Understanding Endocrinology and Pharmacology in Donkeys and Mules

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There are endocrine, metabolic, and pharmacological differences between donkeys, mules, and horses. Endocrine and metabolic disorders are frequent in donkeys, and when diagnosed, the disease process and complications (hyperlipemia, insulin dysregulation, obesity, endocrinopathic laminitis) are often advanced. In donkeys suspected of insulin dysregulation with equivocal insulin concentrations, dynamic testing may be indicated, taking into consideration donkey-specific values. Basal adrenocorticotropic hormone and the thyrotropin-releasing hormone (TRH) stimulation test are the preferred methods to diagnose pituitary pars intermedia dysfunction (PPID) in donkeys. Pergolide is an effective treatment for PPID in donkeys. Donkeys have faster metabolic rates and higher cellular water content than horses, which may contribute to their ability to metabolize many drugs differently than horses. Extrapolation of doses and dosing intervals from horses to donkeys and mules could be ineffective or lead to side effects. For most drugs used in equine practice, donkeys and mules need higher doses and/or more frequent dosing intervals than horses. Other drugs (e.g., fluoroquinolones, pergolide) have longer half-lives, requiring lower doses or longer dosing intervals. Authors' addresses: Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210 (Toribio); Department of Animal Medicine and Surgery, University of Cordoba, Campus Rabanales, 14104 Cordoba, Spain (Perez-Ecija, Mendoza); e-mail: toribio.1@osu.edu. *Corresponding and presenting author. © 2021 AAEP.

1. Introduction

The donkey (*Equus africanus asinus*) plays important economic, social, and cultural roles throughout the world, particularly in developing countries. The donkey and mule were central to the development of countries such as the United States as well as many others in Europe and Asia. With industrialization, the use of these animals for economic development decreased to the point that they became secondary and, over time, even irrelevant. Uses such as recreational activities, ecotourism, hippotherapy/ondotherapy, as well as companion animals have been increasing in recent decades, mainly in developed countries.¹ The donkey continues to be a valuable asset in developing countries, where the livelihood of many families and local economies depend on these animals. Donkeys are also used as a source of meat, milk, and byproducts for allergic conditions and for the cosmetic industry. Unfortunately, demand for donkey hide from China to produce “Ejiao” and other
products has led to a decline in the worldwide donkey population.2,3

To date, more donkeys are being admitted to veterinary hospitals or are receiving specialized care as a result of economic growth, cultural shifts, awareness of animal welfare, and programs to rescue breeds close to extinction. Therefore, there is a need to increase donkey- and mule-specific knowledge in veterinarians and professionals involved with their use and care. Veterinarians practicing in this species should be familiar with anatomical, physiological, endocrine, and pharmacological differences considering that data extrapolation from horses can lead to misdiagnosis, inadequate treatments, complications, unnecessary expenses, and, in some instances, even death.1,4–6

2. Endocrinology

Hyperlipemia

Hyperlipemia refers to the clinical condition associated with increased triglyceride concentrations (hyperlipidemia).1,7 Hyperlipemia is more frequent in donkeys than other equids, and it seems its higher incidence is a consequence of their efficiency to store lipids and rapid ability to mobilize fat stores.1 It is more frequent in older donkeys, jennies, and smaller donkey breeds.1,7,8 Hyperlipemia is not restricted to donkeys with obesity and insulin dysregulation (ID) because it occurs in donkeys of any age and in good or poor body condition, as well as in donkey foals. As with other equids, predisposing factors include conditions associated with a negative energy balance (e.g., anorexia, fasting), increased energy demands (e.g., late pregnancy, lactation), and concurrent diseases (e.g., stress, endotoxemia, parasitism, liver disease, gastrointestinal disease, laminitis).1,7,8 Obesity, stress, and pregnancy are major risk factors for hyperlipemia in donkeys. Mortality rates in affected donkeys can be up to 80%, which are similar to ponies and miniature horses.1,7,8

Physiologic or pathologic processes that increase energy demands activate hormone-sensitive lipase in adipocytes to induce lipolysis and the release of free fatty acids (FFA) into circulation.1 In the liver, FFA are re-esterified into triglycerides, which are released as very-low-density lipoproteins (VLDL) into systemic circulation. If lipolysis persists and VLDL production exceeds peripheral triglyceride uptake, hyperlipidemia (hypertriglyceridemia) will ensue, resulting in hepatic fatty infiltration, liver dysfunction, and increased risk of liver rupture. In severe hyperlipemia, other organs (kidneys, pancreas, heart, intestines, skeletal muscle) can be infiltrated by triglycerides, compromising their function (Fig. 1).1,7,9

Catecholamines, glucocorticoids, adrenocorticotropic hormone (ACTH), growth hormone (GH), glucagon, and pro-inflammatory cytokines (IL-6, TNF-α) increase lipolysis, while insulin inhibits lipolysis and

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Fig. 1. Diagram of the pathophysiology of hyperlipemia. Physiological needs and pathological processes promote lipolysis from increased concentrations of lipolytic factors (catecholamines, glucocorticoids, adrenocorticotropic hormone [ACTH], growth hormone [GH], glucagon, and tumor necrosis factor alpha [TNFα]) or reduced levels of lipogenic factors (insulin) leading to the release of free fatty acids (FFA) into circulation. Adipocyte lipolysis is mediated by hormone-sensitive lipase (HSL). FFA are used as a source of energy, and the excess is re-esterified in the liver into triglycerides (TGL) that are released into circulation as part of very-low-density lipoproteins (VLDL) to be taken by different tissues and used for energy, storage, or other functions. Lipoprotein lipase (LPL) in the capillaries removes TGL from VLDL to be transferred to cells. Glucocorticoids, GH, TNFα, and azotemia interfere with LPL, reducing TGL removal with subsequent VLDL accumulation in blood (hyperlipidemia). VLDL in high concentrations can infiltrate organs and impair their function. Courtesy of Dr. Ramiro Toribio and adapted from Mendoza et al.1
promotes lipogenesis. Increased concentrations of lipolytic factors (cytokines, hormones), decreased lipogenic hormones (insulin), and insulin insensitivity combined with reduced VLDL removal will ultimately lead to hypertriglyceridemia and clinical hyperlipemia (Fig. 1). Insulin is the main lipogenic hormone, and impaired signaling indirectly facilitates hyperlipemia, particularly in animals with metabolic syndrome and obesity. Hyperlipemia is usually secondary to other conditions, and initial clinical signs are the result of the primary condition. In fact, hyperlipemia often goes unnoticed. Lethargy and anorexia are common findings of hyperlipemia. Fatty infiltration of various organs leading to dysfunction can exacerbate disease progression, additional clinical signs (e.g., diarrhea, dysrhythmias), and laboratory abnormalities (e.g., increased liver enzymes, azotemia, acidaemia, hyperbilirubinemia). Hyperlipemia is easily diagnosed by measuring serum triglyceride concentrations. Equids can be classified as hypertriglyceridemic (200–500 mg/dL, 2.26–5.65 mmol/L); no evidence of tissue fatty infiltration or lipemic/hyperlipemic (> 500 mg/dL, 5.65 mmol/L); there could be fatty infiltration in various organs. Severe hyperlipemia is evident when triglyceride concentrations are > 1000 mg/dL, 11.3 mmol/L. Gross lipemia can be noted with triglyceride concentrations > 500 mg/dL in sitting ethylenediaminetetraacetic acid (EDTA) and serum tubes. However, these cutoff values are somehow arbitrary, are mainly used in ponies, and may not apply to donkeys. In donkeys, lipemia may become grossly evident at higher triglyceride concentrations than ponies and horses, likely due to a different lipid profile. Lipemic serum may interfere with the measurement of various chemistry analytes, falsely changing their values (e.g., pseudohyponatremia). The therapeutic principles for hyperlipemia are aimed at halting fat mobilization, controlling the primary disease, reducing hepatic triglyceride synthesis, avoiding stressful conditions, and restoring a positive energy balance.

In pregnant animals, it is essential to provide a balanced caloric intake, although excessive calories can predispose to other disorders (e.g., insulin dysregulation). In extremis situations, pregnancy termination should be considered. In lactating animals, early weaning is highly recommended. Hyperlipemic donkeys should be encouraged to eat by offering a variety of palatable foodstuff that may stimulate hunger (e.g., honey, apples, carrots). Placing a feeding tube should be considered if gastrointestinal function is normal. Intravenous dextrose may be necessary to reduce lipolysis. Partial parenteral nutrition without lipids may be required in some animals. If hyperglycemia persists or triglyceride concentrations continue to increase over 24 h, regular insulin (0.05–0.1 IU/kg/h, IV) or slow-release insulin (0.10–0.15 IU/kg, q 12–24 h, SQ) should be considered. In donkeys where insulin proves effective, a continuous rate infusion (0.05 IU/kg/h starting rate) together with intravenous dextrose can be implemented. Close glucose monitoring is essential to avoid hypoglycemia. The benefits of heparin or low molecular weight heparin to increase lipoprotein lipase remain to be evaluated. These products should be used with caution in animals with liver dysfunction due to their increased risk of bleeding.

Donkey Metabolic Syndrome

Donkey metabolic syndrome (DMS) was recently recognized and appears to be highly prevalent in donkeys, particularly in developed countries or where food is readily available. DMS shares key features with equine metabolic syndrome (EMS), including obesity, ID, and endocrinopathic laminitis. Clinical signs reported in horses such as reproductive disturbances, diabetes mellitus, and pancreatic insufficiency are poorly characterized in donkeys. Similar to horses and ponies, not every obese donkey has ID, and lean animals can be affected. The incidence is higher in jennies and middle-aged to old donkeys (>8 years of age); however, this condition can be seen in much younger donkeys. Multiple factors likely contribute to the pathogenesis of ID and endocrinopathic laminitis in donkeys. Their energy efficiency associated with reduced physical activity results in obesity, which is a major complicating factor for these disorders. In addition to excessive body weight, adipose tissue produces hormones and cytokines that interfere with insulin signaling and promote a systemic pro-inflammatory state.

Inflammatory mediators and prolonged hyperinsulinemia disrupt lamellar cell function, which together with excessive body weight contribute to the development of endocrinopathic laminitis. Insulin concentrations are often elevated in obese donkeys. Insulin insensitivity interferes with glucose uptake, promotes fat mobilization (lipolysis), and alters endothelial integrity. Cytokines also reduce insulin signaling in the liver, worsening hepatic fatty infiltration. Adipocyte factors (adipokines) such as leptin and adiponectin may contribute to the pathogenesis of ID and endocrinopathic laminitis. The diagnostic principles of EMS also apply to DMS. Donkey-specific body condition score systems have been developed, ranging from 1 (very thin) to 5 (obese) or from 1 (emaciated) to 9 (obese). A neck score system was also developed (0 = thin neck without pal-pable crest; 4 = thick neck, rounded and gross cresty). Fasting glucose and insulin concentrations as well as dynamic tests are the main methods used to diagnose ID in donkeys. Factors that could interfere with the diagnosis of ID include stress, fasting time, carbohydrate-rich diets, physical activity, pain, transport, endocrinopathies (pituitary pars intermedia dysfunction [PPID]), concomitant diseases, and α2-adrenoreceptor agonists. Fasting insulin concentration is the main test used to diagnose ID in horses, with a cutoff value of >50 μIU/mL suggestive of ID. Insulin concentrations differ between assays, and extrapolation can be misleading. Dynamic tests should be considered when baseline insulin results are inconclusive (20–50 μIU/mL). Dynamic protocols have been evaluated in donkeys, demonstrating differences with horses for the intravenous glucose...
tolerance test (IVGTT) and the combined glucose-insulin test. For the IVGTT, glucose (300 mg/kg, 50% dextrose solution) is administered IV as a bolus, and glucose and insulin concentrations are measured at 0 (baseline), 5, 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, 240, and 300 minutes. In insulin-sensitive donkeys, glucose should be back to the normal range by 180 minutes. This test is time-consuming. For the combined glucose-insulin test, glucose (150 mg/kg, IV) is administered as a bolus and immediately followed by regular human insulin (0.1IU/kg, IV). Glucose and insulin concentrations are determined at the same time points as the IVGTT. While horses are considered ID if glucose concentrations are above baseline at 45 minutes, donkeys would be considered ID if glucose concentrations are at or above baseline at 60 minutes. The test can be simplified by collecting blood samples at baseline and at 60 minutes. A serum insulin concentration of > 100 µIU/mL at 60 minutes also supports ID. The intravenous insulin tolerance test and frequently sampled intravenous glucose tolerance test (FSIGTT) have also been investigated in healthy and obese donkeys. FSIGTT results are comparable between donkeys and horses. The FSIGTT is not a practical test, and its main use is in research. Oral carbohydrate tolerance tests, whether using dextrose or corn syrup, remain to be evaluated in donkeys, but dynamics likely differ between species. Leptin and adiponectin cutoff values for donkeys with evidence of ID and endocrinopathic laminitis have not been reported. Therapeutic approaches for DMS have not been established, and clinicians rely on protocols for EMS. They are focused on promoting weight loss, improving insulin regulation, and controlling signs of endocrinopathic laminitis. To promote weight loss, caloric restrictions and increased physical activity are central to success. Due to their energy efficiency and ability to subsist on poor quality feedstuffs, dietary management should rely on low-quality hay and elimination of access to grain, concentrates, and carbohydrate-rich pastures. Commercial diets to manage ID and obesity in horses may not be appropriate for donkeys. Access to paddocks to promote physical activity is encouraged. Grazing should be avoided in early morning or after rainfall. Grazing muzzles may be used with caution, and some clinicians avoid their use in donkeys because of concerns of inducing stress, which could trigger additional problems. The presence of other animals (donkeys, horses, goats) is recommended to reduce stress and promote physical activity. Weight loss in donkeys must be a very slow process due to risk of other conditions such as hyperlipemia. Information on the pharmacology of drugs to manage ID or obesity in donkeys is lacking, and equine doses are generally used. Levothyroxine sodium is used in donkeys at equine doses (0.1 mg/kg, q24h, PO). Metformin has not been evaluated in donkeys, but it is occasionally administered (15–30 mg/kg, q12h, PO). Thiazolidinediones (pioglitazone) and sulfonfonylureas (glyburide) have not been assessed in donkeys. Considering the clinical benefits of these and other drugs to manage energy dysregulation in other species, including horses, evaluating their pharmacologic properties in donkeys would be valuable.

Pituitary Pars Intermedia Dysfunction

PPID is common in geriatric donkeys, partly due to their longevity. The condition is often underdiagnosed, and epidemiological studies are lacking. Breed and gender do not appear to be risk factors. The pathogenesis of PPID in donkeys and mules is likely similar to horses and ponies, but mechanistic data are lacking. Clinical signs are similar between donkeys, horses, and ponies, with hypercortisolism being common. It is important to note that some donkey breeds have long haircoats. Lethargy could be overlooked due to their calm behavior. Laminitis is a consistent finding in donkeys with PPID. Hyperhidrosis, ID, abnormal fat distribution (supraorbital, neck, shoulder, tail base), muscle wasting, reproductive problems, predisposition to infections, endoparasitism, and orthopedic problems also occur in donkeys. Polyuria is infrequent. Information on PPID in mules is minimal. Baseline ACTH concentrations and the TRH stimulation test are the main diagnostic tests for PPID diagnosis in donkeys. ACTH concentrations in healthy donkeys are higher than in healthy horses and mules. Similar to horses, donkeys exhibit seasonal variations in ACTH concentrations that should be taken into consideration when measuring baseline ACTH concentrations or performing the TRH stimulation test. Donkeys have higher plasma ACTH values in the fall compared to horses. Basal cortisol concentrations are similar in healthy donkeys and horses. Similar to horses, hypercortisolism is a rare finding in donkeys with PPID. Blood samples to measure ACTH should be collected in EDTA tubes, processed rapidly, and shipped on ice. The ACTH chemiluminescent immunoassay works well with donkey samples. It is important to take into consideration stressful conditions and drugs (e.g., a2-adrenergic agonists, glucocorticoids) that could alter ACTH concentrations. The dexamethasone-suppression test and the combined dexamethasone-TRH test are not reliable methods in donkeys. For the TRH stimulation test, a donkey is considered PPID positive if plasma ACTH concentrations are higher than 110 pg/mL 10 minutes after injecting 1 mg of TRH intravenously. It is important to note that this study had a small number of animals, and a large population of donkeys would necessary to further validate these values. Pergolide, a dopamine (D2) receptor agonist, is the drug of choice to treat PPID in donkeys. The pharmacokinetics of pergolide differs between donkeys and horses. After repeated dosing,
pergolide achieves higher plasma concentrations in donkeys, indicating that lower doses may be sufficient to ameliorate the signs of PPID in donkeys.35 However, pharmacodynamic information is lacking, and donkeys are typically treated with 0.25 to 0.5 mg/250 kg, q24h, PO often with clinical improvement. It is recommended to monitor animals early in treatment for potential side effects. In animals with anorexia, the dose should be reduced or discontinued. Bromocriptine, another dopamine D2 receptor agonist, and cyproheptadine, a 5-HT receptor antagonist, have not been evaluated in this species. Repeated measurements of basal ACTH concentrations may be necessary to assess response to treatment and adjust dosing.

Thyroid Gland
Information on thyroid diseases in donkeys is lacking. Donkeys have higher plasma-free and total triiodothyronine (fT3, tT3), free and total thyroxine (fT4, tT4), and reverse T3 (rT3) concentrations than values reported for horses.29–31 No gender differences for thyroid hormones have been documented in donkeys. Similar to horses, young donkeys have higher fT4, tT4, and rT3 concentrations.31 Drugs such as phenylbutazone and dexamethasone reduce thyroid hormone (TH) concentrations in horses;32,33 however, their effects on asinine thyroid function have not been investigated. Their use could potentially lead to a misdiagnosis of hypothyroidism.

Parathyroid Gland
Serum total calcium, total magnesium, and phosphorus concentrations in donkeys are within the reference range of values reported for horses. One study found higher ionized calcium, complexed magnesium, and calcitriol concentrations but lower parathyroid hormone (PTH) concentrations and protein-bound magnesium in donkeys compared to horses.34 Nutritional secondary hyperparathyroidism may be seen in donkeys consuming diets with low calcium or high phosphorus content35 but also occurs with the ingestion of oxalate-rich plants.36 Clinical signs (facial swelling, lameness, upper airway stridor, and neurological signs), diagnosis, and treatment are similar to horses.

3. Pharmacology
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)
Most NSAIDs used in horses are metabolized faster in donkeys.37–49 Therefore, for many of these drugs to reach therapeutic levels, either the dose or dosing frequency will have to be increased.37 Phenylbutazone mean residence time (MRT) is shorter and clearance is faster in donkeys compared to horses.32,44 Miniature donkeys clear phenylbutazone even faster than average sized donkeys.44 Miniature donkeys will need more frequent dosing as higher doses could potentially lead to renal and gastrointestinal injury. Flunixin meglumine appears to have faster tissue penetration in donkeys than horses.37,45 Flunixin meglumine appears to have faster tissue penetration in donkeys than horses.37,45,52,53 This indicates that more frequent dosing will be required to achieve adequate analgesia with these drugs. Meloxicam reduces the systemic inflammatory response from endotoxemia in donkeys and could be a safer alternative to flunixin meglumine. In contrast to most NSAIDs, intravenous carprofen has a slower clearance and larger AUC in donkeys,43 while intravenous ketoprofen has faster clearance in donkeys than horses.48 Except for flunixin meglumine, NSAID pharmacokinetic studies in mules are lacking.

Sedatives, Analgesics, and Anesthetics
Donkeys and mules are considered stoic animals, and their response to pain may be subtle or go unnoticed, which could have negative consequences (e.g., hyperlipemia, laminitis). For this reason, analgesia is very important to ameliorate the pain-stress cycle. Sedatives and tranquilizers used in horses are routinely administered to donkeys and mules. The dose of α2-adrenoreceptor agonists (e.g., xylazine) often needs to be increased by 50% for pain management in donkeys.55 However, analgesia from xylazine is less intense and of shorter duration than for detomidine and romifidine.56 For these reasons, detomidine and romifidine have been proposed as better options for pain management in donkeys.56 Acepromazine provides satisfactory tranquillization in donkeys,57 although some donkeys may require twice the acepromazine dose used in horses to achieve good tranquillization. Acepromazine is not an effective analgesic.57 Butorphanol also enhances the sedative and hypoalgesic effects of α2-adrenoreceptor agonists in donkeys.58 Tramadol is an effective analgesic in donkeys.59 Transdermal fentanyl patches provide good pain relief in donkeys.60 Metamizole (dipyrone) has a shorter half-life in donkeys than horses.38 In donkeys, ketamine has a shorter half-life and faster clearance than in mules and horses.61 Guaifenesin (glyceryl guaiacolate) has a longer half-life in donkeys than horses, and recovery time could be prolonged, requiring close supervision in donkeys.62 Intravenous propofol is a safe option for anesthesia induction and maintenance.62 Propofol can be combined with ketamine to lower the dose, and this combination produces longer anesthesia time, better muscle relaxation, and smoother recoveries than ketamine alone.63 By reducing the dose, the propofol and ketamine or guaifenesin, ketamine, and xylazine

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combinations can be used to maintain anesthesia in donkeys.\textsuperscript{63,64} Thiopental is a good induction agent in donkeys and mules but is rarely used.\textsuperscript{63} Induction time is faster with thiopental, but recovery is quicker and better with propofol.\textsuperscript{65} Alfaxalone with midazolam time to induction is faster compared to ketamine and midazolam, but recovery time is shorter with the ketamine and midazolam combination.\textsuperscript{66} Induction and recovery with either combination is acceptable after sedation with xylazine.\textsuperscript{67} The combination xylazine, diazepam, and ketamine is effective and safe in donkeys and mules.\textsuperscript{63} Inhaled anesthetics such as halothane, isoflurane, or sevoflurane have similar properties in donkeys and horses.\textsuperscript{37} Epidural lidocaine provides good regional analgesia to donkeys, but morphine is less effective.\textsuperscript{37} Local anesthetics are used in a similar manner and appear to be equally effective in donkeys, mules, and horses.

**Antimicrobials**

Similar to NSAIDs, compared to horses, donkeys and mules have a faster metabolism for a number of antimicrobial drugs, with faster clearances, lower MRTs, and shorter half-lives.\textsuperscript{37,49} For most antimicrobials, donkeys and mules require higher doses or shorter dosing intervals.\textsuperscript{37,49} Aminoglycosides (amikacin and gentamicin) have similar pharmacology between horses and donkeys.\textsuperscript{40} Fluoroquinolones (enrofloxacin and marbofloxacin) are cleared slower in donkeys, and once-a-day dosing interval is preferred.\textsuperscript{47} For many other antimicrobials used in equine practice, information in donkeys and mules is lacking but necessary for better treatments. In addition to appropriate criteria for antimicrobial selection in donkeys is the implementation of antimicrobial stewardship practices to reduce bacterial resistance. Similar to other equids, donkeys are susceptible to the toxic effects of ionophores.

**Antiparasitic Drugs**

Caution must be taken when using macrocyclic lactones (ivermectin, moxidectin, abamectin, eprinomectin) in donkeys, particularly those in poor body condition due to the higher risk of neurotoxicity compared to horses.\textsuperscript{37} Imidocarb dipropionate is an effective treatment for piroplasmosis. Of interest, donkeys and mules are overly sensitive to this drug, and hepatic side effects can be observed.\textsuperscript{67} Doses for donkeys and mules should be lower than for horses. Imidocarb dipropionate toxicity results from acetylcholinesterase inhibition and premedication with anticholinergic drugs such as glycopyrrolate (0.0025 mg/kg/IV) or N-butylscopolammonium bromide (0.1–0.2 mg/kg/IV) 5 to 10 minutes prior to imidocarb administration is recommended.\textsuperscript{37} Fenbendazole is a benzimidazole commonly used against strongyles in horses, donkeys, and mules. Oral fenbendazole is not very effective at eliminating lungworms in donkeys and horses.\textsuperscript{40} Moxidectin (400 μg/kg, PO) is the treatment of choice for lungworms in donkeys.\textsuperscript{37} Pyrantel pamoate in paste and granule formulations have poor intestinal absorption in donkeys but good efficacy (＞95%) against intestinal strongylidae. Psoroptic and choriopthic mange is treated similar to horses (pyrethroids, sulfur, ivermectin, moxidectin, eprinomectin).

**Other Drugs**

Prokinetic drugs such as lidocaine, metoclopramide, and cisapride are occasionally used in donkeys under protocols similar to horses, but pharmacological information, including efficacy studies, is lacking.

### 4. Summary

The evolution of the donkey occurred under environmentally harsh conditions, leading to adaptations for energy conservation, including the ability to digest poor-quality feedstuff, a unique capacity to accumulate adipose tissue, and efficient fat mobilization under increased energy demands or food scarcity. These features also predispose donkeys to obesity, dyslipidemias, insulin dysregulation, metabolic syndrome, pituitary pars intermedia dysfunction, and endocrinopathic laminitis. Endocrine and metabolic diseases are frequent in donkeys. Differences in hormone dynamics and testing protocols for endocrinopathies between donkeys and horses support species-specific approaches for appropriate diagnosis and treatment. In addition, donkeys and mules have distinct pharmacological features leading to differences in the way they metabolize and respond to drugs used in equine practice. Most of these drugs work well and are safe for donkeys and mules; however, some when used under equine protocols can lead to subdosing, overdosing, toxicities, and even death. Therefore, a basic knowledge of drugs used in horses, donkeys, and mules is important.

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**Declaration of Ethics**

The Authors have adhered to the Principles of Veterinary Medical Ethics of the AVMA.

**Conflict of Interest**

The Authors have no conflicts of interest.

### References and Footnotes


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