Metabolic diseases may be inherited or acquired, the latter being more common and significant. Metabolic diseases are clinically important because they affect energy production or damage tissues critical for survival.

While the development of metabolic diseases is largely related to production or management factors, the pathogenesis of each disease is primarily related to alterations in metabolism. In most cases the basis of disease is not a congenital or inherited error in metabolism, but rather an increased demand for a specific nutrient that has become deficient under certain conditions. Diseases such as hypocalcemia, hypomagnesemia, and hypoglycemia are augmented by management practices that are directed toward improving and increasing production. They are therefore correctly considered production diseases. However, they are also metabolic diseases because management of the animal is directed at production, which at its peak, is beyond the capacity of that animal’s metabolic reserves to sustain a particular nutrient at physiologic concentrations. For example, parturient paresis of cows (occurs when the mass of calcium in the mammary secretion is greater than the cow’s diet or its skeletal reserves can supply. Comparable situations occur with magnesium and glucose metabolism, and with phosphorus in relation to postparturient hemoglobinuria.

Most production-induced metabolic diseases result from a negative balance of a particular nutrient. In some cases, dietary intake of the nutrient is rapidly reduced because of an ongoing, high metabolic requirement for that nutrient. Examples include pregnancy toxemia of ewes, protein-energy malnutrition in beef cattle, fat cow syndrome in dairy cattle, and hyperlipemia in ponies. Furthermore, some diseases may be precipitated when producers, primarily due
to economic concerns, are compelled to not supplement animals that already have a substandard nutritional plane.

Exertional rhabdomyolysis of horses is another production-induced metabolic disease. In this case, the production activity (draft or racing) is maintained by and matched to a level of caloric intake. Management decisions not to work or race these horses without a concomitant decrease in caloric intake may result in accumulation of muscle glycogen to dangerous levels. Disease results when work is resumed and the production of lactate exceeds its metabolism.

Metabolic diseases are generally acute states that dramatically respond to the systemic administration of the deficient nutrient or metabolite, although affected animals may require subsequent dietary supplementation to avoid recurrence. An important aspect of dealing with production-induced metabolic diseases is accurate and rapid diagnosis. Ideally, diagnostic tests can be used to predict the occurrence of disease before its clinical onset.

**HYPOCALCEMIA:**

**MILK FEVER:**

Parturient paresis is an acute to peracute, afebrile, flaccid paralysis of mature dairy cows that occurs most commonly at or soon after parturition. It is manifest by changes in mentation, generalized paresis, and circulatory collapse.

**Etiology:**

At or near the time of parturition, the onset of lactation results in the sudden loss of calcium into milk. Serum calcium levels decline from a normal of 10-12 mg/dL to 2-7 mg/dL. Commonly, serum magnesium is increased, serum phosphorus is decreased, and cows are hyperglycemic. The disease may be seen in cows of any age but is most common in high-producing dairy cows >5 yr old. Mechanisms of hypocalcemia include decreased absorption from the intestines; increased loss of calcium from the kidneys, milk or sweat; or inhibition of osteolysis due to alterations in parathyroid hormone, calcitonin, or vitamin D
Clinical Findings and Diagnosis:

Parturient paresis usually occurs within 72 hr of parturition. The disease can contribute to dystocia, uterine prolapse, retained fetal membranes, metritis, abomasal displacement, and mastitis.

There are 3 discernible stages of parturient paresis:

During stage 1, animals are ambulatory but show signs of hypersensitivity and excitability. Cows may be mildly ataxic, have fine tremors over the flanks and triceps, and display ear twitching and head bobbing. Cows may appear restless, shuffling their rear feet and bellowing. If calcium therapy is not instituted, cows will likely progress to the second, more severe stage.

Cows in stage 2 are unable to stand but can maintain sternal recumbency. Cows are obtunded, anorectic, and have a dry muzzle, subnormal body temperature, and cold extremities. Auscultation reveals tachycardia and decreased intensity of heart sounds. Peripheral pulses are weak. Smooth muscle paralysis leads to GI stasis, which can be manifest as bloat, failure to defecate, and loss of anal sphincter tone. An inability to urinate may be manifest as a distended bladder on rectal examination. Cows often tuck their heads into their flanks, or if the head is extended, an S-shaped curve to the neck may be noted.

In stage 3, cows lose consciousness progressively to the point of coma. They are unable to maintain sternal recumbency, have complete muscle flaccidity, are unresponsive to stimuli, and can suffer severe bloat. As cardiac output worsens, heart rate can approach 120 bpm, and peripheral pulses may be undetectable. If untreated, cows in stage 3 may survive only a few hours.

Differential diagnoses include toxic mastitis, toxic metritis, other systemic toxic conditions, traumatic injury (eg, stifle injury, coxofemoral luxation, fractured pelvis, spinal compression),
calving paralysis syndrome (damage to the L6 lumbar roots of sciatic and obturator nerves), or compartment syndrome. Some of these diseases, in addition to aspiration pneumonia, may also occur concurrently with parturient paresis or as complications.

**Treatment:**
Treatment is directed toward restoring normal serum calcium levels as soon as possible to avoid muscular and nervous damage and recumbency. Recommended treatment is IV injection of a calcium gluconate salt, although SC and IP routes are also used. A general rule for dosing is 1 g calcium/45 kg (100 lb) body wt. Most solutions are available in single-dose, 500 mL bottles that contain 8-11 g calcium. In large, heavily lactating cows, a second bottle given SC may be helpful because it is thought to provide a prolonged release of calcium into the circulation. SC calcium treatment alone may not be adequately absorbed due to poor peripheral perfusion and should not be the sole route of therapy. No matter what route is used, strict asepsis should be employed to lessen the chance of infection at the injection site.

Calcium is cardiotoxic; therefore, calcium-containing solutions should be administered slowly (10-20 min) while cardiac auscultation is performed. If severe dysrhythmias or bradycardia develop, administration should be stopped until the heart rhythm has returned to normal. Endotoxic animals are especially prone to dysrhythmias caused by IV calcium therapy.

Administration of oral calcium avoids the risks of cardiotoxic side effects and may be useful in mild cases of parturient paresis. Calcium propionate in propylene glycol gel or powdered calcium propionate (0.5 kg dissolved in 8-16 L water administered as a drench) is effective and avoids the potential for metabolic acidosis caused by calcium chloride. Oral administration of 50 g of soluble calcium results in ~4 g calcium being absorbed into the circulation.

Hypocalcemic cows typically respond to therapy immediately.
Tremors are seen as neuromuscular function returns. Improved cardiac output results in stronger heart sounds and decreased heart rate. Return of smooth muscle function results in eructation, defecation, and urination once the cow rises. Approximately 75% of cows stand within 2 hr of treatment. Animals not responding by 4-8 hr should be reevaluated and retreated if necessary. Of cows that respond initially, 25-30% relapse within 24-48 hr and require additional therapy. Incomplete milking has been advised to reduce the incidence of relapse. Historically, udder inflation has been used to reduce the secretion of milk and loss of calcium; however, the risk of introducing bacteria into the mammary gland is high.

**Prevention:**

Use of the dietary cation-anion difference (DCAD), which decreases the blood pH of cows during the late prepartum and early postpartum period. This method is more effective and more practical than lowering prepartum calcium in the diet. The DCAD approach provides an excess of anions over cations in the diet by adjusting the components of the diet, adding anionic salts to the ration, or both. Adding excess anions to the diet is believed to enhance calcium resorption from bone and absorption from the GI tract.

An important strategy for decreasing blood pH in periparturient cattle is reducing the potassium content of the diet. Including corn silage as a major portion of the dry cow’s diet is essential as it tends to have the lowest content potassium of available forages. Alfalfa is another forage source that may prove beneficial in maintaining proper blood pH.

Administration of vitamin D$_3$ and its metabolites is effective in preventing parturient paresis. Large doses of vitamin D (20-30 million U, s.i.d.), given in the feed for 5-7 days before parturition, reduces the incidence. However, if administration is stopped
Hypocalcemic tetany in horses is an uncommon condition associated with acute depletion of serum ionized calcium and sometimes with alterations in serum concentrations of magnesium and phosphate. In lactating mares, high milk production and grazing of lush pastures appear to be predisposing factors. Hypocalcemia after prolonged physical activity (e.g., endurance rides) results from sweat loss of calcium, increased calcium binding during hypochloremic alkalosis, and stress-induced high corticosteroid levels. Corticosteroids inhibit vitamin D activity, which leads to decreased intestinal absorption and skeletal mobilization of calcium.

more than 4 days before calving, the cow is more susceptible. Dosing for periods longer than those recommended should be avoided due to potential toxicity. A single injection (IV or SC) of 10 million IU of crystalline vitamin D given 8 days before calving is an effective preventive. The dose is repeated if the cow does not calve on the due date. Newer compounds used (where available and approved) in lieu of vitamin D and less likely to cause hypervitaminosis include 25-hydroxycholecalciferol, 1,25-dihydroxycholecalciferol, and 1α-hydroxycholecalciferol. After calving, a diet high in calcium is required. Administering large doses of calcium in gel form (PO) is commonly practiced. Doses of 150 g of calcium gel are given 1 day before, the day of, and 1 day after calving.

Use of synthetic bovine parathyroid hormone (PTH) may prove to be superior to administration of vitamin D metabolites. Vitamin D metabolites enhance GI calcium absorption, whereas PTH enhances GI calcium absorption and stimulates bone resorption. PTH is administered either IV 60 hr before parturition, or IM 6 days before parturition. Drawbacks to the use of PTH include increased labor requirements for administration, as well as the availability of such compounds.

HYPOCALCEMIA IN HORSES

Hypocalcemic tetany in horses is an uncommon condition associated with acute depletion of serum ionized calcium and sometimes with alterations in serum concentrations of magnesium and phosphate.
The severity of clinical signs corresponds with the serum concentration of ionized calcium. Increased excitability may be the only sign in mild cases. Severely affected horses may show synchronous diaphragmatic flutter, anxious appearance, and signs of tetany including increased muscle tone, stiffness of gait, muscle tremors, prolapse of the third eyelid, inability to chew, trismus, salivation, recumbency, convulsions, and cardiac arrhythmias. In lactating mares, if not treated, the disease may take a progressive and sometimes fatal course over 24-48 hr.

Differential diagnoses include tetanus, endotoxemia, colic, exertional rhabdomyolysis or other muscle disorder, seizure disorder, laminitis, and botulism.

IV administration of calcium solutions, such as 20% calcium borogluconate or solutions recommended for treatment of periparturient paresis in cattle, usually result in full recovery. These solutions should be administered slowly (over 20 min) at 250-500 mL/500 kg, diluted at least 1:4 in saline or dextrose, and the cardiovascular response should be closely monitored.

HYPOCALCEMIA IN SHEEP AND GOAT

Characteristically, the disease occurs in outbreaks with more cases in late gestation. The incidence is usually <5%, but in severe outbreaks, 30% of the flock may be affected at one time. The onset is sudden and almost invariably follows—within 24 hr—an abrupt change of feed, a sudden change in weather, or short periods of fasting imposed by circumstances such as shearing, crutching, or transportation. In early hypocalcemia, a stiff gait or ataxia, tremors, tetany, constipation, and/or depressed rumen motility are seen. As the disease progresses, signs include increased heart and respiratory rates, regurgitation of rumen contents, bloat, depression, and eventually, if untreated, opisthotonos and/or death.

Treatment should be initiated immediately, usually as IV calcium
borogluconate (50-150 mL of a 23% solution). Oral administration of a calcium gel or the SC administration of calcium solutions helps prevent relapse. During treatment, the heart should be monitored, and therapy slowed or stopped if arrhythmias occur. An alternative mode of therapy would be to add 50-150 mL of a 23% calcium borogluconate or gluconate solution to 1 L of a 5% dextrose solution. The more hypocalcemic an animal is (ie, the worse the clinical signs are), the more cardiotoxic the intravenously administered calcium becomes.

Hypocalcemia in small animals:

Puerperal hypocalcemia is an acute, life-threatening condition usually seen at peak lactation, 2-3 wk after whelping. Small-breed bitches with large litters are most often affected. Hypocalcemia may also occur during parturition and may precipitate dystocia.

Panting and restlessness are early clinical signs. Mild tremors, twitching, muscle spasms, and gait changes (stiffness and ataxia) result from increased neuromuscular excitability. Behavioral changes such as aggression, whining, salivation, pacing, hypersensitivity to stimuli, and disorientation are frequent. Severe tremors, tetany, generalized seizure activity, and finally coma and death may be seen. Hyperthermia may occur in severe cases. Prolonged seizure activity may cause cerebral edema. Tachycardia, hyperthermia, polyuria, polydipsia, and vomiting are sometimes seen.

Slow IV administration of 10% calcium gluconate is given to effect (0.5-1.5 mL/kg over 10-30 min; 5-20 mL is the usual dose). This usually results in rapid clinical improvement within 15 min. Muscle relaxation should be immediate.

Once the animal is stable, the dose of calcium gluconate needed for initial control of tetany may be diluted in an equal volume of normal (0.9%) saline and given SC, TID, to control clinical signs. (Calcium chloride cannot be given SC.) Alternatively, 5-15 mg of elemental calcium/kg/hr can be continued IV.
The bitch may remain nonresponsive after correction of hypocalcemia if cerebral edema has developed. Cerebral edema, hyperthermia, and hypoglycemia should be treated if present. Fever usually resolves rapidly with control of tetany, and specific treatment for fever may result in hypothermia.

It is best not to let the puppies or kittens nurse for 12-24 hr. During this period, they should be fed a milk substitute or other appropriate diet; if mature enough, they should be weaned. If tetany recurs in the same lactation, the litter should be removed from the bitch and either hand raised (<4 wk of age) or weaned (>4 wk of age).

After the acute crisis, 25-50 mg of elemental calcium/kg/day in 3 or 4 divided doses is given PO for the remainder of the lactation. Vitamin D supplementation is used to increase calcium absorption from the intestines. The concentration of serum calcium should be monitored weekly. The dosage of 1,25-dihydroxyvitamin D$_3$ (calcitriol) is 0.03-0.06 µg/kg/day. Calcitriol has a rapid onset of action (1-4 days) and short half-life (<1 day).

**Magnesium:**

Magnesium (Mg) homeostasis is not under direct hormonal control but is mainly determined by absorption from the GI tract; excretion by the kidneys; and the varying requirements of the body for pregnancy, lactation, and growth. Magnesium in the extracellular fluids represents ~1% of total body Mg, bone contains 50-70%, and the remainder is in the intracellular compartment. Therefore, plasma Mg does not provide an indication of intracellular or bone Mg stores. Intracellular Mg is required for activation of enzymes involving phosphate compounds such as ATPases, kinases, and phosphatases; synthesis of RNA, DNA, or protein; and stabilization of membranes. Extracellular Mg is involved in the regulation of membrane channels as well as in excitation-contraction coupling in skeletal muscle. Low ionic Mg concentrations accelerate the transmission of nerve impulses.
Ruminants are more prone to hypomagnesemia than nonruminant and monogastric animals. The variation in Mg metabolism between species is due mainly to anatomic and physiologic differences in digestive tracts. Ruminants absorb Mg less efficiently than nonruminants (35% vs 70% of intake). The rumen is the main site of absorption, and there are active transport mechanisms. Absorption from the large intestine occurs with high Mg intakes. In nonruminants, the small intestine is the main site of absorption. Differences in Mg metabolism within some species are attributable to variation in absorption efficiency of Mg from the gut, and in others to variation in reabsorption of Mg by the kidney tubules.

**Hypermagnesemia:**

Hypermagnesemia (plasma Mg concentration >2 mg/dL [1.1 mmol/L]) is a rare condition that has been reported only in monogastric animals. Horses show signs of sweating and muscle weakness within 4 hr of receiving excessive oral doses of magnesium sulfate for constipation. This is followed by recumbency, tachycardia (120 bpm), and tachypnea (60 breaths/min). Signs subside following treatment with slow IV infusion of calcium gluconate (23% solution). Hypermagnesemia has been reported in cats with renal failure that were receiving IV fluid therapy. As plasma Mg concentrations exceed 2.5 mmol/L, there may be ECG changes with prolongation of the PR interval; at 5 mmol/L deep tendon reflexes disappear, followed by hypotension and respiratory depression. Cardiac arrest may occur with blood Mg levels >6.0-7.5 mmol/L.

**HYPOMAGNESMIC TETANY IN ADULT CATTLE & SHEEP:**

Hypomagnesemic tetany is a complex metabolic disturbance characterized by hypomagnesemia (plasma Mg <1.5 mg/dL [<0.65 mmol/L]) and a reduction in the concentration of Mg in
the CSF (<1.0 mg/dL [0.5 mmol/L]), which lead to hyperexcitability, muscular spasms, convulsions, respiratory distress, collapse, and death. Adult lactating animals are most susceptible due to the loss of Mg in milk. Hypomagnesemic tetany occurs mainly when animals are grazed on lush grass pastures or green cereal crops, but can occur in lactating beef cows fed silage indoors. It is rare in nonlactating cattle but has occurred when undernourished cattle were introduced to green cereal crops.

**Etiology:**
The disorder occurs after a decrease in plasma Mg concentration when absorption of dietary Mg is unable to meet the requirements for maintenance (3 mg/kg body wt) and lactation (120 mg/kg milk). This can arise after a reduction in food intake during inclement weather, transport, or when cows graze short-grass dominant pastures containing <0.2% Mg on a dry-matter basis. Low herbage availability (<1,000 kg dry matter/hectare) results in liveweight losses during lactation, and plasma Mg decreases because insufficient Mg is obtained from body tissues mobilized during loss of liveweight to support lactation. Mg absorption from the rumen may be reduced when potassium and nitrogen intakes are high and sodium and phosphorus intakes are low. Soils that are naturally high in potassium and those fertilized with potash and nitrogen are high-risk areas for hypomagnesemic tetany. The more complex mineral interactions are likely to be involved in herds in which hypomagnesemic tetany occurs in first- and second-calving cows as well as in older cows.

Cows often do not develop signs of hypomagnesemic tetany until blood calcium concentrations are <8 mg/dL (2.0 mmol/L), which commonly occurs in cattle grazing green cereal crops. The hypocalcemia arises from either a reduction in calcium intake or absorption, or both. Lush grass pastures and green cereal crops may predispose cattle to metabolic alkalosis (urine pH >8.5) with a reduced available pool of calcium, thereby increasing the risk of hypocalcemia. Urine Mg concentrations are a useful guide to Mg status and are undetectable in cows with hypomagnesemia.
Clinical Findings:
In the most acute form, affected cows, which may appear to be grazing normally, suddenly throw up their heads, bellow, gallop in a blind frenzy, fall, and exhibit severe paddling convulsions. These convulsive episodes may be repeated at short intervals, and death usually occurs within a few hours. In many instances, animals at pasture are found dead without observed illness, but an indication that the animal had convulsions before death may be seen from marks on the ground. In less severe cases, the cow is obviously ill at ease, walks stiffly, is hypersensitive to touch and sound, urinates frequently, and may progress to the acute convulsive stage after a period as long as 2-3 days. This period may be shortened if the cow is transported or driven to a fresh pasture. When animals have hypocalcemia and hypomagnesemia, the signs shown depend on which predominates. With hypomagnesemia, tachycardia and loud heart sounds are characteristic signs.

Clinical signs of hypomagnesemia in sheep occur when hypomagnesemia (plasma Mg <0.5 mg/dL [0.2 mmol/L]) occurs concomitantly with hypocalcemia (plasma Ca<8 mg/dL [2.0 mmol/L]). The disease in lactating ewes occurs under essentially the same conditions and has the same clinical signs as in cattle.

Diagnosis:
Diagnosis is usually confirmed by response to treatment, followed by confirmation of hypomagnesemia in samples taken prior to treatment. Tetany usually occurs when plasma Mg is <1.2 mg/dL (0.5 mmol/L) in cattle and <0.5 mg/dL (0.2 mmol/L) in sheep. Urine Mg is usually undetectable in cows with hypomagnesemia. Mg concentrations <1.8 mg/dL (0.75 mmol/L) in the vitreous humour of the eye removed from animals within 24 hr after death are indicative of hypomagnesemia.

Treatment:
Animals showing clinical signs require treatment immediately with combined solutions of calcium and Mg, preferably given slowly IV while monitoring the heart. The response to treatment is slower in animals with hypomagnesemia than in animals
with hypocalcemia alone, due to the time it takes to restore Mg in the CSF. The animal should not be stimulated during treatment, as this could trigger fatal convulsions. Additional Mg sulfate (200 mL of a 50% solution/cow) can be given SC. After treatment, cows should be left to respond without stimulation, and then moved off the tetany-prone pasture, if possible. Animals must be provided with hay treated with 2 oz (60 g) of Mg oxide daily; if this is not done, the condition can recur within 36 hr after therapy.

**Prevention:**
Mg has to be given daily to animals at risk because the body has no readily available stores. Daily oral supplements of Mg oxide (2 oz [60 g] to cattle and 1/3 oz [10 g] to sheep) should be given in the danger period. Most Mg salts are unpalatable and must be combined with other palatable ingredients such as molasses, concentrates, or hay. Feeding hay alone may be all that is required to prevent hypomagnesemic tetany in herds in which only old cows (>6 yr) are affected. If slow-release intraruminal Mg devices are administered, it is recommended that the animals also be provided with hay. Fertilizers containing Mg are effective in increasing herbage Mg only on certain soil types. Herbage may be dusted with powdered Mg oxide (500 g/cow), or sprayed with a 2% solution of Mg sulfate at intervals of 1-2 wk. If rainfall exceeds 40-50 mm within 2-3 days of dusting, the herbage will require another dusting.

Out-wintered stock should be protected from wind and cold and provided with supplementary food. Sheep and cattle should have access to hay, particularly when grazing either green cereal crops or pastures fertilized with potassium or nitrogen (or both).

**Hypomagnesemic tetany in calves:**
Magnesium absorption efficiency in calves fed milk falls from 87% at 2-3 wk to 32% at 7-8 wk of age. Hypomagnesemic tetany occurs in 2- to 4-mo-old calves being fed milk only, or in younger calves with chronic scours while being fed milk replacer.
Clinical Findings:
Clinical signs are similar to those of hypomagnesemic tetany in adult cattle (see above) and include hyperexcitability, muscular spasms, convulsions, and death.

Diagnosis:
Hypomagnesemic tetany in calves must be differentiated from acute lead poisoning, tetanus, strychnine poisoning, polioencephalomalacia, and enterotoxemia caused by the toxin of *Clostridium perfringens*. Analysis of bone aids diagnosis—normal bone has a calcium:Mg ratio of 70:1; in hypomagnesemic calves, the ratio may be ≥90:1.

Treatment, Prevention, and Control:
Affected calves require prompt treatment with a 10% solution of magnesium sulfate (100 mL, SC) followed by 10 g Mg oxide, PO, SID. Provision of good-quality legume hay and a starter ration from 2 wk of age prevents the disorder.

POSTPARTURIENT HEMOGLOBINURIA:

Cows affected with this disease of rapid intravascular hemolysis develop severe anemia and weakness, and milk production drops markedly. The disease is seen worldwide. The exact cause is unknown, but the most likely predisposing factors are phosphorus deficiency, which increases osmotic fragility of erythrocytes, and copper deficiency in which increases susceptibility of erythrocytes to oxidative injury. Hemolytic or oxidative plant toxins (often from *Brassicas* spp, sugar beets, or green forage), selenium deficiency, and ketoacidosis probably contribute. Most affected cattle are in week 2-5 of lactation. Beef and nonlactating cattle are rarely affected.

Clinical disease is rare but, when it occurs, the case fatality rate is high (10-30%). The incidence of subclinical disease is unknown; many postparturient dairy cows have blood or hemoglobin in their
urine, and the source is rarely established. With clinical disease, rapid intravascular hemolysis leads to severe anemia, tachycardia, weakness, hemoglobinuria with dark brown or red urine, and pallor over several days. Milk production drops rapidly over sequential milkings. Affected cows also may have fever, diarrhea, and tachypnea. Cows that survive the hemolytic crisis may take several months to recover completely. Convalescent cows and cows with subclinical disease develop icterus and evidence of increased erythrogenesis.

Diagnosis is usually made by recognition of clinical signs, particularly dark urine and anemia. Hemoglobinuria may best be diagnosed by noting failure of the urine to clear with centrifugation (ruling out hematuria) and presence of concurrent severe anemia (making hemoglobinuria more likely than myoglobinuria). Intravascular hemolysis caused by Babesia or Theileria may be ruled out by blood film analysis, and standard laboratory methods can be used to rule out leptospirosis or bacillary hemoglobinuria. Diagnostic testing and feed or pasture analysis can be performed to identify toxic plants and deficiency of phosphorus, copper, and other antioxidants.

Transfusion of large quantities of whole blood is the best treatment for severely affected cows. Crystalloid fluids may be beneficial if blood is not available and may protect the kidneys against toxic and anoxic damage. Treatment with sodium acid phosphate (60 g in 300 mL of sterile water, IV followed by SC, every 12 hr) or copper glycinate (120 mg available copper) may halt hemolysis. Use of these products is not approved in lactating cows. Correction of mineral deficiencies and elimination of plant toxins from the diet may help prevent recurrence.

Ketosis:

Ketosis is a common disease of adult cattle. It typically occurs in dairy cows in early lactation and is most consistently characterized by partial anorexia and depression. Rarely, it occurs in cattle in late gestation, at which time it resembles pregnancy toxemia of ewes. In
addition to inappetence, signs of nervous dysfunction, including pica, abnormal licking, incoordination and abnormal gait, bellowing, and aggression are occasionally seen. The condition is worldwide in distribution, but is most common where dairy cows are bred and managed for high production.

**Etiology and Pathogenesis:**

The pathogenesis of bovine ketosis is incompletely understood, but it requires the combination of intense adipose mobilization and a high glucose demand. Both of these conditions are present in early lactation, at which time negative energy balance leads to adipose mobilization and milk synthesis creates a high glucose demand. Adipose mobilization is accompanied by high blood serum concentrations of nonesterified fatty acids (NEFA). During periods of intense gluconeogenesis, a large portion of serum NEFA is directed to ketone body synthesis in the liver. Thus, the clinicopathologic characterization of ketosis includes high serum concentrations of NEFA and ketone bodies and low concentrations of glucose. In contrast to many other species, cattle with hyperketonemia do not have concurrent acidemia. The serum ketone bodies are acetone, acetoacetate, and β-hydroxybutyrate (BHB).

Ketosis in very early lactation are usually associated with fatty liver. Both fatty liver and ketosis are probably part of a spectrum of conditions associated with intense fat mobilization in cattle. Ketosis cases occurring closer to peak milk production, which usually occurs at 4-6 wk postpartum, may be more closely associated with underfed cattle experiencing a metabolic shortage of gluconeogenic precursors than with excessive fat mobilization.

The exact pathogenesis of the clinical signs is not known. They do not appear to be associated directly with serum concentrations of either glucose or ketone bodies. There is speculation that they may be due to metabolites of the ketone bodies.

**Epidemiology:**

All dairy cows in early lactation (first 6 wk) are at risk of ketosis. The incidence in lactation is estimated at 5-16%, but incidence in individual herds varies substantially. Ketosis occurs in all parities.
(although it appears to be less common in primiparous animals) and does not appear to have a genetic predisposition, other than being associated with dairy breeds. Cows with excessive adipose stores (body condition score ≥3.75 out of 5.0) at calving are at increased risk of ketosis, compared with those with lower body condition scores. Lactating cows with hyperketonemia (subclinical ketosis—serum BHB concentrations >12 mg/dL) are at increased risk of developing clinical ketosis, compared with cows with lower serum BHB concentrations.

**Clinical Findings:**
In cows maintained in confinement stalls, reduced feed intake is usually the first sign of ketosis. If rations are offered in components, cows with ketosis often refuse grain before forage. In group-fed herds, reduced milk production, lethargy, and an “empty” appearing abdomen are usually the signs of ketosis noticed first. On physical examination, cows are afebrile and may be slightly dehydrated. Rumen motility is variable, being hyperactive in some cases and hypoactive in others. In many cases there are no other physical abnormalities. CNS disturbances are noted in a minority of cases. These include abnormal licking and chewing, with cows sometimes chewing incessantly on pipes and other objects in their surroundings. Incoordination and gait abnormalities occasionally are seen, as are aggression and bellowing. These signs occur in a clear minority of cases, but because the disease is so common, finding animals with these signs is not unusual.

**Diagnosis:**
The clinical diagnosis of ketosis is based on presence of risk factors (early lactation), clinical signs, and ketone bodies in urine or milk. When a diagnosis of ketosis is made, a thorough physical examination should be performed because frequently ketosis occurs concurrently with other peripartum diseases. Especially common concurrent diseases include displaced abomasum, retained fetal membranes, and metritis. Rabies and other CNS diseases are important differential diagnoses.

Cow-side tests for the presence of ketone bodies in urine or milk are critical for diagnosis. Caution should be exercised in the use of
such tests within 48 hr after calving. Due to the large surge in plasma NEFA at calving, a positive test for ketones is very common during this period. The majority of commercially available test kits are based on the presence of acetoacetate or acetone in milk or urine. Dipstick tests are convenient, but those designed to detect acetoacetate or acetone in urine are not suitable for milk testing. All of these tests are read by observation for a particular color change. In a given animal, urine ketone body concentrations are always higher than milk ketone body concentrations. Trace to mildly positive results for the presence of ketone bodies in urine do not signify clinical ketosis. Without clinical signs, such as partial anorexia, these results indicate subclinical ketosis. Milk tests for acetone and acetoacetate are more specific than urine tests. Positive milk tests for acetoacetate and/or acetone usually indicate clinical ketosis.

**Treatment:**

Treatment is aimed at reestablishing normoglycemia and reducing serum ketone body concentrations. Bolus IV administration of 500 mL of 50% dextrose solution is a common therapy. This solution is very hyperosmotic and, if administered perivascularly, results in severe tissue swelling and irritation, so care should be taken to assure that it is given IV. Bolus glucose therapy generally results in rapid recovery, especially in cases occurring near peak lactation. However, the effect frequently is transient and relapses are common. Administration of glucocorticoids including dexamethasone or isoflupredone acetate at 5-20 mg/dose, IM, generally results in a more sustained response. Glucose and glucocorticoid therapy may be repeated daily as necessary. Propylene glycol (250-400 g/dose, PO, [~8-14 oz]) acts as a glucose precursor and may be effective as ketosis therapy, especially in mild cases or in combination with other therapies. This dose may be administered twice per day. Overdosing propylene glycol leads to CNS depression.

Ketosis cases occurring within the first 1-2 wk after calving frequently are more refractory to therapy than those cases occurring nearer to peak lactation.
**Prevention and Control:**
Prevention of ketosis is via nutritional management. Body condition should be managed in late lactation, when cows frequently become too fat. The dry period is generally too late to reduce body condition score. Reducing body condition in the dry period may even be counterproductive, resulting in excessive adipose mobilization prepartum. A critical area in ketosis prevention is maintaining and promoting feed intake. Cows tend to reduce feed consumption in the last 3 wk of gestation. Nutritional management should be aimed at minimizing this reduction. After calving, diets should promote rapid and sustained increases in feed and energy consumption. Rations should be relatively high in nonfiber carbohydrate concentration, but contain enough fiber to maintain rumen health and feed intake. Some feed additives, including niacin, calcium propionate, sodium propionate, propylene glycol, and rumen-protected choline, may be beneficial in preventing and managing ketosis. To be effective, these supplements should be fed in the last 2-3 wk of gestation, as well as during the period of ketosis susceptibility.

**PREGNANCY TOXEMIA IN COWS:**

Pregnancy toxemia in cows is similar to the condition in small ruminants and is the result of fetal carbohydrate or energy demand exceeding maternal supply during the last trimester of pregnancy. It is precipitated by large or multiple fetuses, feed low in energy or protein, and health conditions that increase energy demand or decrease ability to take in nourishment (eg, lameness and oral diseases). The fetoplacental unit uses carbohydrate for energy and removes these compounds from the blood in an insulin-independent fashion. When this demand exceeds maternal supply, adipose tissue is mobilized to supply energy as acetate or ketone bodies, sparing carbohydrate consumption by other maternal tissues. However, only a small amount of new carbohydrate is generated from fat metabolism (from glycerol). This condition is more severe than ketosis.
because fetal demand increases during pregnancy, while milk demand can decline in response to negative energy balance. Although the mechanism is unknown, clinical disease develops in some cows with negative energy or carbohydrate balance. Proposed mediators of clinical disease include glucose deficiency with intermittent hypoglycemia, ketone body accumulation with metabolic acidosis or appetite suppression, and death of the fetus with secondary infection and toxemia. Individual cows of any breed can be affected, but herd problems are most common in beef cattle, which frequently are managed so that late pregnancy coincides with the poorest availability of feed. Both thin and fat cows can be affected, but the first noted abnormality often is loss of body condition over 1-2 wk. Decreased appetite, rumination, fecal production, and nose-licking are general signs of illness. With time, affected cows become markedly depressed, weak, ataxic, and recumbent. Opisthotonos, seizures, or coma may be seen terminally. Ketonuria is present from the early stage of disease and is the most specific finding; even mild ketonuria should not be found in normal pregnant cows until a few days before calving. Hypoglycemia is also common, but excited or seizuring cows may have hyperglycemia. With more advanced disease, there may be variable increases in serum activities of muscle or liver enzymes, as well as clinicopathologic evidence of infection, metabolic acidosis, internal organ dysfunction or failure, and circulatory collapse. Hepatic lipidosis in conjunction with large or multiple fetuses is a common necropsy finding; evidence of muscle pressure necrosis and toxemia may also be found.

Successful treatment requires early identification of the disease. There are few differential diagnoses, and pregnancy toxemia must be considered a factor in any disease that affects cattle in late gestation. Cattle that have lost weight but are still eating may be managed by feeding concentrate or propylene glycol (0.5-1 g/kg/day). Anorectic cattle must be treated aggressively, because the decrease in energy intake causes the disease to progress rapidly. Propylene glycol can be force-fed, or dextrose given IV (0.5 g/kg). Cattle with dehydration, organ dysfunction,
or metabolic acidosis should be treated with large volumes (20-60 L/day, PO or IV) of electrolyte fluids; if IV fluid administration is practical, continuous dextrose infusion (5%) is recommended. Protamine zinc insulin (200 U, SC, every 48 hr) may be given after dextrose administration to suppress ketogenesis. Insulin is not approved for use in cattle, however. Recumbent cattle may benefit from good nursing care but rarely respond to treatment. To decrease the energy drain of any cow with pregnancy toxemia, induction of parturition or removal of the fetus by cesarean section should be considered.

On the herd level, the disease can be prevented by adequate attention to nutrition and health care of cattle in late gestation. For the individual cow, recognition of the precarious state of energy and carbohydrate balance during late gestation dictates careful monitoring of energy intake, attitude, and fat mobilization, especially during times of illness or other stress.

**PREGNANCY TOXEMIA IN EWES:**

Pregnancy toxemia in ewes is a disease affecting sheep during late gestation, characterized by feed refusal and neurologic dysfunction progressing to recumbency and death. It is seen more often in older ewes and those carrying multiple fetuses. Pregnancy toxemia is almost never observed in replacement ewe-lambs or yearlings lambing for the first time.

**Epidemiology and Pathogenesis:**

The primary predisposing cause of pregnancy toxemia is inadequate nutrition during late gestation, usually due to insufficient energy density of the ration and decreased rumen capacity as a result of fetal growth. In the last 4 wk of gestation, metabolizable energy requirements rise dramatically. For example, ewes pregnant with twin lambs need ~1.8-1.9 times more energy and protein than maintenance requirements. In late gestation the liver increases gluconeogenesis to facilitate glucose availability to the fetuses. Each fetus requires 30-40 g of
glucose/day in late gestation, which represents a significant percentage of the ewe’s glucose production and which is preferentially directed to supporting the fetuses rather than the ewe. Mobilization of fat stores is increased in late gestation as a method of assuring adequate energy in the face of increased demands of the developing fetus(es) and impending lactation. However, in a negative energy balance, this increased mobilization may overwhelm the liver’s capacity and result in hepatic lipidosis with subsequent impairment of function.

Ewes with a poor body condition score (BCS ≤2.0) or that are overconditioned (BCS ≥4.0) and carrying >1 fetus are most at risk of developing pregnancy toxemia, although it can occur even in ideally conditioned ewes on an adequate ration. Susceptible thin ewes develop ketosis due to a chronically inadequate ration being offered and, in the face of increasingly insufficient energy to meet increasing fetal demands, the ewe mobilizes more body fat with resultant ketone body production and hepatic lipidosis. Overconditioned ewes may have depressed appetites, and adipose mobilization quickly overwhelms the liver’s capacity resulting again in hepatic lipidosis. In addition, there may be a population of sheep that are less responsive to insulin production in the face of inadequate nutrition. Ewes fitting these criteria may quickly shift from subclinical ketosis to clinical pregnancy toxemia if feed intake is acutely curtailed by such events as adverse weather, transport, handling for shearing or preventive medication, or other concomitant disease (footrot, pneumonia, etc). These variants of pregnancy toxemia have been termed primary pregnancy toxemia (thin ewes and inadequate nutrition), estate ketosis (fat ewes), and secondary pregnancy toxemia (ewes suffering from other disease).

**Clinical Findings:**
Early clinical signs can be detected by an observant shepherd. Most cases develop within 1-3 wk of lambing. Onset earlier than day 140 of gestation is associated with more severe disease and increased risk of mortality. Decreased aggressiveness at feeding, particularly with grain consumption, indicates a problem. Ewes may also show signs of listlessness, aimless walking, muscle
twitching or fine muscle tremors, opisthotonos, grinding of the teeth, and as the disease progresses (generally over 2-4 days), blindness, ataxia, and finally sternal recumbency, coma, and death. Cerebral hypoglycemia coupled with ketosis, ketoacidosis, and reduced hepatic and renal function lead to the clinical signs and fetal death. Blood glucose levels may return to normal or even become high terminally, possibly indicating death of the fetus(es). Septicemia develops in the ewe after fetal death.

**Lesions:**
Postmortem changes demonstrate varying degrees of fatty liver, enlarged adrenal glands, and often include multiple fetuses in a state of decomposition indicating premortem death. Very thin ewes may appear starved (e.g., serous atrophy of the kidney and heart fat). However, these signs alone are not pathognomonic for death due to pregnancy toxemia. Postmortem samples of aqueous humor or CSF can be analyzed for β-hydroxybutyrate (BHB). Levels >2.5 and 0.5 mmol/L, respectively, are consistent with a diagnosis of pregnancy toxemia.

**Diagnosis:**
Laboratory findings in individual ewes may include hypoglycemia (often <2 mmol/L), elevated urine ketone levels (evaluated by commercial qualitative test tablets), elevated BHB levels (normal <0.8 mmol/L, subclinical ketosis >0.8 mmol/L, and clinical disease >3.0 mmol/L), and frequently hypocalcemia and hyperkalemia due to severe ketoacidosis. Hypoglycemia is not a consistent finding, with up to 40% of cases having normal glucose levels and up to 20% having hyperglycemia. If the diagnosis needs further confirmation, CSF glucose levels may be more accurate than blood; they remain low even when serum glucose rebounds in advanced cases after fetal death. BHB is a more reliable indicator of disease severity than are blood glucose levels. Nonesterified fatty acids can also be elevated above 0.4 mmol/L, indicating likely hepatic lipidosis resulting in impaired hepatic function.

Pregnancy toxemia should also be considered as a differential diagnosis for periparturient CNS disease. Other CNS diseases to be considered include polioencephalomalacia, pulpy kidney
disease, rabies, lead poisoning, chronic copper toxicity, and listeriosis. These can be differentiated based on clinical and laboratory findings.  

**Treatment:**

Treatment of advanced cases of pregnancy toxemia is frequently unrewarding. If a ewe is already comatose, treatment should focus on the rest of the flock. However, if the ewe or lambs are valuable, then aggressive therapy should be directed against the ketoacidosis and hypoglycemia. Before starting this therapy, it should be determined whether the fetuses are alive (eg, real time or Doppler ultrasound). If the fetuses are alive and within 3 days of a calculated due date (gestation length 147 days), then an emergency cesarean section may be considered but is often economically unfeasible. If the fetuses are dead or too premature to survive a cesarean section, it is less stressful to the ewe to induce early lambing with dexamethasone (15-20 mg, IV or IM). Prophylactic antibiotics (usually procaine penicillin G at 20,000 IU/kg, **SID**) are appropriate if the fetuses are thought to be dead.

Ketoacidosis can be corrected by administering sodium bicarbonate solution IV, followed by balanced electrolyte solution. Hypoglycemia can be treated by a single injection of 60-100 mL 50% dextrose IV, followed by balanced electrolyte solution with 5% dextrose. IV drips and lower dextrose levels in solution might cause less of a diuretic effect; however, this is often impractical in a field setting. Repeated boluses of IV glucose should be avoided as they may result in a refractory insulin response. Insulin can be administered (20-40 IU protamine zinc insulin, IM, every other day). Calcium (50-100 mL of a commercial calcium gluconate or borogluconate solution, **SC**) can be given safely without serum biochemistry data. If serum biochemistry demonstrates hypocalcemia, ~50 mL of a commercial calcium solution can be given by slow IV injection while monitoring the heart. Oral potassium chloride (**KCl**) can be given as well in cases of severe ketoacidosis.

Ewes in the early stages can often be treated successfully with propylene glycol (60 mL, **BID** for 3 days). Adding oral calcium
(12.5 g calcium lactate), oral potassium (7.5 g KCl), and insulin (0.4 IU/kg, SC, SID) has increased survival rates. Oral commercial calf electrolyte solutions containing glucose may also be given by stomach tube at a dose of 3-4 L, QID, or drenched as a concentrated solution. The contributing factors (eg, nutrition, housing, other stressors) should be corrected for the group and feeding management assessed (eg, adequate feeder space, feeding frequency, protection from adverse weather).

A sample of late-gestation ewes can be tested for BHB levels to determine the extent of the risk in the rest of the flock.

**Prevention:**

Ewes should not enter the last 6 wk of gestation with a BCS <2.5; this can be prevented by good feeding management and ration formulation. During the last 6 wk of gestation, grain is required as a source of carbohydrates in the ration to maintain the health of multiple-bearing ewes.

There is some evidence that monensin may be beneficial for late-gestation ewes. It has improved feed efficiency by lowering feed intake. Treated ewes also showed lower serum BHB in late gestation, with no adverse effects on lamb birth weights. Lasalocid has been similarly studied. Again, feed intake was suppressed but lamb survival was better in the treatment group. More work needs to be done with both drugs to assess their use in preventing pregnancy toxemia in prolific ewes.

**Downer cow:**

The term “downer cow” is frequently applied to a mature dairy cow that is still recumbent 3 hr after calving despite treatment for hypocalcemia. Downer cows that are able to actively crawl are often referred to as “creepers” and are considered to have a more favorable prognosis than inactive animals. The cause of the recumbency is, more often than not, elusive even to an experienced clinician. Furthermore, inexperienced clinicians may miss an obvious cause if they do not adopt a systematic approach.
approach to diagnosis.

Vigorous intervention is most likely to be successful within 12 hr of initial recumbency. After 12 hr, some musculoskeletal changes may become irreversible. While some downer cows will rise after >14 days of recumbency, this is the exception. The cow should be thoroughly evaluated at the first visit and a routine protocol of activities performed within the first 12 hr.

**Etiology, Clinical Findings, and Diagnosis:**

A routine evaluation of the clinical signs of recumbent cows should be conducted. The following steps help identify possible etiologic factors.

**Assessment of Demeanor, Type of Recumbency, and Animal Environment:**

The cow may be found in lateral recumbency, which may indicate an unresolved metabolic problem such as hypocalcemia, a psychosomatic problem, or simply ignorance on the part of the dairymen regarding the importance of maintaining sternal recumbency. Signs that the cow has been thrashing with the hind limbs may indicate hypomagnesemia or tetanus.

The second most likely cause of depression is toxemia, the cause of which is most commonly found in the genital tract or mammary gland.

The environment of the animal can have a bearing on the etiology. If the footing is slippery, physical damage to the musculoskeletal system should be suspected. This is much less likely among cows in open space with a dirt or well-bedded surface.

A psychosomatic component should be suspected if there is evidence that the cow has been struggling to rise and/or is showing signs of exhaustion. The probability of a psychosomatic cause is higher if the bedding is dry, slippery straw or if the cow is found with her head in a corner.

The positioning of the hindlimbs may indicate the cause of the recumbency. Limbs splayed out behind the animal may indicate obturator paralysis. Sometimes the upper limb is extended sideways in such a manner that a crease is formed in the skin. This sign is most suggestive of rupture of the adductor muscles and
may occur when the cow struggles to rise on a slippery surface.

Physical Examination:
A routine examination should be performed when the cow is first presented.

Special Examinations:

**Vaginal exploration** is mandatory in every peripartum, recumbent cow and may lead to discovery of a decomposing second fetus. Damage to and infection of the wall of the vagina is common. Metritis and an associated toxemia can contribute to postpartum recumbency.

**Rectal exploration** is essential for differential diagnosis. The degree of uterine involution should be appropriate to the number of days postpartum. Ballottement of fluid in the organ or lack of tonicity should be noted. Unexpected anomalies may be palpated. Adhesions, lumps of necrotic fat, and enlargement or turgidity of the cervix or vaginal wall are all sequelae of a difficult birth. Fracture of the pelvis may be palpated per rectum, particularly if an assistant manipulates the limb. Pelvic fractures can be associated with sciatic nerve paralysis, while upward hip dislocation may be associated with some degree of obturator paralysis.

**Mammary gland examination** should always be performed on recumbent cows. A toxic infection of the udder with an organism such as *Escherichiacoli* can be a primary cause of recumbency.

Blood samples:

Blood show normal plasma mineral levels. Elevated CK is a specific indicator of muscle damage. Plasma AST is also elevated in muscle-damaged cows. In muscle-damaged cows, the urine may contain myoglobin as well as higher than normal levels of protein. Ketonuria and bilirubinuria may be detected but are associated with lowered feed intake. Serum glutamic oxaloacetic acid levels are usually markedly elevated 18-24 hr after the onset of recumbency.

**Treatment:**

Downer cows are often hypocalcemic. If an apparently hypocalcemic cow does not respond to calcium therapy,
phosphorus, magnesium, and potassium should be given as additional treatments pending the results of laboratory tests. Monitoring the blood mineral status is an important part of downercow management.

In most cases, recovery depends on the quality of recumbency management and nursing care. Lateral recumbency must be corrected immediately to avoid regurgitation and inspiration of stomach contents. The animal should be rolled into sternal recumbency. However, if this posture is to be maintained, the limb on which the animal has been lying should be drawn from under the body. Support (eg, straw bale) placed under the shoulder may be required for some animals to maintain sternal recumbency.

Attempting to stabilize a recumbent cow on a concrete surface is highly undesirable but sometimes unavoidable. Bedding the area around and under the cow with wet, sticky manure to a depth ≥6 in. is a common practice. At least 10 in. of dry straw should be distributed over the wet mass. Dermatitis can result, and comfort of the cow is reduced. More seriously, the risk of mastitis resulting from the contaminated environment is very high. A bed of sand ≥10 in. deep is more effective. This usually drains well, and good hygiene can be maintained if the manure is removed several times each day.

Hobbling of the cow may be considered to prevent overabduction that can lead to muscular damage. Ropes should never be used for this purpose. A soft nylon strap may be wrapped twice around the middle of each metatarsus, allowing a distance of at least 3 ft between the legs.

Supportive Care Cows:

It is vital that recumbent cows be provided with clean water at all times. A shallow rubber feed bowl prevents spillage. If the cow does not drink, she must be given fluid therapy either by drench or parenterally. Every effort must be made to roll the cow from one side onto the other every 3 hr. If this is not done, the weight of the cow results in ischemia in the muscles of the hindlimb.

Protection from the elements is essential. Rain and wind can reduce body temperature considerably and worsen shock if present. A
recumbent cow does not require a warm environment; however, in a cold environment, an inactive animal can gradually succumb to hypothermia.

**Prevention:**
All mature dairy cows must be monitored closely during the postpartum period for signs of parturient paresis. The elapse of several hours from the commencement of clinical signs of milk fever until treatment seems to be the critical issue. The use of television surveillance of recently calved cows may be a prudent measure. Every cow that has been successfully treated for hypocalcemia should, if necessary, be moved to a location with a good footing and remain there for 48 hr.

**EXERTIONAL MYOPATHIES IN HORSES (AZOTURIA)**

Exertional myopathies in horses are a syndrome of muscle fatigue, pain, or cramping associated with exercise. Most exercise-associated myopathies result in necrosis of striated skeletal muscle and are therefore termed exertional rhabdomyolysis. Although exertional rhabdomyolysis was previously considered a single disease described as azoturia, tying-up, or cording up, it is now known to comprise several different myopathies, which, despite similarities in clinical presentation, differ significantly in etiopathology. Clinical signs usually are seen shortly after the onset of exercise. Excessive sweating, tachypnea, tachycardia, muscle fasciculations, reluctance or refusal to move, and firm, painful lumbar and gluteal musculature are common signs. Episodes range from subclinical to severe episodes of muscle necrosis with recumbency and myoglobinuric renal failure. The severity varies extensively between individuals and to some degree within the same individual. A diagnosis of exertional rhabdomyolysis is based on demonstration of abnormal elevations in serum CK, lactate dehydrogenase, and AST. Differential diagnoses for reluctance to move, acute recumbency, and discolored urine include lameness, colic, laminitis, fracture,
pleuropneumonia, tetanus, aortoiliac thrombosis, neurologic diseases resulting in recumbency or reluctance to move, intravascular hemolysis, and bilirubinuria. Causes of non-exercise-associated rhabdomyolysis include infectious and immune-mediated myopathies (eg, Clostridium sp, influenza, Streptococcus equi, Sarcocystis), nutritional myodegeneration (vitamin E or selenium deficiency), traumatic or compressive myopathy, idiopathic pasture myopathy, and toxic muscle damage from the ingestion of ionophores (eg, monensin, lasalocid, rumensin). Plants, including white snake root and vitamin D-stimulating species, should also be considered.

Exertional rhabdomyolysis can be either sporadic, with single or very infrequent episodes of muscle necrosis with exercise, or chronic, with repeated episodes of rhabdomyolysis and increased muscle enzyme activity, often with mild exertion. All breeds of horses are susceptible to sporadic exertional rhabdomyolysis.

A diagnosis of sporadic exertional rhabdomyolysis is made on the basis of a horse with no previous history of exertional rhabdomyolysis, signs of muscle cramping and stiffness following exercise, and moderate to marked elevations in serum CK and AST. Immediately on detection of signs of exertional rhabdomyolysis, exercise should cease and the horse should be moved to a well-bedded stall with access to fresh water. The objectives of treatment are to relieve anxiety and muscle pain, as well as to correct fluid and acid-base deficits. Tranquilizers, opioids, or NSAID may be given. Most horses are relatively pain free within 18-24 hr.

Severe rhabdomyolysis can lead to renal compromise due to ischemia and the combined nephrotoxic effects of myoglobinuria, dehydration, and NSAID therapy. The first priority in horses with hemoconcentration or myoglobinuria is to reestablish fluid balance and induce diuresis. In severely affected animals, regular monitoring of BUN and/or serum creatinine is advised to assess the extent of renal damage. Diuretics are contraindicated in the absence of IV fluid therapy and are indicated if the horse is in oliguric renal failure.
Horses should be stall rested on a hay diet for a few days. For horses with sporadic forms of tying-up, rest with regular access to a paddock should continue until serum muscle enzyme concentrations are normal. Because the inciting cause is usually temporary, most horses respond to rest, a gradual increase in training, and dietary adjustment. Endurance horses should be encouraged to drink electrolyte-supplemented water during an endurance ride and monitored particularly closely during hot, humid conditions.

**NUTRITIONAL DISEASES:**

**Copper deficiency**

There are two main causes of copper deficiency in sheep and cattle:

* Low copper levels in plants due to a lack of copper fertilizer in naturally copper deficient soils;

* an induced deficiency caused by the ingestion of excessive levels of molybdenum and sulphur in pasture or feed supplements.

Clinical signs in cattle

Cattle lose coat colour and the coat becomes rough. This can occur in the absence of any production losses. The classical spectacled appearance may occur where the hair around the eyes loses its pigmentation.

Ill-thrift, decreased milk production, infertility and anaemia can occur in adults, and calves have poor growth rates, scouring is often associated with copper deficiency caused by high levels of dietary molybdenum but not when a deficiency is due mainly to low dietary copper sudden death (falling disease) may occur in adults.

Clinical signs in sheep

Abnormalities of the wool (loss of crimp, steeliness and depigmentation) are seen in the early stages of copper
deficiency. anaemia, scouring, III-thrift and infertility may occur in extreme cases. Bone fragility in lambs can occur in spring. Affected animals develop fractures of the ribs and limbs. Unweaned lambs may develop a condition known as enzootic ataxia in which lambs up to four months old progressively lose coordination in their hind limbs. Copper deficiency Causes CNS disease in sheep, goats, and pigs. Swayback is the congenital form in lambs and is characterized by degeneration and necrosis of the cerebrum. The acquired form, enzootic ataxia, affects lambs, kids, and pigs. Affected animals appear normal at birth but develop progressive paraparesis with hyporeflexia and muscle atrophy within the first few months of life. Other signs include diarrhea and unthriftiness and, in lambs, abnormal fleece. Histologically, there is chromatolysis and loss of neurons and degeneration of axons, primarily in the spinal cord and caudal aspect of the brain stem. Animals may improve with copper supplementation, but permanent neurologic deficits are likely in severely affected animals.

LABORATORY TESTS
Liver copper concentration is one of the best indicators of copper status, although this is still not guaranteed. One cause for uncertainty is that individual sheep or cattle develop copper deficiency with different levels of copper in their livers. Another limitation can be the difficulty and cost of obtaining a liver sample by biopsy from live animals. Even after slaughter it is difficult to retain livers from identifiable animals. Nevertheless, liver analyses are still the most accurate indicators of copper status. The concentration of copper in the blood can be an unreliable guide to copper status if it is a molybdenum-induced deficiency. Caeruloplasmin activity in plasma or comparing different plasma inorganic copper fractions (TCA-soluble versus TCA-insoluble) can indicate if molybdenum is involved. Pasture analyses for copper and molybdenum concentration provide only a rough guide to the copper status of sheep and cattle grazing them. Pastures with less than 2.5 ppm copper are sometimes deficient for sheep and cattle. Above 4 ppm copper, they are not deficient, provided molybdenum levels are less than 1.5 ppm.

Preventing copper deficiency in sheep and cattle
Fertilizers
The residual effectiveness of fertilizer copper is well established. One application of 0.8 to 2.5 kg/ha copper (3.3 to 10 kg/ha copper sulphate), according to soil type and locality, will supply copper to sheep and cattle for at least 20 years. A second application of 0.5 kg/ha copper (2 kg/ha copper...
sulphate) 10 years after the first is probably unnecessary, but may be regarded as good insurance. Where too much molybdenum has been applied, extra copper fertilizer may not be effective in correcting the induced copper deficiency, since it can occur even when soil and plant copper levels are high.

**injections**

copper compounds injected under the skin (such as cujec, diethylamine cuproxy quinoline sulphonate) can correct a deficiency, but must be repeated every six months. This method is both less convenient and more expensive than supplying copper through fertilisers.

Licks, drenches, copper needles and drinking water

Copper sulphate can be supplied through licks and drinking water, but the dose rates cannot be controlled. Some animals can get too much and risk toxicity while other, especially with licks, may get too little.

Drenches only have a brief effect and are not recommended for the treatment of copper deficiencies. Sheep are highly susceptible to copper toxicity and care should be taken whenever supplementing livestock. Many liver toxins will cause copper to accumulate in the liver and can lead to secondary copper toxicity. Copper oxide needles are a slow release form of copper administered as a capsule. They are active for 6 to 12 months.

**Cobalt deficiency**

The disease is caused by a deficiency of cobalt in the diet & characterized by anorexia & wasting. Cattle, and sheep are affected, the signs are identical in both, but sheep are more susceptible than cattle. Lambs and calves are more seriously affected than adult. Soils containing less than 0.25 mg/kg cobalt are likely to produce a deficient pasture & leading to cobalt deficiency. No specific signs are characteristic of cobalt deficiency, agradual
decrease in appetite, loss of body weight, emaciation, weakness, pica, pale m.m., affected animals are easily fatigued, sever decrease in milk & wool production, tendor or easily broken wool, diarrhea, lacrimation may be seen in later stages, death occur in 3-12 months.

D.D. ILL thrift diseases:
Copper def., selenium def., parasitism, lack of total digestable nutrients.

Treatment: oral dosing with cobalt 1mg/day for sheep 10mg/day for cattle.
- I.M. injection of vit.B12 100-300mg weekly.

Control: -supplementation of cobalt with the diet ...

Iodine deficiency:
The cardinal sign of iodine deficiency is goiter. the major clinical manifestation is neonatal mortality, with alopecia & visible palpable enlargement of the thyroid gland occurring in some animals.
etiology: iodine def. may be primarily due to deficient iodine intake or secondarily conditioned by high intake of calcium, diet consisting largely of brassic sp. Or gross bacterial pollution of feed stuffs or drinking water.
CLINICAL SIGNS; loss of condition, decreased milk yield, loss of libido in bull, failure to express estrus in cow, high incidence of stillbirth and weak new born, partial or complete alopecia, palpable enlargement of the thyroid gland. Animals which survive the intial dangerous period after birth may recover except for partial persistence of the goiter, the gland may pulsate with normal arterial pulse and may extend down and cause local edema.
TREATMENT; N.B; over dosage of iodine is toxic.
INDIVIDUAL DOSING; 280 mg potassium iodide WEEKLY APPLICATION of tincture of iodine to the inside of the flank; 4 ml for cattle, 2ml for sheep.
PREVENTION; iodine can be provided as fertilizer or in salt or mineral mixture.
**Zinc deficiency (parakeratosis):**

This is a chronic afebrile, non-inflammatory disease affecting the epidermis & is characterized by crusty proliferation and cracking of the skin. The exact cause is not clearly determined, but it is probably of nutritional origin:

- an excess of calcium
- relative deficiency of zinc
- deficiency of unsaturated fatty acid in diet.

**Clinical finding:**

Parakeratosis and alopecia in about 40% of the skin area, the lesions are more marked on muzzle, vulva, anus, tail-head, ears, back of the hind limbs, flank, and neck. Most animals are stunted in growth.

In sheep; loss of wool, thickening of the skin, decrease growth rate, salivation, swollen hocks.

In ram lambs there is impaired testicular growth and complete cessation of spermatogenesis.

In severe cases in young rams, there is drooling of the saliva, parakeratosis. Around eyes, on nose, feet, and scrotum, and shedding of the hooves.

**c.path.**

- skin biopsy
- serum zinc level

**D.D.**

- sarcoptic mange.

**Treatment:** zinc sulphate 2 gm weekly orally, or 1 gm weekly by I.M. injection.

**RICKETS:**

Rickets is a disease of young, growing animals. The most common causes are dietary insufficiencies of phosphorus or vitamin D. Calcium deficiencies can also cause rickets, and while this rarely occurs naturally, poor balanced diets that are deficient in calcium have been said to cause the disease. As in most diets causing osteodystrophies, the abnormal calcium:phosphorus ratio is most likely the cause.

**Clinical Findings and Lesions:**

The characteristic lesions of rickets are failure of both vascular
invasion and mineralization in the area of provisional calcification of the physis. This pathology is most obvious in the metaphyses of the long bones. There may be a wide variety of clinical signs, including bone pain, stiff gait, swelling in the area of the metaphyses, difficulty in rising, bowed limbs, and pathologic fractures. On radiographic examination, the width of the physis is increased, and the nonmineralized physeal area is distorted. In advanced cases, angular limb deformity can be seen due to asynchronous bone growth.

Animals fed all-meat diets are commonly affected. Kittens that are fed beef heart exclusively develop locomotor disturbances within 4 wk, even though the high content of digestible protein (>50% on a weight basis) and fat promotes rapid growth, the animals appear well nourished, and their coat maintains a good luster. The predominant clinical signs are reluctance to move, posterior lameness, and ataxia. The kittens often stand with characteristic deviation of the paws. The skeletal disease becomes progressively more severe after 5-14 wk. The kittens become quiet and reluctant to play; they assume a sitting position or sternal recumbency with the hindlimbs abducted. Normal activities may result in the sudden onset of severe lameness due to incomplete or folding fractures of 1 or more bones. Lameness is the initial functional disturbance in growing dogs and may vary from a slight limp to inability to walk. The bones are painful on palpation, and folding fractures of long bones and vertebrae are common.

Rickets and other bone pathologies have been reported in young pigs housed indoors and fed processed feed. Processing of the feed removes natural vitamin D and other fat-soluble vitamins. Without vitamin supplementation, nutritional osteodystrophy may result. Diets with excessive amounts of calcium (3 times normal concentrations) have caused ricket-like signs in growing Great Danes. Several other bone pathologies such as retained cartilaginous cores, osteochondrosis, and stunted growth were seen in these dogs as well.

**Treatment:**
Correction of the diet is the primary treatment. The prognosis is good in the absence of pathologic fractures or irreversible damage
to the physis. If the animals are housed, exposure to sunlight (ultraviolet radiation) will also increase the production of vitamin D₃ precursors.

Recent studies show that many homemade diets for dogs are deficient in minerals and have altered calcium:phosphorus ratios. Therefore a high-quality commercial food, or one designed by a credentialed veterinary nutritionist, is recommended.

**OSTEOMALACIA:**

Osteomalacia has a pathogenesis similar to that of rickets but it is seen in mature bones. Because bones mature at different rates, both rickets and osteomalacia can be seen in the same animal. Osteomalacia is characterized by an accumulation of excessive unmineralized osteoid on trabecular surfaces.

**Clinical Findings:**

Affected animals are unthrifty, may have abnormal estrus, and may exhibit pica. Nonspecific shifting lamenesses are common. Fractures can be seen, especially in the ribs, pelvis, and long bones. Spinal deformation such as lordosis or kyphosis may be seen.

In horses, nutritional osteodystrophy is known as bran disease, miller’s disease, and “big head.” The diet of pampered horses is often too high in grains and low in forage; such a diet is high in phosphorus and low in calcium. Many of the obscure lamenesses of horses have been attributed to nutritional osteodystrophy. The pathologic changes are similar to those in other species, with the provisos that the bones of the head are particularly affected in severe cases and that gross or microscopic fractures of subchondral bone (with consequent degeneration of articular cartilage and tearing of ligaments from periosteal attachments) are dominant clinical signs. Unilateral facial deformity due to secondary (nutritional) hypoparathyroidism was recently reported in a 1-yr-old filly.

Nutritional osteodystrophy is uncommon in cattle and sheep but is seen occasionally in feedlots. Marrow fibroplasia is not a feature of the condition in these species. Osteoporosis is the dominant lesion,
but “big head” may be seen in goats. Bone deformities in recovered animals can cause obstipation or dystocia.

**Diagnosis:**

To establish a firm diagnosis, the diet should be evaluated for calcium, phosphorus, and vitamin D content. There is radiographic evidence of generalized skeletal demineralization, loss of lamina dura dentes, subperiosteal cortical bone resorption, bowing deformities, and multiple folding fractures of long bones due to intense localized osteoclast proliferation. Laboratory values used to assess renal function should be within normal limits in animals with nutritional osteodystrophy.

**Treatment:**

Affected animals should be confined for several weeks after initiation of the supplemental diet. Response to therapy is rapid; within 1 wk the animals become more active, and their attitude improves. Jumping or climbing must be prevented because the skeleton is still susceptible to fractures. Restrictions can be lessened after 3 wk, but confinement with limited movement is indicated until the skeleton returns to normal (response to treatment should be monitored radiographically).