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Review Article

Donkey Internal Medicine—Part I: Metabolic, Endocrine, and Alimentary Tract Disturbances

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ABSTRACT

Metabolic and endocrine disturbances are common in donkeys. This species has an inherent ability to thrive with limited and poor-quality roughage. Donkeys are extremely efficient in energy storage and mobilization, which predisposes to hyperlipemia, obesity, and metabolic syndrome. The prevalence of dyslipidemias is higher in donkeys than other equids, which is more evident under stressful conditions. Diagnosis of endocrine and metabolic disorders in donkeys should be based on species-specific information considering that differences in a multitude of variables compared with horses have been demonstrated. Protocols to assess endocrine disorders (e.g., pituitary pars intermedia dysfunction, metabolic syndrome, and thyroid illness) are unavailable, and extrapolation from horse data can be misleading. Treatment guidelines for these conditions in donkeys are currently not reported. On the other hand, the typical stoic and hardy behavior of donkeys can hinder prompt diagnosis of gastrointestinal problems, specifically colic, which is commonly caused by dental issues in this species. Moreover, subclinical gastric ulcer syndrome appears to be a common pathology in this species, especially in working donkeys.

1. Introduction

In 2000, the world donkey population was estimated at 43.5 million, but by 2006, it was 41 million (5.7% reduction). Although donkeys are frequent in Africa, Asia, and the Middle East, in some regions with ancestral donkey tradition (Southern Europe), the local populations has shrunk by 80%–90%, with some breeds at the edge of extinction. The industrial revolution, new methods of transportation, cultural changes, and human migration are key factors behind this reduction.

Ironically, despite their central contribution to human civilization, donkeys are often poorly appreciated, overworked, or neglected. Their tolerant and stoic demeanor, capacity to survive with poor-quality diets, resistance to diseases, and tolerance to hard work have turned the donkey into the preferred species for pack and draught work, particularly in remote areas. There is a belief that donkeys are highly tolerant to pain and are stubborn/stupid, which is a misconception. This is based on a noticeable donkey resistance to painful and frightening situations, being their reaction commonly subtler than horses [1,2].

While donkeys' role as a working animal has been largely replaced since the industrial revolution, new utilities for this species have been found. Outdoor activities such as ecotourism, trekking, or hippotherapy/onotherapy have been increasing steadily in recent years. Donkeys are also used as a source of meat and milk, and donkey byproducts can be found in expensive cosmetic products [2,3]. Finally, some people, particularly in developed countries, are maintaining donkeys as companion pets.

The increased awareness for the well-being and care of these animals has also risen the demand for specialized veterinary services, with a growing number of donkeys being admitted to veterinary facilities.

When facing the diagnosis and treatment of donkeys' pathologies, the clinician should keep in mind that there are marked differences between donkeys and horses. Extrapolating clinical data, treatment, and diagnostic protocols from horses to donkeys could lead to misdiagnosis and unnecessary or inadequate treatments [4–7]. Of special interest are pharmacological dissimilarities between donkeys and horses, with a number of drugs having different kinetics, which in most instances goes unnoticed. However, the lack of this knowledge could have undesirable results [8].

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In this review, we provide information on unique donkey characteristics that are relevant to several equine medical specialties, contrasting differences with other equids. Specifically, this review will focus on metabolic diseases such as dyslipidemias and metabolic syndrome; endocrine disturbances such as pituitary pars intermedia dysfunction (PPID); and gastrointestinal disorders such as gastric ulcers, dental problems, and small or large colon disturbances.

2. Metabolic Disturbances

2.1. Dyslipidemias

Their evolutionary adaptations to harsh environmental conditions and ability to thrive with limited and poor-quality roughage have turned donkeys into highly efficient animals for energy storage and mobilization. This efficiency has also made them prone to pathological conditions associated with negative energy balance, in particular those related to excessive lipolysis, excessive hepatic triglyceride synthesis, and release into systemic circulation (dyslipidemia), with serious systemic consequences. Dyslipidemias in donkeys occur secondary to physiological (pregnancy, lactation, and food deprivation) and pathological (stress, gastrointestinal disease, endotoxemia, respiratory problems, liver diseases, parasitism, laminitis, and so forth) processes linked to a negative energy balance. No primary causes of dyslipidemia (as seen e.g., in cats) have been reported in donkeys. Liver disease (19.4%) followed by colic (13.8%) were the most common primary conditions in a study of 449 dyslipemic donkeys [9].

Prevalence of dyslipidemias is higher in donkeys (10%–20%), especially in miniature donkeys, than horses and ponies [10]. This predisposition is more evident in obese, pregnant, lactating, and older animals, perhaps due to reduced insulin sensitivity [11,12], although dyslipidemias can also occur in nonobese donkeys. Because hyperlipemia is associated with a poor outcome in hospitalized donkeys (mortality rates up to 80%), energy balance should be monitored in sick animals early on to avoid excessive lipolysis and hypertriglyceridemia [13].

Depression and anorexia are common in hyperlipemic donkeys. Hyperlipemia can be suspected based on clinical signs, plasma, or serum turbidity but is confirmed by measuring serum triglyceride concentrations. There are point-of-care sensitive triglyceride analyzers available in the market [14], which could be recommendable for farms with large number of donkeys. Clinicians should also know that because the upper reference limit for triglyceride concentrations (248 mg/dL) is higher in healthy donkeys than horses and ponies [15], the accepted definitions for hypertriglyceridemia (<500 mg/dL) and lipemia/hyperlipemia (>500 mg/dL) in horses and ponies may not be suitable for donkeys.

High leptin concentrations have been found in postpartum hyperlipemic mares (>5 ng/mL) [16] and could be expected in hyperlipemic donkeys. Serum leptin concentrations in healthy donkeys (2.7 ± 0.3 ng/mL) are similar to values reported for horses [15]. Sorbitol dehydrogenase, aspartate aminotransferase, gamma-glutamyl transferase, bile acid, creatinine, and urea can also be elevated in dyslipemic donkeys, indicating liver or kidney dysfunction [12]. Cholesterol, very low-density lipoprotein (VLDL), high-density lipoprotein, and nonesterified fatty acid concentrations could yield valuable information in dyslipemic donkeys although they are not routinely measured [17]. Finally, it is important to emphasize that some of these parameters could be falsely increased/decreased due to interferences of lipemic sera on analytical tests.

Although an exhaustive description of the pathogenesis of hyperlipemia is not the scope of this review, briefly, once hormone-sensitive lipase starts body fat mobilization, free fatty acids (FFAs) are released to the bloodstream, and the liver begins to reesterify FFA into triglycerides or VLDLs. Unlike ruminants and cats, the liver of equids does not produce ketone bodies. If lipolysis persists, plasma triglycerides levels increase (hyperlipemia), resulting in macroscopic lipemia (from turbid to creamy plasma) and ultimately fatty infiltration of multiple organs (most commonly the liver, but also kidneys, intestine, pancreas, heart, and skeletal muscle). Severe liver infiltration, in addition to causing dysfunction may lead to hepatic rupture. Cortisol, which increases in stressed animals, may contribute to the development of hyperlipemia by activating hormone-sensitive lipase, fat mobilization [18,19], impairing triglyceride clearance by lipoprotein lipase [10], and reducing insulin sensitivity, emphasizing the relevance of stress as a risk factor for this condition in donkeys [20]. Transport can be stressful for donkeys, and some animals may develop hyperlipemia after transportation [21]. Hormone-sensitive lipase can also be activated by catecholamines, some interleukins, glucocorticoids, adrenocorticotropic hormone (ACTH), and glucagon and is inhibited by insulin [22].

Therapeutic principles for hyperlipemia in equids can be applied to donkeys. These include treatment of the primary problem (colic, pleuropneumonia, and so forth), reducing stress and resolving any condition causing a negative energy balance (e.g., parasites), as well as close monitoring of pregnant and lactating animals [22].

High-calorie foods (i.e., honey) should be administered to prevent FFA mobilization and stimulate insulin release. Enteral feeding via a small-bore nasogastric tube could be considered if the primary condition allows it. If there is intolerance to enteral feeding and hyperlipemia persists, partial parenteral nutrition is indicated [23]. Considering that basal energy requirements are lower in donkeys than horses and even lower in sick donkeys, it is advised to start parenteral nutrition with a low percentage of the estimated needs. There are several reports on the use and efficacy of parenteral nutrition in hyperlipemic donkeys [22,24]. If hypertriglyceridemia persists after 24 hours of treatment or hyperglycemia develops, 0.1 IU/Kg/hr insulin should be administered, joined by a close glycemic control to avoid hypoglycemia and/or regulate insulin dosage. High levels of insulin could have deleterious effects, such as laminitis secondary to hyperinsulinism [25]. Animals with insulin dysregulation (ID) are prone to hyperlipemia, and there is a correlation between triglycerides and insulin levels [26]. Insulin could be administered to inhibit the hormone-sensitive lipase activity. Protamine zinc insulin (40–60 IU IM) administration has been described in a hyperlipemic jenny [22]. Human recombinant insulin can also be administered intravenously to regulate the glycemia when parenteral nutrition is started.

Regular heparin or low molecular weight heparin (LMWH) also increases lipoprotein lipase activity and, although one study proved this activity to be maximal in ponies with hyperlipemia [27], the lack of data in healthy or sick donkeys precludes any recommendation/opposition for this species [28]. Heparin sulfate (25,000 IU, IV) administration has been reported in a hyperlipemic jenny [22]. Authors use dalteparin or enoxaparin (LMWHs) at a similar dose regimen as described for horses as a treatment option.

Finally, nicotinic acid is administered to people to reduce lipolysis and VLDL synthesis [29], but its use and efficacy in donkeys remains to be evaluated [23].

2.2. Donkey or Asinine Metabolic Syndrome

Donkey or asinine metabolic syndrome (DMS) is the compendium of ID, recurrent laminitis and obesity. Each one of these disturbances can also be observed individually and therefore

independently of DMS. Accordingly, not every fat donkey must suffer DMS, and lean donkeys can also develop DMS. The terminology of DMS is similar to equine metabolic syndrome (EMS) because the same disturbances are observed in this species.

Obesity is a common disturbance in donkeys in developing countries (Figs. 1 and 2). This species is highly efficient in using low-quality feedstuff and has lower energy requirements than horses. When able to access to high-quality or calorie-rich feed, donkeys are prone to accumulate adipose tissue, even without overfeeding. In that sense, they can be considered easy keepers.

When assessing body condition score (BCS) in donkeys, morphologic differences with horses should be considered. Because fat distribution is different between these species, BCS scoring system developed for horses [30] must not be used in donkeys. A donkey-specific BCS system ranging from 1 to 9 points (<3 = underweight; 4–6 = optimal condition; and >7 = overweight) has been published [31]. Also, formulas and tapes to estimate body weight in horses should not be used in donkeys [31].

Similar to BCS, neck scoring system for horses [32] should not be applied to donkeys because they have different neck morphology and distribution of fat deposits. A neck scoring system was recently reported for donkey [15]. This score ranges from 0 (thin neck without palpable crest) to 4 (thick neck, rounded and gross cresty).

Similar to horses, a link between obesity, ID (peripheral or tissue insulin resistance), and recurrent laminitis (endocrinopathic laminitis) is evident in donkeys [33] (Figs. 1 and 2), but unlike horses, a direct link between hyperinsulinemia and laminitis has not been demonstrated yet [25]. However, compared with horses, information on metabolic syndrome and ID in donkeys is limited. Other signs of EMS reported in horses, such as hypertension or reproductive disturbances, have not been documented in donkeys. Nonetheless, according to the authors' experience, obese jennets can display reproductive problems in a similar manner to obese mares [34].

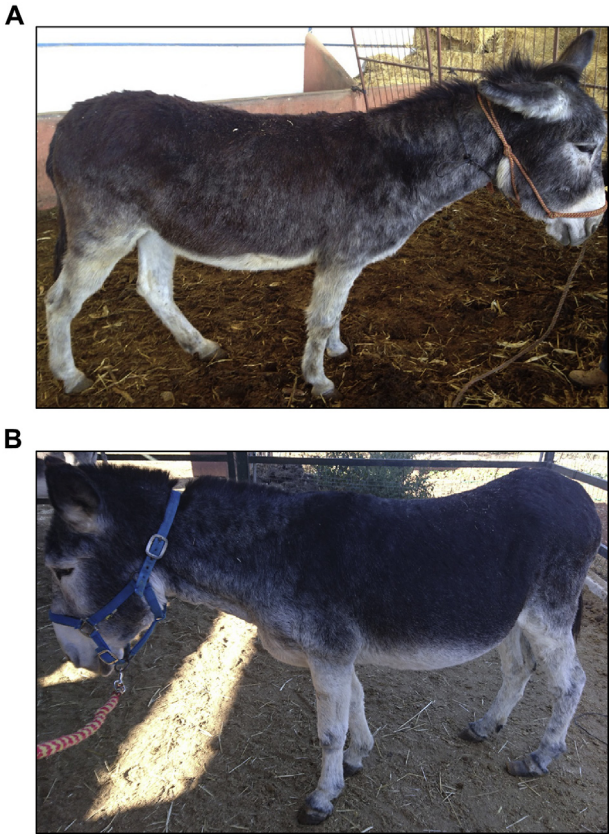

Fig. 1. (A) Six-year-old Andalusian jenny with obesity. Body condition score of 8/9 and neck score of 4/4. (B) Eight-year-old Andalusian jenny with metabolic syndrome. Note the obesity (BCS: 8/9 and neck score 4/4) and long left hindlimb hoof. BCS, body condition score.

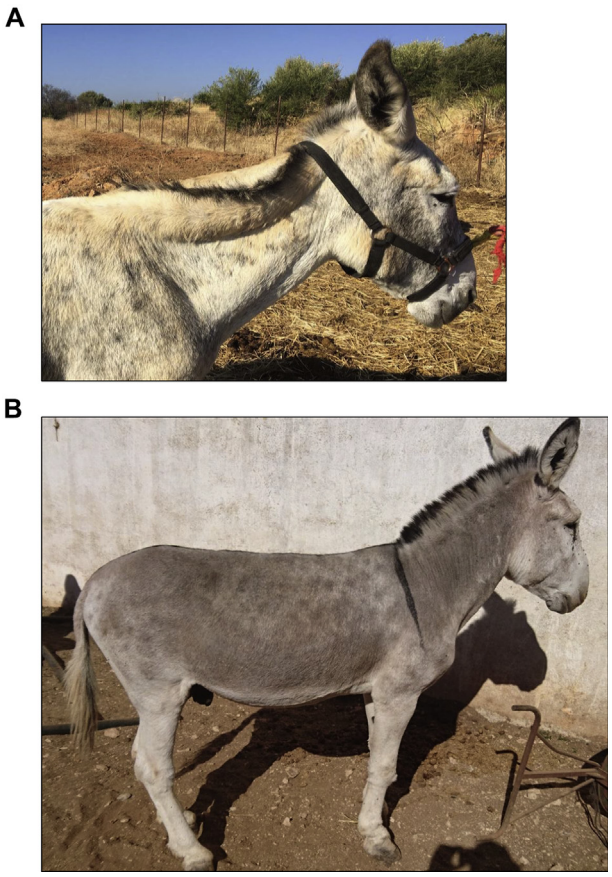

Fig. 2. (A) Twelve-year-old Andalusian jack. Neck score 4/4 (cresty neck appearance). (B) Nine-year-old Andalusian jack with chronic bilateral forelimb laminitis. Hindlimb are positioned under the body to diminish the weight burden on forelimb.

When measuring metabolic parameters in donkeys, it should be noted that many of them may differ with gender [35,36]. For example, healthy nonpregnant jennies have lower glucose and higher triglyceride concentrations than males [15], likely secondary to the effect of sexual hormones on fat distribution and mobilization. Jennies also tend to gain more weight and accumulate more fat than males. Based on the frequently sampled intravenous glucose-insulin tolerance test (FSIGTT), jennies have also proven to show lower insulin sensitivity, thus they could potentially be more prone to disorders linked to ID [33].

Similar to horses [36], geriatric donkeys have lower insulin concentrations, which could be linked to reduced β-cell mass or β-cell sensitivity to glucose [15].

Insulin dysregulation diagnosis in donkeys should be focused on determining basal concentrations of fasting glucose and insulin and performing dynamic tests, although in some cases calculating glucose surrogates could also be useful. According to our clinical experience, factors interfering with this diagnosis are similar to those described in horses (fasting, stress, transport, exercise, pain, current diseases such as acute laminitis, and so forth). Insulin dysregulation has not been thoughtfully studied in donkeys, although previous reports in donkeys [33] and horses [37] have correlated insulin levels over 20 μIU/mL with the presence of laminitis. However, the new guidelines for horses indicate a cutoff

value of 50 μIU/mL for ID [38]. In view of this recent change, it is important to emphasize that donkeys with ID frequently show higher insulin plasma concentrations than horses with ID (personal communication). While lacking more deliberate and species-specific studies, this cutoff insulin level could also be used for the diagnosis of ID in donkeys, taking into consideration both inter-assay and interlaboratory variability.

Reference values for glucose ratios and surrogates in healthy donkeys have been recently described [39]. Reciprocal of the square root of insulin (RISQI) and quantitative insulin-sensitivity check index were similar to horses, but the modified insulin to glucose ratio (MIRG) was higher in donkeys [35]. A higher MIRG could indicate a higher β-cell function in this species [40,41]. Moreover, RISQI and MIRG have also been described in obese and laminitic donkeys [33].

When dynamic tests are used in donkeys, specific protocols should be used [39]. In donkeys, the combined glucose-insulin test (CGIT), intravenous glucose tolerance test (IVGTT), and oral glucose tolerance test have been proved to be different to horses, showing a right-shifted glucose curve in donkeys [42–46]. These results advise a delayed blood sampling in donkeys, at 60–75 minutes for the CGIT and at 150–180 minutes for IVGTT. For every test, it is recommended to allow access to a hay flake the night before to reduce stress and avoid hyperlipemia.

Other dynamic tests such as FSIGTT had results comparable between both species when BCS were similar [35]. Intravenous insulin tolerance test has also been characterized in donkeys but only in 3 days fasting animals, showing a diminished glucose recruitment [47]. This finding could also be related to the high frequency and rapid evolution of hyperlipemia in donkeys.

Donkeys with higher BCS and neck score have higher plasma leptin concentrations [15]. If jennies and males with similar BCS are compared, jennies had higher leptinemia. Older donkeys also have higher leptin levels than younger ones. These results could link this hormone to metabolic disturbances and emphasize its importance because hyperlipemia, ID, and endocrinopathic laminitis are more common in female and older donkeys. Leptin resistance could be a contributing factor to these findings, which tend to be more severe in donkeys than horses [48]. No leptin cutoff value has been established for donkeys, which should be of interest to determine animals at risk of ID, laminitis, and metabolic syndrome. Adiponectin, glucagon, ghrelin, and insulin growth factor 1 plasma concentrations as well as their associations with age, sex, and obesity have also been recently reported in healthy donkeys [15]. These parameters, similar to leptin, could be used as biomarkers for DMS, but information on their changes in sick donkeys is not available.

Incretin hormones (glucose-dependent insulinotropic peptide and glucagon-like peptide-1) released by the intestine have been described to regulate insulin secretion from pancreatic β-cells [49]. Because higher blood concentrations have been demonstrated in hyperinsulinemic horses and ponies, these hormones could also potentially be novel ID biomarkers [50,51].

As long as species-specific indications for the treatment of metabolic syndrome in donkeys are not available, the same basic principles applied to horses with EMS could be used. Thus, drugs and dose regimens are usually extrapolated from horses. When facing endocrine laminitis in donkeys, treatment and diagnosis are not well studied.

When a weight-loss diet is intended for donkeys, their inner capacity of subsisting on poor-quality and low-quantity feedings should be considered (even soaking the feedstuff). Commercially available diets to promote weight loss in horses with metabolic disorders and laminitis may not be appropriate for donkeys because they provide an excess of calories and protein to donkeys. Whenever possible, and in the absence of laminitis, donkeys should be kept in a paddock, allowing them to do some exercise. Nonetheless, when these animals pass a long time in the paddock, they tend to focus on grazing and, due to their ability to ingest high quantities of dry matter in short times, the final objective could not be reached. Due to the intrinsic gregarious behavior of donkeys, the presence of other animals (either donkeys or horses) in the paddock is recommended. Moreover, the presence of other equids could avoid stress and even favor exercise. Grazing should be avoided during the morning (even more in spring) or after rainfall. A muzzle could also be useful in certain conditions. A weight-loss program in donkeys is a slow and patience-demanding process, where losing a 2% bodyweight per month (similar to horses) could be a reasonable goal, although a specific weight-loss program has not been developed for this species.

The effect of levothyroxine sodium administration in donkeys has not been evaluated. It is assumed that doses similar to those used in horses could be used. Metformin pharmacokinetics data are lacking in donkeys. However, a dose of 30 mg/kg/PO q12 hours, has been reported [52]. Other drugs such as pioglitazone or glyburide have not been evaluated in donkeys yet.

3. Endocrine Disorders

3.1. Thyroid Gland Diseases

Information on thyroid diseases of donkeys is lacking. Whether this is due to a low prevalence (similarly to horses) or lack of recognition is unknown. Histological findings consistent with hypothyroidism were described in 4 out of 10 adult donkeys suffering from hypothermia [53]. However, histology is not related to thyroid function or hormones concentrations, and they were not measured in that report.

Few studies have evaluated thyroid hormone (TH) concentrations in donkeys [6]. Donkeys have higher plasma f triiodothyronine (fT3), tT3, fT4, tT4, and reverse T3 concentrations than horses [6]. Considering this finding, reference ranges for horses should not be extrapolated to donkeys because this could lead to a hyperthyroidism misdiagnosis in healthy animals or a fail to recognize hypothyroidism in this species. In addition, because these concentrations can greatly vary depending on laboratory techniques [54–56], clinicians should be familiar with the specific methodology used by their laboratory. Thyroid dynamic tests (thyrotropin-releasing hormone stimulation test, thyroid-stimulating hormone stimulation test, and T3 suppression test) are not characterized in donkeys, and protocols for these tests remain to be established. A better knowledge of hypothalamic-pituitary-thyroid axis physiology could improve our ability to diagnose and treat sick animals.

Age and sex effects on THs have been studied in donkeys. Sexual dimorphism for these hormones has not been demonstrated in donkeys, and its existence is currently unclear in horses [57,58]. Age, in a similar way to horses [59], affects THs, and younger animals have higher reverse T3, fT4, and tT4 levels [6]. This finding could be related to the role of THs in growth, development, and tissue differentiation.

As seen in several species, drugs such as phenylbutazone, dexamethasone, and sulfonamides can modify THs concentrations, competing with transporting proteins or inhibiting thyroid peroxidase enzyme [60–62]. While this principle has not been demonstrated in donkeys, it would be advisable to verify any previous treatment in donkeys before the measurement of these parameters. A prudent clinician should also avoid treatment with the mentioned drugs for a month before thyroid evaluation, discarding false hypothyroidism diagnoses.

3.2. Pituitary Pars Intermedia Dysfunction

Surprisingly, although PPID is suspected to be frequent in donkeys, epidemiological information on PPID in donkeys is lacking.

In donkeys, as observed in horses [63], PPID is more common in older animals (>15 years). No sex or breed predispositions have been demonstrated. Clinical signs are similar in both species. Hypertrichosis is the most common sign although it is occasionally difficult to prove in some breeds due to their hair length. Hyperhidrosis (mostly in summer), laminitis, ID, abnormal fat distribution, and muscle wasting (sarcopenia with a striking pot-belly morphology) are other clinical signs observed in donkeys with PPID (Fig. 3). Polyuria is rarely seen in affected animals. Other signs described for horses (reproductive disturbances, blindness, illness predisposition mainly to infectious and parasitic diseases, bone fractures, and neurological abnormalities) have not been reported in donkeys [63]. Some typical horse signs, such as lethargy, could be easily misdiagnosed in donkeys, due to their characteristic demeanor.

PPID diagnosis in donkeys is commonly empirically extrapolated from protocols oriented to horses [63], using primarily a basal ACTH determination and performing a dynamic test in doubtful cases. Well-designed studies about cutoff values for cortisol and ACTH in this species (also considering seasonal variations) as well as validation of dynamic tests are still needed. Samples for PPID diagnosis should not be taken in animals exercising, suffering acute laminitis, or any other source of pain or stress. Hypercortisolemia is a rare finding in donkeys (personal communication), as previously described in horses [64]. Normal plasmatic cortisol levels are similar in both species [65]. Whether these values are affected by season, as reported in horses, is still uncertain in donkeys.

On the other hand, ACTH levels in healthy donkeys are markedly higher than those in healthy horses [65]. Furthermore, in PPID donkeys, ACTH serum concentrations are frequently higher than in PPID horses. In view of these differences, caution should be taken when extrapolating adrenal axis data from horses to donkeys because we could mistakenly diagnose PPID in a healthy donkey.

In doubtful cases where ACTH concentration is not high enough (early state of the disease), dynamic tests are recommended. Nonetheless, to our knowledge, those tests have not been validated for donkeys. Preliminary data from our research group indicate that thyrotropin-releasing hormone stimulation test should be used preferably in the diagnosis of PPID in donkeys [66], in accordance with the guidelines for the diagnosis of PPID in horses [67].

Fig. 3. Sixteen-year-old Andalusian jenny with pituitary pars intermedia dysfunction. Note the pot belly appearance and dorsal muscle sarcopenia.

Pharmacokinetcs studies for the most commonly used drugs against PPID in horses, such as pergolide, bromocriptine, or cyproheptadine, have not been carried out in donkeys. However, dose regimens reported for horses are being used satisfactorily in PPID donkeys. Anorexia secondary to metformin administration is more commonly observed in donkeys than horses, and sugar-free jam or carrots can be used to give the medication. Sweet flavored meals (i.e., honey or sugar) should be avoided due to the risk of laminitis. When anorexia is too marked, dosage can be lowered or treatment can be halted during several days. Once or twice a year, basal ACTH should be determined in treated donkeys to verify the efficacy of the treatment or readjust the dose of metformin. There are no data available on the percentage of donkeys suffering hypercortisolemia and thus the use of competitive 3β-hydroxysteroid dehydrogenase inhibitors (i.e., trilostane) has not been tested in this species.

4. Alimentary Tract Disturbances

4.1. Dental Diseases

Dental abnormalities are at least as frequent in donkeys as in horses. Because donkeys are not normally used as riding animals, dental disturbances can be unnoticed for the owners until severe secondary problems appear (Fig. 4A). High morbidities have been reported in older donkeys (90%), therefore an annual oral examination is recommended. Diastemata (>50%), wave mouth, and displaced teeth (>40%) are common problems, and frequent complications include weight loss, colic, hyperlipemia, and oral pain [68,69]. Histologically and anatomically, donkeys' and horses' teeth are similar [69]. Congenital deformities of the upper alimentary tract have been described in donkeys and mules, including bifid tongue, and cleft of the mandible, lip, or palate [70,71]. Donkeys are prone to sialoliths although the cause is unclear [72].

4.2. Gastric Diseases

Donkeys are typically stoic and hardy. Intense training, riding, and competition are not common practices in this species, therefore performance loss is not a typical clinical sign of gastric ulcers in this species. Similarly, donkeys are usually fed a forage-based diet and only rarely high quantities of grain or mixed feeding. The aforementioned factors could make us think that gastric ulcers are an uncommon finding in donkeys [73]. Nothing is further from reality. Donkeys are animals that are highly prone to stress although the triggering situation is commonly different to the typical examples in horses (competition and training). For a donkey, as a markedly gregarious animal, transport, estrangement from their paddock-mates, allocation in an isolated paddock, mixing with unknown individuals, or separation of the jenny from her foal could be the most illustrative examples of stressful events compared with training or competition in horses. In modern countries, overfeeding and grain overloading are also predisposing factors for the development of gastric ulcers both in donkeys and horses. Nonsteroidal anti-inflammatory drug (NSAID) administration and other comorbidities such as hyperlipemia and renal disease have also been described as predisposing factors. Recurrent colics (that are even unnoticed for the owner due to donkeys' stoicism), weight loss, or general poor condition are the most common clinical sings observed in donkeys suffering of gastric ulcers. However, no evident clinical signs are also frequent in affected donkeys.

Incidence of gastric ulcers has been proven to be higher in living (51%) [74] donkeys in a study than those carried out on sacrificed or euthanized animals (40%) [75,76]. Sex, breed, or age is not a

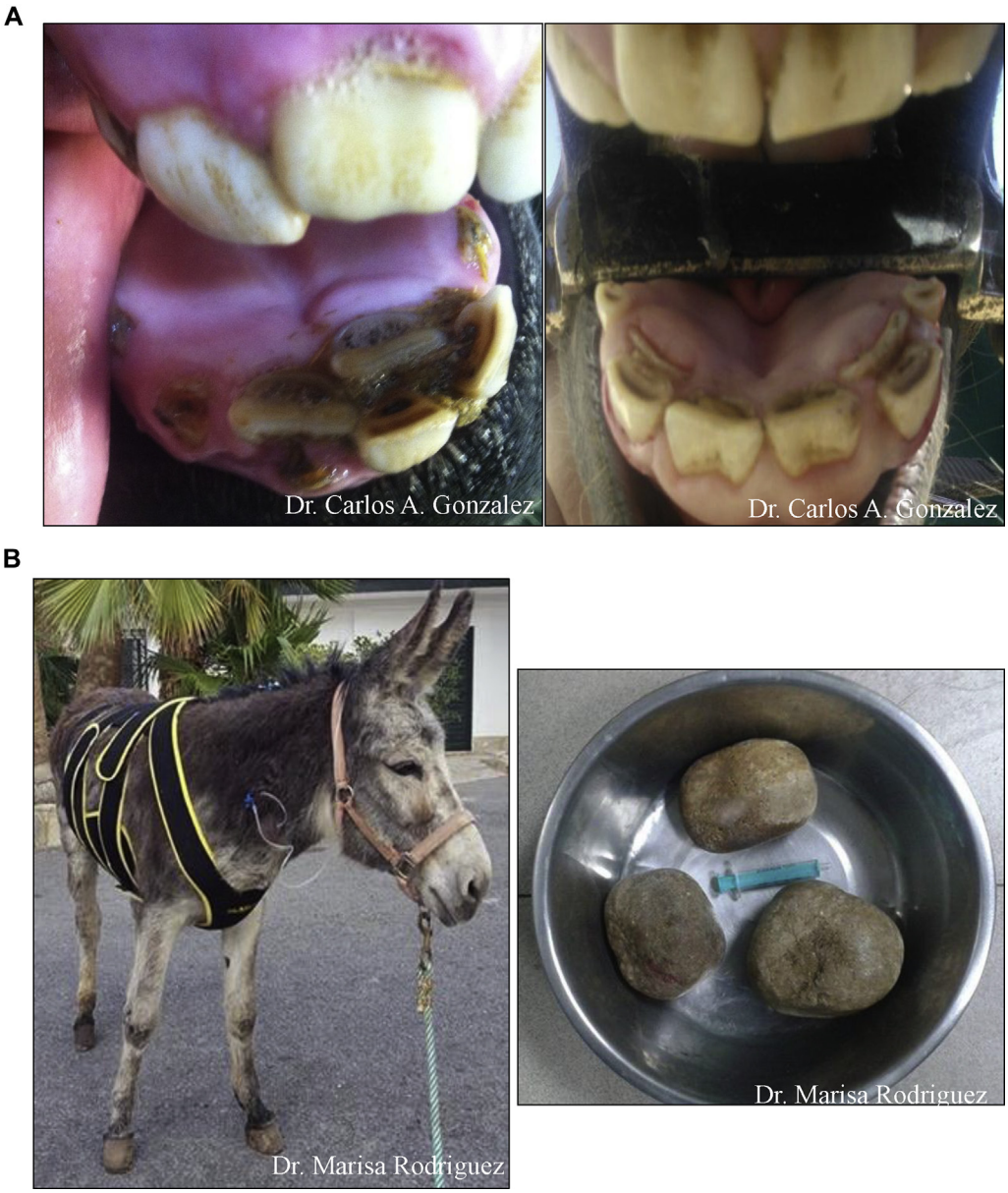

Fig. 4. (A) Incisive retention in two Andalusian jennies. One and a half-year-old on the left and 2.5-y-old on the right (Courtesy of Dr Carlos A. Gonzalez, University of Cordoba, Spain). (B) Six-year-old Andalusian jack after colic surgery due to enteroliths. Note the size of some of the removed enteroliths. (Courtesy of Dr Marisa Rodriguez, Hospital Veterinario San Vicente, Alicante, Spain).

significant factor for developing gastric ulcers. Horse score system [73] can be extrapolated to donkeys [74]. Lesions, as stated for other authors [74–76], are commonly located on the squamous area along the margo plicatus. Al-Mokaddem et al., (2015) also studied the effect of several parasites on gastric ulcers [76]. They found that *Habronema* spp., *Draschia megastoma*, *Gasterophilus* spp., and *Trichostrongylus axei* have only a residual role in the appearance of gastric ulcers in donkeys (Supplementary Material 1). Anecdotally, we have observed in dapple-gray donkeys an intense black mucosal pigmentation during gastroscopies (Supplementary Material 2). This finding was commonly located in the proximal part of the esophagus (near the proximal sphincter) and can be likely a melanin-pigmented area. Motility was normal in every animal with this lesion. Donkey-specific information on drugs that influence gastrointestinal function, gastric acid secretion, or gastric mucous healing is scarce. Omeprazole (4 mg/Kg/PO q 24 hours for a month), the most common gastric ulcers treatment, is often used following dosing protocols for horses, but this drug has not been studied in donkeys at this time.

Phytobezoars show a similar clinical presentation to gastric ulcers in donkeys and have also been reported secondary to persimmon ingestion [77]. Diagnosis via gastroscopy and the administration of cola beverage via nasogastric tube solved the problem in two cases [77]. Similar treatments as used for horses are recommended.

4.3. Small and Large Colon Intestinal Diseases

The use of an abdominal pain scale is unhelpful in donkeys [78]. Rolling is uncommon in donkeys with abdominal pain, even when severe lesions are present. Some animals with strangulating lesions may be dull, inactive, appeared tucked up, continue grazing, but

rarely, they show the typical pawing and rolling observed in horses or lie down. Heart rate would not be used for colic classification and surgery decision in donkeys. For equivalent intestinal lesions, donkeys usually exhibit less pain than horses, a factor that should be taken into consideration when deciding on exploratory laparotomy.

Colon impaction incidence is high in donkeys (50% of the colics seen in one study), with a 51% mortality rate [79]. This reported that high mortality could be influenced by the population used in the study (animals in a charity center, with over-represented geriatric patients) and surgery unavailable. Main predisposing factors for colon impaction in donkeys are dental pathologies, limited pasture and water access, limited exercise, concentrate feeding, and old age (maybe due to dental problems being more common in older donkeys) [80]. More commonly affected region is the pelvic flexure (51%) [80]. Treatment choices and specifications are similar between horses and donkeys for colon impaction.

Another common cause of colic in donkeys is enteroliths (Fig. 4B). This condition is more common in certain geographical areas where donkeys have access to hard water, and their nutrition is rich in alfalfa (i.e., Mediterranean basin regions or California) [81]. Abdominal digital radiography is the preferred imaging diagnostic method, showing higher sensitivity (84%) than non-digital methodologies (76.9%) [82].

Although donkeys are colonized by similar parasites than horses, the parasite burden is commonly higher (especially in nondeveloping countries), which surprisingly is not correlated with clinical signs or BCS, pointing to some degree of resistance [83]. Colic secondary to mesenteric arterial obstructions due to *Strongylus vulgaris* larval migration remains a problem in developing countries [84,85], where animals are seldom dewormed or are not dewormed at all [85].

Necrotizing enteritis due to an equine coronavirus infection has been described in one donkey [86]. Acute onset of clinical signs (depression, colic and more rarely neurologic symptoms such as head pressing, circling, and seizures secondary to hyperammonemia) is common, with high mortality rates in the first 12–24 hours. Because patients commonly die before the etiologic confirmation, this pathogen should be kept in mind when facing an acute high mortality outbreak of colicky donkeys.

Colitis cases have also been reported in donkeys, with typical clinical signs of dullness, anorexia, mild colic, weight loss, and diarrhea [87]. Clinical pathology findings are commonly leucopenia/leukocytosis and hypoalbuminemia. Causes are similar to those described in horses: bacteria (mainly Salmonella and *Clostridium* spp.), virus (coronavirus), parasites (small and large strongyles), sand (Fig. 5A and Supplementary Material 3) and drug-induced (antibiotics and NSAIDs). Therapeutic management of colitis relies on the same principles applied to horses [87] because species-specific studies are not available for donkeys at this time. Treatment is focused on restoring adequate hydroelectrolytic and acid–base status, recovering oncotic pressure with colloids and/or plasma administration, dispensing toxin-neutralizing drugs (smectite, mineral oil, activate charcoal, or psyllium), removing antibiotics or NSAIDs if they are a suspected cause, promoting mucosal healing (misoprostol and omeprazole), and using antiendotoxic-acting drug (polymyxin B), NSAIDs such as pentoxifylline, and suitable antibiotic and local anti-inflammatory agents such as metronidazole. Acute laminitis secondary to colitis-induced endotoxemia should be also prevented with cryotherapy and LMWH, which also would help precluding disseminated intravascular coagulation. A positive energy balance is essential to prevent dyslipidemias.

Intraabdominal neoplasia can be seen in donkeys, typically accompanied by nonspecific and vague signs (inappetence, dullness, behavior changes, weight loss, and chronic colics).

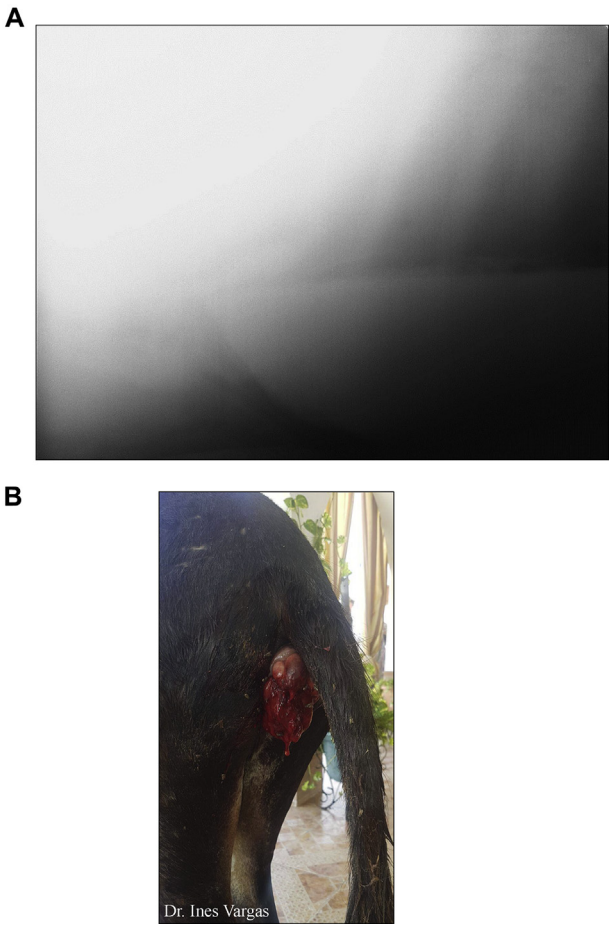

Fig. 5. (A) Lateral abdominal radiography of six-year-old Andalusian jenny with chronic soft feces history. Note the radiopaque appearance of the ventral colon compatible, with sand accumulation. (B) One-year-old mix-breed jack. First degree rectal prolapse secondary to colon impaction.
(Courtesy of Dr Ines Vargas, Seville, Spain).

Unfortunately, those same symptoms can also be observed in donkeys suffering dyslipidemias, colon impaction, or heavy parasitism, therefore ruling out those differential diagnoses is essential in these animals. A pancreatic adenocarcinoma has been reported in a 15-year donkey via laparoscopy [88]. Contrary to other equids with this kind of tumor [89], neither hepatic failure nor metastases were seen in that donkey. An adrenal cortical carcinoma has also been reported in a donkey with anorexia and depression, which died 24 hours after admission. Local invasion of the left kidney as well as metastases in liver, lungs, and heart were found at necropsy [90]. Lymphomas, metastatic gastric squamous cell carcinomas, and mesotheliomas have also been observed. Other neoplasia types have also been vaguely and sporadically described in this species [91].

Rectal prolapse (Fig. 5B) is a common condition, either due to management premises (especially in nondeveloping countries) or secondary to severe parasitosis (e.g., secondary to *Gasterophilus* spp. larvae [92]) or large intestine impaction. Treatment premises are similar to those described for horses.

4.4. Other Gastrointestinal Diseases

Blister beetle toxicosis can occur in donkeys with *Epicauta* spp. infested alfalfa, showing similar clinical signs to horses (gastroenteric signs, more rarely hematuria or cardiac disturbances) [93].

Hypocalcemia and hypomagnesemia have been seen in horses affected by Blister beetle toxicosis, but whether these findings can also be observed in affected donkeys is not known at this time.

Fluoride toxicity (secondary to excessive fluoride in drinking water), characterized by dark to brown dental discoloration, colic, diarrhea, lameness, hoof deformities, exostoses, and abortions has been described in donkeys [94,95].

Finally, donkeys with pyrrolizidine alkaloid poisoning can show signs of liver failure (as well as respiratory disease likely due to pneumotoxicity) [96,97].

5. Conclusions

Endocrine and metabolic diseases are frequent in donkeys. Because information on diagnostic tests and treatment premises is scarce for this species, clinicians should be cautious when extrapolating protocols and drug dosages between both species. In relation to alimentary tract disturbances, similar conditions can be observed in donkeys, but caution should be taken when facing colic in donkeys because they are stoic, and abdominal pain scales described for horses are unhelpful in this species.

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Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jevs.2018.02.001.

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