovale (i.e. atrium secundum defect), or in the most basilar portion of the interatrial septum (i.e. sinus venosus-type defect)
• ASD can occur in isolation or in conjunction with other cardiac anomalies in complex congenital cardiac disease
• The atrial septum forms in the fetus from the septum primum and the septum secundum. The slit-like communication between these septa (i.e. the foramen ovale) allows passage of blood from right to the left atrium in the fetus
• The foramen ovale is functionally closed in normal neonates within 24–48 h of birth, but anatomic closure may not be complete until 9 weeks

PATHOPHYSIOLOGY

• A patent foramen ovale occurs when the foramen ovale fails to close
• Failed formation of 1 of the 2 septa results in the other forms of ASD
• Blood shunts from the higher pressure left atrium to the lower pressure right atrium in foals with ASD, creating a left atrial, right atrial, and right ventricular volume overload
• Size of the ASD determines severity of the volume overload. In horses with a large ASD, the right and left atrial and right ventricular volume overload is severe
• Over time, stretching of the tricuspid annulus occurs, and tricuspid regurgitation develops. As the tricuspid regurgitation becomes more severe, increases in right atrial pressure result in increased hepatic venous pressure and development of clinical signs of right-sided CHF

SYSTEMS AFFECTED

Cardiovascular

GENETICS

• Not yet determined in horses
• Although heritable in other species, it is rare in horses

INCIDENCE/PREVALENCE

These defects are uncommon as isolated congenital defects and more frequently occur in conjunction with complex congenital heart disease, particularly tricuspid and pulmonic atresia.

SIGNALMENT

Most frequently diagnosed in neonates, foals, and young horses, but may be diagnosed at any age.

SIGNS

General Comments

May be detected as an incidental finding, but usually is part of a more complex, congenital cardiac disorder.

Historical Findings

• Exercise intolerance—medium-sized to large ASDs
• CHF—large ASDs

Physical Examination Findings

• No murmur may be present, or a coarse, band- or ejection-shaped, holosystolic murmur with point of maximal intensity in the pulmonic valve area may be detected
• Premature beats or an irregularly irregular heart rhythm of AF may be present with larger ASDs

CAUSES

• Failed closure of the foramen ovale
• Congenital malformation of the interatrial septum

RISK FACTORS

• Premature foal
• Neonatal pulmonary hypertension
• Neonatal respiratory distress syndrome

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Physiologic flow murmur—differentiate echocardiographically
• Pulmonic stenosis (rare)—murmur usually louder; differentiate echocardiographically
• Aortic stenosis (rare)—murmur usually louder; weak arterial pulses; differentiate echocardiographically
• Tricuspid atresia—murmur usually louder; foal is unthrifty, tachycardic, and hypoxemic; differentiate echocardiographically
• Pulmonic atresia—murmur usually louder; may have a continuous machinery murmur; foal is unthrifty, tachycardic, and hypoxemic; differentiate echocardiographically

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

ECG

• Atrial premature depolarizations or AF may be present in horses with right and left atrial enlargement
• Persistent AF has been reported in some affected foals and horses

Echocardiography

• Can determine location of the ASD
• Atrial septal dropout is detected at the ASD location and should be confirmed by visualization in 2 mutually perpendicular planes
• The left and right atria and right ventricle are enlarged, dilated, and have a rounded appearance
• Paradoxical septal motion is detected with a severe right ventricular volume overload
• Pulmonary artery dilatation is seen in horses with a large shunt
• Interrogate the entire atrial septum with pulsed-wave or color-flow Doppler with suspected ASD
• Contrast or color-flow Doppler reveals the shunt from the left to the right atrium through the ASD
• A small amount of positive contrast may be seen in the left atrium in horses with normal pulmonary arterial pressures or with the Valsalva maneuver during contrast echocardiography
• A jet of tricuspid regurgitation may be present in horses with a large ASD and marked right atrial and ventricular volume overload

Thoracic Radiography

Increased pulmonary vascularity and cardiac enlargement may be detected in horses with large shunts.

OTHER DIAGNOSTIC PROCEDURES

Cardiac Catheterization

• Right-sided catheterization can be performed to directly measure right atrial, right ventricular, and pulmonary arterial pressures and to sample blood for oxygen content
• Elevated right atrial, right ventricular, and pulmonary arterial pressures and increased oxygen saturation of right ventricular and pulmonary arterial blood have been seen in horses with larger ASDs

Continuous 24 h Holter Monitoring

Use in identifying intermittent atrial premature depolarizations.

PATHOLOGIC FINDINGS

• Defect in the atrial septum
• Jet lesions along the defect margins and on the adjacent right atrial endocardium
• Left atrial, right atrial, and right ventricular enlargement and thinning of the left atrial, right atrial, and right ventricular free wall in horses with a significant shunt
• Pulmonary artery dilatation in horses with a large shunt or that have developed pulmonary hypertension
• With CHF, ventral and peripheral edema, pleural effusion, pericardial effusion, chronic hepatic congestion, and, occasionally, ascites may be detected

TREATMENT

AIMS

• Management by intermittent monitoring in horses with small ASDs

ATRIAL SEPTAL DEFECT (CONTINUED)

• Palliative care in horses with large ASDs and those with complex congenital cardiac defects

APPROPRIATE HEALTH CARE
• Most affected horses require no treatment and can be monitored on an outpatient basis
• Monitor horses with large shunts on an annual basis
• Affected horses with CHF can be treated for CHF with positive inotropic drugs, vasodilators, and diuretics. Consider humane destruction if CHF develops, however, because only short-term, symptomatic improvement can be expected

NURSING CARE
N/A

ACTIVITY
• Affected horses are safe to continue in full athletic work until significant tricuspid regurgitation or AF develops
• Horses with small defects can be in unrestricted activity and may be able to compete reasonably successfully in upper level athletic competition
• Monitor horses with hemodynamically significant defects echocardiographically on an annual basis to ensure they are safe to ride and compete. These horses can be used for lower level athletic competition but are unlikely to compete at the upper levels of athletic performance
• Affected horses that develop AF need a complete cardiovascular examination to determine if they are safe to use for lower level athletic performance
• Horses with significant pulmonary artery dilatation no longer are safe to ride

DIET
N/A

CLIENT EDUCATION
• Regularly monitor cardiac rhythm; any irregularities of the rhythm, other than second-degree atrioventricular block, should prompt ECG
• Carefully monitor for exercise intolerance, respiratory distress, prolonged recovery after exercise, increased resting respiratory or heart rate, cough, generalized venous distention, jugular pulses, or ventral edema; if detected, obtain a cardiac reexamination

SURGICAL CONSIDERATIONS
• Closure of the ASD would be possible with a transvenous umbrella catheter if the diameter of the umbrella was large enough to close the defect
• Surgical closure is not financially feasible or practical for obtaining equine athletes at this time

MEDICATIONS

DRUG(S) OF CHOICE
N/A

CONTRAINDICATIONS
N/A

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
Frequently monitor cardiac rate, rhythm, and respiratory rate and effort.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Large ASD—AF; CHF.

EXPECTED COURSE AND PROGNOSIS
• Horses with small defects should have a normal performance life and life expectancy
• Horses with moderate defects also have a normal life expectancy. These horses usually perform successfully only at lower levels of athletic competition, and they may develop AF
• Horses with large defects have a guarded prognosis, because they may have a shortened life expectancy and performance life, even at the lower levels of athletic competition
• Affected horses with CHF usually have a guarded to grave prognosis for life. Most such horses being treated for CHF should respond to the supportive therapy and transiently improve; however, once CHF develops, euthanasia is recommended

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Complex congenital cardiac disease, particularly tricuspid and pulmonic atresia, is likely
• Tricuspid regurgitation can develop in horses with significant left atrial, right atrial, and right ventricular volume overload secondary to stretching of the tricuspid annulus
• Pulmonic regurgitation can develop in horses with isolated defects
• Pulmonic valve leaflets may no longer coapt with stretching of the pulmonary artery from the volume overload

AGE-RELATED FACTORS
Young horses are more likely to be diagnosed.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
Breeding affected horses is discouraged. The condition is rare, however, and the heritable nature of this defect in horses is not known.

SYNONYMS
N/A

SEE ALSO
• Atrial fibrillation
• Supraventricular arrhythmias

ABBREVIATIONS
• AF = atrial fibrillation
• ASD = atrial septal defect
• CHF = congestive heart failure

Suggested Reading

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Author Virginia B. Reef
Consulting Editors Celia M. Marr and Virginia B. Reef

BASICS

OVERVIEW
• A form of severe nonexertional rhabdomyolysis due to eating plant material containing toxin hypoglycin A; aka "seasonal pasture myopathy"
• Horses ingest toxin-containing seeds from box elder (*Acer negundo*, midwest USA and Canada) or sycamore maple (*Acer pseudoplatanus*, UK and northern Europe)
• Metabolized hypoglycin A inhibits acyl-coenzyme A dehydrogenase, resulting in massive aerobic metabolism disruption and severe type I muscle fiber damage
• Necrosis of skeletal, respiratory, and cardiac muscles results in myoglobinuria, weakness, recumbency, respiratory difficulty, renal damage, and death in a high proportion of affected horses

SIGNALMENT
• Typically ≤3 years of age
• Any breed or gender

SIGNS
• Weakness, stiffness, rapid progression to recumbency and death in 72 h
• Discolored (red/brown) urine
• Tachycardia, respiratory difficulty
• ± Bright and appetent while recumbent
• ± Subclinical disease in pasture mates

CAUSES AND RISK FACTORS
• Consumption of seeds containing hypoglycin A
• >12 h of pasture access
• Young age, dietary indiscretion
• Competitive feeding situations
• Lack of supplemental feeding, particularly during cold or inclement weather
• Overgrazed pastures

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Conditions causing weakness, stiffness, recumbency, and/or discolored urine such as laminitis, tetanus, colic, viral encephalitides, acute exertional rhabdomyolysis, selenium deficiency, red maple (*Acer rubrum*) toxicity, and other disorders causing intravascular hemolysis/methemoglobinemia.

CBC/BIOCHEMISTRY/URINALYSIS
• Elevated serum creatine kinase (>100 000 U/L in many), aspartate aminotransferase, and lactate dehydrogenase
• Hypochloremia, hypocalcemia, hyponatremia, hyperkalemia
• Azotemia
• Hyperglycemia, hyperlipemia, hyperlactatemia
• Myoglobinuria

OTHER LABORATORY TESTS
• Cardiac troponin I or T
• Methylenecyclopropylacetic acid conjugates (hypoglycin A metabolite) in serum or urine

IMAGING
Echocardiography (in survivors).

OTHER DIAGNOSTIC PROCEDURES
Muscle biopsy—excessive lipid accumulation in type I skeletal muscle fibers.

PATHOLOGIC FINDINGS
• Massive skeletal muscle necrosis
• Cardiac muscle necrosis in ~50% of cases
• Acute tubular necrosis ± pigmenturia

TREATMENT
• Reduce discomfort, prevent further muscle necrosis, restore fluid volume and acid–base and electrolyte status, reverse shock, and prevent renal damage
• Prompt, intensive supportive care. Hospitalization to provide appropriate fluid therapy and to manage recumbency
• IV or oral fluid therapy with balanced electrolyte solutions until myoglobinuria resolves
• Deep bedding, head and eye protection, and limb wraps are indicated for recumbent horses
• ± Slinging

MEDICATIONS

DRUG(S) OF CHOICE
• Analgesics—butorphanol (0.01–0.04 mg/kg IM or IV; or as a CRI at 23.7 µg/kg/h after a loading dose of 17.8 µg/kg IV); lidocaine (CRI at 30–50 µg/kg/min after a loading dose of 1.3 mg/kg IV slowly); and flunixin meglumine (0.5–1.1 mg/kg IV or PO)
• Antioxidant drugs—DMSO (1 g/kg IV or PO as a 10% solution), vitamin C (30 mg/kg IV diluted in fluids), vitamin E (2000–5000 IU PO every 24 h)
• Muscle relaxants—methocarbamol (5–22 mg/kg IV slowly, every 6–12 h) and dantrolene (4–6 mg/kg PO every 12 h). Dantrolene prevents additional muscle necrosis and may speed return of function, but is poorly absorbed in horses that have not eaten within 4 h prior to administration
• Insulin (0.2–0.4 U/kg insulin glargine IV or SC every 24 h) for hyperlipemia

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Avoid NSAIDs in horses with azotemia, myoglobinuria, or profound shock
• Avoid dantrolene in horses with hyperkalemia

FOLLOW-UP

PATIENT MONITORING
Close monitoring of clinical and clinicopathologic variables is essential in affected horses, including serial monitoring of serum muscle enzymes, cardiac troponin, creatinine, and other relevant variables.

PREVENTION/AVOIDANCE
• Prevent access to causative tree species via fencing or tree removal
• Provide supplemental feeding during inclement weather or remove horses from pasture

POSSIBLE COMPLICATIONS
• Acute or chronic renal insufficiency secondary to myoglobinuria
• Acute or chronic cardiac dysfunction
• Atrophy of skeletal musculature

EXPECTED COURSE AND PROGNOSIS
• Guarded to grave prognosis with a 75–80% fatality rate. Surviving horses can have chronic complications
• Survivors require months of rest. Reevaluation including assessment of cardiac function is recommended before return to exercise

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Heart failure
• Renal insufficiency

AGE-RELATED FACTORS
Highest prevalence in young horses.

PREGNANCY/FERTILITY/BREEDING
N/A

SEE ALSO
Exertional rhabdomyolysis syndrome

ABBREVIATIONS
• CRI = constant rate infusion
• DMSO = dimethyl sulfoxide
• NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Valberg SJ, Sponseller BT, Hegeman AD, et al. Seasonal pasture myopathy/atypical myopathy in North America associated with ingestion of hypoglycin A within seeds of the box elder tree. Equine Vet J 2013;45:419–426.

Author Erica C. McKenzie
Consulting Editor Elizabeth J. Davidson

A

AURAL PLAQUES

BASICS

OVERVIEW
Aural plaques are whitish plaques on the inner pinnal surface of horses that are caused by EcPV.

SIGNALMENT
• Common in all sexes and breeds but rarely observed in horses <1 year old
• Incidence ranges from 14.8% of Brazilian horses to 20–24% of horses in the USA
• 85% of Brazilian farms had at least one horse affected

SIGNS
• Depigmented, well-demarcated papules and plaques covered with keratin deposits located on the concave pinnal surface. Lesions are single, multiple, or coalescing and may affect 1 or both pinna
• Horses can be asymptomatic or may resent bridling or handling of the ears
• Symptoms may be aggravated by biting flies

CAUSES AND RISK FACTORS
• Lesions contain EcPV, with EcPV types 3, 4, 5, and/or 6 consistently identified in biopsies
• Abrasions and biting flies, particularly black flies, are likely involved in viral transmission
• Ear grooming is associated with an 8.6-fold increased risk of coalescing (severe) lesions
• Increased horse density

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Sarcoids—more often on the external surface of the pinna or at the margins of the ear. May coexist with aural plaques.

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
Diagnosis is based on classic appearance and can be confirmed by biopsy.

TREATMENT

• Aural plaques are not known to resolve without treatment. Horses without ear sensitivity do not require treatment
• CO_2 laser ablation has been used but long-term efficacy is unknown
• Ear handling and ear clipping should be minimized in affected horses that are not being treated
• Ears should be protected from biting flies to avoid aggravation of the condition

MEDICATIONS

DRUG(S) OF CHOICE
• Topical imiquimod, an immune response modifier with antiviral activity, is the only drug shown to be consistently effective
• Imiquimod 5% cream resolves the plaques in 87–88% of horses and clears the infection with EcPV in 71% of ears biopsied
• Each lesion must be treated. Imiquimod is applied topically as a thin layer 2 or 3 times per week at least every other week until resolution, typically 3–4 months of every other week therapy (9–48 treatments). Alternatively, horses may be treated every 48 h for faster resolution (8–30 applications). A strong local inflammatory response is consistently observed with imiquimod due to its mechanism of action. The exudate and inflammation can make it difficult to handle and clean the ears prior to the next treatment. Sedation is often needed, particularly for the second or third treatment weeks. Inflammation generally resolves 7 days after the last treatment. Owners should be warned of the reaction and temporarily increased sensitivity due to local inflammation

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Imiquimod can cause inflammation of normal skin. No need to wash off the imiquimod until the next treatment is due.

FOLLOW-UP

PATIENT MONITORING
• Monitor for appropriate cleaning, application of imiquimod, and for complete resolution
• Clients may have difficulty cleaning the area sufficiently prior to treatment, resulting in poor contact of the drug with the plaques. Sedation is required for subsequent treatment if the repeated treatment occurs before 7 days after the last application. Inflammation caused by imiquimod can make it difficult to determine if the plaque resolution has occurred. Discontinuation of treatment for 1–2 weeks allows for better evaluation. Reevaluation at 1 month post treatment is strongly recommended. Assume any whitish areas are residual plaques. Recurrence is possible but infrequent within the subsequent 2 years if the plaques were resolved and flies controlled

PREVENTION/AVOIDANCE
• Not possible
• Use of fly repellents with permethrin/pyrethrin (for quick insect knockdown) and piperonyl butoxide (as a pesticide synergist) with fly masks that provide ear coverage may help prevent development

POSSIBLE COMPLICATIONS
• Ear sensitivity and pain
• Imiquimod can cause erosions or ulcers, particularly if applied in a thick layer. Erosions are more common in the first month of treatment. The severity of the reaction decreases as the plaques resolve

EXPECTED COURSE AND PROGNOSIS
• Aural plaques persist without treatment
• Post-treatment skin depigmentation may occur
• Ear sensitivity and head shyness improves after resolution of plaques despite the inflammation and challenges with ear handling during treatment

MISCELLANEOUS

ASSOCIATED CONDITIONS
None known.

AGE-RELATED FACTORS
None known.

ZOONOTIC POTENTIAL
None

SEE ALSO
• Papillomatosis
• Sarcoid

ABBREVIATIONS
EcPV = *Equus caballus* papillomavirus

Internet Resources
University of Minnesota, Veterinarian instructions for Aldara. http://www.vetmed.umn.edu/centers-programs/clinical-investigation-center/completed-clinical-studies/veterinarian-instructions-aldara

Author Erin Malone
Consulting Editor Gwendolen Lorch
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AZOTEMIA AND UREMIA

BASICS

DEFINITION
• Azotemia—the accumulation of nitrogenous waste (e.g. urea, Cr, other nitrogenous substance) in blood, plasma, or serum. • Uremia—the clinical manifestation of azotemia; a multisystem disorder resulting from the effects of uremic toxins on cellular metabolism and function. Cr and BUN typically are measured in serum and used as indices of azotemia

PATHOPHYSIOLOGY
• BUN concentration is determined by the rate of urea synthesis by hepatocytes and rate of clearance by the kidneys. • Increased protein catabolism results in elevated BUN concentration. • Decreased GFR may result from decreased renal perfusion, renal disease, or urinary obstruction. • Azotemia results from resorption of urine following urinary tract rupture. • Cr is a result of muscle creatine metabolism. • Renal excretion of Cr is dependent on GFR. • Cr is not resorbed by renal tubules. • Low BUN concentration may result after prolonged diuresis or as a result of impaired liver function

SYSTEMS AFFECTED
• Depend on the underlying causes. • Generalized effects—depression, weight loss, edema, dehydration. • Gastrointestinal tract—anorexia, uremic stomatitis, uriniferous breath, excessive dental tartar, oral/gastric ulceration, protein losing enteropathy, diarrhea. • Neuromuscular—lethargy, gait imbalance, behavioral changes, seizures. • Endocrine/metabolic—renal secondary hyperparathyroidism, inadequate production of erythropoietin and 1,25-dihydroxycholecalciferol (calcitriol). • Cardiovascular—hypertension, heart murmur, cardiac dysrhythmia. • Hemolymphatic—anemia

GENETICS
Healthy, heavily muscled Quarter Horses might have serum Cr concentrations >2.0 mg/dL.

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
• Neonatal male foals (ruptured bladder at parturition). • Any breed, age, or sex

SIGNS
General Comments
Unless the animal is uremic, clinical findings are limited to the process causing azotemia such as dehydration, urinary outflow tract obstruction, urinary outflow tract, or rupture.

Historical Findings
• Polyuria/polydipsia. • Weight loss. • Anorexia. • Abnormal urination. • Lethargy. • Uriniferous breath. • Poor performance. • Lumbar pain. • Colic. • Poor hair coat. • Prolonged posturing to urinate. • Stranguria

Physical Examination Findings
• Fever. • Anorexia. • Obtundation. • Poor body condition. • Ventral edema. • Oral ulceration. • Excessive dental tartar. • Scleral injection. • Colic. • Distended abdomen. • Urine scald. • Dysuria. • Hematuria. • Halitosis

CAUSES
Prerenal Azotemia
• Renal hypoperfusion caused by decreased circulating volume or decreased blood pressure. • Increased protein catabolism

Renal Azotemia
• AKI or CRF—primary renal dysfunction affecting glomeruli, renal tubules, renal interstitium, or renal vasculature ◦ Prolonged dehydration. ◦ Polycystic kidney disease. ◦ Pigment nephropathy (e.g. hemoglobin, myoglobin). ◦ Nephrotoxic drugs (e.g. NSAIDs, aminoglycoside, tetracycline, polymyxin B). ◦ Toxicities (e.g. cantharidin, red maple leaf, vitamin K3). ◦ Leptospirosis. ◦ Neoplasia

Postrenal Azotemia
• Obstruction of the urinary tract (e.g. urolithiasis). • Rupture of urinary tract

RISK FACTORS
• Prolonged exposure to nephrotoxic drugs, especially with concurrent dehydration. • Rhabdomyolysis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Elevated serum Cr concentration can be seen in healthy, heavily muscled horses.

CBC/BIOCHEMISTRY/URINALYSIS
CBC
Nonregenerative anemia caused by decreased erythropoietin production can occur with CRF.

Biochemistry
• Elevations in serum Cr and BUN concentrations indicate azotemia. In horses, BUN:Cr ratio is unreliable in differentiating AKI and CRF. • Hyponatremia and hypochloremia are common in horses with renal disease and can occur with third-compartment spacing of urine. • Hyperkalemia is a common finding in AKI and uroperitoneum. • Hypercalcemia and hypophosphatemia are often found with CRF; hypocalcemia and hyperphosphatemia can be found with AKI. • Hypercalcemia in renal failure depends upon dietary content and intake of calcium

Urinalysis
• USG >1.020 and urine osmolality >500 mOsm/kg are consistent with prerenal azotemia. • Fluid therapy and some medications (e.g. furosemide, α_2-receptor agonists, corticosteroids) may render the USG value inconclusive. • Dehydrated horses with primary renal disease usually lose the ability to concentrate urine; USG and osmolality are <1.020 and <500 mOsm/kg, respectively

OTHER LABORATORY TESTS
• Blood gas analysis—metabolic acidosis might be present with uremia. • Urine PCR for *Leptospira* sp.

IMAGING
Ultrasonography
• The urinary tract can be examined either transrectally or transabdominally. • Bladder ultrasonography is best performed transrectally using a 5 MHz probe. • Transabdominal ultrasonography of the kidneys is best performed with a 2.5–3 MHz probe. • Assess the size and shape of both kidneys and architecture and echogenicity of the parenchyma. • The renal medulla is more echolucent than the renal cortex. The renal pelvis varies in echogenicity. • With AKI, kidneys may be normal, enlarged, or hydronephrotic, and parenchymal abnormalities are often not detected. • With CRF, kidneys are usually smaller and more echogenic than normal. • Cystic or mineralized areas are more often associated with CRF or congenital anomalies. • Acoustic shadowing represents calculi formation

Renal Scintigraphy
May be used to document renal function but is not commonly performed.

OTHER DIAGNOSTIC PROCEDURES
Urine GGT:Cr Ratio
• Reflects GGT leakage from damaged renal tubular epithelium compared with the normal excretion of Cr. • Calculated as (urine GGT/urine Cr) × 100. • A ratio of >25 suggests proximal tubular damage; this elevation may occur before azotemia develops. • Finding an elevated ratio depends on having enough remaining tubules that can leak GGT; severe renal fibrosis may yield normal values

Fractional Excretion of Electrolytes
• Measurement of electrolytes in serum and urine can be compared to assess renal damage. • Calculated as (urine [electrolyte] × serum Cr/serum [electrolyte] × urine Cr). • Reported reference intervals for sodium fractional excretion range from 0.01 to 0.70. • Poor indicator of renal function

Rectal Examination
• Bladder—determine size, wall thickness, and presence of calculi or mural mass. • Left kidney—determine size and texture. • Ureter—usually not detectable upon palpation, may be enlarged in association with pyelonephritis or ureterolithiasis

A

AZOTEMIA AND UREMIA (CONTINUED)

Ultrasonography-Guided Renal Biopsy
Can be used to confirm the diagnosis of primary renal disease, differentiate AKI from CRF, and identify a specific cause.

Urethrocystoscopy
• To evaluate abnormal urination. • In adult males, a flexible endoscope with an outside diameter of <12 mm and a length of ≥1 m is adequate to evaluate the urethra and urinary bladder. • Normal urethral mucosa is pale pink, with longitudinal folds. • If the urethra is dilated with air (e.g. to aid passage of the endoscope), the mucosa may appear reddened, and a prominent vascular pattern may appear. • The ischial arch and colliculus seminalis are the most common sites of posturination or postbreeding hemorrhage in geldings and stallions. • In the dorsal aspect of the bladder trigone, the ureteral openings can be visualized to determine the source of hematuria or pyuria. • Biopsy of a bladder mass or collection of a sterile urine sample can be obtained

PATHOLOGIC FINDINGS
Dependent on the underlying cause.

TREATMENT

Prerenal Azotemia
Correct the underlying cause of renal hypoperfusion and/or correct the dehydration.

Renal Azotemia
• Dependent on the underlying cause.
• Supportive care to alleviate clinical signs of uremia; correct fluid, electrolyte, and acid–base abnormalities

Postrenal Azotemia
• Eliminate urinary obstruction or correct cause of urine leakage ◦ Surgical intervention often is required, but correction of any metabolic derangements is paramount

MEDICATIONS

DRUG(S) OF CHOICE
Dependent on the underlying cause.

Fluids
• IV fluid therapy is indicated for most azotemic patients. • Commonly used fluids—0.9% saline, Plasmalyte, lactated Ringer's solution. • Base the amount of fluid administration on dehydration or volume deficit. • Correction of the fluid deficit can occur during the first 6 h without untoward effects, except in patients with hypoproteinemia/hypoalbuminemia and with signs of cardiac disease

CONTRAINDICATIONS
• Use nephrotoxic drugs (e.g. NSAIDs, aminoglycosides) with caution in patients with azotemia. • K^+-containing IV fluid solutions (e.g. Plasmalyte, lactated Ringer's solution) in the presence of hyperkalemia

PRECAUTIONS
• Use caution when administering fluids to horses with AKI and CRF because they may develop significant peripheral and pulmonary edema. • Use IV fluids cautiously in oliguric or anuric patients to minimize overhydration. • Use NSAIDs and corticosteroids with caution. Although they can limit renal inflammation, they can also nonselectively block vasodilatory mediators of renal blood flow under conditions of renal hypoperfusion and are not recommended for CRF. • Horses should be well hydrated when using NSAIDs and aminoglycosides

POSSIBLE INTERACTIONS
Be aware of additive effects of nephrotoxic drugs.

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
• Serum Cr, BUN and electrolyte concentrations within 24 h after initiating fluid therapy, hydration status, and urine outflow. • Monitoring body weight of foals and adult horses may be helpful. • With severe electrolyte or acid-base derangements, more frequent monitoring may be required

POSSIBLE COMPLICATIONS
• Failure to promptly correct prerenal azotemia caused by renal hypoperfusion may result in AKI. • Failure to correct renal azotemia may result in uremia. • Failure to correct postrenal azotemia may result in renal damage or death caused by hyperkalemia and uremia

EXPECTED COURSE AND PROGNOSIS
• Dependent on the underlying cause. • With CRF, serum Cr concentrations >5 mg/dL indicates a marked decline in GFR. A grave prognosis is associated with serum Cr concentrations >10 mg/dL

MISCELLANEOUS

ASSOCIATED CONDITIONS
Dependent on the underlying cause.

AGE-RELATED FACTORS
• AKI may occur at any age, but older horses may be at higher risk for azotemia regardless of the cause. • Ruptured bladder is more common in male neonatal foals

PREGNANCY/FERTILITY/BREEDING
The ability of a mare to maintain a viable pregnancy decreases as renal function decreases.

SYNONYMS
Acute renal failure

SEE ALSO
• Acidosis, metabolic
• Acute kidney injury (AKI) and acute renal failure (ARF)
• Chronic kidney disease
• Potassium, hyperkalemia
• Urolithiasis
• Uroperitoneum, neonate

ABBREVIATIONS
• AKI = acute kidney injury. • BUN = blood urea nitrogen. • Cr = creatinine.
• CRF = chronic renal failure.
• GFR = glomerular filtration rate.
• GGT = γ-glutamyltransferase.
• NSAID = nonsteroidal anti-inflammatory drug. • PCR = polymerase chain reaction.
• USG = urine specific gravity

Suggested Reading
Van Metre DC, Soto DR. Diseases of the renal system. In: Smith B, ed. Large Animal Internal Medicine, 5e. St. Louis, MO: Elsevier Mosby, 2015:873–895.

Author Sandra D. Taylor
Consulting Editor Sandra D. Taylor
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