ABDOMINAL DISTENTION IN THE ADULT HORSE

BASICS

DEFINITION
Process by which the abdomen becomes enlarged leading to a change in its normal contour and shape

PATHOPHYSIOLOGY
The accumulation of fluid, gas, or ingesta in the peritoneal GI tract and/or peritoneal cavity, presence of abdominal masses, increased size of abdominal organs, or abdominal wall abnormalities 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
- Cardiovascular—Fluid sequestration may lead to a decreased circulating volume and hypovolemic shock. Often compounded by the presence of vascular compromise of the GI tract leading to translocation of bacteria and/or toxins to the systemic circulation. Hemoperitoneum may occur from trauma or rupture of mesenteric vessels due to increased traction or trauma (e.g., during foaling), from any other abdominal viscera (e.g., rupture of the spleen or liver), or ascites secondary to heart failure.
- Behavioral—Flank watching, pawing, rolling or violent episodes of thrashing.
- Respiratory—Abdominal distention or herniated abdominal viscera (diaphragmatic hernia) may lead to hypoventilation.
- Musculoskeletal/nervous/ophthalmologic/skin—Due to self-inflicted trauma secondary to abdominal pain.
- Reproductive—Hydrops and ruptured of prepubic tendon is seen in pregnant mares and both conditions will manifest as change in the abdominal contour.

SIGNALMENT
- All horses are susceptible.
- Pregnant mares—hydrops (anytime during pregnancy), uterine torsion (mid-term), uroperitoneum (postpartum), 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—predisposed to fecaliths, enteroliths, and small colon impactions
- Older horses—predisposed to pedunculating lipomas

SIGNS
Historical
The clinical progression should help the clinician differentiate between vascular and nonvascular GI obstructions and other non-GI causes of distention. Also, signalment and geographical location, time of year, and sex should provide clues toward a final diagnosis.

Physical
- Evaluate progression of clinical signs, historical facts, and cardiovascular system.
- Rectal examination is practical, inexpensive, and quick, but evaluates only the caudal abdomen.
- Abdominal ultrasound examination may help determining location, nature, and severity of the cause of colic.

CAUSES
Accumulation of Gas
- Functional obstruction—primary ileus due to increased sympathetic drive. Secondary ileus due to pain (visceral or musculoskeletal), ischemic necrosis (e.g., verminous arteritis), electrolyte abnormalities (e.g., endurance horses), dehydration, inflammation of the bowel (enteritis) or abdominal cavity (peritonitis), and drugs (e.g., α_2 agents, morphine)
- 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
- Grain overload
- Free gas within the abdominal cavity may occur secondary to trauma or anaerobic infections
- Colitis

Accumulation of Fluid
- Hemoperitoneum—ruptured viscera or myenteric vessel
- Uroperitoneum—ruptured bladder secondary to obstructive urolithiasis or traumatic parturition
- 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/mucometria

Solid Mass
- Abscess
- Neoplasia—lymphosarcoma, squamous cell carcinoma, mammary adenocarcinoma, mesothelioma, hemangiosarcoma, and hepatic neoplasia

Body Wall Abnormality
- Hernia
- Prepubic tendon rupture

RISK FACTORS
- Cribbing may predisposed to tympany of the colon and epiploic foramen entrapment.
- Gastric ulcers predispose 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 tympany and large colon displacement or volvulus.
- Colonic impactions often occur in horses that are old or debilitated or that have poor dentition.
- Sudden change in physical activity or sudden stall rest imposed by another injury.
- Sudden change of diet, even hay batch, has been associated with colic and gas distention of the abdomen
- Enterolithiasis occurs frequently in the states of California, Florida, and Indiana.
- Sand impactions are seen frequently in the southern states, including Florida and Arizona, and the coastal states, including California and New Jersey.
- Ileal hypertrophy has been associated with ingestion of Bermuda grass hay.
- Periparturient mares are at increased risk of large colon volvulus, particularly if has happened in the past.
- 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 also associated with abdominal distention:
- Marked subcutaneous edema along the ventral abdomen and thorax—hypoproteinemia, disturbed regional lymphatic drainage (e.g., pleuropneumonia), cardiac failure postoperative following abdominal celiotomy
- Pregnancy
- "Hay belly"—may be diagnosed on history (malnourished or severely parasitized horses, diets high in poor-quality roughage) and by fecal examination
- Pendulous abdomen secondary to Cushing's disease—usually accompanied by other distinctive signs, such as hirsutism
- Extreme obesity—ribs not palpable, fat deposits evident along crest of neck, over tailhead, 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 ultrasound examination findings often provide sufficient information to permit a tentative diagnosis. Some conditions are associated with characteristic findings:
- GI gas accumulation (bloat)—On auscultation of the abdomen, few to no GI sounds may be heard, and increased gaseous distention may be identified on percussion as a hyperresonant "ping"; depending on the inciting cause and the degree of distention present, various degrees of abdominal pain are usually present.
- 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. Progression of the disease is slower than acute abdominal distention due to GI obstruction.
- 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

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within a 24-hr 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 toward the presence of colitis or enteritis.

CBC/BIOCHEMISTRY/URINALYSIS

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

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.
• WBC count, TP level, and SG 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. An increase in WBC count and TP levels and the appearance of degenerate neutrophils are indicative of increasing inflammation within the abdomen.
• Hemoperitoneum—free-flowing blood during the centesis procedure. Should be differentiated from puncture of the spleen during the procedure (PCV of the obtained sample higher than that of the circulating blood).
• Uroperitoneum—ratio of peritoneal fluid to serum Cr >2:1.

IMAGING

• Abdominal radiography may be of benefit in the diagnosis of 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. Standing radiographs of these regions in a 500-kg horse require ≈450 mA and 100 kVp and therefore are mostly available at referral centers.
• Ultrasonography of the abdomen can be used to identify the location, amount, character, and echogenicity of peritoneal fluid and abdominal viscera, particularly thickness of the intestinal wall.

DIAGNOSTIC PROCEDURES

• Laparoscopy permits direct visualization of the abdominal cavity in the standing horse and can be used to provide a definitive diagnosis of the cause of abdominal distention. However, it must be used carefully in cases of abdominal distention to not damage accidentally any abdominal viscera upon entrance in the abdominal cavity. In the presence of GI distention, the ability of identifying 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

• Treatment is 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, trocharization of the cecum and/or large colon may be necessary to improve ventilation. Any horse that is trocharized should be treated preemptively with broad-spectrum antibiotic therapy to reduce and minimize the inherent risk of peritonitis. The site for trocharization is situated within the paralumbar fossa and can be delineated through auscultation and percussion of the distended viscus. The author prefers the highest point possible and on the right side this may coincide with the cecal attachment to the body wall, thereby decreasing the incidence of direct peritoneal contamination. The trocharization site should ideally be situated in the mid-proximal region of the most tympanitic area. A longer catheter may be used in this procedure to ensure that the viscus is entirely decompressed. Following clipping and aseptic preparation of the site, a small bleb of local anesthetic should be injected into the skin and muscle layers. A 5.25-in. (13.3-cm) 14-gauge stiff intravenous catheter with stylet should be used for trocharization. The catheter should be inserted through the skin, muscle layers, and distended viscus with a gentle thrust. The stylet could be removed once the viscus has been penetrated and maintained until no further escaping gas is heard or fluid is seen at the hub of the catheter. The audible escape of gas confirms correct placement within the lumen of the distended viscus. In order to prevent laceration of the bowel wall, the needle/catheter should be held carefully during the decompression phase and the hand should follow gently in the direction that GI motility dictates. As the bowel becomes decompressed, the catheter may require further advancement into the lumen of the viscus. In order to prevent leakage of intestinal contents from the tip of the catheter into the peritoneal cavity, the catheter should not be withdrawn until the decompression process is complete. The catheter is then withdrawn while injecting 10 mL of procaine penicillin or gentamicin. The trocarization site should be wiped clean with alcohol.
• 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.

MEDICATIONS

Drug therapy is dictated by the inciting cause.

FOLLOW-UP

Plans for monitoring are based on cause and treatment.

MISCELLANEOUS

PREGNANCY

• Termination of pregnancy may be indicated in mares with hydrops or nonresolving uterine torsion. In case of mares with hydrops if bred in the future, a different stallion should be selected.
• 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

See Causes.

ABBREVIATIONS

• Cr = creatinine
• GI = gastrointestinal
• PCV = packed cell volume
• SG = specific gravity
• TP = total protein
• WBC = white blood cell

Suggested Reading

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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 herniae include ventral, incisional, and acquired inguinal/scrotal hernia.

SIGNALEMENT

Ventral Hernia

Most frequently seen in older, late-term pregnant mares. The draft breeds appear to be predisposed.

Incisional Hernia

It is a complication of ventral celiotomy in 10%–15% of horses. No breed or sex predilection. Incisional herniation can develop up to 3 mo after ventral celiotomy, but acute form develops within 8 days after surgery.

Acquired Inguinal/Scrotal Hernia

• Inguinal hernia refers to the passage of intestine and/or omentum through the vaginal ring into the inguinal canal. • Scrotal hernia describes presence of herniated contents in the scrotum. • Distal jejunum and ileum are most frequently involved, but omentum or small colon may also herniate.
• Acquired inguinal/scrotal hernia occurs exclusively in the intact male horse but isolated cases of inguinal herniation in geldings and mares have been reported.
• Standardbred, Tennessee Walking Horses, American Saddlebreds, and draft breeds seem to be predisposed.

SIGNS

Ventral Hernia

Mares with ventral hernia walk slowly and often lie down. Often, the herniae are painful and the horses have an increased heart and respiratory rates. A large swelling over the flank or caudal ventral abdomen is present. Orientation of the pelvis and the mammary gland is normal. Signs of colic may be present if the herniated content is compromised.

Incisional Hernia

Brown serosanguineous discharge from the incision and progressive increase in drainage of peritoneal fluid are commonly observed prior to dehiscence. Ventral swelling developing over the abdominal incision site is observed. Gaps in the abdominal wall between sutures may be palpated.

Acquired Inguinal/Scrotal Hernia

Scrotal swelling may be mild in inguinal hernia but marked in horses with scrotal hernia. The testis on the hernia side is usually firmer and cooler compared to the opposite testis. Abdominal pain may vary from mild to severe depending on degree of intestinal strangulation.

CAUSES AND RISK FACTORS

Ventral Hernia

In pregnant mares, old broodmares, and twin gestation. Often associated with degenerative changes in the body wall. It can also be associated with trauma and hydrallantois.

Incisional Hernia

Incisional infection and swelling, postoperative endotoxemia and pain, repeated surgeries, and use of chromic gut suture predispose hernia formation after celiotomy.

Acquired Inguinal/Scrotal Hernia

Inguinal/scrotal hernia often follows breeding activity or strenuous athletic exercise. Large vaginal rings may predispose to herniation, but it also occurs in horses with small to normal-size vaginal rings.

DIAGNOSIS

DIFFERENTIAL DIAGNOSES

Ventral Hernia

Prebubic tendon rupture. Clinical signs are similar; however, the pelvis becomes tilted cranioventrally. Cranioventral displacement of the udder can lead to rupture of blood supply and blood can be observed in the milk of such mares.

Incisional Hernia

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

Acquired Inguinal/Scrotal Hernia

Torsion of the spermatic cord, infectious epididymitis or orchitis, thrombosis of the testicular artery, hydrocele, hematocele, and testicular neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

Unremarkable in absence of secondary intestinal obstruction

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IMAGING

Abdominal Ultrasonography

Transcutaneous abdominal ultrasonographic examination with a 3.5- or 5-MHz transducer is used to rule in herniation, to evaluate the extent of the abdominal wall defect, and to identify hernia contents. May also reveal presence of herniated intestine in acquired inguinal/scrotal hernia or rule out hydrocele, hematocele, and testicular neoplasia

OTHER DIAGNOSTIC PROCEDURES

External Palpation

To define the hernia ring and hernia contents but is more difficult with extensive abdominal edema. Mares with ventral hernia resist deep palpation of affected area. Palpation of inguinal regions and scrota is mandatory in stallions with signs of colic.

Rectal Palpation

• Ruling out prepubic tendon rupture by rectal palpation can be difficult, depending on the defect's location and size of the fetus. Palpation of distended loops of intestine associated with abdominal pain warrants immediate exploratory laparotomy. • Rectal palpation of stallions with inguinal/scrotal herniae reveals presence of a loop of intestine entering the vaginal ring. Multiple loops of distended intestine are usually palpated with intestinal obstruction.

TREATMENT

Ventral Hernia and Incisional Hernia

Ventral or incisional herniae are treated initially conservatively by supporting the ventral abdominal wall, decreasing the amount of local inflammation and edema, and preventing worsening of the condition. Affected horses should be rested, fed with low-bulk feed, and monitored for signs of intestinal obstruction. Abdominal pressure bandage should be applied for 24 hr a day and removed twice daily for cold (initial phase) or warm (chronic phase) hydrotherapy for 20–30 min. Ventral or incisional hernia may resolve with conservative treatment, but for the surgical closure of the abdominal defect 8–12 weeks after its occurrence is usually required. Application of a mesh will be performed 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/Scrotal Hernia

Treatment of acute inguinal/scrotal hernia is surgical. During early phase, when intestinal strangulation has not yet occurred, it may be possible to reduce the hernia using external inguinal/scrotal massages under general anesthesia in dorsal recumbency.

MEDICATION

DRUG(S)

Ventral and Incisional Hernia

Pending surgical correction, the use of NSAIDs (phenylbutazone 2.2 mg/kg PO q12 h) is advocated to decrease abdominal edema. Parenteral broad-spectrum antibiotics are also required for incisional hernia. Resolution of incisional infection is mandatory prior to attempting surgical correction.

FOLLOW-UP

• The prognosis for ventral hernia is guarded. Incisional and inguinal/scrotal herniations warrant a favorable prognosis.
• From 3 to 5 mo of rest is required after surgical correction of both ventral and incisional herniae.

Suggested Reading

Kawcak CE, Stashak TS. Predisposing factors, diagnosis, and management of large abdominal wall defects in horses and cattle. JAVMA 1995;206:607–611.

Mair TS, Smith LJ. Survival and complication rates in 300 horses undergoing surgical treatment of colic. Part 2: Short-term complications. Equine Vet J 2005,37:303–309.

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ABDOMINOCENTESIS

BASICS

OVERVIEW

• Procedure for sampling peritoneal fluid by collection through the abdominal wall
• Fluid is collected into EDTA 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.
• Nucleated cell count in fluid from normal horses is <10,000 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 comprise 0%–36% of the total and eosinophils up to 7%; mast cells and basophils rarely are seen. Normally, few erythrocytes are present.
• Biochemical measurements other than total protein may include lactate as an indicator of intestinal ischemia and creatinine and/or potassium to diagnosis 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 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, an 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 types may reflect those disorders.
• In the face of inadequate intestinal perfusion and ischemia, anaerobic glycolysis can result in increased peritoneal fluid lactate concentration.

SYSTEMS AFFECTED

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

SIGNALMENT

Any breed, age, or sex

SIGNS

• Colic
• Chronic weight loss
• Abdominal distention
• Diarrhea

CAUSES AND RISK FACTORS

• Peritonitis caused by compromised gut wall
• Hemorrhage
• Neoplasia
• Intestinal parasitism and secondary thromboembolism
• Inflammation of abdominal organs
• Breeding and foaling injuries
• Bile or urine leakage
• Postsurgical inflammation
• Abdominal abscess
• Decreased oncotic pressure
• Congestive heart failure

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Peritonitis

• Fluid is an exudate with increased nucleated cell count and a predominance of neutrophils.
• Total protein usually is >2.5 g/dL because of inflammation.
• Bacteria are present in septic peritonitis and may be intracellular or extracellular.
• 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 hr. Neutrophils generally are not degenerate and no bacteria are seen. Increased RBC numbers may be seen.

Hemorrhage

• With a splenic tap, PCV is higher in abdominal fluid than in blood, and small lymphocyte numbers may be increased.
• With hemorrhage into the abdomen, PCV of fluid is lower than that of blood. Platelets are absent, and erythrophagocytosis may be present.
• 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

Diagnosis may be established on finding neoplastic cells in fluid but absence of neoplastic cells does not rule out neoplasia,

ABDOMINOCENTESIS

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.

Uroabdomen
• Typically, peritoneal fluid creatinine and potassium are increased compared to 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 to assess causes of transudates—panhypoproteinemia is consistent with GI protein loss; elevated liver enzymes suggest hepatic disease.
• Serum electrolytes and comparison of serum and fluid creatinine aid in diagnosis of uroperitoneum.

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

IMAGING
Ultrasonography
• May be used to look for intestinal entrapment, intussusception, masses, adhesions, enlarged liver, and enteroliths
• Ultrasonographic location of peritoneal fluid sometimes helps in performing abdominocentesis.

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

OTHER DIAGNOSTIC PROCEDURES
• 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.

TREATMENT
Directed at the underlying cause

MEDICATIONS
None

FOLLOW-UP

POSSIBLE COMPLICATIONS
Accidental enterocentesis (rarely associated with clinical disease) causes increased nucleated cell count in abdominal fluid within 4 hours.

MISCELLANEOUS

AGE-RELATED FACTORS
Foals normally have protein levels similar to peritoneal fluid cell counts (<1500 cells/μL) but lower than adults.

PREGNANCY
No significant differences in fluid from mares that are pregnant or have recently foaled compared with fluid from nonperipartum mares.

ABBREVIATIONS
• GI = gastrointestinal
• PCV = packed cell volume

Suggested Reading

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ABNORMAL ESTRUS INTERVALS

BASICS

DEFINITION/OVERVIEW

Estrus—period of sexual receptivity by the mare for the stallion.

• Abnormal—individual's overt display of sexual behavior for longer or shorter periods than normal. • Abnormal interestrus intervals result from short or long estrus or diestrus intervals.

ETIOLOGY/PATHOPHYSIOLOGY

• Mare—seasonally polyestrus in spring and summer months. • Average estrous cycle—21 days (range: 19–22); period of time between ovulations • Estrus coincides with P4 levels <1 ng/mL. • Estrus and estrous cycle lengths repeatable in individual mare from cycle to cycle.

Key Hormonal Events in the Equine Estrous Cycle

• FSH causes ovarian follicular growth.

• Estradiol (E2) stimulates increased GnRH pulse frequency to decreased LH secretion. • LH surge causes ovulation; E2 returns to basal levels 1–2 days post-ovulation. • Progesterone (P4) rises from basal levels (<1 ng/mL) at ovulation to >4 ng/mL by 4–7 days post-ovulation. • P4 causes decreased GnRH pulse frequency, allowing increased FSH secretion to stimulate a new wave of ovarian follicles to develop during diestrus. • $PGF_2\alpha$ (endometrial origin) is released 14–15 days post-ovulation, causing luteolysis and concurrent decline in P4 levels.

Estrus Length

In normal, cycling mares—average 5–7 days; range 2–12 days

Diestrus Length

Less variable than estrus in normal, cycling mares, averaging 15 +/− 2 days

Sexual Behavior

• Absence of P4 allows onset of estrus behavior even if E2 is present in small quantities.

• Conditions that eliminate P4 and/or >E2 concentrations are likely to induce estrus behavior. Persistence of these conditions results in abnormal estrus periods or interestrus intervals. The converse is also true.

SYSTEMS AFFECTED

• Reproductive • Behavioral • Endocrine

SIGNALMENT

• Any breed • Mares of age >20 years tend to have prolonged transition periods, >estrus duration, fewer estrous cycles per year • Ponies may have longer estrous cycles than horses (average 25 days).

SIGNS

Historical

• Chief complaints—infertility, failure to show estrus, prolonged estrus, split estrus, or frequent estrus behavior • Teasing records—Review methods, frequency, teaser type (pony, horse, gelding), stallion behavior (aggressive/passive, vocalization, proximity), and handler experience.

• Seasonal influence—Individual variation (onset/duration/termination of cyclicity) can be mistaken for estrus irregularity. • Mare's reproductive history—Can clinical abnormalities be linked to estrous cycle length, teasing, foaling, previous injuries, or genital infections?

• Pharmaceutical—Clinical abnormalities related to current and historical drug administration?

Physical Examination

• Body condition—Poor condition/malnutrition may add to/cause abnormal estrous cycles.

• Perineal conformation—Poor vulvar conformation can result in pneumovagina, ascending infection, urine pooling and may result in symptoms consistent with behavioral estrus. • Clitoral size—Enlargement may be related to prior treatment with anabolic or progestational steroids or intersex conditions.

• TRP—Essential to evaluate abnormal cycles; uterine size and tone; ovarian size, shape and location; cervical relaxation. Serial examinations, minimum 3 per week, may be needed (several weeks) to define her estrous cycle.

• U/S—Define uterine and ovarian features, normal and abnormal. • Vaginal examination—To identify inflammation, urine pooling, cervical competency or abnormal conformation. Also identify stage of estrous cycle (appearance, degree of external cervical os relaxation).

CAUSES

Shortened Estrus Duration

• Seasonality—Estrus duration decreases in height of breeding season; more efficient folliculogenesis. • Silent estrus—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

• Seasonality—Erratic estrus behavior with transition periods is common. Vernal transition receptivity can be short or long; protracted estrus behavior most common. • Ovarian neoplasia (GCT, GTCT)—affected mare chronically, anestrus exhibits persistent or frequent estrus behavior or stallion-like behavior • Congenital disorders—Gonadal dysgenesis due to chromosomal defects (e.g., XO, XXX) may underlie anestrus, erratic estrus, or prolonged estrus. • Hormone imbalance—Older mares may fail to ovulate and exhibit prolonged estrus; may be ineffective LH release.

Shortened Interestrus Interval

• Uterine disease—Uterine inflammation may cause atypical endogenous $PGF_2\alpha$ release, luteolysis, and early return to estrus. • Systemic illness—Endotoxin-induced $PGF_2\alpha$ release can cause premature luteolysis and a shortened interestrus period. • Iatrogenic/pharmaceutical—$PGF_2\alpha$ administration, intrauterine infusions, uterine biopsy procedure can cause corpus luteum regression, early return to estrus.

Lengthened Interestrus Interval

• Prolonged corpus luteum (CL) activity:
  ○ A normal diestrus ovulation—if CL is immature, it fails to respond to endogenous $PGF_2\alpha$ release.
  ○ Severe uterine disease may prevent release of uterine $PGF_2\alpha$.
  ○ Early embryonic death after maternal recognition of pregnancy
  ○ Persistent CL
  ○ Luteinization of an ovarian hematoma
  ○ Persistent CLs also associated with consumption of fescue forages

• Pregnancy—CL persists if a conceptus is present. Estrus behavior during pregnancy can be normal.

• Iatrogenic/pharmaceutical:
  ○ Treatment with progestin compounds suppresses behavioral estrus.
  ○ NSAIDs—potential interference with endometrial $PGF_2\alpha$ release; result—prolonged CL activity
  ○ No evidence that chronic PGF_2 treatment (label dosing) inhibits spontaneous formation and release of endogenous $PGF_2\alpha$

• GnRH agonist (deslorelin) implants—stimulate ovulation, associated with prolonged interovulatory intervals; effect more profound if $PGF_2\alpha$ is used during the diestrus period to short-cycle the mare.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Conditions with Similar Symptoms

• Frequent urination:
  ○ Cystitis/urethritis
  ○ Bladder atony
  ○ Urine pooling
  ○ Vaginitis or pneumovagina
  ○ May mimic submissive urination and be confused with behavioral estrus

• Defensive or aggressive behavior can be confused with anestrus—review or alter teasing methods.

Differentiating Causes

• Minimum database—Need full medical and reproductive history, teasing, physical examination, TRP, U/S, vaginal examination

• May be useful—uterine cytology, culture, and biopsy

• Silent estrus—often due to poor detection
  ○ *Diagnosis*—TRP minimum 3 per week with frequent serum P4 assays to detect a short or inapparent estrus period

• Transition period in the Northern Hemisphere extends from February to April; mare begins to develop follicles but not regular estrous cycles.
  ○ Characterized by persistent estrus behavior, irregular estrus periods, or irregular diestrus intervals
  ○ *Diagnosis*—Season, combined with serial TRP and U/S, confirms numerous small to large follicles on both ovaries that fail to progress to ovulatory size.

• GCT/GTCT—any age but more typical in middle-aged or older mares. Affected ovary enlarges; ovulation fossa often fills in; contralateral ovary—smaller, inactive
  ○ U/S–affected ovary—multilocular "honeycomb" appearance

ABNORMAL ESTRUS INTERVALS

- *Diagnosis*—TRP and U/S–endocrine assays

• Gonadal dysgenesis—usually ID when the mare enters the breeding herd and fails to have normal estrous cycles
- *Diagnosis*—TRP and U/S confirm absence of normal ovarian tissue and a juvenile reproductive tract. Karyotyping for a definitive diagnosis.

• Ovulation in diestrus—Corpus luteum formed from a diestrus ovulation may be insufficiently mature to be lysed by endogenous $PGF_2\alpha$ at the end of diestrus. Ovulations after day 10 of the estrous cycle result in persistent CL activity.
- *Diagnosis*—demonstration of a normal reproductive tract with failure of clinical estrus for >2 weeks post-ovulation; P4 levels of >4 ng/mL for >2 weeks

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
• Serum P4 concentrations
- Basal levels of <1 ng/mL indicate no functional luteal tissue.
- Active CL function is associated with P4 levels of >4 ng/mL.

• Serum testosterone and inhibin concentrations
- Mare testosterone values typically <50–60 pg/mL and inhibin values <0.7 ng/mL
- Hormone levels suggestive of a GCT/GTCT (in a nonpregnant mare)—testosterone >50–100 pg/mL (if thecal cells are present), inhibin >0.7 ng/mL, with P4 <1 ng/mL

IMAGING
Transrectal U/S—routine to evaluate equine ovaries reproductive tract.

OTHER DIAGNOSTIC PROCEDURES
• Uterine endoscopy can help identify intrauterine adhesions, glandular or lymphatic cysts, and polyps.
• Uterine cytology, culture, and biopsy

TREATMENT

• Vary teasing methods—Silent estrus may be a reflection of poor teasing management.
• Monitor the problem mare, including TRP and U/S, 3 times weekly to best define the reproductive cycle.
• Poor vulvar conformation—Control pneumovagina by vulvoplasty; a portion of the dorsal vulvar commissure is closed surgically.
• GCT/GTCT—ovariectomy
• Urine pooling, rectovaginal fistula and cervical tears—surgical correction
• Artificial lighting—management tool to initiate earlier ovarian activity
- Mares bred earlier in the season, foal earlier the next year; accommodate breed registries that use the January 1 universal birth date.
- Photostimulation does not eliminate vernal transition; merely shifts it to an earlier time of onset.
- Photostimulation should begin ≥90 days prior to the onset of early season breeding.

MEDICATIONS

DRUG(S) OF CHOICE
• $PGF_2\alpha$ (10 mg IM) or its analogs to lyse CL tissue.
• If follicle is ≥35 mm—deslorelin 2.1 mg implant SC or hCG (2500 IU IV) can stimulate ovulation.
• Altrenogest (0.044 mg/kg PO daily, minimum 15 days) can be used to shorten the duration of vernal transition, provided multiple follicles >20-mm diameter are present and the mare is demonstrating behavioral estrus.
- $PGF_2\alpha$ (10 mg IM) on day 15 of the altrenogest treatment increases the reliability of this transition management regimen.

CONTRAINDICATIONS
$PGF_2\alpha$ and its analogs—contraindicated in mares with heaves, or other bronchoconstrictive disease.

PRECAUTIONS
• Horses
- $PGF_2\alpha$ causes sweating and colic-like symptoms due to its stimulatory effect on smooth muscle cells. If cramping has not subsided within 1–2 h, symptomatic treatment should be instituted.
- Antibodies to hCG can develop after treatment; desirable to limit hCG use to no more than 2–3 times during one breeding season. The half-life of these antibodies ranges from 30 days to several months; typically do not persist from one breeding season to the next
- Deslorelin implants—associated with suppressed FSH secretion and decreased follicular development in the diestrus period immediately following use; results in a prolonged interovulatory period in nonpregnant mares. Implant removal post-ovulation is recommended. Injectable product still available in the United States
- Altrenogest, deslorelin, and $PGF_2\alpha$ should not be used in horses intended for food.

• Humans
- $PGF_2\alpha$ or its analogs should not be handled by pregnant women or persons with asthma or bronchial disease. Accidental exposure to skin—wash off immediately.
- Altrenogest should not be handled by pregnant women or persons with thrombophlebitis and/or thromboembolic disorders, cerebrovascular disease, coronary artery disease, breast cancer, estrogen-dependent neoplasia, undiagnosed vaginal bleeding, or tumors that developed during the use of oral contraceptives or estrogen-containing products. Accidental exposure to skin—wash off immediately.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
• Cloprostenol sodium (250 μg/mL IM), a prostaglandin analog
- Product used similar to natural prostaglandin but fewer side effects
- While not currently approved for use in horses, it is in broad use in the absence of an alternative.

FOLLOW-UP

PATIENT MONITORING
Until normal cyclicity is established or pregnancy confirmed, regular TRP examinations are recommended.

POSSIBLE COMPLICATIONS
Unless corrected, abnormalities in estrus behavior frequently result in infertility.

MISCELLANEOUS

PREGNANCY
• Prostaglandin administration to pregnant mares can cause CL lysis and abortion, especially if <40 days pregnant.
• Carefully rule out pregnancy before using any prostaglandin product.

SYNONYMS
• Anestrus • Prolonged diestrus
• Pseudopregnancy • Short estrus

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

ABBREVIATIONS
• CL = corpus luteum
• E2 = estradiol
• FSH = follicle-stimulating hormone
• GCT = granulosa cell tumor
• GnRH = gonadotropin-releasing hormone
• GTCT = granulosa theca cell tumor
• hCG = human chorionic gonadotropin
• LH = luteinizing hormone
• P4 = progesterone
• $PGF_2\alpha$ = PGF, natural prostaglandin ($F_{2\alpha}$)
• TRP = transrectal palpation
• U/S = ultrasound, ultrasonography

Suggested Reading

Hinrichs K. Irregularities of the estrous cycle and ovulation in mares (including seasonal transition). In: Youngquist RS and Threlfall WR, eds. Current Therapy in Large Animal Theriogenology. St. Louis, MO: Saunders Elsevier, 2007;144–152.

McCue PM, Farquhar VJ, Carnevale EM, Squires EL. Removal of deslorelin (Ovuplant™) implant 48 h after administration results in normal interovulatory intervals in mares. Therio 2002;58:865–870.

Author Carole C. Miller
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ABNORMAL SCROTAL ENLARGEMENT

BASICS

DEFINITION/OVERVIEW
A condition causing the gross appearance of the scrotum to deviate from normal size and texture, e.g., scrotal enlargement and/or asymmetry.

ETIOLOGY/PATHOPHYSIOLOGY
• Equine scrotum and associated contents are positioned on a horizontal axis between the hind limbs of the animal and are relatively well protected from external insult.
• Scrotal skin is thin and pliable, and contents are freely movable within the scrotum.
• Blunt trauma (breeding accident, jumping) is the most common cause of scrotal abnormality.
• Trauma can result in scrotal hemorrhage, edema, rupture of the tunica albuginea, hematocoele, hydrocoele, and inflammation.
• Similar signs can occur with inguinal/scrotal herniation, torsion of the spermatic cord, or neoplasia.

SYSTEM AFFECTED
Reproductive

GENETICS
N/A

INCIDENCE/PREVALENCE
Dependent on cause—traumatic, vascular, infectious/noninfectious, neoplastic

SIGNALMENT
• Intact male horses
• Any age

SIGNS
Historical
• 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
• Increased scrotal size (unilateral or bilateral)
• Abnormal testicular position
• Abnormal scrotal temperature (too warm or cold)
• Edema/engorgement of scrotum and/or contents
• Scrotal laceration
• Derangements in systemic parameters (elevated HR, RR, inappetence, CBC abnormalities)
• Any combination of abnormalities may be present and not all signs are present in every animal.

CAUSES
• Three 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/EAV
  ○ Orchitis/epididymitis
• Neoplasia
  ○ Primary scrotal—melanoma, sarcoid
  ○ Testicular neoplasia—seminoma, teratoma, interstitial cell tumor, Sertoli cell tumor
• Noninflammatory scrotal edema
• Hydrocele/hematocele
• Varicocele
• See also: Abnormal Testicular Size

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
• U/S (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
  ○ SN or CF
  ○ 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 best sample for diagnosis (freeze portion of ejaculate and send to approved lab with serum samples).
  ○ **Send samples to an approved laboratory.**
• EIA
• AGID or ELISA, the Coggins test

IMAGING—SCROTAL U/S
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

PATHOLOGICAL 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
Inpatient or Outpatient Treatment?
• Acute scrotal enlargement warrants hospitalization for treatment and care.
• Chronic scrotal enlargement may or may not warrant hospitalization; etiology dependent

ABNORMAL SCROTAL ENLARGEMENT

NURSING CARE
• Cold therapy (cold packs, ice water baths, water hose) 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 hr.
• Scrotal massage with emollient salve—useful to reduce scrotal edema and ischemic injury
• Fluid removal should be considered with hydrocele.
  ○ Use only an aseptically placed needle or an IV catheter.
  ○ Excess fluid accumulation may cause thermal damage to the testes.
• Administration of IV fluids is dependent on systemic status of the horse.

ACTIVITY
The need to restrict activity depends on 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 P/O or IV BID or flunixin meglumine 1 mg/kg IV BID) 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, PRECAUTIONS, POSSIBLE INTERACTIONS, ALTERNATIVE DRUGS
N/A

FOLLOW-UP

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

PREVENTION/AVOIDANCE
N/A

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

EXPECTED COURSE AND PROGNOSIS
N/A

MISCELLANEOUS

ASSOCIATED CONDITIONS, AGE-RELATED FACTORS, ZOONOTIC POTENTIAL, PREGNANCY, SYNONYMS
N/A

SEE ALSO
• Abnormal testicular size

ABBREVIATIONS
• AGID = agar gel immunodiffusion
• CBC = complete blood count
• CF = complement fixation
• EIA = equine infectious anemia
• ELISA = enzyme-linked immunosorbent assay
• EVA = equine viral arteritis
• EAV = equine arteritis virus
• HR = heart rate
• RR = respiratory rate
• SN = serum neutralization
• TRP = transrectal palpation
• U/S = ultrasound, ultrasonography

Suggested Reading

Love CC. Ultrasonographic evaluation of the testis, epididymis and spermatic cord of the stallion. In: Blanchard TL, Varner DD, eds. The Veterinary Clinics of North America: Equine Practice. Stallion Management. 1992;8:167–182.

Varner DD, Schumacher J, Blanchard T, Johnson L. Diseases and Management of Breeding Stallions. Goleta: American Veterinary Publications, 1991.

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Consulting Editor Carla L. Carleton

ABNORMAL TESTICULAR SIZE

BASICS

DEFINITION/OVERVIEW
Any condition causing the gross appearance of a testis to deviate from normal size and texture, e.g., testicular enlargement, reduction, and/or asymmetry

ETIOLOGY/PATHOPHYSIOLOGY
• The testes and epididymides are positioned in a horizontal orientation between the hind limbs of the horse and are freely movable within the scrotum.
• The scrotum and contents, while relatively protected from external insult, are at increased risk for injury during breeding or athletic activity.
• *Acute enlargement* of a testis occurs after trauma, torsion of the spermatic cord, or orchitis/epididymitis.
  ○ May be of bacterial, viral, autoimmune, or parasitic origin
• *Testicular neoplasia* is uncommon in the horse.
  ○ 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.
• *Hypoplastic* and *degenerative testes* are smaller than normal.
• *Testicular degeneration* can be transient or permanent.
  ○ An acquired condition, degeneration may arise from thermal injury, infection, vascular insult, hormonal disturbances, toxins, and age.
• *Testicular hypoplasia* is an irreversible condition.
  ○ Hypoplastic testes are incompletely developed.
  ○ Condition is usually congenital.
  ○ Suspected causes include genetic aberrations, teratogens, cryptorchidism, and postnatal insult.

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

GENETICS
Cryptorchism and testicular hypoplasia are subjected to having genetic components.

INCIDENCE/PREVALENCE
Dependent on etiology

SIGNALMENT
• Intact male horses
• Any age

SIGNS
Historical
• 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
• Increased or decreased scrotal size
• Increased or decreased testicular size
• Abnormal testicular texture (too soft or firm)
• Abnormal testicular position
• Abnormal scrotal temperature (too warm or cold)
• Edema/engorged scrotum and/or contents
• Derangements in systemic parameters (elevated HR, RR, inappetence, CBC abnormalities)

CAUSES
• Three most common
  ○ Trauma
  ○ Cryptorchidism
  ○ Torsion of the spermatic cord
• Testicular degeneration
• Testicular hypoplasia
• Testicular hematoma/rupture
• Neoplasia
  ○ Seminoma
  ○ Teratoma
  ○ Interstitial cell tumor
  ○ Sertoli cell tumor
• Orchitis/epididymitis
  ○ Bacterial infection
  ○ EIA
  ○ EVA, EAV
  ○ *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.
• U/S examination and measurement of the testes is the best means of differentiating the pathologies.

Differentiating Causes
• Duration of problem:
  ○ *Acute*: traumatic injury, torsion of spermatic cord, 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.
• U/S (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:
  ○ SN or CF
  ○ 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 lab with serum samples).
  ○ **Send samples to an approved laboratory.**
• EIA:
  ○ AGID or ELISA, the Coggins test.
• Testicular degeneration:
  ○ Endocrine profile (LH, FSH, testosterone, estrogens) from pooled samples obtained hourly for a minimum of four samples (due to pulsatile release of hormones)
  ○ Abnormal elevation of FSH and low total estrogen concentration are indicative of testicular degeneration.

IMAGING, SCROTAL/TESTICULAR U/S
Testicular parenchyma should appear uniformly echogenic. Aberrations that may be identified by U/S 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

ABNORMAL TESTICULAR SIZE

• Testicular histopathology—diagnose and/or differentiate neoplasia and testicular degeneration/hypoplasia
• Semen evaluation is useful in the diagnosis of testicular degeneration or hypoplasia.
  ○ Oligospermia
  ○ Azoospermia
  ○ Premature release of spermatids

PATHOLOGICAL FINDINGS
N/A

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 hr.
• Sexual rest is indicated in most cases until resolution of the problem.
• Administration of IV fluids is dependent on systemic status of the horse.

ACTIVITY
Restriction depends on cause of the testicular aberration.

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

CLIENT EDUCATION
• Fertility may be permanently lowered.
• Testicular degeneration and subsequent reduction in semen quality can be transient or permanent, depending on the inciting cause.
• 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 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 q30days until resolution of lesions)

CONTRAINDICATIONS PRECAUTIONS, POSSIBLE INTERACTIONS, 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 mo of age in horses.
• Testes may take 4–5 years to reach full size and maturity.

ZOONOTIC POTENTIAL
N/A

PREGNANCY
N/A

SYNONYMS
N/A

SEE ALSO
• Cryptorchidism
• Abnormal scrotal enlargement

ABBREVIATIONS
• AGID = agar-gel immunodiffusion
• CBC = complete blood count
• CF = complement fixation
• EAV = equine arteritis virus
• EIA = equine infectious anemia
• ELISA = enzyme-linked immunosorbent assay
• EVA = equine viral arteritis
• FSH = follicle-stimulating hormone
• GI = gastrointestinal
• HR = heart rate
• LH = luteinizing hormone
• RR = respiratory rate
• SN = serum neutralization
• U/S = ultrasound, ultrasonography

Suggested Reading

Brinsko SP. Neoplasia of the male reproductive tract. In: Savage CJ, ed. Veterinary Clinics of North America: Equine Practice. 1998;14:517–533.
Love CC. Ultrasonographic evaluation of the testis, epididymis and spermatic cord of the stallion. In: Blanchard TL and Varner DD, eds. Veterinary Clinics of North America: Equine Practice. Stallion Management. 1992;8:167–182.
Varner DD, Schumacher J, Blanchard T, Johnson L. Diseases and Management of Breeding Stallions. Goleta: American Veterinary Publications; 1991.

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ABORTION, SPONTANEOUS, INFECTIOUS

BASICS

DEFINITION
Fetal loss >40 days; maternal, placental, or fetal invasion of microorganisms

PATHOPHYSIOLOGY
• Fetal death by microorganisms
• Fetal expulsion after placental infection, insufficiency, or separation
• Premature parturition by microbial toxins, fetal stress, combination mechanisms
• Result: fetal absorption, maceration, autolysis; live fetus incapable of extrauterine survival

SYSTEMS AFFECTED
• Reproductive
• Other organ systems if maternal systemic disease

INCIDENCE/PREVALENCE
• 5%–15% infectious abortion
• Abortion storm, especially EHV-1

SIGNALMENT
Nonspecific, associated specific risk factors

SIGNS
General Comments
• Early pregnancy loss unobserved often termed *asymptomatic*
• Unless complications occur, abortion may occur rapidly; sole sign is relatively normal, previously pregnant mare later found open
• Signs—none to multisystemic and life-threatening
• May be multiple animals
• Most *symptomatic* spontaneous infectious abortions are in second half of gestation

Historical
One or more:
• Vaginal discharge—mucoid, hemorrhagic, serosanguinous
• Premature udder development; dripping milk
• Anorexia or colic; GI disease
• Failure to deliver on expected due date
• Recent (1–16 weeks before presentation) systemic infectious disease
• Other mares, recent abortions
• Inadequate EHV-1 prophylaxis
• History of placentitis
• Previous endometrial biopsy with moderate/severe endometritis or fibrosis
• None/excessive abdominal distention consistent with gestation length
• Behavioral estrus, pregnant mare—may be normal depending on gestation length, time of year, gestation length at time of loss
• Climactic and environmental conditions favor increased ETC (*Malacosoma americanum*) populations and development of MRLS in early and late pregnant mares.
• Possibly geographical location if MRLS and nocardioform placentitits

Physical Examination
• Fetal parts/placental structures protruding through vulvar lips; abdominal straining or discomfort
• Vulvar discharge (variable appearance); premature udder development, dripping milk
• A previously documented pregnancy is inapparent at next examination; evidence of fetal death by palpation, transrectal or transabdominal U/S
• Anorexia, fever, signs of concurrent systemic disease, especially with endotoxemia, dystocia, RFM
• Evidence of placental separation with transrectal or transabdominal U/S

CAUSES
• *Viruses*
  ○ EHV-1 (1P and 1B strains); EHV-4–>7 mo of gestation; rarely EHV-2
  ○ EVA (>3 mo of gestation)
  ○ EIA—direct causal relationship not yet established
  ○ Vesivirus—recent correlation between antibodies of vesivirus and equine abortion
• *Bacteria*
  ○ Placentitis and possible, subsequent fetal infection by *Streptococcus* sp., *Actinobacillus* sp., *Escherichia coli, Pseudomonas* sp., *Klebsiella* sp., *Staphylococcus* sp., nocardioform actinomycetes (to include *Amycolatopsis* sp., *Cellulosimicrobium* sp., *Crossiella* sp., and *Rhodococcus* sp.), *Taylorella equigenitalis* (rare, reportable), and *Leptospira* serovars
  ○ Endotoxemia cause release of $PGF_{2\alpha}$ (especially <80 days of gestation [day 60 in many mares]; may be factor later in gestation, if repeated exposure)
  ○ Exposure to ETC setae in conjunction with MRLS theorized associated with microscopic bowel puncture and bacteremic spread to fetus and/or placenta
• Rickettsiae
• *Ehrlichia risticii*—PHF
• *Fungi*—placentitis caused by *Aspergillus* sp., *Candida* sp., or *Histoplasma capsulatum*
• Protozoa
• *Sarcocystis neurona* or, possibly, *Neospora* sp. in aborted fetuses from EPM affected mares
• MRLS
  ○ Early (≈40–150 days' gestation) and late (>269 days of gestation) abortion syndromes
  ○ Association with ETCs

ABORTION, SPONTANEOUS, INFECTIOUS

RISK FACTORS

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

DIAGNOSIS

• Except for placentitis and abortion secondary to endotoxemia, most abortions are *asymptomatic;* expelled fetus and fetal membranes vary in condition—intact to autolytic
• Definitive causative diagnosis of equine abortion in ≅50%–60% of all cases
• Excluding twins and EHV-1, diagnostic rate may approach only 30% if limited samples are submitted and accompanied by moderate to severe fetal and placental autolysis.

DIFFERENTIAL DIAGNOSIS

Other Causes of Abortion

Abortion, spontaneous, noninfectious
• Twinning
• Fetal abnormalities—teratogenesis
• Umbilical cord abnormalities—excessive twisting; thrombosis
• Placental pathology
• Maternal malnutrition, other noninfectious systemic disease
• Old mare, history of EED or abortion
• Old mare, poor endometrial biopsy (inflammation, fibrosis)
• Endophyte-infected tall fescue pasture, exposure to ergotized grasses, small cereal grains during last month of gestation—no mammary development (agalactia, if term is reached); phytoestrogens; xenobiotics

Other Causes—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—Vulvar Discharge

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

CBC/BIOCHEMISTRY/URINALYSIS

Determine inflammatory or stress leukocyte response, other organ system involvement

OTHER LABORATORY TESTS

Maternal Progesterone

• Indicated if pregnancy outcome is doubtful (prediagnosis of an infectious cause of impending abortion), with suspected endotoxemia
• ELISA or RIA for progesterone may be useful at <80 days of gestation (normal levels vary from >1 to >4 ng/mL, depending on reference lab).
• At >100 days, RIA detects both progesterone (very low >day 150) and cross-reacting 5α-pregnanes of uterofetoplacental origin. Acceptable levels of 5α-pregnanes vary with stage of gestation and laboratory used.

Other Maternal Hormones

See Abortions, noninfectious.

Maternal Serology

• Take serum samples in all cases of abortion in which cause is unknown. Paired sample (21 days later), may be indicated.
• Diagnostic for abortions by *Leptospira* serovars
• Confirms EVA abortion

IMAGING

Transrectal and Transabdominal U/S

• Evaluate fetal viability, placentitis, alterations in appearance of amniotic and/or allantoic fluids.
• Other gestational abnormalities

DIAGNOSTIC PROCEDURES

Pathology, Serology, Molecular Techniques, and Culture

If fetus and membranes are available, sample:
• Fresh/chilled fetal thoracic or abdominal fluid, serum from fetal heart or cord blood, if available
• Fetal stomach content
• 10% Formalin-fixed and chilled/frozen samples of fetal membranes (allantochorion; allantoamnion), fetal heart, lung, thymus, liver, kidney, lymph nodes, thymus, spleen, adrenal, skeletal muscle, and brain

Molecular Techniques

Specific PCR, other molecular analyses, various samples for selected viral infections

Maternal Uterine Swabs

May aid in establishing diagnosis of abortions caused by placentitis

ABORTION, SPONTANEOUS, INFECTIOUS

PATHOLOGICAL FINDINGS

Viruses

- EHV
  - Gross—pleural effusion, ascites, fetal icterus, pulmonary congestion and edema; 1-mm, yellowish-white spots on enlarged liver; fetus is fresh.
  - Histopath (EHV-1 and -4)—areas of necrosis; prominent, eosinophilic, intranuclear inclusion bodies in lymphoid tissue, liver, adrenal cortex, and lung as well as a hyperplastic, necrotizing bronchiolitis; FA staining of fetal tissues; virus isolation from aborted fetus
- EVA
  - Few gross lesions
  - Autolyzed fetus
  - Placental/fetal vascular lesions
- Vesivirus
  - Nonspecific lesions

Bacteria and Fungi

- Fetal infection and placentitis
  - Gross—pleural effusion, ascites; enlarged liver; rare plaques of mycotic dermatitis; placental edema and thickening with fibronecrotic exudate (chorionic surface), especially at cervical star (especially if fungal)
  - Histopath—inflammatory disease; autolysis may make interpretation difficult
- Leptospirosis
  - Gross—fetal icterus and autolysis
  - Histopath—nonspecific; mild, diffuse placentitis

Endotoxemia

Fetus minimally autolyzed

Rickettsiae

Ehrlichia risticii:

- Gross—placentitis
- Histopath—typical fetal lesions include colitis, periportal hepatitis, lymphoid hyperplasia, and necrosis

Protozoa

Sarcocystis neurona—anecdotal reports on histopath, aborted fetuses from EPM plus mares

MRLS

Path 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
- Aborting mares—only prophylactic therapy for metritis or endometritis. Therapy limited to intrauterine, may include a systemic component
- Preexisting GI disease and complications may warrant hospitalization and intensive care

NURSING CARE

Most affected horses require limited nursing care, except for endotoxemia and gram-negative septicemia, dystocia, RFM, metritis, and laminitis.

ACTIVITY

Paddock exercise to permit observation

CLIENT EDUCATION

Inform owners of possible complications of abortion.

MEDICATIONS

DRUG(S) OF CHOICE

- Altrenogest 0.044–0.088 mg/kg PO daily—start later during gestation, continue longer, or use only short periods of time depending on serum progesterone levels during first 80 days of gestation, clinical circumstances, risk factors, clinician preference. Note—Serum levels reflect only endogenous progesterone, 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.

CONTRAINDICATIONS

Altrenogest only used to prevent abortion in cases of endotoxemia or placentitis (>270 days of gestation) if fetus is viable.

PRECAUTIONS

Altrenogest—absorbed through skin; wear gloves and wash hands.

ALTERNATIVE DRUGS

Injectable progesterone (150 to 500 mg oil base IM)

FOLLOW-UP

PATIENT MONITORING

- 7–10 days postabortion—TRP and U/S, monitor uterine involution
- Assess genital tract health—vaginal speculum, uterine culture and cytology, endometrial biopsy
- Base treatment on clinical results. Uterine culture <14 days postpartum or postabortion is affected by contaminants at parturition

PREVENTION/AVOIDANCE

Vaccines

- A killed-virus EHV-1 vaccine, 5, 7, and 9 mo of gestation; approved for abortion prevention in pregnant mares; 2-mo interval due to short-lived vaccinal immunity
- EVA vaccine; not specifically labeled for abortion prevention
  - MLV
  - Only open mares 3 weeks before anticipated exposure to infected semen or in enzootic conditions
  - Isolate first-time vaccinated mares, 3 weeks after exposure to infected semen.
  - Some countries forbid importation of horses with titers to EVA.

ABORTION, SPONTANEOUS, INFECTIOUS

Additional Prophylactic Steps

• Segregate pregnant mares from horses susceptible/exposed to infections.
• Isolate immunologically naïve individuals until immunity to enzootic infections is established/enhanced. Depending on infectious agent, protection may only be accomplished postpartum.
• Limit transport of pregnant mares to exhibitions or competitions.
• Isolate aborting mares, proper disposal of contaminated fetal tissues
• Proper diagnostics to ID infectious cause
• Correct poor perineal conformation, prevent placentitis.
• Prevent pregnant mare exposure to ETCs until 7–8 weeks after ETC death.
• Insecticides to control ETCs; consider toxicity of insecticides.

POSSIBLE COMPLICATIONS

Future fertility and reproductive value impaired by dystocia, RFM, endometritis, laminitis, septicemia, trauma to genital tract

EXPECTED COURSE AND PROGNOSIS

• Most patients recover with appropriate treatment.
• Complications—significant impact on mare's survivability and future fertility
• Prognosis—guarded for pregnancy maintenance with endotoxemia and placentitis

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Abortion, noninfectious
• Dystocia
• EHV-1
• Endometritis
• EPM
• EVA
• Metritis
• Pericarditis, MRLS
• Placental insufficiency
• Placentitis
• PHF
• Premature placental separation
• RFM

AGE-RELATED FACTORS

Immunologic status of young mares

SEE ALSO

• Abortion, noninfectious
• Dystocia
• Endometrial biopsy
• Endometritis
• Fetal stress/viability
• High-risk pregnancy
• Metritis
• Placental insufficiency
• Placentitis
• Premature placental separation
• RFM

ABBREVIATIONS

• EED = early embryonic death
• EHV = equine herpesvirus
• EIA = equine infectious anemia
• ELISA = enzyme-linked immunosorbent assay
• EPM = equine protozoal encephalomyelitis
• ETC = eastern tent caterpillar
• EVA = equine viral arteritis
• FA = fluorescent antibody
• MRLS = mare reproductive loss syndrome
• PCR = polymerase chain reaction
• PHF = Potomac horse fever
• RIA = radioimmunoassay
• RFM = retained fetal membranes/placenta
• TRP = transrectal palpation
• U/S = ultrasound, ultrasonography

Suggested Reading

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ABORTION, SPONTANEOUS, NONINFECTIOUS

BASICS

DEFINITION
Fetal loss >40 days (term *stillbirth* may apply >300 days) associated with a variety of noninfectious conditions

PATHOPHYSIOLOGY
• Fetal death/premature parturition from some intrinsic structural or functional defect or exposure to xenobiotics
• Fetal expulsion <80 days of gestation after CL loss as 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, or live fetus incapable of extrauterine survival

SYSTEM AFFECTED
Reproductive

INCIDENCE/PREVALENCE
• 5%–15% spontaneous abortion, multiple risk factors
• Breed predisposition for twinning

SIGNALMENT
• Nonspecific
• Breeds—Thoroughbred, draft mares, Standardbreds, related breeds (twinning)
• Mares >15 years
• Maiden American Miniature Horse mares—anecdotal placental insufficiency

SIGNS
General Comments
• Depending on cause, time of fetal death, stage of gestation, duration of condition, and whether pregnancy ended in dystocia or with RFM, dam may show few signs or, in extreme cases, suffer life-threatening multiorgan system disease.
• Most in second half of gestation

Historical
• Signs consistent with labor at unexpected stage of gestation
• Dystocia, birth of nonviable foal
• Vaginal discharge—mucoid, hemorrhagic, or serosanguinous
• Premature udder development; dripping milk
• Anorexia or colic
• Recent systemic disease
• Moderate/severe endometritis or fibrosis
• Failure to deliver on expected due date
• None/excessive abdominal distention consistent with stage of gestation
• Behavioral estrus in pregnant mare—normal for stage of gestation; dependent on time of year and stage of pregnancy when lost
• Geographical location—endophyte-infected fescue pastures/hay and/or ergotized grasses or grains

Physical Examination
• Fetal/placental structures protruding through vulvar lips; abdominal straining or discomfort
• Vulvar discharge (variable appearance), premature udder development, dripping milk
• Previously diagnosed pregnancy absent at next examination; fetal death determined by palpation or transrectal/transabdominal U/S
• Twin fetuses identified by transrectal/transabdominal U/S
• Evidence of placental separation or hydrops of fetal membranes during transrectal/transabdominal U/S
• Signs of concurrent, systemic disease, dystocia, or RFM
• Note—Signs variable. Mares pregnant at early check can remain asymptomatic but abort; unobserved, early in gestation. Abortion may be rapid without signs.

CAUSES
Twins
• Twin pregnancies that persist >40 days—≅70% end in abortion/stillbirth.

Luteal Insufficiency/Early CL Regression
• Anecdotal, somewhat controversial
• Caused by increased levels of luteal progesterone at <80 days of gestation

Placental Abnormalities
• Umbilical cord torsion—cord twists are normal, must be evidence of vascular compromise, e.g., cord thrombus, to confirm diagnosis
• Long umbilical cord/cervical pole ischemia disorder
• Confirmed body pregnancy
• Placental separation
• Villous atrophy or hypoplasia
• Hydrops

Fetal Abnormalities
• Developmental abnormalities—hydrocephalus; anencephaly
• Fetal trauma
• Chromosomal abnormalities

Maternal Abnormalities
• Concurrent maternal disease, maternal stress
• Trauma
• Malnutrition—starvation; selenium deficiency
• Severe maternal anxiety—anecdotal
• Moderate to severe endometritis or fibrosis
• Maternal chromosomal abnormalities

Xenobiotics
• Ergopeptine alkaloids associated with fescue toxicosis or ergotism (prolonged gestation is more common)
• Phytoestrogens—anecdotal
• Xenobiotics causing maternal disease—cardiac glycosides, taxine alkaloids, carbamates, organophosphates
• Xenobiotics causing placental and/or fetal disease—originally suspected with respect to MRLS; considered less likely at present time
• Possible deleterious effects of medications on pregnancy—EPM therapies (anecdotal)
• Repeated large doses of corticosteroids during late gestation

ABORTION, SPONTANEOUS, NONINFECTIOUS

Iatrogenic Causes
• $PGF_{2\alpha}$—may require repeated injections if >40 days of gestation
• Procedures mistakenly done on a pregnant mare—AI; intrauterine infusions; samples taken for cytology, culture, or biopsy

RISK FACTORS
• Family history of twinning or noninfectious, spontaneous abortion
• Systemic maternal disease
• Grazing endophyte-infected fescue, ergotized grasses, or plants producing phytoestrogens (anecdotal) late in gestation
• Exposure to xenobiotics

DIAGNOSIS
• Most mares asymptomatic before aborting
• Fetus(es)—variable condition, fresh to autolytic
• Definitive diagnosis possible ≅50%–60% of cases
• Excluding twins and EHV-1, diagnosis is only 30% if few samples are submitted and moderate/severe autolysis of fetal and placental tissues.

DIFFERENTIAL DIAGNOSIS

Other Causes of Abortion
• Infectious, spontaneous abortion
• Placentitis—by physical examination or by lab diagnostics

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 Vulvar Discharge
• Normal parturition
• Dystocia unassociated with abortion
• Normal estrus
• Endometritis
• Metritis or RFM
• Mucometra or pyometra

CBC/BIOCHEMISTRY/URINALYSIS
Determine inflammatory/stress leukocyte response, other organ system involvement

OTHER LABORATORY TESTS

Maternal Progesterone
• Indicated with history of abortion or in an old mare, previous biopsy presence of endometritis or fibrosis
• ELISA or RIA <80 days of gestation; acceptable levels are >1 to >4 ng/mL, depending on reference lab
• >100 days of gestation, RIA detects progesterone (may be very low >150 days) and cross-reacting 5α-pregnanes of uterofetoplacental origin
• Decreased maternal levels of 5α-pregnanes with cases of equine fescue toxicosis

Maternal Estrogens
• Reflect fetal estrogen production and viability, especially conjugated estrogens, e.g., estrone sulfate

Maternal Relaxin
• Decreased maternal relaxin concentration—thought associated with abnormal placental function

Maternal Prolactin
• Decreased prolactin secretion, late gestation, associated with fescue toxicosis and ergotism

Maternal T_3/T_4
• Anecdotal reports of lower levels in mares with history of conception failure, EED, or abortion
• Significance of low T_4 levels is unknown.

Cytogenetic Studies
• If suspect maternal chromosomal abnormalities
• Difficult if fetus autolysis

Maternal and Fetal Assays for Xenobiotics
• Indicated in cases of specific intoxications
• Sample the dam's whole blood, plasma, or urine samples
• Sample fetal serum from heart blood, thoracic or abdominal fluid, liver, and kidney

Feed Analysis
Indicated for specific xenobiotics—ergopeptine alkaloids, phytoestrogens, heavy metals, or endophyte (*Neotyphodium coenophialum*)

IMAGING
Transrectal/transabdominal U/S to confirm pregnancy, diagnose twins, evaluate fetal viability and development, assess placental health, diagnose other gestational abnormalities, e.g., hydrops of fetal membranes

DIAGNOSTIC PROCEDURES
• If entire fetus and placenta are available, appropriate samples for pathology, histology, culture, and serology
• Fresh/chilled fetal thoracic or abdominal fluid or serum from fetal heart or cord blood (if available); fetal stomach contents; 10% formalin-fixed and chilled/frozen samples of fetal heart, lung, thymus, liver, kidney, lymph nodes, spleen, adrenal gland, skeletal muscle and brain; 10% formalin-fixed and chilled/frozen fetal membranes (i.e., allantochorion and allantoamnion)
• Uterine swabs from dam may be useful to establish placentitis diagnosis
• Unless cause is obvious, e.g., twins, iatrogenic, rule out infectious causes of abortion, especially if multiple mares are at risk.

ABORTION, SPONTANEOUS, NONINFECTIOUS

PATHOLOGICAL FINDINGS

Twins

• Two fetuses, often dissimilar in size, with one mummified or severely autolytic
• Avillous chorionic membrane at point of contact of two placentae

Placental Abnormalities

• Umbilical cord torsion—confirm with evidence of vascular compromise
• Villous atrophy or hypoplasia may suggest endometrial fibrosis.
• Placental edema, gross and histopathological, consistent with equine fescue toxicosis
• Hydrops allantois and amnion—a gross diagnosis if dam suffers prepartum death

Fetal Abnormalities

Developmental abnormalities—hydrocephalus; anencephaly; gross and histopath confirmation

TREATMENT

APPROPRIATE HEALTH CARE

• Treatment only if early diagnosis of the pathologic process, before irreversible fetal or placental compromise occurs
• Main therapeutic approach to twinning—early selective reduction
• Late-gestation twin diagnosis—pregnancy may be maintained until term, in some instances, with progestin and antibiotic therapy.
• Mares with abortion history—evaluate and treat before rebreeding; progestin supplementation may be appropriate, especially with suspected luteal insufficiency (anecdotal) or early luteal regression, but this therapy is controversial and is contraindicated in some circumstances; ET may be indicated for mares with a history of repeated abortion.
• Signs of fescue toxicosis or ergotism can be treated with D_2-dopamine receptor antagonists; cases of abortion, i.e., stillbirth, frequently occur before therapy begins.
• Aborting mares generally only require prophylactic therapy for metritis or endometritis.
• Most patients managed on an ambulatory basis
• Systemic maternal disease may need hospitalization and intensive care.

NURSING CARE

Most noninfectious abortions require limited nursing care, unless systemic disease develops.

ACTIVITY

Limit to paddock exercise to allow observation.

CLIENT EDUCATION

Problem mares are likely to have future reproductive problems.

MEDICATIONS

DRUGS OF CHOICE

See specific topics.

History of Abortion, Endometritis, or Fibrosis

• Treat with altrenogest 0.044–0.088 mg/kg PO daily.
• Begin 2–3 days after ovulation or at diagnosis of pregnancy; continue to at least 100 days of gestation.
• Taper dose gradually during a 14-day period at end of treatment.

Altrenogest

• Start later in gestation, continue longer, or use for only short periods of time depending on serum progesterone levels during the first 80 days of gestation (>1 to >4 ng/mL), clinical circumstances, risk factors, and clinician preference.
• If used near term, altrenogest often discontinued 7–14 days before expected foaling date, unless otherwise indicated by assessment of fetal maturity/viability or questions arise regarding accurate gestational age

CONTRAINDICATIONS

• Uses of altrenogest—prevent abortion of viable fetus, for noninfectious placentitis, and endotoxemia
• Monitor fetal viability at least weekly to avoid retaining a dead fetus in utero or lead to development of pyometra.
• Altrenogest absorbed through skin; wear gloves and wash hands.
• Anecdotal success of supplemental progestin to maintain equine pregnancy

ALTERNATIVE DRUGS

• Progesterone 150–500 mg oil base IM daily
• T_4 supplementation—anecdotal success treating subfertile mares; use remains controversial, considered deleterious by some clinicians

ABORTION, SPONTANEOUS, NONINFECTIOUS

FOLLOW-UP

PATIENT MONITORING

• 7–10 days post-abortion—TRP, U/S, or both; evaluate uterine involution.
• Rate of involution depends on therapy used, presence of systemic disease, secondary complications.
• Further examination—vaginal speculum, uterine cytology/culture, endometrial biopsy

PREVENTION/AVOIDANCE

• Early recognition of at-risk mares
• Records of double ovulations
• Early twin diagnosis (<25 days, as early as day 14 or 15)
• Selective embryonic/fetal reduction
• Managing preexisting endometritis before next breeding
• 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.
• Careful use of medications in pregnant mares
• Avoiding exposure to known toxicants.

POSSIBLE COMPLICATIONS

• Recovery uneventful after many asymptomatic abortions
• Dystocia, RFM, metritis, laminitis, septicemia, endometritis, reproductive tract trauma may impact the mare's future well-being and reproductive value.

EXPECTED COURSE AND PROGNOSIS

Uneventful recovery in most cases with appropriate treatment

MISCELLANEOUS

AGE-RELATED FACTORS

• Development of chronic endometritis and endometrial fibrosis
• Maiden American Miniature Horse mares

PREGNANCY

Pregnancy associated by definition

SEE ALSO

• Abortion, infectious
• Endometritis
• Fetal stress/distress/viability
• High-risk pregnancy
• Hydrops allantois/amnion
• Metritis, postpartum
• Multiple ovulations
• Placental insufficiency
• Placentitis
• Premature placental separation
• RFM
• Twin pregnancy

ABBREVIATIONS

• AI = artificial insemination
• CL = corpus luteum
• EED = early embryonic death
• EHV = equine herpesvirus
• ELISA = enzyme-linked immunosorbent assay
• EPM = equine protozoal encephalomyelitis
• ET = embryo transfer
• MRLS = mare reproductive loss syndrome
• RIA = radioimmunoassay
• RFM = retained fetal membranes/placenta
• U/S = ultrasound, ultrasonography

Suggested Reading

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ACER RUBRUM (RED MAPLE) TOXICOSIS

BASICS

OVERVIEW

• An equine disease that follows ingestion of wilted or dried *Acer rubrum* (red maple) leaves and is characterized by methemoglobinemia, hemolytic anemia, and Heinz-body formation
• Most frequently reported in the eastern half of North America, where trees are more prevalent
• The specific toxin has not been identified, but apparently is found only in wilted or dried leaves, because the disease has not been induced using fresh leaves.
• Clinical findings are consistent with oxidative injury to RBCs, resulting in the formation of methemoglobin (i.e., oxidation of iron in hemoglobin from ferrous to ferric form), Heinz bodies (i.e., precipitated oxidized hemoglobin), 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 predilections
• No gender predilections
• No age predilections
• No genetic basis

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.
• Historical findings include lethargy, weakness, anorexia, and perhaps colic or fever.
• Physical examination findings include yellow or brown mucous membranes, red or brown urine, tachycardia, polypnea, and dehydration.

CAUSES AND RISK FACTORS

It usually occurs during the 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

• Consider all causes of equine hemolytic anemia, which include oxidant poisons, EIA, immune-mediated hemolytic anemia, piroplasmosis, and liver failure.
• 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 of laboratory findings may be difficult because of the hemolysis, with resultant discoloration of the serum and urine.
• Decreased PCV, hemoglobin, and erythrocyte count confirm anemia, whereas increased MCHC and MCH 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.
• BUN 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.

ACER RUBRUM (RED MAPLE) TOXICOSIS

OTHER LABORATORY TESTS
The percentage of methemoglobin in the blood often is elevated.

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
N/A

PATHOLOGICAL FINDINGS
• Gross findings include generalized icterus, enlarged spleen, and discolored kidneys. Petechiae and ecchymoses may be present on serosal surfaces.
• Histopathologic findings include erythrophagocytosis by macrophages, renal pigment casts and sloughed epithelial cells, splenic and hepatic hemosiderin, and centrilobular hepatic lipidosis. Pulmonary thrombosis has been reported in one horse.

TREATMENT
• The decision regarding inpatient or outpatient treatment depends on severity of the clinical signs and ability of the owner to care for the animal. Frequently monitor progression of the methemoglobinemia and anemia.
• Give IV fluids to replace fluid deficits and to maintain adequate renal perfusion.
• Blood transfusion may be needed with severe anemia.
• Limit physical activity of anemic animals.
• Continuous nasal oxygen administration may be helpful.
• Offer a high-quality diet, especially because affected horses often lack an appetite.

MEDICATIONS
DRUG(S) OF CHOICE
• Ascorbic acid has been used for its antioxidant effects (30–50 mg/kg q12h added to IV fluids).
• It also can be given orally but may take several doses to achieve adequate tissue levels.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Do not treat methemoglobinemia with methylene blue because of its poor efficacy in horses and reports that it may increase Heinz-body formation.
• NSAIDs may be necessary to control pain but can compromise renal function.

FOLLOW-UP
PATIENT MONITORING
Monitor methemoglobinemia and anemia, and adjust therapy based on the severity and speed of progression.

PREVENTION/AVOIDANCE
• Instruct owners not to plant red maples.
• Prune or remove existing trees only when no leaves are on the trees.
• Owners should check for fallen branches immediately after storms.

EXPECTED COURSE AND PROGNOSIS
• Prognosis depends on the quantity of leaves ingested and how soon veterinary care is sought after ingestion.
• Death is attributed to severe methemoglobinemia or anemia or to renal failure secondary to pigment nephropathy.

MISCELLANEOUS
ASSOCIATED CONDITIONS
Laminitis can occur during or after the course of the disease.

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

ABBREVIATIONS
• EIA = equine infectious anemia
• MCH = mean corpuscular hemoglobin
• MCHC = mean corpuscular hemoglobin concentration
• PCV = packed cell volume

Suggested Reading

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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^-
• Plasma bicarbonate level is ≅ 24 mEq/L.
• pH of arterial blood ranges from 7.35 to 7.45.

PATHOPHYSIOLOGY
• Fixed acid is produced via normal metabolic processes in large quantities daily.
• 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, the remainder in the distal nephron.
• The minimum pH (4.5) of the tubular fluid limits secretion of H^+.
• Titratable acidity increases minimally in acidotic patients.
• In most species, production of ammonia with subsequent excretion of ammonium ion is the major mechanism by which the kidney handles an acid load.
• Intracellular and extracellular buffering of H^+ occurs immediately or within minutes and is accomplished by proteins (primarily albumin and hemoglobin), phosphates, and bicarbonate.
• Carbonate storage in bone also is a significant site of intracellular buffering.
• The most important buffer is HCO_3^-, because it is present in high concentrations and the end product of its activity, CO_2, is readily eliminated by the lungs.
• Respiratory compensation responds within minutes and is effective for mild and moderate acidemia.
• Definitive regulation of H^+ and HCO_3^- levels is accomplished by the kidney.
• Renal processing of an acid load begins within hours but may take days to normalize pH.
• Inability to excrete H^+, loss of HCO_3^-, increased production of H^+ (i.e., lactic acidosis), 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 in body fluids.

SYSTEMS AFFECTED
Respiratory
• Peripheral and central 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 muscle fatigue and worsening metabolic status, especially in neonates.

Cardiovascular
• Decreased cardiac contractility
• May predispose to arrhythmias
• Vasodilation of arterioles; constriction of veins
• Vascular effects may be offset by catecholamine effects.

Neuroendocrine
• Catecholamine release
• CNS depression
• CSF acidosis in acute situations
• Vasodilation of cerebral vessels leading to increased cerebral blood flow and CSF pressure

Renal
• The kidney responds to low arterial pH by increasing H^+ excretion and generating increased levels of HCO_3^- to bring the systemic pH back to normal.
• This response begins within hours, but it may take days to be effective.

Metabolic
• Inhibition of anaerobic glycolysis
• Insulin resistance
• Decreased affinity for oxygen–hemoglobin binding, enhancing release of oxygen to the tissues
• Increased protein catabolism
• Increased ionized calcium concentration

SIGNALMENT
Any equine

SIGNS
• Historical and physical examination findings vary primarily with the underlying cause.
• Weakness, depression, and tachypnea are clinical signs specific to acidosis.

CAUSES
• Many diseases result in metabolic acidosis via more than one mechanism.
• Loss of bicarbonate most commonly is seen in horses with colitis; RTA results in HCO_3^- loss both directly and indirectly, depending on the type of tubular dysfunction.
• Renal failure results in an inability to excrete H^+ and accumulation of uremic acids.
• Increased H^+ production (i.e., lactic acidosis) is seen with diseases producing decreased effective circulating blood volume—hypotension or hypovolemia caused by inadequate intake, hemorrhage, isotonic or hypotonic fluid loss or sequestration (e.g., uroperitoneum, peritonitis, pleuritis, ascites, nonstrangulating types of colic), strangulating lesions of the GI tract, endotoxemia, or cardiac failure.
• Chronic causes of hypoxemia produce lactic acidosis.
• Grain overload produces metabolic acidosis via production of lactic acid, fluid sequestration in the GI tract, secretion into the GI tract, and endotoxemia.
• High-intensity anaerobic exercise results in production of lactate, which can affect fluid balance/SID and result in metabolic acidosis, however, this is short-lived.
• Severe exertional rhabdomyolysis associated with anaerobic exercise produces lactic acidosis.
• Acute or end-stage hepatic failure may result in metabolic acidosis due to failure of the detoxification systems of the liver.
• Asphyxia at parturition may cause multiorgan damage or failure, which can result in metabolic acidosis in neonates.
• Accumulation of exogenous acids is uncommon, as this is usually caused by ingestion of toxic substances; it may be seen with salicylates, propylene or ethylene glycol, paraldehyde, and methanol.
• Malignant hyperthermia is uncommon but has occurred in anesthetized horses and results in severe lactic acidosis.
• Proteins are weak acids; conditions producing significant hyperproteinemia (e.g., chronic infection, immune-mediated disease, plasma cell myeloma, lymphoma) produce metabolic acidosis.
• Excessive or inappropriate fluid therapy, especially in neonates, produces free-water excess and dilutional acidosis.
• TPN can lead to metabolic acidosis when cationic (i.e., lysine, arginine) or sulfur containing amino acids are metabolized, as H^+ is formed.
• Endotoxemia produces acidosis via several mechanisms—hypotension, decreased cardiac contractility, tissue ischemia, fluid shifts, hypoxemia, hepatic damage, etc.

RISK FACTORS
• Patients with chronic renal failure or chronic hypoxemia (i.e., COPD) may be at greater risk for acidosis with progression of their primary problem or if acid load develops for other reasons.
• Horses on acetazolamide for HYPP may develop acidosis more readily, as acetazolamide is a carbonic anhydrase inhibitor that causes increased HCO_3^- excretion.
• Highly anionic diets have been suggested to induce metabolic acidosis in equine.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Some causes of metabolic acidosis can be identified on physical examination (i.e., diarrhea, dehydration, colic with ischemic lesions).
• Decreased HCO_3^- levels are also seen in conditions with chronic respiratory alkalosis; P_{CO_2} is low if compensation is occuring, but pH will be normal or mildly increased.

LABORATORY FINDINGS
Drugs That May Alter Lab Results
• Excessive anticoagulant may falsely decrease results via dilution.
• Excessive sodium heparin may alter HCO_3^- levels, because it is an acidic compound.

Disorders That May Alter Lab Results
With poor peripheral perfusion or cardiovascular shunt, results of blood gas analysis on samples taken from peripheral vessels may differ from those taken elsewhere or not reflect the overall systemic condition.

Valid If Run in Human Lab and if sample submitted properly?

CBC/BIOCHEMISTRY/URINALYSIS
• Measurement of serum electrolytes and protein levels is important to determine the cause and to guide treatment.
• Calculation of the anion gap also may be useful, especially in mixed acid-base disorders.

ACIDOSIS, METABOLIC

• Proportionate changes in sodium and chloride levels occur with alterations of fluid balance.
• Normal sodium levels with hypochloremia or hyperchloremia indicate acid-base imbalance.
• Disproportionate changes in Na^+/Cl^- usually are associated with simultaneous acid-base imbalance and hydration abnormalities.
• Albumin/protein levels are not considered when calculating the anion gap; however, because proteins are weak acids, hyperproteinemia can produce the condition—dehydration, chronic infection, and neoplasia.
• Urinalysis and fractional excretion of electrolytes are useful in cases of renal failure and RTA.

Horses Affected with Hyperchloremia and Normal AG

• Loss of HCO_3^-—diarrhea, type II 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.
• Addition of Cl^-—fluid therapy with Cl^--containing fluids (i.e., 0.9% NaCl, KCl), salt poisoning, TPN, NH_4Cl, or KCl supplementation
• Cl^- retention—renal failure, type I or IV RTA, and acetazolamide therapy

Horses Affected with Increased AG

Accumulation of unmeasured anions:
• Lactate—conditions with hypovolemia or hypotension (e.g., shock, sepsis, cardiac failure, ischemic/inflammatory types of colic); conditions with inflammation or fluid sequestration (e.g., pleuritis, peritonitis, uroperitoneum, grain overload); conditions utilizing anaerobic glycolysis (e.g., anaerobic exercise, severe exertional rhabdomyolysis, malignant hyperthermia)
• Phosphates, sulfates, and organic acids—renal failure, toxic ingestion

OTHER LABORATORY TESTS

Total CO_2
• Measured by many labs using the same sample submitted for electrolytes
• Closely approximates HCO_3^-, because most CO_2 is carried in the blood as bicarbonate
• Respiratory alkalosis also decreases Tco_2; differentiation can only be made with blood gas analysis.
• Analyze rapidly with minimal room-air exposure within the sample tube as CO_2 will decrease.

IMAGING

Diagnosis of cardiac, renal, and hepatic failure can be facilitated via ultrasonography.

DIAGNOSTIC PROCEDURES

Biopsy for suspected organ failure and cytology and microbiology of exudates or effusions may be useful with inflammation or infection.

TREATMENT

• Directed at the primary cause. Alkalinizing therapy is described below.
• Replacement of fluid losses with balanced isotonic fluids may be all that is needed to restore acid-base status in mild cases.
• With hypovolemia caused by hemorrhage, hypertonic saline, colloids, or blood transfusion may be necessary to restore effective circulating volume in addition to crystalloid therapy.
• Specific electrolyte losses should be addressed, i.e., K^+, Ca^{2+}, in GI cases. Levels may change with alkalinizing therapy.

MEDICATIONS

DRUG(S) OF CHOICE

• Alkalinizing therapy is reserved for patients with a pH < 7.2 that persists following rehydration or volume replacement.
• Sodium bicarbonate is most frequently utilized.
• The bicarbonate deficit is calculated as follows: Base deficit × body weight (kg) × 0.3 (ECF space [0.5 in foals]) = HCO_3^- (mEq)
• A negative BE or 24 − (total CO_2 or HCO_3^-) can be used for the base deficit.
• In acute cases, $\frac{1}{2}$ the deficit can be given safely over 30 min, in fluids or as a 5% solution to adults.
• Isotonic bicarbonate (1.3%) is a good choice in neonates or severely affected adults with colitis.
• Correction to a pH >7.2 and BE ≥−5 is usually adequate, especially with organic acidoses, because these are metabolized once the primary problem improves.

CONTRAINDICATIONS

Sodium bicarbonate cannot be mixed with calcium.

PRECAUTIONS

• Use bicarbonate therapy cautiously in patients with respiratory compromise, because the CO_2 that is generated may not be eliminated, causing a further decrease in pH.
• Hyperosmolar solutions may cause vascular irritation and affect tonicity of the CSF.
• Sodium 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 too-rapid administration of bicarbonate since both CO_2 and H_2CO_3 cross the blood-brain barrier.

POSSIBLE INTERACTIONS

Alkalinizing therapies (i.e., HCO_3^-). Lactate can combine with Ca^{2+} in crystalloid solutions that form a harmful precipitate.

ALTERNATIVE DRUGS

• Replacement IV fluid solutions with other alkalinizing agents (e.g., lactate, citrate) are effective, because these are metabolized to HCO_3^-. Adequate hepatic function must be present, so these may not be useful in severely acidotic, hypoxemic, or septic patients.
• Oral rehydration solutions (1–2 gallons PO q2h in adults without ileus) have been used as primary therapy or an adjunct to IV fluid therapy in less severe cases.
• THAM, tromethamine, can be used as an alkalinizing agent. Its use does not increase CO_2 or sodium levels, and can be useful in patients with pneumonia or hypernatremia.

FOLLOW-UP

PATIENT MONITORING

Serial blood gas analysis to evaluate efficacy of therapy should be repeated within a few hours of initial treatment and thereafter according to patient response.

POSSIBLE COMPLICATONS

• Electrolyte abnormalities—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 CONDITIONS

• Asphyxia during parturition in neonates of any gestational age
• Conditions associated with premature neonates

ZOONOTIC POTENTIAL N/A

PREGNANCY

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

SYNONYMS

Nonrespiratory acidosis

SEE ALSO

• Causes of colitis • RTA

ABBREVIATIONS

• AG = anion gap
• BE = base excess
• COPD = chronic obstructive pulmonary disease
• CSF = cerebrospinal fluid
• ECF = extracellular fluid
• GI = gastrointestinal
• HYPP = hyperkalemic periodic paralysis
• RTA = renal tubular acidosis
• SID = strong ion difference
• TPN = total parenteral nutrition

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ACIDOSIS, RESPIRATORY

BASICS

DEFINITION
• Increase in blood P_{CO_2}
• Homeostatic mechanisms maintain normal blood levels within a narrow range.
• Arterial levels range from 35–42 mm Hg.
• Venous levels range from 43–49 mm Hg.

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 bicarbonate ion and hydrogen.
• Most CO_2 is transported in the blood as bicarbonate. 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.
• The three forms of CO_2 exist in equilibrium in the blood, but the P_{CO_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.
• Hypercapnia is uncommon in conscious patients, because the respiratory center responds to even minor abnormalities by increasing minute ventilation.
• Respiratory acidosis results from disease or alteration of the respiratory center in the medulla and peripheral chemoreceptors that control respiration, the mechanical components (i.e., chest wall, respiratory muscles), or the conducting airways, alveoli, and pulmonary vasculature, which are directly involved in gas exchange, by causing hypoventilation, barriers to diffusion, or V/Q mismatching.
• Because CO_2 diffuses very readily across the respiratory membrane in direct proportion to ventilation, hypoventilation usually has the most significant effect on blood levels.
• Hypermetabolism, as seen with malignant hyperthermia, may produce CO_2 in greater amounts than the lung can eliminate.
• Increased CO_2 also develops as a compensatory response of the lungs to metabolic alkalosis.

SYSTEM AFFECTED
Respiratory—See Pathophysiology.

SIGNALMENT
• Any horse
• Almost every anesthetized patient develops some degree of hypercapnia when breathing spontaneously.
• Because of their size, equines are especially predisposed to hypoventilation under anesthesia.

SIGNS
Historical Findings
• Respiratory noise may be heard, especially with exercise, in cases of upper airway obstruction.
• Exercise intolerance may be reported with many causes.

Physical Examination Findings
• None if minute ventilation is increased via increased tidal volume; if not, tachypnea may be present.
• Anesthetized animals with very high levels of CO_2 may have increased rate or depth of respiration.
• 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
• Nasal edema, cysts, mass lesions, or infection of the paranasal sinuses; laryngeal or pharyngeal paralysis; soft-palate displacement; pharyngeal or epiglottal cysts; and tracheal masses or collapse all cause upper airway obstruction and impede airflow into the lungs.
• Injury or disease of the thorax, diaphragm, or pleura may restrict movement of the chest wall or respiratory muscles or lead to atelectasis because of fluid, blood, air, or intestinal organs in the pleural space.
• Uroperitoneum, diseases producing portal hypertension (e.g., cardiac or liver failure), and other diseases that result in large volumes of peritoneal fluid also may restrict diaphragmatic movement. Some may lead to pleural effusion as well.
• Displacement or distention of the intestine can restrict diaphragmatic movement.
• Weakness or paralysis of the respiratory muscles can be seen with neurologic dysfunction—encephalitis, botulism, tetanus, cranial or spinal trauma, and so on.
• Severe cases of pulmonary disease (e.g., viral, bacterial, or interstitial pneumonias), allergic small airway disease, and COPD affect gas exchange, ventilation, and diffusion.
• Hypoventilation caused by lung collapse, muscle relaxation, and decreased sensitivity of the respiratory centers to CO_2 occurs in all anesthetized horses. Heavy sedation also may produce temporary hypercapnia via muscle relaxation and respiratory center insensitivity.
• Exhaustion of the CO_2, absorbent, improper ventilator settings, or improper set up of the breathing system can lead to hypercapnia under anesthesia as well.
• Pregnant animals are more prone to hypoventilation under 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, which increases the volume of abdominal contents and may predispose to hypercapnia under anesthesia.
• 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—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.
• Diseases resulting in metabolic alkalosis may have a compensatory hypercapnia—upper GI obstruction, early large colon impactions or simple obstructions, supplementation with bicarbonate or other alkalinizing agents. Measurements of pH in these cases often are still higher than normal, because compensatory hypoventilation is limited once hypoxemia develops.

LABORATORY FINDINGS
Drugs That May Alter Lab Results
N/A

Disorders That May Alter Lab Results
• With poor peripheral perfusion or cardiovascular shunt, results of blood gas analysis on samples taken from peripheral vessels may differ from those taken elsewhere or not reflect the overall systemic condition.
• Exposure to room air via air bubbles in the sample may change the P_{CO_2} level, because the sample equilibrates with the air.

ACIDOSIS, RESPIRATORY

• Cellular metabolism of RBCs continues after sampling; if not measured quickly, CO_2 levels may be falsely elevated.

Valid If Run in Human Lab?
Yes, if properly submitted.

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, syringes should be 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 will be valid for 3–4 hr.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• Capnography or capnometry to measure CO_2 indirectly from expired gases.
• Samples of end-tidal gases reflect arterial P_{CO_2} levels, because this gas is essentially alveolar gas.
• Continuous monitoring on anesthetized or ventilated patients.
• $\dot{V}/\dot{Q}$ mismatch is always present in anesthetized or recumbent patients, and end-tidal levels may underestimate arterial levels by ≅10–15 mm Hg.

TREATMENT

• Emergency therapy occasionally may be necessary for upper airway obstructions—passage of a nasotracheal tube or tracheotomy.
• Definitive therapy for hypercapnia involves resolution of the primary disease process affecting ventilation, diffusion, or gas exchange; improvement of ventilation usually is most effective.
• Avoid excessive anesthetic depth. Lightening of anesthesia may improve ventilation and decrease P_{CO_2} levels. If depth is adequate, controlled ventilation is necessary when hypoventilation is severe (i.e., >60 mm Hg).
• In neonates, postural therapy and coupage may improve gas exchange. Improvement of overall status, especially cardiovascular and neurologic, may improve respiratory function dramatically.
• With severe lung disease, treat hypercapnia with controlled ventilation. This generally is not feasible in adults, but neonates respond well. Heavy sedation or muscle relaxant therapy may be necessary in some individuals; however, most relax once respiratory function improves.

MEDICATIONS

DRUGS OF CHOICE

Doxapram
• A respiratory stimulant that may be a useful adjunct (0.5–1 mg/kg IV or an infusion of 0.02–0.05 mg/kg per min) in emergency resuscitation and some patients, especially foals with neurologic 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

Other Drugs
Anti-inflammatory therapy with corticosteroids or bronchodilator therapy with α_2-agonists or xanthine derivatives may be useful in patients with allergic airway disease and COPD once environmental factors are controlled.

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, and so on.
• Oxygen toxicity can develop with inspired P_{O_2} >50% or if Pa_{O_2} >100 mm Hg is maintained for prolonged periods (10–12 hr).

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
N/A

FOLLOW-UP

PATIENT MONITORING
• Decreased respiratory effort should be seen quickly after improvement of ventilation.
• Use serial arterial blood gas analysis or capnometry to assess adequacy of ventilation and monitor progress, especially during weaning.

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 the resultant acidosis predispose patients to cardiac arrhythmias, especially under anesthesia.
• The Pa_{CO_2} level greatly affects cerebral blood flow and CSF pressure.
• Severe or prolonged hypercapnia may contribute to brain damage or herniation in cases with head trauma.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Disorders that result in metabolic alkalosis

AGE-RELATED FACTORS
Neonates, especially premature foals, may be more prone to hypercapnia because of decreased compliance of the lungs and lack of strength (i.e., immaturity) of the chest wall.

ZOONOTIC POTENTIAL
N/A

PREGNANCY
See Risk Factors.

SYNONYMS
• Hypercapnia
• Hypercarbia
• Hypoventilation

SEE ALSO
See specific diseases in Causes.

ABBREVIATIONS
• CNS = central nervous system
• COPD = chronic obstructive pulmonary disease
• CSF = cerebrospinal fluid
• GI = gastrointestinal
• $\dot{V}/\dot{Q}$ = ventilation/perfusion

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ACTINOBACILLOSIS

BASICS

OVERVIEW
• Acute rapidly progressive septicemia due to *Actinobacillus equuli* or *A. suis*–like organisms in neonatal foals.
• *A. equuli* is a gram-negative coccobacillary to rod-shaped pleomorphic organism that produces flat gray 1- to 3-mm colonies after 24-hr incubation on blood agar. *A. equuli* is a normal inhabitant of the mucous membranes of the alimentary tract.
• Fetal infection may follow transplacental infection. The kidneys are a frequent site of neonatal infection.
• In adults, infection is frequently endogenous and results from fecal contamination or spread from oral mucous membranes. Adults have 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 of any age and use

SIGNS
Foals
• Acute onset, depression, diarrhea, recumbency, distended painful joints, sudden death
• Fever may not be present and foals may be hypothermic. If left untreated, foals may progress rapidly to septic shock.
• Bone and joint infections in neonates may not be obvious for days to weeks and may be unaccompanied by signs of systemic disease.

Adults
• Signs are generally referable to the affected organ system.
• Primary peritonitis due to *Actinobacillus* has been reported in adult horses.

CAUSES AND RISK FACTORS
Foals
• Commonly seen associated with failure of passive transfer of immunoglobulins. Perinatal stress, prematurity, and/or unsanitary environmental conditions may predispose the foal.
• Portals of entry include respiratory tract, gastrointestinal tract, placenta, and umbilical remnant.

Adults
• Pneumonia and pleuropneumonia may develop secondary to viral infection or stressful events including but not limited to general anesthesia, athletic events, transport over prolonged distance, and other environmental stressors and concurrent illnesses.
• Trauma may predispose to abscess formation.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Foals
• Any other cause of neonatal sepsis including bacterial, viral, and fungal agents
• Gram-negative organisms are the most common bacterial agents isolated in cases of neonatal sepsis, although infections with only gram-positive pathogens have been reported.
• Foals with equine herpevirus type 1 and equine viral arteritis infections may appear identical to foals with bacterial infection.
• Foals with perinatal hypoxic-ischemic anoxic or inflammatory insults may present with nearly identical clinical signs, depending on severity.

Adults
• Any other cause of fever
• Any other cause of peritonitis
• Any other bacterial, viral, or fungal agent causing pneumonia or pleuropneumonia

Other causes of respiratory distress, fever, coughing, and nasal discharge should be considered, including:
• 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 is occasionally present with in utero infections. Hyperfibrinogenemia is common in postnatal infections.
• Increased creatinine and/or blood urea nitrogen with renal involvement
• Metabolic acidosis, hypoxemia, and hypercapnia may be observed with 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 are possible.
• Low PCV in longstanding infection due to anemia of chronic disease
• Other abnormalities, depending on body system involved

OTHER LABORATORY TESTS
N/A

IMAGING
Foals
• Thoracic radiographs may demonstrate pulmonary involvement. Radiographs of affected joints may not show acute changes; bony involvement may take days to become radiographically apparent.

ACTINOBACILLOSIS

• Ultrasonographic examination of the umbilical remnant may demonstrate focal infection. Ultrasonographic examination of kidneys may be abnormal.

Adults

Radiographic and ultrasonographic evaluation of affected body system may be beneficial.

OTHER DIAGNOSTIC PROCEDURES

Foals

• Blood culture may be diagnostic.
• Bacterial culture of synovial fluid may be diagnostic and should be attempted in affected joints.
• Kidneys frequently have multifocal microabscesses at post-mortem examination.

Adults

• Culture of affected body system may be diagnostic.
• Culture of peritoneal fluid may be diagnostic.
• Culture and cytology of transtracheal aspirates and thoracocentesis fluids may be diagnostic. Because *A. equuli* is a normal inhabitant of equine gastrointestinal mucosa, results should be interpreted cautiously.

TREATMENT

Foals

Affected foals are quite ill and are best managed in a hospital. Administer intranasal oxygen supplementation as needed.

MEDICATIONS

DRUG(S) OF CHOICE

Foals

• Administer isotonic polyionic balanced fluids or 0.9% NaCl to maintain adequate hydration and fluid balance. Intravenous plasma as required based on serum or plasma IgG concentrations.
• Intravenous dextrose or parenteral nutrition as needed for nutritional management.
• Broad-spectrum antimicrobial therapy, gentamicin 12 mg/kg IV SID or amikacin 25–30 mg/kg IV SID and potassium penicillin 10,000 IV/kg IV QID or ceftiofur sodium 10 mg/kg IV QID. Monitor plasma creatinine concentration. Therapeutic drug monitoring desirable.
• Foals with systemic inflammatory response syndrome (SIRS) or multiple organ dysfunction syndrome (MODS) may require more intensive fluid management and inopressor therapy.
• Foals with severe respiratory disturbance may require assisted ventilation.
• Regional limb perfusion and/or direct instillation with antimicrobials of choice for septic joints

Adults

Antimicrobial therapy based on culture and sensitivity results

MISCELLANEOUS

Antimicrobial therapy should be modified based on response and culture/sensitivity results. Therapeutic monitoring of aminoglycoside levels should be performed. Continue treatment until clinical signs have resolved and white blood count, differential, and fibrinogen concentration are within normal limits for 48 hours.
Actinobacillus spp. were commonly isolated from foals lost to mare reproductive loss syndrome (MRLS) and adult horses affected by pericarditis during the same time period.

ABBREVIATIONS

• SIRS = systemic inflammatory response syndrome
• MODS = multiorgan dysfunction syndrome
• MRLS = mare reproductive loss syndrome

Suggested Reading

Stewart AJ, Hinchcliff KW, Saville WJ, et al. Actinobacillus sp. bacteremia in foals: Clinical signs and prognosis. J Vet Intern Med 2002;16:464–471.

Author Pamela A. Wilkins
Consulting Editor Ashley G. Boyle and Corinne R. Sweeney

ACUTE ADULT ABDOMINAL PAIN–ACUTE COLIC

BASICS

DEFINITION
Clinical signs associated with discomfort originating within the abdominal cavity. May develop acutely or progressively. Considered chronic when persist for >3–4 days.

PATHOPHYSIOLOGY
• It originates primarily from the gastrointestinal tract but may also arise from other abdominal structures such as liver, spleen, kidneys, uterus, bladder, or peritoneum.
• Intestinal pain may originate from increased intramural tension, tension on the mesentery, regional or generalized ischemia, mucosal inflammation, smooth muscle spasms associated with hypermotility, or a combination of any of these.
• Nonstrangulated lesions have no compromise to the local blood supply.
• Intraluminal lesions (impaction, foreign body, concretions), extraluminal lesions (adhesions, strictures), mural lesion (thickening), as well as spasmodic colic, intestinal displacement, ileus, and inflammatory bowel disease are usually considered nonstrangulated lesions.
• Strangulated lesions, such as torsion and incarceration, are usually associated with compromised local blood supply, intestinal necrosis and cardiovascular shock.

SYSTEMS AFFECTED
• Gastrointestinal—anywhere from the stomach to the small colon can be involved. The large colon and the distal part of the small intestine are most commonly involved.
• Cardiovascular system—dehydration and endotoxemia may lead to shock and result in organ failure.
• Other systems can be the source of abdominal pain.

SIGNALMENT
Nonspecific. There may be an age, breed, or sex predisposition for a specific problem (e.g., intussusception of the small intestine is more commonly seen in young horses; pedunculated lipomas are commoner on older horses; large colon torsion commonly seen around parturition in mares; pain from the reproductive tract is seen in pregnant or postpartum mares and in stallions of breeding age).

SIGNS
General Comments
Signs of abdominal pain may be subtle initially and are often easily missed and the source of pain may be difficult to identify.

Historical
Signs can appear acutely or following an episode of anorexia, depression, and/or decrease in fecal output. History of change in exercise regimen, diet, or availability of drinking water may also precede the signs of colic, which can be of different intensity:
• Mild—decrease in appetite, and fecal output, mild depression, yawning, extended neck and rolling of the upper lip in Flehmen-like response, teeth grinding
• Moderate—pawing at the ground, flank watching, groaning, posture for urinating but only a small quantity of urine is passed, leaning against the wall, kicking the abdomen with the hind legs, ears pinned backward, lying down more frequently, may attempt 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
Signs may vary, depending on stage of the disease:
• General findings—abdominal distention, sweating, increase in respiratory rate, elevated or subnormal body temperature, abnormal quality and quantity of feces
• Cardiovascular findings—congested mucous membrane, increase in capillary refill time and in heart rate, dehydration and cold extremities are suggestive of a strangulated lesion or to a severe inflammatory process such as colitis or peritonitis
• Gastrointestinal findings—increase, decrease or absence in gut motility, gas-filled resonant viscus on percussion. Gastric reflux on passage of the nasogastric tube is most commonly associated with lesions located at the level of the stomach or small intestine.
• Abnormalities on rectal examination—distention of a viscus by gas, liquid, or food; displacement of a viscus; thickening of the intestinal wall; uterine or renal abnormalities; findings will assist in the differentiation among problems involving the small intestine, large colon, cecum, small colon, or nongastrointestinal lesions

CAUSES
Gastrointestinal
• Gastric—gastric ulcers, gastric distention or impaction, gastric rupture, gastric tumor
• Small intestine—nonstrangulated obstructive lesion: duodenal ulcer, duodenojejunal enteritis, ascarid impaction, ileal impaction, ileal hypertrophy, stricture. Strangulated obstructive lesion: incarceration of a segment of the small intestine into the epiploic foramen, a space/rent in the mesentery/inguinal ring/gastrosplenic ligament, strangulation by a lipoma, volvulus, adhesions, etc.
• Large intestine—nonstrangulated obstructive lesion: ulceration, colitis, impaction, idiopathic gas distention, mild displacement, nephrosplenic entrapment, enterolith, adhesions, sand impactions. Strangulated obstructive lesion: volvulus, herniation, incarceration, thromboembolic infarction
• Cecum—nonstrangulated obstructive lesion: impaction, adhesions. Strangulated obstructive lesion: cecal-cecal or ceco-colic intussusception, thromboembolic infarction, torsion, incarceration
• Small colon—nonstrangulated obstructive lesion: impaction, enterolith. Strangulated obstructive lesion: incarceration, strangulating lipoma, submucosal hematoma, thromboembolic infarction
• Reproductive—uterine torsion, uterine 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
• Others—peritonitis, hemoperitoneum

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

DIAGNOSIS

N/A

DIFFERENTIAL DIAGNOSIS
Other causes of pain that might mimic pain originating from the abdominal cavity include myositis, pleuropneumonia, neurologic diseases such as rabies, and musculoskeletal injuries.

CBC/BIOCHEMISTRY/URINALYSIS
Increase in PCV and TP in face of dehydration. Possible hypoproteinemia secondary to protein loss in the intestinal lumen and/or in the abdominal cavity. Leukopenia in acute inflammatory process and endotoxemia or leukocytosis in chronic inflammatory process. Possible metabolic acidosis related to cardiovascular shock and release of lactic acid and/or loss of bicarbonate and electrolytes (colitis) or metabolic alkalosis if a large amount of gastric reflux is present, resulting in loss of chloride. Hypokalemia and hypocalcemia can be present, especially if the horse has been anorexic or is a lactating mare. Hypochloremia and hyponatremia may be present in colitis. Alkaline phosphatase may be increased. Azotemia is found in horses with severe dehydration or urinary tract disease. The increase in some or all of the following is suggestive of liver disease: GLDH, AST, GGT, conjugated bilirubin and bile acids. A selective increase in serum GGT in a horse with colic is suggestive of a displacement of the right colon.

OTHER LABORATORY TESTS
Abdominal Paracentesis
• Normal fluid has a pale, clear yellow color.
• Turbidity of the sample indicates an elevation of WBCs, RBCs, or contamination with intestinal contents.
• Increase of the protein level and WBCs is indicative of primary peritonitis or secondary to morphologic change of the viscera.
• A sanguineous fluid is probably indicative of intra-abdominal bleeding or a strangulated obstructive lesion.
• A foul-smelling reddish-brown fluid with an increase in the RBC, WBC, and protein is indicative of presence of necrotic bowel.
• Presence of plant materials in the absence of an enterocentesis suggests intestinal rupture.
• Few leukocytes or cells should be present if an enterocentesis was performed.

ACUTE ADULT ABDOMINAL PAIN–ACUTE COLIC

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

IMAGING

Radiographs
May be useful in the identification of sand impactions or enteroliths in adults. In foals they help in the localization of gas, fluid, and impaction distention. May also help to identify congenital abnormality such as atresia coli.

Ultrasonography
Evaluate the amount, quality, and characteristics of abdominal fluid; motility, wall thickness and diameter of small intestine and its location; evaluation of the nephrosplenic space for presence of intestine; motility and wall thickness of the large intestine; other abnormal findings, such as intussusceptions, abscesses, or adhesions.

Endoscopy
- Gastroscopy—evaluation of the stomach for ulcers, impaction, or tumor. In small horses, the duodenum may also be observed.
- Cystoscopy—evaluation of the urethra, bladder, and opening of the ureters for inflammation or calculi.
- Laparoscopy—visualization of abdominal viscera

Nuclear scintigraphy
Can be used to assess motility, presence of inflammation and infection of the gastrointestinal tract, and the reticuloendothelial function

OTHER DIAGNOSTIC PROCEDURES
Exploratory laparotomy or laparoscopy.

TREATMENT
- Horses should be taken off feed until diagnosis of the underlying problem.
- Indication for an exploratory laparotomy includes: signs of severe abdominal pain, unresponsiveness to medical treatment, moderate to severe abdominal distention, ileus or progressive reduction in gut motility, progressive increase in heart rate or heart rates above 60–70/min, cardiovascular compromise or deterioration, presence of moderate to severe gas distention or of a displacement of the large colon on rectal examination, gas distention of small intestine on rectal examination, gastric reflux, abnormal paracentesis findings, or presence of severe impaction of the large colon or the cecum. Animals presenting with these signs should be referred to a surgical facility.
- Supportive treatment for medical and surgical cases includes intravenous fluids, gastric decompression if necessary, electrolyte replenishment, and control of the abdominal pain.

MEDICATIONS

DRUG(S) OF CHOICE
- Analgesics—control the abdominal pain
- NSAIDs—dipyrone 10 mg/kg, flunixin meglumine 0.5–1.1 mg/kg IV, IM q8 h, phenylbutazone 2.2–4.4 mg/kg IV q12–24 h, ketoprofen 1.1–2.2 mg/kg, α_2-blockers such as xylazine 0.25–0.5 mg/kg IV, IM, detomidine 5–10 μg/kg IV, IM, or romifidine 0.02–0.05 mg/kg IV, IM can also be given if the pain is not controlled by NSAIDs.
- The narcotic analgesics such as butorphanol 0.02–0.075 mg/kg IV or meperidine (pethidine 2 mg/kg) can be given alone or in conjunction with xylazine. These two drugs potentiate each other.
- Any drugs should be used judiciously as they may mask clinical signs and may lead to postponement of surgery, thereby decreasing the chance of survival. Furthermore, most of these drugs have a detrimental effect on gastrointestinal motility.
- Spasmolytics (indicated in spasmodic colic)—hyoscine 20–30 mL IV and *N*-butylscopolammonium bromide 0.3 mg/kg
- Laxatives—for treatment of impactions
  - Mineral oil—10 mL/kg via nasogastric tube
  - Osmotic laxative—diluted disodium 0.5 g/kg or magnesium sulfate 0.5–1 g/kg in 4 L of warm water via nasogastric tube.
  - Dioctyl sodium succinate (DSS) 10–30 mg/kg of a 10% solution via nasogastric tube.
  - Fluids, via an indwelling nasogastric line (4–5 L/hr) or intravenously
- Parenteral fluid treatments—In cases of dehydration or moderate to severe impaction problems, intravenous fluid (100–200 mL/kg/day). If cardiovascular shock is present, hypertonic saline (2 L of 7% NaCl in an adult horse) prior to balanced electrolyte solutions. Electrolyte imbalances should be corrected, especially hypokalemia and hypocalcemia, which are important for intestinal motility. Moderate to severe bicarbonate deficit should be corrected as well as low plasma protein level (<45 g/L).
- Treatment of endotoxemia—flunixin meglumine 0.25 mg/kg q6 h. Other antiendotoxemic treatments include hyperimmune plasma (see Endotoxemia).
- Intestinal motility stimulants (see Ileus)—Postoperative ileus is the most common indication. Metoclopramide (0.1 mg/kg/hr in a constant drip infusion over several hours); lidocaine (1.3 mg/kg IV as a bolus followed by 0.05 mg/kg/min infusion); erythromycin lactobionate (1 g QID IV in 1 L saline).
- Antimicrobial therapy if peritonitis is suspected or if 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
The patient should be monitored 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
- Gastrointestinal rupture
- Peritonitis

AGE-RELATED FACTORS
Older horses are more predisposed to strangulated lipoma and epiploic foramen entrapment; pregnant mares are more predisposed to large colon torsion; and younger horses are more predisposed to ulcer problems, intussusception, and ascarid impactions.

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

SYNONYM
Colic

ABBREVIATIONS
- PCV = packed cell volume
- TP = total protein

Suggested Reading

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Acute Epiglottiditis

BASICS

OVERVIEW
Epiglottiditis is a nonspecific inflammatory disease of the epiglottis.

SIGNALMENT
• Primarily racehorses (2–10 years) in active race training or other horses undergoing repeated, strenuous exercise
• Occasionally seen in older horses (15–18 years) associated with neoplasia
• No known breed or sex predilection

SIGNS
• Chief complaints—variable amount of abnormal respiratory tract noise and exercise intolerance
• Coughing during eating is fairly common.
• Some horses act mildly pained when swallowing.

CAUSES AND RISK FACTORS
• Cause—unknown
• Repeated, strenuous exercise may induce inflammatory changes on the lingual (ventral) mucosal epiglottic surface between this tissue and the dorsal surface of the free edge of the soft palate.
• The role of inhaled particulate matter during galloping, abrasive feed or bedding material during swallowing, and bacterial or viral infections is unknown.

DIAGNOSIS

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

CBC/BIOCHEMISTRY/URINALYSIS
These tests are not typically performed.

OTHER LABORATORY TESTS
Additional laboratory tests are not typically performed.

IMAGING
Imaging is not usually performed.

DIAGNOSTIC PROCEDURES
• During routine endoscopy, the epiglottis may appear swollen and discolored (reddish-purplish), primarily along the lateral margins and ventral (lingual) mucosal surfaces. This swelling may obscure the normal, serrated margins and cause the epiglottis to appear more rounded and bulbous. The ventral mucosal surfaces often are ulcerated, and in more chronic, untreated cases, granulation tissue surrounded by fibrous connective tissue is seen. The epiglottis looks thicker and may be elevated a variable amount into an abnormal axis above the soft palate.
• 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 displace the soft palate dorsally and may experience difficulty replacing the soft palate into a normal position underneath the epiglottis.
• The caudal free margin of the soft palate may have a variable amount of inflammation, ulceration, or thickening. If the inflammatory insult is more diffuse, then inflammation of adjacent structures characterized by reddening, thickening, edema, and ulceration may occur in the corniculate processes of the arytenoids and adjacent nasal pharyngeal mucosa.

TREATMENT

• Outpatient (stall-side) basis
• Discontinue exercise for a minimum of 7–14 days, depending on the extent of the problem.
• If swallowing is difficult or stimulates coughing, hay may need to be eliminated from the diet or, at least, made wet until the inflammation resolves; a complete ration or gruel made from pellets may be easier to swallow.

MEDICATIONS

DRUG(S) OF CHOICE
• Epiglottiditis usually responds to medical therapy consisting of NSAIDs, parenteral corticosteroids, and topical pharyngeal sprays that contain anti-inflammatory and antimicrobial medication.
• With evidence of infection or a fever, antimicrobial therapy may be indicated—IM procaine penicillin G, PO trimethoprim sulfamethoxazole, or IM or IV ceftiofur at normal recommended dosages for 5–7 days.
• 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). Ten to 20 mL of a pharyngeal spray (750 mL of Furacin, 250 mL of DMSO, 1000 mL of glycerin, and 2.0 g of prednisolone) is sprayed slowly, while watching for swallowing, into the pharynx twice daily for 7–14 days through a 10-F catheter introduced into the nasal pharynx via the nasal passages. After the initial IV dose of either phenylbutazone or flunixin meglumine and dexamethasone, oral therapy is continued with phenylbutazone (2.2 mg/kg PO twice daily for 7–14 days) and prednisolone (2.2 mg/kg PO once daily for 7 days). The same dose is then administered orally every other day for three treatments. Subsequently, a dose of 0.45 mg/kg is given orally every other day for three treatments.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
No contraindications

FOLLOW-UP

PATIENT MONITORING
Substantial improvement in the overall appearance of the epiglottis and adjacent tissue and in pharyngeal function usually is seen at follow-up endoscopy after about 1 week of therapy with acute inflammation. Continue rest and therapy until healing is judged complete based on repeated endoscopy performed at about 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, but this usually can be corrected using dorsal midline division or excision with a curved bistoury or a contact laser. Extremely bulbous or fibrotic-appearing entrapping membranes may need to be excised through a laryngotomy.

POSSIBLE COMPLICATIONS
Advise owners that 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—laryngeal tie-forward, soft-palate trim, or excision of fibrous connective tissue on the subepiglottic surface.

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 of the arytenoid cartilage. Resolution of acute inflammation results in complete return to normal exercise tolerance and elimination of abnormal respiratory tract noise. Horses with more chronic or extensive lesions may experience epiglottic deformity and suffer from intermittent to persistent dorsal displacement of the soft palate despite appropriate medical or surgical therapy.

SEE ALSO
• Dorsal displacement of the soft palate
• Inspiratory dyspnea

ABBREVIATION
• 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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Author Norm Ducharme; Eric Tulleners (First Edition)
Consulting Editor Daniel Jean

ACUTE HEPATITIS IN ADULT HORSES (THEILER'S DISEASE)

BASICS

OVERVIEW
• Many conditions can potentially lead to acute liver failure in adult horses, with the most common being a syndrome occurring 4–10 weeks after animals have received an equine biologic. This is usually tetanus antitoxin, but other agents have been implicated—equine serum and encephalitis vaccine. • Acute failure of liver functions leads to various biochemical derangements, with accumulation of some agents, lack of some, and imbalances in others. These biochemical imbalances are responsible for many of the clinical signs seen in this disease.

SIGNALMENT
Predominantly in adult horses

SIGNS
• Usually sudden in onset and rapidly progressive, with death occurring 2–6 days after onset of signs in some cases. • Horses are often very icteric and pass dark urine caused by the presence of bilirubin. • Many have signs of hepatic encephalopathy, which can manifest in various ways that may change during the course of the disease. • Initially, there may be subtle changes in behavior, progressing to excitement or depression with head pressing. • Some may wander aimlessly around the stall or paddock. • Frequent yawning has been reported in some cases. • If animals live long enough and are outside in the sun, they may develop photosensitive dermatitis on white parts of the body. • Possible hemorrhagic diathesis or hemolysis terminally.

CAUSES AND RISK FACTORS
• Most commonly associated with administration of an equine biologic 4–6 weeks before the onset of signs; however, not all cases have been exposed to an equine biologic. • Some epidemiologic evidence suggests that some cases may result from an infectious agent, probably a virus. None has been isolated as yet, however, and attempts to reproduce the disease with material from affected horses have failed.
• Occasional cases caused by *Clostridium novyi* type B have been described.

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 leaf toxicity, wild onion toxicity, phenothiazine toxicity, and nitrate poisoning • Hepatic—anorexia, Theiler's disease, *C. novyi,* bacterial cholangiohepatitis, EIA, EVA, *Strongyle* sp. migration, arsenic toxicity, and halogenated hydrocarbons.
• Posthepatic—cholelithiasis and other causes of biliary obstruction. • Signs of hepatic encephalopathy can be very similar to those of several acute neurologic diseases—rabies, EEE, WEE, 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.

CBC/BIOCHEMISTRY/URINALYSIS
• Bilirubin—moderate increase in unconjugated and conjugated levels • Liver enzymes—increases in SDH (IDH), AST, GGT, and ALP
• Some may assay LDH, particularly isoenzyme 5. • Glucose—normal to low
• Urea—normal to low • Bilirubinuria
• CBC—usually normal

OTHER LABORATORY TESTS
Bromsulfalein clearance—2.2 mg/kg IV. Half-life is determined by sampling at 3, 6, and 9 min after injection; normal half-life is 2.8 +/− 0.5 min. Half-life is prolonged when >50% of liver function is lost. Archaic test.

IMAGING
Ultrasonography may suggest the liver is smaller than normal, with a loss of normal parenchymal structure.

DIAGNOSTIC PROCEDURES
• Liver biopsy is performed on the right side between the 12th and 14th intercostal spaces, where a line drawn from the tuber coxae to the elbow intersects the selected intercostal space. Ultrasound guidance may ensure accurate placement of the biopsy needle.
• Coagulation profile recommended by some before biopsy
• Histopathology defines the nature and severity of the lesions.

PATHOLOGIC FINDINGS
• The liver is usually smaller than normal, but it may be enlarged in peracute cases.
• Generalized icterus
• Histologically, centrolubular to midzonal hepatocellular necrosis, with mononuclear cell accumulation in the portal triads
• Possibly mild bile ductule proliferation in more chronic cases

TREATMENT
• Restrict activity, and avoid sunlight.
• In cases with hepatic encephalopathy, house the horse in a quiet place, preferably padded to avoid injury.
• If the horse is still eating, a high-carbohydrate, low-protein diet is recommended. The protein should be high in BCAAs—two parts beet pulp with one part cracked corn and added molasses. Oat or grass hay is preferred over alfalfa, and the diet should be fed in small amounts five or six times daily.

MEDICATIONS

DRUG(S) OF CHOICE
• Xylazine (0.5–1.0 mg/kg) or detomidine (0.05–0.4 mg/kg) can be used to control the signs of hepatic encephalopathy.
• In hypoglycemic animals, 10% glucose solution at 0.2 mL/kg may be given, followed by continuous drip of 5% glucose solution at 2 mL/kg per hour, reducing after 24 hr to half this rate.
• If the animal is not drinking, administer IV polyionic fluids at maintenance rates.
• Reduced production and absorption of toxic metabolites can be achieved with mineral oil and neomycin (20–30 mg/kg QID), both via stomach tube.

CONTRAINDICATONS/POSSIBLE INTERACTIONS
• Neomycin should not be given for more than 24–36 hr, because it may induce severe diarrhea.
• 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.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
N/A

EXPECTED COURSE AND PROGNOSIS
• Horses with severe hepatoencephalopathy have a poor prognosis, but if the animal survives for a week after the onset of clinical signs, recovery is possible.
• If the SDH (IDH) continues to fall, then the prognosis improves.

MISCELLANEOUS

ASSOCIATED CONDITIONS, AGE-RELATED FACTORS, ZOONOTIC POTENTIAL, PREGNANCY
N/A

ABBREVIATIONS
• ALP = alkaline phosphatase
• AST = aspartate aminotransferase
• BCAAs = branched-chain amino acids
• EEE = Eastern equine encephalomyelitis
• EIA = equine infectious anemia
• EVA = equine viral arteritis
• GGT = γ-glutamyltranspeptidase
• IDH = iditol dehydrogenase (SDH)
• LDH = lactate dehydrogenase
• SDH = sorbitol dehydrogenase (IDH)
• WEE = Western equine encephalitis

Suggested Reading

Divers TJ. Liver disease and liver failure in horses. Proc Am Assoc Equine Pract 1983;29:213–223.

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Consulting Editor Michel Lévy

Acute Renal Failure (ARF)

BASICS

DEFINITION
A consequence of an abrupt, sustained decrease in GFR, resulting in azotemia and disturbances in fluid, electrolyte, and acid-base homeostasis

PATHOPHYSIOLOGY
• Usually prerenal or renal; most commonly due to hemodynamic or nephrotoxic insults
• Except for neonatal bladder rupture and urolithiasis, postrenal failure is uncommon in horses (see Uroperitoneum and Urolithiasis).
• Perpetuated by decreased GFR in damaged glomeruli and tubular obstruction with desquamated tubular epithelial cells and debris

SYSTEMS AFFECTED
• Renal/urologic—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 and increased susceptibility to infection
• Musculoskeletal—acute laminitis in severe cases; often refractory to treatment

GENETICS
N/A

INCIDENCE/PREVALENCE
Low

GEOGRAPHIC DISTRIBUTION
NA

SIGNALMENT
Breed Predilections
N/A

Mean Age and Range
• Foals <30 days of age (especially when receiving nephrotoxic medications) may be at greater risk, but all ages can be affected.

Predominant Sex
None

SIGNS
General Comments
Clinical signs of ARF are vague and nonspecific.

Historical
• Often secondary to other problems leading to hypovolemia and renal ischemia—colic, diarrhea, prolonged exercise, rhabdomyolysis, or septicemia/endotoxemia • Previous administration of nephrotoxic drugs

Physical Examination
• 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. • Rectal examination may reveal an enlarged, painful left kidney. • Laminitis, often rapidly progressive • Markedly azotemic patients may have neurologic deficits—ataxia, hypermetria, and mental obtundation.

CAUSES
Prerenal Failure
• Hemorrhagic, hypovolemic, or endotoxic shock • Prolonged, exhaustive exercise • Severe rhabdomyolysis, vasculitis, or hemolytic diseases
• Disseminated intravascular coagulation

Intrinsic Renal Failure
• Prolonged duration of above disorders, lack of adequate fluid support, or concurrent use of normal dosages of nephrotoxic medications—aminoglycosides; NSAIDs
• Excessive doses of NSAIDs or prolonged use of gentamicin, particularly in dehydrated horses
• Other nephrotoxins include heavy metals (e. g., mercury [in counterirritants or blisters], lead, cadmium), endogenous pigments (e. g., hemoglobin, myoglobin), vitamins D and K_3, and high doses of oxytetracycline, especially when administered to neonates with flexural deformities. • In occasional cases, infectious agents—*Actinobacillus equuli* in neonates; *Leptospira* sp. in all age groups

RISK FACTORS
• Renal hypoperfusion • Exposure to nephrotoxins, particularly in patients with dehydration or primary renal disease

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• All conditions leading to hemorrhagic, hypovolemic, or endotoxic shock; severe rhabdomyolysis; vasculitis and hemolytic diseases; or disseminated intravascular coagulation • Prerenal failure—oliguria with concentrated urine (specific gravity >1.035) and rapid correction of azotemia with rehydration
• Postrenal failure—stranguria, anuria, or uroperitoneum • Chronic renal failure—weight loss, poor body condition, ventral edema, PU/PD, hypercalcemia, and limited improvement of azotemia with fluid therapy

CBC/BIOCHEMISTRY/URINALYSIS
• Normal to high PCV, variable leukogram, CBC changes reflect underlying primary disease process. • Progressive (moderate to severe) increases in BUN (50–150 mg/dL) and Cr (2.0–20 mg/dL) • Variable hyponatremia, hypochloremia, hyperkalemia, hypocalcemia, and hyperphosphatemia—hyperkalemia and hyperphosphatemia more common with intrinsic ARF and uroperitoneum • Mild to moderate metabolic acidosis, severity varying with the underlying disease process; development of renal tubular acidosis may complicate recovery. • Mild to moderate hyperglycemia
• USG— high (>1.035) with prerenal failure, low (<1.020) with intrinsic ARF; specific gravity best assessed in urine collected during initial patient evaluation (before rehydration)
• Intrinsic cases 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 (see Pigmenturia)

OTHER LABORATORY TESTS
• Increased fractional clearances (i.e., excretions) of sodium and phosphorous; 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—may be marked in obstructive postrenal failure • Nephrolithiasis/ureterolithiasis would indicate underlying chronic renal failure and possible "acute-on-chronic" exacerbation of renal failure.

OTHER DIAGNOSTIC PROCEDURES
• Urine collection—Collect initial urine produced by all at-risk horses. • Percutaneous renal biopsy with routine histopathological, immunohistochemical, and electron microscopic evaluation of the sample may provide information regarding cause, severity, and prognosis. Pursued with caution, however, because life-threatening hemorrhage can be a complication. • Central venous pressure >8–10 mm Hg indicates fluid overload and assists with fluid therapy.

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

TREATMENT

AIMS OF TREATMENT
• Address underlying primary condition.
• Improve GFR with fluid therapy and medications aimed at restoring normal renal function.

APPROPRIATE HEALTH CARE
• Properly recognize and treat all underlying primary disease processes, usually on an inpatient basis for continuous fluid therapy.
• Reassess dosage schedule of, and possibly discontinue, potentially nephrotoxic medications.

NURSING CARE
Fluid Therapy
• After initial measurement of body weight, correct estimated dehydration with normal (0.9%) saline or another potassium—poor electrolyte solution over 6–12 hr. • Fluids may be supplemented with calcium gluconate or sodium bicarbonate if hyperkalemia or acidosis requires specific correction. • Monitor for subcutaneous and pulmonary edema—increased respiratory rate and effort as evidence of overhydration. • Monitor urine output. • CVP may be helpful in determining fluid replacement plan. • Use maintenance fluid therapy judiciously in animals not clinically dehydrated.

ACUTE RENAL FAILURE (ARF)

Oral Electrolyte Supplementation
• Sodium chloride (30 g) can be administered in concentrate feed or as an oral slurry/paste BID–QID 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 for grazing grass if appetite is poor

DIET
• Encourage intake by offering a variety of concentrate feeds, bran mash, and hay types.
• Hand-walking or short periods of turn-out to graze grass encourage feed intake.

CLIENT EDUCATION
• Prognosis is most dependent on progression of the underlying primary disease process.
• ARF may complicate recovery, prolong hospitalization and treatment, and increase cost.

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 hr of fluid therapy), this diuretic may be administered 2 times (1–2 mg/kg IV) at 1- to 2-hr intervals; if effective, urination should be observed within 1 hr after the second dose; if ineffective, discontinue treatment.
• Mannitol—has been used in the past as an osmotic diuretic agent for oliguria/anuria unresponsive to furosemide; however, recent evidence suggests that this treatment is not of benefit in critically ill human patients and ROUTINE USE OF MANNITOL IN PATIENTS WITH ARF IS NO LONGER RECOMMENDED.
• Dopamine—has been used in the past as a continuous rate infusion (3–5 μg/kg per minute IV in a 5% dextrose solution) for persistent oliguria/anuria; however, this drug can induce arrhythmias and recent evidence suggests that this treatment is not of benefit in critically ill human patients and ROUTINE USE OF DOPAMINE IN PATIENTS WITH ARF IS NO LONGER RECOMMENDED.
• Antiulcer drugs (e. g., omeprazole 2–4 mg/kg PO q24 h or cimetidine 5–10 mg/kg IV q8 h in anorexic horses) may be useful in decreasing the associated risk of gastric ulcer disease.

CONTRAINDICATIONS
• Furosemide—at repeated dosages can result in electrolyte derangements
• Avoid all nephrotoxic medications.

PRECAUTIONS
• Monitor response to fluid therapy (i.e., urine output)—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.
• Reassess dosage schedule of drugs eliminated by urinary excretion; consider discontinuing all potentially nephrotoxic medications—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
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 hr of treatment and at least daily thereafter.
• Assess magnitude of 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 central venous pressure <8 cm H_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.
• 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, cardiac arrest, and death
• Laminitis—often 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.
• Prognosis for recovery from prerenal failure and nonoliguric intrinsic ARF usually is favorable if azotemia decreases by 25%–50% after the initial 24 hr of treatment; extent of recovery of renal function in patients with intrinsic failure 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 hr of treatment.
• Poor prognosis for patients that have persistent anuria, increased magnitude of azotemia after the initial 24 hr of treatment, that rapidly develop edema, or that remain oliguric >72 hr.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Colic; enterocolitis
• Pleuritis; peritonitis; septicemia
• Laminitis
• Exhausted horse syndrome—multiorgan failure
• Rhabdomyolysis

AGE-RELATED FACTORS
• Neonates with hypoxic-ischemic multiorgan damage or septicemia may have increased risk of intrinsic ARF.
• 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 intrinsic ARF or uroperitoneum.

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

PREGNANCY
Postpartum mares are at risk of hemorrhagic shock and prerenal failure or intrinsic ARF consequent to rupture of a uterine artery.

SYNONYMS
• Acute nephrosis
• Acute tubular necrosis
• Vasomotor nephropathy

SEE ALSO
• Anuria/oliguria
• CRF

ABBREVIATIONS
• Cr = creatinine
• CVP = central venous pressure
• GGT = γ-glutamyltransferase
• GFR = glomerular filtration rate
• GI = gastrointestinal
• PU/PD = polyuria/polydipsia
• USG = urine specific gravity

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ACUTE RESPIRATORY DISTRESS SYNDROME IN FOALS

BASICS

DEFINITION
Respiratory distress is defined as ventilatory efforts in excess of the metabolic demands. ARDS is defined as acute onset of respiratory distress.

PATHOPHYSIOLOGY
• Inflammatory stimuli may initiate events leading to clinical signs of respiratory failure—aspiration pneumonia; viral, bacterial, or fungal infections; thermal injury (i.e., heat stroke), systemic or pulmonary sepsis/endotoxemia, or inhalation of irritant gases, or smoke may be the initiating insult. • A manifestation of SIRS, leading to MODS, resulting in azotemia, liver dysfunction, ileus, or DIC and bleeding • Diffuse injury to pulmonary alveolar epithelium and capillary endothelium, leading to pulmonary edema • Immunosuppression may be a factor associated with development of ARDS/interstitial lung disease in foals infected with *Pneumocystis carinii*.

SYSTEMS AFFECTED
• Primarily respiratory • Often accompanied by dysfunction of the renal, hepatic, and cardiovascular systems and by clotting cascades as disease progresses—MODS

INCIDENCE/PREVALENCE
• Not established, but relatively uncommon
• Worldwide, in areas with hot summer weather

GEOGRAPHIC DISTRIBUTION
Worldwide.

SIGNALMENT
• All ages, but foals 1–8 months of age are predisposed (mean age, 3.5 +/− 1.0 months).
• No sex or breed predilections

SIGNS
• Acute or peracute depression, lethargy, fever, tachypnea, pronounced respiratory effort, nostril flaring, increased abdominal and intercostal effort (i.e., "double expiratory lift" or "heave line" or paradoxical breathing pattern), and cyanosis • Nasal discharge and cough are frequent but inconsistent findings. • Thoracic auscultation—loud bronchial sounds over central airways, with either increased or diminished peripheral airway sounds

CAUSES
• Likely the common end result of a variety of different intrapulmonary (inhaled) or systemic insults that initiate SIRS and lead to MODS
• Heat stress may play a role. Foals with subclinical respiratory disease have limited ability to dissipate body heat. Use of erythromycin during hot weather is associated with increased susceptibility to environmental temperatures. • Viral and bacterial pneumonia can produce respiratory distress in foals with widespread infections throughout the lungs. *Rhodococcus equi* is cultured from approximately 25% of foals with respiratory distress, and opportunistic pathogens (e.g., β-hemolytic *Streptococcus* spp., enteric bacteria, *Actinobacillus* spp., *Pseudomonas aeruginosa, P. carinii*) may be involved in ARDS. • Lesions in affected foals are similar to those in ruminants with atypical interstitial pneumonia, suggesting that intoxication may contribute to this syndrome.

RISK FACTORS
• Unknown • Risk factors—preexisting subclinical to clinical respiratory tract disease; treatment with antimicrobial agents (particularly erythromycin) or bronchodilators, producing significant interactions in some patients; viral, bacterial, or fungal respiratory tract or systemic infection; heat stress; inhaled irritant gases and pneumotoxicants; and immunosuppression

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Viral pneumonia—equine influenza, equine viral arteritis, equine herpesviruses 1 and 4, equine paramyxovirus, and equine adenovirus
• Bacterial pneumonia • *P. carinii* infection
• Pulmonary abscessation or granuloma
• Upper airway dysfunction, with aspiration of oropharyngeal fluids • Ingestion or exposure to xenobiotics

CBC/BIOCHEMISTRY/URINALYSIS
Common abnormalities—neutrophilic leukocytosis, elevated fibrinogen, and anemia

OTHER LABORATORY TESTS
• Arterial blood gas—arterial hypoxemia, hypercapnia, and respiratory acidosis • Blood culture may help to identify bacteria. • Other laboratory abnormalities— dehydration, disseminated intravascular coagulation, and injury to other organs—may be seen.

IMAGING
Thoracic Radiography
• Findings vary, depending on the stage of injury. • Lesions include prominent interstitial patterns, coalescing to alveolar infiltrates, with superimposed, mixed bronchial patterns of varying severity throughout all lung fields. • A prominent miliary reticulonodular pattern is observed commonly in foals with *P. carinii* infection. • Other changes sometimes include consolidating anteroventral pneumonia or diffusely distributed pyogranuloma in foals with concurrent *R. equi* infection.

Transthoracic Ultrasonography
Consolidation, abscesses, or other lesions in some foals

OTHER DIAGNOSTIC PROCEDURES
• Because many foals are near death, ante-mortem culture of respiratory secretions before initiation of treatment may not be practical. • Routine culture of lower airway secretions should be accompanied by cytologic evaluation. • Examination of tracheal wash or bronchoalveolar fluid reveals acute inflammation, with large numbers of neutrophils some with phagocytized bacteria.
• Recognition of *P. carinii* is difficult.
• Transthoracic lung biopsy may be useful, but should not be performed in foals with severe respiratory distress or tendency to bleed.

PATHLOGIC FINDINGS
Gross Findings
• Lungs are diffusely red, wet, heavy, firm, and fail to collapse when chest is opened. • In many instances, lungs have a lobulated appearance, with dark, reddened areas interspersed between areas of more normal appearing tissue. • A substantial number of foals also have other lung lesions (e.g., *R. equi* pyogranuloma) representing preexisting pulmonary disease. • Many foals demonstrate hypoxemia- or sepsis-induced lesions in other organs.

Histopathologic Findings
• Pulmonary lesions—diffuse, necrotizing bronchiolitis; alveolar septal necrosis; and filling of alveolar spaces with large numbers of mononuclear cells, pneumocytes, and epithelioid-like cells with hyaline membranes

TREATMENT

AIMS OF TREATMENT
• Minimize ventilatory and metabolic demands • Reduce core body temperature (in hyperthermic foals) • Reduce lung edema and inflammation • Promote adequate oxygenation • Discontinue predisposing medications (e.g., erythromycin) • Eliminate infectious agents with broad-spectrum antimicrobial therapy • Support fluid and nutritional needs.

APPROPRIATE HEALTH CARE
• Avoid transporting these patients until temperature decreases. Transportation in extreme temperatures may result in their death. • On-farm examinations during high environmental temperatures should be conducted after moving the mare and foal to a controlled environment on the premises or awaiting stabilization and the cooler period of the day before transportation.

NURSING CARE
• These cases are respiratory emergencies and require immediate attention. • Reduce core body temperature using alcohol baths, fans, and/or misters or by carefully moving the mare and foal to a cooler area protected from direct sunlight or to an air-conditioned stall.
• Cold-water enemas provide significant relief, especially when used in conjunction with the above treatments. • Judicious use of chilled IV fluids lowers core temperature; however, rapid infusion of large volumes may exacerbate pulmonary edema. Preferably, fluids should be selected to correct acid-base status and blood electrolyte abnormalities. Balanced electrolytes (e.g., lactated Ringer's solution) are appropriate initial therapy.
• Insufflation of humidified oxygen (10–15

ACUTE RESPIRATORY DISTRESS SYNDROME IN FOALS

L/min) is facilitated by placement of a nasal or transtracheal catheter.

ACTIVITY
Reduce the patient's activity, by confinement to a clean, cool stall with appropriate environmental temperature and humidity control—fans, misters, or swamp coolers.

DIET
• Lowering body temperature may improve feed intake.
• Allow nursing foals adequate time with the mare, and provide high-quality feed.

CLIENT EDUCATION
• Education is aimed at prevention.
• Proper management of the neonate is imperative, because early handling and training of foals to accept physical examination and daily rectal temperature (preferably in the morning, when ambient environmental temperatures are low) allow early detection of subclinical cases.
• Clients should observe mares and foals carefully, on a daily basis, and consult a veterinarian when foals appear to be unthrifty or depressed.
• Removal of foals from extremes of heat and placement in well-maintained stalls providing shade or fans to lower temperature are beneficial.
• Minimize exposure to high environmental temperatures, providing cooler stalls for foals treated with antimicrobial agents (especially erythromycin).

SURGICAL CONSIDERATIONS
• Evaluate thorax for effusion or pneumothorax.
• Evaluate upper airway function to determine patency of the upper airway.
• In HYPP +/+ foals, hyperkalemic episodes may result in laryngeal paralysis.

MEDICATIONS

DRUG(S) OF CHOICE
• The treatment protocol should specifically address inflammation and hyperthermia.
• Use of corticosteroids in stressed foals demonstrating clinical signs of sepsis is controversial; however, single or multiple doses of short-acting corticosteroids (e.g., dexamethasone sodium phosphate [0.05–0.2 mg/kg IV q12–24h], prednisolone sodium succinate [0.5–1.0 mg/kg IV q8–12h]) provide potent, short-duration relief of pulmonary inflammation in many cases.
• NSAIDs (e.g., flunixin meglumine [0.25–1.0 mg/kg q12–24h]) may be useful in reducing body temperature, decreasing the systemic effects of sepsis or endotoxemia, and reducing discomfort.
• Appropriate antibiotic therapy should be guided by bacteriologic culture, if possible.
Use of oral antibiotics (e.g., trimethoprim-potentiated sulfonamides [30 mg/kg q12h]), parenteral antibiotics (e.g., procaine penicillin G [22,000 IU/kg IM q12h]), or cephalosporins (e.g., ceftiofur [2.2–5 mg/kg IM, IV, or SQ q12h]) may be substituted for antimicrobial agents used prior to onset of respiratory distress.

CONTRAINDICATIONS
Discontinue any medications (especially erythromycin/rifampin) and drugs with an effect that may be altered by concurrent therapy with drugs undergoing metabolism by the liver—theophylline, aminophylline.

PRECAUTIONS
• Because sepsis may represent the underlying cause in some foals, overuse of corticosteroids is discouraged.
• Use NSAIDs with caution, due to gastrointestinal and renal effects.

POSSIBLE INTERACTIONS
• Drugs such as erythromycin/rifampin that induce or inhibit hepatic drug metabolizing enzymes may alter the disposition of concurrently used medications (e.g., methylxanthines), leading to side effects.
• Septic animals are more likely to have multiorgan dysfunction, and hepatic and renal function should be monitored during therapy.
• NSAIDs may result in gastrointestinal or renal compromise in anorexic and dehydrated patients.

ALTERNATIVE DRUGS
• Aminoglycosides (amikacin sulfate, gentamicin sulfate) used in combination with β-lactams (penicillins and cephalosporins).
• Rifampin in combination with erythromycin, clarithromycin, or azithromycin may be indicated for *R. equi*.

FOLLOW-UP

PATIENT MONITORING
• Reduction in body temperature and respiratory rate and effort and improvement in mucous membrane color typically indicate clinical improvement.
• Frequent thoracic auscultation may reveal increased bronchovesicular sounds in foals with positive response to therapy.
• Arterial blood gas analysis is the most sensitive indicator function.
• Repeated thoracic radiography is useful; however, overall radiographic appearance may lag behind clinical appearance by days or weeks.

PREVENTION/AVOIDANCE
• Client education regarding prevention and early recognition of respiratory tract disease in foals is beneficial—minimizing heat stress, control of dust, manure dispersal, and plasma therapy on farms with endemic *R. equi*.
• Client education regarding use of anthelmintics and vaccination of mares and foals against respiratory pathogens
• Client education regarding potential adverse effects of use of drugs such as erythromycin during hot weather

POSSIBLE COMPLICATION
Chronic interstitial pneumonia

EXPECTED COURSE AND PROGNOSIS
• The initial prognosis is guarded to poor in most affected foals.
• The mortality rate is high.
• Long-term outcomes vary, but cases that are recognized and treated early respond well.
• In survivors, the diffuse alveolar pattern tends to resolve quickly, whereas increased interstitial pattern resolves over weeks or months.

MISCELLANEOUS

AGE-RELATED FACTORS
• Can occur at all ages
• In 1- to 8-month foals

SYNONYMS
• Bronchointerstitial pneumonia
• ALI
• Interstitial pneumonia
• Respiratory distress

SEE ALSO
• Inspiratory dyspnea
• Expiratory dyspnea

ABBREVIATIONS
• ALI = acute lung injury
• ARDS = acute respiratory distress syndrome
• DIC = disseminated intravascular coagulation
• HYPP = hyperkalemic periodic paralysis
• MODS = multiorgan dysfunction syndrome
• SIRS = systemic inflammatory response syndrome

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ADENOVIRUS

BASICS

OVERVIEW
• Causes 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 the development of respiratory disease in adult horses has been suggested.

SIGNALMENT
• Foals are usually older than 8–10 weeks when clinical signs become present.
• Adenovirus affects primarily Arabians, although other breeds are affected sporadically, in particular, Fell Ponies.
• SCID-affected foals are frequently clinically normal at birth.

SIGNS
• Signs are essentially identical to other causes of foal pneumonia and include fever, tachypnea, dyspnea, depression, and abnormalities on thoracic auscultation.
• Mild to moderate diarrhea may also be present.

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. Due 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 after 2 months of age. Foals that are immunosuppressed for other reasons, such as Fell Pony syndrome, are also susceptible. It has been suggested that adenovirus may predispose foals to bacterial pneumonia and may play a significant role in the pathogenesis of bacterial pneumonia in non-SCID foals. An antigenically distinct adenovirus has been identified in non-SCID foals with diarrhea, usually associated with concurrent rotavirus infection. The role of adenovirus in foal diarrhea is not clear.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Other viral and bacterial causes of pneumonia in immunocompromised foals include, but are not limited to, the following:
• 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 include, but are not limited to, bacterial, viral, and parasitic causes.

CBC/BIOCHEMISTRY/URINALYSIS
Ante-mortem 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 below).

OTHER LABORATORY TESTS
• Antibody titers—SCID foals do not demonstrate a 4-fold rise in antibody titer to adenovirus, whereas non–SCID-affected foals develop a rise in antibody titer in 10 days.
• Virus isolation—Adenovirus may be isolated from normal and infected foals.
• Histopathology—Intranuclear inclusions can be detected in tissues. Ante-mortem testing may demonstrate intranuclear inclusions in conjunctival and nasal epithelial cells. At post-mortem examination there is gross and histologic evidence of lymphoid hypoplasia of the thymus, spleen, and lymph nodes.
• SRID—Precolostral testing of SCID foals also 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 will aid in diagnosis.

IMAGING
• Radiographs are consistent with pneumonia.
• Ultrasonographic imaging of lymphoid tissues may be suggestive of, but not diagnostic for, SCID.

TREATMENT

• There currently is no treatment specifically for adenovirus.
• In non-SCID foals, treatment is primarily supportive, with broad-spectrum antimicrobial coverage provided.
• Foals with SCID and Fell Pony syndrome eventually die, and treatment is not productive. There has been some investigation into immunologic reconstitution of SCID patients by transplantation of bone marrow stem cells. This treatment remains experimental as of the time of this writing.

MEDICATIONS

DRUG(S) OF CHOICE
• Non-SCID foals should be treated for concurrent bacterial infection based on culture and sensitivity results.
• Foals with adenovirus associated with rotavirus should be treated with supportive therapy, including intravenous isotonic polyionic fluid replacement of deficits and nutritional support as warranted.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

CLIENT EDUCATION
• Prevention of SCID requires identification of carriers and removal of them from breeding programs.
• Approximately one of four foals from the mating of two heterozygotes results in an SCID foal.
• Arabian foals should be tested at birth for IgM levels (presuckle) and lymphocyte count. Those foals with an absolute lymphopenia should be closely monitored until 5 months of age. Alternatively, there are genetic tests available now to identify carriers of the genetic defect.
• Recommendations for client education regarding Fell Pony syndrome are not yet established.

MISCELLANEOUS

ABBREVIATIONS
• SCID = severe combined immunodeficiency syndrome
• SRID = serial radial immunodiffusion

Suggested Reading
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ADRENAL INSUFFICIENCY

BASICS

OVERVIEW
• Synonymous with hypoadrenocorticism and "steroid let-down syndrome"
• Characterized by glucocorticoid and mineralocorticoid deficiency caused by adrenal cortex destruction (i.e., primary AI or Addison's disease) or ACTH deficiency (i.e., secondary AI)
• Primary AI—Both glucocorticoid and mineralocorticoid are deficient.
• Secondary AI—Mineralocorticoid secretion usually is normal.

SYSTEMS AFFECTED
• Endocrine
• Cardiovascular
• Renal
• Musculoskeletal
• GI
• Behavioral

SIGNALMENT
Any age, sex, and breed

SIGNS
• Acute cases—muscular weakness, hypotension, anorexia, hemoconcentration, hypothermia, polyuria, 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
• Pituitary-adrenal axis immaturity attributable to prematurity in neonatal foals
• Adrenal hemorrhage and necrosis subsequent to septicemia or severe bouts of endotoxemia

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Acute cases—endotoxemia, septicemia, renal failure, and colitis
• A normal ACTH stimulation test rules out adrenal insufficiency.

CBC/BIOCHEMISTRY/URINALYSIS
• Acute AI is characterized by hemoconcentration, hyponatremia, hypochloremia, hyperkalemia, decreased sodium:potassium ratio (reference range, >27), and hypoglycemia.
• Additional abnormalities—metabolic acidosis and azotemia
• Chronic cases, including secondary AI—mineralocorticoid secretion (i.e., aldosterone) is generally maintained. Therefore, serum electrolytes are within normal limits.

OTHER LABORATORY TESTS
• With insufficient aldosterone secretion, fractional excretion of sodium (reference range, <1%) is increased despite a normal or low serum sodium concentration.
• Administration of exogenous ACTH (1 U/kg IM) resulting in less than a doubling of the cortisol baseline 6–8 hr later is consistent with AI. Alternatively, synthetic ACTH (Cosyntropin 100 μg IV for a neonatal foal) may be used. Less than a doubling of the cortisol baseline 1 hr later is consistent with AI. Because acute AI is life-threatening, dexamethasone (0.044 mg/kg IV) should be administered simultaneously with exogenous ACTH. Serum cortisol is measured 2 hr later, and horses with AI exhibit a negligible increase in cortisol. This eliminates any delay in treatment while diagnostic tests are being performed.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
N/A

TREATMENT

• Complete rest and avoidance of stress, particularly surgery, infection, and trauma.
• Treat the underlying primary cause.
• Provide sodium supplementation (e.g., salt) to horses with increased sodium losses.

MEDICATIONS

DRUGS
• Glucocorticoid and, if necessary, mineralocorticoid replacement. The maintenance dose of prednisolone, which is equivalent to daily corticosteroid secretion in normal adult horses, is approximately 25 mg/day. However exposure to stress dramatically increases corticosteroid requirements. During periods of stress, increase the dose by 2- to 10-fold and divide into 2–3 daily doses.
• Acute AI—dexamethasone in conjunction with IV crystalloid solutions (i.e., normal saline) and dextrose in cases of hypoglycemia. Although dexamethasone has minimal mineralocorticoid activity, 20 mg administered daily is sufficient to maintain adrenalectomized horses alive.
• Mineralocorticoid replacement with fludrocortisone may be considered.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

PATIENT MONITORING
• Monitor electrolytes, renal function, acid-base balance, and hydration status.
• Once the animal is stable, adrenal recovery can be documented by repeating ACTH-stimulation tests.

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 result in laminitis.

EXPECTED COURSE AND PROGNOSIS
N/A

MISCELLANEOUS

ASSOCIATED CONDITIONS, AGE-RELATED FACTORS, ZOONOTIC POTENTIAL, PREGNANCY
N/A

ABBREVIATIONS
• ACTH = adrenocorticotropin hormone
• AI = adrenal insufficiency
• GI = gastrointestinal

Suggested Reading

Toribio RE. The adrenal glands. In: Reed SM, Bayly WM & Sellon DC, ed. Equine Internal Medicine, ed 2. St Louis: Saunders, 2004:1357–1361.

Author Laurent Couëtil
Consulting Editor Michel Lévy

AFLATOXICOSIS

BASICS

OVERVIEW
• Aflatoxicosis is the condition of intoxication by the *Aspergillus* fungal metabolite, aflatoxin.
• Diffuse liver disease is its hallmark with acute and chronic forms dictated by dose and duration of exposure.
• Aflatoxin-contaminated feed grains, especially corn, are the sources of toxin.
• Aflatoxin is usually produced on grain grown during drought conditions.

SIGNALMENT
Younger horses are more susceptible.

SIGNS
• Ponies given single lethal doses of aflatoxin (2 mg/kg) had increased temperatures, elevated heart and respiratory rates, tenemus, bloody feces, and tetanic convulsions.
• Some ponies died within 3 days while others lived for 32 days post-dosing. Ponies administered high oral doses (0.4 mg/kg for 5 days or the equivalent of several ppm in the feed) of aflatoxin were lethargic, anorectic and slightly icteric on the 5th day. Serum liver enzymes were elevated on the 4th day of dosing. Signs of hepatic encephalopathy such as belligerence, somnolence, circling, blindness, and head pressing may occur when serum ammonia levels are sufficiently elevated. Chronic low-level exposure may present as an ill-defined loss of condition.

CAUSES AND RISK FACTORS
The most likely contaminated diets are corn-based, while less likely exposure comes from diets containing peanut and cottonseed meals. Forage is an unproved source of aflatoxin.

DIAGNOSIS

• Signs and lesions of aflatoxicosis reflect liver disease. None are pathognomonic for either acute or chronic aflatoxin poisoning.
• Feed concentrations of several hundred ppb aflatoxin in grain rations, together with appropriate clinical sings, are supportive of a diagnosis.
• Ill-thrift is associated with lower levels of aflatoxin intake.

DIFFERENTIAL DIAGNOSIS
Elevated serum hepatic enzyme levels can occur in association with many multisystemic diseases. Specific causes of hepatic disease include
• Fumonisin-induced mycotoxicosis—detection in feed
• Alsike clover or kleingrass toxicoses—evidence of exposure
• Hepatic neoplasia or abscessation—imaging or biopsy
• Biliary obstruction—serum chemistries and biopsy
• Theiler's disease—history, biopsy
• Pyrrolizidine alkaloid-containing plants such as *Amsinckia* spp., *Crotalaria* spp., and *Senecio* spp. cause chronic progressive liver disease—history of consumption, biopsy

CBC/BIOCHEMISTRY/URINALYSIS
• White blood cell counts, especially lymphocytes, are decreased and serum glucose is decreased. Total serum lipid and cholesterol are increased.
• Elevations of prothrombin time and serum AST, ALT, and GGT were consistent with the severe liver necrosis and biliary hyperplasia seen post-mortem.

OTHER LABORATORY TESTS
• Chemical analysis of feed samples is necessary to confirm the presence of aflatoxin. The inability to obtain samples at the time of exposure often precludes detection of aflatoxin levels consistent with acute intoxication.
• Feed concentrations necessary to induce acute intoxication typically approach the ppm range, while chronic exposure to several hundred ppb is sufficient to induce subclinical liver damage and associated ill-thrift.

IMAGING
N/A

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. Horses suffering only moderate liver damage will benefit from supplementation with high-quality protein, fat-soluble vitamins, and selenium. Management for liver failure includes high-carbohydrate, low-protein diets.

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 function.

PREVENTION/AVOIDANCE
Reliable feed sources are critical when grains are produced during drought conditions. Test grain 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.

ABBREVIATION
• ppb = parts per billion

Suggested Reading

Raisbeck MF. Feed-associated poisoning. In: Robinson NE, ed. Current Therapy in Equine Medicine, ed. 3. Philadelphia: WB Saunders, 1992:366–372.

Author Stan W. Casteel
Consulting Editor Robert H. Poppenga

AFRICAN HORSE SICKNESS

BASICS

OVERVIEW
• Infectious disease affecting the cardiovascular and respiratory systems, characterized by fever and edema
• Not reported in the United States. 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, are susceptible.
• There is no apparent breed, age, or sex predilection.
• Angora goats are also susceptible. Zebras and elephants may serve as natural reservoirs of the virus that causes AHS. 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 mosquitoes and ticks
• 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 hemorrhagica, equine anaplasmosis and equine piroplasmosis may have similar clinical presentation as 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 isolation of virus from whole blood or tissues, or antibodies to AHS virus in serum.
• In the United States, 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 ultrasound 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, 42 antigenic strains 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.

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 21 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.

MISCELLANEOUS

ZOONOTIC POTENTIAL
The disease does not affect humans.

ABBREVIATION
• AHS = African horse sickness

Suggested Reading

Committee on Foreign Animal Diseases of the US Animal Health Association, Foreign Animal Diseases "The Gray Book" online, 1998, http://www.vet.uga.edu/vpp/gray·book/FAD/AHS.htm
The African Horse Sickness Website, The African Horse Sickness Trust, 2005, http://www.africanhorsesickness.co.za/

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AGALACTIA/HYPOGALACTIA

BASICS

DEFINITION
• Agalactia—postpartum lactation failure
• Hypogalactia—subnormal milk production

PATHOPHYSIOLOGY
• Estrogens (fetoplacental unit) in late gestation induce mammary duct development.
• P4 stimulates lobuloalveolar growth.
• Lactogenesis is triggered by the sharp decrease of P4 and sharp increase of prolactin just prior to parturition.
• The increased production of prolactin by the anterior pituitary gland results from suppression of a prolactin inhibitory factor (likely dopamine) and release of a hypothalamic prolactin-releasing factor (proposed to be serotonin).
• Agalactia/hypogalactia may be caused by alterations of hormonal events (endocrine disease), defects in mammary tissue itself (mammary disease), or as a result of systemic illness or disease.

SYSTEMS AFFECTED
• Reproductive
• Endocrine/metabolic

SIGNALMENT
Mores of any breed or age may be affected.

SIGNS
General Comments
• Tall fescue predominant in central and southeast United States; fescue syndrome
  ○ Grazing endophyte-infected fescue—most likely cause of lactation failure
  ○ Predominant finding—agalactia at parturition
• South America—fungus-infected feed, *Claviceps purpurea* (ergot) implicated in agalactia

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

Physical Examination
• Weak, septicemic foal—FPT 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
• Ingestion of tall fescue grass—infected with *Neotyphodium coenophialum* (formerly *Acremonium coenophialum*) or feedstuffs infected with *Claviceps purpurea* sclerotia.
• Ergot alkaloids depress prolactin secretion (dopamine DA_2 receptor agonists and serotonin antagonists).
• Abortion/premature birth affects normal P4, estrogen, and prolactin fluctuations needed 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

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

AGALACTIA/HYPOGALACTIA

TREATMENT

- Mastitis
  - Lactating cow intramammary treatments
  - Systemic antibiotics based on culture/sensitivity
  - Frequent stripping of mammary gland
  - Hot-packs or hydrotherapy
  - Correct nutritional deficiencies.
- FPT foals
  - Nutritional supplementation during period of agalactia
  - Plasma transfusions

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.
  - Not approved by FDA; still experimental product.
  - No known side effects associated with treatment of pregnant mares.
  - Treat minimum15 days prepartum; discontinue when/if lactation is observed at foaling.
  - If agalactic at foaling and not treated prior to parturition, initiate treatment at foaling and continue for 5 days or until lactation ensues.
- TRH—2.0 mg, SQ, BID, 5 days, begin day 1 postpartum
  - Increases serum prolactin, due to its action as a prolactin releasing factor

CONTRAINDICATIONS

- Perphenazine, dopamine receptor antagonist—published, but:
  - Severe side effects in horses preclude its use.
  - Sweating, colic, hyperesthesia, ataxia, posterior paresis
- Metoclopramide used to treat agalactia of unknown origin
  - Significant risk for developing severe CNS 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 No. 1 primary side effect.
- Reserpine (0.5–2.0 mg IM q48h or 0.01 mg/kg PO q24h)
  - Depletes serotonin, dopamine, and norepinephrine in the brain and other tissues
  - GI motility greatly increased; can cause profuse diarrhea
  - Sedation—common side effect
  - Not Food and Drug Administration 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

- FPT
- Malnutrition
- Starvation

SEE ALSO

- Dystocia
- Fescue toxicosis
- Mastitis
- Prolonged pregnancy
- Retained fetal membranes
- FPT

ABBREVIATIONS

- FPT = failure of passive transfer
- P4 = progesterone
- TRH = thyrotropin-releasing hormone

Suggested Reading

Evans TJ, Youngquist RS, Loch WE, Cross DL. A comparison of the relative efficacies of domperidone and reserpine in treating equine "fescue toxicosis." Proc AAEP 1999;45:207–209.

Van Camp SD. Abnormalities of lactation. In: Youngquist RS, Threlfall WR, eds. Current Therapy in Large Animal Theriogenology. St. Louis, MO: Saunders Elsevier, 1997:131–134.

Author Carole C. Miller
Consulting Editor Carla L. Carleton

AGGRESSION

BASICS

DEFINITION
• Behaviors that do, or attempt to do, injury to another with the apparent motivation of causing harm. Predation is generally not considered aggression. • Agonistic behaviors include threats, offensive aggressive behaviors, defensive behaviors, and submissive behaviors. • Occurs in specific contexts or circumstances and is influenced by numerous variables, including internal states (e.g., hormones, hunger, fear), external stimuli (e.g., presence of offspring), learned experiences, etc. • Can be classified in overlapping categories—according to the target, e.g. people, predators, horses, other animals; according to function and motivation, e.g., establishing dominance status, maternal, defensive, redirected, etc.; whether offensive or defensive.

PATHOPHYSIOLOGY
• Not necessarily a pathological condition, but usually a normal, species-typical behavior
• When extreme in frequency or intensity, can be a sign of an underlying pathological condition
• Any pathophysiology that results in pain
• Hypothyroidism and acute liver failure have been associated with aggressiveness.
• Hypertestosteronism in mares—ovarian tumors such as arrhenoblastoma and granulosa-thecal cell; testicular feminization syndrome in mares • Retained testicles in males that may produce testosterone or e.g., estrogen
• Agents that affect the CNS—encephalopathies, rabies • Obsessive-compulsive self-mutilation; generally isolated stallions • Low blood serotonin levels have been associated with aggressive behavior. • Anabolic steroids may cause aggression.

SYSTEMS AFFECTED
• Several behavioral systems of the horse may be affected. • Musculoskeletal, skin, ophthalmic injuries as a consequent of aggression
• Reproductive behaviors may be interrupted; attachment behaviors may be severed between mare and foal, horse and person. • 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. Sympathetic arousal.
• Interference with learning and learned behaviors

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
Maternal aggressive protection of foals is reported more often in Arabian mares.

Age
• Any age • Maternal aggression—more common among mares with unweaned foals
• Playful aggression—most common in young horses and colts • Intermale aggression—more common and intense in mature males

Predominant Sex
Intact males are more likely to show aggression to other horses and people.

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 with the body or 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 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 head-on approach and threat. • Submissive behaviors include deferring to more dominant animal and "snapping" (jaw-waving, teeth-clamping, or *unterlegenheitsgebarde*). Sometimes a slight sucking sound occurs. The ears are usually in a somewhat horizontal position.

Historical
• Vary with the circumstances and kind of aggression shown
• 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 treatment and risk assessment. • Aggressiveness associated with endocrine abnormalities is generally of gradual onset. • 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.

Physical Examinations
• Should be unremarkable, unless some underlying pathology is present • Examine carefully for pain. • Reproductive tract abnormalities • Retained testicles • Mares may have ovarian enlargements and cystic morphology, enlarged clitoris, blind vaginal sac, "cresty neck."

CAUSES
• Pain • Fear/defense • Play aggression usually is inhibited and causes no injuries among unshod horses of similar ages and weight. May 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—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 either is 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. A mare may attack a stallion attempting to mate her, or a stallion may attack a mare that he is attempting to mate. Stallions may fight with each other in the presence or absence of mares. Mares may attack each other for access to stallions or to block access to a stallion. • Endocrine abnormalities

RISK FACTORS
• Inappropriate use of punishment • Horses reared in isolation from other horses may not develop adequate social skills and may develop inappropriately rough play aggression with people. • 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 • Hand feeding treats can lead to "nipping." • Adjacent stabling of horses that exhibit aggression toward each other
• Sharp edges or protruding sharp wires on barriers between horses that engage in aggressive play with each other

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Rule out pathological conditions, especially painful etiologies, before establishing a nonmedical behavioral diagnosis.
• Aberrant, intense, or steadily increasing aggressiveness warrants comprehensive medical workup.
• Nonmedical diagnoses are based on circumstances and behavioral signs exhibited and rule-outs of medical causes.

CBC/BIOCHEMISTRY/URINALYSIS
Dependent on clinical signs

OTHER LABORATORY TESTS
• Dependent on clinical signs
• Self-mutilating directed to right side warrants endoscopic examination for gastric ulcers.

AGGRESSION

• Aggression in mares, especially when accompanied by stallion-like behaviors, warrants testosterone, estrogen, and inhibin assays.
• Karyotyping of mares exhibiting stallion-like behaviors
• Thyroid panels

IMAGING
Transrectal ultrasonography of reproductive organs

OTHER DIAGNOSTIC PROCEDURES
• Rectal palpation
• Vaginal examination

PATHOLOGICAL FINDINGS
Dependent on etiology of aggression

TREATMENT

AIMS OF TREATMENT
• 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 the physical or social environment 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. Referral to an experienced and competent veterinary behaviorist, applied animal behaviorist, or trainer usually is necessary to help the client implement the plan.
• Assess the risks of treating and keeping a horse exhibiting aggression. Factors to consider are length of time the behaviors have been occurring, severity of aggression, number of situations in which the behaviors occur, predictability of the aggression, ease of stopping or preventing it, number of different targets, environment of the horse, and the people and other animals that may interact with the horse.

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 only cures self-mutilation that appears to be self-directed intermale aggression by stallions about 30% of the time. Seventy percent remain unaffected by castration.

MEDICATIONS

DRUGS OF CHOICE
• No drug is approved by the US Food and Drug Administration for use with aggressive problems in horses.
• Pain medications may help to reduce or eliminate pain-elicited aggression.
• Anxiolytics or antidepressants may help with fear-motivated aggression.

CONTRAINDICATIONS
Benzodiazepines may increase aggressive behaviors.

PRECAUTIONS
• Inform clients that use of psychoactive drugs 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
• Rear young foals with other horses. Ideally should remain with mother for 6 mo and allowed access to other foals and (appropriate) horses as much as possible and for as long as possible.
• Sufficient exercise
• Adequate space to play and defer to dominant horses
• Ground work that results in the horse consistently and quickly yielding to the requests of the handler. Most easily accomplished with naïve and young horses
• Avoid inappropriate use of punishment.
• If the aggression is not pathophysiologic, at the first indication there might be an aggressive behavior problem; advise client to seek help from a qualified, accomplished professional who addresses such behaviors.

POSSIBLE COMPLICATIONS
See Client Education.

EXPECTED COURSE AND PROGNOSIS
• Resolution of aggressive and stallion-like behaviors of mases with ovariectomy is good.
• 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 interested in mares. From 5% to 17% retain some aggressiveness toward people.
• Treatment of hypothyroidism with levothyroxine can effectively reduce aggressive behavior in horses.
• Successful treatment of nonmedical causes of aggression is dependent on many variables (see above).

MISCELLANEOUS

ASSOCIATED CONDITIONS, AGE-RELATED FACTORS, ZOONOTIC POTENTIAL, PREGNANCY, SYNONYMS
N/A

SEE ALSO
• Excessive maternal behavior/foal stealing
• Fears and phobias
• Maternal foal rejection
• Male sexual behavior problems
• Endocrine disorders
• Training and learning problems

Suggested Reading

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ALKALINE PHOSPHATASE (ALP)

BASICS

DEFINITION

• Serum ALP is mainly used as a marker for cholestasis. • Routine chemistry panels report total ALP, but nonhepatic tissues (especially bone) may contribute to total ALP. • Is infrequently used as a marker for changes in other tissues; requires isoenzyme separation techniques. • For routine interpretations, the potential contributions by nonhepatic tissues must be taken into account before interpreting increased ALP as evidence for cholestasis. • Reference intervals vary depending on the assay substrate employed; thus, comparisons across labs may not be valid.

PATHOPHYSIOLOGY

• Two genes produce distinct ALP isoenzymes—intestinal ALP and tissue-unspecific ALP. • Generally, the intestinal ALP gene is expressed only in the intestine and the tissue-unspecific ALP gene elsewhere; however, the equine kidney expresses both. • Posttranslational modification (especially glycosylation) produces additional tissue-specific isoforms of ALP (e.g., bone, liver) and affects circulating half-life. • Various ALP forms can be quantified, but only at specialized labs. • 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 usually is not released into blood, and intestinal ALP has a very short half-life of ≅8 min. Thus, serum concentrations normally consist mostly of liver and, to a lesser extent, bone ALP. • Liver ALP activity generally 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 (e.g., carbon tetrachloride toxicity) has little effect. Bile duct ligation leads to nearly 3-fold elevations within 10 days. Presumably, much higher increases would require considerable chronicity. • Recent work suggests that ALP rises with biliary proliferation, as seen with GGT. • Because increased ALP involves enzyme induction, serum ALP increases in acute obstructive jaundice are preceded by 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 (i.e., mucosal cells versus secondary liver changes) is often unclear. • Reproductive—Placental increases during pregnancy; impact on serum concentrations is equivocal. Semen ALP comes mainly from the epididymus and testes. High 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 levels by 6 mo–1 year. • Pregnancy—Equivocal impact on serum ALP; some diseases associated with cholestasis and increased ALP are more common in pregnant mares (e.g., hyperlipemia, Theiler's disease, etc.). • Ponies and donkeys—particularly susceptible to hyperlipemia and hepatic lipidosis • Other factors—depend on the underlying cause

SIGNS

General Comments

Signs do not result directly from increased serum ALP activity but from the underlying disease process.

Historical Findings

• Owners may report icterus, dark yellow/orange urine, anorexia, weight loss, listlessness, and behavioral changes associated with hepatic failure in conditions associated with cholestasis. • Abdominal pain (e.g., sweating, rolling) may occur with acute hepatopathies (i.e., capsular swelling) or biliary obstructions.

Physical Examination Findings

• Icterus is common. • Increased pulse and respiratory rates, fever, photosensitization, weight loss, or obesity vary with the type and severity of the underlying disease process.

CAUSES

Hepatobiliary System

• Metabolic—secondary to severe anemia (see Hematopoietic System), hyperlipemia, or fasting (<50% increase within 2–3 days, nonpathological) • Immune-mediated, infectious—chronic active hepatitis, Theiler's disease (i.e., serum hepatitis), amyloidosis, endotoxemia, viral (e.g., EIA, EVA, EHV in perinatal foals), bacterial (e.g., Tyzzer's disease, salmonellosis), fungal, protozoal (piroplasmosis), and parasitic (e.g., liver flukes, strongyle larval migrans) • Nutritional—hepatic lipidosis • Degenerative—cirrhosis; cholelithiasis • Toxic—pyrrolizidine alkaloid–containing plants (e.g., senecio, crotolaria), alsike clover, aflatoxin, rubratoxin; chemical toxins (e.g., arsenic, chlorinated hydrocarbons, phenol, paraquat) primarily cause hepatocellular injury; cholestasis secondary to hepatocellular swelling may increase ALP; some anesthetics (e.g., halothane) are associated with mild, transient increases. • Anomaly—biliary atresia; portovascular shunts • Neoplastic—primary liver tumors (rare); metastatic neoplasia (uncommon)

Musculoskeletal System

• Rapid bone growth—juveniles • Severe bony lesions

GI System

Severe GI disease—diarrhea

Reproductive System

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

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 lymphosarcoma, leukemias, and so on

RISK FACTORS

Those associated with any disease leading to cholestasis; exposure to serum products in periparturient mares (serum hepatitis); pregnant ponies (hepatic lipidosis), etc. See Causes.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Increases caused by bone ALP mostly are 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 are associated with long-standing conditions involving severe cholestasis—chronic active hepatitis, cirrhosis, cholelithiasis, and lipidosis. • Concurrent obesity and high enzyme levels suggest hyperlipemia/lipidosis, whereas anorexia and weight loss are typical of most other differentials.

LABORATORY FINDINGS

Drugs That May Alter Lab Results

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

Disorders That May Alter Lab Results

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

Valid If Run in Human Lab?

• 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.

CBC/BIOCHEMISTRY/URINALYSIS

• No routine laboratory tests provide a causative or specific diagnosis for increases. • Most suggest a type of injury (e.g., process, cholestasis, insufficiency) rather than a cause. • Others, confirming the presence of cholestasis, support a suspected hepatic origin for the increase.

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 and may contribute to mild hemolytic anemia. • Severe hemolytic anemia (regardless of mechanism) can cause hypoxic injury leading to hepatocellular swelling and secondary cholestasis.

ALKALINE PHOSPHATASE (ALP)

Leukocytes
• Neutrophilia or neutropenia and monocytosis may occur with inflammatory liver disease—bacterial cholangiohepatitis. • 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.
• Hypoglycemia with liver disease carries a guarded prognosis.

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

BUN
Decreased levels (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 (i.e., hemolysis), or decreased hepatic uptake and with fasting

Cholesterol
• May decrease with hepatic insufficiency/shunts
• Sometimes increases with cholestasis and lipid metabolic disorders—hyperlipemia

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—injury, cholestasis, or insufficiency.
• Assesses enterohepatic circulation, adequate hepatocellular perfusion, and hepatobiliary function.
• More sensitive than ALP for cholestasis

Ammonia
Serum concentrations are affected by hepatic uptake and correlate inversely with hepatic functional mass.

Clearance Tests (BSP, ICG)
• Prolonged clearance intervals with decreased functional mass or cholestasis
• Accelerated clearance (possibly masking insufficiency) with hypoalbuminemia

Serology
Depends on the degree of suspicion for specific diseases—viral, fungal, and so on

Coagulation Tests
May be prolonged with hepatic insufficiency/shunting—prothrombin time; activated partial thromboplastin time.

IMAGING
Ultrasonography—useful for assessing liver size, shape, position, and parenchymal texture; may help to detect focal parenchymal lesions (e.g., abscesses, neoplasms) and abnormalities in the biliary tree (e.g., dilatations, obstructions) or large vessels (e.g., shunts, thrombosis).

DIAGNOSTIC PROCEDURES
Aspiration cytology or biopsy for microbiologic testing, cytologic imprints, and histopathological evaluation may provide specific diagnostic information.

TREATMENT

• Decision regarding outpatient versus inpatient treatment depends on the severity of disease, intensity of supportive care required, need for isolation of infectious conditions, and so on.
• Fluid and nutritional support may be needed.
• Anorexic and hypoglycemic cases may benefit from IV 5% dextrose (2 mL/kg per hr); otherwise, fluid support depends on specific electrolyte and acid-base abnormalities.
• Avoid negative energy balance, especially in ponies and donkeys, to avoid/treat hyperlipemia and hepatic lipidosis.
• Toxicities or hepatic insufficiency may warrant efforts to reduce production/ absorption of toxins.
• Mineral oil by nasogastric tube helps to reduce toxin absorption.
• Lactulose (0.3 mL/kg q6h) by nasogastric tube is suggested to combat GI ammonia production/absorption but also causes diarrhea.
• A high-carbohydrate, low-protein diet reduces ammonia production.
• Specific therapy, including surgery, depends on the specific underlying cause.

MEDICATIONS

DRUG(S) OF CHOICE
Depend on the suspected cause and observed complications

CONTRAINDICATIONS
Depend on the suspected cause and observed complications

PRECAUTIONS
• Depend on the suspected cause
• With suspected hepatic insufficiency, assess coagulation profiles before invasive procedures.

POSSIBLE INTERACTIONS
Depend on the underlying cause

ALTERNATIVE DRUGS
Depend 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—Initial evaluation at 1- to 2-day intervals helps to establish the disease course; subsequent testing can be at increasing intervals, depending on signs and severity.

PREVENTION/AVOIDANCE
Depends on the underlying cause

POSSIBLE COMPLICATIONS
Depend on the underlying cause

EXPECTED COURSE AND PROGNOSIS
Depend on the underlying cause

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Depend on the underlying cause
• One study showed ALP values >900 IU/L were associated with increased risk of nonsurvival (hazard ratio = 10.66).

AGE-RELATED FACTORS
• See Signalment.

ZOONOTIC POTENTIAL
Depends on the underlying cause

PREGNANCY
See Signalment.

SYNONYMS
N/A

SEE ALSO
• See Causes.

ABBREVIATIONS
• BSP = sulfobromophthalein
• EHV = equine herpesvirus
• EIA = equine infectious anemia
• EVA = equine viral arteritis
• GGT = γ-glutamyltransferase
• GI = gastrointestinal
• ICG = indocyanine green

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ALKALOSIS, METABOLIC

BASICS

DEFINITION

• A disruption of acid-base homeostasis producing decreased H^+ concentration reflected by alkalemia—increased pH and high plasma HCO_3^-, Tco_2, or BE.
• Normal plasma bicarbonate level in horses is ≅24 mEq/L.
• Normal pH of arterial blood ranges from 7.35 to 7.45.
• Hypoventilation should increase CO_2 levels to lower pH; however, respiratory compensation is limited once hypoxemia develops.

PATHOPHYSIOLOGY

• The kidney normally is extremely capable of responding to a high pH, correcting metabolic alkalosis (MAK) via excretion of HCO_3^- into the urine. Even with daily administration of high bicarbonate levels, the alkalosis is short lived in normal horses. Therefore, MAK persists only when an initiating factor develops simultaneously with conditions in which renal excretion of HCO_3^- is impaired or reabsorption is enhanced.
• Excessive loss of H^+, retention of HCO_3^-, and contraction of ECF volume without loss of HCO_3^- (i.e., contraction alkalosis) are the common mechanisms thought to initiate MAK.

SYSTEMS AFFECTED

Respiratory

Peripheral and central chemoreceptors sense high pH in blood or CSF and depress ventilation to decrease removal of CO_2; hypercapnia and hypoxemia may follow.

Cardiovascular

• Cardiac arrhythmias
• Arteriolar vasoconstriction
• Decreased coronary blood flow

Neuroendocrine

• Decreased cerebral blood flow caused by vasoconstriction
• Neurologic signs (e.g., delirium, seizures, lethargy, stupor) are rare but can be seen with severe alkalemia.
• Neuromuscular excitability and tetany may occur.

Metabolic

• Increased affinity of oxygen-hemoglobin binding, which inhibits release of oxygen to the tissues
• Decreased ionized calcium concentration

Renal

The kidney responds to high pH by very effective HCO_3^- excretion under otherwise normal conditions. This response develops within hours, but it may take days to complete.

SIGNALMENT

• All breeds, ages, and sexes
• Horses used for endurance exercise may be more likely to be affected.

SIGNS

• Recent participation in endurance events or other exercise of long duration and moderate intensity may be included in the history.
• Physical examination findings vary with the primary cause.

CAUSES

• Some causes may include both an initiating factor(s) and condition(s) that encourage maintenance of alkalosis.
• GI loss of H^+ is seen with gastric reflux that occurs with anterior enteritis, ileus, or early small intestinal obstruction.
• Salivary loss of Cl^- occurs with dysphagia, esophageal trauma or obstruction, and esophagostomy.
• Cl^- loss is seen with gastric reflux, excessive sweating (especially in endurance horses), and diuretic therapy (especially with furosemide).
• K^+ depletion is associated with anorexia, restriction of GI intake, polyuric renal failure, and diuretic therapy (especially with acetazolamide).
• Endurance horses with exertional rhabdomyolysis present with MAK, likely associated with the loss of fluid and electrolytes via sweating.
• Equine sweat contains large amounts of chloride and potassium relative to serum levels. Fluid loss can be extreme with moderate-intensity exercise over long periods, especially in warm, humid conditions. Therefore, fluid and electrolyte losses can be very significant—even life-threatening—in sweating horses.
• Most of the mentioned conditions involve contraction alkalosis—fluid loss/shifts involving Na and Cl but not HCO_3^-.
• Bicarbonate therapy may result in MAK in race horses, especially if also given diuretics.
• Because proteins are weak acids, hypoproteinemia (especially albumin) produces MAK.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Increased bicarbonate levels also are seen in conditions with respiratory acidosis. Pco_2 is high but the pH close to normal or high on blood gas analysis.
• Compensation may be very effective in chronic respiratory acidosis.

LABORATORY FINDINGS

Drugs That May Alter Lab Results

• Excessive anticoagulant may falsely decrease results via dilution.
• Excessive sodium heparin may alter HCO_3^- levels.

Valid If Run in Human Lab?

Yes, if properly submitted

CBC/BIOCHEMISTRY/URINALYSIS

• Measurements of serum electrolytes, protein levels, and serum chemistries are important to determine the cause and to guide treatment.
• Proportionate changes in sodium and chloride levels occur with alterations of fluid balance. Normal sodium levels with hypochloremia or hyperchloremia indicate acid-base imbalance, whereas disproportionate changes usually are associated with simultaneous acid-base imbalance and hydration abnormalities.
• Potassium and chloride are decreased in horses that sweat excessively. Potassium may be low because of the primary cause or as a response to the extracellular shift of H^+.
• Ionized calcium is decreased.
• Magnesium may be decreased, especially with sweat loss and colic.
• Urinalysis may reveal decreased urine pH.

OTHER LABORATORY TESTS

• Many labs measure Tco_2 using the same sample submitted for electrolytes.

ALKALOSIS, METABOLIC

• The T_{CO_2} closely approximates HCO_3^-, because most CO_2 is carried in the blood as bicarbonate.
• Like MAK, respiratory alkalosis also results in high T_{CO_2}. These conditions can be differentiated only by complete blood gas analysis.
• The T_{CO_2} must be analyzed rapidly and with minimal room-air exposure within the sample tube, because CO_2 can dissipate from the sample.

TREATMENT

• Treatment of the primary cause is essential.
• Replacement of fluid losses with isotonic fluids may be all that is needed 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.

MEDICATIONS

DRUGS OF CHOICE

• With hypochloremia, give fluids containing chloride, or the alkalosis will not be corrected even if hydration is restored.
• Saline or Ringer's solution with added calcium and KCl is the fluid of choice.
• With excessive potassium loss, PO supplementation is necessary if the horse remains anorexic.

CONTRAINDICATIONS

Any alkalinizing therapy (i.e., LRS) can worsen the alkalosis. Check contents of oral electrolyte therapies closely.

PRECAUTIONS

• Give calcium-containing solutions slowly to avoid arrhythmias.
• Monitor cardiac rhythm during administration.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

Oral rehydration solutions have achieved good results in horses, being very effective in mild cases and an excellent adjunct to IV therapy. From 1–2 gallons can be given PO every few hours to adults without ileus.

FOLLOW-UP

PATIENT MONITORING

Serial blood gas analysis and measurement of electrolytes and calcium are very important in evaluating efficacy of therapy; repeat within a few hours of initial treatment and thereafter according to patient response.

POSSIBLE COMPLICATIONS

• Hypokalemia
• Hypocalcemia
• Other, rare complications—cardiac arrhythmias, colic, synchronous diaphragmatic flutter, tetany, and neurologic signs

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Hypochloremia
• Hypokalemia
• Respiratory acidosis

SEE ALSO

• Exertional rhabdomyolysis
• Exhausted horse syndrome
• Heat exhaustion
• Hyperthermia

ABBREVIATIONS

• BE = base excess
• CSF = cerebrospinal fluid
• ECF = extracellular fluid
• GI = gastrointestinal
• LRS = lactated Ringer's solution
• MAK = metabolic alkalosis

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ALKALOSIS, RESPIRATORY

BASICS

DEFINITION

• A decrease in blood P_{CO_2} and pH
• Arterial P_{CO_2} tensions of <35 mm Hg
• Venous P_{CO_2} tension <43 mm Hg

PATHOPHYSIOLOGY

• Most (65%–70%) CO_2 combines with water almost instantaneously to form carbonic acid, which then dissociates into bicarbonate ion and hydrogen. Therefore, most CO_2 is transported in the blood as bicarbonate, with some bound to proteins (especially deoxygenated hemoglobin) and a small amount dissolved directly into plasma.
• In the lungs, the reverse occurs, and CO_2 passively diffuses out of capillaries and into the alveoli.
• These three forms of CO_2 exist in equilibrium in the blood, but P_{CO_2} as measured by blood gases depends on the dissolved portion.
• Alveolar CO_2 then is removed mechanically by ventilation as inspired air displaces alveolar gas, which is expired.
• Respiratory alkalosis is present with hyperventilation or when tissue production of CO_2 drops but ventilation remains unchanged.

SYSTEMS AFFECTED

• The brain is most affected by CO_2 levels, because hypocapnia decreases cerebral blood flow.
• Low pH affects acid-base balance, protein binding, and electrolyte levels directly in the blood and via effects on the kidney.
• The kidney responds to low pH by generating more H^+ and excreting more HCO_3^-. It also reabsorbs Cl^- to maintain electroneutrality. Alkalosis decreases serum potassium and ionized calcium levels.
• Severe alkalemia can cause venoconstriction and predispose to arrhythmias, and it may result in hyperexcitability of muscle and nervous tissue.

SIGNALMENT

Any horse

SIGNS

Respiratory rate, volume, or both usually are increased.

CAUSES

Acute

• Usually is a temporary change in response to a stimulus causing hyperventilation
• Physiologic causes of hyperventilation—exercise, fever, and hyperthermia
• Psychological causes—pain, anxiety, excitement, and fear
• Stimulation of medullary respiratory centers by CNS disorders, early septicemia, acidosis, or endotoxemia may result in hyperventilation.
• Anemia, hypovolemia, and hypoxemia of any cause increase respiration in response to tissue hypoxia.

Chronic

• May result from chronic respiratory disease (e.g. pleuropneumonia) or chronic, painful conditions (e.g., laminitis, septic arthritis)
• Overventilation with mechanical ventilators produces low P_{CO_2} in anesthetized patients and sick neonates.
• Hypothermia or decreased metabolic rates seen with prolonged general anesthesia may lower tissue CO_2 production and produce respiratory alkalosis in patients ventilated at appropriate settings.
• Also seen as a compensatory response to primary metabolic acidosis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Physiologic states or disease processes that present with tachypnea—fever, hyperthermia, excitement, anxiety, painful conditions, hypoxemia, metabolic acidosis, and CNS derangements; most of these can be differentiated with history and physical examination findings.
• Most acute problems have low pH and low P_{CO_2}.
• Chronic respiratory alkalosis results in compensatory metabolic acidosis, in which bicarbonate is low and pH should be normal, because compensation is very effective in this circumstance.
• Acute metabolic acidosis has low bicarbonate. Often, pH remains low in severe cases, because respiratory compensation rarely is complete.

LABORATORY FINDINGS

Disorders That May Alter Lab Results

• With poor peripheral perfusion or cardiovascular shunt, results of blood gas analysis on samples taken from peripheral arteries may differ from those taken elsewhere or may not reflect the patient's overall systemic condition.

ALKALOSIS, RESPIRATORY

• Prolonged exposure to air may alter CO_2 levels, because RBC metabolism continues and equilibration with room air may occur.

Valid If Run in Human Lab?
Yes, if properly submitted

OTHER LABORATORY TESTS
• Blood gas analysis is the definitive laboratory test.
• Venous samples may be adequate to identify the condition, but arterial samples are necessary to evaluate adequacy of pulmonary function as a cause.
• Handheld analyzers are now available and easy to use. Some require only small amounts of whole blood; otherwise, heparinize syringes before sampling.
• Perform sampling anaerobically. Immediately evacuate any air bubbles present, and cap the needle with a rubber stopper.
• Analysis should be performed within 15–20 min. If not, samples can be stored on ice, and results will be valid for 3–4 hr.

DIAGNOSTIC PROCEDURES
• Capnography is an indirect method of measuring CO_2 levels.
• Samples of ET gases reflect arterial P_{CO_2}, because ET gas is essentially the same as alveolar gas.
• Continous monitoring can be performed on anesthetized or ventilated patients via a gas-sampling port incorporated into the endotracheal tube or attached to an adapter.
• Because some $\dot{V}/\dot{Q}$ mismatch usually is present, ET levels may underestimate arterial tension by 10–15 mm Hg.
• Periodically compare values obtained via capnography with those via blood gas analysis.

TREATMENT

• Most often, treatment of the primary problem resolves the need for hyperventilation, or metabolic rate will increase and normal P_{CO_2} levels return.
• Alteration of ventilator settings in anesthetized patients is necessary to return CO_2 and pH to normal; however, this may decrease oxygen levels.

MEDICATIONS

PRECAUTIONS
• Monitor ventilated patients continuously for airway obstruction caused by accumulation of secretions, movement of endotracheal tube, kinking of tubing or hoses, and so on.
• Inspiratory pressure should range from 20 to 30 cm H_2O in normal patients.
• Pressures of $\geq$40 cm H_2O may be utilized in patients with abdominal distention—those anesthetized for colic surgery.
• Pressures of >40 cm H_2O compromise venous return and cardiac output.

FOLLOW-UP

PATIENT MONITORING
• Decreased respiratory effort should be seen quickly after resolution of the primary problem.
• Evaluate repeat blood gases analyses soon after institution of mechanical ventilation to ensure appropriate settings have been selected. Further evaluation thereafter is dictated by the patient's condition.

POSSIBLE COMPLICATIONS
Severe alkalemia can result in neurologic signs from decreased cerebral blood flow, muscular excitability, and cardiac arrhythmias.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Hyperchloremia
• Hypokalemia
• Metabolic acidosis

PREGNANCY
Pregnant females often hyperventilate because of decreased lung volume caused by abdominal distention from the gravid uterus.

SYNONYMS
• Hypocapnia
• Hypocarbia

ABBREVIATIONS
• ET = end-tidal, refers to gas expired at the end of expiration, which should be the alveolar gas most recently involved in gas exchange
• $\dot{V}/\dot{Q}$ = ventilation-perfusion ratio

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ALOPECIA

BASICS

DEFINITION
• Alopecia is 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. It is a loss or lack of the hair from skin areas where it is normally present.
• Alopecia is congenital or acquired.
• *Congenital* alopecia is rare in horses.
• *Acquired* alopecia can be subdivided into *infectious* and *noninfectious* causes. 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.

PATHOPHYSIOLOGY
• *Acquired* alopecia represents a disruption in the growth of the hair follicle with or without damage to the hair bulb, follicular wall, hair shaft, or both. 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 adnexa (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.

SYSTEM 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.
• 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 dermatophiliosis
• 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 dermatophiliosis. Folliculitis and furunculosis due to *Staphylococcus* spp. and *Corynebacterium pseudotuberculosis* are 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* causes alopecia. Other fungal causes are mycetoma and the subcutaneous mycosis such as phycomycosis and pythiosis.
• 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., and *Trombiculid* spp.).
• 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 anecdotal reports and one case report in 2006; however, diagnosis is questionable.
  ○ 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

ALOPECIA

- 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.
• 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 helps 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, multifocal well-circumscribed alopecia that progresses to diffuse alopecia. The mane and tail 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
  a. 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 mo later. Alopecia resolves spontaneously if the initiating factor is no longer present, and new anagen hairs grow.

  b. Anagen effluvium—a reaction pattern characterized by shedding during anagen arrest. Severe stresses such as high-dose cytotoxic therapy, infection, or metabolic disease halts anagen hair growth and results 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 either have 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.
• Perform skin scrapings to rule out ectoparasites.
• Perform bacterial and DTM 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 non-affected 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.

PATHOLOGICAL 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

• Alopecia areata has two 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

AIMS OF 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)
• 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

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 dermatophiliosis are zoonotic.

PREGNANCY
• Post-partum 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
• Telogen effluvium = telogen defluxion or defluvium
• Anagen effluvium = anagen defluxion or defluvium

SEE ALSO
• Dermatophytosis
• Pemphigus foliaceus
• Bacterial folliculitis
• Dermatophilosis
• Linear alopecia
• Sarcoids

ABBREVIATION
• DTM = dermatophyte test medium

Suggested Reading

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AMITRAZ TOXICOSIS

BASICS

OVERVIEW
• Amitraz is a formamide acaricide widely used for the control of mites and ticks in veterinary medicine.
• While not approved for use in horses, it is sometimes used intentionally for ectopararsite control and accidental exposures may occur. Amitraz may be deliberately administered intravenously to alter performance in athletic horses.
• Amitraz has complex pharmacological and toxicological effects in animals. It acts on α_2-adrenergic receptors in the central nervous system and 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.
• Amitraz-induced central nervous system stimulation or depression appears to be dose dependent with high doses causing depression while low doses result in hyperreactivity to external stimuli, and in some cases, to aggressive behavior.
• Amitraz reduces smooth muscle activity in the gastrointestinal tract. Clinically and experimentally, this results in a reproducible and reversible impaction colic syndrome.
• Amitraz depresses respiratory rate centrally, probably by inhibiting respiratory neurons located in the ventral portion of the brain. α_2-Adrenergic agonists can reduce both sensitivity of the breathing center to increased P_{CO_2} and tidal volume, thus accentuating respiratory depression.
• Amitraz inhibits antidiuretic hormone and thus may promote diuresis.
• Amitraz and its active metabolite both induce hyperglycemia and hypoinsulinemia by inhibiting insulin secretion mediated by α_2-adrenergic receptors located within the pancreatic islets.
• Amitraz is more slowly metabolized in ponies than sheep, which may explain its toxicity in equines.
• Clinical signs of amitraz toxicosis are usually referable to the central nervous or gastrointestinal systems.

SIGNALMENT
N/A

SIGNS
• Affected horses display signs of tranquilization, depression, ataxia, muscular incoordination, and impaction colic, which may persist for days.
• The impaction colic syndrome is characterized by rapid cessation of gastrointestinal sounds, gastrointestinal stasis, extensive impaction, and tympany throughout the large colon.

CAUSES AND RISK FACTORS
• Amitraz toxicity after topical application is due either to deliberate exposure for parasite control or accidental exposure.
• Because of its known sedative/tranquilizing actions, amitraz may be deliberately administered intravenously to alter performance in athletic horses.
• Amitraz in stored solutions may break down to the highly toxic *N*-3,5-dimethylphenyl-*N*-methyl formadine derivative and more easily induce toxicosis.
• In a chronic low-dose toxicity study in horses, there were no demonstrable adverse effects from amitraz.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Signs of colic can be due to many other disorders.
• Signs of depression and ataxia can be due to viral disease (e.g., rabies, equine encephalomyelitis, West Nile virus), hepatoencephalopathy, meningitis, and 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

PATHOLOGICAL FINDINGS
In an experimental model, 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 absorption.
• If ingested, activated charcoal (1–4 g/kg PO in water slurry [1 g of AC in 5 mL of water]) can be administered via nasogastric tube to reduce absorption.
• Laxatives and/or a laxative diet may be used to manage the gastrointestinal effects.
• Oxygen and mechanical ventilation may be necessary if respiratory depression is severe.
• Fluid therapy may be beneficial.

MEDICATIONS

DRUG(S)
• 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 for amitraz-intoxicated horses.
• Yohimbine is a α_2-adrenergic antagonist with 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 approved to reverse sedative and analgesic effects of medetomidine in dogs. It is considered a new generation of α_2-adrenergic antagonists due 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 has a higher affinity for α_2-adrenergic receptors and is more efficacious in reversing amitraz toxicity in cats than yohimbine. A suggested dose for horses is 0.1mg/kg IV.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• While used in humans to treat amitraz-induced bradycardia, atropine is contraindicated in horses due to the known sensitivity of horses to the anticholinergic effects on gastrointestinal motility.
• Adverse drug interactions are possible with heterocyclic antidepressants, xylazine, benzodiazepines, and macrocyclic lactones.

FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS
The impaction colic effects of amitraz toxicosis may persist for days, but affected horses usually return to normal with treatment.

Suggested Reading

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.

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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, the mammalian body converts it to an excretable form, urea. To a lesser extent, ammonia is eliminated by conversion to glutamine.
• Reference intervals for plasma ammonia are 7.6–63.4 μmol/L, but are very dependent on the type of assay and reported units. Hyperammonemia is when concentrations exceed the established laboratory reference intervals.

PATHOPHYSIOLOGY
• Blood ammonia is derived primarily from dietary nitrogen with the gastrointestinal tract action of bacterial proteases, ureases, and amine oxidases resulting in the major source of blood ammonia.
• Ammonia is also 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.
• If functional liver mass is inadequate, ammonia is not converted to urea, and plasma ammonia concentrations increase. Serum 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.
• Other described neurotoxins in hepatic encephalopathy are: alterations in monoamine neurotransmitters due to altered aromatic amino acids, alterations in γ-aminobutyric acid (GABA) and/or glutamate, and increased endogenous benzodiazepine-like substances.

SYSTEMS AFFECTED
• Nervous—Ammonia is neurotoxic and the brain is affected by high plasma concentrations.
• The degree of hyperammonemia does not necessarily correlate to the severity of hepatic encephalopathy signs because 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 (Alzheimer cells).

GENETICS
N/A

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
• Portal-caval shunts have been reported in foals (rare).
• The presence of hyperammonemia is most often associated with diseases of the liver.

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

Historical
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
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—Hepatic encephalopathy is a prominent clinical feature of hepatic failure in the horse, and is associated with acute 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 pyrrolizidine alkaloid toxicity, acute hepatitis, chronic active hepatitis, hepatotoxic drugs or chemicals, Tyzzer's disease in foals, and hyperlipidemia in ponies with associated hepatic dysfunction.
• Portosystemic shunts—acquired or congenital
• Toxicities—urea toxicity/poisoning, ammonium salt fertilizer toxicity

RISK FACTORS
• Horses in known areas with hepatotoxic plants would be prone to develop hepatopathies.
• Administration of equine-derived biologics may induce hepatopathies.
• Feedstuffs contaminated with high levels of urea, nitrogen, or ammonium salts

DIAGNOSIS

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

CBC/BIOCHEMISTRY/URINALYSIS
Findings vary with the nature of the liver disease.
• CBC—microcytosis may occur in animals with portosystemic shunts, but may be difficult to determine in the horse; RBC histograms may be useful.
• Biochemistry—liver enzymes may be normal in animals with portosystemic shunts, but bile acid concentrations as well as 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 (SDH, GDH, ALP, GGT, or AST) and hyperbilirubinemia, hypoglycemia (not common), hyper- or hypocholesterolemia, or late hepatic failure, and low BUN support a diagnosis of liver disease.
• Urinalysis—ammonia 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.
• Coagulation factor production may be decreased in liver failure resulting in prolonged PT and PTT.

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

OTHER DIAGNOSTIC PROCEDURES
Hepatic biopsy is often necessary.

AMMONIA, HYPERAMMONEMIA

PATHOLOGICAL 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.

TREATMENT

AIMS OF TREATMENT
Prevent signs and adverse effects of hepatic encephalopathy.

APPROPRIATE HEALTH CARE
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
Given above

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 with a hepatopathy and related causes

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 a nonabsorbable aminoglycoside (e.g., neomycin). Metronidazole has been used in companion animals and in horses with acute colitis, but caution should be used with this drug because decreased hepatic clearance also 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 benzodiazepam-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.

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 is advised in critical patients.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Inaccuracy is the biggest problem because of the labile nature of ammonia in blood samples. Delay in processing results in false readings of high 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
N/A

SYNONYMS
N/A

SEE ALSO
• Hepatic encephalopathy
• Liver/hepatic diseases
• Hepatic enzyme
• Bile acids

ABBREVIATIONS
• ALP = alkaline phosphatase
• BUN = blood urea nitrogen
• CNS = central nervous system
• GDH = glutamate dehydrogenase
• GGT = γ-glutamyltransferase
• PT = prothrombin time
• PTT = partial thromboplastin time
• SDH = sorbitol dehydrogenase

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AMYLASE, LIPASE, AND TRYPSIN

BASICS

DEFINITION
• Serum amylase or lipase concentrations above laboratory reference interval in horses are suggestive of pancreatic disease.
• Pancreatic disease is 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 the blood comes from a number of sources, including the 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, and lipemia serum
• Other intestinal diseases—colic, gastric reflux, and tachycardia
• Panniculitis (inflammation of adipose tissue) sometimes evident as colic

CAUSES
• Proximal enteritis
• High intestinal obstructions
• Intestinal mucosal damage
• Hyperlipemia
• Cortisol administration
• Heparin-induced lipoprotein lipase activity
• Obstruction to common bile and pancreatic duct
• Renal disease with renal failure
• Pancreatitis
• Panniculitis

RISK FACTORS
Unknown other than risk factors for colic

DIAGNOSIS

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

LABORATORY FINDINGS
Drugs That May Alter Lab Results
N/A

Disorders That May Alter Lab Results
• Hemolysis inhibits lipase activity.
• Lipemia falsely decreases serum lipase activity measured by kinetic assays.

Valid If Run in Human Lab?
Not unless horse reference intervals are available

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 mean 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.

AMYLASE, LIPASE, AND TRYPSIN

OTHER LABORATORY TESTS

• Serum triglycerides above 500 mg/dL would mean hyperlipemia and expected increases in serum lipase or lipoprotein lipase activity.
• Nonesterified fatty acid (NEFA) concentrations >0.5 mEq/L could mean hyperlipemia due to fat mobilization and expected increases in serum lipase activity.
• Urine GGT:creatinine ratio above 25–50 would indicate renal tubular damage and possible impairment of renal excretion of amylase or lipase.
• Abdominocentesis has been used for cytology to define inflammation and for chemical comparisons of peritoneal amylase and lipase concentrations to serum concentrations. Finding peritoneal fluid concentrations above serum concentrations can be indicative of pancreatitis, but this also can be a nonspecific finding in 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

Treatment varies with the underlying cause. There is no specific treatment for pancreatitis in horses.

MEDICATIONS

As appropriate for underlying disease

FOLLOW-UP

PATIENT MONITORING

• Repeat blood and peritoneal fluid activity of amylase, lipase, and typsin.
• Observe every hour for signs of colic.

POSSIBLE COMPLICATIONS

• Small intestinal obstruction, pancreatitis, and hyperlipemia can cause death.
• Distention of the stomach may cause rupture and death due to peritonitis.
• Leakage of amylase and lipase into the peritoneal cavity can induce nonseptic peritonitis.

MISCELLANEOUS

SEE ALSO

• Colic
• Gastric reflux

ABBREVIATIONS

• GGT = γ-glutamyltransferase
• NEFA = nonesterified fatty acid

Suggested Reading

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ANAEROBIC BACTERIAL INFECTIONS

BASICS

DEFINITION
Anaerobic bacterial infections are caused by organisms that live and grow in the absence of molecular oxygen. Anaerobic bacteria are classified as either facultative or obligate, the former growing with or without oxygen. The anaerobic infections discussed here are caused by obligate anaerobic organisms.

PATHOPHYSIOLOGY
Dermal and mucosal surfaces serve as protective barriers to infection. Normal flora and commensal bacteria contribute to this protective barrier. A breach in this protective barrier allows normal flora or commensal bacteria to gain access and potentially allows pathogenic infection to become established. There is a delicate balance between normal flora and commensal bacteria. When this balance is upset, commensal bacteria may become pathogenic or allow normally sterile sites to become contaminated. In other cases, contamination of a wound or an injection site by environmental organisms may lead to infection. Infectious challenge is dependent on inoculum size, virulence of the organism, and microbial resistance. Anaerobic organisms establish invasion through virulence factors, and release of enzymes and toxins; these result in tissue destruction and provide protection from the host's defenses. 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
• Pleuritis

Gastrointestinal System
• Peritonitis
• Abdominal abscesses
• Enteritis
• Colitis

Musculoskeletal System
• Soft-tissue abscesses
• Foot abscesses
• Thrush
• Canker
• Osteomyelitis
• Sequestrums
• Septic arthritis
• Tenosynovitis
• Clostridial myonecrosis

Neuromuscular System
• Botulism
• Tetanus

Vascular System
• Omphalophlebitis/Omphalitis
• Thrombophlebitis

Hematopoietic System
• Septicemia

Reproductive System
• Metritis

INCIDENCE/PREVALENCE
Dependent on the organism, body system infected, and how early the infection is noted and treatment is instituted

GEOGRAPHIC DISTRIBUTION
Worldwide distribution

SIGNALMENT
Any age, breed, and sex can be affected.

SIGNS
Signs are variable depending on what system is involved and which organism is involved.

Upper Respiratory Tract
• Nasal discharge
• Facial swelling and crepitation
• Malodorous exudates

Lower Respiratory Tract
• Cough
• Nasal discharge
• Malodorous breath, sputum, pleural fluid
• Fever
• Inappetance
• Abnormal lung sounds
• Lethargy

Gastrointestinal System
• Abdominal discomfort
• Fever
• Diarrhea
• Inappetance
• Reflux

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

Neuromuscular System
• Stiffness and rigid posture
• Flashing third eyelid
• Trismus (lockjaw)
• Convulsions
• Dysphagia
• Loss of muscle tone leading to recumbency
• Ataxia

Vascular System
• Swollen and painful umbilicus
• Fever
• Lethargy
• Inappetance
• Swollen, hard, painful veins

Hematopoietic System
• Fever
• Depression
• Tachycardia, +/− arrhythmias
• Tachypnea, +/− dyspnea
• Mucous membrane alterations
• Laminitis
• Abdominal discomfort

Reproductive System
• Vaginal discharge
• Fever
• Lethargy
• Endotoxemia

CAUSES *(most common)*
Upper Respiratory Tract
• *Bacteroides* spp.
• *Fusobacterium* spp.
• *Peptostreptococcus* spp.

Lower Respiratory Tract
• *Bacteroides* spp.
• *Clostridium* spp.
• *Eubacterium lentum*
• *Peptostreptococcus* spp.

Gastrointestinal System
• Peritonitis/abdominal abscesses—*Bacteroides* spp., *Fusobacterium* spp., *Peptostreptococcus* spp.
• Enteritis/colitis—*Clostridium* spp. and *Bacteroides* spp.

Musculoskeletal System
• Soft-tissue/foot abscesses and canker—*Bacteroides* spp. and *Fusobacterium necrophorum*
• Osteomyelitis/sequestrums—*Clostridium* spp.
• Septic arthritis/tenosynovitis—*Clostridium* and *Bacteroides* spp.
• Myonecrosis—*Clostridium* spp.

Neuromuscular System
• Botulism—*Clostridium botulinum*
• Tetanus—*Clostridium tetani*

Vascular System
• *Bacteroides fragilis, Propionibacterium acnes, Peptostreptococcus magnus,* and/or *Clostridium septicum*

Hematopoietic System
• *Clostridium septicum*

Reproductive System
• *Bacteroides fragilis, Peptococcus, Peptostreptococcus, and Fusobacterium* spp.

RISK FACTORS
Concurrent diseases, corticosteroid therapy, antibiotic therapy, immunosuppression, leukopenia, tissue anoxia, prior or concurrent aerobic infections, or the presence of a foreign body may also predispose the horse to anaerobic infections.

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)

ANAEROBIC BACTERIAL INFECTIONS

Lower Respiratory Tract
• Aerobic infection (*Streptococcus* spp., *Staphylococcus* spp., *Escherichia coli, Klebsiella, Pasturella, Bordetella* spp.)
• Fungal infection (*Coccidioides, Cryptococcus, Histoplasma, Aspergillus, Candida* spp.)
• *Mycoplasma* infection
• Thoracic trauma
• Esophageal rupture
• Neoplasia—Primary (rare), metastatic (more common)

Gastrointestinal System
• 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

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

Neuromuscular System
• Botulism—Laminitis, myositis/myopathy, exertional rhabdomyolysis, EPM, tick paralysis
• Tetanus—Acute laminitis, hypocalcemic tetany, rabies, HYPP

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

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

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

CBC/CHEMISTRY/URINALYSIS
• Inflammatory leukogram
• Hyperfibrinogenemia
• Elevated total protein
• +/− Anemia of chronic disease
• Clinical 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.
• Clotting profile
• Fluorescent antibody testing
• Direct immunofluorescence testing

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

OTHER DIAGNOSTIC PROCEDURES
• Fecal cultures
• Bone biopsies
• Identification of toxins or spores in feed, gastrointestinal contents, or serum for botulism (extremely difficult)

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.

TREATMENT

AIMS OF TREATMENT
Elimination of infection with effective antimicrobial therapy and exposure to oxygen, drainage of purulent exudates, and debridement of necrotic tissue if possible

APPROPRIATE HEALTH CARE
Initial hospitalization for intensive therapy, antimicrobials, and debridement/drainage. Hyperbaric oxygen therapy can be utilized in areas with extensive tissue necrosis. Once stabilized, the patient may return home for continued care.

NURSING CARE
Dependent on severity/duration of infection, body system affected, and causative organism. 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 intravenous fluids and/or total/partial parenteral nutrition.

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

DIET
The diet will most likely remain unchanged.

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 skin graft 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).

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Ampicillin
Comparable to penicillin in its spectrum, but it is expensive in some countries, limiting its use to foals. Dose: 25–100 mg/kg IV QID.

Cephalosporins
First-generation cephalosporins are generally less efficacious for anaerobic infections compared to penicillins. Cefoxitin (second generation) kills *Bacteriodes fragilis* but may be used less due to expense. Other cephalosporin activity for anaerobic infections is unpredictable.

Trimethoprim-Sulfonamides (TMS)
TMS is effective against some obligate anaerobes but activity is unpredictable. Dose: 15–30 mg/kg BID PO.

Metronidazole
Consistently effective against obligate anaerobes including *Bacteriodes fragilis,* not effective against facultative anaerobes or aerobes. It is rapidly absorbed after oral administration (bioavailability 75%–85%) and distributes well into synovial fluid, peritoneal fluid, cerebrospinal fluid, and urine, but has poor endometrial concentrations. It is used orally in cases of diarrhea caused by *Clostridium difficile.* It can also be given per rectum to horses that are anorexic or are refluxing; the bioavailability is about 30%. Dose: 15–25 mg/kg PO, IV, or per rectum QID–TID.

Chloramphenicol
All obligate anaerobes are susceptible. It has good tissue penetration into CNS, 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.

Rifampin
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.

Tetracyclines
Can be used for anaerobic infections but penicillin-resistant *Bacteroides* spp. are demonstrating tetracycline resistance. Dose: 5–7.5 mg/kg IV BID.

Aminoglycosides
Ineffective against anaerobes due to mechanism of action requiring oxygen activity

CONTRAINDICATIONS
Any drug causing diarrhea or enteritis. Static drugs like chloramphenicol are not recommended for immunocompromised patients.

PRECAUTIONS
Sustained high dose systemic penicillin therapy may have complications including secondary immune-mediated anemia, thrombocytopenia, and procaine reactions. 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.

POSSIBLE INTERACTIONS
Chloramphenicol may affect the metabolism of other drugs. Concurrent administration of cimetidine with metronidazole may decrease the metabolism of metronidazole and increase the likelihood of dose-related side effects.

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

POSSIBLE COMPLICATIONS
The possibility of complications depends on the body system affected and the severity of the disease. 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
Infection of the reproductive tract may result in breeding and conception problems.

ABBREVIATIONS
- EPM = equine protozoal myeloencephalitis
- HYPP = hyperkalemic periodic paralysis
- NSAID = nonsteroidal anti-inflammatory drug

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ANAPHYLAXIS

BASICS

OVERVIEW

• An immediate hypersensitivity reaction (type I) where antigen-antibody reactions involve mast cells and basophils • IgE is most commonly involved. • Previous exposure to an antigen (allergen) is required to stimulate antigen-specific IgE synthesis. IgE molecules bind to and sensitize the mast cell/basophil. Subsequent exposure to allergen results in release of pharmacologically active substances that mediate anaphylaxis. • Sensitization occurs ≈10 days after first exposure to the allergen. It can persist for years. • Clinical signs usually occur within seconds-minutes of antigen reexposure. They range from mild inflammatory reactions to severe, life-threatening disorders (anaphylactic shock).

SIGNS

• Exposure to the allergen may occur by ingestion, inhalation, contact with skin, or systemic introduction (e.g., IV injection).
• Clinical signs are related to a species-specific tissue distribution of mast cells and smooth muscle. The lung and GIT are the primary target (shock) organs in the horse; involvement of skin and feet also may occur. • Signs are attributable to the inflammatory mediators, enzymes, and cytokines released from sensitized cells. These dilate blood vessels and increase vascular permeability (erythema, edema, and emphysema), stimulate smooth muscle constriction especially in the lungs and GIT (bronchospasm, dyspnea, diarrhea, and abdominal pain), and stimulate secretion of airway mucus and gastric acid. • Reactions may be localized or systemic. Additional signs include restlessness, excitement, urticaria, pruritus, piloerection, generalized sweating, salivation, lacrimation, tachycardia, laminitis, and cardiac arrhythmia. • Severe dyspnea, systemic hypotension, and anoxia may lead to recumbency, convulsions, and death from asphyxia, shock, or cardiac arrest. Death may occur within 5min but usually occurs in ≈1hr.
• Alternatively, signs may be transient and disappear spontaneously within a few hours.

CAUSES AND RISK FACTORS

• A wide range of antigens may induce anaphylaxis, but repeated parenteral administration of the same biological preparations at high doses increases the risk of inducing severe reactions. • Reactions can occur at any time in the course of administration including, rarely, after the first injection of a drug (e.g., penicillin). • Agents implicated include, but are not limited to, insect venom, vaccines, blood products, thiamine, vitamin E/selenium, anthelmintics, penicillin, trimethoprim-sulfa, chloramphenicol, aminoglycosides, tetracyclines, halothane, thiamylal, and guaifenesin. • Rarely reactions may occur during initial exposure to highly charged or osmotically active agents (e.g., iodinated radiocontrast media, dextran). These perturb mast cell membranes. • The sensitizing agent is frequently not identified.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Clinical signs within a few minutes to hours after injection or reexposure to a foreign antigen is a hallmark of anaphylaxis. Response to treatment may help confirm the diagnosis.
• Acute pneumonia can resemble anaphylaxis, but horses are usually more toxemic with lung changes prominent in ventral lobes compared to widespread involvement with anaphylaxis.
• An inappropriate dose or route of drug administration (such as intracarotid injection) may result in collapse associated with neurological deficits (e.g., blindness, seizures).

CBC/BIOCHEMISTRY/URINALYSIS

Hemoconcentration, leukopenia, thrombocytopenia, hyperkalemia, increases in hepatic and myocardial enzyme activities, and coagulation deficits are reported. Their diagnostic relevance is uncertain.

OTHER LABORATORY TESTS

Provocative intradermal/conjunctival challenge testing with the suspected antigen may help confirm diagnosis (response time ≈20min), but value is questionable due to high rate of false-negatives and risk of inducing anaphylaxis.

PATHOLOGICAL FINDINGS

• Severe, diffuse pulmonary emphysema, and peribronchiolar edema are common at necropsy.
• Widespread petechiation, 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 may be observed.

TREATMENT

• Therapeutic goals include reversal of the effects of mediators, prevention of their further release and maintenance of respiratory and cardiovascular function.
• Treatment, if required, should be administered immediately; a few minutes' delay may result in death.
• Identify and remove inciting antigen— if possible.
• Less severe reactions may only warrant monitoring.
• Signs suggestive of anaphylactic shock require aggressive therapy.
• Large-volume fluid therapy is indicated in hypotensive patients.

MEDICATIONS

DRUG(S)

• Epinephrine is the most effective treatment of systemic anaphylaxis/shock. Epinephrine can be given at 0.01–0.02 mg/kg of a 1:1000 dilution [1.0 mg/ml] IM or 0.01 mg/kg of 1:10,000 dilution [0.1 mg/ml] IV.
• Corticosteroids potentiate the effect of epinephrine. Rapid-acting glucocorticoids (prednisolone sodium succinate, 0.25–1.0 mg/kg IV) are recommended in cases of local and systemic anaphylaxis; longer-acting glucocorticoids (dexamethasone, 0.05–0.1 mg/kg IV) are less effective for systemic reactions.
• Antihistamines (tripelennamine hydrochloride 1 mg/kg IM) are in common use but provide variable results due to the presence of mediators other than histamine.
• Atropine is of little value.
• Hypotension refractory to IV fluid and epinephrine therapy may be treated with a dilute dobutamine solution (50 mg in 500mL of 5% dextrose). Administer 1–3 μg/kg/min to effect. Ideally, dobutamine administration requires blood pressure and ECG monitoring.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Epinephrine may cause profound excitement and potentiate myocardial ischemia, increasing the risk of arrhythmia.
• Dobutamine potentiates hypoxemia-induced cardiac arrhythmias.
• Glucocorticoid administration has been associated with laminitis.

FOLLOW-UP

PATIENT MONITORING

• Horses with less severe anaphylactic reactions should be monitored carefully.
• Horses with anaphylactic shock warrant intense therapy and monitoring.
• Continuous blood pressure and cardiac monitoring are recommended to determine efficacy of therapy or worsening of cardiac abnormalities.

PREVENTION/AVOIDANCE

Administration of drugs (especially antibiotics) may result in acute anaphylactic reactions and death. Therefore, caution must be used if there is any suspicion that a horse may be sensitized to these agents.

EXPECTED COURSE AND PROGNOSIS

Variable and will depend on the severity of the reaction, speed of diagnosis, and administration of treatment.

MISCELLANEOUS

SEE ALSO

• Eosinophilia and basophilia
• Blood transfusion reactions

Suggested Reading

Swiderski C. Hypersensitivity disorders in horses. Vet Clin North Am 2000;16:131–151.

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ANEMIA

BASICS

DEFINITION
A decrease in the erythrocyte content or oxygen-carrying capacity of blood as a consequence of a decrease in PCV, RBC count, and, except in cases of intravascular hemolysis, a decrease in Hb concentration to less than the lower limit of the laboratory reference interval.

PATHOPHYSIOLOGY
• Anemia is not a disease but a hematologic clinical sign that develops when one or more of the following 3 basic pathophysiologic mechanisms is present:
  ○ Blood loss (internal/external hemorrhage)
  ○ Increased RBC destruction (intravascular or extravascular hemolysis)
  ○ Decreased or ineffective RBC production
• Characterization of anemia in horses as regenerative (due to hemorrhage or hemolysis) or nonregenerative (due to decreased/ineffective marrow production) is assessed most accurately by examination of bone marrow aspirates. Serial monitoring of PCV and plasma TP concentration also may be helpful. Evaluation of immature RBC and RBC indices in peripheral blood is unrewarding in horses as equine reticulocytes or nucleated RBCs are rarely released into circulation until mature, even during intense erythropoiesis.
• The circulating RBC mass is extremely labile due to the effects of breed, age, level of activity, and splenic contraction, which can increase the RBC by ≈50%.
• Nonregenerative anemia occurs when the rate of erythropoiesis is insufficient to replace aged RBCs removed by the mononuclear phagocyte system. Nonregenerative anemia usually develops slowly due to the long life span of equine RBCs (≈150 days).
• Mechanisms associated with nonregenerative anemia may include:
  ○ Diseases that interfere with erythropoiesis (e.g., by shortening erythrocyte life span or decreasing responsiveness to erythropoietin)
  ○ Deficiency or alterations in specific substances necessary for RBC production or
  ○ Diseases that damage or displace normal bone marrow elements and affect RBC precursors alone, or affect all marrow precursors (WBCs, RBCs, platelets)

SYSTEMS AFFECTED
• Although dependent on the severity and rate of development of anemia, the decreased oxygen-carrying capacity, the decreased circulating RBC mass, and reduced blood viscosity are the main consequences of anemia.
• Hemic/lymphatic/immune systems
• Cardiovascular and respiratory systems
• Hepatobiliary, renal, musculoskeletal, and GI systems

SIGNALMENT
There is no breed, sex, or age predilection for anemia, although some specific primary diseases that result in anemia are more likely in some types of horses.

SIGNS
General Comments
Anemia generally occurs secondary to another disease. Clinical signs relate to the compensatory mechanisms activated in response to anemia as well as the primary disease process, which often are more prominent.

Historical
• Vary depending on the primary disease process, although frequently are related to trauma with visible hemorrhage, and exposure to oxidant toxins, medications, parasites, or infectious agents.
• Most common presenting complaints are exercise intolerance, signs of depression, and inappetence.

Physical Examination
• May be subclinical in horses with chronic anemia, although 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 in cases of hemolysis
  ○ Weight loss, polyuria, and polydipsia in chronic renal failure
  ○ Weight loss, fever, and lethargy in cases caused by chronic infectious, inflammatory, neoplastic, or immune-mediated processes

CAUSES
Hemorrhage
• External hemorrhage due to trauma, surgery, or external parasites
• Epistaxis due to guttural pouch mycosis, pulmonary abscess, severe pnuemonia, EIPH, ethmoid hematoma, fungal rhinitis, sinusitis, neoplasia, or trauma
• Hemothorax due to trauma, ruptured pulmonary abscess, ruptured great vessel, or aneurysm
• Hematuria due to pyelonephritis, erosive cystitis, urolithiasis, urogenital neoplasia, trauma, or urethral ulceration
• Hemoperitoneum due to trauma, ovarian hemorrhage, mesenteric vessel rupture, aneurysm, or abdominal abscess
• GI hemorrhage due to ulceration (e.g., gastric or duodenal ulcers in foals, NSAID toxicosis), parasites (particularly large strongyles), granulomatous inflammatory disease, neoplasia (e.g., gastric squamous cell carcinoma), or foreign bodies
• Coagulopathy

Hemolysis
• Immune-mediated disease—secondary immune-mediated anemia (e.g., bacterial, viral, or parasitic antigens, neoplasia, or drugs), autoimmune hemolytic anemia, and NI
• Infectious diseases—piroplasmosis (*Babesia caballi* and *Theirleria equi*), ehrlichiosis (*Anaplasma phagocytophila*), and EIA
• Oxidant-induced—wilted red maple leaf, phenothiazine anthelmintics, wild onions and familial methemoglobinemia
• Iatrogenic; hypotonic or hypertonic solutions administered IV
• Other toxicities—intravenous dimethyl sulfoxide, heavy metal toxicosis, bacterial toxins (*Clostridium* sp.), snake envenomation
• Miscellaneous—end-stage 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 (especially GI) and nutritional deficiency (particularly foals)
• Bone marrow failure—myelophthisis, myeloproliferative disease, bone marrow toxins (e.g., phenylbutazone), radiation, immune-mediated, and idiopathic hypoplastic anemia
• Miscellaneous—chronic renal disease, chronic hepatic disease, and recent hemorrhage or hemolysis

RISK FACTORS
• Depends 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 phenylbutazone administration
• Geographical location for exposure to infectious agents or toxic plants

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Differentiation of the primary disease causing anemia should be the focus of investigations.
• Initial investigations should focus on identifying the basic mechanisms (see Causes) involved using historical, clinical, hematologic and biochemical findings.
• When onset of clinical signs is sudden, or if there is a history of trauma, severe external or internal hemorrhage or severe hemolysis should be suspected.
• Chronic nonregenerative anemia secondary to infectious, inflammatory, or neoplastic conditions usually is indicated when there is fever, weight loss, and dramatic increases in heart and respiratory rates if the horse is subjected to exercise or stress.
• Laboratory error due to insufficient mixing of samples, delay in analysis of samples. or samples left in hot conditions (hemolysis) may result in a falsely low PCV or RBC count and falsely high MCH and MCHC.

CBC/BIOCHEMISTRY/URINALYSIS
• PCV, total RBC count, and (except in cases of intravascular hemolysis) Hb concentrations below the lower limit of reference intervals.
• Reticulocytes, nucleated RBCs, Howell-Jolly bodies, polychromasia, and anisocytosis are

ANEMIA

rarely observed in horses with regenerative anemia and RBC indices are less useful for diagnosis or classification of anemia.
• A moderate increase in MCV (hemolytic anemia) and RDW (hemorrhagic anemia) may occur 2–3 weeks after onset of regenerative anemia. Additionally, increased MCH values may indicate presence of free Hb and hemolysis and decreased MCH, MCHC, and MCV may indicate iron deficiency anemia.
• Heinz bodies may be observed near the cellular margins of RBCs stained with New Methylene Blue in horses with hemolytic anemia due to oxidative injury.
• Spherocytosis, indicative of immune-mediated hemolytic anemia, may be difficult to detect in equine blood smears due to the small size and lack of central pallor of normal RBCs. In addition, rouleaux formation of normal equine RBCs may complicate identication of autoagglutination in cases of immune-mediated hemolytic anemia.
• Neoplastic cells may be observed in blood smears of horses with myeloproliferative disorders.
• Severe neutropenia and thrombocytopenia may be observed in horses with myelophthisis.
• Horses with blood loss usually have a concomitant decrease in PCV and plasma TP, whereas horses with hemolytic anemia usually have decreased PCV, normal plasma TP and marked increases in serum total direct bilirubin concentration with normal liver enzymes.
• Horses with nonregenerative anemia due to inadequate erythropoiesis usually have decreased PCV, normal or increased TP (due to increased globulin and fibrinogen concentrations), and an inflammatory leukogram.
• Bilirubinuria or hemoglobinuria may occur with some hemolytic disorders.
• Isosthenuria in horses with chronic renal failure

OTHER LABORATORY TESTS
• Positive direct Coombs test is evidence for immune-mediated hemolytic anemia.
• Blood diluted with saline (1:4) aids in differentiating erythrocyte autoagglutination from normal rouleaux formation in horses with immune-mediated hemolytic anemia.
• Serum iron 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 test or C-ELISA test for diagnosis of EIA
• Serology for *Babesia, Theileria* or *A. phagocytophila.*
• Identification of organisms in blood smears

IMAGING
• As indicated to diagnose underlying disease processes
• Ultrasonography or radiography may assist in detecting thoracic or abdominal hemorrhage.

OTHER DIAGNOSTIC PROCEDURES
• Bone marrow aspiration or core biopsy may demonstrate increased erythropoiesis and a decreased myeloid-to-erythroid (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. However, this test lacks sensitivity and specificity.
• Endoscopy to assist in detecting respiratory or GI hemorrhage

TREATMENT

AIMS OF TREATMENT
The major aims of therapy in horses with anemia are to identify and eliminate the primary cause, provide nursing care, ensure adequate tissue perfusion, and administer blood transfusions if indicated.

APPROPRIATE HEALTH CARE
• Inpatient medical management may be necessary depending on severity and rapidity of onset of anemia and underlying disease condition.
• Cross-matched whole blood or packed RBC transfusion is recommended if PCV decreases to <0.08–0.12 L/L (<8%–12%).
• Large-volume, isotonic (e.g., lactated Ringer's solution) or small-volume hypertonic saline (7% NaCl) fluid therapy if patient has signs of hemorrhagic shock

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

DIET
• Ensure access to oxidative plant toxins is eliminated.
• Oral iron supplementation in horses with confirmed iron deficiency anemia. However, for horses with external blood loss, iron supplementation is rarely required because most diets are rich in this element.

SURGICAL CONSIDERATIONS
May be indicated in horses with significant uncontrolled internal hemorrhage, although these horses have a high anesthetic risk.

MEDICATIONS

DRUG(S) OF CHOICE
Specific therapy indicated for the primary underlying disease process

PRECAUTIONS
• Severe reactions to blood transfusions may occur and necessitate careful monitoring and prompt therapy (see Blood Transfusion Reactions).
• Hypertonic saline should be used with caution in horses with uncontrolled bleeding as it may cause increased blood loss.
• Corticosteroids should be used with caution in horses with suspected chronic infectious condition.
• Parenteral administration of iron formulations is not recommended because iron deficiency is extremely rare and there is the possibility of serious adverse reactions.

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.

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

MISCELLANEOUS

SEE ALSO
• Hemorrhage, acute
• Hemorrhage, chronic
• Myeloproliferative diseases
• Blood transfusion reactions

ABBREVIATIONS
• EIA = equine infectious anemia
• EIPH = exercise-induced pulmonary hemorrhage
• GI = gastrointestinal
• Hb = hemoglobin
• IV = intravenous
• MCH = mean cell hemoglobin
• MCHC = mean cell hemoglobin concentration
• MCV = mean cell volume
• NI = neonatal isoerythrolysis
• NSAID = non-steroidal anti-inflammatory drug
• PCV = packed cell volume
• RDW = red cell distribution width
• RBC = red blood cell
• TP = total protein
• WBC = white blood cell

Suggested Reading

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ANEMIA, PURE RED CELL APLASIA

BASICS

OVERVIEW

• Pure red cell aplasia is characterized by selective reduction or hypoplasia of erythroid precursors in the bone marrow resulting in development of a nonregenerative anemia. The white cell (granulocytic) and platelet (megakaryocytic) cell precursors are not affected (as they are in aplastic anemia/pancytopenia).
• In horses, pure red cell aplasia has been reported secondary to repeated doses of rhEPO.
• Primary pure red cell aplasia, described in a number of case reports in dogs and cats and considered to be an immune-mediated disorder responsive to treatment with corticosteroids and/or lymphocytotoxic drugs, has not been reported in horses.

SIGNALMENT

Most commonly this anemia is reported in performance horses such as racing Standardbreds and Thoroughbreds.

SIGNS

• Can occur in the absence of other systemic disease
• Signs depend on the severity and duration of anemia and may consist of poor performance, weight loss, signs of depression, inappetence, weakness, mucous membrane pallor, and tachycardia and polypnea (exaggerated when horses subjected to stress).
• Prolonged or severe nonregenerative anemia may cause tissue hypoxia resulting in cardiac, hepatic, and renal dysfunction and can be life-threatening.

CAUSES AND RISK FACTORS

• The strongest risk factor, and likely cause, of the disorder is repeated administration of rhEPO to race horses in order to increase total red cell mass and oxygen-carrying capacity with the aim of enhancing athletic performance.
• Although the mechanism for erythroid hypoplasia is unclear in this syndrome, the recombinant hormone may induce production of anti-rhEPO antibodies that bind endogenous equine erythropoietin, preventing the latter hormone from stimulating RBC differentiation and multiplication in bone marrow.
• Increased frequency of exposure may lead to an exaggerated immune response and more severe clinical signs.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other Causes of Inadequate Erythropoiesis

• Anemia of chronic disease associated with infectious, inflammatory, or neoplastic disorders. In general, these disorders also result in leukocytosis and elevated fibrinogen concentrations.
• Folate deficiency after treatment of EPM with antifolate drugs, which, paradoxically, occurs in horses administered oral folic acid while receiving antifolate drugs. Diagnosis of EPM and exposure to these drugs easily distinguishes this from pure red cell aplasia.
• Aplastic anemia. Granulocytic and megakaryocytic stem cell lines in bone marrow also fail to undergo differentiation resulting in generalized marrow hypoplasia and peripheral pancytopenia.
• Primary myelophthisic disease may cause anemia in the presence of leukopenia or thrombocytopenia. Because the life span of platelets and WBCs is shorter than that of RBCs, clinical signs of thrombocytopenic hemorrhage, infection, and fever typically precede those of anemia.
• Erythropoietin deficiency from chronic renal failure. Signs specifically referable to the renal system will also be present (e.g., polyuria, polydipsia, renal azotemia, reduced urine concentrating ability).

Other Causes of Anemia

• Chronic EIA may also cause significant bone marrow suppression. These horses are sero- or virus-positive for EIAV.
• Regenerative anemia caused by external or internal hemorrhage and infectious (e.g., low-grade equine piroplasmosis, ehrlichiosis), immune-mediated (e.g., immune-mediated hemolytic anemia and its various causes), or toxic (e.g., oxidant-induced) hemolysis may be differentiated from pure red cell aplasia by the presence of icterus, increased bilirubin concentrations, bilirubinuria, and decreased bone marrow M:E ratios.
• Iron deficiency anemia secondary to chronic hemorrhage. Measurement of decreased serum ferritin concentrations can be used to distinguish this condition from pure red cell aplasia.

CBC/BIOCHEMISTRY/URINALYSIS

• Anemia, with PCV 0.16 L/L (16%) or below
• Normal WBC count, platelet numbers and plasma fibrinogen concentrations
• Normal urinalysis

ANEMIA, PURE RED CELL APLASIA

OTHER LABORATORY TESTS
- Reported cases have demonstrated increased serum iron and serum ferritin concentrations.
- Negative Coggins test for EIA and negative Coombs test for immune-mediated hemolytic anemia
- Bone marrow aspiration demonstrates an increased M:E ratio and erythroid hypoplasia, confirming nonregenerative anemia.
- Serum from affected horses may inhibit rhEPO-induced proliferation of erythroid progenitors in vitro.
- Other diagnostic tests appropriate to rule out other disorders on the differential diagnostic list

TREATMENT
- Avoid further rhEPO administration.
- Blood transfusion from a cross-matched donor is warranted if anemia is severe (< 8–12%) and there are clinical signs of tissue hypoxia (e.g. tachypnea, tachycardia, weak pulse pressure, weakness).

MEDICATIONS
DRUG(S) OF CHOICE
Dexamethasone (0.05 mg/kg once daily) has been used to treat horses with pure red cell aplasia, although efficacy is unproven. The dose should be adjusted or discontinued depending on a favorable or negative response, respectively.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Avoid iron supplementation, because the iron binding-capacity of the serum may be exceeded, leading to hepatic necrosis.

FOLLOW-UP
PATIENT MONITORING
- Monitor the degree of anemia with serial PCV measurements over several weeks to months.
- Some horses are nonresponsive and die despite multiple transfusions and steroid administration, whereas others recover completely.

MISCELLANEOUS
SEE ALSO
- Anemia
- Pancytopenia

ABBREVIATIONS
- EIAV = equine infectious anemia virus
- EPM = equine protozoal myeloencephalitis
- M:E = myeloid:erythroid
- PCV = packed cell volume
- RBC = red blood cell
- rhEPO = recombinant human erythropoietin

Suggested Reading

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ANEMIA, HEINZ BODY

BASICS

DEFINITION
• Acute or chronic hemolytic anemia following exposure to agents that oxidize and denature RBC hemoglobin.
• Heme-depleted hemoglobin aggregates onto RBC membranes to form Heinz bodies, resulting in cells more prone to lysis and removal from the circulation by intravascular hemolysis or via the RES (also called mononuclear phagocytic system).

PATHOPHYSIOLOGY
• Exposure of RBCs to oxidant toxins, drugs, or chemicals results in oxidation of sulfhydryl groups and formation of disulfide linkages in the protein component of the hemoglobin molecule.
• The denatured or heme-depleted hemoglobin precipitates to form Heinz bodies, which attach to the RBC membrane and cause increased cell fragility with resultant intravascular hemolysis, or cause deformability changes with subsequent premature RBC removal by the spleen (extravascular hemolysis).
• Many of these toxins also cause methemoglobin formation. This results from ferrous iron (Fe^{2+}) in the hemoglobin molecule being oxidized to the ferric form (Fe^{3+}). Methemoglobin cannot transport oxygen, resulting in tissue hypoxia.
• Heinz body hemolytic anemia and methemoglobinemia may occur solely, or in combination (the latter producing a more severe clinical syndrome) as a consequence of an oxidant insult.

SYSTEMS AFFECTED
• The systems affected by Heinz body anemia are dependent on the severity and rate of development of the hemolytic anemia.
• Hemic/lymphatic/immune system; regenerative anemia is observed and may result in marked RBC hyperplasia in the bone marrow and splenomegaly. Pyrexia may result from release of hemoglobin and other end products of RBC breakdown.
• Cardiovascular and respiratory systems may be involved resulting in increased heart and respiratory rates, a holosystolic heart murmur, and pallor of mucous membranes.
• Renal system involvement can occur when there is significant intravascular hemolysis with hemoglobinemia causing pigment nephropathy and acute renal failure.
• Hepatobiliary system; hemolytic anemia can result in hyperbilirubinemia and icterus, while hypoxia may result in hepatocellular damage.
• GIT involvement can occur due to hypoxic damage to intestines. This may result in motility disorders, colic or diarrhea.
• Musculoskeletal system involvement can occur due to hypoxic damage to laminae, and shock from severe acute hemorrhage may result in laminitis.

INCIDENCE/PREVALENCE
• No incidence or prevalence data currently is available for oxidant-induced hemolytic anemia in horses.
• Horses with red maple leaf toxicosis have a reported case fatality rate of 30 – 40%.

GEOGRAPHIC DISTRIBUTION
• *Acer rubrum* (red maple) is a common tree in the eastern United States.

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

SIGNS
Historical Findings
• Access to wilted or dried leaves or bark of red maple (*A. rubrum*) or other oxidative toxins (e.g. phenothiazine, wild onions). Dried red maple leaves may remain toxic for as long as 30 days.
• Sudden onset of lethargy, inappetence and signs of depression are common presenting signs.
• May result in acute, apparently unexplained death.

Physical Examination Findings
• Signs of anemia including exercise intolerance, weakness, pale or icteric mucous membranes, tachypnea, tachycardia, or holosystolic heart murmur.
• Brown coloration of mucous membranes, serum/plasma or urine in horses with significant methemoglobin formation (generally from wilted red maple leaf intoxication).
• Occasionally affected horses are febrile.
• Oliguria or polyuria due to acute, pigment-induced renal failure.
• Discolored urine from hemoglobinuria.
• Rectal examination may reveal an enlarged spleen.
• Severely affected horses may become debilitated and (sudden) death may occur.

CAUSES
• Ingestion of wilted or dried red maple leaves or bark.
• Ingestion of wild or domestic onions.
• Phenothiazine toxicity (usually through access to ruminant supplements or salt blocks that contain phenothiazine)

RISK FACTORS
• Exposure to toxins (e.g., wilted or dried [not fresh] red maple leaves, onions)
• Possibly higher risk with ingestion of wilted red maple leaves in autumn compared to spring
• Poorly conditioned horses may be at greater risk of phenothiazine toxicosis
• Horses are innately sensitive to oxidant toxins due to a poorly developed protective mechanism of equine RBC to reverse the natural processes of hemoglobin oxidation (due to the large oxygen load it carries).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other diseases causing anemia must be differentiated from Heinz body hemolytic anemia.
• Hemorrhage is usually evident from history. Physical examination findings may indicate thoracic or abdominal disease.
• Horses with EIA will have a positive Coggins or C-ELISA test.
• Horses with piroplasmosis may have intracellular organisms on Giemsa or New Methylene Blue stained blood smears and/or be seropositive or seroconvert on convalescent titer.
• Horses with granulocytic ehrlichiosis may have granular inclusion bodies in the cytoplasm of neutrophils in Giems stained blood smears and/or be seropositive or seroconvert on convalescent titer.
• Horses with immune-mediated hemolytic anemia will have a positive Coombs test. This test gives a negative result in Heinz body anemia.
• Other causes of hemolytic anemia such as envenomation and heavy metal toxicosis (e.g. chronic consumption of lead, copper or selenium) must be differentiated based on history of exposure.
• Horses with chronic inflammatory, infectious or neoplastic disorders may have anemia, e.g. lymphosarcoma (usually a more chronic history, often including weight loss or organ-specific clinical signs) or purpura hemorrhagica (usually a history of exposure to antigens of *Streptococcus equi* or other respiratory pathogens).
• Familial methemoglobinemia is a hereditary disorder described in Standardbreds.
• Nitrate/nitrite toxicity resulting in methemoglobinemia and anemia can be differentiated based on history of exposure.

CBC/BIOCHEMISTRY/URINALYSIS
• Mild to severe anemia; PCV is often <0.20 L/L (<20%).
• Eccentrocytes, RBC fragments and anisocytosis may be observed on direct blood smears.
• Neutrophilic leukocytosis may be present.
• Increased MCH indicates hemoglobinemia and the presence of intravascular hemolysis.
• Serum chemistry abnormalities may include increased total and indirect bilirubin, increased BUN and creatinine concentrations (in horses with hemoglobinuric nephrosis) and increased serum hepatic enzyme activity (reflecting hepatic hypoxia).
• Results of urinalysis may include bilirubinuria, hemoglobinuria (no microscopic hematuria), methemogobinuria and proteinuria.

OTHER LABORATORY TESTS
• Heinz bodies can be visualized using a blood smear stained with New Methylene Blue. They appear as bluish-green, oval to serrated, refractile granules located near the RBC margin or protruding from the cell.
• Negative direct antiglobulin (Coombs) test.
• Increased RBC osmotic fragility.
• Bone marrow aspiration may reveal a regenerative response and increased erythropoiesis is indicated with an M:E ratio <0.5.
• Blood methemoglobin concentration if mucous membranes or urine are brown-tinged. The normal value is ≤1.77% of total hemoglobin. Affected horses may have methemoglobin concentrations >40% total hemoglobin.

IMAGING
• Splenic/hepatic ultrasonography may be used to detect splenic/hepatic enlargement, which may appear hyperechoic or hypoechoic. There

may be some loss of architecture due to increased fluid component.

OTHER DIAGNOSTIC PROCEDURES
• A thorough diagnostic workup should be undertaken to rule out other causes of hemolytic anemia.

PATHOLOGICAL FINDINGS
• Pale or icteric tissues
• Enlarged liver and spleen and severe, diffuse congestion of the kidneys
• If chronic, possible signs of congestive heart failure include pulmonary embolism, pulmonary edema, cardiomegaly, or hepatic congestion.
• Histopathologic lesions might include renal tubular nephrosis with hemoglobin casts, centrilobular hepatic degeneration and necrosis, and phagocytized RBCs and hemosiderin in the spleen and liver.

TREATMENT

AIMS OF TREATMENT
• Treatment of Heinz body hemolytic anemia involves identification and removal of the oxidant source and provision of supportive care.

APPROPRIATE HEALTH CARE
• Even if several days have elapsed since exposure to the oxidant, activated charcoal (8–24 mg/kg PO via nasogastric intubation) should be administered to reduce further absorption of toxin.
• In-hospital medical management may be necessary depending on severity and rapidity of onset of the anemia.
• Balanced IV fluid therapy with isotonic crystalloid solutions to prevent hemoglobin-induced nephropathy and promote diuresis.
• Cross-matched blood transfusion if PCV decreases to < 8–12%, or if there is persistent tachycardia, tachypnea, prolonged CRT, mucous membrane pallor and weak pulse pressure or a poor response to isotonic fluid therapy.
• Oxygen therapy may be useful but often is ineffective if hemoglobin oxygen-carrying capacity is too low.

NURSING CARE
• Close monitoring of catheter asepsis, vital signs, fluid rates (to avoid hemodilution) and blood hematology and clinical chemistry are indicated and likely aid recovery.
• Concomitant monitoring for renal failure induced by hemoglobinuria or hypoxia and for laminitis also is necessary.

ACTIVITY
• Minimize activity and stress.
• No forced exercise

DIET
• Provide the horse with a balanced diet, including good-quality hay and grain.
• Fresh water should be available *ad libitum*.

CLIENT EDUCATION
• The hazards of exposure to wilted red maple leaves (including red maple hybrids) should be explained and suggestions given concerning housing and removal of branches blown down in storms or cut down in areas where horses may have access to them.

MEDICATIONS

DRUG(S)
• There is no specific medicinal treatment for Heinz body anemia and treatment is mainly supportive.
• Along with administration of isotonic IV fluids for pigment-induced nephropathy, furosemide or dopamine may be indicated in cases with oliguria or anuria.
• Dexamethasone (0.05–0.1 mg/kg IV q12–24 h) may help to stabilize cellular membranes and decrease phagocytosis of damaged RBCs.

CONTRAINDICATIONS
• Use of Methylene Blue or other reductive therapy may be detrimental, because these agents may enhance Heinz body formation.

ALTERNATIVE DRUGS
• Vitamin C or ascorbic acid (30 mg/kg twice daily, diluted in IV fluids) may be used as antioxidant therapy in cases involving methemoglobin-associated conditions although there is no strong evidence of efficacy.

FOLLOW-UP

PATIENT MONITORING
• Serial determination of PCV should be performed to assess the bone marrow regeneration and response to treatment. The PCV should remain stable or slowly increase over time.
• Renal function should also be reassessed and signs reflective of laminitis monitored, particularly in horses also receiving corticosteroid therapy.

PREVENTION/AVOIDANCE
• Limiting access to excess phenothiazine, onions, or wilted red maple leaves.

POSSIBLE COMPLICATIONS
• Laminitis
• Nephropathy
• General debilitation
• Abortion, weak foals

EXPECTED COURSE AND PROGNOSIS
• Prognosis for recovery depends on the amount of oxidant ingested and whether or not methemoglobinemia also is present. If the inciting cause can be removed and methemoglobinemia is minimal or absent, the prognosis for recovery is fair to good. Several weeks may be required for full recovery.
• The prognosis is guarded in horses with red maple leaf toxicosis when methemoglobinemia is present.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Methemoglobinemia
• Pigment nephrosis

PREGNANCY
• Horses severely affected, and with general debilitation, may abort or deliver a weak foal.

SYNONYMS
• Methemoglobinemia
• Oxidative hemoglobinemia
• Oxidant-induced hemolysis

SEE ALSO
• Anemia
• Anemia, immune-mediated
• EIA
• Methemoglobinemia

ABBREVIATIONS
• BUN = blood urea nitrogen
• C-ELISA = competitive enzyme-linked immunosorbent assay
• CRT = capillary refill time
• EIA = equine infectious anemia
• GIT = gastrointestinal tract
• IV = intravenous
• MCH = mean corpuscular hemoglobin
• M:E = myeloid:erythroid
• PCV = packed cell volume
• PO = per os
• RBC = red blood cell
• RES = reticuloendothelial system

Suggested Reading

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ANEMIA, IMMUNE-MEDIATED

BASICS

DEFINITION
• IMHA is an acute or a chronic destruction of RBCs associated with immunoglobulin and/or complement attachment to either RBC antigens or foreign antigens coating the surface of RBCs.
• Affected RBCs are most commonly removed by the RES (also called mononuclear phagocyte system) after immunoglobulin-mediated opsonization (extravascular hemolysis).
• Less commonly, they may undergo intravascular, complement-mediated lysis.

PATHOPHYSIOLOGY
• IMHA most commonly occurs secondary to 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); or
  ○ Stimulate the immune system resulting in production of antibodies with cross-reactivity to RBCs (e.g., infectious agents, neoplasia).
• Occasionally, the immune system produces specific autoantibodies to normal erythrocyte antigens (e.g., primary or idiopathic autoimmune hemolytic anemia, NI, or transfusion reaction).
• Antibody- and/or complement-coated RBCs are removed from the circulation by extravascular hemolysis (if removed by the RES) and/or intravascular hemolysis (if complement-mediated).

SYSTEMS AFFECTED
• The hemic/lymphatic/immune systems are involved due to intravascular and/or extravascular hemolysis. In cases where extravascular hemolysis predominates, splenomegaly may occur. Pyrexia may result from release of hemoglobin and other end products of red cell breakdown.
• Cardiovascular and respiratory systems may be involved with increased heart and respiratory rates, holosystolic heart murmur, and pallor of mucous membranes observed.
• Hepatobiliary system—Hemolytic anemia can result in hyperbilirubinemia and icterus while hypoxia may result in centrilobular degeneration.
• The renal system may be involved in cases where significant intravascular hemolysis and hemoglobinemia cause pigment nephropathy.
• The gastrointestinal tract may be involved due to hypoxic damage to intestines resulting in motility disorders, colic or diarrhea.

INCIDENCE/PREVALENCE
• No incidence or prevalence data are available for immune-mediated hemolytic anemia for specific horse populations. Weak evidence from in-practice experience suggests IMHA is a rare consequence of other disease states in adult horses. These forms of IMHA are reported to have a low case fatality rate.
• NI, which is a specific form of IMHA, is reported in foals in most countries, particularly horse studs where there are large numbers of breeding mares.

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

SIGNS
General Comments
IMHA often reflects a primary, underlying disease process such as infection or neoplasia.

Historical
• 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 are common presenting signs.
• There may be a history of exposure to blood transfusion(s) or certain drugs.

Physical Examination
• Signs of anemia—Severity proportional to the degree of anemia.
• Exercise intolerance, weakness, pale or icteric mucous membranes, fever, tachypnea, tachycardia, holosystolic heart murmur, abdominal pain, and hemoglobinuria may be observed.
• Rectal examination may reveal an enlarged spleen.
• In foals with NI, there is usually an acute onset of intravascular hemolysis, with weakness and icterus during the first few days of life.
• Severe debilitation and death may occur in severe cases.

CAUSES
Primary Immune-Mediated
• NI
• Autoimmune hemolytic anemia
• Incompatible blood transfusion

Secondary Immune-Mediated
• Infectious—e.g., EIA, acute viral infections, infection with *Clostridium perfringens*, injection site abscess
• Neoplastic—e.g., lymphosarcoma and hemangiosarcoma
• Drug-associated—e.g., penicillins, cephalosporins, and trimethoprim-sulfamethoxazole
• Microangiopathic—disseminated intravascular coagulation
• Systemic lupus erythematosus

RISK FACTORS
• Foals born to multiparous dams that have previously had a blood transfusion(s), or the mare is known to be 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 must be differentiated from IMHA.
• Horses with hemorrhage (acute or chronic) often have a history of external blood loss or signs referable to thoracic or abdominal disease.
• Horses with Heinz-body anemia (e.g., wilted red maple leaf toxicosis, onion toxicosis, phenothiazine toxicosis) may have a history of exposure to oxidative toxins and presence of Heinz bodies or methemoglobinemia on routine blood analysis.
• Horses with purpura hemorrhagica often have a history of exposure to *Streptococcus equi* ss *equi* or other respiratory tract pathogens. In these cases edema of the legs, abdomen, and face and petechial hemorrhages of mucous membranes are common.

CBC/BIOCHEMISTRY/URINALYSIS
• PCV is often <0.20 L/L (<20%).
• May have neutrophilic leukocytosis
• RBC autoagglutination may be observed, but must be distinguished from rouleaux formation or RBC clumping due to other inflammatory disorders. Spherocytes may be observed in blood smears, but are more difficult to identify in horses due to the lack of central pallor in normal equine RBCs.
• Increased MCH 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 where intravascular hemolysis occurs.

OTHER LABORATORY TESTS
• Positive direct antiglobulin (Coombs) test, which 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.
• Confirmation of true autoagglutination is performed by diluting EDTA-anticoagulated blood 1:4 with physiologic saline solution. RBCs should remain augglutinated with saline dilution.
• 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 (M:E 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;
  ○ 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.

IMAGING
• Splenic/hepatic ultrasound determines splenic/hepatic enlargement and highlights

ANEMIA, IMMUNE-MEDIATED

hyperechoic or hypoechoic areas indicating loss of architecture.
• Radiography of the thorax is usually within normal limits unless a primary neoplasia is the underlying cause.

OTHER DIAGNOSTIC PROCEDURES
A thorough diagnostic workup should be performed to rule out neoplasia and infectious causes of secondary IMHA.

PATHOLOGICAL FINDINGS
• Necropsy findings may include an enlarged liver and spleen and pale or icteric tissues.
• If chronic, there may be signs of congestive heart failure (with pulmonary embolism, pulmonary edema, cardiomegaly), renal tubular nephrosis with hemoglobin casts, and centrilobular hepatic degeneration and necrosis.

TREATMENT

AIMS OF TREATMENT
• 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 and induce diuresis.
• 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 and often are found to have incurable neoplastic disease.
Additionally, long-term administration of corticosteroids may increase the risk of laminitis, tendon laxity, and immunosuppression leading to secondary infections.
• Clients should be educated in preventative measures for NI.

SURGICAL CONSIDERATIONS
Consider splenectomy if the primary cause cannot be identified.

MEDICATIONS

DRUG(S)
• In adults, corticosteroids (dexamethasone, 0.05–0.2 mg/kg IV or IM q12–24h) 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 (2–3 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.

CONTRAINDICATIONS
Corticosteroids may exacerbate underlying infectious diseases so should be used only in horses that are EIA (Coggins) negative and horses free of other infectious disorders.

PRECAUTIONS
• Cross-match blood before blood transfusion.
• Corticosteroid therapy may predispose horses to laminitis and exacerbate an undiagnosed infectious process. They also should be used with caution in pregnant mares.

ALTERNATIVE DRUGS
The immunosuppressive agents azathioprine (5 mg/kg PO once daily) and cyclophosphamide (300 mg/m^2 body surface area) have been used successfully in one horse that was nonresponsive to corticosteroids.

FOLLOW-UP

PATIENT MONITORING
The PCV should be carefully monitored during dexamethasone treatment. The frequency of dexamethasone administration can be increased to twice daily in horses initially commenced on once/day treatment if the PCV does not stabilize within 24–48hr.

PREVENTION/AVOIDANCE
Avoid drugs known to have caused secondary IMHA.

POSSIBLE COMPLICATIONS
• Pigment nephropathy may occur 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 replenish as the immune-mediated response resolves. This may take several weeks in some horses.
• Horses requiring constant corticosteroid treatment (if diagnosed with idiopathic autoimmune hemolytic anemia) may have an incurable underlying disease such as neoplasia (e.g., lymphosarcoma). The prognosis for survival in these horses is poor.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Pigment nephropathy with intravascular hemolysis
• Laminitis

PREGNANCY
Use corticosteroids cautiously in pregnant mares.

SYNONYMS
• Autoimmune hemolytic anemia
• Immune-mediated hemolytic disease

SEE ALSO
• Anemia
• Anemia, Heinz-body
• Babesiosis
• Equine infectious anemia
• Hemorrhage, acute

ABBREVIATIONS
• C-ELISA = competitive enzyme-linked immunosorbent assay
• IM = intramuscular
• IV = intravenous
• EIA = equine infectious anemia
• IMHA = immune-mediated hemolytic anemia
• MCH = mean corpuscular hemoglobin
• M:E = myeloid:erythroid ratio
• NI = neonatal isoerythrolysis
• PCV = packed cell volume
• PO = per os
• RBC = red blood cell
• RES = reticuloendothelial system

Suggested Reading

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ANEMIA, IRON DEFICIENCY

BASICS

OVERVIEW

• Iron is stored in horses as hemoglobin (65% of total iron stores), ferritin, and hemosiderin.
• Iron deficiency may arise from either chronic external loss of blood (most common in adult horses) or dietary deprivation (in young rapidly growing foals). Unless adult horses have inadequate access to soil, pasture or feed, inadequate iron intake is unlikely.
• Iron deficiency results in delayed hemoglobin synthesis, resulting in arrested and ineffective RBC maturation in bone marrow and anemia. The small hemoglobin deficient RBCs (i.e., hypochromic microcytes) produced have reduced deformability and life span.
• Nonregenerative anemia and reduced blood hemoglobin concentration may lead to compromised oxygen delivery to tissues.
• Nonheme, iron-containing enzymes may also be depleted and result in impairment of cell-mediated immunity and neutrophil killing of ingested bacteria.

SIGNALMENT

• No breed or sex predilections
• Rapid growth of foals is associated with high tissue demands for iron. Mare's milk has low iron concentrations (≈0.88 μg/g of milk by 2 weeks and ≈0.6 μg/g by 8 weeks postpartum) and therefore deficiency may occur in foals with limited access to pasture, iron-rich soils, or not consuming forage or grain.

SIGNS

• Initially, clinical signs may be absent or mild due to adequate physiologic compensation for the gradual reduction in oxygenation.
• Lethargy and exercise intolerance may be the first overt clinical signs noted.
• When PCV is <12%, tissue hypoxia can cause tachycardia, tachypnea, pale mucous membranes, systolic heart murmur, and signs of depression.

CAUSES AND RISK FACTORS

Risk factors for chronic hemorrhage may include inadequate preventative anthelmintic use, phenylbutazone administration, and exposure to toxins.

Chronic, Low Grade Hemorrhage

• Severe internal parasitism (*Strongylus vulgaris*, small strongyles) or external parasitism (e.g., heavy infestation of sucking lice—*Haematopinus asini*)
• Bleeding GI, respiratory, and urinary tract lesions (e.g., gastroduodenal ulcers, NSAID toxicosis, neoplasia [especially gastric squamous cell carcinoma], hemorrhagic or erosive cystitis, guttural pouch mycosis, and ethmoid hematoma)
• Coagulopathies leading to chronic blood loss (e.g., heritable coagulopathies, warfarin toxicosis, moldy sweet clover [dicumarol] toxicosis)

Diet

Inadequate dietary intake (foals)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Causes of low-grade, hemolytic anemia must be ruled out including immune-mediated hemolysis, oxidant-induced hemolysis, and parasite-induced hemolysis. Distinguishing features may include hemoglobinemia, hemoglobinuria, and a normal serum protein concentration. Serum iron concentrations may be increased.
• Causes of decreased erythrocyte production must be ruled out including anemia of chronic disease and aplastic anemia. Increased serum ferritin concentrations are typical in anemia of chronic disease and bone marrow morphology is diagnostic for aplastic anemia.

CBC/BIOCHEMISTRY/URINALYSIS

• Normochromic, normocytic anemia is initially observed, but usually develops into a microcytic, hypochromic, nonregenerative anemia in later stages. Microcytosis often precedes hypochromasia.
• Thrombocytosis may be observed.
• Decreased plasma protein and albumin concentrations

OTHER LABORATORY TESTS

Initial Stage

• Decreased stainable iron (Prussian Blue stain) in bone marrow macrophages
• Decreased serum ferritin concentrations (reference range 85–155 ng/mL) where serum ferritin <45 ng/mL is highly indicative of iron deficiency.

Later Stages

• Decreased SI concentration (reference range, 120–150 μg/dL)
• Normal or increased TIBC (reference range, 300–400 μg/dL)
• Decreased percentage transferrin saturation (= 100 × SI/TIBC). Reference range is 30%–50% (Arabian horses ≈68%) with values <16% reflecting insufficient iron available for erythropoiesis.
• Presence of microcytes (decreased MCV) with decreased hemoglobin concentration (hypochromia, decreased MCHC)
• SI, serum ferritin, and TIBC may be affected by conditions other than iron

ANEMIA, IRON DEFICIENCY

deficiency including acute and chronic inflammation, renal disease, and corticosteroid therapy.

OTHER DIAGNOSTIC PROCEDURES

- Cytology of bone marrow aspirate may show a predominance of late rubricytes and metarubricytes, depletion of macrophage iron, and sideroblasts.
- A diagnostic workup of causes of chronic hemorrhage is required.

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% (0.08 L/L) or there are clinical and laboratory signs of tissue hypoxia.

MEDICATIONS

DRUG(S)

- Appropriate treatment of underlying disease process to resolve chronic blood loss
- Oral ferrous sulfate (1.0 g/450 kg body weight) is the safest means to administer iron. Iron requirements for a 450-kg horse are ≈800 mg/day for maintenance and ≈1100–1300 mg/day during pregnancy and lactation.
- Iron cacodylate (1 g/adult horse) may be given slowly IV, but must be used with caution due the possibility of an anaphylactic reaction.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Do not administer iron dextrans due to idiosyncratic reactions (anaphylaxis and sudden death).
- Iatrogenic iron overload has been reported in adult horses given unnecessary oral and/or parenteral iron supplementation.
- Do not give foals iron-containing products during the first 2 days of life as fatal toxic hepatopathies may result.

FOLLOW-UP

PATIENT MONITORING

- Monitor response to therapy of underlying disease and ensure no further hemorrhage.
- Monitor SI, TIBC, and percentage saturation at ≈2-week intervals.
- Discontinue iron supplementation when values for PCV, SI, TIBC, and percentage saturation return to within reference ranges.

PREVENTION AVOIDANCE

Ensure that sucking foals have access to pasture and, when of an appropriate age, forage and grain.

POSSIBLE COMPLICATIONS

May result in death if horses are left untreated

EXPECTED COURSE AND PROGNOSIS

- If the underlying disease is successfully treated, iron deficiency anemia is reversible.
- Weeks of iron supplementation may be required, depending on the severity of anemia and the degree of iron store depletion.

MISCELLANEOUS

SEE ALSO

- Anemia
- Anemia, aplastic (pure red cell aplasia)
- Anemia, Heinz body
- Anemia, immune-mediated
- Hemorrhage, chronic equine infectious anemia

ABBREVIATIONS

- GI = gastrointestinal
- PCV = packed cell volume
- SI = serum iron
- TIBC = total iron-binding capacity

Suggested Reading

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ANESTRUS

BASICS

DEFINITION/OVERVIEW
Period of reproductive inactivity, ovaries small and static. Characterized by indifferent behavior of mare to stallion.

ETIOLOGY/PATHOPHYSIOLOGY
Seasonally polyestrus, estrous cycles (*ovulatory period*) in spring and summer; primarily regulated by photoperiod; light begins a cascade:
• Increasing day length decreases melatonin secretion (pineal gland).
• Decreasing melatonin allows increased production and release of GnRH.
• Increased GnRH stimulates gonadotropin release (FSH and LH).
• FSH promotes folliculogenesis and ultimately the onset of estrus behavior.
• When sufficient LH is present, ovulation occurs; end of vernal transition = onset of cyclicity
Average estrous cycle—21 days (range 19–22); time between 2 ovulations that coincides with progesterone levels of <1 ng/mL. Estrus, estrous cycle lengths—quite repeatable in individual mare, cycle to cycle. Key hormonal events of equine estrous cycle:
• FSH causes follicular growth.
• Estradiol (follicular) stimulates increased GnRH pulse frequency and secretion of LH.
• LH surge causes ovulation; estradiol returns to basal levels 1–2 days post-ovulation.
• Progesterone (CL origin) rises from basal levels (<1 ng/mL) at ovulation to >4 ng/mL by 4–5 days post-ovulation.
• Progesterone causes decreased GnRH pulse frequency and increased FSH secretion; it stimulates a new wave of follicular development beginning in diestrus.
• Endogenous $PGF_{2\alpha}$ (endometrial) is released 14–15 days post-ovulation causing luteolysis and concurrent decline in progesterone levels.

SYSTEMS AFFECTED
• Reproductive
• Endocrine

SIGNS
Historical
• Chief complaint—failure of mare to accept stallion. Rarely reported—stallion-like behavior.
• Teasing—Review methods used, records, frequency, teaser type (pony, horse, gelding), stallion behavior (aggressive/passive, vocalization, proximity), and handler experience.
• Seasonal influences—Evaluate normal individual variation of onset, duration, termination of cyclicity.
• Individual reproductive history—estrous cycle length, teasing response, foaling data, previous genital tract injuries/infections, and relationship to clinical abnormalities.
• Pharmaceuticals—Current and historical drug history may relate to clinical abnormalities.

Physical Examination
• Poor body condition/malnutrition may contribute to anestrus.
• Poor perineal conformation can result in pneumovagina, ascending infections and/or urine pooling, anestrus/infertility.
• Clitoral enlargement may relate to drug history—anabolic steroids, progestational steroids, or intersex conditions.
• TRP is essential to evaluate suspected anestrus mare. Assess uterine size and tone, ovarian size, shape and location, and cervical relaxation. Serial TRP 3 times a week over 1–3 weeks to completely define status.
• Transrectal U/S to define normal and abnormal features of uterus and ovaries
• Vaginal examination (digital and/or speculum) to identify inflammation, urine pooling, cervical competency, conformational abnormalities; determine stage of the estrous cycle.

CAUSES
Normal Physiologic
• *Winter anestrus*—≈20% of mares cycle through the winter (Northern Hemisphere—November to January); most enter a period of ovarian quiescence. Failure to cycle is normal during winter anestrus.
• *Two transitional phases* occur yearly—*autumnal* transition (ovulatory to anestrus) and *vernal* transition (anestrus to cyclicity/ovulatory). Behavioral patterns vary during transition periods. Individual variation in onset and length of transitional periods is normal.
• Behavioral anestrus (silent heat)—a normal estrous cycle as determined by serial TRP, failures to demonstrate estrus
• Pregnancy—After recognition of pregnancy, CL progesterone production continues; majority of pregnant mares exhibit anestrus behavior.
• Pseudopregnancy—Embryo dies after recognition of pregnancy or formation of endometrial cups, resulting in persistent CL activity and behavioral anestrus.
  ○ eCG (by endometrial cups, 35–150 days pregnancy) is luteotropic, role in maintaining primary CL and formation of secondary CLs of pregnancy.
• Postpartum anestrus—>95% of mares reestablish cyclic activity ≤20 days postpartum. Some fail to continue cycling after first postpartum ovulation, due to prolonged CL function or ovarian inactivity.
• Age-related conditions—Puberty occurs at 12–24 mo. Individual variation by age, weight, nutrition, and season. Aged mares can have protracted seasonal anestrus; >25 years may last for senescence, cycles cease.

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 is XO monosomy (Turner's syndrome).
• Intersex conditions—XY sex reversal chromosomal abnormality

Endocrine Disorders
• Cushing's disease—Adenomatous hyperplasia of pars intermedius of pituitary leads to destruction of FSH- and LH-secreting cells and/or overproduction of glucocorticoids.
  ○ May be increased adrenal-origin androgens causing suppression of the normal hypothalamic-pituitary-ovarian axis
  ○ Primary hypothalamic-pituitary-ovarian axis interference is proposed as cause of anestrus.

Ovarian Abnormalities—See Large Ovary Syndrome
• Ovarian hematoma • Ovarian neoplasia

Uterine Abnormalities
Pyometra—Severe uterine infections can destroy the endometrium, prevents formation and release of $PGF_{2\alpha}$, needed for CL regression. Appears as prolonged diestrus or anestrus.

Iatrogenic/Pharmacologic
• Anabolic steroids—Affected mares behave as if in anestrus, silent estrus, or show increased aggression.
• Progesterone/progestin—Continued treatment inhibits estrus behavior.
• NSAIDs—Potential to interfere with endogenous $PGF_{2\alpha}$ release; result is prolonged CL activity. No evidence that exogenous treatment [recommended therapeutic dose] inhibits spontaneous formation and release of endogenous $PGF_{2\alpha}$

RISK FACTORS
Postpartum anestrus occurs more often in early foaling mares and mares in poor body condition at time of parturition.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Differentiating Causes
• Critically review teasing records, general and reproductive history—foaling data, evidence of infections, injuries, medications that may affect reproductive health. • Serial TRP with/without U/S over 2–3 weeks is adequate to differentiate transitional and behavioral anestrus; fewer examinations for pregnancy, hypoplastic ovaries, large ovary syndrome/ovarian neoplasia, pyometra • EED after the formation of endometrial cups, may result in anestrus or pseudopregnancy. • Gonadal dysgenesis and intersex conditions—base on history (anestrus, irregular estrus), TRP and U/S (small ovaries, flaccid uterus and cervix), repeated low serum progesterone concentrations (<1 ng/mL q7days for 5 weeks) and karyotype.

OTHER LABORATORY TESTS
• Serum progesterone
  ○ Basal—<1 ng/mL—no functional CL present.
  ○ Active CL—>4 ng/mL
• Serum testosterone and inhibin
  ○ Mare—<50–60 pg/mL, inhibin <0.7 ng/mL.
  ○ Levels suggestive of GCT/GTCT (in a nonpregnant mare) are—testosterone >50–100 pg/mL (if thecal cells are significant

ANESTRUS

tumor component), inhibin >0.7 ng/mL, progesterone <1 ng/mL.
• Serum eCG—measured by ELISA
• GnRH stimulation test—to ID primary hypothalamic or pituitary dysfunction
• Karyotype—if suspect gonadal dysgenesis or intersex conditions

IMAGING
Transrectal U/S of reproductive tract. See related topics.

DIAGNOSTIC PROCEDURES
Uterine cytology, culture and biopsy—diagnosis, select treatment/monitor progress of pyometra and endometritis

TREATMENT
• Combination—alter management techniques, vary teasing methods to elicit a response from a mare and/or base timing of AI on TRP and U/S.
• Artificial lighting—hasten onset of vernal transition, also known as manipulation of photoperiod. Duration of transition remains unchanged. Expose mare to 14.5–16 hr light/day or, alternatively, to additional 1–2 hr light at 10 hr after dusk (*flash lighting*). A minimum of 60 (some mares up to 90) days of supplemental light is needed to progress from anestrus to cyclicity. Added light typically starts December 1 (Northern Hemisphere).
• Mare due to foal early in the year—add supplemental lighting 2 mo prior to parturition, improve postpartum cyclicity and decrease potential for lactational anestrus.
• Treating a mare with progesterone while she is in anestrus/early vernal transition will suppress ovarian activity. Coupling artificial lighting as described above for 60 days, until minimal ovarian activity is achieved (multiple 15- to 20-mm follicles present), followed by progesterone therapy, can achieve earlier onset of regular estrous cycles.
• Ovarian tumors/ovariectomy
  ○ With removal of a GCT/GTCT, suppression (inhibin) of contralateral ovary is gone, allowing it to recover.
  ○ Latent period for return of ovarian activity is affected by when tumor is removed; e.g., best if OVX is done in autumn, then mare can respond to normal increase in day length as she transitions into the next season.

MEDICATIONS
DRUG(S) OF CHOICE
• $PGF_{2\alpha}$ (Lutalyse [Pfizer] 10 mg IM) or analogs—lyse persistent CL. Multiple injections may be needed with pseudopregnancy.
• Deslorelin injectable GnRH analog to induce ovulation within 48 hr if follicle(s) >30 mm
• hCG 2500 IU IV to induce ovulation in mares with follicle(s) >35 mm • Altrenogest (Regu-Mate [Intervet] 0.044 mg/kg PO daily minimum 15 days) to shorten vernal transition, providing follicles >20-mm diameter are present at onset of treatment and mare is exhibiting behavioral estrus • Its use in seasonally deep anestrus mares is not recommended. • $PGF_{2\alpha}$ (Lutalyse) on day 15 of altrenogest treatment increases the reliability of this transition management regimen.

CONTRAINDICATIONS
$PGF_{2\alpha}$ and its analogs—contraindicated in mares with heaves or other bronchoconstrictive disease

PRECAUTIONS
• Horses
  ○ $PGF_{2\alpha}$ causes sweating and colic-like symptoms due to its stimulatory effect on smooth muscle cells. If cramping has not subsided within 1–2 hr, symptomatic treatment should be instituted.
  ○ Antibodies to hCG can develop. Desirable to limit its use to no more than 2–3 times during one breeding season. Half-life of antibodies ranges from 30 days to several months; typically do not persist from one breeding season to the next
  ○ Deslorelin implants not currently sold in the United States; injectable product is available. Implants were associated with suppression of FSH and decreased follicular development in the diestrus period immediately following implant use; led to prolonged interovulatory period in nonpregnant mares. Implant removal post-ovulation helped some.
  ○ Progesterone supplementation—potential to decrease uterine clearance; its use may be contraindicated in mares with a history of uterine infection.
  ○ Altrenogest, deslorelin, and $PGF_{2\alpha}$ should not be used in horses intended for food.
• Humans—With either product below, accidental skin exposure should be washed off immediately.
  ○ $PGF_{2\alpha}$ or its analogs should not be handled by pregnant women or persons with asthma or bronchial disease.
  ○ Altrenogest should not be handled by pregnant women or persons with thrombophlebitis, thromboembolic disorders, cerebrovascular or 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 [Schering-Plough Animal Health] 250 μg/mL IM), a prostaglandin analog. Used in similar fashion as natural prostaglandin, but fewer side effects. Not currently approved for use in horses, but is an analog in widespread use in absence of an alternative.

FOLLOW-UP
PATIENT MONITORING
• Serial TRP during the breeding season; establish diagnosis for etiology of anestrus behavior.
• Pseudopregnant mares return to normal cyclic activity upon regression of endometrial cups, as eCG decreases.
  ○ eCG can persist up to 150 days.
  ○ If embryonic death is confirmed, intervention up to 150 days may be ineffective.

POSSIBLE COMPLICATIONS
Infertility may result from intractable persistent anestrus.

AGE-RELATED FACTORS
Postpartum anestrus occurs more often in old mares.

MISCELLANEOUS
PREGNANCY
$PGF_{2\alpha}$ to pregnant mares can lyse CL, causing abortion, especially if <40 days pregnant. Rule out pregnancy before injecting this drug or its analogs.

SYNONYMS
• Gonadal dysgenesis • Gonadal hypoplasia
• Lactational anestrus • Postpartum anestrus

SEE ALSO
• Abnormal estrus intervals • Aggression
• Cushing's syndrome • Disorders of sexual development • EED • Endometritis
• Large ovary syndrome • Ovarian hypoplasia
• Ovulation failure • Prolonged diestrus
• Pyometra

ABBREVIATIONS
• AI = artificial insemination
• CL = corpus luteum
• eCG = equine chorionic gonadotropin
• EED = early embryonic death
• FSH = follicle-stimulating hormone
• GCT/GTCT = granulosa cell tumor/granulosa-theca cell tumor
• GnRH = gonadotropin-releasing hormone
• hCG = human chorionic gonadotropin
• LH = luteinizing hormone
• OVX = ovariectomy
• $PGF_2\alpha$ = natural prostaglandin
• TRP = transrectal palpation
• U/S = ultrasound, ultrasonography

Suggested Reading
Hinrichs K. Irregularities of the estrous cycle and ovulation in mares (including seasonal transition). In: Youngquist RS, Threlfall WR, eds. Current Therapy in Large Animal Theriogenology. St. Louis, MO: WB Saunders Elsevier, 2007:144–152.
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ANGULAR LIMB DEFORMITY

BASICS

DEFINITION
ALD is an abnormal rotation from the normal axis of the limb in the frontal plane. Valgus is the lateral deviation of the limb distal to the location of the deformity, 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 (e.g., carpal valgus).

PATHOPHYSIOLOGY
There are two main categories associated with the etiology of ALD—perinatal factors and developmental factors.

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 (manually correctable in the early stages). • 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. If the joints are unevenly loaded while the bones are not yet ossified, the uneven pressure may result in abnormal shape once ossification occurs, leading to permanent ALD.

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).

SYSTEM AFFECTED
Musculoskeletal—One or more joints may be involved in the front limbs and/or hindlimbs, including the fetlock, carpus, and tarsus. Most commonly, the angular limb deformity originates at the carpus. Carpal valgus deformity is the most commonly observed ALD, but tarsal valgus and fetlock varus are also seen commonly.

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.

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
• Natural growth of foals can lead to spontaneous correction of the ALD. However, foals with ALD must be monitored appropriately, as if they do not correct their conformation, there is a limited window during which time surgical intervention can occur prior to various physis closures. • Ideal conformation varies between breeds and type of work desired (i.e., pleasure versus racing). • Each foal will respond differently to treatment.

Historical
• Prematurity/dysmaturity • Placentitis or twinning in the mare • Witnessed or suspected trauma at the physis • Crib-feeding practices on the farm

Physical Examination
• A valgus deformity results in what is termed "splay foot" due to the lateral deviation; outward rotation of the entire limb ("toed out") should not be mistaken for deviation of the limb at the level of the carpus or fetlock (carpal valgus or fetlock valgus). • A varus deformity results in what is termed "pigeon toed" due to medial/axial deviation.

CAUSES

Perinatal Factors
• Prematurity • Dysmaturity • Hypothyroidism • Twin foal • Placentitis • Ligamentous laxity • Perinatal soft tissue trauma • Intrauterine malpositioning

Developmental Factors
• Nutritional imbalances • External trauma to the physis • Overload of a limb • Excessive exercise

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

OTHER 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 (long cassettes will allow for easier assessment of the deformity). Only two views are required for ALD (lateromedial and dorsopalmar/dorsoplantar). If there is evidence of joint problems, oblique images should be included.

OTHER DIAGNOSTIC PROCEDURES
• Examination of the limb in both a standing and a flexed position • Observation of the foal from several angles • Examination from a position perpendicular to a frontal plane through the limb—the toe should point in the same direction as the carpus.
• Observation of the foal at a walk
• Manipulation/palpation of the limb can help determine whether the deformity was caused by perinatal (manual correction) or developmental factors (permanent).

PATHOLOGICAL FINDINGS
• Asymmetric early closure of either the medial or lateral physis due to injuries or inflammation • Delayed ossification

TREATMENT

AIMS OF TREATMENT
To manage ALD, either conservatively or by providing surgical intervention, if needed, in order to correct growth. 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 without adverse consequences.
• For foals with incomplete ossification of the cuboidal bones and deviation of the limbs
• 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.
• 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.

ANGULAR LIMB DEFORMITY

ACTIVITY

Stall Rest

• Effective treatment for newborn foals, specifically for incomplete ossification and straight limbs. The maximum period of rest is 1 month. • Foals with ALD due to disproportionate growth at the level of the physis (>10 degrees) and diaphyseal deformities should be stall rested for 4–6 weeks. • Foals with laxity of the periarticular supporting structures require 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

• Early recognition and treatment are important. • 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. This allows close monitoring to determine if the foal will self-correct or need surgical intervention.

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. Studies have indicated an 80% improvement in foals that have undergone a periosteal transection. The procedure is relatively inexpensive and easy, with the ability to be performed in the field. • Foals should have this surgery at 4 weeks (earlier if the deformity is severe) to 3 months of age (limited growth beyond this time). The timing of surgery also depends on the site of abnormal growth (below). • 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.
• Keep the foal on 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 (MClll/MTlll and proximal phalanx = 2 months, tibia = 4 months, and radius = 6 months). • The bridging is performed on the convex aspect of the affected limb. • The goal is to retard growth on the convex side of the limb, allowing the shorter side of the affected limb to keep growing. • Screws and cerclage wires are the most commonly used implants.
• Current techniques include two screws, one inserted in the center of the epiphysis and one into the proximal physis, with cerclage wire connecting the two in a figure-eight pattern. A more recent technique includes one transphyseal screw, which can be used across the physis of the distal MClll/MTlll, the distal radius and the distal tibia. Surgical staple techniques and small bone plates have also been described for use in transphyseal bridging. Periosteal transaction and elevation are often performed in combination with growth retardation techniques. • A bandage should be maintained for 10–14 days. • Stall rest the foal for 2–3 days following surgery.
• Evaluate radiographically every 2 weeks to assess. • 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 osteotomy, step osteotomy in the sagittal plane and step osteotomy in the frontal plane. • Most frequently performed on MClll/MTlll
• Maintain a bandage and splint or cast for several weeks following surgery.

MEDICATIONS

DRUG(S)

For surgical cases, NSAIDs (flunixin meglumine 1.1 mg/kg IV daily or q12h) and antibiotics (i.e., gentamicin 6.6 mg/kg IV daily or Amikacin 25–30 mg/kg IV daily and potassium penicillin 22,000 IU/kg IV q6h) can be given as needed perioperatively.

CONTRAINDICATIONS

N/A

PRECAUTIONS

NSAIDs can have an ulcerogenic effect on foals. Ulcer prophylaxis may include oral Gastrogard (omeprazole 1–2 mg/kg PO once daily) or ranitidine (10 mg/kg PO q8h or 1.5 mg/kg IV q8h in 250 mL saline) while the foal is in the hospital and receiving NSAIDs.

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 on their own.
• Following transphyseal bridging, the horse should be monitored so that once the correction has taken place and radiographs have confirmed this, the implants are removed to prevent overcorrection. • Foals with incomplete ossification of the cuboidal bones 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 is possible if transphyseal bridging implants are not removed as soon as ALD has been corrected.
• Failure of passive transfer 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. It has been reported that an athletic use was pursued for 80% of foals with ALD of the carpus and 27.3% of foals with ALD of the metacarpus/metatarsus after transphyseal bridging.

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Timing of intervention is important, as the greatest effects of surgical manipulation will occur during the rapid growth phases.

ZOONOTIC POTENTIAL

N/A

PREGNANCY

N/A

SYNONYMS

N/A

SEE ALSO

Flexural limb deformity

ABBREVIATIONS

• ALD = angular limb deformity
• MClll = third metacarpal bone
• MTlll = third metatarsal bone

Suggested Reading

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Author Shannon J. Murray
Consulting Editor Margaret C. Mudge

ANHIDROSIS

BASICS

OVERVIEW
Anhidrosis (also known as dry coat disease or a nonsweater, or as "dry puffers") is the inability to sweat effectively in response to appropriate stimuli. The current theory is that overstimulation of sweat gland β_2-receptors causes diminished function or a period of unresponsiveness of the receptors.

SIGNALMENT
No coat color, age, sex, or breed predilections. Up to 20% of horses may be affected when exercising in a hot, humid climate.

SIGNS
- Extended tachypnea after exercise, later combined with a lack or reduction of sweating
- Horses recently introduced into a hot and humid climate may sweat excessively before showing signs of anhidrosis.
- With acute onset, horses may demonstrate partial or complete absence of sweating when exposed to appropriate stimuli.
- Horses with long-standing anhidrosis may exhibit dry and flaky skin with alopecia, lethargy, and decreased water intake. Body areas that may retain the ability to sweat include under the mane, saddle and halter regions, and the axillary, inguinal, and perineal regions.

CAUSES
- Systemic—Heat-stressed horses may have higher-than-normal levels of circulating catecholamines. Anhidrotic horses have significantly higher levels of epinephrine compared with normal horses at rest. These catecholamines act as β_2-agonists and may overstimulate the sweat gland receptors, which results in either desensitization of the receptor (i.e., the receptor is sequestered away from its normal site to another site within the cell) or down-regulation (i.e., decreased number of receptors). Down-regulation is a long-term mechanism that may involve altered synthesis or degradation of receptor proteins.
- Horses maintained in hot, humid climates are at risk, and exercise magnifies this risk.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Respiratory diseases that cause an increase in the respiratory rate (both obstructive and restrictive diseases)

CBC/BIOCHEMISTRY/URINALYSIS
Dehydration, as evidenced by prerenal azotemia and, possibly, increased urinary specific gravity

DIAGNOSTIC PROCEDURES
Intradermal injections, in the neck area below the mane, of a specific β_2-agonist (e.g., terbutaline sulfate, salbutamol sulfate), serial dilutions (10^{-3} to 10^{-8} [w/v]), and a control injection of sterile saline— read the results at 30 min. Normal horses sweat in response to all dilutions, whereas anhidrotic horses show a diminished response to some or all.

PATHOLOGICAL FINDINGS/HISTOPATHOLOGY
Thickened basal lamina, evidence of poor myoepithelial contraction, thickened connective tissues, and marked reduction of vesicles in the secretory cells. Luminal microvilli often are absent and the lumen of the duct is obstructed with cellular debris.

TREATMENT
- Advise clients that sound environmental management is the only reliable treatment option at present.
- Horses with acute anhidrosis who exhibit signs of heat stress should be immediately taken to a cooler environment, and attempts to reduce the body temperature should be made.
- Restrict to a stall with adequate air movement (i.e., a fan) during hot periods of the day.
- If exercise is necessary, do so during the cooler periods of the day. After exercise, make sure the horse is "cooled off" adequately by hosing it down with water.

ANHIDROSIS

• Concentrates should be fed in decreased amounts. Allow access to cool, fresh water as well as water with electrolyte supplementation.
• Inform clients that these horses will be prone to poor performance and will only improve once the capability to sweat effectively has returned.
• It may not occur again in a horse's lifetime but is usually is a lifelong problem. However, when it does occur attempts to provide a cool, dry environment must be made.
• If exogenous β_2-agonists such as clenbuterol for concurrent respiratory problems are being administered, consider this as a possible cause and cease administration.

MEDICATIONS

DRUG(S) OF CHOICE
• Supplemental electrolytes, especially potassium salts, can be added to the feed or water.
• Some anecdotal reports of success with iodinated casein (10–15 g/day for 4–8 days) and with 1000–3000 IU PO of vitamin E (i.e., natural α-tocopherol) daily for 1 mo.
• Amino acid supplements, especially those with tyrosine, are commercially available. (Tyrosine is necessary for the resensitization of sequestered β_2-receptors.)

PRECAUTIONS
Anaphylaxis has been reported when using injectable vitamin E.

ALTERNATIVE DRUGS
Drugs that either reduce down-regulation or decrease sympathetic drive are still in the investigative stages.

FOLLOW-UP

PATIENT MONITORING
Normal thermoregulatory abilities allow a horse to reduce its body temperature to within normal limits approximately 30 min after exercise. Monitor respiration and rectal temperature post-exercise.

PREVENTION/AVOIDANCE
• Do not expose anhidrotic horses, especially when exercising, to extreme ambient temperatures.
• Exercise during the cooler periods of the day and stall the horse in a cooler environment (e.g., an air-conditioned stall) during the hotter periods of the day.
• Relocating the horse to a more temperate climate may lead to resolution of the clinical signs.
• Avoid administration of exogenous β_2-agonists such as clenbuterol.

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, but not necessarily, 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

SEE ALSO
Skin diseases

Suggested Reading
Hubert JD, Norwood G, Beadle RM. Equine anhidrosis. Vet Clin North Am Equine Pract 2002;18:355–369.

Authors Jeremy D. Hubert and Ralph E. Beadle
Consulting Editor Michel Lévy

ANOREXIA AND DECREASED FOOD INTAKE

BASICS

DEFINITION

Anorexia is the loss of appetite or lack of desire for food. Some conditions that cause anorexia may not lead to complete loss of appetite, but merely reduced food intake.

PATHOPHYSIOLOGY

Appetite Suppression

• Anorexia in general appears to be the result of a modification of central regulation of feeding behavior in the hypothalamus. • Many factors and substances appear to 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, as well as causing dehydration, electrolyte imbalances, acid-base disorders, micronutrient deficiencies, and changes in concentrations of neurotransmitters, hormones, or mediators. • Serotonin agonists decrease food intake, apparently via central histaminergic activity. • The neurotransmitter neuropeptide Y and various cytokines may cause CACS. Cytokines induce anorexia when administered peripherally or directly into the brain. Administration of specific cytokine antagonists mitigates cachexia in experimental animal models. • Other primary disease conditions, such as infection, inflammation, injury, toxins, immunologic reactions, and necrosis, may cause anorexia via cytokines as well. • 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. • 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.

SIGNALMENT

Any signalment

SIGNS

May be a lack of interest in food or an interest only in certain types of food. May note difficulty or inability in prehension, chewing, or swallowing of food, and food may appear at the nostrils. Nasal discharge and cough can occur due to foreign material entering trachea, acquired aspiration pneumonia, or both. Some of the signs seen in horses with anorexia may include the following:

• Increased salivation (ptyalism) due to:
• Inability to swallow • Hypoesthesia of the face (CN-V) • Neurogenic atrophy of the masticatory muscles (CN-V, motor component)
• Bilateral paralysis of facial muscles (CN VII)
• May expel partially chewed food ("quidding")
• Oral lesions

CAUSES

Anorexia

Commonly due to gastrointestinal or abdominal disorders, including colic. May be secondary to one of the following primary disease processes in any organ system:

• Inflammation • Infections (bacterial, viral, fungal, or parasitic) • Injury • Toxins
• Immunologic reactions • Malignancy
• Necrosis • Dehydration • Electrolyte imbalances • Acid-base disorders • Severe respiratory distress • Neurologic disorders
• Uremia or renal tubular acidosis • Cardiac disease • Metabolic disorders • Side effects of medications • Pain

Food prehension problems may be due to:

• Pain in lips, tongue, or mouth (e.g., ulcers, lacerations, dental "points") • Mechanical obstructions (e.g., severe swelling of the lips)
• Nervous dysfunction of the lips or tongue

Mastication problems may be due to:

• Pain (in teeth, mandibles, maxilla, sinuses, muscles, or temporomandibular joint)
• Neurologic dysfunction

Swallowing problems may be due to:

• Pain (in pharynx or esophagus) • Mechanical obstructions in pharynx or esophagus
• Neurologic dysfunction (e.g., CN-IX although questioned lately) • Unpalatable food due to contamination or spoilage

RISK FACTORS

Choke, which is the layperson's term for feed impaction of the esophagus, occurs more commonly in animals that bolt their food or have defective teeth.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Anorexia

• Colic • Esophagitis • Gastrointestinal ileus
• Gastric ulcers and pyloric stenosis • Peritonitis

Secondary to a primary disease process in any organ system

• Renal failure (uremia)
• Renal tubular acidosis
• Cardiac amyloidosis
• Severe respiratory distress
• Depression of the nervous system—especially cerebral disorders
• Inflammation or endotoxemia
• Injury
• Toxins (e.g., monensin, lead)
• Immunologic reactions
• Malignancy
• Necrosis

Secondary to diseases leading to dehydration, electrolyte imbalances, or acid-base disorders

• Hypertriglyceridemia
• Side effect of metronidazole or toltrazuril or cyproheptadine

Dysphagia

Food prehension problems may be due to:

• Mucosal disease—oral erosions or ulcers, swellings, growths, or crusts
• Vesicular stomatitis
• Contact with chemical irritants
• Phenylbutazone toxicity
• Mechanical trauma; yellow bristle grass, foxtails
• Postsurgical complications
• Mechanical obstructions—severe swelling of the lips
• Snake bites
• Bee stings
• Nervous dysfunction of the lips
• Bilateral CN-VII damage
• Yellow star thistle (nigropallidal encephalomalacia) poisoning
• Rabies
• Equine protozoal myelitis
• Verminous encephalitis

Mastication problems may be due to:

• Musculoskeletal problems
• Postsurgical complications
• Pain (in teeth, mandibles, or maxilla (e.g., fractured mandible), sinuses (e.g., sinusitis), temporomandibular joint
• Pain or other problems of masticatory muscles (e.g. myodegeneration)
• Vitamin E/selenium deficiency causing masseteric myopathy
• Botulism or tick paralysis causing paresis of masticatory muscles and tongue
• Tetanus causing trismus
• Mechanical obstructions
• Premolar caps (deciduous teeth)
• Foreign body
• Neurologic problems
• CN-V bilaterally
• CN-XII damage
• Rabies
• Lead toxicity
• Equine protozoal myelitis
• Verminous encephalitis

Swallowing problems may be due to:

• Pain in pharynx or esophagus
• Esophagitis
• Pharyngitis or pharyngeal trauma
• Pharyngeal abscess
• Neoplasia
• Strangles
• Hyoid bone injury
• Mechanical obstructions or abnormalities in pharynx or esophagus
• Esophageal intraluminal occlusion; choke or foreign body
• Esophageal stricture, stenosis, or diverticulum
• Megaesophagus or esophageal ectasia
• Persistent right aortic arch
• Esophageal intramural inclusion cysts
• Rostral displacement of the palatopharyngeal arch
• Dorsal displacement of the soft palate in foals
• Ulcers of the soft palate secondary to dorsal displacement in adult horses
• Pharyngeal foreign body
• Cysts—epiglottic, dorsal pharyngeal, aryepiglottic, soft palate, guttural pouch, or laryngeal
• Strangles or other retropharyngeal abscess causing external compression
• Cleft palate
• Neoplasia of the tongue
• Nervous or neuromuscular problems
• Severe cerebrum or brain stem (forebrain) disease; hydrocephalus, trauma, leukoencephalomalacia, equine protozoal myelitis, verminous encephalitis
• Lead toxicity
• Senecio toxicity
• CN-IX damage

ANOREXIA AND DECREASED FOOD INTAKE

• Guttural pouch disease (CN-IX to CN-XI damage)
• White muscle disease–nutritional muscular dystrophy
• Hyperkalemic periodic paralysis
• Tetanus
• Botulism
• Tick paralysis
• Weak suckle reflex, poor pharyngeal tone
• Prematurity/dysmaturity, neonatal maladjustment syndrome, bacterial meningitis, viral encephalitis, hypoglycemia, or depression in foals
• Electrolyte disorders (hypokalemia and hypocalcemia)
• Post upper respiratory surgical complications
• Postanesthetic myasthenia
• Myotonia congenita
• Rabies
• Ruptured rectus capitus ventralis muscle
• Grass sickness
• Pharyngeal–cricopharyngeal incoordination

CBC/BIOCHEMISTRY/URINALYSIS
• Free (unconjugated or indirect) bilirubin elevations, unless cachexic, in which case bilirubin levels may be normal
• Laboratory findings (CBC, biochemistry, fibrinogen) consistent with the primary disease process (e.g., inflammation, internal organ damage)
• Laboratory findings (CBC, biochemistry, fibrinogen) consistent with a secondary disease (e.g., aspiration pneumonia)

OTHER LABORATORY TESTS
Based on primary disease processes

IMAGING
• Radiography of guttural pouches for swallowing problems
• Fluoroscopy or radiography of barium swallow for swallowing problems
• Radiography of mandible, temporo-mandibular joint and teeth for painful mastication
• Radiographs of thorax for aspiration pneumonia
• Ultrasound of the tongue
• Abdominal ultrasound for primary inflammatory or neoplastic problems

OTHER DIAGNOSTIC PROCEDURES
• Examination of the food supply for evidence of contamination or spoilage
• Careful observation of individual when offered food
• Oral examination for painful chewing
• Passage of a nasogastric tube (for difficulty swallowing) to rule out "choke"
• Neurologic examination for difficulty swallowing
• Endoscopy of guttural pouches for nervous cause of swallowing problems
• Endoscopy of pharynx, larynx, and esophagus for swallowing problems
• Rectal examination for internal organ disease

TREATMENT
Depends on the primary problem

DIET/ACTIVITY
Offer highly palatable and varied feed in cases of anorexia. Supply feed that is easy to chew and swallow in case 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 of 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
Depends 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 (CACS), a syndrome of anorexia and weight loss that occurs secondary to malignancy
• Guttural pouch disease can cause neurologic damage to CN-IX–CN-XI and impair chewing and swallowing as well as causing mechanical obstruction to swallowing.
• Tetanus
• Neonatal maladjustment syndrome may interfere with swallowing or the suckle reflex.
• Moderate jaundice may occur due to increased indirect bilirubin levels in the blood. This is an idiosyncratic finding in the horse that occurs with fasting or decreased intake of feed.
• 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.
• Secondary or conditional PCM involves weight loss with prolonged anorexia.
• Aspiration pneumonia occurs secondary to dysphagia.

AGE-RELATED FACTORS
Cleft palate, hydrocephalus, and nutritional muscular dystrophy (white muscle disease) are noted most commonly in the neonatal period.

ZOONOTIC POTENTIAL
Rabies can cause anorexia or dysphagia. Precautions should be taken while examining and treating the patient.

SYNONYM
Decreased appetite

SEE ALSO
• Aspiration pneumonia
• Botulism
• Cerebral disorders of the central nervous system
• Choke
• Colic
• Dental disease
• Epiglottic cysts
• Esophagitis
• Fractured mandible
• Gastric ulcers
• Gastrointestinal ileus
• Guttural pouch disease
• Lead toxicity
• Monensin toxicity
• Organophosphate toxicity
• Peritonitis
• Pharyngeal abscess
• Phenylbutazone toxicity
• Rabies
• Renal failure (uremia)
• Ruptured rectus capitis ventralis muscle
• Sinusitis
• Snake bites
• Strangles
• Tetanus
• Tick paralysis
• Yellow star thistle poisoning
• Vesicular stomatitis
• Vitamin E/selenium deficiency causing swollen masseter muscles

ABBREVIATIONS
• CACS = cancer-related anorexia/cachexia syndrome
• CN = cranial nerve
• PCM = protein–calorie malnutrition

Suggested Reading

Amory H, Perron MF, Sandersen C, Delguste C, Grulke S, Cassart D, Godeau JM, Detilleux J. Prognostic value of clinical signs and blood parameters in equids suffering from hepatic disease. J Equine Vet Sci 2005;25:18–25.

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Author Gail Abells Sutton
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa

ANTHRAX

BASICS

OVERVIEW
Anthrax is a rapidly fatal septicemic disease of animals and human beings caused by *Bacillus anthracis,* which occurs in localized regions worldwide. In the horse, infection usually results from ingestion of soil, forage, or water contaminated with *B. anthracis* spores. In the animal, the organism germinates and produces exotoxins 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 are formed that are a potential source of infection for other animals.

SIGNALMENT
• Gender, age, or breed disposition have not been reported.
• In cattle, anthrax is reported to occur in adult animals, with males more frequently affected, probably due to differences in grazing habits.

SIGNS
• Fever, depression, and death in <4 days is characteristic of the acute form.
• Severe colic, bloody discharge from body orifices, and painful subcutaneous swellings may be noted.
• A chronic form resulting in pharyngeal edema has been described.
• The peracute form, in which death occurs with few clinical signs, appears to be less common in horses than in ruminants.

CAUSES AND RISK FACTORS
• The source of infection is usually soil contaminated by exudates from infected animals. *B. anthracis* forms spores that are very resistant to environmental conditions and most disinfectants, and these spores may persist in the soil for decades. Ingestion of contaminated soil, feed, or water is the most common route of infection, but the organisms may also be inhaled or inoculated by biting insects.
• Anthrax is most common in tropical and subtropical climates but is seen sporadically in temperate regions, usually in the summer. Anthrax usually occurs in regions with alkaline soils and with climatic cycles of heavy rain and drought.
• Overgrazing increases the risk of disease by increasing the ingestion of soil. Coarse forages may contribute to infection by causing breaks in the oral mucosa.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Lightning strike can be differentiated on the basis of history of storms and absence of post-mortem findings typical of anthrax.
• Colic and enteritis can be differentiated by finding evidence of gastrointestinal disease at post mortem.
• Purpura hemorrhagica has similar signs but is not rapidly fatal.
• Toxicity can be differentiated based on history and lack of post-mortem findings typical of anthrax.
• Malignant edema may appear similar, but crepitation of swellings is not found with anthrax.

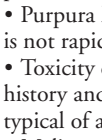
CBC/BIOCHEMISTRY/URINALYSIS
Routine laboratory findings have not been reported.

OTHER LABORATORY TESTS
Bacterial culture of blood or exudate is useful, although results may be negative early in disease or if antibiotics have been administered. Cultures should only be performed in a facility capable of containment to prevent infection of laboratory personnel.

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
• Organisms may be seen by microscopic examination of blood smear or edema fluid. Bacilli are gram-positive, have blunt ends, are encapsulated, and occur singly or in short chains.
• Fluorescent antibody of blood or tissue may be diagnostic.

PATHOLOGIC FINDINGS
• Due to human health risk and danger of environmental contamination, necropsy should not be performed if anthrax is strongly suspected. Diagnosis can be made without necropsy.
• Dark, nonclotting blood from orifices; absence of rigor mortis; splenomegaly; and lymphadenopathy are hallmarks of anthrax.
• Serosal and mucosal hemorrhage and edema of many organs are seen.



TREATMENT

• The high mortality and rapid course of disease usually limit 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 q4–6 h) or oxytetracycline (5–11 mg/kg IV q12 h) is traditionally recommended. Enrofloxacin (7.5 mg/kg PO q24 h or 5 mg/kg IV q24 h) is potentially a good choice in adult horses. Continue treatment for at least 5 days.
• Anthrax antiserum may be useful but is not available in the United States.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

• Regulatory officials should be notified when anthrax is suspected and the premises placed under quarantine.
• Carcasses should not be opened, and may be disposed of by burning or deep (>6 ft) burial with lime. The area can be disinfected with 5% aqueous lye or 10% formaldehyde.
• Susceptible animals should be vaccinated. An avirulent live spore vaccine is administered subcutaneously and provides immunity in 1 week. Some authors recommend a second vaccination in 2–4 weeks. Annual boosters are required to maintain immunity. Severe adverse reactions have been reported; therefore, the vaccine is indicated only in endemic regions. No antibiotics should be administered within 5 days before or after vaccination, or the vaccine organism may be inactivated.

MISCELLANEOUS

ZOONOTIC POTENTIAL
Anthrax is a zoonosis; inhalation or ingestion of spores may lead to fatal disease. Gloves and mask should be worn if it is necessary to contact infected material or animals. Cutaneous anthrax is the most common form in human beings, resulting from inoculation of an open wound with spores.

SYNONYMS
• Woolsorters' disease
• Charbon
• Splenic fever

Suggested Reading
Pipkin AB. Anthrax. In: Smith BP, ed. Large Animal Internal Medicine. Philadelphia: Mosby, 2002:1074–1076.

Author Laura K. Reilly
Consulting Editors Ashley G. Boyle and Corinne R. Sweeney

ANTICOAGULANT RODENTICIDE TOXICOSIS

BASICS

OVERVIEW
• Ingestion of anticoagulant rodenticides interferes with normal blood clotting in horses.
• Anticoagulant rodenticides are the most commonly used class of rodenticides.
• First-generation anticoagulants (i.e., warfarin, pindone, coumafuryl, coumachlor) are short-acting coumarin derivatives requiring multiple feedings to result in toxicosis.
• Intermediate anticoagulants (i.e., chlorophacinone, diphacinone) require fewer feedings than first-generation chemicals and, thus, are more toxic to nontarget species.
• Second-generation anticoagulants (i.e., brodifacoum, bromadialone, difethialone) are highly toxic to nontarget species after a single feeding.
• Most anticoagulant rodenticides commonly used today are long-acting, second-generation anticoagulants, with activity in the body of ≅1 month.
• Coagulopathy has been reported in horses after a dose of brodifacoum of 0.125 mg/kg (equal to ingestion by an average-size horse of 1 kg of bait containing 0.005% brodifacoum).
• Warfarin has been used therapeutically (30–75 mg per 450 kg) in horses with navicular disease, laminitis, venous arteritis, DIC, and thrombophlebitis.

SIGNALMENT
• May affect all animals
• Poisoning can occur after accidental ingestion of bait packages or as a result of malicious intent.
• Poisoning is rare in horses because of the amount of bait needed to be ingested to cause signs.
• Iatrogenic warfarin toxicosis may result from overdosing, dietary vitamin K deficiency, or concurrent use of protein-bound drugs that increase the concentration of active, unbound warfarin.

SIGNS
• Bleeding diathesis ranging from mild to severe
• Hemorrhage—internal or external
• Signs generally manifest within 3–5 days after ingesting bait.
• Signs are similar to those seen with dicumarol toxicosis.

CAUSES AND RISK FACTORS
The mechanism of anticoagulant rodenticide toxicosis is the same as that for dicumarol toxicosis.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Moldy sweet clover ingestion—history of ingesting plant, detection of dicumarol in forage or tissue samples
• DIC—reduced plasma concentrations of platelets and coagulant and anticoagulant proteins; increased concentrations of coagulant byproducts; petechial hemorrhages
• Severe liver disease—clinical pathology, liver biopsy

CBC/BIOCHEMISTRY/URINALYSIS
Blood loss anemia

OTHER LABORATORY TESTS
• Elevated PT and aPTT
• Chemical analysis of whole blood or liver tissue for specific anticoagulant

IMAGING
N/A

DIAGNOSTIC PROCEDURES
N/A

PATHOLOGICAL FINDINGS
Hemorrhages may occur in any part of the body.

TREATMENT

• Blood or plasma transfusions may help.
• Handle horses with care to avoid stress and further hemorrhage.
• Attempt correction of organ dysfunction resulting from accumulation of extravascular blood (e.g., thoracocentesis) only if the situation is life-threatening and after normal blood coagulation is restored.
• Adding alfalfa hay to the diet may help to provide a source of increased dietary vitamin K_1.

MEDICATIONS

DRUG(S) OF CHOICE
• Vitamin K_1 (phytonadione 2.5 mg/kg q12h SQ initially then PO after ≅3 days and continuing for 3–5 weeks) effectively reverses the clotting defect.
• AC at 1–4 g/kg body weight in water slurry (1 g AC in 5 mL water) PO. One dose of cathartic PO with AC if no diarrhea or ileus (70% sorbitol at 3mL/kg or sodium or magnesium sulfate at 250–500 mg/kg).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Do not use vitamin K_3 (menadione) in horses. Vitamin K_3 is ineffective against anticoagulant rodenticide toxicosis and is nephrotoxic.
• Medications that are highly plasma protein bound may exacerbate toxicosis.
• Drugs generally contraindicated are NSAIDs, phenothiazine tranquilizers, local anesthetics, antihistamines, sulfonamide antibiotics, anabolic steroids, and epinephrine.

FOLLOW-UP

PATIENT MONITORING
• Continue monitoring for blood loss.
• Check PT 2–3 days after the last dose of vitamin K_1 to determine if additional treatment is necessary.

PREVENTION/AVOIDANCE
Prevent access to bait packages.

POSSIBLE COMPLICATIONS
N/A

EXPECTED COURSE AND PROGNOSIS
Prognosis is based on the severity of blood loss and damage to organ systems affected by hemorrhage.

MISCELLANEOUS

ASSOCIATED CONDITIONS, AGE-RELATED FACTORS, ZOONOTIC POTENTIAL
N/A

PREGNANCY
• Lactating mares may excrete anticoagulant rodenticides in their milk.
• Monitor foals for any coagulopathies, and treat with vitamin K_1 if PT rises.

SEE ALSO
Dicumarol (moldy sweet clover) toxicosis

ABBREVIATIONS
• AC = activated charcoal
• aPTT = activated partial thromboplastin time
• DIC = disseminated intravascular coagulation
• PT = prothrombin time

Suggested Reading

McConnico RS, Copedge K, Bischoff KL. Brodifacoum toxicosis in two horses. J Am Vet Med Assoc 1997;211:882–886.
Ayala I, Rodriguez MJ, Martos N, Zilberschtein J, Ruiz I, Motas M. Fatal brodifacoum poisoning in a pony. Can Vet J 2007;48:627–629.

Author Anita M. Kore
Consulting Editor Robert H. Poppenga

ANURIA/OLIGURIA

BASICS

• *Anuria*—lack of urine production
• *Oliguria*—decreased urine production (<0.25 mL/kg per hr, or <125 mL/hr in a 500-kg horse)
• Anuria or oliguria may be physiologic or pathological.
• This chapter will focus on intrinsic renal failure causing anuria and oliguria.

SYSTEM AFFECTED

Renal/urologic

SIGNALMENT

Breed Predilections

No age, sex, or bred predisposition documented

CAUSES AND RISK FACTORS

• Physiologic oliguria—hyperosmolality; any disease process leading to renal hypoperfusion (e. g., dehydration, hypotension, low cardiac output).
• Pathological anuria/oliguria—intrinsic ARF or 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 ARF, terminal CRF, 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 PCV in most cases; mild to moderate anemia possible with terminal CRF.
• Moderate to severe increases in BUN (50–150 mg/dL) and Cr (2.0–20 mg/dL).
• Variable hyponatremia, hypochloremia, hyperkalemia, hypocalcemia, and hyperphosphatemia—hyperkalemia and hyperphosphatemia more common with intrinsic ARF; hyperkalemia most apparent with urinary tract disruption and development of uroperitoneum.
• Mild to moderate metabolic acidosis—depending 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 ARF; specific gravity best assessed in urine collected during initial patient evaluation (before rehydration) or while the horse is not receiving fluids.
• Oliguria with intrinsic ARF may be accompanied by mild to moderate proteinuria, glucosuria, pigmenturia, and increased numbers of RBCs and casts on sediment examination.
• Urine pH—normal to acidic, especially with concurrent depletion of body potassium stores

IMAGING

Transabdominal and Ultrasonography

• Kidneys may be enlarged, with loss of detail of corticomedullary junction, in intrinsic ARF.
• Kidneys typically are reduced in size, with increased parenchymal echogenicity, in CRF.

TREATMENT

• Treat anuria/oliguria as a medical emergency because persistent renal hypoperfusion may lead to ischemic 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.

MEDICATIONS

DRUG(S) OF CHOICE

• Fluid therapy to correct renal hypoperfusion—after initial measurement of body weight, correct estimated dehydration with normal (0.9%) saline or another potassium-poor electrolyte solution over 6–12 hr; 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 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 minutes]), 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 two times (1–2 mg/kg IV) at 1–2-hr intervals; if effective, urination should be observed within 1 hour after administration of the second dose; if ineffective, discontinue.
• Based on recent evidences in critically ill human patients the ROUTINE USE OF MANNITOL or DOPAMINE IN EQUINE PATIENTS WITH ARF 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 significant 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.

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 cm H_2O in more critical patients and neonates.

POSSIBLE COMPLICATIONS
• Severe hyperkalemia accompanied by cardiac arrhythmias, cardiac arrest, and death
• Pulmonary and peripheral edema; conjunctival edema may be dramatic.

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 ARF.

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

SEE ALSO
• ARF
• CRF
• Urolithiasis
• Urinary tract obstruction
• Uroperitoneum

ABBREVIATIONS
• ARF = acute renal failure
• CRF = chronic renal failure
• GFR = glomerular filtration rate
• PCV = packed cell volume
• USG = urinary specific gravity
• UTI = urinary tract infection

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Schott HC. Chronic renal failure. In: Reed SM, Bayly WM, eds. Equine Internal Medicine. Philadelphia: WB Saunders, 1998:856–875.

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Consulting Editor Gillian Perkins

AORTIC REGURGITATION

BASICS

DEFINITION
• Occurs when the aortic valve allows blood to leak into the left ventricular outflow tract during diastole, creating a holodiastolic decrescendo murmur with its PMI in the aortic valve area. • The murmur radiates toward the left cardiac apex and the right side.

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 becomes more severe, stretching of the mitral annulus occurs, and mitral regurgitation often develops. Mitral regurgitation compounds the severe left ventricular volume overload, and these horses often rapidly develop congestive heart failure.
• Severe regurgitation results in decreased coronary artery blood flow and decreased myocardial perfusion. • Ventricular arrhythmias may develop secondary to decreased myocardial perfusion.

SYSTEM 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
• Poor performance • Possibly congestive heart failure

Physical Examination
• Grade 1–6/6, decrescendo or musical holodiastolic murmur with PMI in the aortic valve area (left or right fourth intercostal space) radiating to the left apex and right side
• Other, less common findings—bounding arterial pulses, atrial fibrillation, ventricular premature depolarizations, accentuated third heart sounds, and congestive heart failure

CAUSES
• Degenerative changes of the aortic leaflets
• Fenestration of aortic leaflets
• Nonvegetative valvulitis • 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 usually are soft or not detectable and should have PMI in the pulmonic valve area; bounding arterial pulses are not present; differentiate echocardiographically.

CBC/BIOCHEMISTRY/URINALYSIS
May have neutrophilic leukocytosis and hyperfibrinogenemia with bacterial endocarditis

OTHER LABORATORY TESTS
• Elevated cardiac isoenzymes may be present (e.g., cardiac troponin I, CK-MB, HBDH, LDH-1 and LDH-2) with concurrent myocardial disease.
• Positive blood culture may be obtained from horses with bacterial endocarditis.

IMAGING
Electrocardiography
• Ventricular premature depolarizations may be present in horses with severe regurgitation and be caused by poor myocardial perfusion.
• Atrial fibrillation often develops in horses 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 and a nodular thickening of the left coronary leaflet free edge are the most common findings.
• Prolapse of an aortic leaflet (usually the noncoronary or right coronary 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 infrequently are detected.
• Left ventricle—enlarged and dilated, with a rounded apex
• Thinning of the left ventricular free wall and interventricular septum
• Increased septal–to–E point separation may be present.
• Pattern of left ventricular volume overload
• Normal or decreased fractional shortening in a horse with left ventricular enlargement is consistent with myocardial dysfunction.
• Dilatation of the aortic root in horses with longstanding regurgitation
• High-frequency vibrations on the mitral valve septal leaflet usually are detected with M-mode echocardiography and are created by turbulence in the left ventricular outflow tract.
• In some horses, high-frequency vibrations may be visualized on the interventricular septum instead of, or in addition to, vibrations on the mitral valve septal leaflet.
• 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.
• 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 is a good indicator of severity. Size and extent of the regurgitation jet represent another means of semiquantitating its severity, as is strength of the regurgitation signal.
• Continuous-wave Doppler assessment of the spectral tracing of the regurgitation jet also provides an estimate for the severity of regurgitation—a steep slope and a short pressure half-time indicate more severe regurgitation.

Thoracic Radiography
• Left-sided cardiac enlargement may be detected in horses with moderate to severe regurgitation.
• Pulmonary edema may be present in affected horses with congestive heart failure.

DIAGNOSTIC PROCEDURES
Cardiac Catheterization
• Right-sided catheterization may reveal elevated pulmonary capillary wedge pressures and pulmonary arterial pressures in horses with severe regurgitation and concurrent mitral regurgitation.
• Right ventricular and atrial pressures may be elevated in affected horses with congestive heart failure.
• Oxygen saturation of blood obtained from the right atrium, right ventricle, and pulmonary artery should be normal.

Continuous 24-Hour Holter Monitoring
Use in the diagnosis of horses with suspected ventricular premature depolarizations.

PATHOLOGIC FINDINGS
• Focal or diffuse thickening or distortion of one or more aortic leaflets may be present.
• Nodules, bands, plaques, and fenestrations have been described on the aortic leaflets at postmortem examination.
• Flail aortic leaflets, infective endocarditis, or congenital malformations of the aortic valve infrequently are detected.
• Aortic root dilatation usually is present in horses with severe, long-standing 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 in horses with significant regurgitation.
• Atrial myocardial thinning with atrial dilatation has been documented in horses with atrial fibrillation and enlargement.
• Inflammatory cell infiltrate has been detected in horses with myocarditis and aortic regurgitation; however, most affected horses do not have significant underlying myocardial disease.

AORTIC REGURGITATION

TREATMENT

AIMS OF TREATMENT
• 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 congestive heart failure for the congestive heart failure with positive inotropic drugs, vasodilators, and diuretics on an inpatient basis, if possible, 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 congestive heart failure.
• Horses with significant ventricular arrhythmias or pulmonary artery dilatation are no longer safe to ride.

DIET
N/A

CLIENT EDUCATION
• Regularly palpate the arterial pulses to monitor the progression of left ventricular volume overload. Bounding arterial pulses indicate significant left ventricular volume overload. Moderate to severe regurgitation usually is present in these horses.
• Regularly monitor cardiac rhythm; any irregularities other than second-degree AV 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

DRUGS
• Severe regurgitation—Administor enalapril (0.25–0.5 mg/kg PO q24h or q12h) or another ACE inhibitor.
• ACE inhibitors prolong the time to valve replacement in humans with moderate to severe regurgitation.
• The bioavailability of enalapril is poor but 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 include digoxin, furosemide, 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.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
Most other vasodilatory drugs should have some beneficial effect in horses with moderate to severe regurgitation, but they may be less effective than the ACE inhibitors.

FOLLOW-UP

PATIENT MONITORING
• Frequently monitor arterial pulses and cardiac rhythm.
• Reexamine horses with mild to moderate regurgitation by ECG every year.
• Reexamine horses with severe regurgitation by echocardiography every 6 mo to monitor progression of valvular insufficiency and determine if the horse continues to be safe to ride or drive.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Chronic regurgitation—ventricular arrhythmias; atrial fibrillation; mitral regurgitation; congestive heart failure

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 of horse's performance career or shorten life expectancy.
• Affected horses with congestive heart failure usually have severe underlying valvular heart disease and myocardial disease and a guarded to grave prognosis for life. Most affected horses being treated for congestive heart failure respond to the supportive therapy and improve. This improvement usually is short lived, however, and most are euthanized within 2–6 mo of initiating treatment.

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Old horses are more likely to be affected.

ZOONOTIC POTENTIAL
N/A

PREGNANCY
• Affected mares should not experience any problems with pregnancy unless the regurgitation is severe.
• Treat pregnant affected mares with congestive heart failure 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
• Infective endocarditis
• Ventricular septal defect

ABBREVIATIONS
• ACE = angiotensin-converting enzyme
• AV = atrioventricular
• CK-MB = MB isoenzyme of creatine kinase
• HBDH = α-hydroxybutyrate dehydrogenase
• LDH = lactate dehydrogenase
• PMI = point of maximal intensity

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AORTIC ROOT RUPTURE

BASICS

DEFINITION
A defect in the wall of the aorta at the aortic root, usually in the right sinus of Valsalva

PATHOPHYSIOLOGY
• Aortic rupture results in the exsanguination into the thoracic cavity, cardiac tamponade from hemopericardium, or a shunt between the aorta and heart.
• 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

SYSTEM AFFECTED
Cardiovascular

INCIDENCE/PREVALENCE
More frequently occurs in old horses, particularly males

SIGNALMENT
Often occurs during or after breeding or other exercise

SIGNS
General Comments
Often interpreted by owners as colic, because the horse appears distressed, may be looking at its flanks, and acts uncomfortable

Historical
• Acute onset of colic or distress, usually after exercise or breeding
• Less commonly, exercise intolerance; syncope

Physical Examination
• 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 congestive heart failure

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.

RISK FACTORS
• Aortic aneurysm
• Aortitis

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
Elevated serum creatinine and BUN may occur because of impaired renal perfusion, which is associated with sustained ventricular tachycardia and blood loss.

OTHER LABORATORY TESTS
Serum cardiac troponin I and cardiac isoenzymes of creatine phosphokinase and lactate dehydrogenase can be elevated with significant myocardial cell injury.

IMAGING
ECG
Uniform ventricular tachycardia with a heart rate of >100 bpm may be present.

Echocardiography
• Two-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.
• Right atrial or ventricular enlargement if the aorta has ruptured into one of these chambers
• Paradoxical septal motion with severe right ventricular volume overload
• Ruptured tricuspid chordae tendineae or ruptured or flail tricuspid valve leaflet may be detected, particularly with rupture of an aneurysm of the sinus of Valsalva.
• Subendocardial dissection of blood along the left side of the interventricular septum may result in rupture into the left ventricle and left ventricular volume overload.
• Hyperdynamic interventricular septum and left ventricular free wall are associated with left ventricular volume overload, producing increased fractional shortening, until the myocardium starts to fail.
• Rupture of a mitral valve chordae tendineae and a flail mitral valve leaflet may occur, producing acute onset of severe mitral regurgitation.
• Significant left ventricular volume overload can lead to dilatation of the mitral annulus and mitral regurgitation.
• Use color-flow Doppler, pulsed-wave Doppler, or contrast echocardiography to localize the shunt associated with the aortic cardiac fistula.
• Continuous-wave Doppler can be used to determine peak velocity of the shunt flow.

Thoracic Radiography
• An enlarged cardiac silhouette should be present in horses with a large aorticocardiac shunt.
• Pulmonary overcirculation and edema may be detected.

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.

AORTIC ROOT RUPTURE

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
• Post-mortem examination confirms the site and extent of the rupture and the presence of aorticocardiac fistula.
• Path of the dissection can be traced and the rupture into the right atrium, tricuspid valve, right ventricle, or left ventricle confirmed.
• 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 root 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.
• Biatrial and biventricular enlargement usually is detected, and hepatic congestion and pulmonary edema may be present.

TREATMENT

AIMS OF TREATMENT
Palliative care

APPROPRIATE HEALTH CARE
• Closely monitor affected horses with ventricular tachycardia if the tachycardia is uniform, the heart rate is >120 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 >120 bpm, or with clinical signs of cardiovascular collapse, institute antiarrhythmic treatment on an inpatient basis.
• If congestive heart failure also is present, institute treatment for congestive heart failure as well. Consider humane destruction, 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.
• IV lidocaine is rapidly acting and has a very short duration of action. However, it also has CNS effects in horses and, thus, must be used carefully.
• IV procainamide and quinidine gluconate have been effective in converting sustained, uniform ventricular tachycardia but have a slower onset of action.
• IV magnesium sulfate has been successful in converting sustained ventricular tachycardia and is not arrhythmogenic.

ACE Inhibitors
• May be indicated in stallions to decrease resistance to forward flow once ventricular tachycardia has been converted.
• Enalapril (0.5mg/kg PO BID) has no effect on the stallion's libido, breeding performance, or fertility.
• Other vasodilators or antihypertensive drugs can be considered, but their effect on breeding stallions is unknown.

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

Propafenone
• Very effective in converting refractory ventricular tachycardia
• The IV form is not available in the United States (but is available abroad); only an oral form is available in this country.
• May have a synergistic effect with procainamide in horses with refractory ventricular tachycardia

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.

AORTIC ROOT RUPTURE

• Return of venous distention and jugular pulsations or development of ventral edema or coughing indicates the onset of congestive heart failure and worsening of ventricular volume overload.

PREVENTION/AVOIDANCE

• With congenital 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.
• Routine echocardiography of old breeding stallions and high-performance horses potentially at risk may help to identify these horses before development of a tear in the aortic root.

POSSIBLE COMPLICATIONS

• Deterioration of uniform ventricular tachycardia into fatal ventricular arrhythmia
• Severe, acute congestive heart failure from massive right atrial or ventricular, left atrial, and left ventricular volume overload
• Tricuspid valve rupture, leading to massive tricuspid regurgitation and congestive heart failure
• Rupture of a chordae tendineae of the tricuspid or mitral valve, leading to massive tricuspid or mitral regurgitation, respectively, and acute, right- or left-sided congestive heart failure
• Sudden death

EXPECTED COURSE AND PROGNOSIS

• Prognosis for life of affected horses is grave, with sudden death expected in those with extracardiac or intrapericardial rupture.
• Onset of congestive heart failure is likely after development of an intracardiac fistula, and the speed of its development depends on the location and size of the shunt.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Aortic root aneurysm

AGE-RELATED FACTORS

Old horses are more likely to be affected, but horses as young as 4 years have been diagnosed.

PREGNANCY

• 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 tachycardia

ABBREVIATIONS

• CNS = central nervous system

Suggested Reading

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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 CCA-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).
• Toxicity of organic pentavalent forms used as growth promoter in swine (e.g., arsanilic acid, roxarsone) has not been determined for horses.
• Trivalent inorganic arsenicals inhibit cellular respiration and damage capillaries.
• Pentavalent inorganic arsenicals uncouple oxidative phosphorylation, leading to deficits in cell energy.

SIGNALMENT
No breed or sex predilections

SIGNS
• Peracute or acute syndromes are most 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

CAUSES AND RISK FACTORS
Ingestion of arsenic-containing products or arsenic-contaminated soils, water, or feed

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Lead toxicosis—evidence of neurologic dysfunction is likely.
• Mercury toxicosis
• NSAID toxicosis—history of previous use
• Cantharidin toxicosis—evidence of cystitis
• Salmonellosis
• Colitis X
• Acute cyathastomiasis
• Clostridial colitis

CBC/BIOCHEMISTRY/URINALYSIS
• Reflect circulatory shock and possible liver and kidney damage
• Hemoconcentration—elevated PCV and plasma total protein
• Leukopenia with degenerative changes in PMNs
• Azotemia
• Electrolytes—hypokalemia; hyponatremia; hypochloremia
• Hyperglycemia
• Hyperbilirubinemia
• Elevated LDH and CK

OTHER LABORATORY TESTS
• Ante-mortem—measurement of arsenic in urine, whole blood, or GI contents
• Post-mortem—measurement of arsenic in liver or kidney
• Chronic exposures—arsenic can be measured in hair.
• Arsenic is rapidly excreted after exposure ceases.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
N/A

PATHOLOGICAL FINDINGS
Gross
• GI hemorrhage, mucosal congestion, edema, and erosion are either localized or throughout the GI tract, which may be filled with watery, dark-green, black, or hemorrhagic ingesta, with necrotic material from mucosal sloughing.
• Pulmonary edema and epicardial and serosal hemorrhage

Histopathologic
Necrotizing, hemorrhagic typhlocolitis, with necrotizing vasculitis, 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 and acidosis.
• Appropriate fluid therapy

MEDICATIONS

DRUG(S)
• 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 muscular injection, followed by 2–3 mg/kg q4h for 24 hr and then 1 mg/kg q4h 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 q8h is suggested).
• Control abdominal pain.
  ○ Flunixin meglumine (1.1 mg/kg IV or IM q24h for 5 days) or butorphanol tartrate (0.1 mg/kg IV q3–4h up to 48 hr)
  ○ 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
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, AGE-RELATED FACTORS, ZOONOTIC POTENTIAL, PREGNANCY
N/A

ABBREVIATIONS
• CCA = chromated copper arsenate
• CK = creatine kinase
• DMSA = 2,3-dimercaptosuccinic acid, succimer
• GI = gastrointestinal
• LDH = lactate dehydrogenase
• PCV = packed cell volume
• PMN = polymorphonucleocytes

Suggested Reading
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Artificial Insemination

BASICS

DEFINITION/OVERVIEW
• Extended fresh, cooled, frozen semen introduced into the mare's uterus using aseptic technique
• Standard AI—minimum 300–1000 × 10^6 PMS deposited into *uterine body*
• DHI or low-dose AI—1–25 × 10^6 PMS deposited into *tip of uterine horn* (ipsilateral to dominant follicle)

ETIOLOGY/PATHOPHYSIOLOGY
Advantages
• AI increases live cover.
• Efficient use of semen
• Ejaculate divided—several AI doses, greater number of mares bred in a season (120 by AI; 40–80 by live cover)
• Wider use of genetically superior stallions.
• Eliminate cost and risk of transport, mares with foals at side.
• Antibiotics in semen extenders prevent many genital infections.
• Fewer breeding injuries
• Continue using stallions with problems (musculoskeletal and behavioral).
• Protect mares with genital tract impairments or recent surgical repair from further breeding-related trauma.
• Semen quality assessed before AI
• Low-dose AI—stallions with limited availability or costly semen due to
  ○ Excessive size of book
  ○ Low sperm cell production or high percentage of dead sperm
  ○ Use of sex-sorted sperm
  ○ Epididymal spermatozoa collected at the time of castration or stallion's death

SYSTEM AFFECTED
Reproductive

SIGNALMENT
• Thoroughbreds allow only live cover.
• All other breed registries allow AI; may impose restrictions

SIGNS
Historical
Records of mare's prior cycles—help predict days in heat, time of ovulation

Teasing and Physical Examination
• Ovulation timing is critical.
  ○ Predict by her history, teasing response, results of genital tract TRP and U/S.
  ○ During estrus—tease daily; not less than every other day
  ○ On 2nd day of estrus, begin daily or every-other-day TRP.
  ○ Perform U/S, as needed, to determine optimal time to breed.
• TRP—record dominant follicle (35+ mm), uterine edema, relaxing cervix
• Follicle size and growth, increasing uterine estrual edema (cartwheel appearance) evident with U/S
• Preovulatory follicle may become irregular/pear-shaped 12–24 hr preovulation.
• Estrual edema peaks 72–96 hr, decreases to light or absent by 36 hr preovulation in young, normal mares.
• OVD, CH, CL—evidence of ovulation

DIAGNOSIS

PROCEDURAL ISSUES
Timing and Frequency of Breeding
• Depends on semen longevity—affected by stallion idiosyncrasy, semen preservation method (fresh, cooled, frozen)
• Equine ova—short viability, 8–18 hr postovulation

Teasing and Examinations
• GnRH analog or hCG when preovulatory follicle is ≥35 mm to induce ovulation within 36–42 hr. AI as close to ovulation as possible.
• U/S 4–6 hr post-AI for presence of intrauterine fluid (especially new/DUC mare, or if bred with frozen semen) and for ovulation
• Evaluate normal, fertile mares 24–48 hr after AI for ovulation.

Fresh (raw or extended) Semen
• Routine breeding—every other day
  ○ Begin day 2–3 of estrus until they tease out, or
  ○ When a large preovulatory follicle is detected by TRP and U/S.
• Inseminate within 48 hr preovulation to achieve acceptable pregnancy rates.

Cooled Transported Semen
• More intense management; fertility of cooled semen from some stallions decreases markedly >24 hr.
• GnRH analog or hCG when preovulatory follicle is ≥35 mm to induce ovulation within 36–42 hr; order semen—overnight shipment
• Inseminate ≤12–24 hr preovulation for acceptable conception rates.
• Semen with poor post-cooling fertility should be sent *counter to counter* (i.e., airline transport).
  ○ Administer Deslorelin or hCG 24–36 hr before expected semen arrival; ensure ovulation is very close to time of AI.
  ○ No advantage to keeping a 2nd AI dose to rebreed next day. Mare's uterus is best incubator for sperm, not a chilled shipper.

Frozen Thawed Semen
• Precise timing of AI post-thaw longevity is reduced to ≤12–24 hr.
• Mare management—serial, daily teasing, TRP, and U/S
• Deslorelin or hCG when dominant follicle ≥35 mm
• TRP and U/S—TID–QID, ensure AI as close before ovulation as possible; most important, ≤6–8 hr postovulation
• New frozen semen strategy for AI if have multiple doses:
  ○ Deslorelin or hCG when dominant follicle ≥35 mm
  ○ AI at 24 hr and again at 40 hr after injection; ensures viable sperm are available during ovulatory period
  ○ Treat mare if intrauterine fluid is present 4–6 hr after first AI.
  ○ Pregnancy rate is equivalent to a one-time AI 6 hr postovulation, but minus the intensive labor and fewer veterinary examinations.

ARTIFICIAL INSEMINATION

Low-Dose Insemination
• Allows use of a reduced dose of semen (fresh, cooled, frozen)
• Varies with semen quality
  ○ DHI dose has been decreased to as few as 14×10^6 motile, frozen-thawed sperm.
  ○ Average of $60–150 \times 10^6$ of PMS for DHI.
  ○ Semen is deposited at the UTJ, tip of uterine horn ipsilateral to dominant follicle.
• DHI can be either hysteroscopically guided or transrectally guided (with or without U/S).
• Mare management varies according to method of semen preservation.

General Comments
• If ovulation has not occurred within the recommended times for fresh (48 hr), cooled (24 hr), or frozen (6–12 hr) semen, rebreed the mare.
• Older ova or semen—due to poor timing, percentage of EED increases.

OTHER LABORATORY TESTS
Progesterone level of >1 ng/mL confirms ovulation.

IMAGING
U/S

DIAGNOSTIC PROCEDURES
Semen Analysis
• Minimum parameters—volume, motility, concentration
• Morphology—optional, but of particular use if a stallion has fertility problems
• Small sample of cooled or frozen semen should be saved and warmed (at 37° C) to evaluate immediately after AI.
• Slide, coverslip, and pip—prewarm, stallion semen very susceptible to cold shock
• The total number of sperm should be at least $300–1000 \times 10^6$ PMS (concentration [in millions of sperm per mL] × volume used).

Stallion's Disease Status
Should be negative for EIA, EVA, CEM, and venereal diseases

Mare Selection
• Her fertility takes on special significance if using frozen semen or its quality is less optimal.
• Include reproductive history +/− normal estrous cyclicity, results of uterine culture and cytology, presence of intrauterine fluid during estrus.
• Fertility alters by status—normal maiden > normal pluriparous > older maiden, pluriparous or barren mare

Prebreeding Uterine Culture and Cytology of Mare
• All, except young maiden mares, should have at least one negative uterine culture and cytology prebreeding.
  ○ Avoid transmitting infections to the stallion.
  ○ Early identification of possible mare problems
  ○ Maximize the likelihood of first-cycle conception.
• Pregnancy rates are lower and EED higher for mares treated for uterine infections during the same cycle as the AI.

TREATMENT
Prebreeding
• Presence of ≥2-cm height of prebreeding uterine fluid, then LRS uterine lavage immediately before AI
• Does not affect fertility

AI Technique
• Sterile and disposable equipment. Mares are restrained and the perineal area is thoroughly cleansed with a mild detergent, antiseptic solution or soap; then completely remove any residue (minimum three rinses).
• Sterile sleeve on arm and nonspermicidal lubricant applied to dorsum of the gloved hand.
  ○ 250–56 cm (20–22 inch) AI pipet is carried in the gloved hand.
  ○ Index finger is first passed through the cervical lumen. It serves as a guide by which the pipet can readily be advanced (advanced to a position no more than 2.5 cm into the uterine body).
  ○ Syringe with a nonspermicidal plastic plunger (e.g., Air-tite) containing the extended semen is attached to the pipet, and the semen is slowly deposited into the uterus. The remaining semen in the pipet is delivered by using a small bolus of air (1 mL) in the syringe.

Fresh Extended Semen
• Perform AI immediately after collection.
• Semen can be mixed with an appropriate extender for immediate insemination, with semen-to-extender ratio of 1:1 or 1:2, if the ejaculate volume is small and of high concentration.

Cooled Transported Semen
• Semen is collected, diluted in semen extender, and cooled to 5°–6° C for 24–48 hr. With transport, there can be a modest decrease of fertilizing capacity (stallion fertility dependent).
• A semen-to-extender ratio of 1:3 or 1:4 is acceptable; may be as high as 1:19
• Semen longevity optimized by extending the ejaculate to a final sperm concentration of $25–50 \times 10^6$ sperm/mL.

Frozen Thawed Semen
• Frozen semen is packed in 0.5–5 mL straws and stored in liquid N_2.
• A 5-mL straw contains from $600–1000 \times 10^6$ sperm cells.
• Dependent on post-freeze viability of the spermatozoa, only one straw may be needed.
• A 0.5-mL straw contains $200–800 \times 10^6$ sperm cells.
  ○ Number of straws needed depends on post-thaw motility and method of AI.
  ○ Thawing protocols vary and are reported ideally to be paired with a particular freezing method. Seek specific information regarding thawing. In the absence of a recommended protocol, 37° C for 30–60 seconds may provide an acceptable alternative.

ARTIFICIAL INSEMINATION

• If details are not provided with frozen semen received, seek instructions regarding thawing before the day of AI to ensure proper handling.
• Post-thawing, semen should be in the mare within 5 min.
• Post-AI uterine treatment is strongly recommended. The high concentration of sperm cells in a thawed straw and absence of seminal plasma (provides a natural protective effect in the uterus) may induce an acute PMIE.

Low-Dose Insemination Procedures (LDI)

• Sedation of the mare is recommended. Procedure should be performed quickly (≤10 min) and avoid inducing uterine trauma.
• *Hysteroscopic AI*—introduction of an endoscope into the mare's uterus:
  ○ Approach and visualize the UTJ ipsilateral to the dominant follicle.
  ○ Small catheter is passed through the endoscope's channel and semen deposited at/on the UTJ.
• *DHI*—Pass a flexible AI pipet through the cervix toward the tip of the uterine horn ipsilateral to the dominant follicle.
  ○ Pipet is guided by either TRP or U/S.
  ○ Semen is deposited close to or onto the UTJ.
  ○ *Manual TRP elevation of the tip of the uterine horn may help pass the pipet.*

Post-Breeding

• U/S examination 4–6 hr after AI for presence of intrauterine fluid.
  ○ If present, lavage uterus with sterile saline or LRS, followed by oxytocin beginning 4–6 hr after AI.
  ○ Repeat oxytocin at 2-hr intervals until 8–10 hr post-AI, and again at 12–24 hr until the inflammation resolves.

MEDICATIONS

DRUG(S) OF CHOICE

• Ovulation induction most effective if follicle is ≥35 mm
  ○ Within 36–42 hr with hCG (1500–3000 IU IV); response range is 12–72 hr.
  ○ Within 36–42 hr with GnRH analogue (Deslorelin 1.5 mg IM)
• Ecbolic drugs may be used to treat PMIE and DUC.
• Prostaglandins—Misoprostol for cervical relaxation or intrauterine $PGF_{2\alpha}$ (0.25 mg) 2 hr before deep AI (only with good-quality semen)

CONTRAINDICATIONS

See Endometritis.

PRECAUTIONS

See Endometritis.

FOLLOW-UP

PATIENT MONITORING

• Begin teasing by 11 days post-ovulation.
  ○ Early detection of endometritis—indicated by a shortened cycle due to endogenous prostaglandin release
• U/S for pregnancy 14–15 days post-ovulation includes ruling out potential twins versus lymphatic cyst.
• Follow-up TRP and U/S—24–30 days; confirm heartbeat in the embryo.
• Serial TRP pregnancy examinations—45, 60, 90, and 120 days

POSSIBLE COMPLICATIONS

• AV 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
  ○ With cooled shipments, entire breeding program is at the mercy of airlines/couriers.
• Operator skill—to manipulate and place semen through the cervix, into the uterine lumen or to the tip of the horn, in a proper and timely manner
• Misidentification of stallions/mares

MISCELLANEOUS

PREGNANCY

Cooled Semen

Per cycle pregnancy rates are equivalent to on-farm AI with fresh semen (60%–75%) if semen quality remains good after cooling period of 24 hr at 5–6° C.

Frozen Semen

• Pregnancy rates decrease for most stallions.
• Spermatozoa suffer many stresses; anticipate attrition rate of ≅50% with freezing and thawing.
• First-cycle pregnancy rates—30%–40% (range—0%–70%); wide range between stallions
  ○ Intense breeding management and good quality of semen—positive impact on the pregnancy rate
• Candidate selection for frozen semen breeding
  ○ Most fertile—young, maiden and normal pluriparous mares
  ○ Least fertile—old, maiden or barren and abnormal pluriparous mares
• Older eggs or semen
  ○ Due to poor timing; pregnancy rate decreased by 30 days; increased EED

SYNONYMS

Artificial breeding

SEE ALSO

• Conception failure
• Delayed uterine clearance
• Early embryonic death
• Endometritis
• Semen evaluation, abnormal
• Semen evaluation, normal
• Venereal diseases

ABBREVIATIONS

• AI = artificial insemination
• AV = artificial vagina
• CEM = contagious equine metritis
• CH = corpus hemorrhagicum
• CL = corpus luteum
• DHI = deep horn insemination
• DUC = delayed uterine clearance
• EIA = equine infectious anemia
• EED = early embryonic death
• EVA = equine viral arteritis
• GnRH = gonadotropin-releasing hormone
• hCG = human chorionic gonadotropin
• LRS = lactated Ringer's solution
• OVD = ovulation depression
• PMIE = persistent mating-induced endometritis
• PMS = progressively motile sperm
• TRP = transrectal palpation
• U/S = ultrasound, ultrasonography
• UTJ= utero-tubal junction

Suggested Reading

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ARYTENOID CHONDROPATHY

BASICS

OVERVIEW
• A septic inflammatory process of one or both arytenoid cartilages, resulting in 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.

SIGNALMENT
• Male and Thoroughbred racehorses are more commonly affected. • Incidence increases with age.

SIGNS
• Upper respiratory noise, exercise intolerance, or both • The disease usually worsens gradually, with progressive involvement of one or both arytenoid cartilages. • The condition leads to ventilation interference proportional to the loss of abductory function and the mechanical size of the affected arytenoid cartilages. The more intense the high-intensity exercise occurs, the more severe is the hypoventilation, so 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 resembles that of horses with laryngeal hemiplegia.

CAUSES AND RISK FACTORS
• 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 cartilage sepsis
• In many cases, the inciting cause is never found.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Laryngeal hemiplegia • Congenital malformation of the laryngeal cartilages

CBC/BIOCHEMISTRY/URINALYSIS
Of no value.

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 mm Hg; PaO_2 may be <65 mm Hg in affected horses.

IMAGING
• Lateral radiography of the larynx may reveal enlarged laryngeal cartilages, sometimes with associated osseous metaplasia. • Ultrasound 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.

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 axial 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 leads 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 laser-assisted excision of intralaryngeal granulations if the affected arytenoid cartilage retains abductory function. • 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 (e. g., 250 mL of 90% DMSO, 500 mL of nitrofurazone, and 50 mL of prednisolone [25 mg/mL] mixed with 250 mL of glycerin) 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 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 for 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. • 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 axial surface of the arytenoid cartilage that maintain abductory function may respond to simple "lumpectomy." • 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

ABBREVIATION
• DMSO = dimethylsulfoxide

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Authors Norm Ducharme and Richard P. Hackett
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ASCARID INFESTATION

BASICS

OVERVIEW
• Parasitic roundworm infection caused by *Parascaris equorum*.
• The infection prevalence may be up to 100% in tested farms and up to 80% in foals, with the highest incidence occurring between 100 and 180 days of age.
• The parasite has a direct life cycle that follows the oral-fecal route. Adults, in the small intestine of infected horses, produce large numbers of eggs, which are passed in the feces. The eggs become infective in 10 days to 6 weeks by developing into larvae (L_2). These highly resistant eggs accumulate in the environment, sticking to different surfaces, including the mare's mammary gland. When ingested, the larvae are released in the small intestine and migrate through the intestinal wall into the bloodstream, reaching the liver via the portal circulation. In the liver, they migrate to a hepatic vein, accessing the caudal vena cava and finally the pulmonary circulation. Molting of the larvae occurs in the lungs, followed by tracheal ascending migration and subsequent deglutition. Arrival to the small intestine completes the life cycle, and a final molting and maturation into the adult form take place.

SYSTEMS AFFECTED
• It affects primarily the GI system, causing enteritis, maldigestion, and malabsorption.
• The hepatobiliary and respiratory systems—An exaggerated inflammatory response to migrating larvae, resulting in temporary lung and liver damage in sensitized horses. Varying forms of tracheobronchitis have also been described.

SIGNALMENT
• Any ages, but primarily in foals and weanlings up to 9–12 mo of age
• Debilitated and immunocompromised adult horses can also be infected.

SIGNS
• Decreased growth rate, generalized weakness, a dull hair coat and dry skin, "pot-bellied" appearance, and decreased appetite
• In severe cases, colic due to obstruction can occur.
• Acute colic signs with peritonitis due to perforation of the intestine.
• Coughing and mucopurulent nasal discharge with or without systemic illness may be seen during periods of larval imigration through the lungs.

CAUSES AND RISK FACTORS
The disease is caused by *P. equorum*, the roundworm from the family Ascarididae. Animals at risk are susceptible foals and weanlings grazing on infested pastures.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Any causes of colic, ill thrift, weakness, malabsorption, and malnutrition

CBC/BIOCHEMISTRY/URINALYSIS
• Eosinophilia may be seen during larval migration, 10–40 days postinfection.
• Leukopenia and mild anemia have been reported.
• In severe cases, hypoproteinemia can be detected.

OTHER LABORATORY TESTS
Coprology for detection of the eggs (see Other Diagnostic Procedures)

IMAGING
Adult ascaris may be seen on transabdominal ultrasound, within the intestinal lumen or in the peritoneal cavity after intestinal perforation.

OTHER DIAGNOSTIC PROCEDURES
The infestation is confirmed by fecal flotation techniques.

PATHOLOGIC FINDINGS
• Adult forms are found in the intestinal lumen or free in the abdominal cavity following intestinal perforation.
• Hemorrhagic and edematous lesions around necrotic areas in the lungs, liver, and associated lymph nodes are seen during larval migration.
• Microscopy after larval migration reveals multiple foci of white tracts within a fibrotic liver parenchyma.
• Lymphocytic nodules may develop in the lungs after multiple episodes of reinfection in a sensitized host.

TREATMENT

Treatment is indicated for fecal egg counts greater than 100 eggs per gram. Following sudden and complete paralysis of all ascarids after anthelmintic therapy, small intestinal obstruction or impaction may occur. Emergency surgical intervention for removal of dead parasites and correction of secondary complications such as intussusceptions and intestinal volvulus are then required. Ascarid impaction should be suspected in colicky foals and weanlings with a recent history (24 hr) of deworming.

MEDICATIONS

The regular use of anthelmintics is the treatment of choice for patent infections with *P. equorum* and should be administered to foals and weanlings every 6–8 weeks, starting at 1.5–2 mo of age.

DRUG(S) OF CHOICE
• Anthelmintics available at present do not eliminate migrating larvae. Therefore, preventative therapy should be given until 1 year of age.

ASCARID INFESTATION

• Broodmares should be treated at monthly intervals in the last trimester of pregnancy to reduce environmental contamination.
Recommended anthelmintics:
• Fenbendazole 10 mg/kg PO given for 5 consecutive days (varies in effectiveness against ascarids)
• Pyrantel pamoate 6.6 mg/kg PO
• Levamisole 8 mg/kg PO
• Daily prophylactic administration of pyrantel tartrate (2.64 mg/kg) in the feed also prevents penetration of the intestinal wall by ascarid larvae.
• Moxidectin 0.4 mg/kg PO and ivermectin 0.2 mg/kg PO were advocated to be 100% efficient in eliminating ascarid infection in horses, but resistance to these and other macrocyclic lactone anthelmintics has been identified in Europe, Canada, and the United States in recent years.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

If severe parasite burdens are suspected, anthelmintics that result in paralysis of the parasites (e. g., pyrantel pamoate, piperazine, organophosphates, ivermectin) should be avoided because it may result in small intestinal obstruction or impaction and can lead to intestinal rupture and peritonitis. Therefore, anthelmintics with a slower action such as benzimidazoles are recommended.

FOLLOW-UP

PATIENT MONITORING

Fecal floatation should be conducted in 10% or more of the foals every 4–6 mo. If 10% of foals or more are positive, failure of the anthelmintic therapy and/or the prevention and control strategies should be suspected.

PREVENTION/AVOIDANCE

• Contaminated facilities should be disinfected with a 5% phenolic compound and sprayed with a high-pressure hose.
• Grazing of broodmares, foals, and weanlings on heavily contaminated pastures should be avoided.
• *P. equorum* eggs can remain viable in the environment for many years.
• Frequent removal of manure from stalls and pastures also reduces transmission between foals and reinfection following treatment.

POSSIBLE COMPLICATIONS

Overdose of anthelmintic can result in toxicity.

EXPECTED COURSE AND PROGNOSIS

• Prognosis is favorable in uncomplicated cases, but a delay in growth and development is common.
• Infection rates start to decline at 6 mo of age, and immunity is long lasting. Patent infections are rarely seen in adults except in immunocompromised animals.

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Gastrointestinal obstruction
• Septic peritonitis

ZOONOTIC POTENTIAL

Human infection, although extremely rare, may occur after ingestion of a viable egg.

PREGNANCY

Transplacental infection with *P. equorum* is not known to occur, nor is the transfer of ascarid larvae in colostrum.

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Author Carlos Medina-Torres
Consulting Editors Henry Stämpfli and Olimpo Oliver-Espinosa

Aspartate Aminotransferase (AST)

BASICS

DEFINITION
• Catalyzes transamination of 2-oxoglutarate and L-aspartate to glutamate and oxaloacetate
• Present in many tissues—liver, striated muscle, erythrocytes, and others
• 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, increased AST activity will occur with hemolysis because of the high AST content in erythrocytes.
• Magnitude of the elevation generally is proportional to the number of hepatocytes affected, not to the severity of a particular insult.
• With skeletal muscle injury, magnitude of AST elevation is not necessarily proportional to the extent of tissue injury.
• Increases above the reference interval occur with intramuscular injections and in downer animals.
• AST is a sensitive indicator of hepatocellular and striated muscle injury; however, because it is present in many tissues, AST lacks specificity. Other biochemical tests need to be examined concurrently with AST to localize the source of the increase (i.e., SD for liver and CK for muscle).
• After tissue injury AST activity increases more slowly and remains increased longer than SD or CK.
• Increased SD, with normal or increased AST, indicates acute or ongoing hepatocellular injury. If serial serum chemistry analyses reveal continuously or progressively increased activities of both enzymes, ongoing hepatocellular injury is likely. During treatment of hepatic disease, the enzymes can be used to monitor cessation of the insult. If, after documenting recent hepatocellular injury, serial serum chemistry analyses reveal increased AST and progressively decreasing or normal SD activity, cessation of the original insult is likely. Because of its longer half-life, AST may increase even after cessation of the 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 SD may be seen together.

SYSTEMS AFFECTED
• Musculoskeletal
• Hepatobiliary
• Cardiovascular (myocardium)
• Hemic (erythrocytes)

GENETICS
N/A

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
• Depends on the primary disease process and secondary complications

SIGNS
Historical
• Depend on the cause of the increases in AST activity
• Strenuous exercise or overtraining

Physical Examination
• Depends on the cause of the increases in AST activity
• Muscle disorders—reluctance or inability to move, stiffness, and recumbency
• Liver disorders—jaundice, neurologic deficits, discolored urine, anorexia, abdominal pain, weight loss, and fever
• Clinical signs due to hepatic failure generally do not appear until 75% of the hepatic functional mass is lost.

CAUSES
• Degenerative conditions—cirrhosis, rhabdomyolysis, and choleliths
• Anomaly, congenital diseases—polysaccharide storage myopathy; biliary atresia
• Metabolic diseases—shock, hypovolemia, hypoxia caused by severe anemia or during anesthesia, and severe GI disease
• Neoplastic or nutritional diseases—primary neoplasia, metastatic neoplasia, leukemia, hepatic lipidosis, and vitamin E/selenium deficiency
• Infectious and immune-mediated diseases—hepatitis of various causes (e.g., viral, bacterial, protozoal, fungal, parasitic), serum sickness, amyloidosis, endotoxemia, and chronic active hepatitis
• Toxic or trauma—pyrrolizidine alkaloid-containing plants, ferrous fumarate in newborn foals, cottonseed, castor bean, oaks, and alsike clover; fungal toxins, such as aflatoxins, cyclopiazonic acid, fumonisin, phalloidin (i.e., mushrooms), rubratoxins; blue-green algae; and chemical compounds/elements, such as ethanol, chlorinated hydrocarbons, carbon tetrachloride, monensin, copper, iron, and petroleum and its products

RISK FACTORS
• Risk factors vary according to the specific disease.
• Familial disease, exposure to infected animals, overweight and miniature ponies, poor nutrition, excessive exercise, exposure to toxic compound or plants, or excessive exercise
• Halothane anesthesia, particularly of prolonged duration, may result in hepatic injury in horses.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
See Causes.

CBC/BIOCHEMISTRY/URINALYSIS
CBC
• Erythrocytes—liver disease may cause nonregenerative anemia and morphologic changes (e.g., acanthocytes, target cells, nonspecific poikilocytosis, normochromic microcytosis in portosystemic vascular shunts); severe anemia of any cause may produce cellular injury from tissue hypoxia.
• Leukocytes—leukocytosis or leukopenia may be seen with inflammatory diseases and leukemia; morphologic changes of the leukocytes (e.g., neutrophil toxicity in inflammation; neoplastic cells) 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.

Serum/Plasma Biochemistry Profile
• Glucose—increased in diabetes mellitus, glucocorticoid influence (e.g., exogenous, endogenous); decreased in end-stage liver disease, sepsis/endotoxemia
• BUN—increased in severe rhabdomyolysis from secondary renal injury; decreased in liver insufficiency and end-stage liver disease from decreased conversion of ammonia to urea
• Albumin—decreased in end-stage liver disease from decreased production; minimally to mildly decreased in inflammation
• Globulins—generally increased in end-stage liver disease and with chronic antigenic stimulation
• SD—increased with acute and ongoing hepatocellular injury
• ALP—increased with concurrent cholestatic disease
• GGT—increased with cholestatic disease or hepatocellular injury
• CK—increased with acute or ongoing muscle injury
• Conjugated bilirubin—increased in cholestatic disease
• Unconjugated bilirubin—increased with anorexia and prehepatic cholestasis (i.e., massive in vivo hemolysis)
• Cholesterol—may be increased with cholestasis and lipid disorders, and decreased in hepatic insufficiency.
• Triglycerides—increases may be associated with hepatic lipidosis.
• Because of high AST activity in erythrocytes, hemolysis falsely elevates serum/plasma AST activity.
• Prolonged in vitro exposure of serum or plasma to erythrocytes falsely increases AST activity even before visible signs of hemolysis are present. To avoid this confounding factor, prompt separation of plasma/serum from the cellular components of blood is strongly recommended.
• If laboratory analysis will not occur within 1–2 days, freeze the plasma/serum.

Urinalysis
Bilirubinuria—Conjugated bilirubin, detected by the commonly used dipstick and diazo tablet methods, indicates cholestatic disease and should not be increased if only hepatocellular injury is present.

OTHER LABORATORY TESTS
SBA
• Sensitive test for hepatobiliary disease, but not specific for the type of hepatobiliary disease
• May be increased with cell injury, cholestasis, or hepatic insufficiency/decreased functional mass; specificity for the latter condition is greatly

ASPARTATE AMINOTRANSFERASE (AST)

increased when SBA are increased in cases with normal or minimally increased markers for hepatocellular injury (e.g., SD, AST, GGT) and cholestasis (e.g., ALP, GGT, conjugated bilirubin).
• Main advantage over plasma ammonia, a more specific test for hepatic insufficiency/ decreased functional mass, is that immediate sample analysis is not necessary.

Plasma Ammonia

• Hepatic insufficiency/decreased functional mass is indicated if fasting or challenge ammonia concentration is increased.
• A sensitive and specific test, because it is not affected by other factors (e.g., cholestasis). However, ammonia measurement requires special handling, which limits its general availability.
• Consult reference laboratory for specific sample submission requirements.

Coagulation Tests and Fibrinogen

• The liver manufactures many of the coagulation factors; 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.

Serologic Tests

Helpful in detecting infectious causes

Toxicology

• Analysis of tissue biopsy material, feed, ingesta, serum/plasma, or other body fluids may indicate presence of a toxin.
• Contact reference laboratory regarding sample selection and submission recommendations.

Bacterial, Fungal, or Viral Culture

• May establish a definitive diagnosis regarding the infectious agent involved and help to guide treatment.
• Request bacterial antibiotic sensitivity to determine appropriate antibiotic therapy.
• Contact reference laboratory regarding sample selection and submission recommendations.

Sulfobromophthalein and Indocyanine Green Dye—Clearance Tests for Evaluation of Hepatic Function

These tests have been replaced by plasma ammonia and SBA.

IMAGING

Ultrasonography for Liver Disease

• Limited by position and size of the liver
• Evaluate size, echogenicity, shape, and position.
• Useful for guidance when obtaining biopsy material for cytology, histopathology, and microbiology
• Helpful in the evaluation of muscle and tendon injuries
• Other diagnostic imaging modalities such as radionucleotide imaging are expensive and available only at select institutions.

OTHER DIAGNOSTIC PROCEDURES

• Aspiration cytology and histopathology of formalin-fixed tissue (particularly liver)
• Cytology has the advantages of simplicity, quicker turnaround, better individual cellular detail, and better recognition of individual infectious organisms.
• Histopathology has the advantage of allowing examination of the tissue architecture and lesion distribution.
• Success of these procedures depends on the quality of the sample, area sampled, and the disease process itself; some hepatic diseases do not have significant microscopic alterations.

PATHOLOGICAL FINDINGS

Pathological findings will depend on the primary disease process and complications.

TREATMENT

AIMS OF TREATMENT

Depend on the primary disease process and secondary complications

APPROPRIATE HEALTH CARE

Depends on the primary disease process and secondary complications

NURSING CARE

Depends on the primary disease process and secondary complications

ACTIVITY

Depends on the primary disease process and secondary complications

DIET

Depends on the primary disease process and secondary complications

CLIENT EDUCATION

Depends on the primary disease process and secondary complications

SURGICAL CONSIDERATIONS

Depends on the primary disease process and secondary complications

MEDICATIONS

DRUG(S) OF CHOICE

Depends on the primary disease process and secondary complications

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 the coagulation panel results.

PRECAUTIONS

Depends on the primary disease process and secondary complications

POSSIBLE INTERACTIONS

Depends on the primary disease process and secondary complications

ALTERNATIVE DRUGS

Depends on the primary disease process and secondary complications

FOLLOW-UP

PATIENT MONITORING

Serial serum biochemical analyses to monitor progression or improvement of the disease process (see Pathophysiology)

PREVENTION/AVOIDANCE

Depends on the primary disease process and secondary complications

POSSIBLE COMPLICATIONS

Depends on the primary disease process and secondary complications

EXPECTED COURSE AND PROGNOSIS

Depends on the primary disease process and secondary complications

MISCELLANEOUS

ASSOCIATED CONDITIONS

Depend on the primary disease process and secondary complications

AGE-RELATED FACTORS

See Signalment.

ZOONOTIC POTENTIAL

Infectious diseases such as salmonellosis

PREGNANCY

See Signalment.

SYNONYMS

Previously known as glutamate oxaloacetate transaminase (SGOT)

SEE ALSO See Causes.

ABBREVIATIONS

• GI = gastrointestinal
• ID = iditol dehydrogenase
• SBA = serum bile acids

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Consulting Editor Kenneth W. Hinchcliff

ASPIRATION PNEUMONIA

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 (e.g., administration of medication into the lung via a nasogastric tube). • Characterized by ventral consolidation of the lungs • Other organ systems may be involved depending on the primary cause.

SIGNALMENT
• No sex or breed predisposition has been observed.
• Foals appear more prone to GI reflux and subsequent AP.

SIGNS

Historical Findings
• Dysphagia, ptyalism, or discharge of food, water, or milk from the nostrils may have been observed before the onset of respiratory signs. • Recent history of drenching or nasogastric intubation should be investigated.

Physical Examination Findings
• Clinical signs—depression, anorexia, fever, tachypnea, dyspnea, nasal discharge, and coughing.
• Foul-smelling breath or nasal discharge suggests anaerobic infection. • Abnormal lung sounds are often heard on 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 musculature—white muscle disease and hyperkalemic periodic paralysis • Diseases causing pharyngeal obstruction—strangles, pharyngeal abscess, neoplasia, foreign body, dorsal displacement of the soft palate, rostral displacement of the palatopharyngeal arch, and cysts • Congenital abnormalities—cleft palate and hypoplasia of the soft palate
• Iatrogenic causes—pharyngeal and laryngeal surgery

Esophageal Disorders
• Esophageal obstruction—foreign body, feed impaction, stricture, compression (e.g. abscess, neoplasia) • Megaesophagus • Esophageal diverticulum • Esophageal fistula

GI Reflux
Gastric outflow obstruction is usually secondary to ulcer disease in foals.

Accidental Inhalation of a Foreign Body
Administration of fluids by drenching or nasogastric tube

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Acute bronchopneumonia—often follows viral infection or stressful events (e.g., anesthesia, transportation, strenuous exercise)
• Pleuropneumonia—possible complication of AP, bronchopneumonia, pulmonary abscess, or secondary to thoracic trauma or esophageal rupture; auscultation, percussion, ultrasonography, radiography, or thoracocentesis helps confirm pleural effusion.
• Interstitial pneumonia—thoracic radiography most commonly reveals marked increase in overall lung opacity. • Respiratory distress syndrome—severe respiratory distress noted 24–48 hours after birth caused by surfactant deficiency; thoracic radiography typically shows diffuse, ground-glass appearance of the lungs with air bronchograms.

CBC/BIOCHEMISTRY/URINALYSIS
• Elevated WBC count with absolute neutrophilia is common. • Band neutrophils may be present.
• Hyperfibrinogenemia, hyperglobulinemia, and anemia are common findings with chronic pneumonia.

OTHER LABORATORY TESTS
• Increased blood and tissue concentrations of lead are diagnostic for lead toxicity. • Decreased whole-blood selenium concentration and glutathione peroxidase activity with increased serum creatinine kinase (CK) and aspartate amino-transferase (AST) are consistent with white muscle disease. • Hyperkalemic periodic paralysis may be diagnosed by genetic testing or by finding hyperkalemia during clinical episodes.

IMAGING
• Thoracic radiography commonly reveals ventral patchy opacity often obscuring the cardiac silhouette.
• Contrast radiography may help to diagnose causes of esophageal diseases. • Thoracic ultrasonography is a sensitive means of detecting pleural effusion.

OTHER DIAGNOSTIC PROCEDURES
• Tracheobronchial aspiration for cytology, gram stain, and culture (both aerobic and anaerobic); with pleural effusion, collect fluid sample by thoracocentesis for cytology and culture • Endoscopy of the respiratory and upper GI tracts may help to identify the primary cause.

PATHOLOGIC FINDINGS
• Consolidation of the ventral region of the lungs
• Acute cases—severely affected areas are hemorrhagic and edematous. • Chronic cases—affected lung may be necrotic and filled with purulent material. • Pleural space involvement—fibrinous exudate and adhesions

TREATMENT

• Treat severe dyspnea according to the cause—restore airway patency, drain pleural effusion, etc. • Nasal oxygen (6–10 L/min) if severe hypoxemia (PaO_2 < 60 mm Hg) • The primary disease must be treated. • Stall rest is imperative. • Dysphagic horses may be fed via an indwelling nasogastric tube. • With pleural effusion, thoracocentesis or placement of indwelling chest tubes can achieve drainage; a one-way valve attached to the tube prevents pneumothorax. • Administer fluid therapy as needed.

MEDICATIONS

DRUG(S) OF CHOICE
• Promptly initiate systemic administration of broad-spectrum antimicrobials while waiting for culture results. • Preferred combinations include sodium or potassium penicillin (22,000–40,000 IU/kg IV q6h), aminoglycoside (gentamicin [6.6–8.8 mg/kg IV q24h] or amikacin [15–20 mg/kg IV or IM q24h] for foals), and metronidazole (15–25 mg/kg IV or PO q6–8h). • Other antimicrobial choices include procaine penicillin G (22,000 IU/kg IM q12h), trimethoprim-sulfamethoxazole (30 mg/kg PO q12h), ceftiofur (1–5 mg/kg IV or IM q12h), or chloramphenicol (20–50 mg/kg PO q6–8h for adults and foals >1 week). • Administer antimicrobial drugs systemically until the horse's condition is stable and improving; treatment may then be switched to long-term oral antimicrobials. • NSAIDs—flunixin meglumine (1.1 mg/kg PO or IV q12–24h) or phenylbutazone (2.2–4.4 mg/kg PO or IV q12h)

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Use aminoglycosides and NSAIDs with caution in horses with compromised renal function or dehydration.

FOLLOW-UP

PATIENT MONITORING
• Monitor clinical signs, especially respiratory rate and efforts, and rectal temperature. • Follow progress of pulmonary lesions by radiography. • Ultrasonography helps to monitor pleural effusion.

PREVENTION/AVOIDANCE
• Prevent or avoid exposure to primary causes.
• Vitamin E and selenium supplementation for white muscle disease

POSSIBLE COMPLICATIONS
• Lung abscess • Pleuritis • Disseminated intravascular coagulation • Laminitis • Thrombophlebitis • Septicemia

EXPECTED COURSE AND PROGNOSIS
• Expect a long and protracted course of treatment.
• Prognosis is guarded.

MISCELLANEOUS

SEE ALSO
• Hemorrhagic nasal discharge
• Pleuropneumonia
• Acute respiratory distress syndrome

ABBREVIATIONS
• AP = aspiration pneumonia
• GI = gastrointestinal

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ATHEROMA OF THE FALSE NOSTRIL

BASICS

OVERVIEW
• An epidermal inclusion cyst of the false nostril (nasal diverticulum)
• Also called false nostril cyst
• Present at birth and becomes apparent with age as the cyst enlarges
• Usually a cosmetic issue only
• The term "atheroma" is a misnomer as it implies a sebaceous cyst.
• The false nostril cysts in horses are not sebaceous cysts.

SIGNALMENT
• Any age
• Usually becomes apparent after weaning to 3 years of age. Most often at yearling 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 at the area of the nasomaxillary notch
• Typically unilateral, but can be bilateral
• Not painful on palpation
• Size increases with age and can reach a size of up to 5cm
• Usually not associated with respiratory compromise unless very large

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 keratinized and nonkeratinized squamous epithelial cells and keratinous debris.
• Histologically, the cyst lining is comprised of 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
• Histological evaluation

TREATMENT

• Do nothing. 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.
• A technique has been reported using intralesional injection of neutral-buffered 10% formalin after aspirating the cyst contents. Injection of formalin until leakage around the needle is seen (2–4.5 mL). There is transient swelling within 24 hours of injecting the formalin. Desiccation of the cyst occurs after a few weeks.

MEDICATIONS

DRUGS
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 atheroma 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
N/A

SEE ALSO
N/A

Suggested Reading

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Atopic Dermatitis

BASICS

DEFINITION
Chronically relapsing, inflammatory, pruritic skin disease resulting from a predispostion to develop IgE-mediated hypersensitivities to inhaled or cutaneously absorbed environmental allergens

PATHOPHYSIOLOGY
The complete pathomechanism of equine AD is unknown. Susceptible animal is sensitized to environmental allergens resulting in the production of allergen-specific IgE. Upon further exposure to percutaneously absorbed or inhaled allergens, an immediate type I hypersensitivity ensues. The reaction commences by binding of allergen-specific IgE to FcεRIα receptors on mast cells ultimately causing degranulation and liberation of inflammatory mediators such as histamine, cytokines, chemokines, and proteolytic enzymes. The culmination of these inflammatory processes is pruritus and/or urticaria.

SYSTEMS AFFECTED
• Skin • Respiratory

GENETICS
• Genetic predisposition and heritability of AD in horses are unknown. AD must have a genetic component due to the clinical observation that the disease appears more often within certain breeds. • One stallion with AD has five offspring with AD, each from a different mare—suggesting a dominant mode of inheritance.

INCIDENCE/PREVALENCE
True incidence is unknown; estimated at 2%–4% of the equine population; within the top 10 most common equine dermatoses

GEOGRAPHIC DISTRIBUTION
Recognized worldwide; local environmental factors (temperature, humidity, and flora) influence the seasonality, severity, and duration of signs.

SIGNALMENT
Breed Predilections
Arabians, Thoroughbred, Quarter Horses, and Warmbloods have been reported to be predisposed.

Mean Age and Range
Mean 5–6.5 years of age (2–12 years); signs may be mild the first year and usually progress each year.

Predominant Sex
• Both sexes affected equally • In a recent small regional study, males (geldings > stallions) were twice as likely as mares to develop AD.

SIGNS
General Comments
• Hallmark sign—chronic relapsing seasonal or nonseasonal pruritus and/or urticaria (rubbing, itching, biting themselves, stomping, tail flicking, rarely head shaking, and agitation) • Primary lesions are wheals representing an urticarial reaction and/or papules. • Secondary lesions reflect self-induced trauma from intense pruritus at the affected body site and consists of alopecia, excoriations, erosions to ulcers, scale, lichenification, hypopigmentation, and mane and tail loss. Lesions may be symmetrical. • Urticaria in AD may be pruritic or nonpruritic.

Historical
• Most commonly affected sites include face, pinnae, chest, ventral thorax and abdomen, extremity extensor and flexor surfaces • Other common sites include the mane, dorsolateral neck, croup, and tail base. • Clinical signs may begin in any season and progress from seasonal to nonseasonal. • Symptoms become progressively more severe with time.

Physical Examination
• Clinical signs of atopy-associated recurrent airway obstruction include head shaking, snorting, bilateral mucopurulent nasal discharge, conjunctivitis, dry unproductive coughs, labored breathing, stomping, and face rubbing on front legs or objects and exercise intolerance. • Uncommon clinical signs are head shaking and laminitis.

CAUSES
• Airborne pollens (trees, grasses, weeds) • Mold spores (indoor and outdoor) • Animal danders (mouse, cat, cow, poultry, goat) • Possibly storage and house dust mites

RISK FACTORS
• Temperate environments with long allergy seasons, high pollen and mold spore levels • Concurrent pruritic dermatoses, such as insect hypersensitivity or ectoparasitic disease (summation effect)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Insect hypersensitivity—may occur concurrently with AD • Ectoparasites (pathogens and incidentals) • Cutaneous adverse food reaction—rare • Contact hypersensitivity • For respiratory disease—respiratory infection (bacterial, fungal, viral), congestive heart failure, and bronchitis

CBC/BIOCHEMISTRY/URINALYSIS
Eosinophilia is rare.

OTHER LABORATORY TESTS
Serologic Allergy Tests
• Detects relative levels of allergen-specific IgE in the serum • Controversy exists as to the usefulness of serum allergy tests in horses; the author does not recommend the use of these tests. • A positive result does not always correlate with clinical manifestation of allergy; therefore, results of these tests must be interpreted cautiously. • The effects of antihistamines and corticosteroid administration on test results are unknown. • Many false-positive and -negative results occur with the currently available assays. Lack of repeatability of test results and sensitivity are common. • Do not use to diagnose cutaneous adverse reaction to food or supplements.

IMAGING
N/A

OTHER DIAGNOSTIC PROCEDURES
Intradermal Testing
• Detects levels of allergen-specific IgE in the skin directed to a panel of allergens that are region specific and thought to be clinically-relevant to the patient's disease. • IDT is the gold standard test for allergen hypersensitivity identification in horses. • Performed for identification of allergens to include in ASIT, possible avoidance or decrease in exposure • Intradermal injection of allergens results in raised turgid wheals. The reaction is given a subjective score (usually 0–4+) based on its size and turgidity compared to the positive and negative controls. • Reactions are interpreted at 15–30 min for an immediate IgE-mediated type I hypersensitivity and 4 hr for the IgE-mediated late-phase reaction. • Normal horses have one or more positive intradermal reactions. • Interpret results in terms of the horse's environment, clinical signs, and history to determine allergens that should be avoided and included in ASIT. • Before performing IDT, a withdrawal period of 14 days is observed for oral and topical antihistamines as well as topical steroid preparations and 30 days for parenteral corticosteroids. • Cytology from erosions or ulcers shows a neutrophilic exudate with intra- and/or extracellular cocci representative of a secondary folliculitis. • Perform skin scrapings to rule out ectoparasites. • Perform bacterial and DTM cultures to determine bacterial species and susceptibility and/or dermatophyte infections.

PATHOLOGICAL FINDINGS
• Skin biopsy—will not rule out other differential diagnosis such as insect or food hypersensitivity • Histopathological changes—epidermal hyperplasia with superficial and deep, perivascular to interstitial dermatitis wherein the eosinophil is the predominant inflammatory cell. Concurrent focal eosinophilic infiltrative and/or necrotizing mural folliculitides and/or eosinophilic granulomas are possible.

TREATMENT

AIMS OF TREATMENT
Reduce pruritus and secondary infections.

APPROPRIATE HEALTH CARE
Outpatient medical management

NURSING CARE
Frequent bathing using cool water (antimicrobial shampoos, sulfur/salicyclic acid, +/− colloidal oatmeal rinses or leave-on conditioners) helps to remove allergens, crusts, bacteria, and debris; control secondary infections; hydrate dry skin; and provide antipruritic effects.

ACTIVITY
Avoid offending allergens if possible by changing environment.

DIET
Essential fatty acid supplementation may be beneficial in some cases.

ATOPIC DERMATITIS

CLIENT EDUCATION
• Imperative to discuss the progressive nature of the disease • Advise disease is not curable, but rather manageable and life-long therapy may be needed. • Advise that commitment to proper management of horses with AD can lead to a horse that has a good quality of life and can continue to work. • Discuss that therapeutic modifications over the life of the horse are to be expected. • Due to the potential hereditary factor, owners should be advised to remove affected individual from breeding stock.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE

Allergen-Specific Immunotherapy
• Subcutaneous administration of gradually increasing doses of causative allergens in an attempt to reduce sensitivity • Allergens for inclusion are based on correlation of history with positive intradermal results and knowledge of local flora. • A useful nonsteroidal long-term treatment alternative when signs last longer than 2 mo or when nonsteroidal forms of therapy are ineffective • Anticipated improvement may be seen as early as 2 mo; however, minimum treatment duration of 12–14 mo is necessary to determine efficacy. • Reports indicate 50%–75% of horses with AD show at least a 50%–100% improvement in clinical signs with ASIT.

Corticosteroids
• Best selection—prednisolone, greater bioavailability than prednisone, tablets or syrup (compounded) at 0.5–1.5 mg/kg q24h until control achieved; then reduce to lowest-dose alternate-day regimen, for example, 0.2–0.5 mg/kg q48h • For horses that do not respond to prednisolone, try dexamethasone powder or injectable. Initial loading oral or IV dose of 0.02–0.1 mg/kg q24h for 3–5 days; then taper to 0.01–0.02 mg/kg q48–72h for maintenance. • Repository injectable corticosteroids should be avoided as withdrawal upon an adverse reaction is not possible.

Antihistamines—A Nonsteroidal Alternative for Long-term Control
• Not useful when moderate to severe pruritus is present; rather use as a preventative either before the onset of severe pruritus or in a maintenance regimen to suppress pruritus once controlled. • Pharmacokinetic data for the use of antihistamines in horses are limited. Anecdotal reports suggest that H_1-receptor antagonist hydroxyzine hydrochloride/pamonate (0.5–1 mg/kg q8h), chlorpheniramine (0.25 mg/kg q12h), diphenhydramine (0.75–1.0 mg/kg q12h), or pyrilamine malate (1 mg/kg q12h) may decrease pruritus and provide a steroid-sparing effect. • Antihistamines should be given at least 10–14 days before efficacy is determined. If no response, select another class of antihistamine.

Tricyclic Antidepressants
Used to control hypersensitivity with a stress or psychogenic component. Horses may respond to doxepin HCl (0.5–0.75 mg/kg q12h PO) or amitriptyline (1–2 mg/kg q12h PO).

CONTRAINDICATIONS
• Due to the anticholinergic properties of antihistamines and tricyclic antidepressants, do not use in patients with a history of cardiac arrhythmias, colic, glaucoma, or urinary retention disorders. Antihistamines may thicken mucus in the respiratory tract. Extra caution should be used in horses with respiratory problems due to excess mucus. • Avoid corticosteroid use during pregnancy and lactation unless the benefits outweigh the risks. Risks are likely low.

PRECAUTIONS
• Corticosteroids—Use judiciously to avoid iatrogenic hyperglucocorticism, diabetes mellitus, polydipsia and polyuria, aggravation of bacterial folliculitis, decreased muscle mass, weight loss, poor wound healing, and behavior changes. • Antihistamines—can produce sedation and/or behavior changes, whole body or fine tremors or seizures. High doses of antihistamines cause birth defects in laboratory animals. Antihistamines should only be used in pregnant or lactating animals if the benefits outweigh the risks. Do not administer antihistamines intravenously in the horse due to potential CNS stimulation. • Note drug withdrawal times and regulations pertaining to horse show or racing associations.

POSSIBLE INTERACTIONS
• If diuretics such as furosemide are given with corticosteroids, an increased risk of electrolyte imbalances due to calcium and potassium losses exists. • Prednisolone interacts with phenytoin, phenobarbital, rifampin, erythromycin and the anticholinesterase drugs, neostigmine and pyridostigmine. • Antihistamines have an additive effect when combined with other CNS-depressant drugs, such as tranquilizers.

ALTERNATIVE DRUGS
Polyunsaturated omega 3 and 6 fatty acids—variable response in decreasing pruritus; provide support for epidermal barrier function and anti-inflammatory properties. Use as adjunctive therapy. Response noted within 2–8 weeks after starting therapy. Exact dosing for horse is lacking; the author uses 180 mg of EPA/10 lb q24h.

FOLLOW-UP

PATIENT MONITORING
• Examine patient every 2–6 weeks when a new course of therapy is commenced. • Monitor pruritus, self-trauma, secondary bacterial dermatitis, and possible adverse drug reactions.
• Once an acceptable level of pruritus is achieved, examine patient every 4–12 mo.
• CBC, serum biochemical profile, and fibrinogen are recommended within the first week of starting corticosteroid therapy and then every 1–4 mo thereafter if chronic corticosteroid therapy cannot be avoided.

PREVENTION/AVOIDANCE
• Avoidance of allergens is not always possible or practical, especially as many patients have multiple allergens contributing to their disease.
• Prevention of the disease may be possible if patient is moved to another region of the country.

POSSIBLE COMPLICATIONS
• Secondary bacterial dermatitis • Secondary laminitis, colic, and iatrogenic hyperadrenocorticism due to chronic steroid administration

EXPECTED COURSE AND PROGNOSIS
• Not life-threatening unless intractable pruritus persists • No reports of spontaneous remission exist.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Insect hypersensitivity • Eosinophilic granulomas • Allergic conjunctivitis and rhinitis • Recurrent airway obstruction • Inflammatory airway disease • Summer pasture–associated obstructive pulmonary disease

AGE-RELATED FACTORS
Severity worsens with age.

ZOONOTIC POTENTIAL
N/A

PREGNANCY
• Corticosteroids—contraindicated during pregnancy • Antihistamines—no information on teratogenicity is available for horses; consider this before treating pregnant mares.

SYNONYMS
Equine atopy

SEE ALSO
• Insect hypersensitivity • Urticaria • Bacterial dermatitis • Ectoparasites

ABBREVIATIONS
• AD = atopic dermatitis • ASIT = allergen specific immunotherapy • IDT = intradermal test • DTM = dermatophyte test medium

Suggested Reading
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Author Gwendolen Lorch
Consulting Editor Gwendolen Lorch

Atrial Fibrillation

BASICS

DEFINITION
• An irregularly irregular cardiac rhythm, with variable-intensity heart sounds and pulses and inconsistent diastolic intervals
• Can be sustained or paroxysmal (resolving spontaneously within 48 hr of onset)

PATHOPHYSIOLOGY
• A critical atrial mass must be present for the condition to occur.
• Predisposing factors—large atrial mass, high vagal tone, shortened and nonhomogeneous effective refractory period, potassium depletion, atrial premature depolarizations, rapid atrial pacing
• Produces no change in cardiac output at rest without underlying cardiac disease
• During high-intensity exercise, produces a marked increase in the heart rate response and fall in cardiac output and exercise capacity
• Present in many horses with CHF but is not the cause of CHF

SYSTEM AFFECTED
Cardiovascular

SIGNALMENT
Higher incidence in Standardbreds, Draft, and Warmblood horses

SIGNS
General Comments
Causes exercise intolerance in performance animals, but often an incidental finding in sedentary horses

Historical
• Exercise intolerance
• Exercise-induced pulmonary hemorrhage—often profuse
• Weakness or collapse

Physical Examination
• 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.
• 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.
• Sinus rhythm with multifocal ventricular premature depolarizations—Need ECG to differentiate.

CBC/BIOCHEMISTRY/URINALYSIS
Low plasma potassium or urinary fractional excretion of potassium may be present.

OTHER LABORATORY TESTS
• Elevated cardiac isoenzymes (e.g., CK-MB, HBDH, LDH-1 and LDH-2, cardiac troponin I) may be present but are usually within the normal range.
• RBC potassium concentrations may be decreased.

IMAGING
ECG
• No P waves, replaced by baseline "f" waves
• 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 normal in appearance.

Echocardiography
• Most 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 sinus rhythm.
• Mild left atrial enlargement with sustained AF
• Atrial enlargement due to congenital defects or AV valve insufficiency may be present.

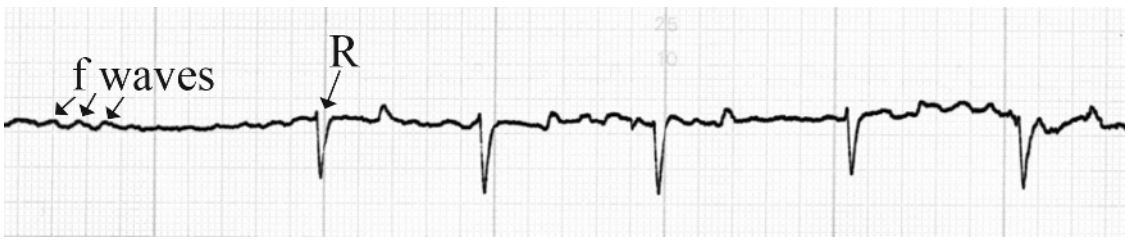

Figure 1.

Base-apex lead, 25 mm/sec, 5 mm = 1 mV.

ATRIAL FIBRILLATION

DIAGNOSTIC PROCEDURES

Continuous 24-Hour Holter Monitoring

Use in horses with suspected paroxysmal AF to identify underlying arrhythmias.

Exercise Electrocardiography

• Useful to detect exercise-induced arrhythmias and to determine 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 long-standing 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 OF TREATMENT

• Restoration of sinus rhythm and athletic performance in horses with exercise intolerance but no, or minimal, underlying heart disease
• Palliative care for horses with AF in conjunction with CHF

APPROPRIATE HEALTH CARE

• Monitor horses for 24–48 hr to determine if the condition will resolve without treatment (i.e., paroxysmal).
• In horses with AF and CHF, institute treatment for congestive heart failure—for example, using digoxin (0.0022 mg/kg IV) and furosemide (1–2 mg/kg IV, not PO).
• If AF is sustained, CHF is not present, and exercise intolerance is present, pharmacological or electrical cardioversion should be considered.

NURSING CARE

• Perform continuous ECG throughout attempted conversion to sinus rhythm.
• Keep horses quiet and unmoving during quinidine treatment.

ACTIVITY

• AF cases should not perform high-intensity exercise.
• AF cases usually can perform successfully as pleasure horses, in lower-level athletic competition, as broodmares, and as breeding stallions.

DIET

• Oral potassium supplementation may be indicated with low plasma potassium, low RBC potassium, or low urinary fractional excretion of potassium or with excessive sweating.
• Potassium chloride salt can be added to the feed (1 tbsp BID, gradually increasing to 1 oz BID).

CLIENT EDUCATION

• Discuss treatment-associated risks with owners—see Possible Complications.
• Discuss predisposing factors with owners to minimize the likelihood of future episodes.

SURGICAL CONSIDERATIONS

• Successful transvenous electrical conversion of horses under general anethesia has been described.
• This utilizes a biphasic current delivered between electrodes placed in the right atrium and left pulmonary artery using pressure waveforms, echocardiography, and radiography to guide and confirm electrode placement.
• Initial reports of success rates from one center are very encouraging.

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 10 mg/kg.

Quinidine Sulfate

• Indicated in horses with sustained AF
• Administered via nasogastric intubation at 22 mg/kg q2h to a total of four to six treatments, then q6h until the horse shows signs of toxicity or has converted to sinus rhythm.

CONTRAINDICATIONS

• Do not administer quinidine sulfate or gluconate to affected horses with CHF.
• Horses with a resting heart rate of >60 bpm and/or grade 3/6 or louder systolic murmurs are likely to have CHF.

PRECAUTIONS

Quinidine is associated with the following complications.

Cardiovascular

• Prolonged QRS duration—indicates quinidine toxicity.
• Rapid supraventricular tachycardia—treat aggressively with digoxin to slow heart rate.
  ○ Digoxin is recommended in conjunction with quinidine in horses with myocardial dysfunction or rapid heart rate during quinidine treatment.

ATRIAL FIBRILLATION

- ○ If heart rate exceeds 100 bpm, consider digoxin—0.011 mg/kg PO or 0.0022 mg/kg IV.
- ○ If a heart rate exceeds 150 bpm, consider digoxin (0.0022 mg/kg IV) and sodium bicarbonate (1 mEq/kg IV).
- ○ If the heart rate remains high, administer propranolol—0.03 mg/kg IV.
- ○ 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 heart rate or to improve myocardial contractility.

• Ventricular arrhythmias require treatment unless ventricular rhythm is slow (<100 bpm), uniform, and no R-on-T is detected.
• Treat ventricular arrhythmias with magnesium sulfate—2–5 mg/kg bolus IV q5min to 50 mg/kg total or propranolol—0.03 mg/kg IV.
• Hypotension—monitor and treat, if severe, with intravenous fluids to effect and, if necessary, phenylephrine (0.1–0.2 μg/kg per minute IV to effect).
• Sudden death—Try to prevent with continuous ECG and treatment of any arrhythmias that occur.

GI
• Flatulence—resolves on return of quinidine plasma concentrations to negligible levels.
• Oral ulcerations—Prevent by not administering quinidine via nasogastric tube.
• Diarrhea—indicates quinidine toxicity, resolves on return of quinidine plasma concentrations to negligible levels.
• Colic—indicates quinidine toxicity; treat with analgesics as needed.

Respiratory
Upper respiratory tract obstruction—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

POSSIBLE INTERACTIONS
Quinidine competes with digoxin for binding to plasma protein, causing potential digoxin toxicity.

ALTERNATIVE DRUGS
Oral, but not intravenous, flecanide and intravenous amiodarone have recently been proposed.

FOLLOW-UP

PATIENT MONITORING
• Perform continuous ECG during treatment, because antiarrhythmic drugs are also arrhythmogenic.
• Measure QRS duration before each dose; discontinue treatment if QRS duration ≥25% of the pretreatment value.
• Discontinue treatment if rapid supraventricular tachycardia, ventricular arrhythmia, diarrheal colic, ataxia, convulsions, bizarre behavior, urticaria, upper respiratory tract obstruction, or laminitis occurs.
• Following conversion, perform 24-hour Holter monitoring. If atrial ectopy is found, rest and corticosteroid therapy may be indicated.
• Riders should regularly monitor cardiac rhythm; any irregularities or poor performance should prompt reexamination.

ATRIAL FIBRILLATION

PREVENTION AVOIDANCE
• Discontinue administration of furosemide and bicarbonate milkshakes.
• Administer potassium or other electrolyte supplementation, if indicated.
• See Supraventricular Arrhythmias.

POSSIBLE COMPLICATIONS
• If AF is not or cannot be treated, clinical signs will persist.
• Some horses with AF also have exercise-induced ventricular arrhythmias; this possibility should be explored if AF is not or cannot be treated and the horse is to continue to be used for ridden exercise—see Ventricular Arrhythmias.

EXPECTED COURSE AND PROGNOSIS
• Most horses with little or no underlying cardiac disease convert to sinus rhythm with quinidine therapy.
• Recurrences occur in ≅25% of horses with a suspected duration of atrial fibrillation of ≤4 mo.
• Recurrences occur in ≅60% of horses with a duration of atrial fibrillation of >4 mo.
• Recurrence is mostly likely during the first year after conversion but can occur at any time.
• Prognosis for return to the previous level of athletic performance is excellent in converted horses without significant underlying cardiovascular disease.
• Horses with sustained AF that do not convert to sinus rhythm 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.
• 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 congestive heart failure respond to the supportive therapy and improve for a short time but are euthanized within 2–6 mo of initiating treatment.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Any cardiac disease resulting in atrial enlargement predisposes to atrial fibrillation.

AGE-RELATED FACTORS
• Old horses are more likely to have significant underlying cardiac disease with valvular insufficiency and atrial enlargement.
• These horses usually are not candidates for conversion because of significant underlying cardiac disease.

PREGNANCY
• Affected pregnant mares without underlying cardiac disease and congestive heart failure should not experience any problems.
• Affected pregnant mares with CHF can be treated for the underlying cardiac disease with positive inotropic drugs (e.g., digoxin) and diuretics (e.g., furosemide).

SYNONYMS
A fib

SEE ALSO
• Congestive heart failure
• Mitral regurgitation
• Tricuspid regurgitation
• Supraventricular arrhythmias
• Ventricular arrhythmias

ABBREVIATIONS
• AF = atrial fibrillation
• AV = atrioventricular
• CK-MB = MB isoenzyme of creatine kinase
• CHF = congestive heart failure
• GI = gastrointestinal
• HBDH = α-hydroxybutyrate dehydrogenase
• LDH = lactate dehydrogenase
• RBC = red blood cell

Suggested Reading

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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 hr 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 one of the two 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 congestive heart failure.

SYSTEM 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
May be detected as an incidental finding, but usually is part of a more complex, congenital cardiac disorder

Historical
• Exercise intolerance—medium-size to large ASDs
• Congestive heart failure—large ASDs

Physical Examination
• No murmur may be present, or a coarse, band- or ejection-shaped, holosystolic murmur with PMI in pulmonic valve area may be detected.
• Premature beats or an irregularly irregular heart rhythm of atrial fibrillation 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
Electrocardiography
• Atrial premature depolarizations or atrial fibrillation may be present in horses with right and left atrial enlargement.
• Persistent atrial fibrillation 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 two 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 at 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.

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-Hour Holter Monitoring
Use in identifying intermitent 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 congestive heart failure, ventral and peripheral edema, pleural effusion, pericardial effusion, chronic hepatic congestion, and, occasionally, ascites may be detected.

ATRIAL SEPTAL DEFECT

TREATMENT

AIMS OF TREATMENT
• Management by intermittent monitoring in horses with small ASDs
• 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 congestive heart failure can be treated for congestive heart failure with positive inotropic drugs, vasodilators, and diuretics. Consider humane destruction if congestive heart failure 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 atrial fibrillation 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 atrial fibrillation 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 AV 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, CONTRAINDICATIONS, PRECAUTIONS, POSSIBLE INTERACTIONS, 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—atrial fibrillation; congestive heart failure

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 atrial fibrillation.
• 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 congestive heart failure usually have a guarded to grave prognosis for life. Most such horses being treated for congestive heart failure should respond to the supportive therapy and transiently improve; however, once congestive heart failure 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
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
• ASD = atrial septal defect
• AV = atrioventricular
• PMI = point of maximal intensity

Suggested Reading

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AURAL PLAQUES

BASICS

OVERVIEW
• Aural plaques are whitish plaques on the inner surface of the pinna of horses.
• Likely related to papilloma virus infection
• May or may not be associated with varying degrees of ear sensitivity
• Lesions do not spontaneously regress.
• Treatment has been unsuccessful until recently.

SIGNALMENT
• Common in both sexes and all breeds.
• Not frequently observed in horses <1year of age.

SIGNS
• Depigmented, well-demarcated papules and plaques covered with keratin deposits located on the concave surface of the pinna. Lesions are single, multiple, or coalescing and may affect one or both pinna.
• Horses can be asymptomatic or may resent bridling or handling of the ears.
• Head shaking has been rarely reported.
• Symptoms may be aggravated by biting flies.

CAUSES AND RISK FACTORS
• Bovine papilloma virus is suspected.
• Abrasions and insect bites may be involved in transmission.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Sarcoids—usually identified on the external surface of the pinna or at the margins of the ear. They may be coexistent 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.

PATHOLOGICAL FINDINGS
Histologic features consistent with papilloma virus infection including papillated epidermal hyperplasia, koilocytosis, and increased numbers and size of keratohyalin granules.

TREATMENT

• Multiple treatments are advocated but none have been shown consistently effective.
• CO_2 laser ablation, corticosteroids, tretinoin, and Eastern blood root in zinc chloride have all been tried with variable results and recurrence is common.
• Management of affected horses often involves minimizing resistance to ear handling and protecting ears from biting insects.

MEDICATIONS

DRUG(S) OF CHOICE
• Imiquimod (Aldara) has recently been evaluated in a clinical trial and is effective at removing the plaques. Recurrence rates are as yet undetermined.
• Imiquimod is applied topically as a thin layer 2–3×/week every other week until resolution (typically 3–4 mo of every other week treatment).

AURAL PLAQUES

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
A strong local inflammatory response is consistently observed with imiquimod due to its mechanism of action. This can make it difficult to clean the ears prior to the subsequent treatment. Sedation is often needed, particularly for the second or third treatments of the treatment weeks. Owners should be warned of the reaction and temporarily increased sensitivity due to local inflammation.

FOLLOW-UP

PATIENT MONITORING
• Monitoring for complete resolution is important. Imiquimod causes enough local reaction that it can be difficult to determine if the plaques are still present. One to 2 weeks without treatment allows better evaluation and recheck evaluation at 1 mo post-treatment is strongly recommended.
• Each lesion must be treated. No effect is observed on untreated lesions.

PREVENTION/AVOIDANCE
• *Generally* not possible
• Use of fly repellents with permethrin/pyrethrin (for quick insect knockdown) and piperonyl butoxide (as a pesticide synergist) in addition to fly masks that provide ear coverage may help prevent development of additional lesions.

POSSIBLE COMPLICATIONS
• Ear sensitivity and pain on cleaning
• Imiquimod can cause skin erosions or ulcers, particularly if applied in a thick layer. Erosions appear to be more common in the first month of treatment. The amount of reaction seems to decrease as the plaques resolve.

EXPECTED COURSE AND PROGNOSIS
• Aural plaques persist without treatment.
• Post-treatment skin depigmentation may occur.
• Initial results with imiquimod treatment suggest that after resolution of the plaques, horses are less sensitive to ear manipulation than prior to treatment.

MISCELLANEOUS

ASSOCIATED CONDITIONS
None known

AGE-RELATED FACTORS
None known

ZOONOTIC POTENTIAL
None

PREGNANCY
Does not affect disease or treatment

SEE ALSO
• Papillomatosis
• Sarcoid

Suggested Reading

Berman B, Hengge U, Barton S. Successful management of viral infections and other dermatoses with imiquimod 5% cream. Acta Dermatol Enereal 2003;suppl 214:12–17.

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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 SUN (serum urea nitrogen) typically are measured in serum and used as indices of azotemia.

PATHOPHYSIOLOGY
• Serum urea concentration is determined by rate of urea synthesis by hepatocytes and rate of clearance by the kidneys. • Increased protein catabolism results in elevated SUN. • Decreased GFR may result from decreased renal perfusion (i.e., prerenal azotemia); primary renal disease, either insufficiency or failure (i.e., renal azotemia); or urinary obstruction (i.e., postrenal azotemia). • Azotemia results from resorption of urine when urinary tract rupture (i.e., postrenal azotemia) results in accumulation of urine in the body cavities (abdomen) or subcutaneously.
• Creatinine is a result of muscle creatine metabolism; serum levels reflect the rate of synthesis and rate of excretion. • Rate of synthesis is relatively constant except in the face of rhabdomyolysis. • Renal excretion is dependent on GFR. • Creatinine is not resorbed by renal tubules. • Low serum urea levels may result after prolonged diuresis or as a result of impaired liver function. • There is no clinical significance to decreased creatinine levels.

SYSTEMS AFFECTED
• Generalized or systemic effects—depression, weakness, weight loss, edema, and dehydration
• Gastrointestinal—anorexia, uremic stomatitis, uriniferous breath, excessive dental tartar, gingivitis, oral/gastric ulceration, mild protein-losing enteropathy, diarrhea, and melena
• Neuromuscular—dullness, lethargy, gait imbalance, tremors, behavioral changes, seizures, and stupor • Endocrine/metabolic—renal secondary hyperparathyroidism, inadequate production of erythropoietin and 1,25-dihydrocholecalciferol, decreased hormone clearance that prolongs plasma half-life (e.g., parathormone, gastrin), decreased tissue sensitivity (e.g., insulin, parathormone), decreased hormone production (i.e., testosterone), and hypersecretion to reestablish homeostasis (i.e., parathormone)
• Cardiovascular—elevated blood pressure, heart murmur, and cardiac dysrhythmia
• Respiratory—dyspnea • Hemic/lymphatic/immune— anemia and impaired immune function

GENETICS
No genetic predisposition

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
All ages, breeds, and sexes

SIGNS
General Comments
• Azotemia does not always equate to clinical signs of disease described here. • Unless the animal is uremic, clinical findings are limited to the process causing azotemia—dehydration, urinary outflow tract obstruction, or rupture.

Historical
• Weight loss • Anorexia • Abnormal urination
• Depression • Lethargy • Dental tartar
• Uriniferous breath • Poor performance
• Lumbar pain • Colic • Abdominal distension
• Poor hair coat • Prolonged posturing to urinate • PU/PD

Physical Examination
• Fever • Anorexia • Depression • Oral pallor
• Poor body condition • Ventral edema • Oral ulceration • Excessive dental tartar • Scleral injection • Colic • Distended abdomen • Urine scalding • Dysuria • Hematuria • Halitosis

CAUSES
Prerenal Azotemia
• Renal hypoperfusion caused by decreased circulating volume or decreased blood pressure
• Protein catabolism associated with fever, infection, trauma, myositis, thermal injury, and corticosteroid therapy • General anesthesia
• Prolonged exercise

Renal Azotemia
Acute or chronic renal failure—primary renal dysfunction affecting glomeruli, renal tubules, renal interstitium, or renal vasculature and impairing 60%–75% of renal function

Postrenal Azotemia
• Obstruction of the urinary tract • Rupture of the urinary outflow tract

RISK FACTORS
Medical Conditions
• Renal disease • Diarrhea • Endotoxemia
• Acute blood loss • Septic shock • Prolonged exercise • Urolithiasis • Exposure to nephrotoxic chemicals or plants • Dehydration • Acidosis
• Hepatic disease • Neoplasia

Drugs
• Aminoglycosides
• NSAIDs
• Diuretics

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Prerenal azotemia—dehydration, hypovolemia, acute blood loss, decreased cardiac output, exhaustive disease syndrome, some colic cases
• Renal azotemia
  ○ *Acute renal failure* with increased or decreased urine output is suggestive of vitamin K_3 toxicity, red maple leaf toxicosis, aminoglycoside toxicosis, other nephrotoxic chemicals, vasomotor nephropathy, abnormal kidney size, and rarely leptospirosis.
  ○ *Chronic renal failure* with progressive weight loss, PU/PD, pitting edema, other signs over several weeks or months suggests chronic glomerulohephritis or pyelonephritis, amyloidosis, polycystic kidney disease, renal hypoplasia, and nephrolithiasis.
• Postrenal azotemia—abrupt decrease in urine output and acute signs of uremia, abdominal distension, stranguria and signs of colic may suggest ruptured ureter, ruptured bladder, or obstructive urolithiasis.

CBC/BIOCHEMISTRY/URINALYSIS
CBC
Nonregenerative anemia caused by decreased erythropoietin production occurs with chronic renal failure.

Biochemistry
• Consider hydration status, presenting complaint and physical exam findings when interpreting SUN/Cr levels.
• In horses, the SUN:Cr ratio is unreliable in differentiating acute from chronic renal failure.
• Correcting dehydration deficits and restoring renal perfusion dramatically reduces SUN and Cr in patients with prerenal azotemia.
• Relieving outflow obstruction or correcting the rent in the excretory pathway rapidly decreases the degree of azotemia in patients with postrenal azotemia.
• Hyponatremia and hypochloremia are common in horses with renal disease and can occur with third-compartment spacing of fluid as in uroperitoneum.
• Hyperkalemia is a common finding in urinary tract disruption and uroperitoneum.
• Calcium and phosphorus levels vary in renal disease.
• Hypercalcemia and hypophosphatemia often are found with chronic renal failure; hypocalcemia and hyperphosphatemia are seen with acute renal failure.
• Hypercalcemia in renal failure depends on dietary content and intake of calcium.

Urinalysis
• Urine specific gravity >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, steroids) may render the urine specific gravity value inconclusive.
• Dehydrated horses with primary renal disease usually lose the ability to concentrate urine;urine specific gravity and osmolality are <1.020 and <500 mOsm/kg, respectively.
• Urine specific gravity does not differentiate postrenal, prerenal or primary renal azotemia.

IMAGING
Radiography
Rarely is used to evaluate the urinary tract in adult horses but is useful in foals and miniature horses

Ultrasonography
• The urinary tract can be examined either transrectally or transabdominally.
• Bladder ultrasonography is best performed transrectally using a 5-MHz probe.
• Transcutaneous ultrasonography of the right or left kidney is best performed with a 2.5- or 3-MHz probe.
• Assess the size and shape of both kidneys and the architecture and echogenicity of the parenchyma.

AZOTEMIA AND UREMIA

• The renal medulla is more echolucent than the renal cortex. The renal pelvis varies in echogenicity.
• With acute renal failure, kidneys may be normal or enlarged, and parenchymal abnormalities often are not detected.
• With chronic renal failure, kidneys are smaller and more echogenic than normal.
• Cystic or mineralized areas more often are associated with chronic renal disease or congenital anomalies.
• Acoustic shadowing represents calculi formation.

Renal Scintigraphy
May be used to document renal function but commonly is not performed

OTHER DIAGNOSTIC PROCEDURES

Urine GGT:Cr Ratio
• Reflects GGT leakage from damaged renal tubular epithelium containing GGT compared to the constant 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 values in the normal range.

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 0.01–0.70 in healthy horses.
• 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; enlarged in association with pyelonephritis or ureterolithiasis

Ultrasound-Guided Renal Biopsy
Can be used to confirm the diagnosis of primary renal failure, to differentiate acute from chronic renal disease, and to identify a specific cause

Urethrocystoscopy
• Extremely useful diagnostic aid when evaluating abnormal urination, especially in geldings and stallions.
• In adult male horses, 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 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 also be obtained.

Renal Scintigraphy
May be used to document renal function but is rarely performed

TREATMENT

PRERENAL AZOTEMIA
• Correct the underlying cause of renal hypoperfusion and/or correct the dehydration deficit.
• Fluid replacement is primary therapy.
• More aggressive treatment in conditions that can lead to primary renal damage or failure

PRIMARY RENAL AZOTEMIA
• Measures to stop or reverse the immediate cause
• Supportive care to alleviate clinical signs of uremia; to correct fluid, electrolyte, and acid–base abnormalities; and to resolve the problems associated with decreased renal hormones

POSTRENAL AZOTEMIA
• Eliminate the urinary obstruction or correct the cause of urine leakage.
• Surgical intervention often is required, but correction of any metabolic derangements is paramount.
• Solute diuresis can follow correction of postrenal azotemia; thus, additional fluid therapy may be required to prevent dehydration.

FLUIDS
• IV fluid therapy is indicated for most azotemic patients.
• Commonly used fluids—0.9% saline, Ringer's, and lactated Ringer's solution.
• Base the amount of fluid administered on the dehydration or volume deficit.
• Correction of the fluid deficit can occur during the first 6 hr without untoward effects, except in patients with hypoproteinemia/hypoalbuminemia and with signs of cardiac disease.

MEDICATIONS

DRUGS OF CHOICE
Treat any patient exhibiting signs of shock appropriately.

CONTRAINDICATIONS
Use nephrotoxic drugs (e.g., aminoglycosides, NSAIDs) with caution in patients with azotemia.

PRECAUTIONS
• Use caution when administering fluids to horses with chronic renal failure, 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 cautiously. Although they can limit intrarenal inflammation, they also nonselectively block vasodilatory mediators of renal blood flow under conditions of renal hypoperfusion and are not recommended for chronic renal failure.
• Use caution with drugs requiring renal excretion. Horses should be well hydrated when using aminoglycosides and NSAIDs.
• Be aware of adverse reactions and toxic effects that may require altering dosage schedules.

FOLLOW-UP

PATIENT MONITORING
• Serum urea nitrogen, Cr, and electrolyte concentrations 24 hr after initiating fluid therapy; hydration status; and urine outflow.
• In neonates, monitoring body weight may be helpful.
• With severe acid-base derangements, more frequent monitoring may be required.

POSSIBLE COMPLICATIONS
• Failure to promptly correct prerenal azotemia caused by renal hypoperfusion may result in ischemic renal failure.
• Failure to correct renal azotemia may result in uremia.
• Failure to correct postrenal azotemia (e.g., urinary tract obstruction, uroperitoneum) may result in renal damage or death caused by hyperkalemia and uremia.

MISCELLANEOUS

AGE-RELATED FACTORS
• Primary renal failure may occur at any age, but older horses may be at higher risk for azotemia regardless of the cause.
• Postrenal azotemia caused by ruptured bladder is more common in neonatal foals.

PREGNANCY
The ability of a mare to maintain a viable pregnancy decreases as renal function decreases.

SYNONYMS
N/A

SEE ALSO
• Renal failure, acute
• Renal failure, chronic
• Urinary tract obstruction

ABBREVIATIONS
• GFR = glomerular filtration rate
• GGT = γ-glutamyltransferase
• PU/PD = polyuria/polydipsia

Suggested Reading

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