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CHAPTER 3

CLINICAL APPROACH TO COMMONLY ENCOUNTERED PROBLEMS

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3.1—Syncope and Weakness

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Syncope is a clinical syndrome consisting of a generalized weakness, sudden collapse, and a transient cessation of consciousness. Syncopal episodes are uncommon in horses, and generally few or no premonitory warning or presyncopal (faintness) signs are evident to the rider or handler. The subsequent loss of consciousness and collapse may be potentially harmful or dangerous to the horse and the rider. Despite the infrequent reports of true syncopal episodes in horses, the clinical signs are sufficiently dramatic to cause great concern on the part of the owner. Syncope in horses has been virtually unstudied. Consequently, most of the following information has been drawn from studies of persons and other animal species.

Although presyncopal signs have been well described in human beings (i.e., dizziness, yawning, confusion, and spots before the eyes), these signs are generally not evident in horses. Horses may stumble initially and go down or collapse completely. The depth and duration of unconsciousness may vary, but generally unconsciousness lasts for a few minutes. Horses may be slightly unsteady or struggle during recovery. After a syncopal attack, the horse will completely recover and appear normal.

Pathophysiology

Syncope results from a sudden reduction in cerebral blood flow and subsequent cerebral ischemia. Cerebral blood flow is maintained primarily by arterial blood pressure and cerebrovascular resistance. In response to falling or rising systemic blood pressure, the cerebral blood flow autoregulatory mechanism automatically regulates cerebral vessels to constrict or dilate. This control phenomenon maintains a constant cerebral blood flow despite fluctuations in arterial blood pressure, whether or not these fluctuations are physiologic or pathologic. If perfusion pressure in human beings falls below 60 mm Hg, the cerebral blood flow autoregulatory mechanism may fail. Mean resting arterial pressure measured at the carotid artery in horses has been reported to be 97 ± 12 mm Hg at a heart rate of 42 ± 10 beats/min.[1] Systolic pressure in horses experiencing syncope has not been determined.

Disturbances in oxygen supply to the brain generally result from three primary causes: anoxia, anemia, and ischemia. Although a variety of conditions or diseases may cause these disturbances, all three potentially deprive the brain of its critical oxygen supply.[2] Anoxia generally is described as insufficient oxygen reaching the blood so that arterial oxygen content and tension are low. This insufficiency results from an inability of oxygen to cross the alveolar membrane (e.g., pulmonary disease) or low oxygen tension in the environment (e.g., high altitude). In situations of mild hypoxia, the cerebral blood flow autoregulatory mechanism maintains oxygen delivery to the brain. When the hypoxia is severe or the compensatory mechanism fails, cerebral hypoxia occurs and syncope may result.

Anemia is defined functionally as a decreased oxygen-carrying capacity of the blood. This may be characterized

by several mechanisms, including a reduction in the amount of hemoglobin available to bind and transport oxygen or changes in hemoglobin that interfere with oxygen binding (e.g., methemoglobin). If the anemia is severe, the oxygen concentration drops below the metabolic requirements of the brain despite increased cerebral blood flow.

Finally, cerebral ischemia results when cerebral blood flow is insufficient to supply cerebral tissue. Any disease that greatly reduces cardiac output, such as myocardial infarction or an arrhythmia, ultimately may result in cerebral ischemia. If any of these aforementioned conditions occurs and cerebral blood flow is interrupted or stops with resultant cerebral underperfusion, consciousness is lost. If tissue oxygenation is restored immediately, consciousness generally returns quickly without sequelae.

Areas of the brain that maintain or control consciousness have been the subject of much debate and research. Generally, the level of activity of the brain (alertness) is maintained through sensory input to the ascending reticular activating system in the rostral brainstem, thalamus, and cerebral cortex. More specifically, the bulboreticular facilitatory area within the reticular substance of the middle and lateral pons and mesencephalon is considered to be the central driving component of the excitatory area of the brain. Recent studies have identified the role of the midbrain reticular formation and the thalamic intralaminar nuclei in maintaining consciousness and arousal in animals and human beings.[3] Syncope may result if regional cerebral blood flow to this area is disrupted for any reason.

In horses, syncope may be cardiogenic or extracardiac (neurocardiogenic) in origin. The primary cause of syncope in horses is generally cardiovascular disease. Cardiogenic syncope may result from (1) myocardial disease, (2) cardiac dysrhythmias (i.e., atrial fibrillation and third-degree heart block), (3) congenital heart disease, (4) pulmonary hypertension or stenosis, and (5) pericardial disease. Although many of these conditions are uncommon in horses, atrial fibrillation has been associated with several reports of syncope.[4]

Cardiovascular disease, resulting in an inability to regulate heart rate or in stroke volume, ultimately decreases cardiac output. Atrial fibrillation can lead to heart rates greater than 240 beats/min with submaximal exercise. The lack of effective atrial contraction prevents complete ventricular filling at the end of diastole, thus causing a great reduction in effective cardiac output. Complete heart block may be persistent or intermittent and also has been associated with syncopal episodes in horses. When the block is complete and the pacemaker below the block fails to function, syncope occurs. This situation has been reported in human beings and horses as Morgagni-Adams-Stokes syndrome. This syndrome is the most frequent arrhythmic cause of syncope in human beings.[5] Morgagni-Stokes-Adams attacks result from an advanced atrioventricular block and usually involve a momentary sense of weakness followed by an abrupt loss of consciousness. After cardiac standstill or prolonged periods of asystole, unconsciousness results from cerebral ischemia. These "cardiac faints" have been reported to occur several times a day in human beings. Additional, less common causes of cardiogenic syncope usually involve the distal conduction system (His-Purkinje system) and may be persistent or episodic. Heart block involving the atrioventricular node or proximal conduction system may be congenital or drug induced (e.g., digitalis). Sick sinus syndrome, a condition described in elderly human beings, involves impaired sinoatrial impulse formation or conduction and has been associated with cerebral anoxia. With any of these conditions, cardiac output does not increase sufficiently during skeletal muscle exercise to meet peripheral oxygen demands. Blood preferentially flows to exercising muscle, resulting in systemic arterial hypotension, which results in cerebral ischemia leading to weakness or syncope.

Extracardiac causes of syncope indirectly may involve the cardiovascular system and were referred to previously as vasovagal or vasodepressor syncope. The term *neurocardiogenic syncope* more accurately describes this phenomenon. Neurocardiogenic syncope is the most common type of syncope reported in human beings and often is precipitated by stress or pain.[6] Although not specifically described in horses, a similar mechanism of collapse likely may exist. The critical cardiovascular features include hypotension and paradoxical sinus bradycardia, heart block, or sinus arrest after sympathetic excitation. Additionally, cardiac asystole may occur as an extreme manifestation of neurocardiogenic syncope. The mediating mechanisms of neurocardiogenic syncope are not well understood; however, several theories have been proposed. Hypercontractile states may cause excessive stimulation of the myocardial mechanoreceptors (C fibers) located in the left ventricle. The result is an exaggerated parasympathetic afferent signal carried by the vagus and glossopharyngeal nerves with a subsequent decrease in sympathetic tone. Inhibition of sympathetic vasoco strictor activity results in vasodilation, which may be especially evident during periods of vigorous activity and increased heart rates and blood pressure. The excess vagal activity produces bradycardia and a decrease in cardiac output. This combination, along with a decrease in peripheral vascular resistance, ultimately leads to syncope.

Regardless of the specific cause, syncope results from a sudden fall in cerebral blood flow. The loss of consciousness is caused by a reduction of oxygenation to the parts of the brain that maintain consciousness. In horses, syncope usually is caused by a fall in systemic blood pressure resulting from a decrease in cardiac output.

Additional, less common causes of syncope in horses may include neurologic disease from space-occupying lesions or increased intracranial pressure. Syncopal episodes have been reported in foals with severe respiratory or congenital heart disease.[7] After minimal exercise or restraint in these foals, hypoxia and subsequently reduced cerebral blood flow may result in syncope. Certain drugs, specifically phenothiazine tranquilizers (acepromazine), have been reported to cause syncope in horses. These tranquilizers produce antiadrenergic effects primarily through α_1-blockade with resultant vasodilation and hypotension. If phenothiazine tranquilizers are administered to severely hypovolemic horses or to horses that have hemorrhaged, severe hypotension and syncope may result.

Several disorders often are confused with syncope and should be differentiated carefully by an accurate history and thorough physical examination. These disorders include (1) epilepsy, (2) hypoglycemia, (3) narcolepsy and cataplexy, (4) cerebrovascular disease, and (5) hyperkalemic periodic paralysis.

Epileptic seizures generally differ from syncope in that they have immediate onset and involve loss of consciousness, tonic and clonic convulsive activity with opisthotonos, and changes in visceral function (urination and defecation). Seizures commonly last for several minutes and often are followed by a postictal phase in which the horse may pace, appear blind, and not recognize its surroundings.

Metabolic disturbances such as hypoglycemia frequently are observed in neonatal foals and may be associated with weakness or syncopal-like episodes. Typically, foals are premature or are subject to perinatal stress with subsequent increased glucose use following hypoxia or sepsis. Serum glucose determination is necessary to evaluate hypoglycemia.

Narcolepsy, an abnormal sleep tendency, and cataplexy occasionally may be difficult to distinguish from syncope as a cause of unconsciousness. Attacks of narcolepsy or cataplexy may be preceded by signs of weakness (buckling at the knees) followed by total collapse and areflexia. Rapid eye movements may occur with an absence of spinal reflexes. No other neurologic abnormalities are observed between attacks, although animals may appear sleepy between episodes. Provocative testing with physostigmine (0.05 mg/kg) may induce narcoleptic attacks and might be helpful in differentiating syncope from narcolepsy or cataplexy.

Cerebrovascular disease associated with head trauma and subarachnoid hemorrhage may cause temporary unconsciousness in horses. Clinical signs resulting from brain trauma generally are associated with focal cerebral dysfunction and therefore are readily distinguishable from syncope.

Hyperkalemic periodic paralysis causes weakness and collapse without alterations in consciousness. This autosomal dominant disorder has been reported in certain lines of registered Quarter Horses, Paints, and Appaloosas. A reliable DNA-based test is available to diagnose hyperkalemic periodic paralysis in horses.

Evaluation of Syncope

A thorough evaluation of syncope in the horse consists of the following:

1. *History:* Emphasis should be placed on obtaining a detailed history. The onset and the duration of the problem along with performance history should be determined.
2. *Physical examination:* After a thorough physical examination and determination of vital signs, a detailed cardiovascular and neurologic examination should be performed. In addition to heart rate at rest and pulse characteristics, a thorough cardiac auscultation should be performed in a quiet room to identify any murmurs or cardiac dysrhythmias. An electrocardiogram and echocardiogram also provide valuable information. A neurologic examination should evaluate reflexes and sensory and motor function carefully to identify any central or peripheral neuropathies.
3. *Complete blood count and biochemical profile:* To rule out other potential causes of syncopelike episodes (e.g., hypoglycemia and sepsis), a complete blood count and biochemical profile should be performed. Additionally, serum lactate dehydrogenase (isoenzymes 1 and 2) and creatine kinase (CK-2) concentration determinations may be helpful in identifying cardiac dysfunction.
4. *Exercise/stress test:* A thorough cardiac evaluation should be performed following strenuous exercise, including auscultation and an electrocardiogram. If available, a high-speed treadmill may be helpful in this phase of the evaluation. If any cardiac abnormalities are detected on physical examination, exercise testing on a treadmill will allow a more thorough evaluation of the cardiovascular system, although care must be taken to ensure that such testing does not exacerbate the condition of the horse.

Diagnosis of the cause of syncope in horses is not always easy, because the cause should be considered a symptom complex rather than a primary disease. In addition to the infrequent reports of syncope, the history is often vague and the neurologic and cardiovascular examinations may not lead to a specific cause. Even in the absence of apparently overt cardiovascular disease (e.g., atrial fibrillation), cardiac dysrhythmias cannot be excluded as the possible cause of syncope.

Treatment of Syncope

Options for treating syncope in horses are limited. The frequency of the syncopal attacks and the underlying

cause (i.e., cardiogenic or neurocardiogenic) may determine if a course of treatment should be undertaken. Generally, treatment of syncope should be directed toward preventing or correcting the cause of the decreased cerebral perfusion. An accurate pathophysiologic diagnosis is essential for treating cardiogenic syncope. A few reports in the literature indicate successful treatment of syncope in horses associated with atrial fibrillation.[4] A horse with a complete heart block returned to work after implantation of a transvenous cardiac pacing system.[8]

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3.2—Polyuria and Polydipsia

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The complaint of excessive urination and drinking may be encountered with some frequency in equine practice. Before pursuing a lengthy diagnostic workup, verifying that 24-hour urine production and voluntary water consumption exceed reference ranges is important. Urine production in adult horses may range from 15 to 30 ml/kg/day, and values as high as 48 ml/kg/day have been reported.[1-4] Daily urine volume is affected by diet; more water is lost in the urine in horses fed pelleted diets and legume hays than in horses fed grass hay. The latter excrete more water in feces.[5,6] Generally, any component of the diet that increases renal solute load increases urine volume (e.g., high salt content in the diet). Voluntary water intake also is affected by the ambient temperature (Table 3.2-1). When temperatures are high and evaporative water losses increase to cool the horse, voluntary water intake also increases. Diet and climatic conditions therefore must be considered when interpreting water consumption and urine production data. Water requirements are proportional to metabolic body size rather than to body mass. Thus larger horses, particularly draft breeds, require less water per kilogram than do smaller horses, ponies, or miniature horses. In addition, fat is low in water content compared with lean body tissue, and fat animals require proportionately less water than do lean animals.[7]

Some owners may misinterpret polyalkiuria (frequent urination usually of small volume) as polyuria. Quantitative collection of urine for a 24-hour period may be required to verify excessive urine production. Several simple collection apparatuses have been described.[8,9]

Maintenance of Water Balance in Health

Maintenance of water homeostasis depends on establishing a balance between intake and excretion such that plasma osmolality remains constant (within approximately 2% of normal).[10] The primary determinant of renal water excretion is antidiuretic hormone (ADH).[11] ADH is a polypeptide synthesized in three nuclei in the hypothalamus (suprachiasmatic, paraventricular, and supraoptic nuclei)[12] and transported from the latter two nuclei in secretory granules down axons of the

TABLE 3.2-1

Voluntary Water Consumption in Healthy Horses

	WATER CONSUMPTION	
AMBIENT TEMPERATURE	**ml/kg/day**	**L/450 kg**
5°–16° C (41°–61° F)	44–61	19.8–27.5
25° C (77° F)	70	31.5

Data from Tasker JB: Fluid and electrolyte studies in the horse. III. Intake and output of water, sodium and potassium in normal horses, *Cornell Vet* 57:649-657, 1967; Rose BD: *Clinical physiology acid-base and electrolyte disorders,* New York, 1989, McGraw-Hill Information Services; and Groenedyk S, English PB, Abetz I: External balance of water and electrolytes in the horse, *Equine Vet J* 20:189-193, 1988.

supraopticohypophyseal tract into the posterior lobe of the pituitary where ADH is stored. Some ADH enters the cerebrospinal fluid or portal capillaries of the median eminence from the paraventricular nucleus.[11] In addition, neurons from the suprachiasmatic nucleus deposit ADH in other areas in the central nervous system.[12] In human beings, lesions of the posterior pituitary or supraopticohypophyseal tract below the median eminence usually do not lead to permanent central diabetes insipidus because ADH still has access to systemic circulation in these cases.[11] The clinical importance of these anatomic relationships in horses is not known.

ADH increases renal water reabsorption and urine osmolality by augmenting water permeability of luminal membranes of cortical and medullary collecting tubules. ADH augments urea, and in some species NaCl, accumulation in the interstitium, therefore promoting medullary hypertonicity. The primary stimuli for ADH release are plasma hyperosmolality and depletion of the effective circulating blood volume. Osmoreceptors in the hypothalamus detect changes in plasma osmolality of as little as 1%.[11] Although the threshold for ADH release in the horse is not known, 24-hour water deprivation in healthy ponies resulted in approximately an 8 mOsm/kg increase in plasma osmolality (about 3%), from 287 ± 3 mOsm/kg to 295 ± 4 mOsm/kg, which was associated with an increase in plasma ADH concentration from 1.53 ± 0.36 pg/ml to 4.32 ± 1.12 pg/ml.[13] In another study of ponies, water deprivation for 19 hours resulted in an increase in plasma osmolality from 297 ± 1 mOsm/L to 306 ± 2 mOsm/L.[14] In human beings, plasma osmolalities of 280 to 290 mOsm/L stimulate ADH release. The organs that sense changes in effective circulating blood volume include arterial and left atrial baroreceptors. These stretch receptors function indirectly as volume sensors by responding to the reductions in intraluminal pressure that typically accompany loss of plasma volume. Reduced activation of these receptors by hypovolemia or heart failure is a potent cause of ADH release, even in the absence of increased plasma osmolality. ADH secretion also may be stimulated by stress (pain), nausea, hyp glycemia, and certain drugs including morphine and lithium.[11]

When the need for water in body fluids cannot be met by conservation via the renal/ADH axis, thirst is stimulated. Thirst is regulated primarily by plasma tonicity; however, in human beings the threshold for stimulation of thirst is approximately 2 to 5 mOsm/kg greater than that for stimulation of ADH release.[11] Thirst is controlled by osmosensitive neurons in close proximity in the hypothalamus to osmoreceptors that mediate ADH secretion.[12] Thirst is sensed peripherally by oropharyngeal mechanoreceptors as dryness of the mouth. Thirst also may be stimulated by volume depletion through an incompletely understood mechanism. Experimental ponies drank when their plasma osmolalities increased by 3% after water deprivation, when plasma Na concentrations increased by approximately 5%, and after induction of a plasma volume deficit of 6%.[14]

Mechanism of Urine Concentration

For the kidney to make concentrated urine, ADH must be produced, the renal collecting tubules must respond to ADH, and the renal medullary interstitium must be hypertonic. Generation of medullary hypertonicity is initiated in the thick ascending limb of the loop of Henle by active transport of NaCl out of the lumen. Because the thick ascending limb is impermeable to water, active resorption of NaCl results in hypotonicity of the fluid entering the distal tubule in the renal cortex (Figure 3.2-1, *A*). The distal tubules and cortical portions of the collecting ducts are permeable to water (Figure 3.2-1, *B*), which is reabsorbed down its concentration gradient into the interstitium. Reabsorbed water is transported rapidly out of the interstitium by the extensive cortical capillary network, and interstitial hypertonicity is preserved. Urea remains in the lumen of the distal tubule and cortical collecting duct and is concentrated further. Luminal fluid flows into the medullary collecting duct, which is permeable to water and urea when under the influence of ADH (Figure 3.2-1, *C*). Water is reabsorbed down its progressively steeper concentration gradient as luminal fluid moves through the medullary collecting ducts. Some urea also is reabsorbed into the interstitium. Reabsorbed water is removed efficiently by the vasa recta in the renal medulla. Because these blood vessels also are arranged in a hairpin loop, minimal loss of medullary interstitial solute occurs with water removal. Some reabsorbed urea enters the loop of Henle (Figure 3.2-1, *D*) and thus is recycled, helping to maintain medullary hypertonicity. In the absence of ADH, the collecting ducts are relatively impermeable to water and urea, resulting in water and urea loss in urine and reduction of medullary solute. Prolonged diuresis of any cause may result in the loss of medullary hypertonicity (medullary washout) with subsequent impairment of renal concentrating ability. Water is reabsorbed down its concentration gradient from the thin descending limb of the loop of Henle (Figure 3.2-1, *E*) as a consequence of medullary hypertonicity. This segment of the nephron is impermeable to NaCl and urea, thus the osmolality of luminal fluid in the most distal portion of the loop approaches that of the interstitium. The thin ascending limb of the loop of Henle is permeable to NaCl, which diffuses down its concentration gradient into the interstitium (Figure 3.2-1, *F*). As previously mentioned, this segment is also permeable to urea, and some interstitial urea enters the tubule lumen by diffusion down its

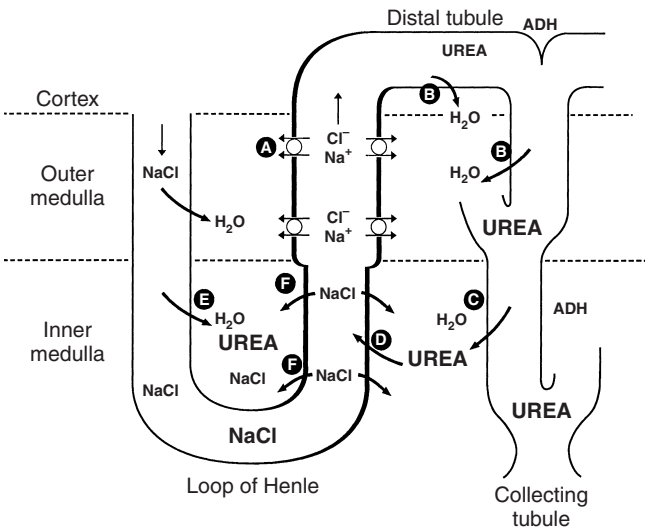

Figure 3.2-1 The countercurrent hypothesis identifies the roles of sodium chloride and urea transport in the generation of concentrated urine.

(From Hansen B: Polyuria and polydipsia. In Fenner WR: *Quick reference to veterinary medicine,* ed 2, Philadelphia, 1991, JB Lippincott. Adapted from Jamison RL, Maffly RH: The urinary concentration mechanism, *N Engl J Med* 295:1059-1067, 1976.)

concentration gradient. Luminal fluid entering the thick ascending limb of the loop of Henle is thus hypotonic to the interstitium.

When luminal fluid reaches the thick ascending limb of the loop of Henle, approximately 80% of the glomerular filtrate has been reabsorbed. Therefore only 20% of the glomerular filtrate is available for reabsorption via the action of ADH.[15,16]

Primary Polydipsia

Excessive water intake may result in water diuresis. Primary polydipsia has been described in horses residing in the southern United States during months when ambient temperature and humidity are high. Apparent psychogenic polydipsia may result from boredom, especially in stalled, young horses.[8] Psychogenic polydipsia also has been reported anecdotally in horses with chronic liver disease and central nervous system signs that had been treated with intravenous fluids.[17] Primary disorders of thirst are poorly understood in horses.

Causes of Polyuria With Secondary Polydipsia

Increased urine flow may be induced by solute or water diuresis (Box 3.2-1). Solute diuresis results in increased urine flow because of excessive renal excretion of a nonreabsorbed solute such as glucose or sodium. During solute diuresis, the urine osmolality is equal to or higher than the plasma osmolality. Primary renal insufficiency or failure (33% or fewer intact nephrons) result in solute diuresis, because each functional nephron must filter an increased amount of solute to maintain daily obligatory solute excretion. Fractional clearances of solutes such as Na, K, and Cl therefore appropriately increase. Solute diuresis caused by glucosuria occurs in hyperglycemic horses when the maximal renal reabsorptive capacity for glucose is exceeded (180 to 200 mg/dl).[18] Solute diuresis caused by glucosuria has been reported in horses with pituitary adenoma and in a hyperglycemic horse with bilateral granulosa cell tumors.[19,20] Primary diabetes mellitus, a common cause of hyperglycemia and glucosuria in other species, is uncommon in the horse, although type 2 diabetes mellitus was diagnosed in a 15-year-old Quarter Horse mare.[21] Primary renal tubular glucosuria caused by a defect in proximal tubular glucose reabsorption (as is seen in Basenji dogs with Fanconi-like syndrome)[15] has not been reported in horses. Psychogenic salt consumption also has been reported to cause solute diuresis in a horse.[22] Postobstructive solute diuresis is not diagnosed commonly in horses because nephrolithiasis and ureterolithiasis are uncommon; when they occur, the condition is often bilateral and associated with chronic renal failure, and treatment is usually unsuccessful.[23,24]

Decreased water resorption in the collecting tubules or inappropriately large voluntary water intake causes water diuresis. The osmolality of the urine during water diuresis is less than that of plasma. Water diuresis may be caused by insufficient ADH secretion, insensitivity of the receptors of the distal collecting duct and collecting tubules to the action of ADH, renal medullary solute washout, or apparent psychogenic polydipsia. Insufficient secretion of ADH (central diabetes insipidus) may be associated with adenoma of the pars intermedia of horses but has never been documented[25] and with head trauma and potassium depletion in other species. A case of idiopathic central diabetes insipidus was reported in a Welsh pony.[26] Insensitivity of collecting duct receptors to ADH may occur during endotoxemia and hyperadrenocorticism (glucocorticoid excess associated with tumors of the pars intermedia). In other species, potassium depletion, hypercalcemia, and the administration of certain drugs (including gentamicin) have been reported to cause insensitivity of the collecting duct receptors to ADH.[15] Congenital diabetes insipidus also has been reported in other species.[26] True nephrogenic diabetes insipidus implies isolated dysfunction of response to ADH by collecting tubules that are not associated with other structural or metabolic lesions of the kidney. The occurrence of nephrogenic diabetes insipidus in two sibling Thoroughbred colts has suggested that the condition might be heritable in some horses.[27] Renal medullary washout (loss of medullary Na,

BOX 3.2-1

CAUSES OF POLYURIA AND POLYDIPSIA

Solute Diuresis

Primary renal insufficiency or failure
Glucosuria (adenoma of the pars intermedia of the pituitary)
Psychogenic salt consumption
Diabetes mellitus
Postobstructive diuresis

Water Diuresis

Insufficient antidiuretic hormone (central diabetes insipidus)
  Adenoma of the pars intermedia of the pituitary
  Head trauma
  (Potassium depletion)*
Insufficient response of collecting ducts to antidiuretic hormone
Acquired nephrogenic diabetes insipidus
  Hyperadrenocorticism (glucocorticoid excess with adenoma of the pars intermedia of the pituitary)
  Endotoxemia
  (Drugs: gentamicin, lithium, methoxyflurane, amphotericin B, propoxyphene, etc.)
(Congenital nephrogenic diabetes insipidus)
Renal medullary solute washout
  Chronic diuresis of any cause
  Inappropriate renal tubular sodium handling
Apparent psychogenic polydipsia
(Chronic liver disease)
(Polycythemia)
(Pyometra)
(Hypercalcemia)
(Potassium depletion)

Iatrogenic

Intravenous fluid therapy
Excess dietary salt
Drugs:
  Diuretics
  Glucocorticoids
  (Drugs causing acquired diabetes insipidus)

Modified from Hansen B: Polyuria and polydipsia. In Fenner WR: *Quick reference to veterinary medicine,* ed 2, Philadelphia, 1991, JB Lippincott.
*(), Not reported in horses.

Cl, and urea) leading to water diuresis may result from chronic diuresis of any cause. Diuresis is associated with increased tubular flow rates and inability to resorb sodium and urea adequately from the tubular lumen. Enhanced medullary blood flow may deplete medullary solute further. Water diuresis also has been reported in association with pyometra, hypoadrenocorticism (chronic renal sodium loss), chronic liver disease (increased aldosterone concentration promotes sodium retention, smaller daily load of urea for excretion caused by decreased conversion of ammonia to urea), primary polycythemia, hypercalcemia, and potassium depletion in other species.[15]

Approach to the Horse With Polyuria and Polydipsia

Iatrogenic causes of polyuria and polydipsia (see Box 3.2-1) should be ruled out by careful assessment of the history and by documentation of return to normal urine volume and water intake after withdrawal of intravenous fluids, excess dietary salt, or drugs implicated in causing polyuria and polydipsia (Figure 3.2-2). Verification of 24-hour urine volume and water intake should be undertaken for horses suspected of having polyuria and polydipsia that do not display obvious polyuria (frequent large volume urination and wet stall) and polydipsia (water bucket always empty and overt thirst). Hemogram, serum biochemistries, and urinalysis should be assessed for all horses with polyuria and polydipsia. A hallmark finding in horses with polyuria and polydipsia is a decreased urine specific gravity (USG). Identification of other abnormalities on laboratory tests (e.g., increased blood urea nitrogen or creatinine concentrations, hyperglycemia, and hypokalemia) necessitates ruling out the presence of underlying diseases (such as renal insufficiency and adenoma of the pars intermedia of the pituitary) using specialized laboratory tests.

The hydration status of horses then should be assessed carefully. Those horses that are dehydrated should be rehydrated judiciously with intravenous fluids, taking care not to overhydrate horses with renal insufficiency. After rehydration, when possible, creatinine clearance should be determined by using a urine collection apparatus to allow 24-hour volumetric urine collection. A creatinine clearance value below the reference range (1.46 to 3.68 ml/min/kg)[28] suggests that renal insufficiency with decreased glomerular filtration rate and solute diuresis are likely present. A creatinine clearance within the reference range indicates that central diabetes insipidus (CDI), nephrogenic diabetes insipidus (NDI), or apparent psychogenic polydypsia (APP) is present. To distinguish among these differential diagnoses, an exogenous ADH challenge test should be performed (see the subsequent discussion).

Horses with polyuria and polydipsia that are well hydrated and healthy based on physical examination and results of hemogram and serum biochemistry determinations should be subjected to a water deprivation test to assess renal ability to conserve water.[2,29,30] Water

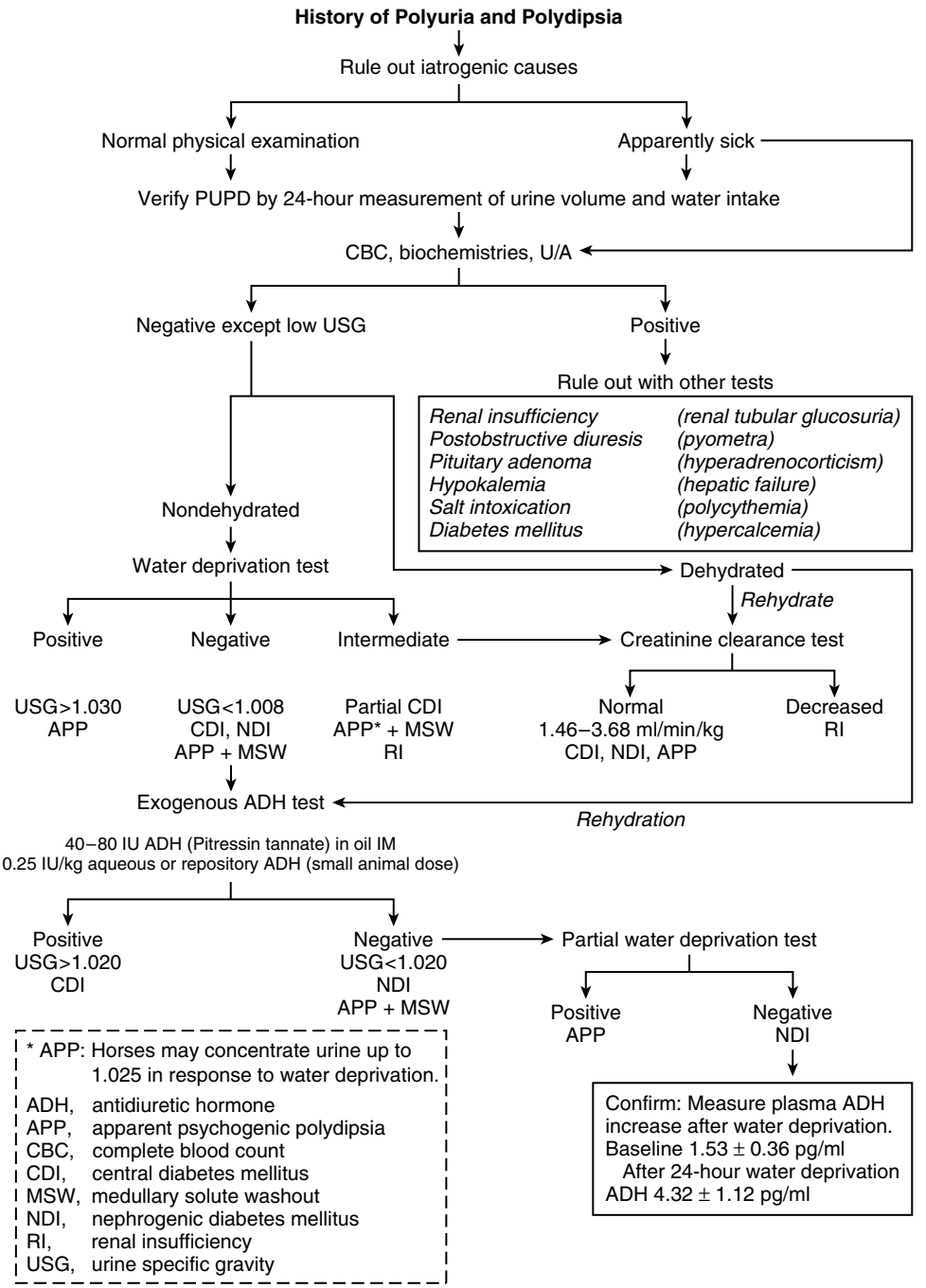

Figure 3.2-2 Approach to the polyuric patient. *PUPD,* Polyuria and polydipsia; *U/A,* Urinalysis.

(Modified from Hansen B: Polyuria and polydipsia. In Fenner WF: *Quick reference to veterinary medicine,* ed 2, Philadelphia, 1991, JB Lippincott.)

deprivation testing is contraindicated in a dehydrated horse with a low USG. Such horses have already undergone an endogenous water deprivation test (clinical dehydration is present) and have responded with an inappropriately low USG. The following guidelines for interpretation of water deprivation test results are based on practical experience and the limited data available. A positive response to water deprivation (USG >1.030) indicates that the horse has APP, whereas a negative response (USG <1.008) after 24 hours of water deprivation or greater than 5% weight loss[31] is consistent with a diagnosis of CDI, true NDI, insensitivity of collecting duct receptors to ADH, or apparent psychogenic polydipsia and medullary solute washout (APP plus MSW). Horses with a negative response to water

deprivation testing should undergo an exogenous ADH challenge. Some horses may have an intermediate response to water deprivation. An intermediate response is consistent with partial CDI or APP plus MSW or renal insufficiency, and assessment of creatinine clearance is indicated. Consult Chapter 18 for a more detailed discussion of water deprivation testing.

An evaluation of a response to the administration of exogenous ADH is indicated for horses that do not concentrate their urine adequately during water deprivation testing, for horses that require rehydration and subsequently demonstrate creatinine clearance values within reference ranges, and for rehydrated horses for which creatinine clearance determinations are impractical. Two regimens for exogenous ADH administration have been reported: 40 to 80 IU ADH as Pitressin tannate in oil intramuscularly[32] or 0.25 IU/kg aqueous or repository ADH intramuscularly. A few reports of responses of horses to exogenous ADH administration have been made, and the following recommendations are based on clinical experience. A positive response to exogenous ADH (USG >1.020) confirms the diagnosis of CDI. A negative response (USG <1.020) implies that NDI or APP plus MSW is present.[31]

MSW may result in a decreased USG despite the presence of adequate ADH. A partial water deprivation test should result in an increase in USG in horses with APP plus MSW but should have no effect on horses with true NDI or insensitivity of collecting duct receptors to ADH. The horse is allowed to consume its normal diet and water ad libitum. Voluntary water consumption is monitored closely for 3 to 4 days to establish a baseline. Water available to the horse then is decreased by 5% to 10% of the baseline voluntary intake. Water should be offered in aliquots several times a day to prevent the horse from consuming most of the water in a short time. Water intake should never be restricted below maintenance requirements (about 40 ml/kg/day). During water restriction, the horse is allowed to eat its regular diet. The horse should be weighed daily if possible and should be observed carefully for signs of dehydration (prolonged capillary refill time, increasing heart rate, prolonged skin tenting, and hypernatremia). Moderate water restriction in the face of continued intake of dietary solutes facilitates reestablishment of the corticomedullary osmotic gradient.[15] Results of partial water deprivation tests in horses have been reported infrequently.

The diagnosis of true NDI or insensitivity of collecting duct receptors to ADH may be confirmed by measuring plasma ADH concentrations before and after partial water deprivation. ADH concentrations have been reported to increase from baseline values of 1.53 ± 0.36 pg/ml to 4.32 ± 1.12 pg/ml after 24 hours of water deprivation in ponies.[13]

Because CDI, NDI, and APP are uncommon in horses, the presenting complaint of polyuria and polydipsia usually signifies other underlying disease. The most likely underlying disease is renal insufficiency. Pituitary adenoma should be considered in horses with compatible clinical signs (hirsutism, weight loss, and laminitis) and supporting laboratory data (hyperglycemia and failure of suppression of cortisol production by dexamethasone).[33] Medullary washout may be a more common complication of primary diseases and their therapy in horses than has been reported to date. Potential causes of diuresis compatible with the case history and clinical signs should be investigated, and a partial water deprivation test should be considered when horses exhibit polyuria and polydipsia.

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3.3—Edema

Kenneth W. Hinchcliff

Edema is the excessive and abnormal accumulation of fluid in the interstitium. Interstitial fluid accumulates because of imbalances in the rates with which fluid enters and exits the interstitium. Factors that increase the rate of fluid flux from the capillary or impair lymph drainage sufficiently to overwhelm normal compensatory mechanisms result in accumulation of fluid and the development of edema.

Physiology

The volume of interstitial fluid and lymph fluid in the normal horse is 8% to 10% of body mass,[1] or 36 to 45 L in a 450-kg horse. Interstitial fluid consists of water, protein, and electrolytes. Compared with plasma, interstitial fluid has a slightly lower concentration of cationic electrolytes, a slightly higher concentration of chloride, and a much lower concentration of protein (1.2 versus 0.2 mOsm/L of water).[2] The amount and function of plasma proteins within the interstitial space are not inconsequential. A constant circulation of plasma proteins occurs between the vascular and interstitial spaces, with about half of the protein circulating every 24 hours in human beings. More than half of the plasma protein content of the body is contained within the interstitial space at any one time. Plasma proteins within the interstitial space are important in the transport of water-insoluble substances from the vascular space and in resistance to infection.[3]

Interstitial fluid is contained within the interstitium, the intercellular connective tissues that lie between the cellular elements of the vascular and cellular compartments of the body. The extracellular tissue of the interstitium, except in the case of bone, consists of a three-dimensional collagen fiber network embedded in a proteoglycan gel matrix.[4] Interstitial water exists as free water and as water within the proteoglycan gel. Normally, only a small proportion of interstitial fluid exists as free water, most of the water being contained in the interstitial gel. However, in edematous states, the proportion of fluid as free water within the interstitium increases.[2]

The source of interstitial fluid is the intravascular space. The volume of interstitial fluid is determined by the functional relationships of three major anatomic structures: the capillary, the interstitial space, and the lymphatics.[5] Functionally, the volume of fluid that accumulates in the interstitium is determined by the rate of ingress of fluid from the vascular space, the compliance of the interstitium, and the rate at which fluid is evacuated from the interstitium. The net rate of ingress of fluid from capillaries into the interstitium is determined by a number of factors acting across the capillary membrane, the effects of which are related by Starling's equation:

$$J = Kf[(P_c - P_t) - \sigma(\pi_p - \pi_t)]$$

in which J equals the volume flow across the capillary wall; Kf equals the filtration coefficient of the capillary wall (volume flow per unit time per 100 g of tissue per unit pressure); P_c equals capillary hydrostatic pressure; P_t equals interstitial fluid hydrostatic pressure; σ equals the osmotic reflection coefficient; π_p equals the colloid osmotic

(oncotic) pressure of the plasma; and π_t equals the colloid osmotic (oncotic) pressure of the interstitial fluid.[6] Although all these factors act in concert to determine the rate of net fluid efflux from the capillary, considering them individually is conceptually easier.

FILTRATION (Kf) AND REFLECTION (σ) COEFFICIENTS

Together the filtration and reflection coefficients describe the properties of the capillary membrane that determine the ease with which water, protein, and other plasma constituents move from the vascular space to the interstitium. The filtration coefficient, which is the product of the hydraulic permeability and surface area of the capillary, is a measure of the ease with which water crosses the capillary membrane. The reflection coefficient is an indicator of the degree to which the capillary membrane resists the passage of a substance, such as protein. A reflection coefficient can be defined for each substance; a reflection coefficient of 0 indicates that the molecule crosses the membrane as readily as does water, whereas a value of 1 indicates that the membrane is impermeable to the substance. The reflection coefficient for a substance may vary with the anatomic site of the capillary[7,8]: Capillaries in the liver are permeable to albumin, whereas capillaries in muscle are much less permeable and cerebral capillaries are among the least permeable to albumin.

The movement of fluid and protein across the vascular membrane is assumed to be passive, with plasma water and protein exiting the vascular space through pores in the capillary membrane. However, the rate with which various plasma constituents cross the capillary membrane varies considerably depending on the constituent and the tissue. For example, muscle capillary pores are permeable to water molecules (reflection coefficient of 0) but much less permeable to albumin (reflection coefficient of approximately 0.9).[2] Movement of solutes across the endothelium is not understood fully, being complex, but is affected by the concentration of the solutes on either side of the membrane, solute charge and interaction with other solutes, and capillary pore configuration.[9]

Together the filtration and reflection coefficients partially determine the rate of fluid flux across the capillary wall, and the composition of the fluid. For a given hydrostatic and oncotic pressure difference, tissues with higher filtration coefficients (whether because of a larger capillary surface area or more porous capillaries) will have a greater fluid flux. Conversely, under the same circumstance, increases in the reflection coefficient of the capillary wall reduce fluid flux. The differential permeability of the capillary membrane to water and protein has important consequences in the maintenance of the oncotic pressure difference between plasma and interstitial fluid.

HYDROSTATIC AND COLLOID OSMOTIC PRESSURES

Transcapillary fluid flow is results from an imbalance between the hydraulic forces favoring movement of water from the capillary into the interstitium and the forces favoring movement of water in the reverse direction. The forces contributing to fluid movement out of the capillary are the intracapillary hydrostatic pressure and the interstitial colloid osmotic pressure, whereas those forces favoring movement of fluid from the interstitium to the capillary are the interstitial hydrostatic pressure (if it is positive) and the plasma colloid osmotic pressure.[10]

The principal force favoring fluid efflux from the capillary is the hydrostatic pressure within the capillary. Capillary hydrostatic pressure varies among different tissues and decreases along the length of the capillary. Hydrostatic pressure within a capillary is determined by the arterial and venous pressures and by the precapillary and postcapillary resistances.[11] Specifically, capillary pressure is determined by the ratio of the postcapillary resistance (R_a) to the precapillary resistance (R_v), and the arterial (P_a) and venous (P_v) pressures:

$$P_c = \frac{(R_v/R_a)P_a + P_v}{1+(R_v/R_a)}$$

Thus a small increase in venous pressure has a much greater effect on capillary pressure than does an increase in arterial pressure. For this reason the hydrostatic pressure is greater in capillaries below the heart (e.g., legs) than in those above the heart (e.g., head).

The colloid osmotic pressure of the plasma is the principal force minimizing fluid efflux from the capillary. The colloid osmotic pressure is generated because the plasma and interstitial fluid are separated by a semipermeable membrane—the endothelium—and vary slightly, but significantly, in composition. As noted previously, the interstitial fluid has a lower protein concentration than does plasma but has an essentially identical electrolyte concentration. The difference in protein concentration across the semipermeable endothelium generates an osmotic force that tends to draw water from the interstitium into the plasma.

In addition to the capillary hydrostatic pressure, the colloid osmotic pressure and negative hydrostatic pressure of the interstitial fluid favor fluid movement out of the capillary. Fluid flux across the capillary results from the summation of these forces (Table 3.3-1). These figures should be recognized as representing the forces at the midpoint of an idealized capillary and that the forces are dynamic, changing between tissues and even along the length of the capillary. In fact, a large net flux of fluid from the capillary occurs at its arteriolar end, where capillary hydrostatic forces are greatest and plasma

TABLE 3.3-1

Mean Forces (mm Hg) Influencing Fluid Movement Into or Out of the Capillary

HYDROSTATIC PRESSURES	
Mean capillary pressure	17.0
Interstitial pressure	–5.3
Total hydrostatic pressure favoring filtration	22.3
COLLOID ONCOTIC PRESSURES	
Plasma oncotic pressure	28.0
Interstitial oncotic pressure	6.0
Total oncotic pressure opposing filtration	22.0
TOTAL PRESSURE FAVORING FILTRATION	0.3

Data from Guyton AC: *Textbook of medical physiology,* ed 8, Philadelphia, 1986, WB Saunders.

oncotic forces are least, and a net flux of fluid into the capillary toward its venous end, where capillary hydrostatic forces are least and plasma oncotic pressure is greatest.

The small imbalance in filtration forces results in a net efflux of fluid from the capillary into the interstitial tissue. This fluid does not accumulate in the interstitium; it is removed by the lymphatics.

LYMPHATICS

The lymphatics drain the interstitium of fluid and substances, notably proteins, that are not absorbed by the capillaries. The lymphatics represent the only means by which interstitial protein is returned to the circulation. Interstitial fluid, and with it protein, moves down a pressure gradient into lymphatic capillaries through clefts between the lymphatic endothelial cells. Lymphatic endothelial cells are supported, and the lymphatic capillaries maintained patent, by anchoring filaments that attach the endothelial cells to surrounding connective tissue. Lymphatic fluid progresses centripetally through progressively larger vessels before draining into the great veins of the chest. Lymphatic valves prevent the retrograde flow of fluid from the lymphatics. Lymph is propelled by factors extrinsic to the lymphatics, including muscle activity, active and passive motion, posture, respiration, and blood vessel pulsation. Exercise causes a significant increase in lymph flow, at least in part because of the increase in tissue pressure that is associated with muscle contraction, although passive motion also increases lymph flow. Standing results in significant diminution or cessation of lymph flow from, and the prompt accumulation of interstitial fluid in, the lower extremities of human beings. In addition to the extrinsic factors affecting lymph flow, coordinated contractions of lymphatic vessels contribute substantially to the centripetal flow of lymph.[12]

Mechanisms of Edema Formation

Simply stated, accumulation of excessive fluid in the interstitial spaces—edema—results from an imbalance of the rates of fluid filtration from the capillaries and drainage by the lymphatics. Perturbations of one or more of the forces that affect filtration across the capillary alter the rate at which fluid enters the interstitium. Increases in capillary hydrostatic pressure, decreases in plasma oncotic pressure, and increases in interstitial oncotic pressure all favor increased fluid filtration. Conversely, increased interstitial hydrostatic pressure and decreased interstitial oncotic pressure act to inhibit fluid filtration.

Box 3.3-1 lists the fundamental mechanisms of accumulation of excessive interstitial fluid. Increases in capillary hydrostatic pressure, which occur with venous obstruction or arteriolar dilation, such as that associated with inflammation, increase net fluid efflux. The edema that occurs with congestive heart failure likely has an increase in capillary hydrostatic pressure as one of its causes, although the mechanism is complex.[13] Posture also affects capillary hydrostatic pressure; capillaries below the level of the heart have higher hydrostatic pressures than do capillaries above the level of the heart.

A decrease in the oncotic gradient across the capillary endothelium, which occurs with a decreased plasma oncotic pressure or an increased interstitial oncotic

BOX 3.3-1

PATHOGENESIS OF EDEMA

Increased Capillary Hydrostatic Pressure

Venous obstruction
- Thrombophlebitis
  - Compression (mass, tourniquet)

Venous congestion
- Posture (dependent limbs)
- Congestive heart failure

Arteriolar dilation
- Inflammation
- Increased body water

Decreased Plasma Oncotic Pressure

Panhypoproteinemia
Hypoalbuminemia

Increased Interstitial Oncotic Pressure

Increased capillary permeability

Decreased Lymph Flow

Lymphatic obstruction

pressure, results in an increase in efflux of fluid from the capillary. A decrease in plasma oncotic pressure decreases the oncotic gradient that favors movement of fluid into the capillary. Consequently, the capillary hydrostatic pressure, which favors filtration, predominates and fluid accumulates in the interstitium. Plasma oncotic pressure decreases when plasma protein concentration declines. Albumin is the plasma protein that exerts the preponderance of the oncotic force[8]; therefore clinically, edema often is associated with hypoalbuminemia. An increase in the permeability of the capillary membrane greatly increases fluid and protein transport into the interstitium and decreases the ability of the membrane to maintain a difference in oncotic pressure between the plasma and the interstitium.[5] Capillary permeability increases when the endothelium is damaged, such as by vasculitis or inflammatory reactions.

Lymphatic obstruction prevents the removal of interstitial fluid and protein. Filtration of fluid and passage of small amounts of protein into the interstitial space continues in the presence of lymphatic obstruction. The interstitial fluid is reabsorbed by the capillaries; however, the protein is not. Consequently, the protein content of the interstitial fluid gradually increases, with a resultant increase in interstitial oncotic pressure that favors filtration of fluid. The increased interstitial oncotic pressure causes fluid to accumulate in the interstitium, thus exacerbating the edema.[2]

Alterations in the magnitude of one or more of Starling's forces may be offset by compensatory changes in lymph flow and other of Starling's forces. In concert, Starling's forces and lymph flow act as "edema safety factors" to prevent the excess accumulation of interstitial fluid and development of frank edema. For example, lymph flow increases with the increased filtration associated with increased capillary hydrostatic pressure. Thus a larger volume of fluid enters and is removed from the interstitial space. The interstitial protein concentration decreases as increased fluid flow washes protein out of the interstitial space. Reduced interstitial space protein concentration increases the oncotic gradient, inhibiting fluid efflux from the capillary, and decreases the rate of movement of fluid from the capillary to the interstitial space.[6]

Diagnostic Approach to the Patient With Edema

Edema is not of itself a disease; rather it is a sign of a disease process. Therefore the diagnostic approach to the patient with edema is based on an understanding of the pathogenesis of edema and a knowledge of the diseases likely to be involved (Box 3.3-2). The diagnostic approach

BOX 3.3-2

COMMON CAUSES OF PERIPHERAL OR VENTRAL EDEMA IN HORSES

Congestive Heart Failure
- Valvular disease
- Myocarditis
- Monensin toxicosis

Vasculitis
- Equine viral arteritis
- Equine ehrlichiosis
- Purpura hemorrhagica
- Equine infectious anemia

Venous Obstruction and Congestion
- Catheter-related thrombophlebitis
- Disseminated intravascular coagulation
- Tight bandages
- Tumors
- Immobility

Cellulitis
- Staphylococcal
- Clostridial
- Counterirritant application

Lymphatic Obstruction
- Ulcerative lymphangitis
- Lymphadenitis *(Streptococcus equi, Corynebacterium pseudotuberculosis)*
- Lymphosarcoma
- Tumors

Hypoalbuminemia
- Parasitism
- Pleural and peritoneal effusions
- Protein loss (gastrointestinal, renal, or wounds)
- Inadequate production (starvation)
- Hemodilution (subsequent to hemorrhage)

Shock
- Hemorrhagic
- Endotoxic

Pleuritis
- Late-Term Pregnancy
- Prepubic Tendon Rupture
- Starvation
  - Inadequate intake
  - Malabsorption

to an animal with edema should not be any different than for any other sign of disease. A clinical examination, including history and physical examination, permit the development of a list of potential diagnoses and dictate the appropriate subsequent steps in confirming the diagnosis. The reader is referred to those sections of the text that deal with specific diseases for a description of the appropriate diagnostic aids.

When taking the history of a horse that has edema, one should focus on acquiring those facts that have the greatest diagnostic use in differentiating among those diseases that have edema as a sign. One should consider the following aspects:

- Housing, season, and geographic region
- Vaccine and parasiticide administration
- Exposure to other horses and diseases present within the herd
- The duration of the edema, its distribution, and the presence of any other clinical signs

One should investigate the remainder of the history depending on the responses to initial questions.

The physical examination should begin with a visual evaluation of the attitude and physical condition of the horse. The temperature, pulse, and respiration should be recorded. Although the physical examination should be complete, particular attention should be paid to those body systems that the preliminary examination indicates may be involved in the disease process. The physical examination reveals the distribution and severity of edema. Edema that is localized to one extremity or is not bilaterally symmetric is more likely to be caused by local factors (e.g., lymphangitis or venous obstruction) than by systemic disease. Conversely, edema that involves several areas of the body and has a symmetric distribution is likely to be associated with systemic disease (e.g., the ventral edema of congestive heart failure).

Following the initial clinical examination, the clinician will have developed an ordered list of potential diagnoses. Confirmation, or elimination, of these diagnoses depends on subsequent diagnostic procedures, including the response to therapy. Sections of this text deal with the specific disease processes for appropriate diagnostic procedures.

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3.4—Changes in Body Weight

Jonathan H. Foreman

An unwelcome or unexpected change in the body weight of a horse is a commonly encountered problem in equine practice. Although obesity may be a more common problem, weight loss often represents a more serious situation, with potentially severe consequences. Normal or acceptable body weight is also in the eye of the beholder, because a horse with a given body weight might look overweight as an endurance horse, appropriate as a Thoroughbred racehorse, or too thin as a show hunter.

Whether dealing with a problem of weight loss or weight gain, the veterinarian always should investigate the feeding practices of the horse. Not uncommonly the owner reports that the horse is receiving 3 lb of grain twice daily when the actual measuring device (usually the everyday coffee can) differs in net grain weight once

the volume of the measuring device and grain density are taken into account. Observing firsthand the feeding practices of the stable may be necessary to document that the horse actually is getting the reported amount of grain 2 or 3 times daily. Hay should be examined for type, quality (color, texture, leafiness, and steminess), mold, weeds, and potentially toxic plants. The horse in question should be observed eating hay and grain to ensure that it really does consume the amounts the owner or feeder reports.

The veterinarian also should observe nursing foals when they suckle. The udder should be examined before and after nursing to ensure that the mare actually is producing sufficient milk and that the foal actually is nursing the mare completely until her udder is empty. The milk itself should be examined from both halves of the udder to see that it appears grossly normal (no evidence of mastitis). The nostrils of the foal should be examined after nursing to determine the presence of milk reflux caused by dysphagia, esophageal obstruction, or gastric reflux associated with gastrointestinal ulcers.

Decreased Body Weight

Losses in body weight are usually insidious and chronic but may be surprisingly rapid in the face of acute overwhelming systemic infections (Box 3.4-1). Causes have been classified variously as gastrointestinal, nutritional, infectious, or hypoproteinemic.[1,2] Differential mechanisms include decreased feed intake, decreased absorption of nutrients, decreased nutrient utilization, and increased loss of energy or protein leading to a catabolic "sink."[1-3]

Decreased feed intake may be caused by management factors, poor dentition, dysphagia, or esophageal obstruction. Management factors leading to weight loss may be multifactorial and include inadequate amounts of feed, inadequate quality of feed, or inability of the horse to eat the proper amounts of the feed given. A horse with severe lameness (e.g., chronic laminitis) may not be able to ambulate to the feed source. A horse low on the pecking order in a pasture hierarchy may be unable to eat because it cannot approach the feed without the other horses bullying it and fending it away. The feed must be palatable and digestible. Appropriate amounts and types of concentrates must be fed considering the work schedule or pregnancy status of the horse. Proper investigation of stable feeding practices is described earlier.

Poor dentition may cause the horse not to eat some or all of its grain or hay. Parrot-mouthed horses or aged horses with receding incisor teeth (more than 25 years old) may have difficulty in tearing off grass when grazing. A horse with one or more oral sores from a poorly fitting bit or from sharp cheek teeth may exhibit partial or complete inappetence because of pain associated with chewing. Sharp cheek teeth, wave mouth, or step mouth may lead to poor digestion and incomplete absorption of nutrients because of inadequate mastication of hay leading to poor fiber use during the hindgut (cecum) fermentation process.

Dysphagia has many causes, including abnormal prehension, chewing, or swallowing.[4] Abnormal prehension

BOX 3.4-1

MECHANISMS AND DIFFERENTIAL DIAGNOSES FOR DECREASED BODY WEIGHT

Decreased Dietary Intake

- Inadequate diet
- Lameness
- Pecking order
- Poor dentition
- Dysphagia
- Esophageal obstruction

Maldigestion and Malabsorption

- Lactose intolerance
- Gastrointestinal ulceration
- Parasitism
- Diarrhea
- Inflammatory intestinal disease
  - Granulomatous enterocolitis
  - Eosinophilic enterocolitis
  - Lymphocytic/plasmacytic enterocolitis
- Gastrointestinal neoplasia

Inappropriate Hepatic Utilization

- Inadequate circulation and respiration
  - Heart failure
  - Chronic obstructive pulmonary disease

Increased Rate of Protein and Energy Loss

- Infection
  - Pneumonia
  - Pleuritis
  - Peritonitis
  - Equine infectious anemia
- Protein-losing eneropathy
  - Diarrhea
  - Gastrointestinal ulceration
  - Parasitism
  - Inflammatory intestinal disease
  - Gastrointestinal neoplasia
- Renal disease (glomerular)
- Increased metabolic energy use
  - Chronic pain
  - Secondary hyperadrenocorticism

can be caused by tongue lacerations; dental, mandibular, or maxillary fractures; damage to nerves supplying the tongue or facial musculature (local trauma, equine protozoal myelitis, or polyneuritis equi); or central neurologic disease (equine protozoal myelitis). Basal ganglia lesions caused by poisoning by ingestion of yellow star thistle or Russian knapweed prevent normal prehension in the pharynx.[5] Swallowing abnormalities may be caused by neurologic (equine protozoal myelitis, viral encephalitis, or guttural pouch infection), muscular, or physical obstructions such as strangles, abscesses, or guttural pouch distention.[4] Muscular causes include hyperkalemic periodic paralysis in Quarter Horse foals, vitamin E or selenium deficiency in neonates, botulism in neonates and adults, and local trauma subsequent to laryngeal surgery (laryngoplasty).

Esophageal obstruction usually presents acutely because an apparently dysphagic horse regurgitates food from its nostrils while attempting to eat or drink. Chronic choke, or anorexia related to painful swallowing caused by partial esophageal obstruction may lead to weight loss without the owner realizing that the horse is not eating adequately. Esophageal endoscopy is usually diagnostic, but positive contrast radiography may be helpful and is sometimes necessary to establish an accurate diagnosis.

If the horse with weight loss has been observed fully to ingest adequate amounts of good-quality hay and grain, then decreased feed absorption must be considered the reason for weight loss. Maldigestion and malabsorption are not easily confirmed diagnoses, but tests based on luminal absorption of simple sugars (xylose or glucose tolerance tests) have been used to document malabsorption syndromes.[3,6,7] These tests are described in greater detail in Chapter 13.4. Malabsorption may be caused by parasitism, diarrhea, and inflammatory or neoplastic intestinal disease.

Gastrointestinal parasitism results in weight loss because of several mechanisms.[2] Parasites may compete directly for nutrients within the lumen of the bowel. Malabsorption may result from a lack of mucosal integrity, a decrease in intestinal villi size and number (and subsequent decrease in mucosal absorptive surface area), and a decrease in digestive enzymes that originate in the mucosa. Competition of parasites for protein sources may result in decreased availability of amino acids for production of digestive enzymes or mucosal transport proteins. Increased mucosal permeability caused by leakiness in mucosal intercellular bridges may result in mucosal edema and increased transudation of intercellular fluid and its associated electrolytes, amino acids, and sugars into the lumen of the intestine.

Chronic diarrhea results in partial or complete anorexia, which contributes directly to weight loss. More rapid (decreased) gastrointestinal transit time results in increased losses of incompletely digested dietary feedstuffs. Malabsorption may result from decreased transit time and from villus blunting caused by specific pathogens, such as in viral diarrhea (see Chapter 13.4). Bacterial pathogens may compete directly for luminal nutrients. Mucosal invasion by viral and bacterial pathogens may cause mild to severe degrees of mucosal sloughing (ulcers), which result in maldigestion, malabsorption, and increased mucosal losses of intercellular fluid (e.g., in parasitism).

Given that the horse has adequate feed intake and absorption, inappropriate hepatic use of amino acids and sugars must be considered as a differential diagnosis for weight loss. Chronic liver disease may result in weight loss because of inappetance, maldigestion (caused by inadequate bile acid production), and inadequate or improper processing of amino acids into normal plasma proteins in the liver. These abnormalities may result in lowered concentrations of serum albumin, liver-dependent clotting factors (factors II, VII, IX, and X), and total plasma or serum protein. Lowered circulating proteins (especially albumin) may result in decreased plasma colloid osmotic pressure and thus may manifest as peripheral dependent edema in the distal limbs, pectoral region, and ventral midline. This peripheral edema may mask further weight loss by making the torso of the horse appear to be heavier than it actually is. Decreases in clotting factors may result in bleeding diatheses. Hyperlipemia, hyperlipidemia, fatty liver syndrome, and ketosis may be seen in poorly fed ponies and in miniature horses with acute anorexia or overwhelming energy demands, such as pregnancy or lactation.[8]

Increased loss of protein or energy is a common cause of decreased body weight in horses. Luminal losses of fluid, electrolytes, and nutrients were described earlier for intestinal parasitism and diarrhea. Acute inflammatory protein losses may occur into major body cavities in overwhelming infections such as pleuritis or peritonitis. Chronic abscessing pneumonia, pleuritis, and peritonitis often result in increased, rather than acutely decreased, serum total protein because of increased γ-globulin production in response to chronic antigenic stimulation from the chronic infection. These chronic infections also usually have weight loss as an additional clinical sign because of the continuing catabolic processes associated with the infection itself. Equine infectious anemia is a type of persistent systemic infection that in its symptomatic form may result in chronic weight loss and varying levels of anemia.[9] Asymptomatic equine infectious anemia carriers may have no weight loss or other obvious clinical signs but can infect pasture mates via vector transmission.

Protein-losing enteropathy is not a definitive diagnosis but rather is a group of diseases, each of which results in luminal losses of fluid, electrolytes, plasma proteins, and

nutrients. Mechanisms of protein and fluid loss were described earlier for intestinal parasitism and diarrhea. Gastrointestinal ulcers have been reported to result in lowered serum total protein and weight loss.[10] One of the early indications of nonsteroidal antiinflammatory drug toxicity is detection of a lowered serum total protein. Horses with such a condition also may manifest varying degrees of inappetence and colic, especially associated with the immediate postprandial period. Intestinal neoplasms (usually lymphosarcoma) often manifest as a protein-losing enteropathy with weight loss.[11]

Acute or chronic renal diseases, especially involving glomerulonephritis, can result in urinary protein loss and subsequent body weight loss.[12] Horses with this condition may have polyuria and polydipsia as associated clinical signs. Owners or handlers often report polyuria as increased wetness in stall bedding. The veterinarian should question owners thoroughly regarding the water intake of the horse. The veterinarian may need to observe stable watering habits, often including actually measuring the volume of the water buckets to establish definitively the presence of polydipsia. Turning off automatic waterers in the stall or pasture and offering the horse measured volumes of water from additional buckets may be necessary to establish a diagnosis of polydipsia. Urine puddles in stalls or collected urine samples may foam excessively because of increased protein concentrations. Increased urinary protein concentrations can be diagnosed quickly on the farm with the proper interpretation of urine dipstick protein indicators.

Neoplasms or abscesses within the thorax or abdomen serve as catabolic energy and protein sinks, resulting in chronic weight loss.[11-13] Chronic pain, such as that associated with severe, unresponsive laminitis, results in increased catabolism and weight loss, probably because of chronically elevated systemic catecholamine levels. Increased circulating epinephrine and norepinephrine levels result in a whole-body catabolic state with increased breakdown of stored energy sources and ultimately result in chronic weight loss. Similar weight loss caused by systemic catabolism can result from chronically elevated serum cortisol associated with pituitary adenoma and secondary hyperadrenocorticism.

Heart murmurs and resultant heart failure can cause weight loss because of inefficiency of circulation of nutrients and oxygen to peripheral tissues. Chronic obstructive pulmonary disease or heaves may result in weight loss because of an increase in the work of breathing and poor oxygenation of peripheral tissues. Although ventral abdominal musculature may hypertrophy and result in a heave line, weight loss is manifested by increased depth between the ribs and decreased muscular thickness and definition along the dorsal midline. Suckling foals with severe pneumonia may manifest weight loss if they become inappetent because of decreased suckling related to their severe dyspnea.

An appropriately taken history should document the type, amount, and quality of feed and hay being provided daily. Documentation of deworming products used and intervals of administration is critical. The history also may document the presence of anorexia, depression, polyuria, polydipsia, diarrhea, or other important historical signs that may point more quickly toward a specific cause of the weight loss.

The physical examination should reveal the presence of weight loss, a cardiac murmur, pneumonia or pleuropneumonia (increased lung sounds), chronic obstructive pulmonary disease (increased abnormal expiratory lung sounds), dental abnormalities, peripheral edema, urine staining on the hindlimbs, diarrhea, icterus, nasal discharge (dysphagia, pneumonia), fever, or hirsutism (secondary hyperadrenocorticism). The rectal examination may document the presence of intraabdominal masses (abscesses or neoplasms), enlarged left kidney, thickened intestinal or rectal wall, colonic displacement, gritty peritoneal surfaces (peritonitis), gritty feces (sand impaction), or diarrhea.

Fecal flotation may serve as an adequate screening tool to determine whether any evidence of parasitism exists. In the event of a positive fecal flotation, Baermann sedimentation may be necessary to determine quantitatively the severity of the patent parasitic load in the horse with weight loss. Fecal occult blood may be positive with gastrointestinal ulceration or neoplasms, but parasites or a recent rectal examination also may result in positive results.

Routine hematologic testing (complete blood count and fibrinogen) should assist in diagnosing infectious conditions such as pleuritis or peritonitis. Decreased serum or plasma total protein and albumin concentrations are evidence of hypoproteinemia and make the following conditions more likely: severe malnutrition, protein-losing enteropathy (diarrhea, parasitism, ulceration, intestinal neoplasms, or inflammatory intestinal disease), glomerular disease, acute pleuritis or peritonitis, or chronic liver disease. Increased total protein concentrations, especially γ-globulins, make chronic closed-cavity infections such as abscesses, peritonitis, or pleuritis more likely. Increased β-globulin fractions suggest the presence of parasitism.

Routine serum biochemistries should aid in diagnosing renal (renal azotemia, electrolyte abnormalities) and liver disease (increased γ-glutamyltransferase, aspartate aminotransferase, serum alkaline phosphatase, and lactate dehydrogenase). Urinalysis should reveal increased protein levels on dipstick or quantitative analysis in the event of glomerular protein losses. Metabolic alkalosis may be evident in the aftermath of salivary bicarbonate losses caused by dysphagia or esophageal obstruction.

Endoscopy may aid in diagnosing causes of dysphagia or esophageal obstruction. Lengthy endoscopes are necessary for examination of large adult horses for suspected gastrointestinal ulcers, but shorter endoscopes may suffice for foals or shorter-necked adults (e.g., Arabians and ponies).

Peritoneal fluid analysis documents the presence of a transudate (equivocal infection) or exudate (probable infection).[14,15] Aerobic and anaerobic peritoneal fluid cultures should be performed if intraabdominal infection is suspected. Exfoliative cytologic examination rarely may document the presence of neoplastic cells from intraabdominal neoplasms.[11-16]

Nonroutine tests should be performed only as indicated and should include oral absorption tests (see Chapter 13.4) and biopsies of the liver, kidney, or intestinal wall. Abdominal or thoracic ultrasonography should help to rule out abnormalities of the liver or kidneys and may document the presence of abnormal fluid (peritonitis or pleuritis) or masses (abscesses or neoplasms). Cardiac ultrasound should be definitive in the event of a murmur and suspected heart failure. Radiography also may be helpful to document the presence of thoracic masses or chronic obstructive pulmonary disease, but increased pleural fluid obscures visualization of other intrathoracic structures.

Increased Body Weight

Overfeeding may be the most common cause of obesity in horses and also may be the easiest to correct. The veterinarian should investigate the feeding practices of the stable and feed and hay sources thoroughly. Novice horse owners, single horse owners, and pony owners commonly overfeed their animals.

Ponies seem to be particularly susceptible to obesity, perhaps because their size renders them more easily overfed. However, at least one author has proposed that this tendency toward obesity in ponies receiving modern confinement diets may be because of their having evolved in the inhospitable ice age climates of northern Europe.[17] In that era, the lack of readily available grazing feedstuffs might have placed greater selection pressure on survival of ponies with more efficient dentition and better nutrient and fluid absorption from the gastrointestinal tract. The author argues that those ponies that had greater feed conversion efficiency would have been stronger, had longer lives, and been more available for breeding. Current illustrations of this theory may lie in the Welsh and Connemara pony breeds that still thrive and flourish in the wild in the inhospitable north Atlantic climates of the western coasts of Wales and Ireland, respectively.

Pregnancy in mares is a normal physiologic event that leads to increased body weight. Surprisingly, many new owners of mares may not know that their new purchase is pregnant. For an earlier negative pregnancy diagnosis to have been in error is not uncommon. Any mare that is gaining weight in an unexpected manner should be examined rectally, and by ultrasonography if necessary, for a possible pregnancy.

Hypothyroidism has been reported to be associated with weight gain and failure to become pregnant in broodmares.[18] Evidence for hypothyroid-associated weight gain and infertility was lacking in surgically created hypothyroid pony[19] and Quarter Horse[20] subjects. An abundance of field experience exists, however, from which to infer a relationship between obesity, hypothyroidism, and infertility in mares.[17] Documentation of hypothyroidism must be by performance of a thyroid-stimulating hormone or thyroid-releasing hormone stimulation test,[21,22] because resting thyroid levels vary diurnally[23] and do not truly reflect thyroid function. One must also remember that only 5 days of normal phenylbutazone therapy results in abnormally low resting serum thyroid levels because of direct competition of phenylbutazone with thyroid hormone for serum protein-binding sites.[21] The diagnosis and treatment of hypothyroidism is described in greater detail elsewhere in this text.

Differential diagnoses for increased body weight include overfeeding, pregnancy, hypothyroidism, and other conditions that result in abdominal distention, such as bloat, ascites, uroperitoneum, fetal hydrops, and rupture of the prepubic tendon or abdominal wall musculature. The latter conditions are described in greater detail in Chapter 16.

Feeding practices should be investigated and observed firsthand if necessary. A positive pregnancy status should be an easy historical and rectal diagnosis. Most hematologic and biochemical tests are normal in the pregnant or simply overweight horse. Thyroid status should be assessed appropriately, not by simple resting thyroid hormone concentrations, but by thyroid-stimulating hormone or thyroid-releasing hormone stimulation tests that have been described previously and that are presented elsewhere in this text.[21,22]

Education of the client is important regarding feeding practices, especially if the overweight horse is determined simply to have been overfed by a novice owner. Dangerous consequences, including colic and laminitis, should be explained to the client.

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3.5—Abdominal Distention

Jonathan H. Foreman

Increases in body weight because of overeating or pregnancy must be distinguished from increases in body girth caused by bloat, ascites, uroperitoneum, fetal hydrops, or ruptured prepubic tendon. In each of these conditions, body weight actually may increase because of fetal growth or fluid accumulation. More important, however, a perceptible change in the shape of the abdomen of the horse occurs.

Bloat usually is associated with colic signs in horses and is caused by gaseous intestinal distention resulting from ileus or simple obstruction of the large, or rarely small, intestine. Ileus caused by diarrhea, peritonitis, colic surgery, or parasympatholytic agents (e.g., atropine) can result in sufficient accumulation of intraluminal gas to be manifested as tympany, bloat, and mild to severe abdominal pain.[1] If optic topical atropine application is overly aggressive, secondary ileus and bloat may result. Rapid and severe gas production may follow grain overload; cecal and colonic fermentation of readily available carbohydrate sources results in rapid-onset colonic tympany and abdominal distention.[2] Exhaustion in endurance horses also is associated with intestinal shutdown and subsequent abdominal distention.[3] In any of these bloat conditions, abdominal auscultation in the flank area reveals decreased or absent intestinal motility sounds (borborygmi) and perhaps increased gaseous distention sounds (pinging). Decreased borborygmi in the right flank are specific for cecal ileus.

Simple colonic obstruction also results in tympany and bloat. Strangulating obstruction results in greater pain than usually is manifested in simple obstruction and bloat. Colonic displacements are more common in older postpartum mares.[4] These horses often initially show mild colic signs and progressively develop more dramatic pain and abdominal distention. Miniature horses with simple obstructions caused by fecoliths often have bloat as the initial clinical sign.[5] Such cases have the additional complication that rectal examination may be impossible for differentiation of the source of the bloat. Even in full-sized horses, rectal examination may reveal that the abdomen is so filled with distended colon that the examiner can push an arm into the rectum no farther than wrist-deep. Colonic or cecal bloat can be relieved by trocarization through the flank, but relief is merely palliative and is usually temporary because the cause of the obstruction still has not been resolved.

Ascites does not occur commonly in horses and usually is caused by peritonitis or abdominal neoplasms.

Peritonitis is caused by septicemia, laparotomy, intestinal leakage, internal abscess, or a penetrating external wound resulting in inflammation and usually infection of the peritoneal lining of the abdomen. Such inflammation results in increased fluid production by the squamous abdominal epithelium. Initially, this increased abdominal fluid may be characterized as a transudate (low cell count and low total protein). If inflammation with infection persists, the character of the fluid may change to that of an exudate (increased cell count >5000 nucleated cells/μl, increased neutrophil count, increased degenerate neutrophils, microscopically visible bacteria, and increased total protein).[6,7] These increases in abdominal fluid volume can be substantive and can result in abdominal distention that eventually becomes clinically apparent. Fluid ballottement in the equine abdomen is not an easily performed diagnostic technique but may be easier in foals, ponies, or miniature horses than in full-sized horses.

Ascites also may result from abdominal neoplasms. Tumors reported to cause ascites and weight loss in horses include lymphosarcoma, squamous cell carcinoma, mammary adenocarcinoma, and mesothelioma.[8,9] Although rare, mesothelioma may cause the most fluid production, because it is a tumor of the fluid-producing cells of the peritoneal lining. Mesothelioma may result in the production of large volumes of fluid (several liters) in a short time (24 hours) after a similarly large volume is drained from the same horse via abdominal catheterization or trocarization.

Ascites also may result from any condition that produces lowered serum total protein and albumin. With lowered intravascular colloid osmotic pressure, fluid diffuses or moves from the vasculature and results in dependent peripheral edema. Fluid also may accumulate within the major body cavities (i.e., the thorax and the abdomen).[7] The mechanisms for such low-protein conditions include poor protein intake, malabsorption, poor hepatic utilization, and increased rate of protein loss such as in glomerular renal disease, peritonitis/pleuritis, or gastrointestinal transudation (diarrhea or ulceration). Causes of peripheral edema are described elsewhere in this text.

Increased preload because of right ventricular heart failure also can result in a transudate fluid accumulation within the abdomen.[7] A horse with right ventricular heart failure usually has tricuspid insufficiency and manifests other signs of right ventricular heart failure, such as a murmur, exercise intolerance, jugular pulse, and edema of the ventral abdomen, pectoral muscles, and distal limbs. Severe mitral insufficiency also can result in right ventricular heart failure, but only after the development of left ventricular heart failure and its associated pulmonary edema, which is manifested by exercise intolerance, coughing, epistaxis, and increased respiratory effort.

Uroperitoneum results from leakage of urine from some part of the urinary tract into the abdomen and most commonly is associated with a ruptured bladder in neonatal foals (usually male). Uroperitoneum also may result from a necrotic bladder caused by neonatal sepsis and urachal abscesses. Such foals often have pendulous, bloated abdomens that ballotte more easily than do the abdomens of adult horses with accumulation of fluid. Abdominal fluid actually may smell like urine, and peritoneal fluid creatinine concentrations will be high—often more than twice those of peripheral blood.[10-12] Because most classically described neonatal urinary bladder tears are dorsal near the trigone, the foal still may be able to produce a stream of urine despite having a leaking bladder. A ruptured urinary bladder abscess should be suspected in a foal with sepsis that initially responds to therapy for sepsis and then, several days later, has acute-onset depression, anorexia, ileus, and abdominal distention. Adults horses rarely have uroperitoneum; however, uroperitoneum has been associated with ruptured urinary bladders during stressful parturition in mares that manifest mild postpartum abdominal pain and abdominal distention.[12,13]

Fetal hydrops results from an accumulation of excessive amounts of fluid within the amnion (hydrops amnion) or chorioallantois (hydrops allantois).[14] Hydrops results in a bilaterally pendulous abdomen in a late-term pregnant mare. A rapid accumulation of fluid over 10 to 14 days may makes walking or perhaps even breathing difficult for the mare. A diagnosis may be made after taking history and performing a rectal examination, although palpating the fetus is usually difficult because the excess fluid causes the uterus to descend out of reach of the examiner. If necessary, a percutaneous ultrasonographic examination may be used to confirm the diagnosis by documenting the presence of increased intrauterine fluid within the fetal membranes.

A ruptured prepubic tendon results in a unilateral lowering of the abdominal margin and apparent distention of the abdomen only on the affected side. The condition is associated routinely with later-term pregnancy in mares and is thought to occur simply because of the increased weight of the pregnant uterus pressing downward on the abdominal wall. Rupture of the rectus, transverse, or oblique abdominal muscles also can result in ventral dropping or herniation of the abdomen late in gestation.[14] Ruptures may be more common in older or more sedentary mares, probably because of decreased abdominal wall strength and tone. Other than a focal abdominal wall hernia, a unilateral prepubic tendon rupture results in the only form of prominent unilateral abdominal distention in horses. Mares with ruptured prepubic tendons may have elicitable pain in the local abdominal wall and may demonstrate a reluctance to walk. They may need

assistance during parturition, because they may have difficulty performing an effective abdominal press to aid in fetal expulsion.

Pregnancy, diarrhea, colic signs, colic surgery, and the use of parasympatholytic agents should be evident from the history. The rate of onset of abdominal distention may help to distinguish more acute conditions (e.g., gastrointestinal bloat from grain overload) from more chronic conditions (e.g., ascites caused by heart or liver failure). Signalment and history may assist in indicating specific conditions. A depressed, 48- to 72-hour-old male foal with fluid abdominal distention may be a likely candidate to have a ruptured urinary bladder and uroperitoneum. Miniature horses with bloat and colic signs frequently have simple obstructions owing to fecoliths or enteroliths.

A complete physical examination reveals the presence of a murmur that may be associated with heart failure and ascites. Other signs of heart failure also may be evident on physical examination. An actual defect in the integrity of the abdominal wall may be palpable on external examination of the abdomen in a mare with a ruptured prepubic tendon or ruptured abdominal wall musculature.[14] The veterinarian should attempt ballottement to discern the presence of increased free abdominal fluid in suspected ascites or uroperitoneum. Fever may indicate the presence of an infectious peritonitis or umbilical abscess.

A rectal examination is a critical part of examining a horse with bloat or colic but may be difficult to accomplish if colonic distention is dramatic or if the patient is small (i.e., a foal, pony, or miniature horse). A rectal examination further may document advanced pregnancy, resulting in mild bilateral abdominal distention (normal pregnancy), abnormal or severe bilateral distention (hydrops or bilateral ruptured prepubic tendon), or unilateral distention (unilateral ruptured prepubic tendon or focal abdominal wall hernia). A rectal examination also may reveal abnormalities of the urinary tract (enlarged kidney or ureter, abscess, or neoplasm), which may result in uroperitoneum in adults.

An ultrasonographic examination may be helpful and is sometimes necessary to examine the distended abdomen and fetus in a pregnant mare. Such an examination must be performed percutaneously in late gestation. Ultrasonography can determine the location of increased abdominal fluid (intrauterine or extrauterine) and the health status of the fetus. Percutaneous placement of base-apex electrocardiographic leads across the abdomen of the mare may help to document that the fetus is still viable if an ultrasound examination does not produce definitive evidence (heart movement or gross fetal movement).[15]

Cardiac ultrasonography may help to document the presence of a cardiac valvular defect that can be the cause of ascites in a horse with heart failure. Abdominal radiography may assist in the diagnosis of abdominal distention caused by intestinal obstruction in a foal or miniature horse. Percutaneous ultrasound examination also may assist in documenting the source of abdominal distention (e.g., intussusception) in smaller horses or foals[16,17] and in characterizing umbilical and urachal abnormalities.[17]

Complete blood counts and plasma fibrinogen concentrations assist in diagnosing inflammatory conditions such as infectious peritonitis. Urachal or urinary bladder abscesses also may be associated with inflammatory leukograms. Blood or peritoneal fluid cultures may assist in documenting the offending bacterial agent(s). Foals or adults with uroperitoneum have elevated serum urea nitrogen, creatinine, and potassium and decreased serum sodium, chloride, and bicarbonate concentrations.[10,11]

Abdominocentesis should be attempted to distinguish the cause of ascites. Care must be taken, however, in obtaining peritoneal fluid from late-term pregnant mares to avoid penetrating directly into the distended uterus. Analysis of peritoneal fluid reveals abdominal fluid to be a transudate (equivocal infection) or exudate (probable infection).[6,7] Fluid should be cultured aerobically and anaerobically when infectious peritonitis is suspected. Exfoliative cytologic examination rarely may document the presence of neoplastic cells.[8,9] Peritoneal fluid creatinine concentration approaches or often exceeds (more than twice) that of serum if uroperitoneum is present.[10,11] Serum and peritoneal urea nitrogen concentrations are less reliable for such a diagnosis because the peritoneal membrane does not differentially sequester urea nitrogen (but does creatinine) within the abdominal cavity.

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3.6—Dysphagia

Laurie A. Beard

Normal Eating

Normal eating is complex and requires normal anatomic structures and neurologic function. The process of eating can be divided into prehension (uptake of food into the oral cavity) and deglutition (transport of food from the oral cavity to the stomach). Prehension requires the lips to grasp and the incisors to tear the food.[1] Motor innervation to the tongue, lips, and muscles of mastication is provided by the hypoglossal, facial, and trigeminal nerves. Sensory input is important for successful prehension and requires intact olfactory, optic, and trigeminal nerves, providing smell, sight, and sensation of the rostral oral mucosa and lips. Normal prehension depends on the central nervous system to coordinate movements of the tongue and lips.

Deglutition involves mastication, swallowing, and transport of food through the esophagus to the stomach. Mastication or chewing of food initiates mechanical digestion and insalivation. Mastication is specifically a function of the molars to grind feed and the tongue and buccal muscles to position the food. The facial nerve provides motor and sensory fibers to the tongue and pharynx. The glossopharyngeal nerve provides sensory fibers to the caudal third of the tongue. The trigeminal nerve is sensory to the teeth and provides the important parasympathetic fibers to the parotid salivary gland. Function of this gland is critical to help liquefy food and provides a small amount of digestive enzymes.

Swallowing is complex and is performed in a series of steps. Initially, food must be moved to the base of the tongue and formed into a bolus. This action requires coordinated movements of the tongue and pharynx. Second, the bolus is forced caudally. As this action takes place, the oropharynx relaxes and the soft palate elevates to seal the palatopharyngeal arch and nasopharynx.[1] Next, the bolus enters the oropharynx and the hyoid apparatus swings rostrodorsally, which draws the larynx and the common pharynx forward.[1,2] The epiglottis is tipped caudally and prevents the bolus from entering the larynx. Finally, the bolus is moved into the common pharynx with pharyngeal muscle contractions and enters the open cranial esophageal sphincter. The sphincter closes to prevent esophagopharyngeal reflux and aerophagia. Herbivores are unique, because breathing continues uninterrupted during swallowing, unlike other animals.[1] The glossopharyngeal, vagus, and spinal accessory nerves provide sensory and motor fibers to the pharynx, larynx, and soft palate.

The esophageal phase of eating involves the transport of the food bolus to the stomach, with primary peristaltic waves, which are generated by continuous contraction of the pharyngeal peristalsis. The bolus is transported to the caudal esophageal sphincter, which relaxes to allow the bolus to enter the stomach and then contracts to prevent gastroesophageal reflux. If reflux does occur, esophageal clearance is achieved by secondary peristaltic waves. Antiperistalsis is normal in ruminants during eructation and regurgitation but is not normal in horses.[1]

Dysphagia

Dysphagia is defined as difficulty in swallowing but often is used to describe problems with eating.[2] Problems with eating may include problems with prehension, mastication, swallowing, and esophageal transport. In this section, the term *dysphagia* is used in the broader sense to describe problems with eating. Dysphagia can result from a number of disorders affecting any part of the upper gastrointestinal system (oral cavity, pharynx, and esophagus). Clinical

signs of dysphagia vary depending on the cause and the location of the problem but may include ptyalism (excessive salivation), gagging, dropping food, nasal discharge, and coughing. Dysphagia can result from morphologic or functional disorders. The causes of these diseases may be acquired or congenital. Morphologic causes of dysphagia include abnormal anatomy, obstruction of the upper gastrointestinal tract, inflammation, and pain. Examples of anatomic abnormalities include a cleft palate and subepiglottic cysts.[3,4] Obstruction of the upper gastrointestinal tract most commonly includes feed impactions of the esophagus but also can include pharyngeal obstructions secondary to retropharyngeal lymph node masses or severe guttural pouch tympany.[5-10] Inflammatory conditions resulting in pain and dysphagia include periodontal diseases, foreign bodies, pharyngitis, epiglottitis, and mandibular or maxillary fractures.[3,6]

Functional disorders resulting in dysphagia include neurologic, neuromuscular, and muscular diseases. Functional disorders frequently result in problems with swallowing but less commonly involve mastication and prehension and rarely occur with esophageal transport. Neurologic diseases resulting in dysphagia may be peripheral or central. Peripheral neurologic problems frequently result from abnormalities of the guttural pouch but also can include toxic peripheral neuropathies, such as lead toxicity. Problems of the guttural pouch include infection (tympany, empyema, or mycosis), iatrogenic problems (infusion of caustic substances), and trauma (rupture of the longus capitis muscle from the basisphenoid bone and hemorrhage into the guttural pouch).[2,11,12] Central neurologic diseases may result in problems in prehension, mastication, or swallowing. Specific examples include equine protozoal myelitis, viral encephalitis (rabies and eastern and western encephalitis), toxic neuropathies (leukoencephalomalacia and nigropallidal encephalomalacia), and cerebral trauma.[1,2,7,13-15] Neuromuscular problems resulting in dysphagia generally present as a systemic disease and include diseases such as botulism and organophosphate toxicity.[1,2,16,17] Muscular diseases resulting in dysphagia are rare but include nutritional muscular dystrophy (white muscle disease) in foals.[18]

BASIC APPROACH TO DYSPHAGIA

The initial evaluation of dysphagia focuses on determining whether morphologic or functional abnormalities exist. To answer these questions best, a thorough history, physical examination (including observation of the horse eating), and additional tests (e.g., endoscopic examination and radiographs) are required. A history of an acute onset of dysphagia is often consistent with trauma, whereas a slow progressive onset of clinical signs is more consistent with a neurologic problem such as guttural pouch mycosis, equine protozoal myelitis, or toxicities. The clinician should assess exposure of the horse to toxic substances or plants (lead or yellow star thistle). A history of treatment before the onset of dysphagia suggests trauma or injury to the pharynx. Use of a balling gun or flushing of guttural pouches may result in iatrogenic injury to the pharynx, esophagus, and guttural pouches. The clinician should determine concurrent problems in other horses (e.g., strangles or other bacterial infections of the submandibular lymph nodes).

In performing the physical examination, the clinician should pay close attention to the head and neck. Because rabies is a potential cause of dysphagia, protective measures while performing a careful and thorough physical examination are necessary. Ideally, all clinicians working on horses should have an adequate rabies antibody titer. An examination of the oral cavity is best accomplished with a mouth speculum, good light, and if necessary, the administration of sedation. The teeth should be examined carefully for retained deciduous caps, sharp points or hooks, wave mouth or step mouth, dental fractures, or patent infundibula.[3] Foreign bodies may become wedged between the molars or under the tongue. The tongue should be examined for lacerations, foreign bodies, and evidence of neoplasia. The throat latch area and neck should be examined for heat or swelling, which might be caused by a ruptured esophagus. The lungs should be auscultated carefully to determine if the horse shows evidence of aspiration pneumonia resulting from dysphagia.

A valuable activity is to watch the horse eat. The distinction between dysphagia and anorexia is important. Dysphagic horses usually are hungry and will attempt to eat. Problems with prehension generally suggest a primary neurologic problem. Watching the horse try to graze and eat hay or grain may be necessary. Ingestion of yellow star thistle or Russian knapweed results in basal ganglia lesions (nigropallidal encephalomalacia). Horses with these lesions are unable to prehend food (with lack of coordination of the lips and tongue), but they can swallow.[14] Their ability to drink water should be evaluated carefully, because some horses continue to drink despite having difficulty in swallowing. Horses that expel food while chewing may have problems with mastication. Coughing and nasal discharge indicate aspiration of food into the trachea. Problems with swallowing or regurgitation may cause aspiration. Esophageal obstruction results in regurgitation of food through the nares. Regurgitation often is observed during feeding but may occur shortly after or even hours after feeding. Ptyalism, without dysphagia, may result from ingestion of legume plants (especially second-cutting red clover) contaminated with *Rhizoctonia leguminicola*. This fungus produces a mycotoxin called slaframine, which has parasympathomimetic properties.[19] The excess salivation disappears once the animal stops feeding on the plant.

MORPHOLOGIC ABNORMALITIES

Morphologic abnormalities that cause dysphagia are easier to diagnose than are functional disorders. Morphologic problems of the oral cavity generally result in problems of prehension or mastication. An oral examination (as outlined earlier) is particularly useful. The passing of a nasogastric tube, endoscopic examination, and radiographs (if necessary) are other diagnostic tests that may help to identify the anatomic localization and cause of dysphagia. Complete obstruction of the esophagus can be excluded if a nasogastric tube is passed successfully into the stomach. Feed impactions of the esophagus are common in horses. Esophageal impactions of feed may occur because of poor mastication or esophageal strictures or diverticulum.[5-7] The most common sites for obstructions occur in the cranial esophagus, at the thoracic inlet, and at the base of the heart.[7] Other esophageal abnormalities include rupture, fistula, cyst, megaesophagus, and neoplasms.[5,20] An endoscopic examination allows visualization of the nasal passageways, nasopharynx, guttural pouches, pharynx, larynx, and esophagus. Inflammation of the pharynx, larynx, or esophagus is assessed best by endoscopic examination. Partial obstructions of the pharynx often result in dyspnea, especially during exercise, and sometimes can cause dysphagia. Retropharyngeal masses, guttural pouch tympany, and rarely neoplasms may result in pharyngeal obstruction and collapse.[2,9,10] Depending on the length of the endoscope available, the clinician can evaluate all or part of the esophagus for inflammation or obstruction.

Radiographs can provide additional information in horses with morphologic causes of dysphagia; however, they are not required in all situations. Radiographs of the skull can help demonstrate the presence of periodontal disease, fractures of the mandible or maxilla, lesions of the temporomandibular joint, or radioopaque foreign bodies.[3] Radiographs of the larynx or pharynx are indicated in cases of pharyngeal obstruction and are especially useful to evaluate retropharyngeal masses, neoplasms, or trauma.[8-10] Radiographs of esophageal perforations reveal subcutaneous air, which shows up as extraluminal radiolucencies.[6] Contrast studies of the esophagus, with the use of barium sulfate, may help differentiate cases of esophageal strictures, dilation, or diverticulum.[5] Radiographs of the thorax are indicated in horses with nasal discharge and abnormal thoracic auscultation because of the concerns of aspiration pneumonia.

FUNCTIONAL ABNORMALITIES

Functional disorders that cause dysphagia are more difficult to diagnose and should be pursued after morphologic causes are not identified. The clinician also should consider a functional abnormality if the initial physical examination provides strong evidence of a neurologic, neuromuscular, or muscular problem. The initial step to evaluate functional causes of dysphagia is to perform a neurologic examination. The neurologic examination helps establish a neuroanatomic localization by (1) assessing brain, brainstem, and spinal cord functions; (2) determining if the problem is focal, multifocal, or diffuse; and (3) determining if the problem is a peripheral or central problem.

Cerebral disease usually manifests as seizures, head pressing, wandering, depression, and changes in mentation. Brainstem function can be assessed by cranial nerve examination. Evaluation of an abnormal response of the cranial nerves should establish the location of the problem within the brainstem. For example, the optic nerve can be assessed by the menace response (requiring the facial nerve) and by the pupillary light reflex (requiring the oculomotor nerve). Abnormalities of the oculomotor, trochlear, and abducens nerves manifest as strabismus or lack of a pupillary light reflex. Facial nerve paralysis (ear, eyelid, and muzzle droop) and vestibular disease (circling, nystagmus, and head tilt) often occur together because of the close proximity of these nerves as they exit the brainstem.[21] Endoscopic examination is a valuable tool to determine if pharyngeal or laryngeal paralysis is present. These problems may be caused by peripheral or central diseases. The dorsolateral wall of the medial compartment of the guttural pouch contains a plexus of nerves, including the glossopharyngeal nerve; branches of the vagus, spinal accessory, and hypoglossal nerves; and the cranial cervical ganglion. Mycotic plaques, empyema, and trauma (hematoma) of the guttural pouch can result in pharyngeal paralysis, dorsal displacement of the soft palate, laryngeal hemiplegia, and occasionally Horner's syndrome.[1,2,11,12,21] The clinician should obtain skull radiographs in many horses with dysphagia, and they are especially helpful when traumatic injuries are suspected. Rupture of the longus capitis muscle results in ventral deviation of the dorsal pharynx and narrowing of the nasopharynx. Bony fragments may be evident ventral to the basisphenoid bones in these horses.[12] Otitis media and pathologic fracture of the petrous temporal bone frequently result in vestibular disease and facial nerve paralysis and occasionally in glossopharyngeal and vagus nerve involvement. An endoscopic examination of the guttural pouches is helpful with this problem, because the distal stylohyoid bone is thickened and irregular. Ventrodorsal, lateral, and rostrolateral oblique radiographs also may reveal osseous changes of the stylohyoid bone, tympanic bulla, or petrous temporal bone.[21]

The clinical examination should include an evaluation of gait. Signs of ataxia, generalized weakness, and hypermetria along with cranial nerve signs may be observable with brainstem involvement. The clinician should

evaluate the horse at the walk, trot, down an incline, over a step, and backing and turning in tight circles. The clinician may wish to place the feet of the horse in abnormal positions and determine if the horse can reposition the leg correctly in a reasonable time. Generalized weakness (without ataxia) may manifest with a decrease in tail, eyelid, and tongue tone and muscle fasciculations. Weakness generally suggests a neuromuscular (botulism, organophosphate poisoning) or muscular problem.[16-18] Equine lower motor neuron disease results in generalized weakness and weight loss; however, horses are not dysphagic and do not exhibit cranial nerve abnormalities.[22] Ataxia or hypermetria along with dysphagia suggests a diffuse or multifocal disease that affects the spinal cord and brainstem. Examples of such diseases include equine protozoal myelitis, rabies, equine herpes myeloencephalopathy, polyneuritis equi, and a migrating parasite.[12,23,24] Further diagnostic tests are indicated in these cases, such as an evaluation of spinal fluid for cytologic abnormalities and chemistry and Western blot analysis for antibodies to *Sarcocystis neurona*.[25] Grass sickness, a disease found in Great Britain and in other northern European countries, results in ileus and colic. Grass sickness can result in dysphagia, with problems in swallowing or esophageal transport.[26] Grass sickness is regarded as a fatal disease, resulting in ileus of the gastrointestinal tract, dysphagia, and weight loss, which most likely is caused by an unidentified neurotoxin. Grass sickness can be defined as a dysautonomia characterized by pathologic lesions in autonomic ganglia, enteric plexi, and specific nuclei in the central nervous system.[27] Additional information about the specific causes of dysphagia are covered elsewhere in this text.

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3.7—Respiratory Distress

Bonnie R. Rush

Respiratory distress is defined as labored breathing and is characterized by an inappropriate degree of effort to breathe based on rate, rhythm, and subjective evaluation of respiratory effort.[1] Dyspnea is the sensation of arduous, uncomfortable, or difficult breathing that occurs when the demand for ventilation exceeds the patient's ability to respond.[2] Dyspnea describes a symptom rather than a clinical sign, and although the term often is used, dyspnea is not technically applicable in veterinary medicine. The clinical signs of respiratory distress vary with the severity and origin of impaired gas exchange. Clinical signs commonly observed in horses with respiratory distress include flared nostrils, exercise intolerance, inactivity, exaggerated abdominal effort, abnormal respiratory noise (stridor), anxious expression, extended head and neck, cyanosis, and synchronous pumping of the anus with the respiratory cycle.[1] Horses with chronic respiratory distress may develop a heave line resulting from hypertrophy of the cutaneous trunci and abdominal muscles, which assist during forced expiration.[3] Respiratory distress usually results from inefficient exchange of oxygen and carbon dioxide caused by primary pulmonary disease, airway obstruction, or impairment of the muscles and supporting structures necessary for ventilation. In some cases, ventilation increases in the absence of impaired gas exchange in response to pain, metabolic acidosis, or high environmental temperature. Familiarity with the mechanics of breathing and control of ventilation in healthy and diseased lungs facilitates the diagnosis and treatment of respiratory distress.[3,4]

Control of Ventilation

The partial pressure of oxygen (Pa_{O_2}) and carbon dioxide (Pa_{CO_2}) in arterial blood are maintained within a narrow range through rigid control of gas exchange.[2] The center controller of respiration in the medulla alters the rate and depth of respiration via efferent signals to the muscles of respiration in response to afferent signals from chemoreceptors in the peripheral vasculature and central nervous system and mechanoreceptors in the upper and lower respiratory tract, diaphragm, and thoracic wall. The central controller therefore adjusts alveolar ventilation to the metabolic rate of the individual.[4]

SENSORS

The chemoreceptors identify changes in metabolism and oxygen requirements and provide feedback to the central controller, thus allowing for modification of ventilation. Central chemoreceptors respond predominantly to hypercapnia, whereas peripheral chemoreceptors respond to hypoxia and hypercapnia. Central chemoreceptors, located in the ventral medulla, monitor alterations in the pH of intracerebral interstitial fluid and cerebrospinal fluid. The blood-brain barrier is impermeable to bicarbonate and hydrogen ions but is freely permeable to carbon dioxide. Therefore acidification of the intracerebral interstitial fluid and stimulation of the central chemoreceptors occur predominantly in response to hypercapnia. The severity of acidosis in the intracerebral interstitial fluid caused by hypercapnia is amplified by two features of the central nervous system: (1) hypercapnia produces cerebral vasodilation, increasing the delivery of CO_2 to the central nervous system, and (2) cerebrospinal fluid has poor buffering capacity because of low total protein concentrations.[2]

Peripheral chemoreceptors are located in the arterial circulation and respond to acidemia, hypercapnia, and hypoxemia. The carotid bodies are situated at the bifurcation of the common carotid artery, and the aortic bodies are located near the aortic arch. These receptors relay information to the central controller regarding arterial gas tensions via the glossopharyngeal and vagus nerves. Their responsiveness to alterations in Pa_{CO_2} is less consequential than the central chemoreceptors; however, the peripheral chemoreceptors are solely responsible for the hypoxic ventilatory drive. The peripheral chemoreceptors demonstrate a nonlinear response to low arterial oxygen tension. They are insensitive to alterations in Pa_{O_2} above 100 mm Hg, exhibit moderate response to arterial O_2 tensions between 50 and 100 mm Hg, and demonstrate a dramatic increase in responsiveness when the partial pressure of oxygen falls below 50 mm Hg in the arterial circulation.[2] The respiratory pattern elicited by hypoxia differs from that stimulated by hypercapnia.[5,6] Hypoxia evokes an increase in respiratory frequency, whereas hypercapnia triggers an elevation in tidal volume. In addition, hypoxia stimulates recruitment of the inspiratory muscles, whereas hypercapnia potentiates the activity of inspiratory and expiratory muscles.

The sensitivity of peripheral chemoreceptors should be considered in the treatment of patients with complex acid-base and blood-gas abnormalities. A patient suffering from impaired gas exchange caused by pulmonary disease and metabolic acidosis resulting from shock manifests respiratory distress in response to hypoxemia, hypercapnia, and acidosis. Oxygen supplementation likely will improve the patient's arterial oxygen tension. Such treatment, however, may abolish the hypoxic ventilatory drive and consequently slow the ventilatory rate. This decreased ventilation could exacerbate respiratory acidosis

and may result in decompensation of the patient.[4] To avoid life-threatening acidemia, treatment of metabolic acidosis in addition to oxygen supplementation is indicated.

Receptors located in the upper and lower respiratory tract respond to mechanical and chemical stimuli and relay afferent information to the central controller of respiration via the vagus nerve.[1,2] Vagal blockade abolishes tachypnea in horses with pulmonary disease; therefore these receptors are likely to play an important role in development of respiratory distress associated with primary pulmonary disease.[7-9] Pulmonary stretch receptors, also called slow-adapting stretch receptors, are located within smooth muscle fibers in the walls of the trachea and bronchi.[1,2,4] These receptors are stimulated by pulmonary inflation and inhibit further inflation of the lung (Hering-Breuer reflex). Conversely, at end expiration these receptors stimulate inspiratory activity. These receptors are considered to be partially responsible for controlling the depth and rate of respiration.

Irritant receptors (rapid-adjusting stretch receptors) are believed to be located between epithelial cells of the conducting airways.[2] They are not likely to function in regulation of breathing in a normal resting horse.[4] Stimulation of these receptors by noxious stimuli triggers bronchoconstriction, cough, tachypnea, mucus production, and release of inflammatory mediators.[1,2] Irritant receptors can be triggered by exogenous stimuli (smoke, irritant gases, dust) or by endogenously produced inflammatory mediators including histamine and prostaglandins. Production of histamine, prostaglandins, and other inflammatory mediators increases in horses with chronic obstructive pulmonary disease (COPD).[10-12] Stimulation of irritant receptors by these inflammatory mediators may be responsible in part for bronchoconstriction, mucus production, and tachypnea observed in horses with allergic airway disease. In addition to their role as chemoreceptors, irritant receptors also function as mechanoreceptors.[1] An abrupt change in end-expiratory lung volume, such as occurs with pneumothorax or pleural effusion, produces a tachypneic breathing pattern attributed to stimulation of irritant receptors. Juxtacapillary receptors are believed to be located within the wall of the alveolus. Stimulation by increased interstitial fluid volume triggers the sensation of difficult breathing.[2] Nonmyelinated C fibers are located in the pulmonary parenchyma, conducting airways, and blood vessels. These receptors respond to pulmonary edema, congestion, and inflammatory mediators, and stimulation activates a tachypneic breathing pattern. In addition, C fiber receptors may stimulate the release of pulmonary neuropeptides, which produce bronchoconstriction, vasodilation, protein extravasation, and cytokine production.[1] Increased negative pressure (upper airway obstruction) within the airway stimulates mechanoreceptors of the larynx and produces prolongation of inspiratory time and activation of upper airway dilator muscles.[13]

CENTRAL CONTROL OF RESPIRATION

The central controller consists of a group of motor neurons in the pons and medulla that receive input from the peripheral and central receptors and initiate phasic activity of diaphragmatic, intercostal, and abdominal respiratory muscles.[2] The medullary respiratory center, which is located in the reticular formation, controls the rhythmic pattern of respiration. The dorsal respiratory group coordinates inspiratory activity by assimilating afferent information from the glossopharyngeal and vagus nerves and transmits efferent signals to the muscles of inspiration and neurons in the ventral respiratory group. The ventral respiratory group consists of inspiratory and expiratory motor neurons. This nucleus is relatively inactive at rest and has a more dominant role during exercise. The apneustic center, located in the pons, provides stimulatory input to inspiratory motor neurons. Damage to the apneustic center, from trauma or neonatal maladjustment syndrome, results in prolonged inspiratory gasps interrupted by transient expiratory efforts.[4] The pneumotaxic center, also located in the pons, inhibits the inspiratory centers and regulates the volume and rate of respiration. The pneumotaxic center is not required to maintain a normal respiratory rhythm; instead, this center functions to fine tune the respiratory rhythm,[2] receiving afferent input from the vagus nerve regarding Pa_{O_2}, Pa_{CO_2}, and pulmonary inflation.

EFFECTORS OF RESPIRATION

The muscles required for ventilation include the diaphragm, the external and internal intercostal muscles, and the abdominal muscles. The single most important muscle required for the inspiratory phase of the respiratory cycle is the diaphragm. Contraction of the diaphragm forces the abdominal contents back, increasing the length of the thoracic cavity, and pulls the ribs abaxially, increasing the width of the abdominal cavity. In addition, the external intercostal muscles participate in inspiration by pulling the ribs abaxially to increase the width of the thoracic cavity. The net effect is an increase in the size of the thoracic cavity, producing subatmospheric intrathoracic pressure, to drive inspiration and pulmonary inflation. Expiration at rest is a passive process in most species and relies on elastic recoil of the lung to create positive intrathoracic pressure.[14] In horses, the first portion of expiration relies on elastic recoil of the lung to the point of relaxation volume, whereby the tendency for pulmonary collapse equals the tendency for expansion by the thoracic wall. However, horses further decrease lung volume by active compression of the chest wall, through contraction

of the internal intercostal muscles and muscles of the abdominal wall.[15] Conversely, the first part of inhalation is passive until the relaxation volume is reached, at which point the diaphragm and external intercostal muscles complete the inspiratory phase. Mechanical (abdominal distention, trauma to the thoracic wall) and neuromuscular (botulism, phrenic nerve damage, nutritional muscular dystrophy) dysfunction of the diaphragm and intercostal muscles prevent expansion of the thoracic wall and produce hypoventilation, hypoxemia, and respiratory distress.[4] Horses with torsion of the large colon develop significant abdominal distention and respiratory distress. Respiratory failure caused by impaired diaphragmatic function plays an important role in the pathophysiology and mortality associated with this intestinal accident.

The diameter of the conducting airways is an important determinant of the degree of pulmonary resistance and work of breathing and is controlled by the autonomic nervous system. Vagal-mediated parasympathetic stimulation causes airway narrowing and is one mechanism of bronchoconstriction associated with allergic airway disease. Administration of atropine results in rapid relief of bronchoconstriction in some horses with COPD, demonstrating the important role of parasympathetic bronchoconstriction in the pathogenesis of this disease.[16,17] β_2-Receptor stimulation produces smooth muscle relaxation and bronchodilation. β_2-Adrenergic receptors are abundant throughout the lung; however, sympathetic innervation is sparse and β-receptors within the lung must rely on circulating catecholamines for stimulation.[4] Airways must be constricted for β_2-receptor stimulation or atropine blockade to produce increased airway caliber.[18,19] β-Adrenergic receptors are less abundant than β_2-receptors and play no important role in the regulation of airway diameter. However, α-receptors appear to be upregulated in horses with COPD and contribute to bronchoconstriction associated with this disease.[20]

Nonadrenergic-noncholinergic (NANC) innervation also contributes to large airway diameter. Smooth muscles of the trachea and bronchi relax in response to activation of the inhibitory NANC system. In COPD-affected horses with clinical signs of airway obstruction, inhibitory NANC function is absent.[21] Failure of the inhibitory NANC system may result from the inflammatory response during acute COPD or may be an inherent autonomic dysfunction of the conducting airways of COPD-affected horses.

Hypoxemia

Respiratory distress most often originates from inadequate pulmonary gas exchange to meet the metabolic demands of the individual, resulting in hypoxia and hypercapnia. Hypoxia results from one or more of five basic pathophysiologic mechanisms: hypoventilation, ventilation-perfusion mismatch, right to left shunting of blood, diffusion impairment, and reduced inspired oxygen concentration. The degree of hypercapnia and response to oxygen supplementation varies depending on the mechanism of impaired gas exchange. Determination of these two parameters is useful in identifying the pathophysiologic process predominantly responsible for the development of hypoxia.[22]

HYPOVENTILATION

The hallmark of hypoventilation is hypercapnia.[22] The elevation in Pa_{CO_2} is inversely proportional to the reduction in alveolar ventilation; halving alveolar ventilation doubles Pa_{CO_2}.[2] The reduction in arterial oxygen tension is almost directly proportional to the increase in CO_2. For instance, if Pa_{CO_2} increases from 40 to 80 mm Hg, then the Pa_{O_2} decreases from 100 to 60 mm Hg. Therefore hypoxemia resulting from hypoventilation is rarely life-threatening. In addition, oxygen supplementation easily abolishes hypoxemia caused by pure hypoventilation. Acidosis caused by hypercapnia is the most clinically significant feature of hypoventilation and may threaten the life of the patient.[22] Metabolic alkalosis or central nervous system depression (head trauma, encephalitis, narcotic drugs) can produce hypoventilation; however, horses with these disorders may not demonstrate clinical signs of respiratory distress. The following disorders can cause alveolar hypoventilation, and affected patients usually demonstrate clinical signs of respiratory distress: mechanical (abdominal distention, trauma to the thoracic wall) and neuromuscular (botulism, phrenic nerve damage, nutritional muscular dystrophy) dysfunction of the diaphragm and intercostal muscles, restrictive pulmonary disease (silicosis, pulmonary fibrosis, pneumothorax, pleural effusion), and upper airway obstruction.[4]

VENTILATION-PERFUSION MISMATCH

Ventilation-perfusion (V-Q) mismatch is the most common cause of hypoxemia and is characterized by unequal distribution of alveolar ventilation and blood flow.[4] Pulmonary regions that are overperfused in relation to ventilation (low V-Q ratio) contribute disproportionate amounts of blood with low arterial oxygen content to the systemic circulation.[2,22] Respiratory diseases characterized by low V-Q ratios include COPD, pulmonary atelectasis, and consolidation.[4] If ventilation exceeds perfusion (high V-Q ratio), the ventilated pulmonary units are inefficient for CO_2 elimination and O_2 uptake. Ventilation of poorly or nonperfused units is wasted ventilation, termed *alveolar dead space*.[2,22] Conditions associated with high V-Q ratios include pulmonary thromboembolism and shock (low pulmonary artery pressure). Patients with V-Q mismatch often have a normal

arterial P_{CO_2}. The ventilatory drive to maintain normal Pa_{CO_2} is powerful. Because the CO_2 dissociation curve is basically a straight line (direct relationship), increased ventilation efficiently decreases Pa_{CO_2} at high and low V-Q ratios. Because the nearly flat shape of the O_2 dissociation curve, increasing ventilation is inefficient for proportionally increasing the arterial P_{O_2}. Only pulmonary units with moderate to low V-Q ratios benefit from increased ventilation. Therefore the increased ventilatory effort to maintain normal Pa_{CO_2} is wasted and unnecessarily increases the work of breathing. Oxygen supplementation increases Pa_{CO_2} in patients with a V-Q mismatch. However, elevation in arterial O_2 is delayed compared with hypoventilation and in some cases may be incomplete.[22] Compensatory mechanisms are present to minimize unequal distribution of ventilation and perfusion in diseased lungs to prevent the development of hypoxemia until pulmonary pathologic condition is severe.[23] Reflex pulmonary arterial constriction (hypoxic vasoconstriction) prevents perfusion of unventilated alveolar units and attempts to redirect blood flow to alveoli that are ventilated adequately. Airway hypocapnia causes bronchoconstriction of airways that conduct to unperfused alveolar units, redirecting air flow to better perfused alveoli.

SHUNT

Shunt is defined as blood that is not exposed to ventilated areas of the lung and is added to the arteries of the systemic circulation.[22] Shunting can occur as an extreme form of V-Q mismatch or with direct addition of unoxygenated blood to the arterial system. *Physiologic shunting* is defined as perfusion of nonventilated or collapsed regions of the lung and occurs with pulmonary consolidation, atelectasis, and edema. Congenital heart disease, such as tetralogy of Fallot and some cardiac septal defects, is an example of a direct right-to-left shunt wherein unoxygenated blood from the right side of the heart is added to oxygenated blood from the left side of the heart. In these conditions, hypoxemia cannot be abolished by increasing the oxygen content of inspired air. The shunted blood is never exposed to the higher concentration of inspired oxygen in the alveolus, and the addition of a small amount of shunted blood with its low O_2 content greatly reduces the P_{O_2} of arterial blood. Compared with breathing room air, the decrement in P_{O_2} is much greater at P_{O_2} levels associated with the inhalation of O_2-enriched air because the O_2 dissociation curve is so flat at high P_{O_2} levels. Only hypoxemia caused by right-to-left shunting behaves in this manner when the patient is permitted to inspire high percentages of oxygen (70% to 100%). Shunts do not usually cause hypercapnia.[23] Chemoreceptors detect excess arterial CO_2, and ventilation increases to reduce the content of CO_2 in unshunted blood until arterial P_{CO_2} reaches the normal range. In some cases of shunt, the arterial P_{CO_2} is below normal because of hyperventilation stimulated by the hypoxemic ventilatory drive.

DIFFUSION IMPAIRMENT

Gas exchange between the alveolus and the capillary occurs by passive diffusion, which is driven by the property of molecules to move randomly from an area of high concentration to one of low concentration.[23] Factors that determine the rate of gas exchange include the concentration gradient between the alveolus and capillary blood, solubility of the gas, surface area available for diffusion, and the width of the air-blood barrier. Diseases characterized by pure diffusion impairment are rare in veterinary medicine.[4] Diffusion impairment can occur with pulmonary fibrosis, interstitial pneumonia, silicosis, or edema caused by increased width of the barrier or decreased surface area available for gas exchange. The clinician should recognize that the major component of hypoxemia for these conditions is a V-Q mismatch; however, diffusion impairment can contribute to the severity of hypoxemia. Supplemental oxygen therapy is effective in treating hypoxemia caused by diffusion impairment because it creates a more favorable concentration gradient and increases the driving pressure of oxygen to move from the alveolus into the blood. Transport of CO_2 is less affected by diseases of diffusion impairment because of its greater solubility compared with O_2.[23]

REDUCTION OF INSPIRED OXYGEN

Hypoxemia resulting from decreased inspired oxygen content is uncommon and occurs only under special circumstances. High altitude and iatrogenic ventilation with a low oxygen concentration are the most common circumstances in which hypoxemia is attributed to reduction of inspired oxygen content.[22]

Most pulmonary diseases in horses incorporate more than one of these pathophysiologic mechanisms for the development of hypoxemia. Horses with pleuropneumonia, for example, may develop hypoxemia caused by hypoventilation (extrapulmonary restriction by pleural effusion), V-Q mismatch (accumulation of exudate and edema within alveoli and conducting airways), and diffusion impairment (exudate and edema within the interstitial spaces).

Obstructive Disease

The location (intrathoracic or extrathoracic) and nature (fixed or dynamic) of airway obstruction determines whether impedance to air flow occurs during inspiration, expiration, or both.[3] The phase of the respiration cycle affected by air flow obstruction are prolonged and may be associated with a respiratory noise (stridor or wheeze).[24,25]

The horse is an obligate nasal breather and can only breathe efficiently through the nares.[4] Therefore upper airway obstruction within the nasal passages cannot be bypassed by mouth breathing. In addition, approximately 80% of the total airway resistance to air flow is located in the upper airway.[25] A 50% decrease in the radius of an airway increases its resistance by sixteenfold (Poiseuille's law).[14] Therefore small changes in the upper airway diameter dramatically affect the overall resistance to air flow and work of breathing for the horse. Extrathoracic airway pressures are subatmospheric during inspiration; therefore poorly supported structures in the upper airway narrow or collapse during inspiration (dynamic collapse). The most common cause of non–fixed upper airway obstruction in horses is laryngeal hemiplegia, which produces inspiratory stridor during exercise. Intraluminal masses and arytenoid chondritis cause fixed upper airway obstruction and produce inspiratory and expiratory respiratory distress.[3]

Twenty percent of the total airway resistance is attributable to the small airways.[25] Although the radius of individual bronchioles is small, many of them exist and the sum or collective radius is large, with the result that their overall contribution to pulmonary resistance is low.[23] Because the resistance of the bronchioles is low, advanced disease must be present for routine measurements of airway resistance to detect an abnormality, and obstruction of these airways must be extensive before a horse would suffer from respiratory distress. During pulmonary inflation, intrathoracic pressures are subatmospheric. Small airways are pulled open by negative intrathoracic pressure and stretched parenchymal attachments at high lung volumes. Thus resistance to air flow in small airways is low during the inspiratory phase of respiration.[24] During exhalation, intrathoracic pressure is positive and the diameter of small airways is decreased, and bronchioles may even close at low lung volumes. Therefore resistance to air flow in small airways is greatest during the expiratory phase. In horses with COPD, the airway diameter is reduced by inflammatory exudate, edema, and bronchoconstriction.[16,17] As lung volume decreases during expiration, the narrowed bronchioles are compressed shut (dynamic airway collapse) and trap air distal to the site of closure.[4] This is an example of severe flow limitation, which may lead ultimately to the development of emphysema. Flow limitation forces horses with COPD to breathe at higher lung volumes and maintain a higher functional residual capacity to reduce or avoid dynamic airway collapse. Affected horses attempt to reduce the end-expiratory lung volume by recruiting abdominal muscles to increase the intrathoracic pressures during expiration. However, the greater the end-expiratory pressure, the greater is the likelihood of small airway compression and collapse. Hypertrophy of the cutaneous trunci and expiratory abdominal muscles, especially the external abdominal oblique, produces the characteristic heave line associated with COPD.[4] Because dynamic airway narrowing and collapse occurs during exhalation, wheezes are loudest at end expiration in horses with COPD.[16,17]

Restrictive Disease

Restrictive disease is less common than is obstructive pulmonary disease in horses.[4] By definition, restrictive disease inhibits pulmonary expansion and leads to inspiratory respiratory distress.[26] The vital capacity and compliance (pulmonary or chest wall) decrease, expiratory flow rates and elastic recoil increase, and airway resistance is normal. The characteristic respiratory pattern in horses with restrictive pulmonary disease is rapid, shallow respiration at low lung volumes.[4] This strategy takes advantage of high pulmonary compliance at low lung volumes and decreases the work of breathing. This respiratory pattern has the disadvantage of increased ventilation of anatomic dead space.[26] Restrictive diseases may be classified as intrapulmonary (pulmonary fibrosis, silicosis,[27] and interstitial pneumonia[28,29]) and extrapulmonary (pleural effusion, pneumothorax, mediastinal mass, botulism, and nutritional muscular dystrophy).[4] Hypoxemia observed in horses with intrapulmonary restrictive disease is attributed to V-Q mismatch and diffusion impairment. Stimulation of juxtacapillary receptors may contribute to respiratory distress observed in these patients.[26] The pathophysiologic mechanism for hypoxemia in horses with extrapulmonary restriction is hypoventilation.[4] In cases of pleural effusion and pneumothorax, respiratory distress is likely to be exacerbated by thoracic pain.

Nonpulmonary Respiratory Distress

Respiratory distress does not always originate from dysfunction of the pulmonary system and its supporting structures. Nonpulmonary respiratory distress can occur because of inadequate oxygen-carrying capacity of the blood, compensation for metabolic acidosis, pain, and hyperthermia.

Impaired oxygen-carrying capacity of the blood may occur because of anemia (blood loss, hemolytic, or aplastic) or dysfunction of red blood cells (methemoglobinemia, carbon monoxide toxicity). In these cases, the arterial P_{O_2} tension is normal; however, the oxygen content of the blood is reduced greatly.[2] Tachypnea and respiratory distress occur in response to impaired oxygen delivery and tissue hypoxia.[3]

The respiratory system can compensate for metabolic acidosis by increasing ventilation to lower Pa_{CO_2} and attenuate acidemia.[2] The ventilatory drive increases in

response to stimulation by peripheral chemoreceptors by circulating hydrogen ions. Hypocarbic compensation for mild to moderate metabolic acidosis is effective in returning blood pH to normal until renal compensatory mechanisms can be established.[2]

Pain and anxiety are physiologic causes of tachypnea and hyperpnea. Horses with musculoskeletal pain are unlikely to demonstrate significant respiratory distress; however, rhabdomyolysis and laminitis are painful musculoskeletal conditions that may produce tachypnea.[3] Marked respiratory distress is observed frequently in horses with abdominal pain; however, the respiratory distress is not caused solely by pain and is exacerbated by abdominal distention, shock, acidosis, and endotoxemia.

Hyperthermia caused by fever, high environmental temperature, exercise, and heat stress can produce respiratory distress in horses. Tachypnea and elevation in body temperature are the most prominent clinical signs in horses with anhydrosis.[30] Hyperpnea is an effective mechanism for heat dissipation in human beings, dogs, and ruminants.[3] Unfortunately, increased ventilation is an inefficient mechanism for heat dissipation in horses and appears to be wasted effort.[3,4]

Clinical Evaluation of Respiratory Distress

A thorough physical examination is essential to determine the origin of respiratory distress, identify concurrent disease, and direct further diagnostic testing. Prolonged inspiration is consistent with restrictive or extrathoracic, nonfixed, obstructive disease, whereas horses with intrathoracic airway obstruction exhibit expiratory difficulty.[3,24] Respiratory distress associated with inspiration and expiration may indicate an extrathoracic fixed obstruction. Stridor is an abnormal respiratory noise that usually is generated by obstruction of the upper airway and is audible most often during inspiration.[3] Horses with nonpulmonary respiratory distress demonstrate increased rate and depth of respiration, without producing abnormal respiratory noise.

Thoracic auscultation identifies abnormal respiratory sounds (crackles and wheezes) or regions of decreased breath sounds caused by pleural effusion, pneumothorax, or pulmonary consolidation. Percussion of the thoracic wall generates a resonant and hollow sound when performed over regions of normal lung. Pleural effusion and pulmonary consolidation sound dull and flat during thoracic percussion, whereas pneumothorax produces a hyperresonant sound.[31]

Normal air flow occurs in laminar flow; therefore normal horses at rest do not generate easily audible sounds.[4] Respiratory sounds are generated from vibration in tissue and sudden changes in pressure of gas moving within the airway lumen. Airway narrowing and exudate generate audible sounds by creating disturbances in laminar flow, turbulence, and sudden changes in pressure of moving gas.[14] Crackles are intermittent or explosive sounds, generated by bubbling of air through secretions or by equilibration of airway pressures after sudden opening of collapsed small airways. The generation of crackles requires an air-fluid interface, and these abnormal lung sounds occur in horses with pneumonia, interstitial fibrosis, COPD, pulmonary edema, and atelectasis.[4] Wheezes are continuous, musical sounds that originate from oscillation of small airway walls before complete closing (expiratory wheeze) or opening (inspiratory wheeze).[14] Expiratory wheezes are the hallmark of obstructive pulmonary disease.[24]

Arterial blood gas determination provides a quantitative evaluation of pulmonary function, alveolar ventilation, and acid-base status and may identify the origin of respiratory distress (hypercapnia, hypoxemia, or acidemia).[22] The clinician may determine the pathophysiologic mechanism of hypoxemia by examining the Pa_{CO_2} level and by investigating the response of Pa_{O_2} to supplemental oxygen therapy. In addition, serial blood gas monitoring can determine response to bronchodilator, parasympathomimetic, or antiinflammatory therapy.

Additional diagnostic tests that may be indicated in horses with respiratory distress include thoracic radiography, thoracic ultrasonography, endoscopic examination of the upper airway, and atropine challenge. The findings during thoracic auscultation and percussion are valuable in determining indication for ultrasonography versus radiography. Pulmonary consolidation, abscessation, fibrosis, interstitial pneumonia, peribronchial infiltration, and mediastinal mass are differentiated and diagnosed readily via thoracic radiography. Thoracic ultrasonography is superior to radiography in detecting and characterizing pleural fluid and peripheral pulmonary abscessation and consolidation in horses. Air reflects the ultrasound beam; therefore ultrasonography does not image deep pulmonary lesions if the overlying lung is aerated.[32] An endoscopic examination of the upper airway is indicated in horses with inspiratory stridor and suspected upper airway obstruction.[33] Horses with extreme respiratory distress may resent endoscopic examination, and forced examination may precipitate a respiratory crisis. Atropine administration in horses with COPD may provide rapid relief of respiratory distress, if the major component of airway obstruction is reversible bronchoconstriction. Horses that respond to an atropine challenge likely will respond favorably to bronchodilator therapy. Incomplete response to atropine in horses with COPD indicates that exudate or fibrosis is contributing to airway obstruction, and limited response to bronchodilator therapy is anticipated.[16,17]

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3.8—Cough

Catherine W. Kohn

Cough, a sudden explosive expulsion of air through the glottis, is a common sign of respiratory disease and a reflex pulmonary defense mechanism. Coughing facilitates the removal of noxious substances and excessive secretions from the airways by creating maximum expiratory airflow. A high-velocity airflow generates the shear forces required to separate mucus from the airway walls, enabling expulsion of exudate and debris from the airway.[1] An understanding of the cough reflex provides insight into the pathophysiology of diseases characterized by cough.

The cough reflex has been studied infrequently in horses. Descriptions of the cough cycle and the neural basis of cough presented in this section are based on data from other species. The author infers that similar events occur in horses. Because differences exist among species

regarding the cough reflex,[2] studies on horses will be required to define the physiologic events of the cough reflex in this species.

Cough Cycle

The cough cycle has four phases: inspiration, compression, expression, and relaxation.[1] Deep *inspiration,* which immediately precedes cough, increases lung volume. As lung volume increases, the ability to generate maximum expiratory airflow increases because of the greater force of contraction achieved by the muscles of respiration when their precontraction length increases and because of the greater elastic recoil pressure of the lung at high lung value.[3] Thus precough expansion of lung volume maximizes the velocity of expiratory airflow. Achievement of maximum expiratory airflow rates requires a relatively gentle expiratory effort, and airflow maxima are therefore independent of effort.[2]

After deep inspiration, the glottis closes. While the glottis remains closed, *compression* of the chest cavity occurs by contraction of the thoracic and abdominal musculature during an active expiratory effort. Compression of the chest results in an increase in pleural pressure from 50 to 100 mm Hg.[2] This increase in pleural pressure is transmitted to pressure in the intrathoracic airways and trachea. Intraalveolar pressures actually exceed intrapleural pressures by an amount equal to the elastic recoil pressure of the lung.[4]

Expression occurs when the glottis opens abruptly, thus producing a gradient in airway pressure (atmospheric at the pharynx and high in the alveoli), and air is expired forcefully. The occurrence of dynamic airway compression in larger airways maximizes the velocity of airflow toward the mouth (Figure 3.8-1). The intraairway pressures vary in the respiratory system according to the instantaneous transpulmonary pressure.[3] At the equal pressure point, the airway pressure equals the pleural pressure. Toward the mouth from the equal pressure point (downstream), the pleural pressure is greater than intrathoracic airway pressure, and the intrathoracic airways therefore are compressed dynamically. Partial collapse of the airways downstream of the equal pressure point maximizes airflow velocities in these airways by decreasing their diameter. At high lung volumes, the equal pressure point likely is in the larger airways and therefore only the intrathoracic trachea may be subject to dynamic compression and maximal airflow velocity.[4] Maximum airflow velocity produces high shearing forces that dislodge mucus and debris from airway walls, thus facilitating expectoration. Cough is therefore most effective as a defense mechanism for clearing the larger airways in healthy animals. Removal of noxious substances from the smaller peripheral airways depends on the presence of mucus in the airways, and irritants that stimulate cough also may stimulate mucus production.[5]

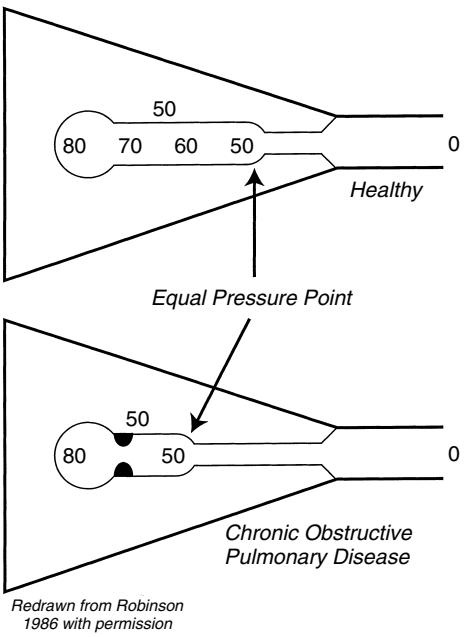

Figure 3.8-1 Dynamic airway compression during cough or maximum expiratory airflow. Lungs are represented at total lung capacity. When chronic obstructive pulmonary disease is present, the equal pressure point moves toward the alveoli. This peripheral migration of the equal pressure point results in dynamic compression in more peripheral airways during cough than would be found in a healthy individual.

(Redrawn from Robinson NE: Pathophysiology of coughing. In Proceedings of the thirty-second convention of the American Association of Equine Practitioners, Nashville, 1986, pp 291-297.)

In diseases characterized by increased resistance in small peripheral airways caused by partial obstruction (e.g., chronic obstructive pulmonary disease [COPD]), maximal expiratory flow rates are reduced. When small airways are obstructed partially, the equal pressure point moves toward the periphery of the lung during coughing because pressures in airways downstream of the partial obstruction are lower than are pressures in those airways in healthy lungs (see Figure 3.8-1). This shift in the equal pressure point subjects more peripheral airways to dynamic compression. Coughing is likely to be less effective as a clearance mechanism when obstructive diseases of the small airways are present. Bronchodilator therapy may increase the effectiveness of cough in such patients by increasing expiratory airflow rates.[4]

The sound of cough is generated by vibration of laryngeal and pharyngeal structures caused by the rapid expulsion of air immediately after opening of the glottis,[3] by narrowing and deformation of airways, and by vibration of surrounding lung tissue. Variations in the sound

of cough most likely relate to the quantity and quality of mucus in the airway.[6]

At the end of cough, *relaxation* occurs. Intrapleural pressure falls, and the muscles of expiration relax. Transient bronchodilation occurs.[1]

Neural Basis of the Cough Reflex

The afferent input for the cough reflex is carried predominantly in the vagus nerves, and the cough reflex depends uniquely on vagal afferents in the species studied.[5,7,8] Sensory myelinated nerves in the larynx respond to mechanical and chemical irritation and mediate cough and changes in airway diameter.[7] Debate continues about the identity of receptors that initiate cough in the lower airways; however, all the receptors described is this section likely contribute to the cough response.[8] *Rapidly adapting receptors* are located in the airway mucosa in the region of the carina and are stimulated primarily by mechanical deformation produced, for example, by inhaled particles, mucus, or cellular debris accumulating near the carina. Chemical irritants (e.g., ammonia fumes, ozone, and inflammatory mediators) evoke cough by stimulation of receptors located in the peripheral airways. *Pulmonary C fibers* may mediate a chemically evoked cough, although this issue still is debated. Chemical mediators known to stimulate pulmonary C fibers and cough when inhaled as aerosols by human beings include bronchodilator prostaglandins, bradykinin, and capsaicin.[8] Forced expiration during coughing may be facilitated by the modulating effects of information from these receptors on central respiratory neurons.

Bronchoconstriction is a constant component of cough,[3,6] and stimuli of cough also may cause bronchoconstriction; however, cough and bronchoconstriction are separate airway reflexes. Inhalation of dust and irritant gases causes reflex bronchoconstriction in the species studied. Reflex bronchoconstriction has a slow onset and is long lasting compared with the cough reflex.[9] Bronchoconstriction may increase the efficiency of cough by decreasing airway diameter and therefore increasing airflow velocity. In some cases, bronchodilating drugs may suppress the cough reflex by desensitizing airway receptors that elicit cough.[6]

Sensory nerves mediating bronchoconstriction and cough are distributed unevenly along the airways.[7] Laryngeal receptors and sensory nerves in the extrapulmonary airways may be more sensitive to mechanical stimuli, whereas intrapulmonary receptors may respond preferentially to chemical mediators and irritants.

Little is known about the brainstem neuronal pathways of the cough reflex. In the cat, the cough center is reported to be in the medulla at the level of the obex, alongside the solitary nucleus of the vagus and close to the expiratory neurons of the respiratory center. On the motor side of the cough reflex, the vagal, phrenic, intercostal, and lumbar nerves and motor portions of the trigeminal, facial, hypoglossal, and accessory nerves are distributed to the striated and smooth muscles of respiration, the vocal fold abductors and adductors, and glands of the respiratory tract.[3]

Stimuli of Cough

Cough may be stimulated by airway smooth muscle contraction (bronchoconstriction), excessive mucus production, presence of inhaled particles in the airways, release of inflammatory mediators (infectious diseases), exposure to cold or hot air, intramural or extramural pressure or tension on the airways (tumor, granuloma, abscess, or decreased pulmonary compliance caused by restrictive disease such as interstitial fibrosis or pleuritis), sloughing of airway epithelial cells, and enhanced epithelial permeability (pulmonary edema).[5] Epithelial sloughing and enhanced epithelial permeability theoretically increase the accessibility of cough receptors to the mechanical or chemical agents that stimulate them. Loss of the integrity of the epithelial lining of the respiratory tract is a common feature in many respiratory diseases associated with cough (infectious diseases); however, a cause-and-effect relationship between alterations in respiratory epithelium and cough has not been established.[5]

Diseases of the respiratory tract may alter the sensitivity of the cough reflex.[5] For example, viral diseases may increase the responsiveness of cough receptors to stimuli.

Deleterious Consequences of Cough

Although cough is an important defense mechanism of the respiratory system that promotes expectoration of inhaled noxious substances and voluminous airway secretions, cough may lose its original defensive function and may contribute to the morbidity and discomfort associated with bronchopulmonary disease.[8] This is especially true when the effort to cough is intense and when multiple coughs occur sequentially. Chronic coughing is exhausting and, especially in foals, may decrease food intake. Paroxysmal or persistent cough may impair respiration. Coughing may have profound effects on the cardiovascular system. During the deep inspiratory phase of cough, the rise in intraabdominal pressure because of contraction of the diaphragm and the fall in intrathoracic pressure combine to aspirate blood from the vena cava to fill the right atrium and ventricle abruptly.[3] Because the pleural pressure decreases, the pulmonary artery pressure also decreases. During the expiratory phase of cough, an initial increase in systemic arterial blood pressure and a simultaneous and commensurate increase in cerebral

venous and cerebrospinal fluid pressures occur. However, venous return to the heart soon decreases and within a few heartbeats, filling of the heart and stroke volume decrease.[2,3] Hypotension ensues. Falling arterial blood pressure in the face of high cerebral venous pressures reduces the effective perfusion pressure of the brain. Cerebral hypoperfusion and anoxia may occur. Cough-induced syncope has been reported in human beings[2] and in dogs.[10]

In chronic cough, bronchial muscular hypertrophy may develop. Bronchial mucosal edema or emphysema may accompany chronic cough. During cough inspiration, inflammatory debris may be aspirated into previously uncontaminated areas of the lung. Cough in dogs has been associated with pneumothorax (from rupture of preexisting pulmonary bullae) and lung lobe torsion.[11] Rib and vertebral fractures have been reported in human beings with powerful coughs but have not been reported in horses.[2,3]

Clinical Approach to the Coughing Horse

Cough is a common sign of respiratory disease in horses (Figure 3.8-2). Cough is an indication of mechanical or irritant stimulation of cough receptors for which the potential causes are diverse. Many clinical approaches exist for anatomic localization of the origin of the cough stimulus in respiratory disease and for discovery of the cause. All methods have in common a systematic and thorough evaluation of the history and physical examination of the patient. To aid the clinician in formulating a rational approach to diagnosis, diseases associated with cough may be grouped according to those characterized by fever (current or historical) and those characterized by lack of an elevated body temperature. The clinician should keep in mind that exceptions to generalizations always occur concerning disease processes, and the following discussion therefore serves only as a guide to develop a logical approach to differenting diseases characterized by cough.

COUGH WITH FEVER

Horses with cough and fever should have a thorough physical examination (see Chapter 7 for a complete description of a physical examination for horses with respiratory disease). A minimum laboratory database for the coughing horse with fever should include the results of a hemogram and a fibrinogen determination. The clinician carefully should auscultate the thorax of the horse in a quiet room with the horse breathing quietly. If the horse is not dyspneic or hypoxemic, the clinician also should undertake auscultation during forced breathing. A plastic bag loosely held over the nostrils of the horse forces the horse to increase tidal volume and respiratory rate. This maneuver causes many horses with exudate in the airways to cough, and deep breathing may be frankly painful for some horses with pleuropneumonia. Auscultation during forced breathing is not necessary in horses with obviously abnormal lung sounds during quiet breathing and is not advisable in horses with pneumonia (especially aspiration pneumonia) or in horses with foreign material in the trachea. Crackles and wheezes heard repeatedly during the inspiratory and early expiratory phases of breathing suggest that pulmonary parenchymal disease is present. Accentuated normal bronchovesicular sounds sometimes are present in horses with pulmonary consolidation, because of referral of sounds from the aerated lung. Absence of lung sounds in dependent portions of the thorax indicates that pulmonary consolidation, atelectasis, or fluid in the pleural cavity may be present. Thoracic percussion and sonographic evaluation are particularly helpful in documenting the presence of fluid in the pleural cavity. Ultrasonography also may show pleural irregularities and superficial parenchymal abscessation, atelectasis, or consolidation. Thoracic radiographs are especially helpful in demonstrating deeper parenchymal disease. Many equine practitioners do not have access to thoracic radiography but can perform thoracic ultrasonography.

Abnormal lung sounds, percussion irregularities, and sonographic evidence of fluid or consolidation are indications for performing transtracheal aspiration (TTA) and bronchoalveolar lavage (BAL). When both procedures are to be performed on the same patient, the clinician should perform TTA first to obtain a sample for culture before the airway is contaminated by the BAL tube. Many practitioners prefer to obtain TTA samples transendoscopically to avoid percutaneous aspiration. Despite the development of guarded culture swabs for transendoscopic use, this technique does not always prevent contamination of lower airway fluid samples. One study demonstrated that *Pseudomonas* spp. and anaerobic bacteria in cultures of tracheal fluid obtained transendoscopically should be viewed as potential contaminants.[12]

Cytologic evaluation of the TTA/BAL, indicating an increase in polymorphonuclear leukocytes (PMNs), is consistent with parenchymal disease. Some PMNs may be degenerate. Although some clinicians feel that PMNs may be seen in the tracheal aspirates of normal horses, few PMNs are found in bronchoalveolar lavage fluids from healthy horses (4.4 ± 3.3 cells to 8.9 ± 1.2 cells/μl).[13] How well the results of cytologic evaluation of BAL fluids represent the environment of the lower airways is a matter of some debate. Bronchoalveolar lavage fluids are harvested from a focal area of the lung. If parenchymal disease is not generalized, bronchoalveolar lavage may miss the diseased region. Results of BAL fluid analysis

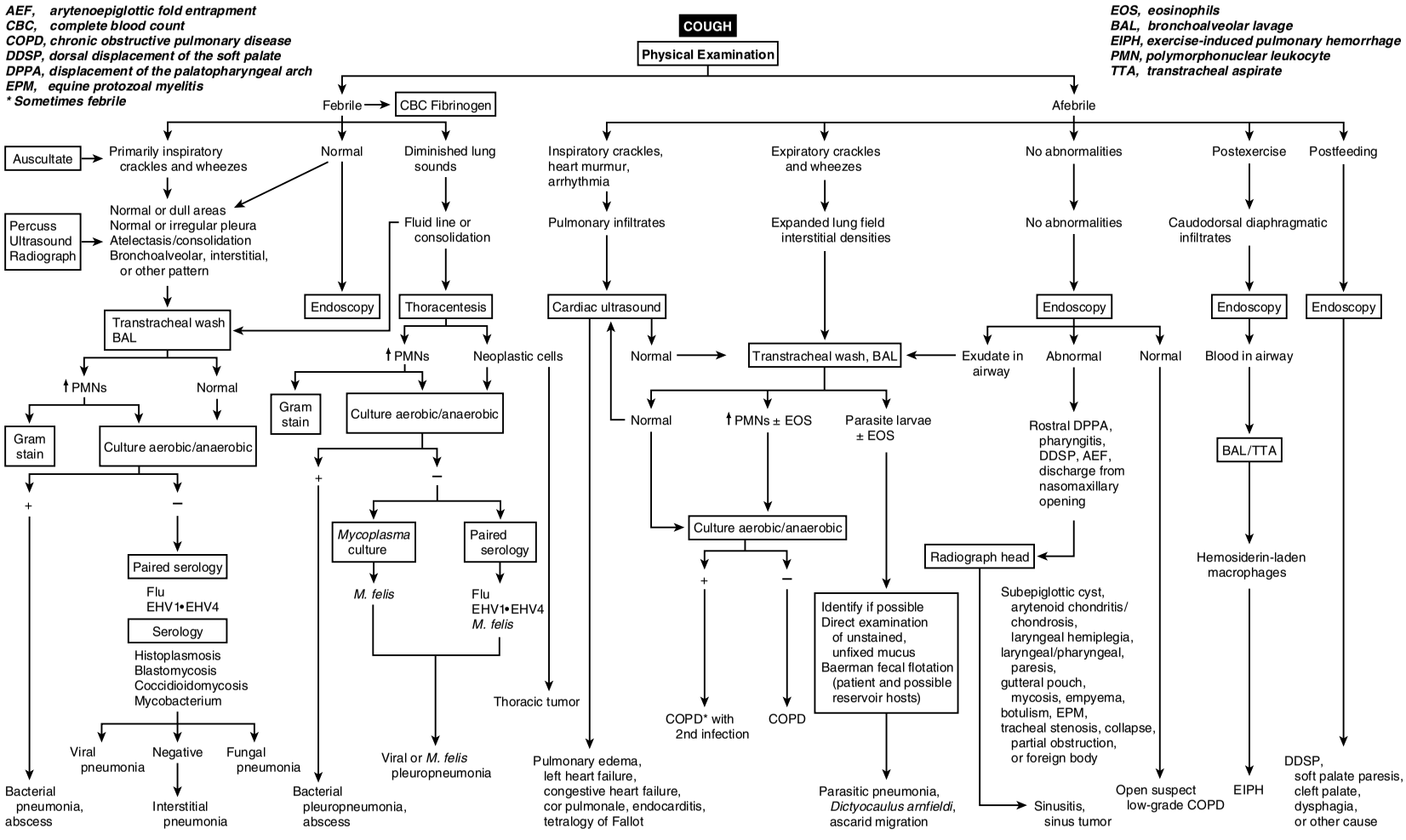

Figure 3.8-2 Approach to cough. *EHV1, 4,* Equine herpesvirus 1 or 4.

are normal in some horses with pneumonia and pleuropneumonia. Transtracheal wash fluid consists of secretions from both lungs, and TTA cytologic examination was abnormal in all horses with pneumonia and pleuropneumonia in one study.[14] The prevalence of PMNs in TTA fluid from horses without lower respiratory tract disease has not been determined.

The presence of degenerate PMNs and extracellular or intracellular bacteria in TTA/BAL fluid is consistent with the diagnosis of a septic process. The clinician should evaluate a Gram stain to guide the initial choice of antimicrobial agents while awaiting results of culture and sensitivity determinations. Growth of aerobic or anaerobic bacteria in a culture of TTA fluid confirms the presence of bacterial pneumonia if clinical and radiographic findings are also consistent with this disease process. Contamination of cultures of airway secretions obtained via TTA occasionally may occur. Lack of growth of bacterial pathogens from TTA fluid suggests that viral, interstitial, or fungal pneumonia might be present. These possibilities should be investigated by evaluating paired serum samples taken 10 to 14 days apart for influenza virus, equine herpesvirus 1 (EHV1), EHV4, rhinovirus, and equine viral arteritis. Serologic testing for histoplasmosis, blastomycosis, coccidioidomycosis (southwestern United States especially), and possibly mycobacteria should be evaluated. Fungal cultures of tracheal fluid should be evaluated when other more common causes of pneumonia have been ruled out and if the clinical signs of the patient are consistent with this diagnosis. Negative results on serologic tests and fungal cultures in patients with a significant interstitial pattern on thoracic radiographs should prompt consideration of the diagnosis of interstitial pneumonia, a condition for which the inciting cause has not been established and for which the prognosis is grave.

Percussion, radiographic, or ultrasonic evidence of increased intrapleural fluid is an indication for thoracocentesis. Many horses with bacterial pleuropneumonia have elevated pleural fluid PMN concentrations, and PMNs may be degenerate. Intracellular or extracellular bacteria may be seen on cytologic evaluation. Occasionally, frankly neoplastic cells may be identified in thoracic fluid (usually squamous cells or lymphocytes). Many cytologists are uncomfortable diagnosing thoracic neoplasia based solely on an evaluation of pleural fluid. Thoracic fluid should be cultured aerobically and anaerobically. A positive culture identifies the cause of bacterial pleuritis; however, often pleural fluid cultures may be negative. Cultures of TTA fluid are more likely to be positive in horses with pleuropneumonia, and TTA cultures should be performed routinely for these patients. Primary viral pleuritis, although rare in the author's experience, has been reported in horses, and paired serologic examinations for influenza virus and EHV1/EHV4 may be helpful when cultures are negative. One case of pleuritis caused by *Mycoplasma felis* has been reported.[15] Culture of pleural fluid and paired serologic examinations for this organism should be performed in patients for which other tests have not proved diagnostic.

Intrathoracic neoplasms may cause cough with or without accompanying fever. Confirmation of a thoracic tumor may require an ultrasound-guided biopsy or an exploratory thoracotomy and a biopsy. Secondary bacterial pleuritis may complicate thoracic neoplasms, and aerobic and anaerobic cultures of thoracic fluid from patients suspected of having thoracic neoplasms should be performed.

Some febrile coughing horses have no abnormalities on auscultation, percussion, thoracic radiography, or ultrasound. In such patients, occult pulmonary disease may be present and TTA/BAL and culture of TTA fluid are indicated. Alternatively, such horses may have upper airway disease (sinusitis, sinus tumor, guttural pouch empyema), and an endoscopic evaluation is also indicated.

COUGH WITHOUT FEVER

When auscultation of the thorax demonstrates primarily expiratory crackles and wheezes, thoracic percussion often reveals a caudoventral expansion of the lung borders. These findings suggest that COPD may be present. Thoracic radiographs usually show increased interstitial densities; radiographs are useful to rule out occult underlying pulmonary disease (such as a well walled-off abscess) but are not required for diagnosis in most cases. TTA and BAL are indicated. Horses with COPD usually have an increase in well-preserved PMNs, and sometimes eosinophils, in TTA and BAL fluids. Growth of pathogens in aerobic or anaerobic culture of TTA fluid identifies secondary bacterial infection. No growth in cultures of TTA fluid is also consistent with the diagnosis of COPD. Occasionally, TTA/BAL fluids may contain parasite larvae or many eosinophils. If horses historically have been housed with donkeys or mules, one should suspect *Dictyocaulus arnfieldi* infestation. Coughing horses younger than 18 months of age with eosinophilic TTA fluid may be experiencing an aberrant migration of *Parascaris equorum* larvae. The clinician should attempt to identify the larvae, although this may be difficult. A direct cytologic evaluation of unfixed, unstained, or iodine-stained mucus may be helpful to identify larvae of *D. arnfieldi*. The clinician should perform a Baermann flotation on feces from the patient and potential reservoir hosts, but the test may not demonstrate ascarid larvae, because pulmonary migration may occur early in the prepatent period.[16] The diagnosis of pulmonary ascarid migration is based on ruling out other causes of pneumonia.

When TTA/BAL fluids have no abnormal cells, cultures still should be assessed. For afebrile coughing horses

with thoracic auscultation findings of inspiratory crackles and wheezes and cardiac murmur or arrhythmia, one should take thoracic radiographs. The presence of diffuse pulmonary infiltrates in a bronchoalveolar pattern suggests that pulmonary edema may be present. A complete ultrasonic evaluation of the heart is indicated.

Some coughing, afebrile horses have no abnormalities on auscultation or percussion, and endoscopy of the upper airway and trachea is indicated. Some horses have endoscopic evidence of exudate in the trachea and likely have low-grade COPD. The clinician should take thoracic radiographs of these horses if possible and perform TTA/BAL testing followed by culture of TTA fluid. A transtracheal aspirate should not be obtained immediately after tracheoscopy because bacteria on the endoscope may contaminate airway cultures.

In other patients, cough may be a symptom of upper airway obstructive disease (dorsal displacement of the soft palate, rostral displacement of the palatopharyngeal arch, arytenoepiglottic fold entrapment, subepiglottic cyst, arytenoid chondritis/chondrosis, laryngeal hemiplegia, or tracheal stenosis, collapse, or partial obstruction) or maxillary or frontal sinusitis with discharge into the nasal passages via the nasomaxillary opening or laryngeal/pharyngeal paresis. The latter may be a symptom of guttural pouch mycosis, empyema, or systemic disease (e.g., botulism or equine protozoal myelitis). Cough also may be a symptom of a tracheal foreign body (e.g., a twig or TTA catheter) in the airway. One should suspect horses with cough but no abnormalities on endoscopic examination of having low-grade COPD.

Cough after exercise or feeding also should prompt an endoscopic evaluation. Evidence of hemorrhage in the trachea after exercise indicates that exercise-induced pulmonary hemorrhage is likely. This diagnosis can be confirmed by finding hemosiderin-laden macrophages in BAL or TTA fluid. Thoracic radiographs may show interstitial densities and pleural thickening in the caudodorsal lung field. Postprandial cough may be associated with soft palate paresis, dorsal displacement of the soft palate, cleft palate (neonates and foals), or dysphagia of any cause.

A detailed description of diagnostic and therapeutic strategies for diseases of the respiratory system can be found in Chapter 7.

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3.9—Changes in Body Temperature

Melissa T. Hines

Assessment of body temperature is an essential part of every physical examination. As with all mammalian species,

horses normally maintain their core body temperature within a narrow range despite extremes in environmental conditions. The core temperature may vary by approximately 1° C (2° F) between individuals. In adult horses, the average normal body temperature is 38.0° C (100.5° F), whereas in neonatal foals the temperature tends to be slightly higher, ranging from 37.8° to 38.9° C (100.0° to 102.0° F). A diurnal variation of up to 1° C (2° F) may occur, with the low point typically in the morning and the peak in the late afternoon.

Control of Body Temperature

The set-point is the crucial temperature that the body attempts to maintain, primarily via neuronal control operating through temperature centers in the hypothalamus.[1,2] Peripheral and central thermoreceptors sense changes in ambient and core body temperatures and activate feedback mechanisms that bring the temperature back to the set-point. Specifically, the anterior hypothalamic-preoptic area contains large numbers of heat-sensitive neurons and lower numbers of cold-sensitive neurons that function as temperature detectors. Peripheral receptors, which are generally most sensitive to low temperatures, are located in the skin and in some deep tissues, such as the spinal cord, abdominal viscera, and around certain great veins. The anterior hypothalamic-preoptic area and the peripheral receptors transmit signals into the posterior hypothalamic area, subsequently activating autonomic and behavioral effector responses to regulate body temperature.

When the body temperature is too high, heat loss increases and heat production diminishes. Increasing blood flow to the skin is an effective mechanism for heat transfer from the body core to the surface. In response to changes in core body temperature and environmental temperature, the sympathetic nervous system regulates the degree of vasoconstriction and thus the amount of blood flow. Heat is lost from body surfaces to the surroundings by several physical mechanisms, including radiation, conduction, and convection. Evaporation is also an important mechanism of heat loss in horses.[3] The rate of sweating controls to some extent the amount of evaporative heat loss. However, even when the animal is not sweating, water evaporates insensibly from the skin and lungs, causing continual heat loss. In horses, evaporative heat loss, primarily though increased sweating but also through increased respiration, becomes more important as the ambient temperature rises and during exercise.[3,4] In addition to increased heat loss when the body temperature rises, the horse also decreases temperature further by inhibiting means of heat production, such as shivering, and by behavioral responses, such as seeking shade, wind currents, and wading into water.

Mechanisms that increase body temperature come into play when the body temperature is too low.[2] Heat is conserved by stimulation of the posterior hypothalamic sympathetic centers leading to cutaneous vasoconstriction and piloerection. Heat production also increases and may occur through increased muscle activity ranging from inapparent contractions to generalized shivering. Shivering may increase heat production by 4 to 5 times baseline. The primary motor center for shivering is in the posterior hypothalamus, which normally is stimulated by cold signals from the peripheral receptors and to some extent the anterior hypothalamic-preoptic area. Signals from heat sensitive neurons in the anterior-hypothalamic-preoptic area inhibit the center. Digestion of food also contributes to total body heat. Sympathetic stimulation may increase the rate of cellular metabolism, increasing heat production by chemical thermogenesis. Cooling also increases the production of thyrotropin-releasing hormone, ultimately increasing thyroid hormones and cellular metabolism, and further contributing to chemical thermogenesis. In addition to these physiologic adaptations, behavioral responses to conserve heat also occur, such as adopting a huddled stance, aggregating in groups, and seeking shelter.

Conditions of Increased Body Temperature

Elevation of the body temperature above normal is one of the most common clinical problems encountered, and although classically associated with infection, a variety of disorders may cause increased body temperature. One should distinguish between conditions of hyperthermia, in which the temperature set-point is unaltered, and true fever, in which the set-point actually increases.

HYPERTHERMIA

The body temperature may become elevated without an increase in the set-point when a loss of equilibrium occurs in the heat balance equation. Increased heat production or absorption of heat beyond the ability of the body to dissipate heat may occur. In some conditions, impaired heat loss also may occur. Hyperthermic conditions include problems such as exercise-related hyperthermia, heat stroke, malignant hyperthermia, anhidrosis, central nervous system disorders, and reactions to certain toxins or drugs. In general, these conditions do not respond to treatment with antipyretic drugs.

EXERCISE-RELATED HYPERTHERMIA

During sustained or high-intensity exercise, increased heat production is associated with muscular activity.[3,4] The heat produced may exceed the ability of the body to lose heat, resulting in an increased core body temperature.

Typically, the temperature returns to normal with rest as heat loss mechanisms remain activated. Elevated temperature also may occur with the intense muscle activity associated with generalized seizures.

HEAT STROKE

Heat stroke occurs when the body temperature rises above a critical temperature, leading to multisystemic problems. In horses, signs of heat stroke may develop when the body temperature is above 41.5° C (107° F), which most often occurs in association with exercise in environmentally stressful conditions. Although horses can acclimatize to various weather conditions to some extent, the efficiency of evaporative heat loss may be compromised significantly in hot, humid weather.[4,5] Susceptibility to heat stroke may increase if sweating leads to dehydration and electrolyte imbalances. Once the body temperature reaches the critical point, the homeostatic mechanisms of thermoregulation fail, resulting in peripheral vasoconstriction, decreased cardiac output, and decreased blood pressure. Affected horses are lethargic, with weak flaccid muscles. Prostration, circulatory shock, disseminated intravascular coagulation, multiple organ failure, and death may occur.

ANDHIDROSIS

Especially in hot, humid climates, horses may develop anhidrosis, which is characterized by a partial or total loss of the ability to sweat.[6] Because of the resulting impaired heat loss, hyperthermia may develop. Clinical signs of poor performance, increased respiratory rate, and poor hair coat also are observable.

MALIGNANT HYPERTHERMIA

Malignant hyperthermia encompasses a group of inherited skeletal muscle disorders in which calcium metabolism is altered.[7] Although the condition is most common in human beings and pigs, it has been reported in several species, including horses.[8,9] The disorder is characterized by a hypermetabolic state of muscle that generally is induced by halogenated inhalation anesthetics, depolarizing skeletal muscle relaxants, and occasionally local anesthetics or stress. Clinical signs include a rapid increase in core body temperature, skeletal muscle rigidity, and tachycardia. Affected animals may develop significant acidosis and muscle necrosis and in some cases may die. In pigs, malignant hyperthermia has been linked to a single point mutation in the gene for the skeletal muscle ryanodine receptor, but a genetic basis has not yet been established in horses.[7]

CENTRAL NERVOUS SYSTEM DISORDERS

Any condition affecting those areas of the hypothalamus involved in thermoregulation may alter the body temperature, with hyperthermia being more common than hypothermia.[1,2] Thus central hyperthermia occurs in association with a variety of conditions, including hemorrhage, neoplasms or abscesses, infectious/inflammatory changes, and degenerative disorders. Central hyperthermia usually is characterized by a lack of any diurnal variation, absence of sweating, resistance to antipyretic drugs, and excessive response to external cooling.

CERTAIN TOXINS OR DRUGS

Occasionally, hyperthermia has been associated with toxins or drugs. Exposure to compounds that act to uncouple oxidative phosphorylation, such as the wood preservative pentachlorophenol, potentially could cause a significant rise in body temperature.[10] Foals treated with the antibiotic erythromycin are at risk of developing hyperthermia.[11] Such predisposition has been attributed to a reaction to the erythromycin itself or to an alteration of the thermoregulatoy system of the foal by mechanisms not yet described. Environmental conditions may exacerbate the development of hyperthermia, with foals exposed to high ambient temperatures and direct sunlight being at greatest risk.

Pathogenesis of True Fever

In true fever the set-point for the desired core body temperature increases and then is maintained by the same mechanisms that maintain the normal body temperature. Although primarily associated with infectious diseases, fever is also a prominent component of many inflammatory, immunologic, and neoplastic conditions. Although the pathogenesis of the febrile response is complex, essentially all of these conditions initiate fever by stimulating the release of endogenous pyrogens (Figure 3.9-1).

Endogenous pyrogens are substances with the biologic property of fever induction.[12,13] Initially endogenous pyrogen was assumed to be a single molecule produced by leukocytes, thus the name leukocytic or granulocytic pyrogen. Now, multiple cytokines are known to act as pyrogens, and a variety of cell types produce them, with monocytes and macrophages predominating. Currently, the following cytokines are thought to be intrinsically pyrogenic in that they produce a rapid-onset fever via direct action on the hypothalamus without requiring formation of another cytokine: interleukin-1α (IL-1α) and IL-1β, tumor necrosis factors (TNF) α and β, interferon-α, and IL-6. IL-1α and IL-1β and TNF-α appear to be among the most potent pyrogens. Many endogenous pyrogens use the cell-signaling apparatus gp130. Cytokines that act through this receptor include IL-6, IL-11, oncostatin M, ciliary neurotrophic factor, cardiotropin-1, and leukemic inhibitory factor. From a clinical standpoint,

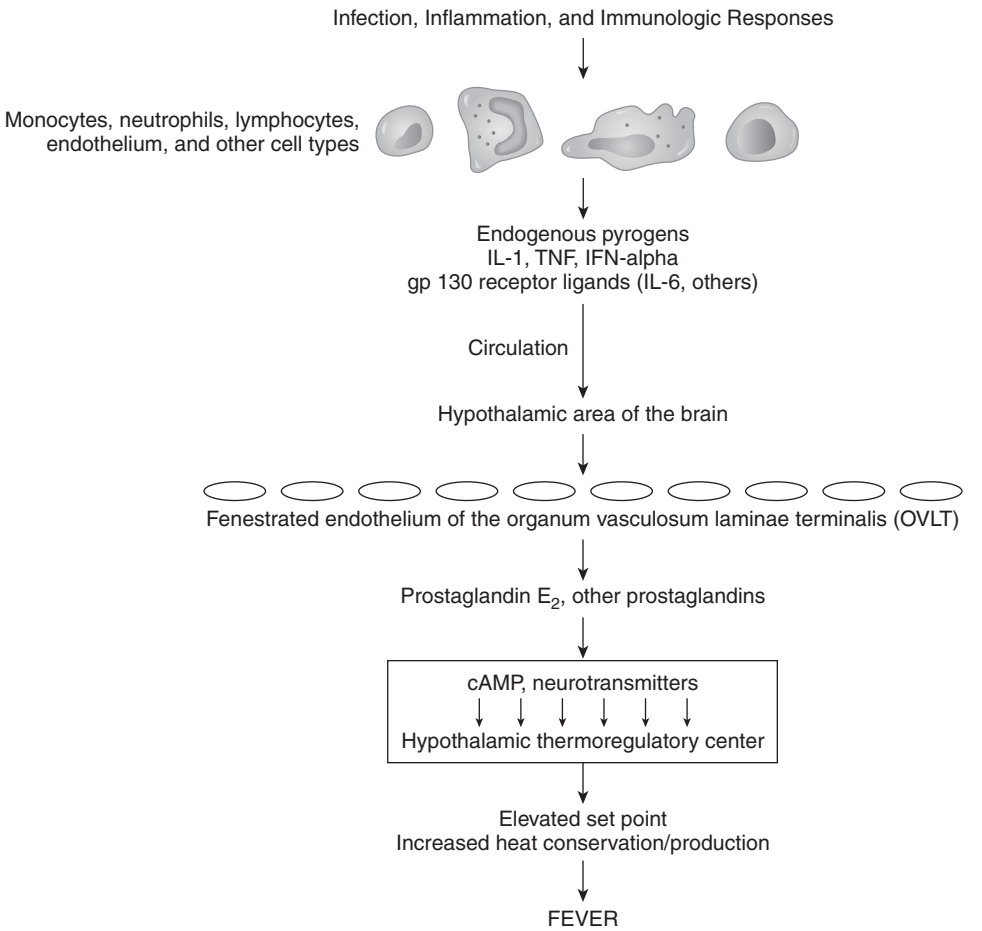

Figure 3.9-1 Schematic representation of the pathogenesis of fever. *cAMP,* Cyclic adenosine monophosphate; *IFN,* interferon; *IL,* interleukin; *TNF,* tumor necrosis factor.

several pyrogenic cytokines are produced during most febrile diseases and contribute to the febrile response.

The precise mechanism of action of pyrogenic cytokines in the central nervous system is still unclear. Endogenous pyrogens probably act on the circumventricular organs or organum vasculosum laminae terminalis (OVLT), a rich vascular network associated with neurons of the preoptic anterior hypothalamus.[13-15] Ablation of the OVLT prevents fever after a peripheral injection of endogenous pyrogens but has no effect when endogenous pyrogens are injected directly into the brain tissue.[14] In the region of the OVLT the blood-brain barrier is minimal, and endothelial cells lining this region may allow direct movement of endogenous pyrogens into the brain or they may release arachidonic acid metabolites in response to endogenous pyrogens, which then move into the brain. The production of arachidonic acid metabolites, particularly prostaglandin E_2 via the cyclooxygenase 2 (COX-2) pathway is clearly important in the pathogenesis of fever, because COX inhibitors, and specifically COX-2 inhibitors, effectively reduce the febrile response but have no effect on the normal body temperature. The prostaglandins do not act directly but initiate neuronal signaling by producing a cascade of changes in cyclic nucleotides, calcium, and monoamines leading to a higher set-point in the hypothalamic thermoregulatory center.

Physiologic mechanisms exist to control the febrile response and prevent extremes that are incompatible with life. Multiple feedback mechanisms limit the activity of the pyrogenic cytokines and many endogenous cryogens or antipyretics have been identified.[16,17] For example, IL-10, which can be induced by pyrogenic cytokines, inhibits further production of IL-1 and TNF. Arginine vasopressin and α-melanocyte-stimulating hormone act within the brain to decrease fever.[16-19] When administered to human beings, α-melanocyte-stimulating hormone is a much more potent antipyretic than acetaminophen. Nitric oxide also has been shown to have an antipyretic role, mediated by cyclic guanosine monophosphate, in the anterior hypothalamic-preoptic region.[20]

The cytokines that act as endogenous pyrogens have a variety of biologic effects. Therefore the onset of fever is accompanied by several hematologic, immunologic, and metabolic changes referred to as the acute phase response. In particular, IL-6 and IL-11 induce the synthesis of acute phase proteins by hepatocytes, including fibrinogen, C-reactive protein, haptoglobin, and others. Similarly, hypoferremia, hypozincemia, and hypercupremia are cytokine mediated, as is the activation of lymphocytes, which in turn produce additional cytokines.

Pyrogenic cytokines, particularly IL-1 and TNF-α cause membrane perturbation with an increase in phospholipases and the production of arachidonic acid.[12,13] The subsequent production of mediators depends on the metabolic pathways for arachidonic acid in the target tissue. Prostaglandins induced by endogenous pyrogens stimulate the muscle catabolism associated with fever and induce collagenase synthesis from synovial cells, contributing to the muscle and joint pain often seen with fever. Local tissue responses to IL-1β and TNF-α may stimulate afferent neural impulses that lead to behavioral responses associated with fever, such as lethargy and anorexia. As expected, treatment with COX inhibitors can diminish many of the signs of fever.

Effects of Fever

Fever is a normal physiologic response with beneficial and adverse effects to the animal. With the exception of some viral infections, the elevation in temperature is generally not high enough to affect pathogens directly. However, studies on bacterial infections in several species have demonstrated an increase in survival with fever, which is thought to be caused primarily by enhanced host defenses.[21-23] In addition, the concentration of iron, which is required by many bacteria for multiplication, decreases during the acute phase response.[24-26] If the temperature becomes extremely high, many of the beneficial effects are reversed.[2,27,28] In rabbits the severity of bacterial infection increases when the body temperature in more than 3° C (5° F) above normal. The increased catabolism, variable anorexia, and increased metabolic rate can lead to muscle wasting and weakness when fever is prolonged. Although seizures induced by fever are uncommon in horses, they can be seen in neonates when the temperature is above 42° C (108° F).[29] In debilitated animals, prolonged fever has been associated with cardiovascular failure.

Approach to Fever

Increased body temperature is a common clinical sign with diverse causes (Figure 3.9-2). Fortunately, in many cases the cause may be readily apparent based on the signalment, history, and physical examination. Conditions of increased temperature such as exercise-related hyperthermia and malignant hyperthermia are often apparent from the history. Infectious diseases remain the most common cause of fever, and often localizing clinical signs such as nasal discharge or diarrhea aid in the diagnosis. In other cases, an increased temperature may be one component of another obvious condition, such as neoplasm, immune-mediated disease, or a drug reaction.

Fever of Unknown Origin

Fever of unknown origin exists when fever is prolonged with no other specific signs. In many cases, the cause is a common disease with an unusual presentation. The specific criteria used to define fever of unknown origin in the horse in a review of 63 cases included the following: (1) illness of at least 3 weeks' duration associated with nonspecific signs, (2) body temperature of at least 38.6° C (101.5° F) on several occasions, and (3) no clear diagnosis after an initial complete blood count and serum biochemical profile.[30] The most common cause was found to be infection, which was responsible for 43% of the cases. Other causes included neoplasms in 22% of cases, immune-mediated diseases in 6.5%, and miscellaneous diseases including toxic hepatopathy, parasitism, and others in 19%. In 9.5% of cases, no diagnosis was made. Therefore diagnosis of fever of unknown origin requires a systematic approach with emphasis on the evaluation of infectious disease.

The clinician can have the body temperature taken twice daily over a period of time to document fever and identify any pattern. Although some inconsistencies in the precise terminology used to define patterns of fever exist, *intermittent fevers* generally are characterized by recurring paroxysms of elevated temperature followed by periods of normal temperature, such as those fevers that demonstrate diurnal variation. Intermittent fevers most often are associated with infectious causes, particularly viral infections, although they may be seen with a variety of other conditions. In most cases of intermittent fever the temperature tends to peak in the late afternoon or evening, though this is not always the case. *Remittent fevers* are those in which diurnal variation is exaggerated without a return to normal body temperature or those with a cyclic pattern in which the temperature elevation lasts for several days, such as may be seen with equine infectious anemia virus. *Biphasic fevers,* in which an initial rise in body temperature precedes a period of normal temperature and then a second rise, are characteristic of certain diseases such as equine monocytic ehrlichiosis (Potomac horse fever). Sustained fevers are those in which the elevation of temperature is consistent.

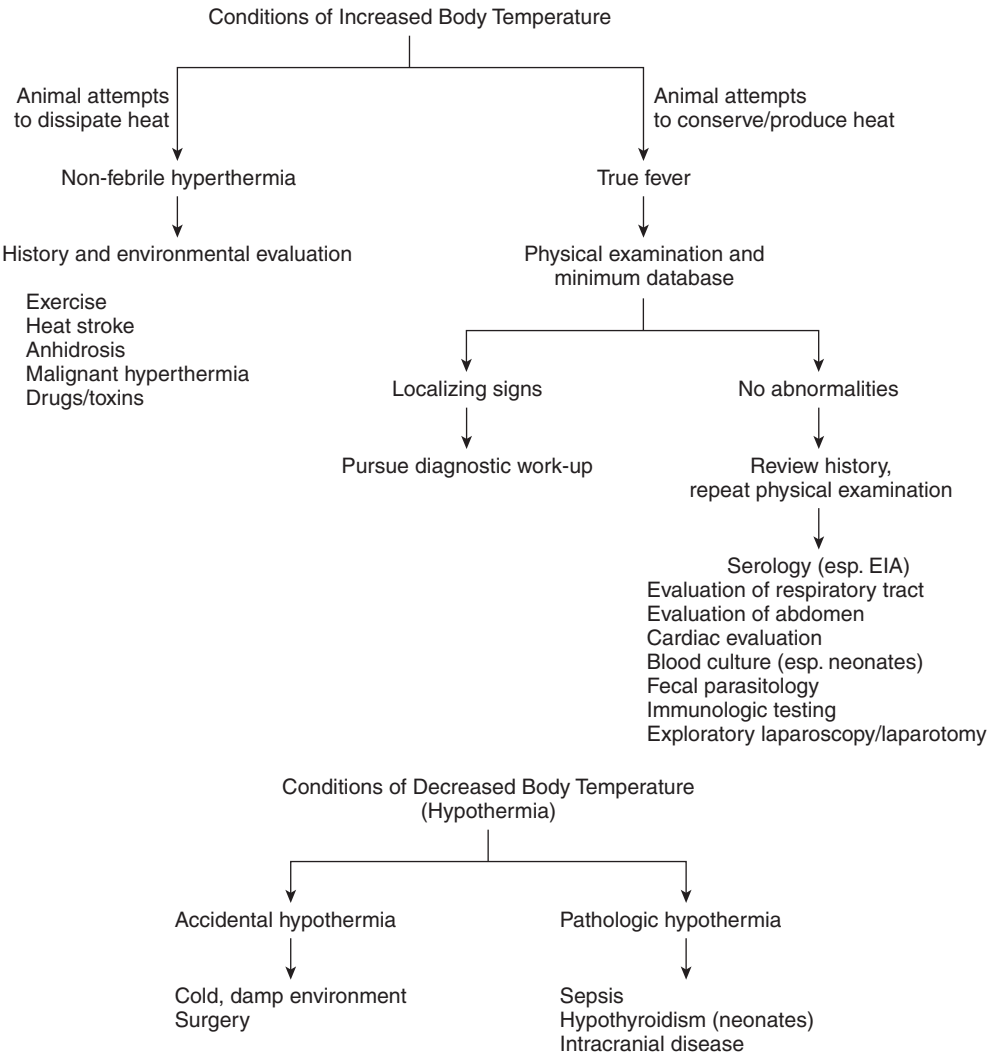

Figure 3.9-2 Approach to changes in body temperature.

A complete history is important when one is investigating fever of unknown origin. Any exposure to *Streptococcus equi* ssp. *equi* (strangles) may be significant because of the association of this organism with internal abscessation. Travel history may be relevant, especially regarding diseases with a geographic influence such as babesiosis and coccidioidomycosis.

The clinician always should perform a careful physical examination, including rectal palpation. Repeating the physical examination may yield new information. The clinician also should perform a complete neurologic examination, because disorders of the central nervous system may cause aberrations in temperature through pyrogenic cytokines or in some cases through direct effects on thermoregulatory centers.

Ancillary diagnostic tests usually are required to diagnose fever of unknown origin. A minimum database, including complete blood count, fibrinogen, biochemical profile with bile acids, and urinalysis should be performed. Hemoparasites occasionally may be seen on the blood smear, but the apparent absence of organisms does not rule out a parasitemia that is below readily detectable limits. Abnormalities consistent with chronic infection or inflammation, including anemia, hyperfibrinogenemia, and hyperglobulinemia are common but nonspecific findings. If an elevation of serum protein occurs, further assessment by serum protein electrophoresis and specific immunoglobulin quantitation may be indicated. A monoclonal gammopathy is characteristic of plasma cell myeloma and other tumors of the reticuloendothelial system, both of which may initiate fever directly and increase susceptibility to bacterial infection. In general, immunodeficiencies may be associated with chronic infections. If the serum protein is low, one should investigate the causes of hypoproteinemia, including decreased production because of significant hepatic disease, increased

gastrointestinal or renal loss, or loss into a third space. The presence of hypercalcemia can be helpful in establishing a diagnosis, because in horses, hypercalcemia most often is linked with renal disease or neoplasms.

Infections of the respiratory tract and abdomen frequently are associated with fever of unknown origin in the horse, and therefore one should evalute these systems thoroughly. Careful auscultation of the thorax using a rebreathing bag should be performed at rest and, if possible, after exercise. Endoscopy, including examination of the guttural pouches can be useful. Diagnostic imaging of the thorax, including radiographs and ultrasound, often is indicated. The clinician also should include thoracocentesis in evaluation of the thorax, for abnormalities occasionally are apparent even without increases in the volume of pleural fluid. Pleuroscopy, which allows direct visual examination of the pleural space and which may facilitate biopsy of any masses, can be helpful in establishing a diagnosis, especially when neoplasia is suspected.

Peritonitis and abdominal abscessation are common causes of fever of unknown origin, and one should include abdominocentesis in the diagnostic plan. The peritoneal fluid should be evaluated for protein, cellularity, and cell morphology, and culture should be performed. One should remember that although many neoplastic conditions involve the abdomen, neoplastic cells are not always observed in the peritoneal fluid. In cases of gastric squamous cell carcinoma, gastroscopy is helpful in establishing the diagnosis. Radiographs of the abdomen may be useful, especially in neonates, and ultrasound of the abdomen may help to identify fluid for collection or abnormalities that indicate further evaluation, such as abdominal masses or pathologic liver conditions.

Gastrointestinal parasitism is a common clinical problem in the horse, although it is associated only occasionally with fever. However, one should examine feces for parasite ova in horses with fever of unknown origin. In cases of suspected gastrointestinal protein loss, diarrhea, or melena, one should consider diagnostic procedures such as fecal culture, polymerase chain reaction for *Salmonella,* rectal mucosal biopsy, or absorption tests.

Bacterial endocarditis can cause a fever of unknown origin, although the condition is not as common in horses as in some other species. In the study by Mair, Taylor, and Pinsent, the authors identified endocarditis in 3 of 63 cases of fever of unknown origin.[30] In each case a murmur they did not identify initially became apparent several weeks after the onset of illness. Therefore a thorough cardiac evaluation, including echocardiography, is indicated.

Blood cultures are generally most useful in neonates but can yield valuable information in adult horses with fever as well. Ideally, one should collect three to five samples at least 45 minutes apart when the horse is not in a regimen of antibiotic therapy. Sampling just before and during a temperature rise is most likely to yield a positive culture.

The clinician should consider equine infectious anemia as a differential diagnosis for horses with fever of unknown origin and should perform a serologic examination. Recently, a serologic test for detection of antibodies to the M protein of *Streptococcus equi* ssp *equi* was developed as an aid in the diagnosis of internal abscessation.[31] Serologic tests for equine babesiosis, brucellosis, and coccidioidomycosis are also available.

Immune-mediated disorders such as autoimmune hemolytic anemia, immune-mediated thrombocytopenia, systemic lupus erythematosis, vasculitides, and rheumatoid arthritis have been implicated as causes of fever of unknown origin, but more commonly in human beings and small animals than in horses. However, appropriate diagnostic tests, such as the Coombs' test, skin biopsy, and antinuclear antibody testing may be useful in some cases.

Exploratory laparoscopy or laparotomy is indicated when abdominal involvement is evident or the animal is becoming progressively debilitated. Occasionally, bone marrow aspiration may be useful, particularly in those cases with persistent abnormalities in circulating cell populations. In cases in which a specific diagnosis has not been made, therapeutic trials with antimicrobials may help, and in cases of suspected immune-mediated disease, corticosteroids may help.

Hypothermia

Hypothermia occurs when the core body temperature drops below accepted normal values. In clinical cases, hypothermia can be characterized as accidental or pathologic (see Figure 3.9-2). In accidental hypothermia a spontaneous decrease in the core body temperature occurs independent of actual disruption to the thermoregulatory system. These cases often can be identified from the history. Mild accidental hypothermia sometimes occurs with surgical procedures. Most often, accidental hypothermia is associated with exposure to cold or cold, damp environments, which can lead to severe hypothermia and death. Neonates are particularly susceptible to hypothermia, although central thermoregulation through the hypothalamus is normal.[32,33] Sick foals often decrease their activity and nutritional intake and have alterations in circulation. They also have a large ratio of surface area to body weight, enhancing heat loss. Geriatric and otherwise debilitated animals are also at increased risk of hypothermia.

One should consider pathologic causes of hypothermia when no clear reason for accidental hypothermia is evident. Pathologic hypothermia occurs in association with disorders that decrease metabolic activity or directly affect the thermoregulatory center and occurs with

endocrine disorders, sepsis, and intracranial disease. In horses, hypothyroidism is probably an uncommon clinical problem; however, impaired thermoregulation has been seen in foals with congenital hypothyroidism.[34] Lesions of the thyroid gland also have been associated with hypothermia in donkeys.[35] Hypothermia has been observed with septicemia and shock, especially in neonates, in which 24% of septic foals were found to have a decreased body temperature.[36]

The ability to generate heat through shivering is impaired or lost when the body temperature becomes too low. The animal experiences a decrease in the metabolic rate of most tissues. Heart rate, cardiac output, glomerular filtration, and blood pressure may decrease.

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3.10—Diarrhea

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Diarrhea, defined as an increase in the frequency, fluidity, or volume of bowel movements, is a commonly encountered clinical problem in the horse. Diarrhea may occur as a primary disease of the gastrointestinal tract or as a secondary response to another disease process, such as sepsis, endotoxemia, or hepatic disease.

The function of the equine gastrointestinal tract is complex and involves maintenance of normal fluid balance and digestion and absorption.[1-3] As a result of dietary intake and endogenous secretions, normally a large volume of fluid enters the gastrointestinal tract, most of which is reabsorbed. In the adult horse absorption occurs predominantly in the large bowel, where a volume of water approximately equal to the total extracellular fluid volume of the animal, or about 100 L, is recovered during the course of the day. Because the large colon is the primary site of water resorption, most significant diarrheal disease in the adult horse involves the colon. In young foals, however, small intestinal disorders such as rotaviral infection also may result in diarrhea.[4]

A second critical function of the large bowel is that of microbial digestion of carbohydrates and, to some extent, protein or nonprotein nitrogen.[1-3] Microbial fermentation of carbohydrates in the cecum and colon results primarily in the production of volatile fatty acids, which are absorbed readily, providing up to 75% of the energy requirement of the horse. Therefore maintaining a stable environment for the microbial population is important. In general, efficient function of the large bowel requires mechanisms that limit the rate of digesta passage, provide optimal conditions for microbial digestion, and allow for efficient transport of solutes and water.

The characteristics of normal equine feces vary somewhat with diet. Generally, equine feces are tan, brown, or greenish, and although approximately 75% water, they are well formed. An adult horse on a diet of grass hay and approximately 3 lb of oats per day produces about 20 to 28 g of feces per kilogram of body mass per day or about 11 to 13 kg of feces per day.[5] In cases of diarrhea, the amount of feces may increase up to tenfold, with horses producing more than 200 g/kg/day, or more than 90 L of diarrhea. As a result, diarrhea can cause significant losses of electrolytes and water and significant systemic acid-base imbalances. However, despite large water losses, horses with chronic diarrhea seldom develop severe dehydration or electrolyte abnormalities because they compensate for increased fecal losses.

Mechanisms of Diarrhea

Inflammation within the bowel plays a central role in the pathogenesis of diarrhea. Several basic mechanisms of diarrhea have been described, and in most diarrheal diseases, more than one mechanism is involved. These mechanisms include the following:

1. *Malabsorption:* Malabsorption results from a decrease in the functional absorptive surface area of the gastrointestinal tract. Villus atrophy in the small intestine, seen with rotaviral enteritis and infiltrative bowel disease, can result in malabsorption because of the loss of functional epithelium and maldigestion caused by decreased production of digestive enzymes. A number of insults to the colon result in inflammation and disruption of absorptive cells and tight junctions, leading to decreased absorptive capacity and decreased ability to retain absorbed fluid, that is, increased loss. Several inflammatory mediators, such as histamines and prostaglandins, contribute to the colonic inflammation. These mediators are produced primarily by inflammatory cells in the lamina propria and inhibit absorption through a variety of mechanisms.[6-10]
2. *Increased secretion:* The increased secretion of solutes and water by the inflamed colon can contribute significantly to the development of diarrhea. Although the precise mechanisms of secretion in the equine colon are not understood fully, active secretion and passive fluid loss occur.[6-12] Control of active secretion is complex, involving two primary pathways: first, the activation of adenyl cyclase, resulting in an increase of intracellular cyclic adenosine monophosphate concentrations, and second, the activation of calcium channels, leading to increased intracellular calcium concentrations.[11,12] Cyclic adenosine monophosphate and calcium stimulate specific secretory activities, primarily through chloride channels. In some cases of diarrhea, bacterial enterotoxins such as those produced by certain strains of *Escherichia coli* and *Salmonella* stimulate adenyl cyclase activity, thus increasing active secretion. This is true hypersecretory diarrhea. Also, a number of inflammatory mediators produced by the inflamed colon, particularly prostaglandin E, increase intracellular concentrations of cyclic adenosine monophosphate and to some extent calcium, thereby increasing active secretion by mucosal cells.[11-13] Inflammation also enhances passive fluid loss through a number of factors, such as changes in hydrostatic pressure in the colonic capillaries, mucosal damage, and loss of tight junctions. In cases of severe mucosal injury, the loss of protein can decrease vascular oncotic pressure and further potentiate fluid exchange across the endothelium.

3. *Decreased transit time (abnormal motility):* Progressive motility must be present for diarrhea to occur. Primary motility disorders causing diarrhea are not well recognized, although diarrhea associated with stress or excitement may represent this phenomenon. Inflammation is known to influence gastrointestinal motility, in addition to altering absorption and secretion. However, the precise significance of the altered motility in the pathogenesis of diarrhea is not clear. Sufficient retention time and thorough mixing are required for digestion and absorption of nutrients and fluid to occur, and decreased intestinal transit time has been recognized in association with many gastrointestinal diseases, including infectious diarrhea. Absorption of endotoxin and the release of inflammatory mediators, including prostaglandins, disrupts normal motility patterns.[14] In some cases of acute colitis, a period of ileus may occur without diarrhea. With diarrheal diseases, the elimination of gut contents is part of the normal host defense mechanism, and thus decreasing motility is not indicated in most cases.
4. *Osmotic overload:* Any increase in osmotically active particles within the intestinal lumen can result in diarrhea. The increase can be associated with the administration or ingestion of osmotically active substances such as magnesium sulfate. The increase also may be associated with overloading of the intestine with carbohydrates or occasionally lipids beyond the amount that can be digested and absorbed. Therefore sudden dietary changes that result in significant shifts in gut flora and changes in fermentation or gastrointestinal diseases that result in malabsorption or maldigestion also may result in an osmotic diarrhea. In foals the loss of villus epithelial cells in the small intestine associated with disorders such as rotavirus infection and clostridiosis may lead not only to malabsorption but also to maldigestion caused by the decreased production of lactase.[4,15] The resulting lactose intolerance allows excess lactose to enter the large intestine, increasing the osmotic load.
5. *Increased hydraulic pressure from the blood to the lumen:* This mechanism of diarrhea is more common in chronic conditions, such as congestive heart failure or inflammatory bowel disease. The condition may result from decreased oncotic pressure associated with hypoproteinemia, increased capillary hydrostatic pressure (as in heart failure), or decreased lymphatic drainage associated with inflammation of lymphatics and lymph nodes.

Understanding the mechanisms of diarrhea can be helpful in directing therapy. However, one must remember that most disorders that cause diarrhea, whether infectious or noninfectious, do so through inflammatory mechanisms resulting in multiple functional alterations.

Diagnostic Approach to the Patient With Diarrhea

Diarrhea is a common, and sometimes fatal, clinical problem of adult horses and foals. A number of specific causes for acute and chronic diarrhea have been identified (Tables 3.10-1, 3.10-2, and 3.10-3). A comprehensive evaluation may help in establishing a diagnosis and

TABLE 3.10-1

Differential Diagnoses for Acute Diarrhea in Adult Horses

CAUSES	MAJOR DIAGNOSTIC TEST(S)
COMMON	
Salmonellosis	Fecal culture or polymerase chain reaction (PCR), culture of rectal mucosal biopsy
Potomac horse fever (equine monocytic ehrlichiosis)	PCR (feces, peripheral blood), paired serologic tests
Clostridiosis (*Clostridium difficile, C. perfringens*)	Fecal culture, toxin analysis
Antibiotic-associated diarrhea	History
Nonsteroidal antiinflammatory toxicity (primarily right dorsal colitis)	History and supportive clinicopathologic findings, ultrasonography, exploratory surgery with biopsy
Undiagnosed	Other conditions ruled out
LESS COMMON	
Cantharidin toxicity	
Parasitism (strongylosis, cyathostomiasis, other)	
Aeromonas, Campylobacter	
Sand	
Carbohydrate overload	
Arsenic toxicity, other toxicities	
Thromboembolic disease	
Anaphylaxis	

TABLE 3.10-2

Differential Diagnoses for Chronic Diarrhea in Adult Horses

CAUSE OF DIARRHEA	MAJOR DIAGNOSTIC TEST(S)
Chronic salmonellosis	Fecal culture or polymerase chain reaction, culture of rectal mucosal biopsy
Sand	Fecal sedimentation
Parasitism (strongylosis, cyathostomiasis)	Fecal egg count, empirical deworming
Nonsteroidal antiinflammatory toxicity (primarily right dorsal colitis)	History and supportive clinicopathologic findings, ultrasonography, exploratory surgery with biopsy
Inflammatory or infiltrative disorders	Histopathologic exam, absorption tests (supportive but nonspecific)
Inflammatory bowel disease (granulomatous, lymphocytic-plasmacytic, or eosinophilic enterocolitis)	
Mucosal lymphosarcoma	
Amyloidosis	
Dietary: abnormal fermentation	History
Neoplasms: lymphosarcoma, squamous cell carcinoma	Histopathologic exam
Peritonitis, abdominal abscessation	Peritoneal fluid analysis, ultrasound, exploratory surgery
Nongastrointestinal causes (chronic liver disease, congestive heart failure, renal disease)	Physical exam, clinicopathologic findings

developing a treatment plan (Box 3.10-1). However, even in severe cases a definitive diagnosis often is not made, making the problem particularly frustrating.[16,17]

HISTORY AND PHYSICAL EXAMINATION

One should consider the signalment and history carefully when evaluating a patient with diarrhea. Age is particularly important because several disorders, such as foal heat diarrhea and rotavirus, are age related. The genetic background also may be significant, because diarrhea has been associated with certain heritable immunodeficiencies, and granulomatous bowel disease has been identified in three sibling horses.[18-20] Establishing whether the diarrhea is acute or chronic is important. Other historical questions of particular relevance include dietary changes, deworming program, involvement of single versus multiple animals, exposure to sand, and the use of medications, especially antibiotics and nonsteroidal antiinflammatory drugs.[21-23] Other concurrent diseases, stress, possible exposure to toxins, weight loss, water consumption, and salt availability also may be significant. The information obtained helps to prioritize differential diagnoses and direct further testing.

The clinician should perform a complete physical examination. The body condition of the horse and the presence of any edema should be noted. The presence of fever, dehydration, or signs of endotoxemia may help in assessing the severity of the disease and differentiating the cause, because some causes of diarrhea are not associated typically with systemic signs of illness. Careful evaluation of the abdomen should be performed. Visible abdominal distention is often an indication of large intestinal distention, which may occur in association with acute colitis. However, distention also may be visible with

TABLE 3.10-3

Differential Diagnoses for Diarrhea in Foals

CAUSE OF DIARRHEA	MAJOR DIAGNOSTIC TEST(S)
Salmonellosis	Fecal culture or polymerase chain reaction (PCR)
Clostridiosis (*Clostridium difficile, C. perfringens*)	Fecal culture, toxin analysis
Endotoxemia, gram-negative septicemia	Blood culture, physical exam, complete blood count, sepsis score
Antibiotic-associated diarrhea	History
Foal heat diarrhea	History, physical exam
Viral: rotavirus; rarely coronavirus or adenovirus	Electron microscopy, enzyme immunoassay
Protozoan: cryptosporidiosis	Fecal analysis
Secondary lactose intolerance	Oral lactose tolerance test, response to therapy
Rhodococcus equi	Culture, PCR
Lawsonia intracellulare	Fecal PCR, serologic testing
Gastric ulcer disease syndrome	Gastric endoscopy
Strongyloides westeri	Fecal egg count
Sand	Fecal sedimentation

BOX 3.10-1

OUTLINE OF DIAGNOSTIC APPROACH TO DIARRHEA

I. Signalment, history, and physical examination
II. Clinical pathology
  1. Minimum database: complete blood count, fibrinogen, and serum chemistry profile
    a. Assess hydration, acid-base status, electrolyte abnormalities, and protein status.
    b. Assess renal and hepatic function.
    c. Assess endotoxemia.
  2. Serum protein electrophoresis and immunoglobulin quantitation
  3. Serologic testing: *Ehrlichia risticii* and *Lawsonia intracellulare*
  4. Peritoneal fluid analysis
III. Evaluation of feces
  1. Gross appearance: severity, hemorrhage, odor, and presence of sand
  2. Direct smear: evaluation of protozoan populations and presence of leukocytes and epithelial cells
  3. Parasite evaluation: including evaluation for *Cryptosporidium parvum,* especially in foals
  4. Evaluation of bacterial pathogens
    a. Gram stain and spore stain
    b. Aerobic and anaerobic culture (culture of multiple samples or rectal mucosal biopsy for *Salmonella*)
    c. Clostridial toxin analysis
    d. Polymerase chain reaction: *Salmonella, E. risticii, and L. intracellulare*
  5. Foals: evaluation of viral pathogens, primarily rotavirus (electron microscopy and enzyme immunoassay)
IV. Diagnostic imaging: radiography and ultrasonography
V. Endoscopic examination: stomach, rectum, and descending colon
VI. Absorption tests (glucose or xylose absorption): primarily for chronic protein-losing enteropathy
VII. Histopathologic examination
VIII. Toxin evaluation: cantharidin in urine or gastrointestinal contents, arsenic in liver, or other
IX. Response to therapy

extreme dilation of multiple loops of small intestine. Careful auscultation of the abdomen can be useful in assessing motility. Generally, progressive borborygmi heard about every 3 to 4 minutes on both sides of the abdomen suggests normal motility of the cecum and colon. Auscultation behind the xiphoid process may help to identify the presence of sand or gravel if one hears particles grinding together during contractions of the colon.[24] Particularly in foals, transabdominal palpation and ballottement may be useful to identify increased abdominal fluid or large masses near the body wall. Transrectal palpation can be helpful in assessing the size of intestinal segments, consistency of contents, and wall thickness as well as in identifying masses, enlarged lymph nodes, or mesenteric arteritis.

CLINICAL PATHOLOGY

Routine analysis of blood work rarely identifies a specific cause of diarrhea but can be important in directing appropriate supportive care and may help to establish whether diarrhea is caused by another condition, such as hepatic or renal disease. Some important parameters to evaluate include the presence of leukopenia, particularly neutropenia with a left shift and toxic changes in the white blood cells. These abnormalities suggest endotoxemia, which also may be associated with thrombocytopenia and coagulopathies. One also should evaluate the concentration of protein, as well as the albumin/globulin ratio. Significant hypoproteinemia, especially hypoalbuminemia caused primarily by protein loss, may occur with acute and chronic diarrhea. Hyperglobulinemia may indicate a chronic inflammatory condition. Disturbances in acid-base balance, especially metabolic acidosis, and electrolyte abnormalities frequently occur in cases of acute diarrhea but are uncommon in chronic diarrhea. Because of the dehydration frequently seen with acute diarrhea, prerenal azotemia is common and is important to recognize because some therapies, especially nonsteroidal anti-inflammatory medications, may worsen the condition. In a study of 122 horses with acute diarrhea, horses with azotemia and clinicopathologic findings consistent with hemoconcentration and hypoproteinemia were less likely to survive.[17]

The diagnostic and prognostic value of serum protein electrophoresis has been evaluated in horses with chronic diarrhea.[25] Significantly higher levels of β_1-globulin were found in horses with larval cyathostomiais than in other horses, and such values in conjunction with a decreased albumin were helpful in diagnosing intestinal parasitism. However, a normal β_1-globulin concentration was not a reliable indicator of the absence of the disease. Significantly lower albumin concentrations and significantly higher α_2-globulin concentrations were found in horses that did not survive, suggesting that these parameters are nonspecific indicators of the severity of inflammatory changes within the intestinal wall. Parasitic infections, particularly strongylosis, also may be associated with elevated serum concentrations of immunoglobulin G(T).[26]

Infrequently, immunodeficiencies are associated with diarrhea.[18,19] Therefore in some cases, further evaluation of immune status may be indicated and may include specific immunoglobulin quantitation, evaluation of

specific lymphocyte subsets, or functional assays. One should consider genetic testing for severe combined immunodeficiency in sick foals of Arabian breeding.

Analysis of peritoneal fluid may be useful in some cases of diarrhea. Abnormalities in the peritoneal fluid may reflect the severity of inflammation and in some cases may help to establish a specific diagnosis. Increases in protein and sometimes nucleated cell count may be seen in association with ulcerative colitis.[23] In cases of bacterial peritonitis, one may find organisms on cytologic examination or culture. Occasionally, one may identify neoplastic cells in the peritoneal fluid, although their absence does not rule out the presence of neoplasia.

EVALUATION OF FECES

Evaluation of the feces may yield important information in cases of diarrhea. Even the gross appearance of the feces can be helpful. For example, profuse, watery diarrhea is not generally consistent with a diagnosis of right dorsal colitis. Frank blood in the feces suggests bleeding into the distal colon from mucosal damage. Hemorrhagic, foul-smelling feces often are seen in association with clostridial diarrhea. One also can assess the feces for the presence of occult blood, which indicates bleeding from any source. Although excess sand in the feces is readily apparent in some cases, other cases require mixing the feces in a rectal sleeve with water and allowing the sand to settle.

Microscopic examination of the feces for evidence of parasitism and evaluation of viable protozoal populations also may be useful. A direct smear of fresh feces allows for observation of the motility of ciliates and can be used as a screen for the presence of ova and oocysts, although more sensitive techniques, including fecal flotation and sedimentation, are recommended for evaluation of parasitism. Ideally, a quantitative method that allows for estimation of the number of eggs per gram of feces, such as McMaster's or Stolley's, is recommended. However, one must remember that fecal examination for parasites sometimes can be misleading, giving false-negative results. *Cryptosporidium parvum* infection can be difficult to diagnose, but oocysts can be detected in the feces by acid-fast staining or by immunofluorescence assay.[27]

Fecal samples also can be examined microscopically for leukocytes and epithelial cells. In general the cellularity increases with the severity of diarrhea. Fecal leukocytes and epithelial cells are increased in salmonellosis, but are not specific for this disorder.[28] More than 10 leukocytes per high-power field may indicate salmonellosis.

Evaluation of the feces for infectious agents is essential in the diagnostic evaluation of horses with diarrhea. *Salmonella* and *Clostridium* species are among the most common causes of bacterial diarrhea in horses. Other less common bacterial agents include *Campylobacter* spp., *Aeromonas* spp., and particularly in weanling age foals, *Lawsonia intracellulare*.[29,30] Although primarily a respiratory pathogen, *Rhodococcus equi* also can cause diarrhea, particularly in foals 2 to 4 months of age.[31] *Escherichia coli* is an uncommon cause of diarrhea in foals, unlike in calves and piglets. However, enterotoxigenic strains, characterized by the presence of virulence factors, have been identified in foals. Gram stain and spore stain of fecal smears can help to identify and quantitate the bacterial populations present, particularly clostridial species. However, although large numbers of gram-positive rods or spores have been identified in foals with clostridial enterocolitis, the results of direct staining may be misleading.[32,33] In one study, *Clostridium perfringens* was cultured from 59% of samples in which no gram-positive rods were visible. Some clostridial strains also are likely part of the normal microflora.[34] Large numbers of yeast in the feces should alert the clinician to the possibility of candidiasis, especially in compromised neonatal foals.

Fecal culture is used commonly to establish a diagnosis in cases of bacterial diarrhea. When culturing feces, especially if an outside laboratory is used, one must consider proper sample handling, particularly for anaerobic clostridia.[35] *Salmonella* spp. are one of the most significant bacterial pathogens in equine feces.[36] Although the number of *Salmonella* spp. organisms isolated from the feces of horses with clinical salmonellosis is generally greater than from horses with asymptomatic infections, the volume of feces in horses with profuse diarrhea may decrease recovery. Culture of multiple fecal samples, typically five, is recommended to increase the sensitivity. Culture of a rectal mucosal biopsy or rectal scraping is an alternative to fecal cultures and may increase sensitivity, because *Salmonella* spp. are intracellular organisms. Identifying clostridial species requires anaerobic culture. However, evaluating the presence of toxin in cases of suspected clostridial diarrhea also is critical, because *Clostridium* spp., particularly *C. perfringens* type A, may be present in normal equine feces.[34] Depending on the clostridial species and the laboratory, toxin can be assessed by detecting preformed toxin in the feces, toxin being produced by the isolate in culture, or the toxin gene in the isolate.[32-35]

An increasing number of polymerase chain reaction (PCR) assays are available for detecting causative agents of equine diarrhea. In comparing a PCR with microbial culture for detection of salmonellae in equine feces and environmental samples, the PCR method was found to be more sensitive and more rapid and required submission of fewer samples.[37,38] Currently, PCR is also available for detection of *Ehrlichia risticii,* the causative agent of Potomac horse fever, in feces and peripheral blood.[39,40] Fecal PCR analysis also has been shown to be useful in documenting equine proliferative enteropathy caused by

Lawsonia intracellulare.[30] Serologic methods, evaluating the presence of antibodies, are additional diagnostic tests used for diagnosis of *Ehrlichia* and *Lawsonia*.[30,40]

Rotaviral infection is associated with diarrhea in foals and is most common in foals from 1 to 4 weeks of age.[4,41] One generally makes a diagnosis by detecting the virus by electron microscopy or the viral antigen by enzyme immunoassay (Rotazyme, Abbot Laboratories, North Chicago, Illinois), which is generally more sensitive than direct electron microscopy.[42] Coronavirus appears to have a low prevalence in foals but has been isolated from a horse with diarrhea.[43]

Less commonly used tests include evaluation of fecal osmolality and electrolyte concentrations (sodium and potassium). If the concentration of sodium plus potassium is much less than the osmolality, the result indicates the presence of osmotically active nonelectrolytes, confirming an osmotic diarrhea.

DIAGNOSTIC IMAGING

Diagnostic imaging, although particularly useful in foals, also can be valuable in adult horses. In foals, radiographs can detect gas distention in the lumen of the gastrointestinal tract, and the gas pattern may help to differentiate ileus from mechanical obstruction. Occasionally, gas may be seen within the bowel wall in severe cases of clostridial necrotizing enterocolitis. In adult horses, abdominal radiography is limited somewhat by having the proper facilities and equipment to perform the procedure safely. However, radiographs can be effective in identifying radiodense material, such as enteroliths and sand. Ultrasonography can be used in horses of all ages to evaluate the amount and character of the peritoneal fluid, masses, intestinal distention, and wall thickness. In cases of right dorsal colitis, the diagnosis has been supported by ultrasonographic evidence of thickening of the right dorsal colon. Altough isotope-labeled white blood cell scintigraphic scans also may help identify colonic ulcerations, the availability and sensitivity of the procedure are limited.

OTHER DIAGNOSTICS

Endoscopic examination of the stomach and proximal duodenum may reveal the presence of neoplasms or ulceration. Diarrhea and inappetance are common clinical signs in symptomatic foals with ulceration of the squamous gastric mucosa. Endoscopy also can be used for inspection of the mucosa of the rectum and descending colon, allowing for evaluation of mural masses or mucosal inflammation.

Absorption tests are used primarily in cases of chronic diarrhea or weight loss to evaluate the small intestinal absorptive capacity. Oral glucose and oral xylose absorption tests have been used.[44,45] Although the plasma concentration of glucose may reflect glucose metabolism as well as absorption from the gastrointestinal tract, the assay has been shown to be reliable in the diagnosis of significant malabsorptive conditions. Xylose is influenced less by the metabolic status of the horse, but the compound is more expensive than glucose, and the assay is not available in many laboratories. Results of both assays are nonspecific, but abnormal results support malabsorption and may indicate the necessity of biopsy.

Diagnosing neoplasms and chronic inflammatory or infiltrative disorders often requires histopathologic examination. A rectal mucosal biopsy is easy to collect and also can be cultured, but the area that can be reached for biopsy is limited. Laparoscopy allows for visualization of the abdomen and certain biopsies. One can obtain full thickness intestinal biopsy during exploratory celiotomy.

Diarrhea is a component of the clinical syndrome associated with several toxins. Cantharidin (blister beetle toxin) can be detected in urine or gastrointestinal contents.[46,47] One can measure lead in the blood and liver, selenium in the blood and liver, or arsenic in the liver if they are suspected.[47,48] One should consider oleander toxicity in horses with diarrhea, arrhythmias, and renal disease, especially if exposure is possible.[47] Oleandrin is detectable in urine and gastrointestinal contents.

EVALUATION OF RESPONSE TO THERAPY

Evaluating the response to empirical therapy may be helpful in some cases of chronic, undiagnosed diarrhea. Dietary changes may decrease diarrhea in some cases, and often a diet of grass hay alone is recommended. In cases in which right dorsal colitis is suspected but cannot be confirmed, using pelleted feed may be beneficial. Addition of psyllium mucilloid and corn oil to the diet also may be beneficial in right dorsal colitis. Psyllium mucilloid also has been used in cases in which sand was suspected as contributing to the diarrhea. Any medications that the horse has been receiving, especially nonsteroidal antiinflammatory drugs or antibiotics, should be discontinued in case they are contributing to the diarrhea.

Transfaunation can be used in an attempt to restore normal flora. Fresh colonic or cecal contents are considered the best source of organisms, but feces can be used. A number of commercial probiotics are available, but their efficacy has not yet been established.

A course of corticosteroids can be tried in cases of chronic diarrhea in which infectious causes have been ruled out. Treatment with a larvicidal anthelmintic may be beneficial in some cases, and sometimes is used with corticosteroids. Some horses with chronic diarrhea have responded to iodochlorhydroxyquin (10 g/450 kg/day for 2 weeks). This drug sometimes has been used concurrently with trimethoprim-sulfa. Occasionally, transfusion with plasma seems to suppress diarrhea in young horses.

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3.11—Clinical Assessment of Poor Performance

Melissa T. Hines

Any decrease in performance may be critical to the equine athlete. Numerous factors influence performance, including genetics, training, desire, and overall health. Peak athletic performance requires optimal function of all body systems, particularly those involved in locomotion and oxygen transport.

Approach to Poor Performance

Determining the cause of poor performance in those horses without overt clinical disease often is challenging.[1-4] In a study by Martin, Reef, Parente et al. of 348 cases of poor performance, a definitive diagnosis was established in 73.5% of cases after in-depth examination, which included the use of a high-speed treadmill.[3] Subtle abnormalities may be sufficient to impair performance, and in some cases, problems may be evident only during exercise, contributing to the difficulty of making a diagnosis. Additionally, multiple problems may occur concurrently. In a study by Morris and Seeherman of 275 racehorses with a history of poor racing performance, 84% were found to have more than one abnormality.[2] Therefore determining the actual clinical significance of any given problem may be difficult.

Equine athletes presented for poor performance should undergo a comprehensive evaluation, the basic components of which include a history, detailed physical examination, and laboratory screening. The clinician should emphasize examination of the respiratory, musculoskeletal, and cardiovascular systems, because these systems most often are linked to performance problems. In many cases, standardized exercise testing, generally on a high-speed treadmill, is critical in identifying the problem. Endoscopic examination of the upper airways during exercise has proved particularly useful.

History

Obtaining a complete history is a fundamental part of evaluating poor performance. The clinician should establish the use of the horse, the time in training, and the specifics of the training program. Determining whether the horse has never performed as expected or has experienced a decline in the level of performance is crucial. If the horse has never performed as expected, one should consider a lack of ability, congenital abnormalities, or training problems. A change in performance, either sudden or insidious, often is associated with an acquired problem. The clinician should characterize specifically the decline in performance, including the intensity of exercise at which signs are observed and whether performance is abnormal from the onset of exercise or declines during an exercise bout. In those cases in which performance drops off during exercise, the clinician should determine whether the decline is acute or gradual and whether any other signs such as stridor are associated with it.

Other elements of the history with particular relevance to athletic performance include any previous respiratory disease, respiratory noise, or respiratory distress associated with exercise. Any change in gait also may be significant. Establishing the feeding practices, changes in appetite or body condition, the type of tack used, and whether sweating is appropriate is important. The clinician should determine the response to any medications that have been used, such as phenylbutazone or furosemide. The information obtained in the history may help direct the investigation.

General Physical Examination and Laboratory Screening

The clinician should perform a complete physical examination in all cases. Hematologic testing and a biochemical profile are indicated, although in most horses presented for poor performance without obvious clinical abnormalities, routine evaluation of a single sample is within normal limits. Because exercise can induce some changes in laboratory parameters, such as an increase in the packed cell volume and neutrophil count, considering the time of sample collection relative

to exercise is important.[5-7] Potentially significant findings include changes consistent with chronic inflammation, such as anemia, hyperglobulinemia, and possibly hyperfibrinogenemia. Subclinical infections may have only slight alterations in the leukocyte count and differential. Viral infections, especially in the early stages, may be associated with a leukopenia and neutropenia. A decrease in the neutrophil-to-lymphocyte ratio has been associated with overtraining, although this is not a reliable correlation.[7]

Horses at rest normally maintain a significant proportion of red blood cells and hemoglobin in the splenic reserve.[5,6,8] Thus although total body hemoglobin increases in response to training and may correlate with performance, such cannot be determined from a resting sample. Special techniques must be used to document total red cell mass or hemoglobin.[8,9] Anemia can decrease the oxygen-carrying capacity during exercise, resulting in suboptimal performance.

Signs of organ dysfunction in horses presented for poor performance are not common findings. Muscle enzymes may be elevated, although many cases of myopathy are subclinical and require evaluation of muscle enzymes after exercise.[10] Much attention has been paid to the importance of electrolytes and exercise; however, abnormalities seldom are found. In general, circulating electrolyte concentrations are regulated tightly and may not reflect closely the total body electrolyte status.[11] However, a concentration of potassium consistently below 3 mEq/L may suggest a potassium deficit. Chronic electrolyte deficiencies may be detected by performing renal fractional excretion of electrolytes.

Evaluation of the Respiratory System

The clinician should give careful attention to examining the respiratory tract, because abnormalities of this system frequently influence performance. The examination should include evaluation of air flow from the nares and percussion of the sinuses, as well as assessment of any cough or nasal discharge. Careful palpation of the larynx may reveal an increase in prominence of the muscular process of the left arytenoid cartilage resulting from a loss of mass of the left dorsal cricoarytenoid muscle associated with idiopathic hemiplegia. The clinician can use the laryngeal adductor response test, or slap test, to evaluate adduction of the arytenoid cartilages by slapping the withers during expiration and evaluating movement of the contralateral arytenoid by endoscopy or palpation. The clinician should perform a thorough auscultation of the trachea and lungs. Having the horse rebreathe from a plastic bag placed over the nostrils increases the respiratory rate and tidal volume, accentuating sounds. In addition to auscultation, one should note the character and pattern of respiration, including the presence of any abdominal component, and the recovery time. Percussion of the thorax may be useful in establishing the lung border and any dull or hyperresonant areas, as well as in detecting pleural pain.

Dynamic obstruction of the airway is among the most common causes of poor performance in the equine athlete.[2,3,12-14] In the study by Morris and Seeherman of 275 racehorses evaluated for poor performance, 40% were found to have dynamic obstruction.[2] Similarly, in the study by Martin, Reef, Parente et al. of 348 racehorses and show horses with poor performance, 148 (42.6%) had dynamic obstruction of the airways.[3] Of these 148 affected horses, 39 were found to have multiple airway abnormalities. An additional 22 horses had dynamic airway obstruction concurrently with a cardiac arrhythmia. In both studies of poor performance the most common conditions causing airway obstruction were dorsal displacement of the soft palate and idiopathic left laryngeal hemiplegia with arytenoid collapse. Other conditions diagnosed included dynamic pharyngeal collapse, epiglottic entrapment, subepiglottic cyst, rostral displacement of the palatopharyngeal arch, and redundant alar folds. An important note is that many of the horses with airway obstruction did not have a history of abnormal respiratory noise and did not have abnormalities at rest. Also, not all abnormalities observed at rest caused obstruction. Therefore these studies emphasize the importance of treadmill videoendoscopy as a component of the evaluation of poor performance. In most cases, the clinician should perform a treadmill videoendoscopy regardless of the history and physical examination findings.

Endoscopy also can be useful in identifying respiratory problems other than dynamic airway collapse. For example, one can identify narrowing of the ventral nasal meatus associated with sinusitis, nasal masses, and pharyngitis. If the endoscope is sufficiently long, tracheal injury and secretions in the lower respiratory tract can be visualized. Sampling of airway secretions by bronchoalveolar lavage may aid in the diagnosis of low-grade respiratory infections, small airway inflammatory disease, or exercise-induced pulmonary hemorrhage. In some cases, evidence of inflammation and retropharyngeal lymphadenopathy on endoscopic examination of the guttural pouches has been associated with dorsal displacement of the soft palate, which may result from neuropathy of the pharyngeal branch of the vagus nerve.[15]

Radiographs and ultrasound may be indicated on evaluation of the respiratory system of horses with poor performance, especially in those horses with evidence of lower respiratory tract disease. Radiographs also can be useful in assessing upper respiratory disorders, allowing for the evaluation of soft tissue masses or fluid accumulations. In addition, sometimes one can identify abnormalities of

the pharyngeal and laryngeal structures such as thickening of the soft palate or hypoplasia of the epiglottis.

Evaluation of the Cardiovascular System

Any decrease in cardiac output potentially can limit performance, making thorough evaluation of the cardiovascular system essential. On basic physical examination, the clinician should evalutate the mucous membrane color, capillary refill time, and arterial and venous peripheral pulses, although finding abnormalities in these parameters in horses presented for decreased performance is uncommon. One should perform careful auscultation of the heart on both sides of the thorax to evaluate the cardiac rhythm and murmurs. Many horses have murmurs that are of little clinical significance.[2,16] In the study by Martin, Reef, Parente et al., 102 of the 348 horses were found to have murmurs, the most common being mitral regurgitation.[3] In all cases the murmur was determined to be clinically unimportant.

The clinician can use electrocardiography to evaluate the cardiac rhythm further, and ideally should perform the procedure before, during, and after exercise using radiotelemetry. Cardiac arrhythmias were the only abnormality found in 33 of the 348 horses evaluated by Martin, Reef, Parente et al. and were found in conjunction with dynamic airway obstruction in 22 horses.[3] However, in the study by Morris and Seeherman, arrhythmias were noted in just 2 of 275 horses.[2] The most frequent arrhythmias observed include atrial and ventricular premature depolarizations. Ventricular tachycardia and paroxysmal atrial fibrillation also have been noted. Changes in the T wave, once thought to be related to poor performance, and second-degree atrioventricular block have been found to have no effect on exercise capacity.[17]

Echocardiography before and after exercise helps to evaluate cardiac function. Martin, Reef, Parente et al. found decreased fractional shortening indicating left ventricular dysfunction after exercise in 19 horses, only 8 of which had echocardiographic changes at rest.[3] Six of the 19 horses had clinically significant arrhythmias. Myocardial disease may contribute to left ventricular dysfunction and arrhythmias. Elevations in myocardial fractions of creatine kinase, lactate dehydrogenase, and troponin support myocardial disease but are not present in all cases.

Evaluation of the Musculoskeletal System

A surprising number of horses presented for poor performance are found to be lame, even when lameness is not part of the presenting complaint.[1,2,4] Therefore the clinician should perform a complete lameness examination in all cases. In some horses presented for poor performance, the gait asymmetry may be subtle and only discernable at high speed, making diagnosis by traditional methods difficult. In these cases, gait analysis on the treadmill and advanced diagnostic techniques such as nuclear scintigraphy, thermography, and computed tomography or magnetic resonance imaging may be useful. One also should perform a neurologic examination to identify any deficits that could contribute to poor performance.

Myopathy can lead to decreased performance. In many cases the condition is subclinical and requires an exercise challenge test to make the diagnosis.[3,10] One should measure creatine kinase before exercise and ideally 4 to 6 hours after an exercise bout consisting of 15 to 30 minutes at the trot. In normal horses, this light exercise rarely causes more than a threefold increase in creatine kinase. An increase of fivefold or more indicates exertional rhabdomyolysis. A muscle biopsy can help to define the myopathy. In the study by Martin, Reef, Parente et al., 10 of 348 horses developed clinical exertional rhabdomyolysis after exercise, and an additional 53 demonstrated subclinical myopathy as demonstrated by increased creatine kinase levels after exercise.[3]

Exercise Testing

Exercise testing provides a mechanism for evaluating a range of body systems under standard exercise conditions. In particular, measurements of cardiorespiratory and metabolic function taken during an exercise test provide information about the capacity and efficiency of key body systems involved in energy production. From a clinical standpoint, exercise testing is generally most useful in assessing the effect on performance of abnormalities found on a physical examination. Testing also may help to establish the reason for reduced athletic capacity in horses that have no abnormalities on basic examinations. Exercise testing can be done in the field, which mimics the condition in which the horse actually performs. However, most testing is currently done on a treadmill, which provides more standard conditions and an opportunity to perform a greater range of measurements. The specific protocol used for exercise testing may vary somewhat.[1,18,19] Occasionally a high-speed test is performed in which the horse is accelerated rapidly to maximum speed and run to fatigue. However, the most common type of test is an incremental test in which the speed increases every 1 to 2 minutes until the horse reaches fatigue, allowing for the generation of data during submaximal and maximal exercise. In most cases the test is performed with the treadmill at a slope of 10%. This slope is not so steep as to be completely unrepresentative of normal exercise,

and yet it ensures that maximum intensity exercise can be performed without reaching speeds that may be too fast for horse safety. Some parameters that can be assessed in an exercise test include heart rate, blood lactate level, arterial blood gases, total red cell volume, stride length, and oxygen uptake. As previously discussed, treadmill videoendoscopy is often valuable.

HEART RATE DURING EXERCISE

Evaluation of the heart rate during exercise provides an indirect index of cardiovascular capacity and function. Several heart rate monitors are available.[20] Radiotelemetry also can be used to evaluate the heart rate and rhythm, particularly at the end of exercise. Because the stroke volume does not change greatly with increasing exercise speed, the heart rate provides a guide to changes in cardiac output. In general, a linear increase in heart rate occurs with increasing exercise speed up to the point at which the maximal heart rate is reached.[21-23] The maximal heart rate (HRmax) is identified when no further increase in heart rate occurs despite an increase in exercise speed. The HRmax does not change with training state, although the speed at which it is reached increases with increasing fitness.

One reference point for comparison of cardiovascular capacity is the treadmill speed at a heart rate of 200 bpm (V_{200}). At a heart rate of 200 bpm, most horses are close to the point of onset of blood lactate accumulation. The V_{200} can be calculated by linear regression analysis or plotted using measurements taken at three to four submaximal exercise speeds, without the horse reaching maximal exercise. One should take care when using the V_{200} to assess exercise capacity, because at a heart rate of 200, horses may be exercising at different proportions of their HRmax and therefore their maximal oxygen uptake (VO_{2max}). In general, however, horses with the highest cardiovascular and metabolic capacities have the highest V_{200} values; that is, the better horses reach a heart rate of 200 at higher speeds than those with a lower exercise capacity. The V_{200} increases with training and can be useful for monitoring changes in fitness. The better quality Thoroughbreds have a V_{200} of 8 to 9 m/sec in an exercise test with the treadmill set at a 10% slope. Values less than 7 m/sec are abnormal and if found in a fit horse indicate decreased cardiac capacity.

Another measurement of cardiovascular capacity is the treadmill speed at which the horse reaches HRmax, known as V_{HRmax}. This value correlates with VO_{2max} and exercise capacity but requires the horse to exercise up to maximal speeds so that a plateau in heart rate can be identified.

Heart rate measurements are helpful in determining the actual significance of cardiac abnormalities such as murmurs and arrhythmias. In horses with functional cardiac disease the reduced stroke volume necessitates higher heart rates to maintain adequate cardiac output. Also, studies in Standardbred racehorses have suggested that horses with musculoskeletal problems have an increased V_{200} and that monitoring the V_{200} may help to identify subclinical lameness.

BLOOD OR PLASMA LACTATE MEASUREMENT

Exercising muscles produce lactate to some extent during all intensities of exercise, but production increases exponentially with the intensity of exercise.[23-25] As exercise becomes more intense, the aerobic energy contribution becomes insufficient to meet total energy requirements, and increased anaerobic metabolism results in increased lactate production. Lactate diffuses from muscle to blood, and therefore blood or plasma concentrations of lactate reflect muscle lactate. Some evidence suggests that whole blood concentrations most accurately measure lactate accumulation, because red blood cells actively take up lactate.[25-28]

The rate of increase of lactate in the blood may be used as an indirect indicator of cardiovascular and metabolic capacity. Horses with the highest aerobic capacities because of a high maximal cardiac output tend to have lower lactate values at submaximal exercise intensities than those with lower aerobic capacities. Lactate values can be used to compare horses or to evaluate training in the same horse. The treadmill speed at which a plasma lactate of 4 mmol/L (V_{LA4}) is reached is one measure of lactate production, and a high value reflects good aerobic capacity. The V_{LA4} has been used to monitor changes in fitness. In fit Thoroughbred horses 3 years of age and over, values for V_{LA4} range from 8.0 to 9.5 m/sec. Horses that are not fit or have respiratory disease have lower values. Another useful reference is the blood or plasma lactate at conclusion of the 10 m/sec exercise step of the incremental test, and highly fit, athletic horses usually have values less than 5 mmol/L. High-quality sprint horses, which perform largely under anaerobic conditions and have a high anaerobic capacity, may have high peak lactate values.

OXYGEN UPTAKE

The measurement of oxygen uptake (VO_2) is critical to assessing athletic performance.[21,22] The VO_{2max} has been used as a key indicator of exercise capacity in human athletes since the 1950s. As the VO_2 increases linearly with increasing treadmill speed, VO_{2max} can be identified when VO_2 reaches a plateau despite an increase in speed. The Thoroughbred horse has VO_{2max} values that are higher than those of many other mammalian species when expressed on a mass-specific basis. The major factor responsible for the high VO_{2max} in athletic horses is their

high oxygen-carrying capacity, which arises from a high maximum stroke volume and to some extent a large arteriovenous oxygen content difference. The VO_{2max} is a good index of changes in fitness and a measurement of exercise capacity in performance horses.

MAXIMUM OXYGEN PULSE

The oxygen pulse is defined as the VO_2/heart rate and is expressed as ml/kg/beat. This value provides an indication of the maximum stroke volume, and in high-quality horses, values range from 0.66 to 0.76 ml/kg/beat. Those horses with cardiac problems resulting in low cardiac outputs and individuals with low VO_{2max} values usually have values in the range of 0.5 to 0.56 ml/kg/beat. The maximum oxygen pulse also has been shown to correlate with treadmill total run time.

ARTERIAL BLOOD GAS ANALYSIS DURING EXERCISE

Arterial blood gas analysis during exercise may be indicated, especially in horses in which respiratory disorders are the suspected cause of poor performance. For an accurate blood gas analysis, one should take into account the temperature of the blood because it may reach 42° C during maximal exercise. At exercise intensities above 65% VO_{2max}, athletic horses become hypoxemic, although the extent varies between individuals.[29-32] Horses with low VO_{2max} values do not necessarily have a significant decrease in arterial oxygen tension.

HEMATOCRIT AND TOTAL RED CELL VOLUME DURING EXERCISE

The total volume of red cells is a major determinant of oxygen-carrying capacity, and therefore measurement of red cell volume can give some index of exercise capacity. A postexercise packed cell volume test is not a reliable indicator of total red cell volume primarily because of plasma volume variations, but it does provide a rough estimate of total circulating red cells.

One can make an accurate determination of red cell volume by techniques that use dye dilution following mobilization of the splenic erythrocyte pool to measure the plasma volume. Although total red cell volume increases with training, some evidence indicates that Standardbred racehorses with overtraining syndrome may develop an abnormal red cell hypervolemia that contributes to poor performance.[9]

PEAK RUNNING SPEED AND TOTAL RUN TIME

The peak treadmill running speed and the total run time may indicate exercise capacity. In some studies of human athletes, the peak treadmill running speed during an exercise test was shown to be a predictor of performance. Athletic Thoroughbred racehorses can complete 60 seconds at 13 m/sec during an incremental exercise test at a 10% slope.

STRIDE LENGTH

Athletic horses are thought to have better stride characteristics.[4,33] Some studies have shown a correlation between maximum stride length and the treadmill run time. An accelerometric device has been used to provide quantitative information about locomotory variables that may be useful in evaluating performance.[33]

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