Vlaams Diergeneeskundig Tijdschrift

FACULTEIT DIERGENEESKUNDE
accredited by EAEVE

NOVEMBER-DECEMBER 2018
VOL. 87 - NR 6

VERSCHIJNT TWEEMAANDELIJKS
PUBLISHED BIMONTHLY
ISSN 0303 9021
WWW.VDT.UGENT.BE
GENT X

Afgiftekantoor 9099 Gent X
v.u. Luc Peelman
Salisburylaan 133 - B-9820 Merelbeke

UNIVERSITEIT GENT

VLAAMS DIERGENEESKUNDIG TIJDSCHRIFT

2018, vol. 87, nr. 6

INHOUD

Coverfoto: Nadia Eeckhout

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De laatste decennia worden ***varkens*** meer en meer ***als hobbydier*** gehouden. Er bestaan tientallen verschillende rassen. Het Vietnamese hangbuikvarken en de Kunekune uit Nieuw-Zeeland of kruisingen zijn zeer populair. Net zoals andere varkens beschikken ze over een uitstekend reuk- en gehoorvermogen. Ze houden ervan om te wroeten in de grond en te grazen. Soms kunnen ze dominant en zelfs agressief gedrag vertonen, vooral bij onaangepaste huisvesting en verzorging. De vruchtbaarheid is gelijkaardig als deze van commercieel gehouden varkens. De puberteit treedt echter iets vroeger op, de dracht is iets korter en de worpgrootte kleiner. Veel voorkomende gezondheidsproblemen zijn obesitas, overgroei van de klauwen, zonnebrand, ecto- en endoparasitaire infecties, diarree bij jonge biggen en tumoren bij oudere dieren (cf. pg 347).

Tekst: Dominiek Maes en Nadia Eeckhout

VLAAMS DIERGENEESKUNDIG TIJDSCHRIFT
ISSN 0303-9021
http://vdt.UGent.be

Hoofdredacteur en verantwoordelijke uitgever: Luc Peelman
Coördinator en eindredacteur: Nadia Eeckhout
Redacteur rubriek "Uit het verleden": Luc Devriese

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Druk: Graphius
Eekhoutdriesstraat 67, B-9041 Oostakker

Publiciteit:
Boerenbond – Media-Service, Diestsevest 40, B-3000 Leuven
Tel. 016 28 63 33

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Editor-in-chief and publisher: Luc Peelman
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Printed by: Graphius
Eekhoutdriesstraat 67, B-9041 Oostakker

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The use of desoxycorticosterone pivalate in dogs with hypoadrenocorticism: a retrospective study of eight cases

Het gebruik van desoxycorticosterone-pivalaat bij honden met hypoadrenocorticisme: een retrospectieve studie van acht gevallen

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ABSTRACT

In this article, the use of desoxycorticosterone pivalate is retrospectively reviewed in eight dogs with primary hypoadrenocorticism, presented at the Small Animal Department of Ghent University. The results showed that desoxycorticosterone pivalate provided adequate mineralocorticoid replacement in all cases, also in the dogs that had previously been treated with fludrocortisone acetate. A starting dosage of 1.5 – 2.2 mg/kg SC was used, with a fixed dosing interval of 28 days in most of the cases. Each time, prednisolone was added to the therapy as glucocorticoid supplementation. No side effects related to desoxycorticosterone pivalate therapy were noted and all owners were satisfied with the treatment consisting of desoxycorticosterone pivalate and prednisolone.

SAMENVATTING

In deze retrospectieve studie wordt het gebruik van desoxycorticosterone-pivalaat beschreven bij acht honden met primair hypoadrenocorticisme die aangeboden werden op de vakgroep Kleine Huisdieren (Faculteit Diergeneeskunde, UGent). Uit de resultaten bleek dat desoxycorticosterone-pivalaat adequaat was voor de supplementatie van mineralocorticoïden in alle gevallen, ook bij de honden die voordien behandeld werden met fludrocortisone-acetaat. Een aanvangsdosis van 1,5 – 2,2 mg/kg SC werd gegeven met een vast doseringsinterval van 28 dagen in de meeste gevallen. Ter supplementatie van de glucocorticoïden werd aan de behandeling telkens prednisolone toegevoegd. Er werden geen bijwerkingen gezien die aan desoxycorticosterone-pivalaat konden worden toegeschreven en de eigenaren van de honden waren allen tevreden over de behandeling met desoxycorticosterone-pivalaat en prednisolone.

INTRODUCTION

Canine hypoadrenocorticism (HA), also known as Addison's disease, is an uncommon endocrine disease with an overall prevalence of 0.13 to 0.5%, and with a higher prevalence in certain breeds (Reusch, 2000; Feldman and Nelson, 2004; Hanson et al., 2016). The majority of dogs with HA have primary HA, most often caused by an immune-mediated lymphocytic adrenalitis, resulting in both glucocorticoid (GC) and mineralocorticoid (MC) deficiencies (Peterson et al., 1996; Feldman and Nelson, 2004). There are no pathognomonic signs for HA. Usually, dogs present with a variety of non-specific, waxing and waning signs. Most often, these are gastrointestinal in origin, such as anorexia, vomiting and diarrhea, sometimes with associated blood loss. However, as the disease progresses, dogs can present in circulatory shock, i.e. acute Addisonian crisis. Azotemia and non-regenerative anemia are often noted, although an absent or reversed stress leukogram and hyperkalemia, often combined with hyponatremia, are more important features. A low sodium-to-potassium ratio of less than 27 to 1 is more specific. These findings, especially the abnormal serum electrolyte levels, can raise the suspicion of HA. However, an adrenocorticotropic hor-

mone (ACTH) stimulation test remains mandatory to confirm the diagnosis. Serum cortisol concentrations below 2 mcg/dL or 50 nmol/L before and one hour after ACTH administration are diagnostic (Peterson et al., 1996; Feldman and Nelson, 2004; Klein and Peterson, 2010a; Lathan and Thompson, 2018).

Short-term treatment of dogs with an Addisonian crisis includes aggressive intravenous fluid therapy with 0.9% saline and the administration of GC. If available, short-acting MC are given as well. Long-term treatment requires lifelong replacement of deficient MC and GC hormones. Fludrocortisone acetate (FC), a potent synthetic MC formulation with some GC activity, can be used orally at a starting dosage of 0.01 mg/kg twice daily (Feldman and Nelson, 2004; Meeking, 2007; Klein and Peterson, 2010b; Lathan and Thompson, 2018). Since 2016, desoxycorticosterone pivalate (DOCP) has been registered for the treatment of canine HA in most European countries by Dechra Pharmaceuticals (Zycortal®, United Kingdom). As DOCP only has MC activity, prednisolone must be administered daily. A starting dosage of DOCP of 2.2 mg/kg SC every 25 days is suggested by the manufacturer and has been reported by Feldman and Nelson (2004). Bates et al. (2013) and Lathan and Thompson (2018) have recently proven that lower dosages and longer dosing intervals of DOCP are effective as well. Likewise, at the Post Congress day of the European Society of Veterinary Endocrinology (ESVE) in Göteborg (2016), it has been suggested to use lower dosages at a fixed time interval of 28 days. According to Feldman and Nelson (2004), Klein and Peterson (2010b) and Lathan and Thomspon (2018), follow-up with a physical examination and the measurement of serum electrolyte concentrations should be performed 10 days and 25 days post injection, in order to determine the need for adjustment of the dosage and/or dosing interval. If potassium levels are high and/or sodium levels low at day 10, the dose of DOCP should be increased by 5 - 15%, whereas the dosage interval can be decreased by 1 - 2 days if this is noted at day 25 (or 28). If the potassium levels are low and/or sodium levels high at day 10, a dose reduction of 5 - 15% should be performed, and if noted at day 25 (or 28) the dosage interval can be prolonged by 1 - 2 days. This should be carried out until achieving stabilization of the DOCP dosage (Klein and Peterson, 2010b; Lathan and Thompson, 2018). Once the adequate dose and interval have been determined, the patient should be monitored twice a year with a physical examination and serum electrolyte measurement (Feldman and Nelson, 2004; Klein and Peterson, 2010b; Lathan and Thomspon, 2018). With appropriate treatment, prognosis is excellent, with normal quality of life and life expectancy in more than 80% of the treated dogs. However, timely diagnosis and treatment are important, as a lacking diagnosis can result in a fatal Addisonian crisis (Van Zyl and Hyman, 1994; Meeking, 2007; Klein and Peterson, 2010b; Lathan and Thompson, 2018).

MATERIALS AND METHODS

Case selection

Medical records of all dogs diagnosed with primary HA and treated with DOCP (Zycortal®, Dechra Veterinary Products NV, Lille, Belgium) at the Small Animal Department of the Faculty of Veterinary Medicine (Ghent University) between January 2016 and September 2017 were reviewed retrospectively. These included both newly diagnosed cases and cases that were previously treated with FC. Dogs were excluded if follow-up, including electrolyte measurement, was not available for at least one month.

Procedures

Signalment, history, physical examination, serum electrolyte concentrations, side effects of and response to therapy were extracted from the medical files. A standardized questionnaire was used to evaluate the owner's opinion concerning costs, number of control visits and blood draws, as well as the clinical condition of their dog during the treatment with DOCP and prednisolone.

Objectives

The objective of this retrospective study was to give a detailed description of the use of DOCP in a series of dogs with primary HA.

RESULTS

Signalment

The median age at presentation was four years (range 1 - 9 years). Five out of the eight dogs were male. All but one were pedigree dogs, of the following breeds: bearded collie, papillon, English cocker spaniel, Leonberger, standard poodle, Shih Tzu and Irish terrier.

History, clinical signs and physical examination at initial presentation

Six dogs had been newly diagnosed, of which five were emergency cases, presented with an acute Addisonian crisis. Of these five dogs, one dog presented with signs of hypovolemic shock, with severe hypotension and stupor, while the other four expressed signs of dehydration. Five newly diagnosed cases presented with acute lethargy and anorexia, although this was chronic in one new case. Vomiting was noted in four of them and polyuria/polydipsia was present in three cases. Three of these five dogs also had chronic and intermittent complaints, namely lethargy, intermittent anorexia, episodic vomiting and diarrhea or polyuria/polydipsia. The remaining two cases had been receiv-

ing GC and FC before presentation. Both dogs were monitored with frequent clinical controls and measurement of serum electrolyte concentrations. Both were switched to GC and DOCP due to insufficient control of the disease, manifested by vomiting, anorexia and lethargy in one case and persistent GC side effects (polyuria/polydipsia, polyphagia and/or poor skin condition) with abnormal electrolyte levels in both cases.

Laboratory findings at initial presentation

One dog showed mild regenerative anemia and all dogs had an absent or reversed stress leukogram. Five dogs had elevated levels of serum urea, of which one showed mild azotemia and two more pronounced azotemia. One dog was severely hypoglycemic and one dog presented with mild hyperalbuminemia. All dogs had abnormal serum electrolyte levels, six of which showed hyperkalemia and seven hyponatremia. In half of the cases, the electrolyte abnormalities were severe, with potassium values above 7 mmol/l in four and sodium levels below 125 mmol/l in one case (reference intervals 3.5 - 5.8 and 144 - 160 mmol/l, respectively).

Treatment

Stabilization and initial treatment with DOCP and prednisolone

Both dogs previously treated with FC and one other dog were not hospitalized at the time of the first DOCP injection. The other five dogs that suffered from an Addisonian crisis, were initially stabilized with adequate fluid therapy, using 0.9% saline. In four cases, IV boli of glucose 50% at 0.5 - 2 g/kg (Glucose Sterop 50 mg/ml, Laboratories Sterop, Brussels, Belgium) and in three dogs, short-acting human insulin at 0.1 IU/kg (Humuline Regular Cartridge 100 IU/ml, Eli Lilly Benelux NV, Brussels, Belgium) were administered. As a result, three of the hospitalized dogs had normal electrolyte levels at the time of DOCP administration, one still had slight abnormalities and in one case, it was not remeasured. The starting dosage of 2.2 mg/kg SC, as prescribed by the manufacturer, was given to six dogs, while two dogs received a lower starting dosage of 1.5 mg/kg SC. All dogs had normal serum electrolyte levels ten days after the DOCP injection, although one dog showed borderline hyperkalemia. Prednisolone was also administered to all dogs, at a dosage of 0.11 - 0.5 mg/kg/day PO, which in all but two cases was divided over two gifts. Both dogs that were switched to DOCP, had a doubling of the previously given dosage of prednisolone. Clinical signs resolved in all dogs within ten days.

Second injection with DOCP

From the six dogs that were started on 2.2 mg/kg DOCP, three had a subsequent 10% decrease in DOCP dosage, while a larger dose reduction of 20% was performed in the two other dogs. According to the guidelines of the manufacturer (Table 1), this reduction was based on the sodium:potassium ratio, which was approximately 34 in the first three cases and significantly higher in the last two cases. Therefore, it was opted to implement an even higher dose reduction in these two cases. The last dog (previously treated with FC) was kept on the same starting dosage of 2.2 mg/kg, but the dosage interval was increased based on serial electrolyte measurements. A fixed interval rate of 64 days was eventually achieved in this dog. Two other dogs were started on 1.5 mg/kg. One of these dogs had a dose reduction of 10%. The other dog (also previously treated with FC) needed an increase of 10%, due to borderline hyperkalemia at day ten post injection.

Further follow-up

Long-term follow-up was available in four dogs. For three of those dogs, the maintenance dosage of DOCP varied between 1.2 - 1.8 mg/kg every 28 days. The maintenance dosage was reached after two dosage adjustments of DOCP in these dogs. For the dog, for which interval prolongation was chosen above dose reduction, the dosage remained 2.2 mg/kg with a fixed extended interval of 64 days. The maintenance dosage for prednisolone was 0.08 - 0.28 mg/kg/d PO, given once daily in all but one case.

Owner satisfaction and side effects during treatment

There was a high owner satisfaction rate for the treatment of HA with DOCP and prednisolone, based on a scale ranging from unsatisfied to very satis-

Table 1. Guidelines for dosage adjustment of Zycortal® according to the manufacturer (Dechra Veterinary Products, United Kingdom). Administering the second dose of Zycortal Suspension.

If the day 10 Na^+/K^+ ratio is:		25 days after the first dose, administer Zycortal suspension, as follows:
> 34	Do not	Decrease dose to: 2.0 mg/kg
> 32 to 34	administer	Decrease dose to: 2.1 mg/kg
27 to 32	dose 2	Continue 2.2 mg/kg
24 to < 27	on day 10	Increase dose to: 2.3 mg/kg
< 24		Increase dose to: 2.4 mg/kg

fied, with seven owners being very satisfied and one satisfied. For the owners of the two dogs that were switched from FC to DOCP, the satisfaction rate was notably higher than during the treatment with FC. Two dogs, which were immediately started on DOCP, experienced polyuria/polydipsia during the treatment with DOCP and prednisolone, which resolved after a reduction of the prednisolone dose. No adverse effects attributable to DOCP were noted.

DISCUSSION

Pure bred, young to middle-aged dogs were overrepresented in this case series, although two dogs were older. A female predisposition was not observed in the present cases, in contrast to the literature, in which a predisposition of 69% has been stated (Feldman and Nelson, 2004). This could be due to the small number of cases in this retrospective study.

Most of the cases (63%) were presented as an emergency, which could be explained by the dogs being selected from a referral university clinic. Most dogs (also 63%) showed gastrointestinal signs, and all of them presented with anorexia and lethargy, which is consistent with the literature. The clinical signs can be attributed to the lack of GC, which are vital for maintaining the mucosal gastric barrier, blood pressure, blood glucose and body temperature and for stress counterregulation. The lack of MC also contributes to clinical signs, as they play a role in water homeostasis by promoting renal sodium resorption and potassium excretion (Meeking, 2007; Klein and Peterson, 2010a; Lathan and Thomspon, 2018).

Only one dog showed mild regenerative anemia, which was most likely due to gastrointestinal bleeding since high urea levels were also present. Dehydration could have falsely elevated the levels of packed cell volume in other cases, masking anemia. The presence of dehydration was also evident based on hyperalbuminemia in one dog. Dehydration and/or gastrointestinal bleeding could explain the high percentage of dogs with increased urea. One dog had unmeasurably low blood glucose levels, which could be attributed to the lack in GC causing decreased hepatic gluconeogenesis and increased insulin sensitivity, combined with the anorexia and vomiting in a toy breed dog (Feldman and Nelson, 2004; Klein and Peterson, 2010a; Lathan and Thompson, 2018).

All dogs showed abnormal serum electrolyte concentrations, which is mainly caused by the lack of MC. As described in the literature, serum levels of sodium and potassium normalized in most of the present cases (7/8) within 24 hours after initiating fluid therapy (Feldman and Nelson, 2004; Klein and Peterson, 2010b; Lathan and Thompson, 2018).

The first dog being treated with DOCP followed the protocol suggested by the manufacturer (Table 1). A starting dosage of 2.2 mg/kg SC was administered and the dog was then monitored at day 10, day 25 and every five days thereafter until the sodium-to-potassium ratio dropped beneath 32, eventually resulting in a fixed interval of 64 days. Gaining experience with DOCP, following new guidelines that were discussed at the ESVE Post-Congress day, and considering the recent literature, all following dogs had a fixed interval of 28 days and two dogs were treated with a lower starting dosage of 1.5 mg/kg SC (Bates et al., 2013; Lathan and Thompson, 2018). However, one of these dogs needed an increase of the dosage at the time of the second injection of DOCP. Due to sodium-to-potassium ratios being markedly higher than 34, a dose reduction of 20% was performed in two other dogs, which is a larger dose reduction than the 5 - 15% dose reduction suggested in the literature (Klein and Peterson, 2010b; Lathan and Thomspon, 2018). For both dogs that were switched from FC to DOCP, FC was immediately stopped after injection with DOCP, but with a doubling of the previously administered prednisolone dosage. Both dogs were switched to DOCP due to insufficient control of the serum electrolyte concentrations with FC, whilst already expressing GC side effects. After the switch to DOCP, the serum electrolyte concentrations normalized rapidly and the GC side effects disappeared or improved greatly. Baumstark et al. (2014) suggested that DOCP is more effective than FC in the treatment of HA. However, an earlierer study of Kintzer and Peterson (1997) with 205 dogs showed no difference regarding efficacy of MC replacement and survival time between DOCP and FC.

The starting dosage of prednisolone was notably lower in two cases and higher in one case, than the dosage of 0.22 - 0.3 mg/kg/day reported in the literature. However, the two dogs receiving a lower dosage were previously treated with FC and GC before the first administration of DOCP. In most cases (75%), the maintenance dosage of prednisolone was lower than the dosage of 0.2 mg/kg/day reported in the literature (Van Zyl and Hyman, 1994; Kintzer and Peterson, 1997; Reusch, 2000; Klein and Peterson, 2010b), although a similar dosage has recently been described (Lathan and Thompson, 2018).

It should be mentioned that the main limitations of this study were the relatively small number of dogs and all limitations inherent to the retrospective nature of this study.

CONCLUSION

In conclusion, DOCP was successful in maintaining normal serum electrolyte concentrations in eight dogs with HA, both in newly diagnosed cases and in dogs previously treated with FC. A fixed dosage interval of 28 days was deemed effective and practical. A dose reduction of DOCP was possible in 75% of the cases at the time of the second injection. In one out of

the two cases treated with a lower starting dosage (1.5 mg/kg), treatment was effective; however, an increase in DOCP dosage was necessary for the dog that was previously treated with FC.

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General anesthesia for surgical treatment of urethral obstruction in nine goats

Algemene anesthesie voor de chirurgische behandeling van urinewegobstructie bij negen geiten

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ABSTRACT

Nine pygmy goats underwent surgical treatment for obstructive urolithiasis in a period of six months. In two cases, (second) revision surgery was necessary resulting in a total of twelve procedures under general anesthesia. Different anesthetic protocols were applied: analgesia was provided by an opioid (12/12) combined with either benzodiazepine (10/12) or an alpha-2 agonist (2/12). Anesthesia was induced with propofol (10/12) or ketamine (2/12) and maintained with isoflurane (8/12) or sevoflurane (4/12) in oxygen in a semi-closed circle system with continuous monitoring during anesthesia. Minor complications were mild bradycardia (4/12), hypotension (3/12), metabolic acidosis (1/12) and hypothermia (12/12). In four cases, epidural anesthesia was performed; in one of those four cases, severe complications developed (paralysis, 1/4). The goat was euthanized later. Although urethral obstruction increases the risk of general anesthesia, the selection of an appropriate anesthetic protocol, adequate preoperative examination/ preparation and detailed monitoring throughout anesthesia reduced the incidence of severe complications in this case series.

SAMENVATTING

Over een periode van zes maanden werden negen dwerggeiten chirurgisch behandeld voor obstructie van de urinewegen. In twee gevallen was een (tweede) revisie-operatie nodig, wat resulteerde in twaalf procedures onder algemene anesthesie. Verschillende anesthesieprotocollen werden toegepast. Analgesie werd voorzien door middel van een opioïd in combinatie met ofwel benzodiazepine (10/12) of met een alfa-2 agonist (2/12). De anesthesie werd geïnduceerd met propofol (10/12) of ketamine (2/12), waarna deze werd onderhouden met isofluraan (8/12) of sevofluraan (4/12) in zuurstof in een semigesloten cirkelsysteem en onder continue monitoring. Geregistreerde complicaties waren milde bradycardie (4/12), hypotensie (3/12), metabole acidose (1/12) en hypothermie (12/12). In vier gevallen werd door middel van een epidurale anesthesie bijkomende analgesie voorzien, waarbij er zich bij één geit een ernstige complicatie (paralyse, 1/4) ontwikkelde met euthanasie tot gevolg. Hoewel een obstructie van de urinewegen het anesthesierisico verhoogt, werd de kans op ernstige complicaties in de voorliggende casussen vermeden door de keuze van een adequaat anesthesieprotocol, een goed(e) preoperatief (-ve) onderzoek/ voorbereiding en een nauwgezette perioperatieve monitoring.

INTRODUCTION

Urolithiasis, resulting in urethral obstruction, is commonly seen in male small ruminants (Fortier et al., 2004; Kinsley et al., 2013; Hunter et al., 2012; Gazi et al, 2014). The etiology is multifactorial (Gugjoo et al., 2013) and involves both anatomic and dietary factors (Ewoldt et al., 2008). Uroliths are frequently observed in the processus urethralis or in the distal sigmoid flexure, due to the narrow urethral diameter in these areas (Ewoldt et al., 2008). During the formation of uroliths, debris in the urinary tract, mucoproteins and cells form a nidus, which serves as a basis for later precipitation of crystals (Gazi et al., 2014; Videla and van Amstel, 2016). Calcium carbonate, calcium phosphate, struvite or calcium oxalate stones are the most common types in small ruminants (Kinsley et al., 2013; Videl and van Amstel, 2016). Depending on the number and size of the uroliths, (partial) obstruction of the urinary tract can occur (Gazi et al., 2014).

Signs of discomfort, such as abnormal stance, failure to urinate or strangury, vocalization, anorexia, teeth grinding, ventral edema at the level of the abdomen and kicking the abdomen, can be seen, as well as tachycardia and tachypnea (Ermilio and Smith, 2011; Videla and van Amstel, 2016). Deep abdominal palpation of the distended bladder in the caudal abdomen, transabdominal ultrasonography or plain radiography can contribute to achieve a diagnosis (Ermilio and Smith, 2011; Gazi et al., 2014; Videla and van Amstel, 2016).

In an early stage, conservative treatment can be attempted with spasmolytic agents, fluid therapy, medical dissolution of the uroliths by acidification of the urine, cystocentesis, retrograde catheterization and flushing (Hunter et al., 2012; Gazi et al., 2014; Videla and van Amstel, 2016). However, surgical treatment is necessary when medical management is unsuccessful (Ermilio and Smith, 2011). Several surgical procedures have been described (Gugjoo et al., 2013; Kinsley et al., 2013; Gazi et al., 2014; Videla and van Amstel, 2016), either under general anesthesia or under sedation, in combination with a local and/or epidural block (Kinsley et al., 2013; Gazi et al., 2014; Videla and van Amstel, 2016). Typical concerns in (small) ruminant anesthesia are tympany, profuse salivation, regurgitation and aspiration pneumonia. In addition, anesthesia of a patient with urolithiasis can be quite challenging due to the impact on the cardiovascular and respiratory function but also due to electrolyte and acid-base disbalances (George et al., 2007; Freitas et al., 2012). The objective of this retrospective case series was to describe different anesthetic protocols and the occurrence of possible minor and major complications during anesthesia of pygmy goats for obstructive urolithiasis.

Twelve procedures under general anesthesia

In a period of six months (August 2016 – March 2017), nine (pet) goats were admitted to the clinic of the Faculty of Veterinary Medicine (UGhent) with a similar history of abdominal discomfort, apathy and unsuccessful attempts to urinate. After a general clinical examination, venous blood gas analysis, biochemistry, ultrasonographic and radiographic examination, all cases were referred for surgical treatment of urinary tract obstruction (without bladder rupture) under general anesthesia (Tables 1 and 2). Goat 1 underwent three different surgical procedures on separate occasions and goat 8 was operated twice. The surgical procedures included tube cystotomy (Silcoat Foley Catheter, Servoprax GmbH, Wesel, Germany) (three cases) or cystotomy (one case), marsupialization of the bladder (three cases), urethrostomy (two cases), amputation of the processus urethralis (one case), transposition of the penis (one case) and vesiculopreputial anastomosis (one case). The type of surgery was determined depending on the presence or absence of ventral edema at the level of the abdomen, the condition of the urethra and bladder and the preference of the individual surgeon in each case. Two weeks after the initial surgery, the tube cystotomy of patient 1 was obstructed and the decision was made to perform a urethrostomy instead (1B). Three months later, the same goat (1C) (weight loss from 31kg to 21kg over a period of three months) was re-presented at the clinic for persistent urinary problems. A rupture of the urethra was diagnosed, and a third revision surgery (vesiculopreputial anastomosis) was performed. Patient 8 was referred for recurrent symptoms of urinary obstruction eleven days after the initial surgery (urethrostomy (8A)) and a marsupialization of the bladder (8B) was performed during the second surgery.

In all goats, a catheter (Venocan™ Plus IV Catheter, 14G, 2.1 x 50mm, Kruuse, Langeskov, Denmark) was placed in the jugular vein, and antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs) were administered before anesthesia, except in case 1C, where NSAIDs and antibiotics were administered during surgery (Table 3). Different anesthesia protocols were applied, depending on the individual anesthetist's preference and the patient's condition (Table 3). In all cases, premedication consisted of an opioid, methadone (Comfortan 10 mg mL^{-1}, Eurovet Animal Health BV, AE Bladel, the Netherlands) or morphine (Morfine HCL 10 mg mL^{-1}, Laboratoires Sterop NV, Brussels, Belgium), combined with either midazolam (Midazolam B Braun 5 mg mL^{-1}, Braun, Meslunger, Germany) (seven cases), diazepam (Ziapam 5 mg mL^{-1}, Ecuphar, Oostkamp, Belgium) (three cases) or xylazine (Xyl-M 2%, VMD, Arendonk, Belgium) (goats 3 and 7). Induction of anesthesia was performed with

Table 1. Preoperative venous blood values in nine goats undergoing surgical treatment of urolithiasis under general anesthesia (Jackson and Cockcroft, 2002).

	Reference	Goat 1A	Goat 1B	Goat 1C	Goat 2	Goat 3	Goat 4	Goat 5	Goat 6	Goat 7	Goat 8A	Goat 8B	Goat 9
Glucose (g dL^{-1})	*40-60*	149	x	x	259	129	107	x	97	160	263	208	101
pH (mmHg)	*7.35-7.45*	7.49	x	x	7.389	7.45	7.428	x	7.54	7.515	7.35	7.435	7.165
pCO_2 (mmHg)	*35-45*	32.4	x	x	42.2	31.1	34	x	38.2	26.8	33.4	34.7	33.2
HCO_3^- (mmol L^{-1})	*25-30*	24	x	x	24.9	20.9	22	x	31.9	21.1	18.2	22.8	11.7
Packed cell volume (%)	*25-35*	40	x	x	37	35	25	x	35	44	43	36	42
B.E. (mEq L^{-1})	*-5 +5*	1.2	x	x	-0.1	-2.3	-2.0	x	8.8	-0.5	-6.3	-1	-15.8
Na^+ (mmol L^{-1})	*135-156*	142	x	x	142.5	143.6	152.3	x	140.2	143	133.1	145.4	142.6
K^+ (mmol L^{-1})	*3.4-6.1*	4.38	x	x	3.92	4.61	3.19	x	4.41	4.06	4.22	3.63	4.61
Ca^{2+} (mmol L^{-1})	*2.3-2.9*	1.08	x	x	1.1	0.96	0.93	x	0.96	1.08	0.97	1.15	1.04
Cl^- (mmol L^{-1})	*98-110*	104	x	x	98	107	112	x	96	103	89	104	107
Urea (mmol L^{-1})	*4-8.6*	6.9	**13.1**	**x**	**41.1**	**18.3**	**22.1**	**38.8**	**19.3**	x	**46**	**13.3**	3.5
Creatinine (µmol L^{-1})	*54-123*	**89**	**382**	**x**	**820**	**210**	**183**	**571**	**298**	x	x	**98**	**68**

X= not performed or saved. The different patients are referred by number (1 to 9). The letters A to C refer to the different times the same patient underwent surgical treatment under general anesthesia. Aberration from the reference values are clarified in bolt. Reference values are clarified in italics.

propofol administered intravenously (IV) (Propo Vet Multidose 10 mg mL^{-1}, Zoetis Belgium SA, Louvain-La-Neuve, Belgium) (ten cases) or ketamine administered IV (Ketamidor 100 mg mL^{-1}, Richter Pharma AG, Wels, Austria) (goats 6 and 7) (Table 3). With the aid of a laryngoscope, endotracheal intubation was performed in each case with the animal in a sternal position. Intubation was smooth in all but one case (case 6), where several attempts were needed, due to poor visualization of the larynx and swallowing attempts. The diameter of the endotracheal tube (Kendal Curity, Minneapolis, USA) depended on the size of the patient. In 4/12 patients, an epidural injection was performed in sternal recumbency, with 0.1 mg kg^{-1} morphine and 0.5 mg kg^{-1} bupivacaine hydrochloride (Marcaïne 0.5%, Aspen Pharma Trading Limited, Dublin, Ireland) (Spinal needle Quicke, 22G/0.7 mm x 65 mm, Temena SAS, France). Anesthesia was maintained with isoflurane (IsoFlo, Aesica Queenborough Limited, Kent, UK) (eight cases) or sevoflurane (SevoFlo, Zoetis Belgium SA, Louvain-la-Neuve, Belgium) (four cases) in oxygen in a semi-closed circle system (Dräger-AV 1, Drägerwerk AG Lübeck, Germany). The animals breathed spontaneously (7/12) or were mechanically (5/12) ventilated, depending on the spontaneous respiratory rate and results of the arterial blood gas analysis during anesthesia (Table 2). Lactated Ringer's solution (Vetivex 5000 mL, Dechra Limited, North Yorkshire, UK) was administered at a low rate (1 mL kg^{-1} h^{-1}) until urine could be drained from the bladder. Patients were monitored thoroughly during anesthesia using standard monitoring equipment (Table 2; Figures 1, 2 and 3). Monitoring of the patients included electrocardiography (ECG), pulse oximetry, measurement of the body temperature and monitoring of invasive blood pressure obtained through the placement of a catheter (Venocan™ Plus IV Catheter, 22G, 0.9 x 25mm, Langeskov, Denmark) in the auricular artery (Datex-Ohmeda S/5, Helsinki, Finland) that was used in addition to collect arterial blood samples (Radiometer ABL5, Denmark, Copenhagen) (Table 2). Furthermore, inspired and expired concentrations of oxygen, carbon dioxide (CO_2) and the volatile anesthetic agent (sevo- or isoflurane) were recorded (Datex-Ohmeda DivGE Healthcare Finland OY, Helsinki, Finland).

Only minor complications were noted during maintenance of anesthesia (Table 4). In case 1B, metabolic acidosis was diagnosed in an arterial blood sample taken 15 minutes after induction of anesthesia, which was treated with 8.4 g of sodium bicarbonate over 30 minutes (Bicarbonate de Sodium 8.4% B52l, Melsungen, Germany) (Table 2).

Slight bradycardia was observed in cases 1C, 2 and 9, but the arterial blood pressure remained stable (Figures 1 and 2). In case 7, more pronounced bradycardia was noted: the heart rate in this goat varied around 60 beats per minute (bpm) throughout the anesthesia, but dropped to 42 bpm 30 minutes after induction of anesthesia (Figure 2). Simultaneously, the mean arterial pressure (MAP) abruptly decreased from 60 to 30 mmHg (Figure 1). The end-tidal concentration of sevoflurane was decreased to 1.3%, a bolus of 10 mL kg^{-1} Lactated Ringer's solution (Baxter, Lessines, Belgium) was administered over 10 minutes (Baxter Colleague, Baxter Healthcare SA, Zürich, Switzerland) and a constant rate infusion (CRI) of dobutamine hydrochloride (Dobutrexmylan, Synthon BV, Nijmegen, the Netherlands) was started at a rate of 0.5 µg kg^{-1} $minute^{-1}$. The MAP increased from 30 to 70 mmHg and the heart rate from 45 to 60 bpm (Figures 1 and 2). Fifteen minutes later, slight swallowing and positive palpebral reflexes were noted. The end-tidal sevoflurane concentration was again increased and adjusted according to the responses in arterial blood pressure and heart rate. In goat 3, hypotension (MAP 45 mmHg) was observed at the start of anesthesia, with a normal heart rate of 85 beats per minute (Figures 1

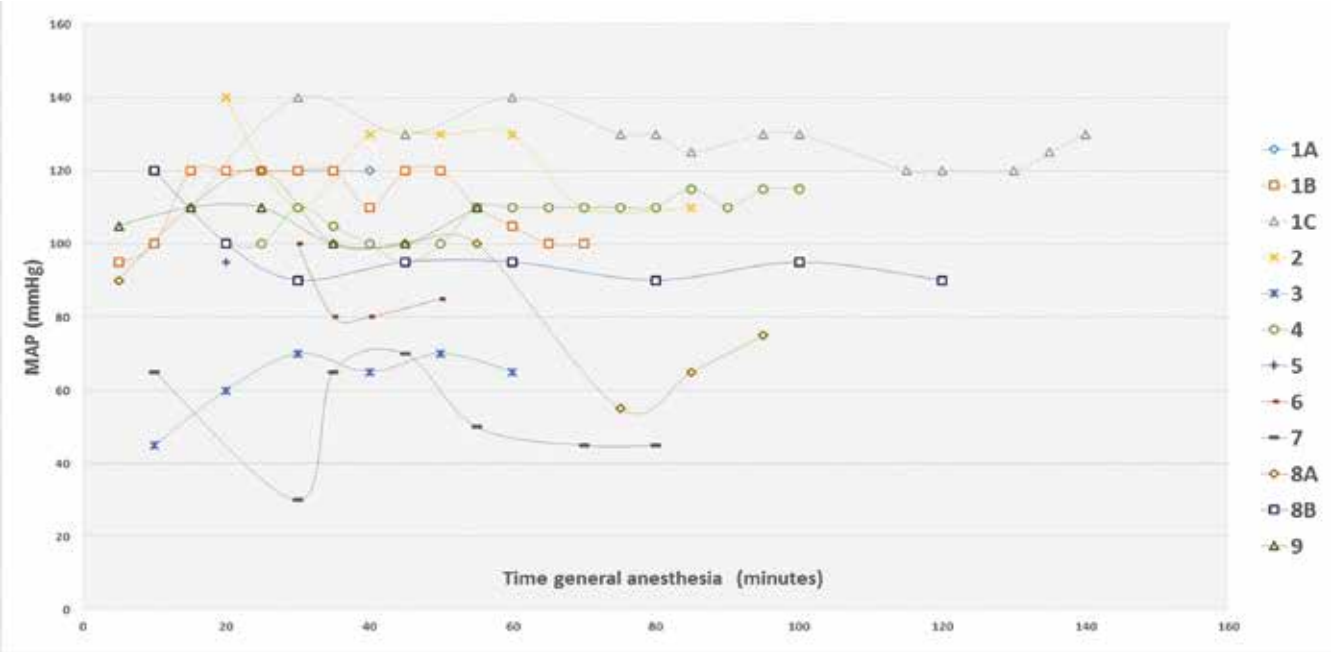

Figure 1. Mean arterial blood pressure (MAP) in mmHg of the patients during anesthesia for surgical treatment of urolithiasis. Hypotension (MAP < 65 mmHg) was observed in three cases (3, 7, 8A) during the anesthesia.

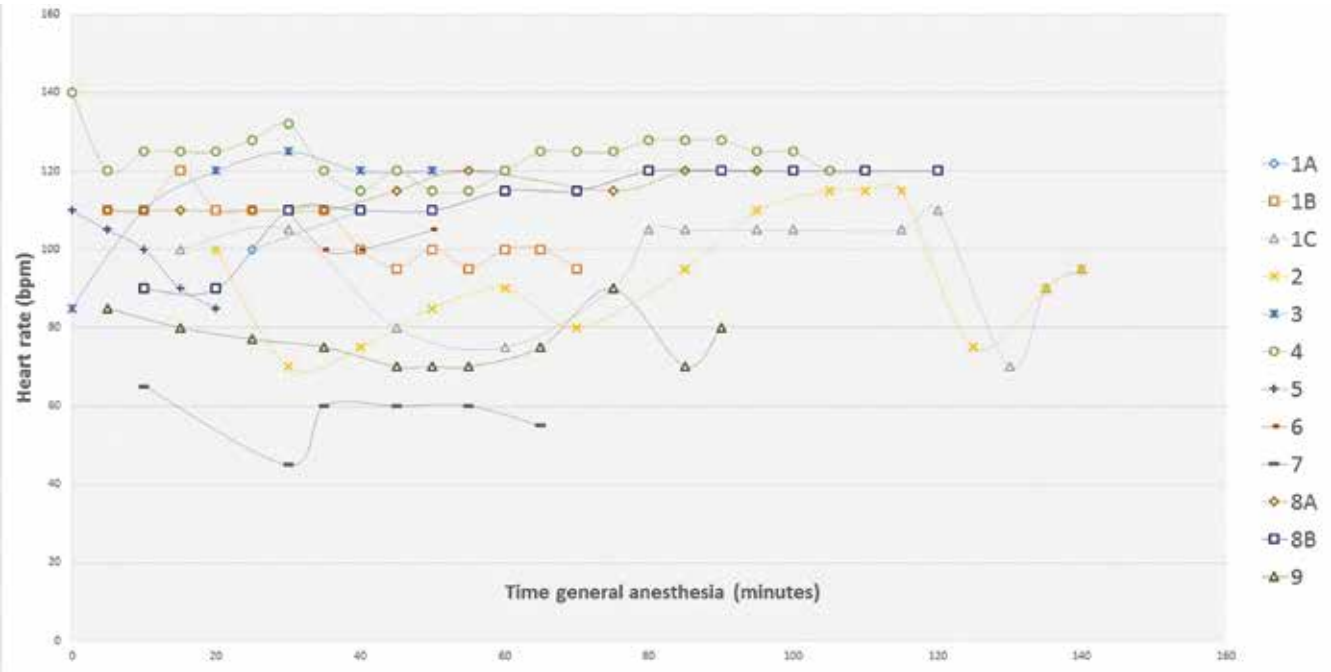

Figure 2. Graphic presentation of the heart rate (beats per minute, bpm) of patients during anesthesia for surgical treatment of urolithiasis. Mild bradycardia (heart rate < 70 to 90 bpm) was observed in three cases (1C, 2 and 9) and more pronounced bradycardia was noted in case 7.

and 2). A bolus of 10 mL kg^{-1} Lactated Ringer's solution was administered over 10 minutes (Baxter Colleague, Baxter Healthcare SA, Zürich, Switzerland), and a CRI of dobutamine hydrochloride was started at a rate of 2 µg kg $minute^{-1}$. The MAP increased to 70 mmHg and the pulse rate increased to 120 beats per minute (Figure 1). Administration of dobutamine was discontinued after 20 minutes. Heart rate and arterial blood pressure remained stable during the remaining time of the anesthesia (Figures 1 and 2). In case 8A, a bolus of 1 mg kg^{-1} ketamine was administered IV because of movement of the patient at the start of the surgery. Immediately thereafter, a drop in mean arterial pressure (MAP) from 100 to 55 mmHg was noted, which spontaneously increased again to 65 and 70 mmHg, respectively 5 and 10 minutes later (Figure 1).

After extubation, the animals were placed in a clean stable with a heating lamp until normothermia was reached (all goats had developed hypothermia during anesthesia) (Table 4). The recovery of the pa-

Table 2. Arterial blood gas values from an arterial blood sample taken from the auricular artery (Radiometer ABL 5, Denmark, Copenhagen) analysis per-operative of goats undergoing surgical treatment of urolithiasis in general anesthesia. In case 1B samples were taken at 15, 35 and 50 minutes after the start of anesthesia. During anesthesia, a correction for the low pH and bicarbonate was performed by administrating sodium bicarbonate (Bicarbonate de Sodium 8.4% B52l, Germany, Meslungen). Body temperature (°C) at the end of anesthesia and the total anesthesia time in minutes.

	1A	1B (#=3)			1C (#=2)		2	3 (#=1)	4 (#=2)		5	6	7	8A	8B	9 (#=1)
Time of sample after induction (minutes)		**15'**	**35'**	**50'**	**45'**	**105'**		**25'**	**46'**	**81'**						
pH (mmHg)	x	**7.27**	7.33	7.35	7.38	7.36	x	7.31	**7.21**	**7.26**	7.38	x	x	x	x	x
pCO_2 (mmHg)	x	37	39	37	47	**28**	x	**50**	**50**	**50**	35	x	x	x	x	x
pO_2 (mmHg)	x	421	440	443	434	216	x	98	241	158	364	x	x	x	x	x
Saturation (%)	x	100	100	100	100	100	x	97	100	99	100	x	x	x	x	x
HCO_3^- (mmol L^{-1})	x	**17**	**20**	**20**	27	**20**	x	25	**22**	**22**	**20**	x	x	x	x	x
SBC (mmol L^{-1})	x	17	20	21	26	14	x	23	20	20	21	x	x	x	x	x
tCO_2 (Vol%)	x	40	47	48	**64**	23	x	59	52	52	47	x	x	x	x	x
ABE (mmol L^{-1})	x	**-9**	-5	-4	2	**-14**	x	-2	-5	**-6**	-4	x	x	x	x	x
SBE (mmol L^{-1})	x	**-9**	-5	-4	3	**-15**	x	-1	-4	-4	-4	x	x	x	x	x
Packed cell volume (%)	x	17	x	x	x	25	x	30	16	18	32	x	x	x	x	x
Ventilation?	No	No			Yes		Yes	No	No		No	Yes	Yes	No	No	Yes
Duration of anesthesia (minutes)	90	70			140		150	70	110		25	50	100	110	125	90
Rectale temperature (°C)	x	**35.**5			x		x	**37**	**35.9**		38	**37.3**	**37.5**	x	**37.3**	**34**

X = not performed; # = total amount of blood gases analysed. The different patients are referred by number (1 to 9). The letters A to C refer to the different times the same patient underwent surgical treatment under general anesthesia. Aberration from the reference values are clarified in bolt.

tients was generally smooth, although after the first surgical procedure, goat 1 was not able to stand during the first six hours after epidural injection. After the surgery, case 8B was unable to stand. A supportive treatment was started, consisting of an infusion of crystalloids, administration of meloxicam (0.5 mg kg^{-1} subcutaneously (S.C.)) on day 0, 2 and 4 and a single dose of 0.1 mg kg^{-1} morphine intramuscularly (IM) on the first postoperative day. Because the animal was still unable to stand with signs of complete paralysis and absence of pain sensation on the second postoperative day, a single dose of 0.5 mg kg^{-1} of dexamethasone was administered IV. From the third postoperative day onwards, a treatment with vitamin B1 (10 mg kg^{-1}) was started and physiotherapy was applied at four-hour intervals. Because no signs of improvement were seen after nine days, further examinations were performed (radiography, myelography and computed tomography (CT)). On radiography of the abdomen (right-left and ventral-dorsal view), mineral opacities caudal to the urinary bladder and cranial to the pubis were observed. On myelography, no anomalies were seen. On CT, a bony defect with mild displacement of a fragment was visible centrally at the caudo-dorsal endplate of L7, suggestive for osteochondrosis dissecans. In the caudal abdomen and in the surroundings of the penis, reactive tissue was seen, probably due to inflammation from the surgery. In the cranial mediastinum, a cystic lesion was noted. Bilaterally in the adductor muscles, more pronounced right then left, some irregular hypo-attenuated lesions were visible ventrally to the ischium. This was probably due to myositis, edema or contusion. The presence of uroliths in the bladder and in the penile urethra, already observed on radiography, were also confirmed. No abnormalities were found at the level of the spinal cord and due to the lack of improvement, after consideration with the owners, the decision was made to euthanize the goat, using 60 mg kg^{-1} sodium-pentobarbital IV. (Release, Garbsen, Germany). No autopsy was performed, according to the owner's wishes.

After surgery, the goats remained hospitalized and the treatment with antibiotics and NSAIDs was continued (Table 3). The choice of antibiotics depended on the type of surgery. Meloxicam 0.5 mg kg^{-1} (Rheumocam 20mg mL^{-1}, Boehringer Ingelheim, Ingelheim, Germany), flunixin meglumine 1.1 mg kg^{-1} (Emdofluxin 50, Emdoka BVBA, Sint-Niklaas, Belgium) or ketoprofen 2 mg kg^{-1} (Ketofen 10%, Merial Belgium NV, Diegem, Belgium) were used as NSAIDs, the choice depending on the clinician's preference. Morphine 0.1 mg kg^{-1} was administered intramuscularly when the patient showed symptoms of pain (4 out of 12). The scoring of pain was done subjectively without the use of a pain scale by the treating veterinarian. All patients received 1 g kg^{-1} ammonium chloride (NH_4^+) orally once a day (magisterial preparation). Propylene glycol 0.5 mL kg^{-1} (Propylenglycolum, Fraver Laboratoria, Belgium) was administered orally once a day in obese patients, to reduce the risk for Fatty Liver Syndrome. In 6/12 cases, vitamin B1 (Thiamine B1, magisterial preparation) 10 mg kg^{-1} was given orally twice a day to support the nervous system and in case the patients were

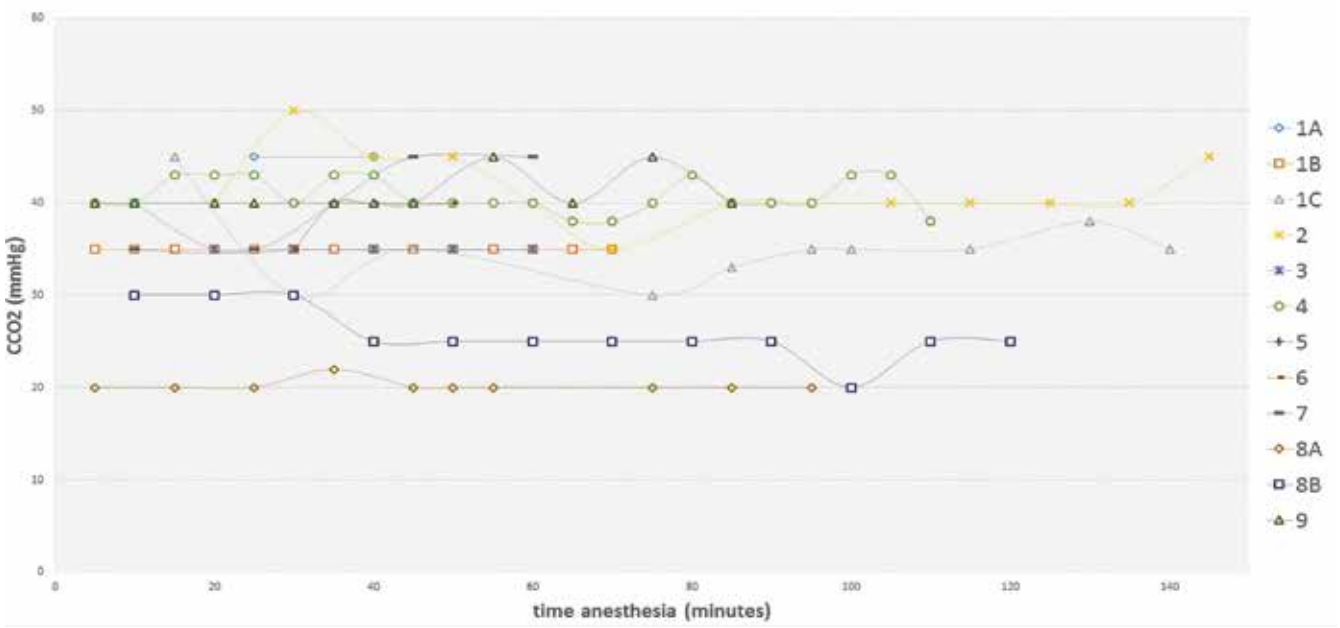

Figure 3. End tidal CO_2 monitoring (mmHg) of the patients undergoing surgical treatment for urolithiasis. The end tidal CO_2 concentration was used to determine the decision-making in the adaptation of the patient's (mechanical) ventilation.

not eating. The length of treatment with vitamin B1 and propylene glycol depended on the clinical improvement of the patient. During the first days after surgery, intravenous crystalloids were administered for general support and adjusted as needed based on measurement of the packed cell volume, kidney values and electrolyte concentrations in venous blood samples. Bethanecholchloride (Myocholin-Glenwood 10 mg, Glenwood GmbH, München, Germany) was administered orally at 0.29 mg kg^{-1} in case 7 due to bladder atony postoperatively. In case 3, furosemide 0.5 mg kg^{-1} (Dimazon 5%, Intervet International BV, Boxmeer, the Netherlands) was administered once because of a high urea (24 mmol L^{-1}) and creatinin (435 µmol L^{-1}) concentration.

DISCUSSION

General anesthesia of (small) ruminants can be challenging because of the anatomical and physiological differences compared to other species (Taylor, 1991; Lin, 2015; Riebold, 2015). Tympany, profuse salivation, regurgitation and aspiration pneumonia are some typical concerns in animals with multiple stomachs (Taylor, 1991). Preanesthetic starvation (12 to 24 hours) and water restriction (6 to 12 hours) can reduce the risk of ruminal tympany, regurgitation and aspiration during anesthesia (Ewing, 1990; Taylor, 1991; Galatos, 2011; Dzikiti, 2013; Lin, 2015). Unfortunately, starvation prior to anesthesia is not an option in case of emergency procedures (Carroll and Hartsfield, 1996; Riebold, 2015). Endotracheal intubation with sufficient cuffing of the tube is essential to avoid (aspiration)pneumonia in ruminants when regurgitation or salivation would occur (Galatos, 2011; Taylor, 1991). The placement of a stomach tube could be useful in cases with long anesthetic procedures to release ruminal gas (Ewing, 1990; Taylor, 1991) and avoid a tympanic patient, which might compromise the cardiovascular and respiratory systems (Taylor, 1991). The risk of anesthesia is further increased in patients suffering from urolithiasis with obstruction of the urinary tract (Freitas et al., 2012).

In case of urinary tract obstruction, electrolyte imbalances can rapidly occur (Freitas et al., 2012; Ermilio and Smith, 2011) and progress to severe acid-base disbalances (George et al., 2007; Freitas et al., 2012). These abnormalities include metabolic acidosis, hyponatremia, hyperkalemia, azotemia and hyperphosphatemia (George et al., 2007; Ermilio and Smith, 2011; Videla and van Amstel, 2016). Electrolyte imbalances must be corrected before anesthesia (Ermilio and Smith, 2011), e.g. hyperkalemia (> 6 mmol L^{-1}) has important effects on the cardiac function, with the risk of fatal arrhythmias during anesthesia (Ewoldt et al., 2006; Videla and van Amstel, 2016). However, in contrast to other species, the concentrations of potassium and phosphate can remain within normal values in ruminants with urinary tract obstruction (Ewoldt et al., 2006; George et al., 2007). All the goats in the present case series were normokalemic before the induction of anesthesia (Table 1). The best-known biochemical parameter for goats with urolithiasis is azotemia (George et al., 2007). Blood urea nitrogen and creatinin levels should therefore always be assessed (Videla and van Amstel, 2016). In all patients, urea and creatinin values were indeed in-

Table 3. Anesthesia protocols used in nine goats undergoing surgical treatment of urolithiasis under general anesthesia.

	Surgery	Position	Premedication (IV)	Induction (IV)	ETT	Epidural	Ventilation	NSAID and antibiotics	Remarks
Goat 1A 33 kg 4y MC	Tube cystotomy	Dorsal	0.1 mg kg^{-1} Methadone 0.3 mg kg^{-1} Midazolam	3 mg kg^{-1} Propofol	8	Yes	S	0.5 mg kg^{-1} Meloxicam 45 mg kg^{-1} Neomycin	*Postoperative* Prolonged recovery + unable to stand for several hours (6 hours). Ammonium chloride 1 g 10 kg^{-1} PO
Goat 1B 31 kg 4 Y MC	Urethrostomy	Sternal	0.4 mg kg^{-1} Midazolam 0.1 mg kg^{-1} Morphine	4 mg kg^{-1} Propofol	8	No	S	0.5 mg kg^{-1} Meloxicam 45 mg kg^{-1} Neomycin	*Anesthesia* Correction pH with sodium bicarbonate 0.11 mg kg^{-1} Ketamine during surgery *Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO
Goat 1C 21 kg 4 Y MC	Vesiculopreputial anastomosis	Dorsal	0.2 mg kg^{-1} Morphine 0.2mg kg^{-1} Diazepam	3.8 mg kg^{-1} 8 Propofol		No	AC TV = 200 mL PIP: 6-8 F: 14-26 PEEP: 1-8	0.5 mg kg^{-1} Meloxicam 1.1 mg kg^{-1} Sodium-ceftiofur during surgery 45 mg kg^{-1} Neomycin postoperative	*Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO 0.1 mg kg^{-1} Morphine (I.M. Day 1)
Goat 2 40 kg 6 Y MC	Tube cystotomy	Dorsal	0.1 mg kg^{-1} Methadone 0.3 mg kg^{-1} Midazolam	2.6 mg kg^{-1} Propofol	7	Yes	C	1.1 mg kg^{-1} Flunixin meglumine 13.4 mg kg^{-1} Sulfadoxine + 2.7 mg kg^{-17} Trimethoprim	*Postoperative* 0.1 mg kg^{-1} Morphine (I.M. Day 1) Ammonium chloride 1 g 10 kg^{-1} PO 5d Propyleenglycol PO 5d 0.5 mL kg^{-1} Infusion 4d
Goat 3 25 kg 4 Y MC	Right sided para-median marsupilization	Dorsal	0.06 mg kg^{-1} Xylazine 0.1 mg kg^{-1} Morphine	4 mg kg^{-1} Propofol	5.5	Yes	S	0.5 mg kg^{-1} Meloxicam 45 mg kg^{-1} Neomycin	*Anesthesia* 12 mgh^{-1} Dobutamine + bolus fluids 10 mL kg^{-1} due to hypotension *Postoperative* Furosemide 0.5 mg kg^{-1} Ammonium chloride 1 g 10 kg^{-1} P.O.
Goat 4 13 kg ? Y M	Cystotomy	Dorsal	0.1 mg kg^{-1} Midazolam 0.1 mg kg^{-1} Methadone	3 mg kg^{-1} Propofol	6	No	S	1.1 mg kg^{-1} Flunixin meglumine 7 mg kg^{-1} Amoxicilline	*Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO 5d Propyleenglycol PO 0.5 mL kg^{-1} Vitamine B1 PO 1 gram 100 kg^{-1}
Goat 5 43 kg ? Y M	Amputation processus urethralis	Dorsal	0.1 mg kg^{-1} Morphine 0.3 mg kg^{-1} Diazepam	5 mg kg^{-1} P Propofol	8	No	S	1.1 mg kg^{-1} Flunixin meglumine 13.4 mg kg^{-1} Sulfadiazine + 2.7 mg kg^{-1} trimethoprim	*Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO 3d
Goat 6 40 kg 3 Y MC	Transposition of the penis	Dorsal	0.2 mg kg^{-1} Diazepam 0.1 mg kg^{-1} Methadone	1.75 mg kg^{-1} Ketamine + 2x 0.87 mg kg^{-1} Ketamine	8	No	AC TV= 350 PIP= 19-21 Freq= 8-10	2 mg kg^{-1} Ketoprofen 45 mg kg^{-1} Neomycin	*Anesthesia* Difficult intubation *Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO 5d 0.1 mg kg^{-1} Morphine (I.M. Day 1 + 2) Propyleenglycol PO 0.5mL kg^{-1} Vitamine B1 PO 1 g 100 kg^{-1}
Goat 7 35 kg 4 Y MC	Tube cystotomy	Dorsal	0.1 mg kg^{-1} Methadone 0.06 mg kg^{-1} Xylazine	1.7 mg kg^{-1} Ketamine	8	No	AC TV= 250 PIP= 17-20 Freq= 17	Preoperative 2 mg kg^{-1} Ketoprofen Postoperative 1.1 mg kg^{-1} Flunixin meglumine 45 mg kg^{-1} Neomycin 3 days after change to 13.4 mg kg^{-1} Sulfadiazine + 2.7 mg kg^{-1} Trimethoprim	*Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO Propylene glycol P.O. 0.5mL kg^{-1} Vitamine B1 PO 1 g 100 kg^{-1} Myocholine 0.29 mg kg^{-1} P.O.
Goat 8A 40 kg 11 Y MC	Urethrostomy	Dorsal	0.3 mg kg^{-1} Midazolam 0.1 mg kg^{-1} Morphine	3 mg kg^{-1} Propofol	10	No	S	0.5 mg kg^{-1} Meloxicam 7 mg kg^{-1} Amoxicillin	*Anesthesia* Local infusion of procaine without adrenaline 1 mg kg^{-1} ketamine IV *Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO Propylene glycol PO 0.5 mL kg^{-1} Vitamin B1 PO 1 g 100 kg^{-1}
Goat 8B 36 kg 11 Y MC	Marsupialization	Dorsal	0.2 mg kg^{-1} Midazolam 0.1 mg kg^{-1} Methadone	2.5 mg kg^{-1} Propofol	10	Yes	S	0.5 mg kg^{-1} Meloxicam 2 days postoperative 45 mg kg^{-1} Neomycin 0.5 mg kg^{-1} Dexamethasone IV Day 2 postoperative	*Postoperative* Unable to stand after epidurale: further examination RX, myelogram and CT followed by euthanasia. Morphine 0,1 mg kg^{-1} IM day 1+ 2 postoperative Ammonium chloride 1 g 10 kg^{-1} PO Propylene glycol PO 0.5 mL kg Vitamin B1 PO 1 g 100 kg^{-1}
Case 9 34 kg 4 Y MC	Marsupialization	Dorsal	0.3 mg kg^{-1} Midazolam 0.1 mg kg^{-1} Morphine	2.75 mg kg^{-1} Propofol	7.5	No	AC TV= 400 PIP= 11-15 Freq=10-15	0.5 mg kg^{-1} Meloxicam 45 mg kg^{-1} Neomycin	*Postoperative* Ammonium chloride 1 g 10 kg^{-1} PO Vitamin B1 PO 1 g 100 kg^{-1}

Abbreviations: PO = per os, IM = intramuscular, TV= tidal volume (mL), PIP= peak inspiratory pressure (cmH_20), PEEP= positive end expiratory pressure (cmH_20), F= frequency (breaths per minute), S= spontaneously, AC= assisted-controlled ventilation, C= controlled ventilation, ETT = endotracheal tube (internal diameter in mm), kg= kilograms, Y= years, MC= male castrated.

creased before surgery and gradually decreased in the postoperative period (Table 1).

After thorough examination and correction of electrolyte disorders, an anesthetic protocol may be chosen (Riebold, 2015). In food producing animals, national legislation must be taken into account when choosing the anesthetic protocol. Although minor surgery in goats can often be performed under sedation, usually combined with loco-regional or epidural anesthesia (Galatos, 2011; Taylor, 1991), more invasive surgery warrants the use of general anesthesia. The choice of anesthetic drugs must be well considered, since the excretion of drugs may occur through the kidneys, both directly and indirectly (Freitas et al., 2012). Most goats (10 out of 12) in this case series were premedicated with an opioid, methadone (6/12) or morphine (5/12) in combination with a benzodiazepine, diazepam (3/10) or midazolam (7/10) (Table 2). The choice between morphine or methadone and diazepam or midazolam was made on the preference of the anesthesiologist or medication available in stock. Opioids are metabolized by the liver while their metabolites, which are water soluble, are mostly excreted by urine and partially in the feces by biliary secretion (Kukanich and Wiese, 2015). Benzodiazepines are metabolized in the liver by reduction or glucuronide conjugation and later excreted by the urine (Posner and Burns, 2009). Benzodiazepines are mild sedatives, with anxiolytic but no analgesic effects (Galatos, 2011). For this reason, they are often combined with opioids during premedication. Their effects on the cardiovascular and respiratory systems are minimal compared to xylazine and are therefore the choice of preference in cases with urethral obstruction (Valverde and Doherty, 2008; Galatos, 2011). Although it has been stated that hypoxemia may occur due to a decrease in ventilation, this was not observed in this case series (Galatos, 2011). Diazepam has more tissue irritating properties and it is therefore not advised to administer the drug intramuscularly, in contrast to midazolam, which is water soluble (Galatos, 2011). Injection of benzodiazepines IV should be performed slowly to avoid excitation (Valverde and Doherty, 2008; Galatos, 2011). In this case series, no excitation was noticed after administration of benzodiazepines IV. Two goats however were premedicated with xylazine, a frequently used α_2-adrenoreceptor agonist, with potent sedative and some analgesic and muscle relaxant effects (Galatos, 2011; Lin, 2015). The response to the α_2-adrenoreceptor agonists is very variable between breeds and even differs individually (Valverde and Doherty, 2008; Riebold, 2015). Side effects seen after administration of an α_2-adrenoreceptor agonist are marked salivation (Kokkonen and Eriksson, 1987), respiratory depression, hypercapnia, hypoxemia, bradycardia, initial hypertension followed by hypotension and an increase in urine production in combination with hyperglycemia and hypoinsulinemia (Ewing, 1990; Ermilio and Smith, 2011; Galatos, 2011; Riebold, 2015). Therefore, the use of α_2-adrenoreceptor agonists in animals with cardiopulmonary disease, hypovolemia or urinary tract obstruction must be avoided if possible (Ewing, 1990; Galatos, 2011). Nevertheless, in this cases series, xylazine was used in the premedication of cases 3 and 7, because there was only a partial obstruction of the urethra, with suspicion of bladder atony in case 3. In the authors' opinion, avoiding the use of α_2- agonists would have been more appropriate. Indeed, during anesthesia of both cases, marked salivation, hypotension, as well as bradycardia and hypoventilation (necessitating mechanical ventilation) were observed (Figure 1). Finally, the use of acepromazine (0.05 – 0.1 mg kg^{-1}) could have been considered (Taylor, 1991; Carroll and Hartsfield, 1996; Riebold, 2015), but this drug is not frequently used in small ruminants (Galator, 2011). The onset of action is quite slow, and the level of sedation is less profound (Valverde and Doherty, 2008), while the vasodilatory effect may result in hypotension and hypothermia. For these reasons, acepromazine was not used during premedication in the present case series.

Induction of anesthesia was either performed with propofol or ketamine. In one of the goats, in which ketamine had been used, endotracheal intubation was quite challenging. This goat had been premedicated with a combination of diazepam and methadone. Prassinos et al. (2005) studied the comparison of propofol, ketamine and thiopental as induction agent in goats and reported difficult intubation in some goats receiving ketamine as induction agent. In the authors' experience, endotracheal intubation of small ruminants is indeed more difficult after induction with ketamine. These observations about the difficulties to intubate can be explained by the fact that laryngeal and pharyngeal reflexes may still be present after an induction with ketamine (Clarke et al., 2014).

During maintenance of anesthesia, hypotension, MAP below 65 mmHg, was noted in three cases (Clarke et al., 2014) (Table 4). In two of these (case 3 and 7), xylazine had been administered during premedication. One of the potential side effects of an α_2-agonist is indeed hypotension (Ewing, 1990; Ermilio and Smith, 2011; Galatos, 2011; Riebold, 2015). Hypotension can also appear as a consequence of epidural anesthesia (Borer-Weir K., 2014), which could also explain the hypotension noted in case 3. This can be explained by either sympathetic blockage or cardiovascular depression caused by the local anesthetic, or by the increase in epidural pressure during the injection. Therefore, epidural injections should be avoided in cardiovascular instable patients (Borer-Weir, 2014).To address the hypotension, in both cases, the concentration of the inhalation agent was reduced, since volatile anesthetics cause a dose-dependent decrease in blood pressure (Clarke et al., 2014, Steffey

Table 4. Frequency of complications during general anesthesia of goats undergoing surgery for urolithiasis.

Complication	Frequency (%)
Hypothermia	100% (12/12)
Bradycardia	33% (4/12)
Complications after epidural	25% (1/4)
Hypotension	25% (3/12)
Metabolic acidosis	8% (1/12)

et al., 2015; Riebold, 2015). Further treatment may include a bolus of crystalloids or the administration of inotropes or vasopressors. In this case series, a bolus of crystalloids was administered over 10 minutes, and dobutamine hydrochloride was infused at a constant rate of 2 µg kg minute^{-1} (case 3) and 0.5 µg kg minute^{-1} (case 7). In both cases, a significant improvement of the MAP was obtained. Clarke et al. (2014) described a constant rate infusion of 5-7 µg kg minute^{-1} of dobutamine or dopamine. Ephedrine (0.02 - 0.06 mg kg^{-1} I.V.) could have been used as an alternative for dobutamine to increase cardiac contractility and systemic vascular resistance (Riebold, 2015). Calcium-borogluconate can be useful in cases with hyperkalemia and increase cardiac contractility, but can cause bradycardia (Riebold, 2015) and was therefore not the preferred choice in this case series.

The normal heart rate in goats varies from 70 to 90 beats per minute (Jackson and Cockcroft, 2002). Bradycardia was observed in four cases (Table 4). In case 7, xylazine, which is known to cause bradycardia, had been administered during premedication. During the period of the pronounced bradycardia, the plane of anesthesia was considered deep, which is known to contribute to bradycardia (Galatos, 2011). In the other three cases, the arterial blood pressure remained stable and above 70 mmHg, so no interventions were undertaken.

Hypoventilation, hypercapnia and hypoxemia are commonly seen during anesthesia of ruminants (Tagawa et al., 1994; Carroll and Hartsfield, 1996) and are often caused by anesthetic agents (Lin, 2015). Orotracheal intubation is advised to protect the airways and to allow proper ventilation and supplementation of additional oxygen (Carroll and Hartsfield, 1996). Arterial blood gas analysis was not performed in all cases, but in case 3, a relatively pronounced difference between $paCO_2$ (50mmHg) and end tidal CO_2 (average 39 mmHg) was found (Figure 3). In case 3, the patient was kept in spontaneous ventilation during the entire procedure. The difference in PaO_2 and end tidal CO_2 was caused by alveolar dead space. In case 1B, the first arterial blood sample during anesthesia revealed a low pH, Base Excess (BE) and bicarbonate concentration, suggesting metabolic acidosis. These values were corrected by administration of sodium bicarbonate. Although salivation causes large losses of bicarbonate in ruminants, bicarbonate rarely needs to be administered during anesthesia (Riebold, 2015). Also, metabolic acidosis is rarely seen in case of obstructive urolithiasis. The most common causes are the absorption of D-lactate from the gastrointestinal tract and sodium loss in case of secretory diarrhea. Sepsis or other causes of systemic shock can also lead to metabolic acidosis due to lactate accumulation, as a result of poor tissue perfusion. This last cause may be the reason for the metabolic acidosis seen in this case due to revision a few days after the first surgery (Walz and Taylor, 2012). However, lactate was not determined and other venous blood values were not recorded before the revision surgery (Table 1).

During recovery, all patients suffered from hypothermia (Table 4). The normal body temperature of goats varies between 39 and 40°C (Jackson and Cockcroft, 2002). During anesthesia of newborns or long procedures (Taylor, 1991), monitoring of the body temperature is important as hypothermia commonly occurs (Lin, 2015; Riebold, 2015). In the present case series, a warming device could have been used to avoid the development of hypothermia. This is usually highly effective, but not all types of warming device are without risk in their use, since burns can occur if excessive heat is applied on the skin depending on the type of device used (Dunlop et al., 1989; Chung et al., 2012).

Analgesia is an important part of anesthesia and more effective when administered before the initial pain stimulus (Galatos, 2011; Riebold, 2015). The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is important to alleviate pain and may provide postoperative analgesia (Anderson and Muir, 2005). In addition, inflammatory reactions, and in this case, the risk of stenosis at the level of the urinary tract can be reduced. In humans, dogs and cats, the use of NSAIDs has been reported to cause an increased risk of acute kidney injury (Paliainen, 2015). The National Institute for Health and Clinical Excellence guidelines 2008 state the nephrotoxicity of NSAIDs and recommend to avoid them in patients with chronic kidney disease until their renal function is evaluated (Nderitu, 2013). In the occurrence of hypotension, the administration of NSAIDs can further decrease the renal function (Garcia, 2016). However, in case of severe kidney dysfunction, caution should be taken to avoid further damage (Videla and van Amstel, 2016). In Iranian Cashmere (Rayeni) goats,the effects of NSAIDs, more specifically flunixin meglumine, ketoprofen and phenylbutazone, were evaluated in a study of Mozaffari and Derakhshanfar (2012). Adverse effects were noted on gastrointestinal and myocardial tissues. Flunixin meglumine was the least toxic while phenylbutazone caused the worst side effects as evidence was shown on necropsy at the end of the study. Patients in this case report were treated with flunixin or meloxicam. Visceral analgesia can indeed be achieved with flunixin (Anderson and Muir, 2005). In these case series, NSAIDs were administered in the clinic before

transfer to the surgery department. Alpha-2 agonists, like xylazine or detomidine, provide dose-dependent analgesia, but their use is limited by the sedative and cardiovascular effects (Carroll and Hartsfield, 1997). Opioids, such as morphine (0.05 - 0.1 mg kg^{-1}) or butorphanol (0.05 - 0.2 mg kg^{-1}), are also proven to provide good analgesia in ruminants (Riebold, 2015). In addition, Riebold (2015) described constant rate infusions of ketamine (bolus of 0.5 mg kg^{-1}, CRI of 10 µg kg min^{-1}) or lidocaine (loading dosage of 2.5 - 5 mg kg^{-1}, CRI of 50 - 100 µg kg^{-1} min^{-1}) to provide analgesia in goats, but these were not applied in this case series.

Reduction of the amount of anesthetics and analgesia per- and postoperatively can be achieved by the use of an epidural (Anderson and Muir, 2005). Epidural anesthesia achieved with local anesthetics and opioids has been described to provide analgesia (dos Santos Silva et al., 2017). A lumbosacral epidural anesthesia was performed in four out of twelve procedures using morphine and bupivacaine hydrochloride with the patient placed in a sternal position. The epidural space was entered as described by Skarda (1996) at the lumbosacral intervertebral joint, after surgical preparation of the skin in the region of L6-S1. Neurological anomalies caused by hematoma formation, infection or nerve injury may be associated with epidural anesthesia with occurring symptoms of pain, numbness or paraplegia (Sawai et al., 2016). Injuries of the spinal cord or nerve root can occur with or without the presence of a hematoma due to spinal compression (Kane, 1981; Sawai et al., 2016). Irritation of the nerves by the local anesthetic caused by direct toxicity of the agents (Kane, 1981; Sawai et al., 2016; Kobayashi et al., 2017) or by their osmotic effect can occur (Sawai et al., 2016). Spinal cord ischemia and thrombosis of the spinal arteries caused by hypotension can be considered as main cause of paraplegia in terms of anesthetic management related factors (Kane, 1981; Auroey et al., 1997; Sawai et al., 2016; Kobayashi et al., 2017). Hypotension can also occur as a result of epidural anesthesia (Kane, 1981). Lastly, lumbar puncture can aggravate venous engorgement causing neurological compression (Sawai et al., 2016). Patient 8B was unable to stand after the epidural with loss of deep pain sensation. Possibly, the spinal cord or meninges had been traumatized, since no hypotension occurred during the anesthetic procedure (Skarda, 1996). Nevertheless, the identification of the cause of paraplegia is essential (Sawai et al., 2016). Dexamethasone was administered once at a dosage of 0.5 mg kg^{-1}. Since there was no improvement of the patient's condition, further medical imaging examination was performed, including radiography, myelography and CT scans. On CT, no obvious spinal abnormalities were discovered that could have explained the condition, but a bony defect with mild displacement of a fragment was visible centrally at the caudodorsal endplate of L7, suggestive for osteochondrosis dissecans. Komasawa et al. (2016) described paraplegia of a man due to compression of the spinal cord by bone wax. The fragment at the level of L7 revealed at CT might therefore provide a possible explanation for the condition of the goat. However, in human medicine, magnetic resonance imaging (MRI) has been advised in several case reports to evaluate the spinal cord and determine the cause of paraplegia (Komasawa et al., 2016; Sawai et al., 2016). In this case, MRI was not performed but could have provided additional information. The owners opted the goat to be euthanized and did not wish to have a necropsy performed. One other case (1A) was unable to stand during several hours after surgery; however, this was not unexpected, since the inability to stand after epidural injection of bupivacaine for up to 11 hours, given its long duration of action has been reported (Skarda, 1996; Skada and Tranquilli, 2007).

CONCLUSIONS

Special considerations must be made when ruminants are placed under general anesthesia due to their anatomical and physiological properties which may lead to tympany, regurgitation and salivation. The use of an endotracheal tube is important to avoid (aspiration) pneumonia.

In case of obstructive urolithiasis, a good physical evaluation and assessment of the bloodwork should be performed prior to surgery. Electrolyte disbalances must be corrected before anesthesia. In one case of this case series, metabolic acidosis was present, which needed correction with bicarbonate during anesthesia.

The choice of anesthetics must be well considered due to the possible side effects of the drugs. Xylazine is not recommended because of an increased urinary production in combination with hyperglycemia and hypoinsulinemia. In addition, cardiovascular side effects (hypotension and bradycardia) can be observed, which was seen in the cases (2/12) which received xylazine.

Fluids should be given initially in a conservative way until the obstruction is relieved.

Epidural anesthesia (4/12) can be a good way to provide additional analgesia; however, in this case series, it resulted in a complication with paralysis in one case.

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Uit het verleden

Gent : Een gespan werd door een tram aangereden : het paard gedood.

Treatment of a malignant peripheral nerve sheath tumor by intravenous administration of combretastatin A4-phosphate in a dog

Behandeling van een maligne perifere zenuwschedetumor door intraveneuze toediening van combretastatine A4-fosfaat bij een hond

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ABSTRACT

A fifteen-year-old, male, castrated American Staffordshire terrier was presented with a subcutaneous, ulcerated mass on the right carpal joint. Thoracic radiographs and abdominal ultrasound were both negative for metastatic disease. Punch biopsies revealed the histopathological diagnosis of a malignant peripheral nerve sheath tumor. Due to the extent of the primary mass, local excision was not possible, and amputation of the limb was not an option for the owner. The dog was treated with intravenous administration of combretastatin A4-phosphate, a vascular disrupting agent. A biopsy was taken before and after treatment and power-Doppler ultrasound and contrast-enhanced ultrasound were performed to assess pre- and posttreatment evaluation of the tumor vasculature. The treatment resulted in massive necrosis of the tumor.

SAMENVATTING

Een vijftienjarige, mannelijke, gecastreerde Amerikaanse staffordshireterriër werd aangeboden met een subcutane, ulceratieve massa ter hoogte van het rechter carpaal gewricht. Thoraxradiografieën en een abdominale echografie waren beide negatief voor metastasen. Er werden punchbiopten genomen van de massa waaruit histopathologisch een maligne perifere zenuwschedetumor werd gediagnosticeerd. Doordat de primaire massa zo uitgebreid was, was chirurgische excisie onmogelijk en amputatie van de voorpoot was geen optie voor de eigenaar. De hond werd intraveneus behandeld met combretastatin A4-phosphate, een stof die het cytoskelet van immature bloedvaten verstoord. Voor en na de behandeling werd een biopt genomen en via “power-doppler ultrasound” en contrastechografie werd de doorbloeding van de tumor voor en na de therapie opgevolgd. De behandeling resulteerde in massale necrose van de tumor.

INTRODUCTION

Cancer is an important cause of death in companion animals (Farese et al., 2012). Pets with cancer often have very advanced (locally invasive and/or metastatic) disease when presented to a veterinarian (Farese et al., 2012).

Soft tissue sarcomas, such as peripheral nerve sheath tumors (PNST), are a heterogenous population of mesenchymal tumors that comprise around 15% and 7% of all skin and subcutaneous tumors in dogs and cats, respectively (Liptak and Forrest, 2013). Most dogs that are presented with a soft tissue sarcoma are between three and twelve years old (Targett et al., 1993). There is no specific breed or sex predilection for soft tissue sarcomas (Liptak and Forrest, 2013). PNSTs are most commonly located on the extremities (Brehm et al., 1995). In the early stage of the disease,

clinical presentation of a PNST is indistinguishable from other causes of lameness (da Costa et al., 2008). Treatment consists of surgical excision, amputation of the affected limb, radiation or, sometimes, palliative administration of corticosteroids (Targett et al., 1993; Saunders et al., 1998).

Whenever surgery is not an option, other therapies might have potential. Apart from chemotherapy and radiation, the use of drugs such as vascular disruptive agents (VDA) might be explored. Treatment with a VDA is not yet approved by the US Food and Drug Administration (FDA) in companion animals, but recent (pre)clinical studies in dogs have demonstrated positive results (Abma et al., 2017; Abma et al., 2018).

Combretastatin A4-phosphate (CA4P) is a vascular disrupting agent that is originally derived from the tree called "Combretum caffrum", a South African willow. It is a tubulin-binding agent that destabilizes the microtubules and disrupts the endothelial cells of the immature tumoral vasculature (Young and Chaplin, 2004), leading to endothelial cell death and resulting in ischemia and necrosis of the tumor cells (Kanthou et al., 2004). CA4P is an effective antivascular agent that interferes with regrowth of blood vessels by activating cell death pathways (Kanthou et al., 2004). Vascular disrupting agents such as CA4P are very specific and also selective in their target for vascularization because they only focus on the immature vessels. Immature vasculature present in the central part of the tumor is sensitive, whereas vessels of the periphery and surrounding normal tissues are mature and therefore will not be destroyed (Siemann et al., 2005). Despite its selectivity, there is proof that CA4P can be toxic for dividing endothelial cells after prolonged exposure (Galbraith et al., 2001). In animals, it has been confirmed that dividing cells that are present in the gastrointestinal tract and lymphoid tissues, are affected when CA4P is administered at or above the maximum tolerated dose (Zweifel and Rustin, 2010).

In this case report, a fifteen-year-old dog with an inoperable PNST on the carpus that received CA4P treatment, is described. Special attention is given to the different methods that can be used to assess the treatment effect of such vascular disruptive agent and the clinical results of treatment with CA4P.

CASE REPORT

A fifteen-year-old, male, castrated American Staffordshire terrier was presented with a large mass on the right carpal joint. In the past, a PNST had already been removed twice from the same location. On both occasions, it recurred after six months. The present mass had been growing slowly but consistently over the past year. Despite the extent of the tumor, the dog was not lame.

On physical examination, no abnormalities were found apart from the presence of the mass. The tumor itself was solid with an ulcerative and reddish aspect, and the surrounding tissue was swollen (Figure 1A). Blood analysis did not reveal any abnormalities. Metastasis was ruled out by thoracic radiographs and a complete ultrasound examination of the abdomen.

Local excision, even if marginally, was not an option due to the size of the mass. Therefore, limb ampu-

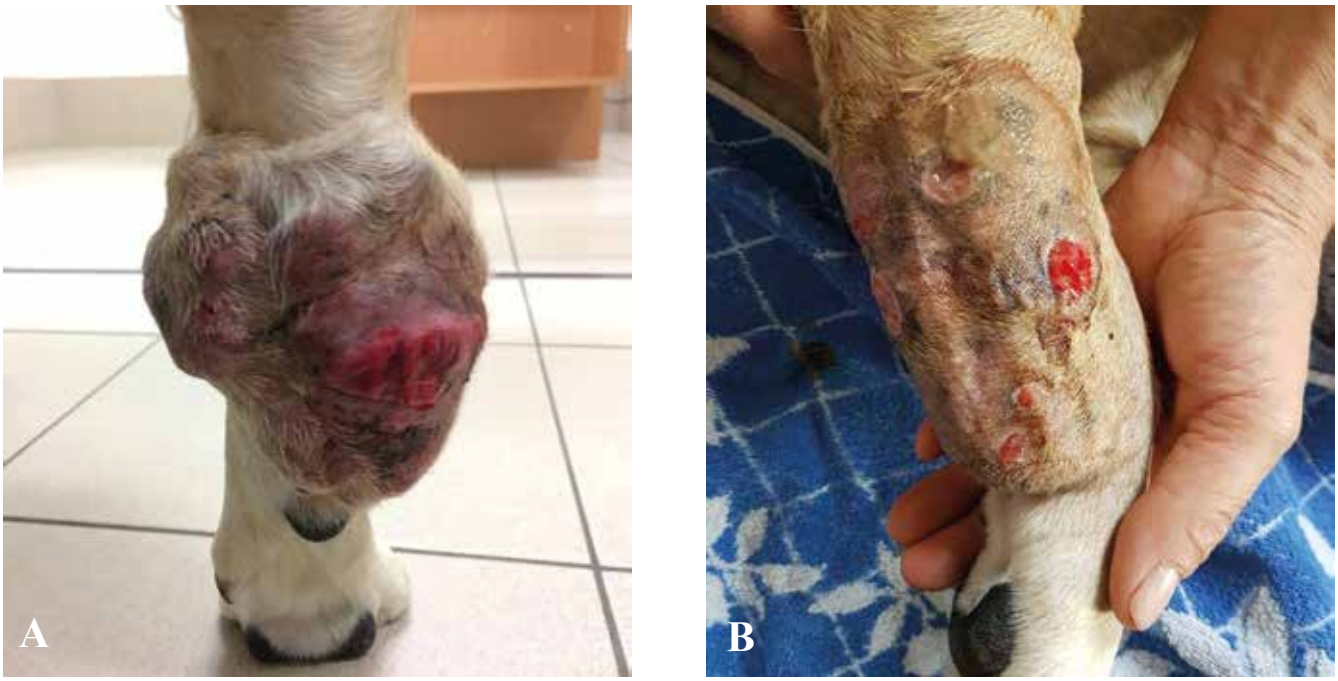

Figure 1 A. Caudal view of the ulcerative and solid tumoral mass at the level of the right carpal joint of a 15-year-old American Staffordshire terrier. B. Macroscopic view of the tumor three weeks after treatment. The mass decreased in size and the overlying skin had a less irritated and less ulcerative aspect. Regions where the biopsies were taken could be seen as small circular wounds (https://doi.org/10.1111/vco.12402).

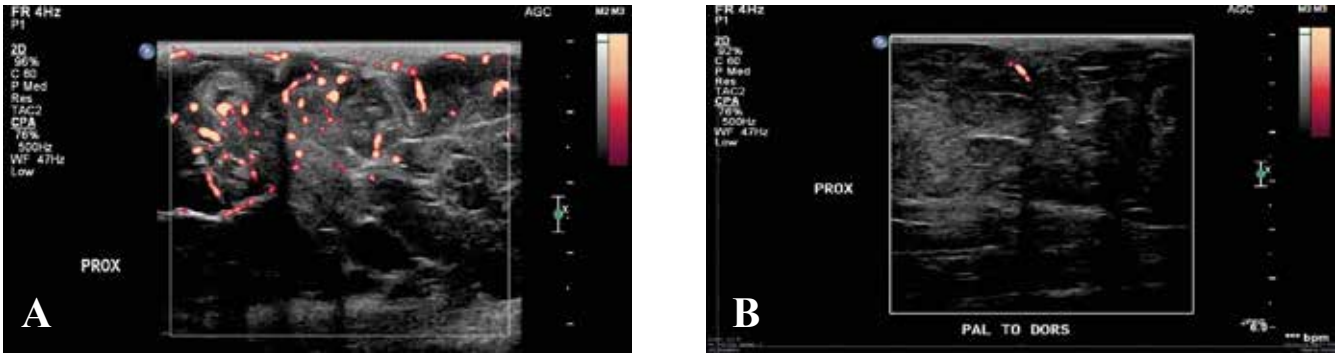

Figure 2 A. Power-Doppler ultrasound images of the tumor before treatment. Blood flow through the tumor is visualized as yellow-red dots. Vascularization is prominent in both the central part of the tumor, as well as at the periphery. B. Power-Doppler ultrasound images of the tumor three days after CA4P treatment. There is minimal blood flow remaining.

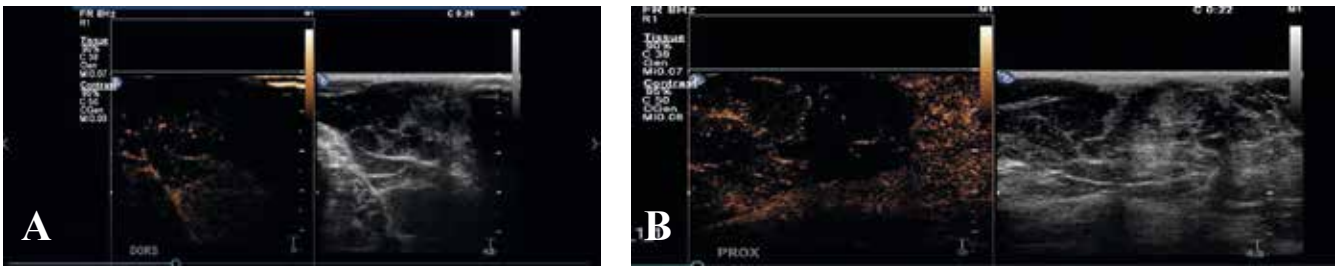

Figure 3 A. B-mode (right) and contrast-enhanced (left) image of the tumor before treatment. The microbubbles, shown in orange, are taken up by the vasculature present in the mass, with a higher uptake in the septa. There is also a diffuse uptake of contrast in a large part of the tumor. B. B-mode (right) and contrast-enhanced ultrasound (left) image of the tumor one day after treatment. The uptake of microbubble contrast is less in het central part of the tumor compared to the periphery; however, the mass can still be identified.

tation with curative intent was advised but declined. The owner reported that the dog had arthrosis in both stifle joints. Furthermore, she firmly believed that a three-legged dog would be an unhappy dog, anyhow. Since PNSTs are not sensitive to chemotherapy, the owner was informed about an ongoing experimental clinical trial on the use of the vascular disrupting agent CA4P in dogs with solid neoplasia.

To obtain more information about the vascularization of the tumor, B-mode, power-Doppler ultrasound (PDUS), contrast-enhanced ultrasound (CEUS) and biopsies were performed. A routine B-mode ultrasonography of the mass was performed and a linear transducer with a frequency of 4Hz was used. On B-mode images, the tumor could be defined as a solid mass. The mass was scanned from a dorsal to palmar region and vasculature was prominent and clearly outspoken in de central part as well as at the periphery of the tumor (Figure 2A). For the CEUS images, a linear transducer of 12-5 MHz was used, combined with a frame rate of 8 Hz. There was a large uptake of microbubbles throughout the septa of the tumor and the uptake went from the periphery to the central part of the tumor (Figure 3A). A biopsy of the mass was taken after all imaging was performed and before the treatment with CA4P was started. The protocol used for the sedation was an intravenous injection of both butorphanol (Dolorex®, 0.2 mg kg^{-1}, MSD, Brussels, Belgium) and dexmedetomidine (Dexdomitor®, 0.005 mg kg^{-1}, Orion Corporation, Espoo, Finland). After sedation and clipping, two six-mm-punch biopsies were taken and sent for histopathologic examination. On the histopathological sections before treatment, hematoxylin and eosin (HE) staining confirmed the diagnosis of malignant PNST (Figure 4A). Additional staining with anti-von Willebrand factor (vWF) was performed to identify vessels in the tissue sections (Figure 5A). Two anti-vWF stainings were made; on each, five fields of view were screened. The anti-vWF-stained slides demonstrated a multitude of viable endothelial cells.

The dog was treated intravenously with a single dose of 75 mg CA4P per m^2 dissolved in 10 mL phosphate buffered saline (PBS), infused over a period of thirty minutes. A PDUS was performed during the infusion and 24 and 72 hours after CA4P-administration. The PDUS images after treatment showed a significant decrease in vascularization compared to the pretreatment images (Figure 2B). Power-Doppler images show that the vascularity index (VI) was at its highest before injection with CA4P. After injection, the VI started to decrease and was low at 24 hours and at its lowest at 72 hours. The vascularization in the central part of the tumor was completely absent; however, in the periphery, a small amount of vascularization remained. One day after treatment, CEUS was repeated. On CEUS images, the uptake of microbubble contrast in the central part of the PNST after treatment

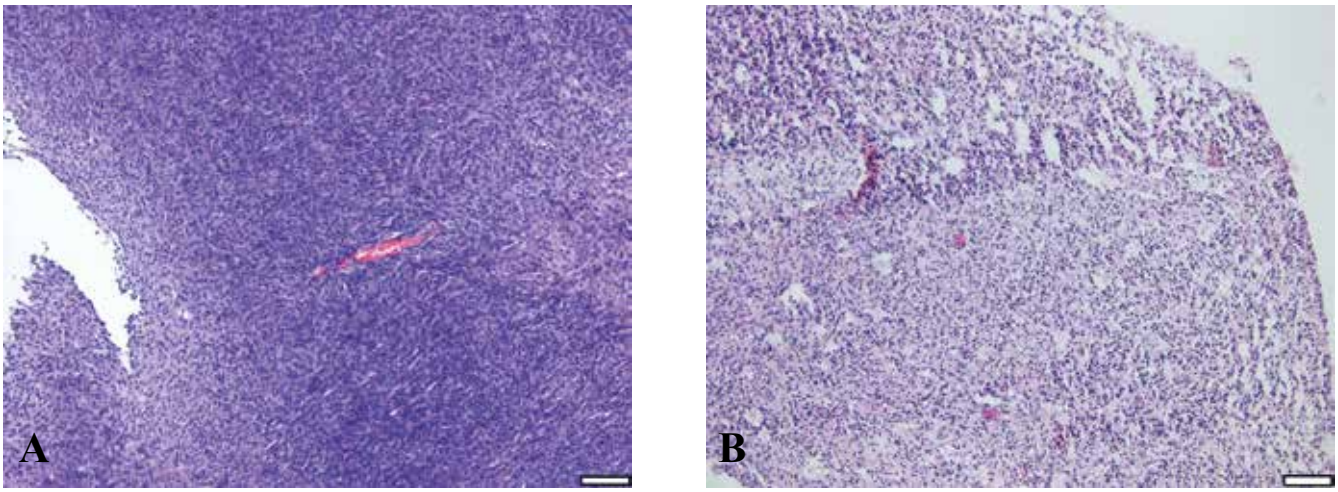

Figure 4 A. Histopathological sections of the tumor before treatment. The tumoral cells are lying in sheets with no differentiation between tumoral cells and fibrovascular stroma. The cells are spindloid with a basophilic nucleus (hematoxylin and eosin; scale bar = 100 µm). B. Histopathological sections of the tumor three days after treatment. Necrosis can be seen as a big region of eosinophilic amorphous material consisted of cellular and nuclear debris (hematoxylin and eosin; scale bar = 100 µm).

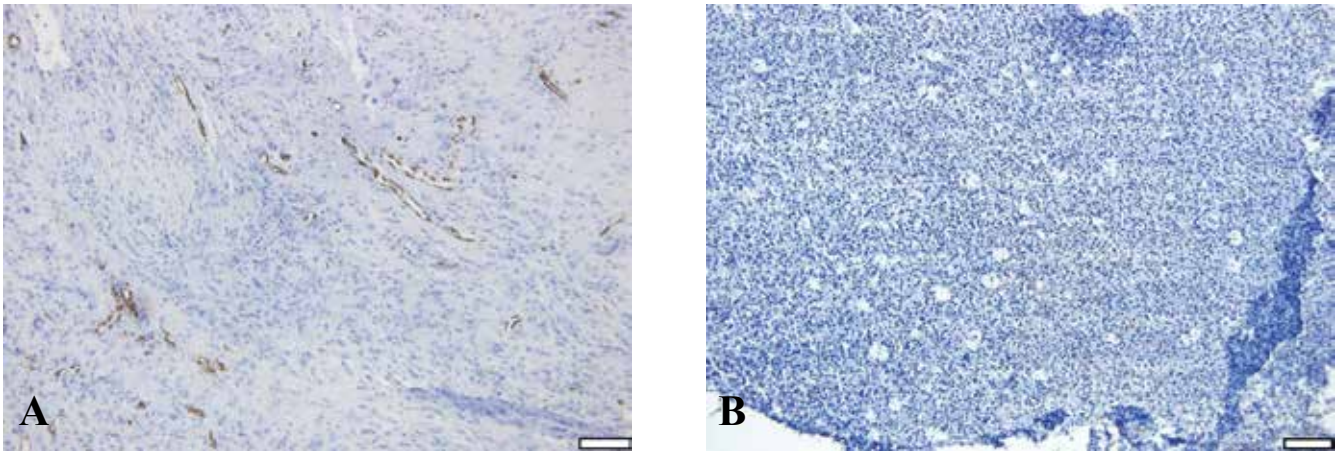

Figure 5 A. Immunohistochemical staining for endothelial cells before treatment. The endothelial cell nuclei are dark brown and the tumoral cells stain blue (anti-von Willebrand factor; Scale bar = 100 µm). B. Immunohistochemical staining for endothelial cells after treatment. There are no endothelial cell nuclei visible after treatment (anti-von Willebrand factor; Scale bar = 100 µm).

was distinctly less than before treatment (Figure 3B). Biopsies were repeated three days after treatment. On the HE-stained slides, the tumor cells displayed signs of karyorhexis (Figure 4B). In the posttreatment biopsies stained with anti-vWF, the endothelial cells were decreased in number from a mean of 0.21% before to a mean of 0.06% after treatment, indicating a reduction in viable endothelial cell density (Figure 5B).

After treatment, the dog remained hospitalized for one week and physical examination was carried out daily. Special attention was given to potential general, cardiovascular and neurological side effects of CA4P treatment. The dog was clinically stable during hospitalization but did experience side effects of CA4P, such as nausea, ataxia on the hind limbs and pain in the tumoral region. Maropitant citrate (Cerenia®, Zoetis, Belgium) was administered intravenously and nausea passed in two hours after treatment. For the tumoral pain, Methadon hydrochloride (Comfortan®, 1 mg kg^{-1}, Dechra, UK) was administered intravenously every four to six hours. The pain disappeared within 96 hours after CA4P administration. The ataxia was self-limiting and disappeared one week and a half after CA4P administration.

Three weeks after treatment, the tumoral mass was macroscopically decreased in size, and the overlying skin had a less irritated and less ulcerative aspect. Small circular wounds were indicative of the regions where biopsies had been taken (Figure 1B).

The dog returned for further follow-up, weekly for one month, and then monthly for five months. Five months after the CA4P treatment, the remaining mass got infected. Because of the poor response to local and systemic treatment, the owner decided to have the dog euthanized.

DISCUSSION

Different options are available when treating a PNST. Local tumor control is the most important consideration in the management of soft tissue sarcomas because of their locally aggressive behavior (Liptak and Forrest, 2013). As such, surgical resection is the main treatment for soft tissue sarcomas. Surgical removal of the mass without adequate margins result in incomplete resection and a high risk of local tumoral recurrence (McKnight et al., 2000; Liptak and Forrest, 2013). In a retrospective study in 51 dogs with a PNST, the overall prognosis after surgical management alone has been shown to be guarded to poor (Brehm et al., 1995). Recurrence and/or development of metastases are associated with decreased survival rate (McKnight et al., 2000). Yet, in this case with a PNST at the level of the carpus in the absence of metastasis, forelimb amputation most likely would have been curative. However, the owner declined such aggressive surgery.

Radiation therapy is often used when treating soft tissue sarcomas. It can be used along with surgery with a curative intent, either preoperatively or postoperatively, or as a sole treatment for pain palliation (Liptak and Forrest, 2013). Similar to other soft-tissue sarcomas, an excellent long-term survival rate may be achieved in some dogs with resection of a PNST followed by radiation (McKnight et al., 2000). Multimodal therapy with marginal surgical excision and postoperative radiation therapy may be limb sparing and reduce patient morbidity (Liptak and Forrest, 2013). The patient described in this case report was not eligible for radiation therapy. Even marginal surgical resection of the tumor would have resulted in a large skin defect, comprising more than half of the leg's circumference. Complications, such as impaired venous and/or lymphatic drainage and the slow healing after free skin grafting, would create a delay in the start of radiation therapy in an attempt to limit the risk of early and late side effects. Palliative radiation therapy was not considered in this case because it has an analgesic rather than a curative intent (Kubicek, 2018); moreover, the tumor was not considered painful to the dog.

The value of chemotherapy in dogs with soft tissue sarcomas, including PNST, is not known (Liptak and Forrest, 2013). In the past, it was claimed that the most promising chemotherapy protocol was doxorubicin (Ogilvie et al., 1989). In the treatment of hemangiosarcoma in dogs, no benefit of combining doxorubicin with another chemotherapeutic agent could be demonstrated (Ogilvie et al., 1996). More recent studies on the efficacy of chemotherapy protocols are not available.

Although not yet FDA-approved as anticancer treatment in domestic animals, CA4P was considered an alternative treatment option in the dog described in this case report. Single IV CA4P treatment resulted in massive necrosis of the malignant PNST. In human patients, CA4P is already FDA-approved for the treatment of several types of cancer and there are preliminary data suggesting that adding CA4P to existing chemotherapy protocols improves overall survival (Garon et al., 2010; Ng et al., 2012; Sosa et al., 2014). Also, the combination of CA4P with radiotherapy is well tolerated in most patients (Ng et al., 2012). Treatment with CA4P can contribute to a longer survival time (Garon et al., 2010). Vascular disruptive agents such as CA4P target and destroy the established tumor vessels. They should not be confused with anti-angiogenic agents (AAA); the last interfere with the de novo synthesis of blood vessels, thus preventing the formation of tumor vasculature (Siemann et al., 2005). The exact mechanism behind CA4P has not yet been completely unraveled, but the main action is the disruption of the cytoskeleton of the immature endothelial cells (Siemann et al., 2005). Binding of CA4P leads to tubulin depolymerization, inhibiting further cell proliferation. Consequently, the immature tumoral vessels collapse, leading to tumor hypoxia and necrosis. Because VDAs such as CA4P only target the immature vessels, there is little to no effect on other types of vasculature (Siemann et al., 2005).

In this case, the vascular shutdown effect of a single dose of IV CA4P was evaluated by monitoring the effect on the vascularization of the tumor by three different means. Histopathology, complemented with immunohistochemistry, is still considered the gold standard to assess the treatment effect of antivascular therapy (Gee et al., 2001). The posttreatment surgical biopsies showed clear evidence of vessel destruction and necrosis. Routine histology slides stained with HE revealed zones with necrotic cells, whereas immunohistochemistry staining with anti-vWF identified less endothelial cells. Obviously, US monitoring of the antivascular effect is a more attractive technique than serial biopsies in clinical patients because it is non-invasive. On B-mode images after treatment, the central part of the tumor was more hypoechogenic than the periphery but more specific information could not be gained. Yet, US techniques, such as PDUS and CEUS, reveal information on tissue perfusion through small vessels and the capillary bed, respectively (Wilson et al., 2009). Before treatment, the blood flow in the PNST was prominent throughout the entire tumor and was obvious on both PDUS and CEUS images. On the posttreatment PDUS and CEUS images, there was a marked decrease in vascularization compared to before treatment. It should be noted that PDUS is extremely sensitive to motion, causing flash artifacts that should not be mistaken for blood flow (Rubin et al., 1994). CEUS is an imaging modality that is not yet available to many clinicians, but is considered a promising, sensitive tool to assess in vivo vascularization (Zhang et al., 2017).

CONCLUSION

Up to now, conventional treatment of PNSTs has consisted of surgery or palliative radiotherapy. Research proves that VDAs significantly destroy the vasculature of tumoral tissue and lead to necrosis of the tumoral mass. The use of VDAs, such as CA4P, should therefore be further explored in novel combination therapies as alternative treatment options for solid tumors whenever radiation therapy, surgical resection, and/or conventional chemotherapy are not an option.

ACKNOWLEDGEMENTS

The dog described in this case report was enrolled in a clinical trial that has been funded in part by the Agency for Innovation & Entrepreneurship under contract number 141020 and by the Belgian Animal Cancer Foundation (BKFD).

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Degenerative granulomatous mural folliculitis and cytotoxic dermatitis in a dog

Degeneratieve granulomateuze murale folliculitis en cytotoxische dermatitis bij een hond

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ABSTRACT

A variant of degenerative granulomatous mural folliculitis with cytotoxic dermatitis is reported in a dog that presented with multifocal, well-demarcated, annular alopecia with peripheral crusting. The skin condition might have been drug-induced and responded well to oral ciclosporin.

SAMENVATTING

In deze casus wordt een variant van degeneratieve granulomateuze murale folliculitis met cytotoxische dermatitis beschreven bij een hond aangeboden met multifocale, goed omschreven, annulaire alopecie met een korstige periferie. De mogelijk medicatie-geïnduceerde huidaandoening vertoonde een uitstekende respons op een orale behandeling met ciclosporine.

INTRODUCTION

Degenerative granulomatous mural folliculitis (DGMF) is a rare and presumed immunological alopecic syndrome in dogs. Only one case has been reported in the scientific literature (Scott, 1999), and a few additional cases have been mentioned in textbooks or abstracts (Gross et al., 1993; Gross et al., 2005; Welle et al., 2009; Miller et al., 2013). The wide range in severity and diversity of lesions noted, both clinically and histopathologically, suggests a multifactorial etiology. The most frequently documented cause of DGMF in dogs is drug reaction (Scott, 1999; Gross et al., 2005; Miller et al., 2013). The condition is clinically characterized by highly variable alopecia that may be multifocal or coalescing and generalized. Scaling and crusting may be present. In long-standing cases, alopecic skin often has a smooth, shiny appearance with variable degrees of hypopigmentation. Pruritus is usually not present (Scott, 1999; Gross et al., 2005; Welle et al. 2009). Histopathologic examination reveals granulomatous to pyogranulomatous mural folliculitis with destruction of follicles and sebaceous glands. There may be pronounced perifollicular granulomatous inflammation. Mural follicular inflammation includes histiocytes, lymphocytes and neutrophils. Multinucleated giant cells may be present. Interface dermatitis and apoptosis (increased eosinophilia of keratinocytes) are generally mild but uncommon (Gross et al., 2005; Welle et al., 2009). Endstage lesions may be severe follicular atrophy and dropout.

Cytotoxic dermatitis (interface) represents a number of reaction patterns that may occur in the skin consequent to the infiltration of reactive T lymphocytes (Yager, 2014; Affolter et al., 2015). This term focuses on cell death of keratinocytes and hence, includes single cell necrosis/apoptosis of basal cell as well as more superficial keratinocytes. This can occur with or without an inflammatory infiltrate that obscures the dermo-epidermal junction. The aim of this report is to describe a mixed pattern of degenerative granulomatous mural folliculitis and cytotoxic dermatitis in a dog.

CASE DESCRIPTION

A seven-year-old, intact, male Miniature poodle was presented to the referring veterinarian with alopecic and crusted lesions on the dorsal neck and thorax. Apart from the skin lesions, the dog appeared to be in good health. One month prior to the onset

Figure 1. Right dorsolateral thorax of the dog. A small area, on the left side of the picture was clipped for visualization. Coalescing and well-circumscribed annular hyperpigmented patches with alopecia in the center and scaling and crusting at the peripheral borders.

Figure 2. Dog in left lateral decubitus, anterior view of the right stifle. Alopecic hyperpigmented skin with patchy hypopigmentation and a shiny appearance.

of the skin condition, the dog had been treated for coughing with amoxicillin clavulanate (Clavubactin, Le Vet Pharma, Oudewater, the Netherlands) at 12.5 mg/kg twice daily for ten days and tolfenamine-acid (Tolfedine, Vétoquinol, Aartselaar, Belgium) at 3 mg/kg once daily for three days. The skin lesions were treated with a topical phytopharmacum containing Melaleuca, Origanum, Cinnamomum and Cymbopogon (Curax gel, Phytovet, Putte, Belgium). In spite of this treatment, the dog had developed new lesions and became pruritic. Systemic treatment was initiated with cefalexin (Therios, Sogeval, Laval, France) at 20 mg/kg twice daily. Whilst on cefalexin therapy, the skin condition had worsened rapidly. Based upon the results of a bacterial culture and antibiotic sensitivity testing, the treatment was changed to marbofloxacin (Marbocyl, Vétoquinol, Aartselaar, Belgium) at 2 mg/kg once daily. As the skin lesions also had failed to respond to the last treatment, the dog was referred with a three-month course of skin disease.

At referral, the history and physical examination revealed no abnormalities other than moderate pruritus associated with an alopecic cutaneous eruption. The condition was more or less symmetrical and limited to the top of the head, the entire neck, over the dorsolateral thorax, and on all aspects of the limbs. The skin lesions were coalescing, well-circumscribed, annular hyperpigmented patches with alopecia in the center and severe scaling and crusting at the peripheral borders. Removal of the crusts revealed ulcerations

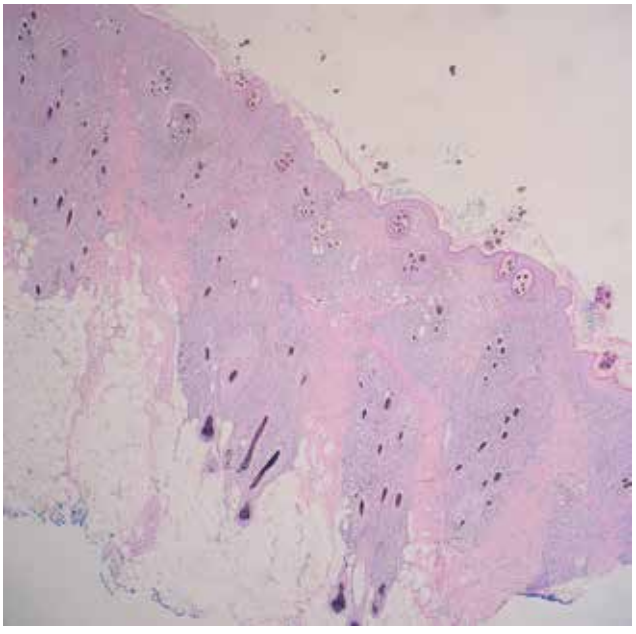

Figure 3. Overview of panfollicular inflammation with loss of sebaceous glands. Hematoxylin and eosin stain, 100x.

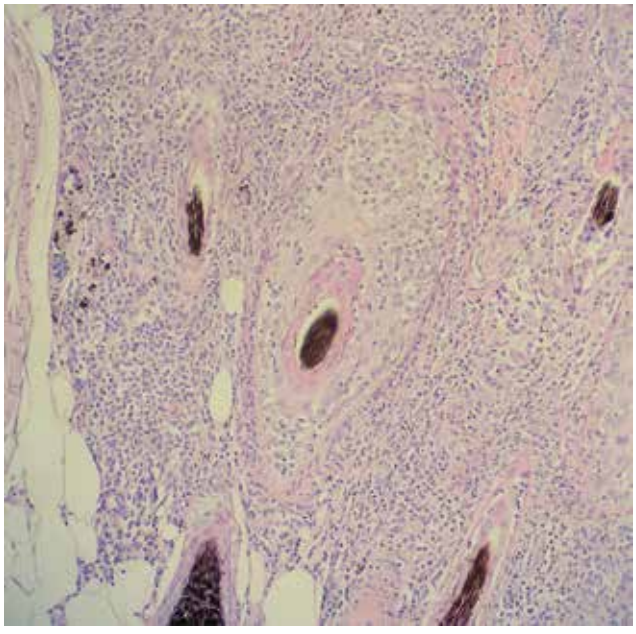

Figure 4. Closer view of an inflamed follicle. Histiocytes within the follicular wall and perifollicular infiltration of mainly lymphocytes and plasma cells. Hematoxylin and eosin stain, 200x.

(Figure 1). The exposed skin on the limbs was hyperpigmented with foci of hypopigmentation and had a smooth shiny appearance (Figure 2). The peripheral lymph nodes were normal. Clinical differential diagnoses included, but were not limited to, cutaneous adverse drug reaction (CADR), erythema multiforme (EM) and generalized discoid lupus erythematosus (GDLE). Two excisional biopsy specimens were taken from the lateral thorax. Histopathological examination showed two reaction patterns. The predominant pattern was a granulomatous to pyogranulomatous mural folliculitis tracking down the full length of the hair follicles (from the infundibulum to the hair bulb) with loss of sebaceous glands (Figure 3). Mural inflammation included mainly histiocytes, neutrophils, lymphocytes and a few multinucleated giant cells (Figure 4). Neutrophilic luminal folliculitis was seen in the superficial portions of the hair follicles. There was a multifocal mild to moderate perifollicular infiltration of lymphocytes, plasma cells and less histiocytes. Endstage lesions were complete drop out of hair follicles and loss of sebaceous glands, often with aggregates of melanophages (Figure 5). The second and minor pattern was a multifocal mild interface dermatitis with scattered transepidermal single cell necrosis, occasionally with lymphocytic satellitosis and a moderate pigmentary incontinence (Figures 6 and 7). These areas occasionally had severe overlying serocellular crusting. The hair follicles showed similar but minor changes. A diagnosis of mixed degenerative granulomatous mural folliculitis and cytotoxic dermatitis was made.

The history and histopathological findings were considered to be consistent with CADR. The dog was treated with ciclosporin oral solution (Neoral Sandimmun, Novartis, Vilvoorde, Belgium) at 6 mg/kg once daily. Six weeks later, a marked clinical improvement was noticed. The dog was no more pruritic and the lesions had progressively regressed. The treatment was continued at the same dosage for another two months. After that time, the lesions had resolved completely and there was residual cicatricial alopecia.

DISCUSSION

The main clinical feature of degenerative granulomatous mural folliculitis is alopecia that may be patchy and multifocal, or coalescing and generalized. Erythema, scaling and crusting may be present. Advanced cases reveal a shiny smooth alopecic skin with variable degrees of hypopigmentation (Scott, 1999; Gross et al., 2005; Welle et al., 2009). The prominent clinical features in the dog of this report were alopecia and crusting. The skin lesions on the dorsolateral thorax were well-demarcated, hyperpigmented patches with alopecia in the center and severe scaling and crusting at the peripheral borders. Severe crusting is not a prominent feature of DGMF. The clinical lesions of the present dog resembled those that have

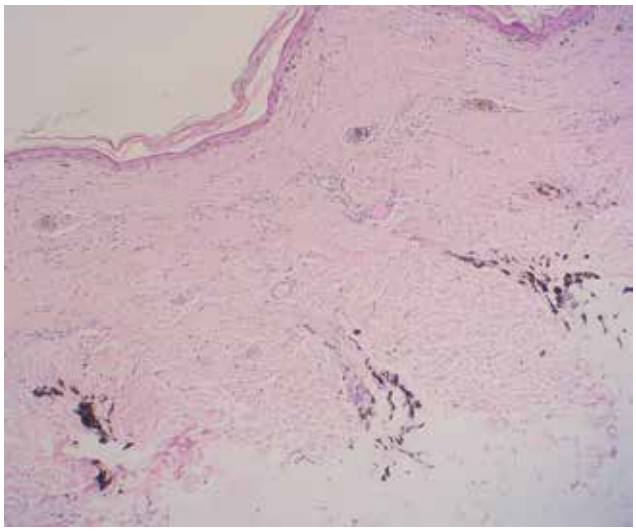

Figure 5. Endstage lesions. Hair follicles are completely erased. Melanomacrophages indicate previous follicular structures. Minimal superficial dermal inflammation. Hematoxylin and eosin stain, 100x.

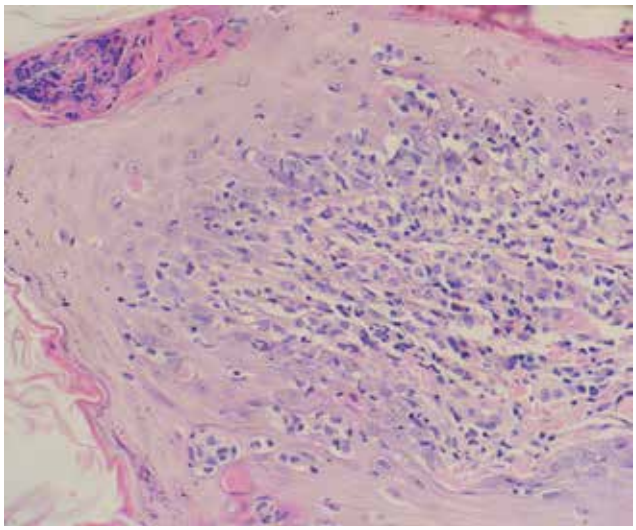

Figure 6. Mild lymphocytic-rich interface dermatitis with scattered keratinocyte apoptosis in multiple epidermal levels. Note suprabasilar keratinocyte apoptosis with lymphocytic satellitosis. Hematoxylin and eosin stain, 400x.

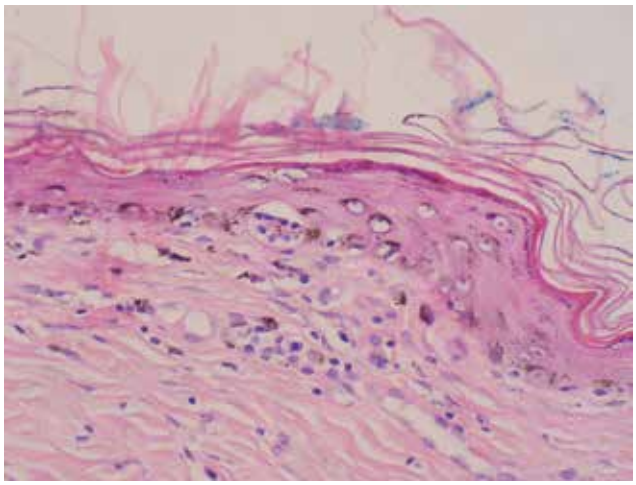

Figure 7. Cell-poor interface dermatitis with a basal keratinocyte apoptosis with lymphocytic satellitosis. Hematoxylin and eosin stain, 400x.

been reported in GDLE (Banovic et al., 2016) and in erythema multiforme (Yager, 2014). The alopecic lesions on the extremities revealed hyperpigmentation of the skin with foci of hypopigmentation and the exposed skin had a smooth shiny appearance. These features were consistent with those described in advanced cases of DGMF.

The predominant pattern on histopathology in the present case was degenerative granulomatous to pyogranulomatous mural folliculitis with loss of sebaceous glands and sequential diffuse effacement and drop out of hair follicles. The histopathology of DGMF may have marked perifollicular granulomatous inflammation tracking down along the hair follicles (Gross et al., 2005; Welle et al., 2009). Perifollicular inflammation in this case was mainly lymphoplasmacytic and mild to moderate. Severe granulomatous perifollicular inflammation was not observed. Histiocytes and giant cells can infiltrate the walls of follicles secondary to follicular necrosis with subsequent granulomatous inflammation towards hair shafts mimicking primary granulomatous mural folliculitis (Gross et al., 1993). A secondary inflammatory event was considered unlikely as granulomatous mural inflammation was present in intact hair follicles. GDLE may be considered as a differential diagnosis clinically and histopathologically. Lymphocytic mural folliculitis does occur in GDLE, although the predominant microscopic feature in this condition is a lymphocyte-rich interface dermatitis (Banovic et al., 2016). In the dog of this report, lymphocytes were mainly part of the perifollicular inflammation. In the present case, the interface dermatitis was only a minor pattern and was multifocal and mild. The cytotoxic component was characterized by a mild interface dermatitis with scattered keratinocyte apoptosis of multiple epidermal levels, very occasionally with a lymphocytic satellitosis. This last finding is also seen in GDLE (Banovic et al., 2016) and is a more florid finding in EM. The histological lesions differed from 'classic' EM in that there was less basilar apoptosis and hydropic degeneration and a lower degree of superficial keratinocyte apoptosis (Gross et al., 2005; Yager, 2014). The histopathologic patterns did not support the diagnosis of GDLE or EM. The skin condition was diagnosed as a variant of DGMF with a lymphocyte-mediated, cytotoxic component.

The history and mixed histopathologic reaction patterns were considered to be compatible with CADR. A drug reaction occurs at least 7-10 days after the first administration of the drug (Scott et Miller, 1999). The dog in the present report developed clinical signs after treatment with amoxicillin clavulanate for ten days and with tolfenamine-acid for three days; both are commonly incriminated drugs. The dog had not received tolfenamine-acid previously and therefore amoxicillin clavulanate was likely to be the causative drug. The owner had observed the initial skin lesions twenty days after amoxicillin clavulanate had been discontinued. This timing of events was unusual as most cutaneous adverse reactions to drugs resolve within two weeks with removal of the suspected agent (Scott and Miller, 1999). The skin condition in the Miniature poodle had rapidly progressed when cefalexin treatment was initiated, which can be considered as a minor rechallenge. Amoxicillin clavulanate and cefalexin are related drugs of the same class, the beta-lactam family of antibiotics. The probability of CADR by applying the Naranjo system was estimated as probable. The drug-induced etiology for the dog reported here must still be regarded as putative as no rechallenge using the suspect medication was performed, a criterion not applicable for ethical considerations.

In conclusion, in this report, a dog is presented with DGMF and cytotoxic dermatitis. The condition might have been drug-induced and responded well to oral ciclosporin.

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An atypical case of pyoderma gangrenosum in a dog

Een atypisch geval van pyoderma gangrenosum bij een hond

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ABSTRACT

Neutrophilic and ulcerative dermatitis is reported in a mixed breed dog. The condition was considered to be an atypical case of pyoderma gangrenosum. Clinically, it had a more superficial ulceration, a more pronounced pustular component and lacked the characteristic cutaneous pain and tenderness of the lesions. The diagnosis of pyoderma gangrenosum was made as a diagnosis of exclusion. The dog showed an excellent response to treatment with ciclosporin (Cyclavance, Virbac, Leuven, Belgium).

SAMENVATTING

In deze casuïstiek wordt een geval van neutrofiele en ulceratieve dermatitis beschreven bij een canis vulgaris. De aandoening werd beschouwd als een atypisch geval van pyoderma gangrenosum. De hond had een uitgesproken pustulaire eruptie en vertoonde meer oppervlakkige ulceraties. Ook ontbrak bij deze letsels de voor pyoderma gangrenosum karakteristieke begeleidende pijn. De diagnose van pyoderma gangrenosum werd gesteld als een diagnose per uitsluitsel. De hond vertoonde een uitste-kende respons op een behandeling met ciclosporine (Cyclavance, Virbac, Leuven, Belgium).

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare, chronic, often destructive, inflammatory skin disease, in which a nodule or pustule breaks down to form a progressively enlarging ulcer with a raised, tender, and undermined border. Lesions may be solitary or multiple and are, almost invariably painful (Gross et al., 2005; Ruocco et al., 2009). They present either in the absence of any apparent underlying disorder or in association with a systemic disease, or may more rarely be linked to many kinds of surgery and various drugs (Ruocco et al., 2009). PG is largely a clinical diagnosis based on clinical features and exclusion of all other causes of ulcerative skin disease (Gross et al., 2005; Ruocco et al., 2009). The histopathology of PG is unspecific and shows massive dermal infiltrations of neutrophils and large crateriform ulcers with neutrophils beneath and adjacent to the ulcers (Gross et al., 2005; Ruocco et al., 2009). The primary objective of biopsy is to rule out other causes of ulceration, i.e. infection, vasculitis, malignancy.

Four clinical and histological variants of PG have been described in humans, i.e. ulcerative, pustular, bullous and vegetative (Weedon, 2002; Ruocco et al.,2009). There is still little information available regarding the characteristics of PG in dogs as only a few cases have been reported in the peer-reviewed literature (Bardagi et al., 2007; Simpson et al., 2013; Declercq, 2015; Nagata et al., 2016). Affected dogs may be febrile and have malaise (Gross et al., 2005). Reported canine PG cases are all typical forms with cutaneous lesions described as painful and deep ulcerative. PG in the dog has a predilection for the trunk, particularly the dorsum (Gross et al., 2005), although limbs, head and neck, tail base and tail, may also be involved (Declercq, 2015). The phenomenon of pathergy or Koebner phenomenon, i.e. new lesions forming in response to minor trauma (Simpson et al.,2013; Nagata et al., 2016) and the clinical finding of cribriform scarring (Simpson et al., 2013), minor human diagnostic criteria, have been documented. Reported effective treatments in the dog include oral prednisolone alone (Declercq, 2015; Nagata et al., 2016) or in conjunction with ciclosporin (Bardagi et al., 2007) or with azathioprine (Simpson et al.,2013).

The aim of this report was to describe an atypical case of PG in a dog.

Figure 1. Large and deep draining ulceration on the head. Note the ectropion of the right lower eyelid.

Figure 2. Distribution of the lesions. Note the large and deep ulceration on the head in contrast to the more superficial aspect of the small ulcers on the body and limbs.

CASE DESCRIPTION

A seven-year-old, mixed breed, spayed, female dog was presented to the referring veterinarian with a fever of 40°C and skin lesions. Pustules and crusts were observed on the bridge of the nose, the dorsal trunk and on the limbs. The lesions were not pruritic or painful. One month prior to the onset of the skin condition, the dog had a dental care treatment for periodontal disease and ten days prior to the onset of the skin condition, the dog underwent surgery for a closed-cervix pyometra. At both of the medical interventions, the dog had been treated with eight-day courses of oral amoxicillin clavulanate (Clavubactin, Le Vet B.V., Oudewater, the Netherlands) 15 mg/kg twice daily and five-day courses of meloxicam oral suspension (Meloxoral, Le Vet B.V., Oudewater, the Netherlands) 0.1 mg/kg once daily. An adverse drug reaction was suspected and all drugs were stopped. Skin biopsies were obtained and submitted for histopathology. The morphologic diagnosis was neutrophilic vasculitis. Treatment with prednisolone (Prednisolone, Kela Laboratories, Sint-Niklaas, Belgium) 2 mg/kg once daily was initiated. Clinical response to immunosuppressive doses of prednisolone was excellent. Dose tapering to 1 mg/kg by the referring veterinarian resulted in severe worsening of the skin problem. The dose of prednisolone was increased to 1.5 mg/kg and ciclosporin (Cyclavance, Virbac, Leuven, Belgium) 6 mg/kg once daily was added. As the dog was febrile and new pustular lesions still had developed over the following few days, the case was referred. In order to fully evaluate the original nature of the dog's skin lesions, the referring veterinarian was advised to stop all immunosuppressive medications. Within the next three days, a deep and exudative ulceration reappeared on the dog's face. Therefore, in the meantime to the referral, a treatment was dispensed of oral enrofloxacin (Baytril, Bayer, Diegem, Belgium) 5 mg/kg once daily combined with oral clindamycin (Clindamycine, Kela Laboratories, Sint-Niklaas, Belgium) 10 mg/kg twice daily.

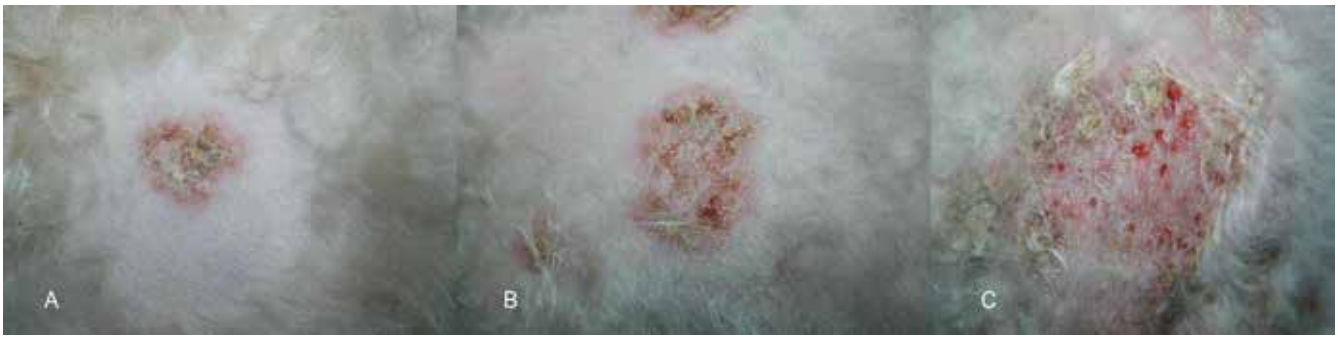

Figure 3. PG lesions on the trunk in various stages of development. A. Well-demarcated clusters of small yellow pustules on an erythematous base. B. The pustules are breaking down to form small ulcers and new pustules are arising at the border. C. Small superficial indolent ulcers with no undermined borders that do not drain.

At admission, the dog was depressed and had a normal rectal temperature. Physical examination revealed widespread skin disease. There were lesions on the face, the medial aspect of both ears, on the dorsolateral neck and trunk, and on the four limbs. The initial lesions were small pustules that broke down to form ulcers. The skin disease was non-painful, neither at the pustular stage nor at the ulcerative stage. The face was more severely affected. There was widespread and deep ulceration with exudation and crusting that had deformed the lower right eyelid causing ectropion (Figure 1). Lesions on other parts of the body, i.e. medial aspects of the ears, neck and trunk, limbs were characterized by multifocal, well-demarcated areas that were studded with small pustules, arising simultaneously or subsequently, on an erythematous base. Pustules broke down to form small and indolent superficial ulcers that did not drain. Peripheral spreading of these focal areas resulted from new pustules arising on the erythematous periphery. The lesions on the legs had coalesced to involve almost the entire limbs (Figures 2 and 3). The peripheral lymph nodes were normal on palpation. Differential diagnosis included, but was not limited to, deep bacterial pyoderma, fungal infection and pyoderma gangrenosum.

Cytology and bacterial culture of intact pustules, and fungal culture and skin biopsies of truncal lesions were performed. Cytological evaluation of the pustule's contents revealed numerous neutrophils and a few macrophages suggesting a purulent-pyogranulomatous inflammation. No microorganisms were detected in any of the cytology samples. While awaiting the findings of both of the cultures and the results of the histopathological examination, the combined antibiotic therapy was continued. At twenty days of treatment, there was no improvement of the skin lesions. Histopathological examination revealed focal and dense subepidermal, neutrophilic infiltrations, not primarily follicular, with dermal hemorraghes (Figure 4). There were multiple crateriform ulcers covered with neutrophils that occasionally penetrated into the deep dermis (Figure 5). No microorganisms were identified on histopathology, on hematoxylin and periodic acid-Schiff stains. No bacterial or fungal growth was obtained from the submitted skin samples.

Pyoderma gangrenosum was diagnosed by exclusion diagnosis. Antibiotics were stopped. Treatment with oral ciclosporin 6.5 mg/kg once daily was initiated. Ten weeks later, the skin lesions had progressively resolved and the treatment was continued, given once every second day for one month and then given once every third day for two months. Therapy was stopped, but seven weeks later, new pustular lesions developed. Treatment with once-daily oral ciclosporin was reinstituted for a month and the dog was finally maintained in remission with six days of treatment a week. There was cicatricial alopecia and permanent scarring of the face (Figure 6).

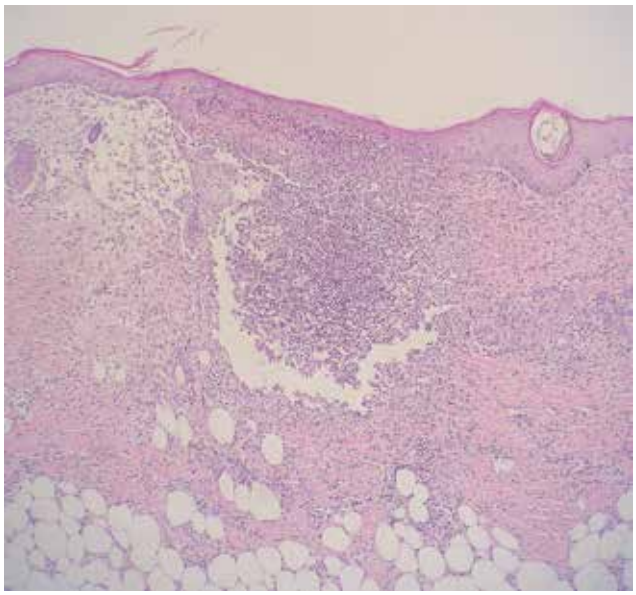

Figure 4. Subepidermal neutrophilic infiltration, not primarily follicular. Note the subepidermal hemorraghe (hematoxylin and eosin stain 200x).

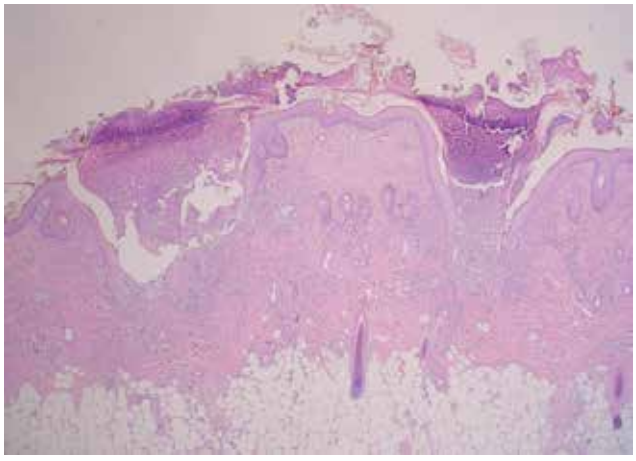

Figure 5. Early ruptured dermal pustules. Small crateriform superficial ulcers with grossly no undermined peripheral borders (hematoxylin and eosin stain 40x).

Figure 6. Healing of the lesions after ciclosporin therapy. Note the cicatricial alopecia and the scarring of the face.

DISCUSSION

PG is a rare inflammatory and ulcerative skin disease of presumed neutrophilic dysfunction (Gross et al., 2005; Ruocco et al., 2009). As histopathology is indicative, but not diagnostic, the diagnosis rests entirely on the clinical presentation and course. Typical clinical features include a painful pustule or nodule that breaks down to form a progressively enlarging deep ulcer with a raised, tender, undermined border that drains exudate. Peripheral growth results from the burrowing extension of the undermined margin or from fresh pustules arising on the border. Lesions may be solitary or multiple, gradually progressive or indolent (Gross et al., 2005; Ruocco et al., 2009). In humans, clinical variants have been described where the ulceration is more superficial and with no undermined border or surrounding erythema (Weedon, 2002; Ruocco et al., 2009). In doubtful atypical cases, the diagnosis is confirmed through a process of elimination of other (infectious) causes of cutaneous ulcers (Ruocco et al., 2009).

The primary skin lesion in the dog of the present report was a small pustule that broke down to form an ulcer. Peripheral growth resulted from new pustules arising on the border. On the dog's head, the lesions had progressed and coalesced to form a deep and large ulceration. On all other parts of the body, pustules had appeared in well-demarcated clusters with a surrounding erythema. The resulting ulcers remained small and superficial and did not drain. There was no pain at any stage of the disease and the peripheral lymph nodes were normal. Except for malaise, there were no systemic signs. The skin condition in the present report was considered to be an atypical case of PG for several reasons. First, the dog presented with an overlap of different types of PG. It had the classical deep ulceration of PG on the head that was progressive and draining. In other parts of the body, there was a more superficial ulceration and a pronounced pustular component. The small ulcers were indolent and had no undermined borders. Secondly, severe pain and tenderness commonly associated with lesions of PG, were not present at any stage of the disease. Lesions in humans have been reported as, almost invariably, painful (Ruocco et al., 2009). This wording may imply that cutaneous pain is not an absolute criterion for diagnosis and it may occasionally be absent. The lesions involved the head, dorsolateral neck and trunk, and limbs, which fits with the description in published canine PG cases.

In atypical cases, as in the present case, the diagnosis is based on exclusion of other causes of similar appearing cutaneous ulcerations. Fungal infection was excluded by a negative culture on Sabouraud's dextrose agar and a negative periodic acid-Schiff staining of the skin biopsies. Cytology samples and bacterial culture of intact pustules could not detect the presence of bacterial microorganisms. The lack of response to antibiotics of different classes, i.e. beta-lactams, fluoroquinolones, lincomycin, and the excellent response to prednisolone and ciclosporin supported a non-infectious etiology of the dog's skin condition. The histopathology findings observed in this dog were similar to those seen in PG, i.e. massive neutrophilic dermal infiltrations (subepidermal pustulations) and crateriform ulcers. Histopathological examination of the skin biopsies, initially obtained by the referring veterinarian, had provided a morphologic diagnosis of neutrophilic vasculitis. This misdiagnosis could be related to the choice of the biopsy site that lacked the massive dermal neutrophilic infiltration. Histopathology of PG may show pronounced dermal hemorrhages (Gross et al., 2005) and a vasculitis may be present as a secondary event (Weedon, 2002). Taken into consideration the pathology result, exclusion of other causes and failure to respond to anti-infectious agents, the diagnosis of PG was made as a diagnosis of exclusion.

Underlying conditions could not be identified. PG has been rarely linked with various drugs and surgery (Gross et al., 2005; Ruocco et al., 2009; Miller et al., 2013). Interestingly, prior to the onset of the skin lesions, the dog of the present report and a dog in another report had been treated with meloxicam (Declercq, 2015). The dog of the present case had developed PG soon after abdominal surgery. Triggering of PG by the administered meloxicam or by surgery cannot be completely discarded.

The number of cases of PG in the veterinary literature is too small to draw any meaningful conclusions regarding comparative treatments. The dog in the present report had been treated consecutively with prednisolone alone, prednisolone in conjunction with ciclosporin and ciclosporin alone. The therapeutic responses to these treatments suggested that concurrent short-term use of prednisolone at an immunosuppressive dose with ciclosporin may be considered as an effective treatment of PG in dogs.

In summary, PG can be a challenging clinical diagnosis. Dogs may present with atypical lesions characterized by a more florid pustular component and a more superficial ulceration that lacks an undermined border, which is normally seen. Cutaneous pain is not an absolute clinical criterion for the diagnosis and it may be absent.

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Uit het verleden

'T ZWIEN

Het zwien is het schoonste der beesten,
Zonder varken wuk zouden we zyn?
't Is er nodig ip al onze feesten,
Ik eet'n alles gèren van 't zwien.

Smout, vet, hespe en spek, hoofdvlees, korteletten en paté
Worsten en bloeling en vette derms, scheutelvlees en zwienepoot.

E'j gie nog dat beestje zien slokken?
't Is altijd zo up zyn gemak.
Het jeunt hem in sop en in brokken,
Zijn pootjes staan ook in de bak.

In 't zwienekot, ge zoudt daar wegsleeren,
Niet dat de zwiens daarmee afzien.
Ze wroeten, ze zoen 't ol ommekeren,
Hoe vulder, hoe schoonder om zien.

Een plaatje die ook nog kan tellen
Voor 's winters os 't vriest gereed te doen:
Een schoon stuksje zwienerauwélle,
Met kole gestoofd in andjoen.

Die gerenoars, 'k kan geen meer rieken,
En koeietong, 'k wil geen meer zien.
En zwijg me van haze of kieken,
Mo geef mi een broksje van 't zwien.

Liedje gebracht door de folkgroep O'Djavel. Auteur van de tekst: F. Vercruysse

A perianesthetic approach of heat stroke in a dog with laryngeal paralysis

De perianesthetische benadering van hitteslag door larynxparalyse bij de hond

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ABSTRACT

In this case report, a seven-year-old, male, castrated Landseer presented with chronic respiratory distress, occasional coughing, dysphonia and exercise intolerance is described. The stress caused by transportation and the physical examination rendered the dog severely dyspneic and cyanotic. At that moment, the core body temperature was increased up to 42.5 °C. Based on the clinical signs, laryngeal paralysis causing heat stroke was the most likely diagnosis. The dog was anesthetized and intensive temperature control methods, like active cooling and fluid therapy, were applied. As soon as the dog was cardiovascularly stable, emergency treatment for laryngeal paralysis was performed. As a result of timely intervention, the dog recovered completely without any persisting complications.

SAMENVATTING

Een zeven jaar oude, mannelijke, gecastreerde landseer werd aangeboden met chronische ademhalingsklachten, occasioneel hoesten, dysfonie en inspanningsintolerantie. Door stress veroorzaakt tijdens het transport en het klinisch onderzoek vertoonde deze hond al snel zeer ernstige dyspneu met cyanose. Op dat moment werd een rectale lichaamstemperatuur van 42,5°C gemeten. Gebaseerd op de klinische symptomen was een hitteslag veroorzaakt door larynxparalyse de meest waarschijnlijke diagnose. De hond werd met spoed onder anesthesie gebracht en intensieve verkoelende behandelingen, zoals actief koelen en vloeistoftherapie, werden uitgevoerd. Vanaf het moment dat de hond cardiovasculair stabiel was, werd een spoedbehandeling voor larynxparalyse uitgevoerd. Dankzij een tijdige interventie herstelde deze hond volledig zonder blijvende complicaties.

INTRODUCTION

Heat stroke is a life-threatening condition that veterinarians regularly face in practice during summer. It is frequently observed in dogs but rarely in felines (Johnson et al., 2006). This complex form of hyperthermia is characterized by body temperatures above 41°C and dysfunction of the central nervous system (Bruchim et al., 2009; Hemmelgarn and Gannon, 2013a). Typical for this condition is the direct lethal damage to organ systems as a result of a non-pyrogenic increase in body temperature (Flournoy et al., 2003). Heat stroke is associated with a systemic inflammatory response, leading to progressive multiple organ failure and possibly resulting in death (Bruchim et al., 2009; Hemmelgarn and Gannon, 2013b).

Multiple organ systems are involved in this condition, with the central nervous system playing a crucial role. Also the gastrointestinal tract, the renal, the pulmonary and the coagulation systems are disturbed. Common side effects of heat stroke are disseminated intravascular coagulation, acute kidney injury, and acute respiratory distress syndrome (Bruchim et al., 2009; Hemmelgarn and Gannon, 2013a). This condition has high mortality rates of 50% to 56%. To achieve an increased chance of survival, early detec-

tion, elimination of the cause, aggressive therapy and critical monitoring are necessary (Flournoy et al., 2003; Hemmelgarn and Gannon, 2013a).

CASE HISTORY

A seven-year-old, male, castrated Landseer was presented at the Small Animal Department, Faculty of Veterinary Medicine (Ghent University) with chronic respiratory distress, occasional coughing, dysphonia and exercise intolerance. The symptoms had gradually started six months before presentation. Since a couple of days before presentation, the dog had become very dull and had developed an inspiratory stridor at rest. At the local veterinarian, the dog was tested for laryngeal paralysis, but findings were inconclusive.

On physical examination, the dog was alert. He showed mixed inspiratory and expiratory dyspnea and stridor. Body weight was 84.5 kg and a body condition score (BCS) of 6/9 was given. He was tachypneic (40/min) and his heart rate was 120 beats per minute (bpm). Rectal temperature at that point was moderately increased (40.5°C). The red mucous membranes showed a capillary refill time (CRT) of less than two seconds. Pulmonary and cardiac auscultations, as well as pulse quality were normal. During consultation, the dog became progressively more dyspneic and cyanotic. Based on the severity of the respiratory symptoms, an extensive preanesthetic examination was not possible. An ASA-score 'V E' (5/5) was given because the patient was not expected to live 24 hours without surgery and was presented as an emergency. An intravenous (IV) catheter was urgently placed into the vena cephalica, followed by induction of anesthesia with propofol (2.1 mg/kg IV, PropoVet® Multidose, Zoetis Belgium S.A., Louvain-la-Neuve, Belgium). By this time, the core body temperature was increased up to 42.5 °C and the heart rate was increased to 229 bpm. Drastic temperature control methods were performed and consisted of applying cold water to the skin with presoaked towels and enhancing evaporation with a fan. At the same time, fluid therapy was initialized. A cooled shock bolus of a Ringer-lactate solution (Vetivex® 500 ml, Dechra Veterinary Products, Belgium) was infused IV at a rate of 90 ml/kg/h over 40 minutes and afterwards continued at a maintenance rate of 5 ml/kg/h throughout the rest of the anesthesia. Laryngeal paralysis was confirmed by laryngeal inspection, and an endotracheale tube, size 11, was placed to secure the airway.

When stabilized, 65 minutes after initiating maintenance anesthesia, the dog was taken to medical imaging, where left-right lateral and ventrodorsal radiographs of the thorax were taken. The caudal esophagus was mildly distended by gas due to stress aerophagia, general anesthesia or polyneuropathy. A diffusely increased lung opacity, likely caused by expiratory phase and obese body condition, as well as an alveolar lung pattern with loss of volume in the right middle and caudal lung lobes, compatible with atelectasis, was visible. Hematology, biochemistry and coagulations tests were performed. Except for a hematocrit of 51%, no abnormalities were detected. All the findings supported the diagnosis of heat stroke due to laryngeal paralysis, probably as a clinical manifestation of a generalized peripheral polyneuropathy, also called geriatric onset laryngeal paralysis polyneuropathy.

With the owner's consent, a unilateral cricoarythenoid lateralization (CAL) was performed. Anesthesia was maintained with isoflurane (IsoFlo® 100%, Zoetis Belgium S.A., Zaventem, Belgium) vaporized in oxygen with an initial setting of 1.8% on the vaporizer. The end tidal isoflurane concentration (F_E´Iso) gradually rose and ranged from 0.61-1.5% over the anesthetic period. An electrocardiogram was connected, to measure the electric activity of the heart muscle and heart rate (HR). The peripheral oxygen saturation (SpO_2) and the end tidal pressure of carbon dioxide (P_E´CO_2) were continuously monitored using a pulse oximeter and by side stream capnography. By non-invasive Doppler blood pressure measurement, a systolic blood pressure of 70 mmHg at the time of induction was estimated. During the rest of the procedure, anesthesia was maintained with isoflurane vaporized in oxygen using a Bain breathing system in the preparation room and a circle rebreathing circuit in the operating room with appropriate fresh gas flows. Manual ventilation was performed in the preparation room and later switched to mechanical ventilation in the operating room. The peak inspiratory pressure (PIP) varied between 12-16 cm H_2O. Respiratory rate (F_R) ranged between 14-19/min. P_E´CO_2 ranged between 19-61 mmHg, with an average of 39 mmHg. The fraction of inspired oxygen (FiO_2) ranged between 88% and 96%, while the peripheral oxygen saturation (SpO_2) varied between 93-99%. Invasive intra-arterial blood pressure measurement via a catheter (20G) in the dorsal pedal artery showed a mean arterial blood pressure (MAP) of 56-77 mmHg. The femoral pulse pressure was checked regularly and quickly changed from a powerful pulse into a weak pulse ten minutes after initiating inhalation anesthesia, but normalized 45 minutes later. During the first 90 minutes, the patient showed hyperemic mucous membranes, followed by normal pink appearance till the end. The CRT stayed less than one during the whole procedure and only normalized, to less than two seconds, at the very end. The palpebral reflexes were monitored regularly and remained negative during the whole procedure. The heart rate started to decrease gradually when active cooling methods were applied and normalized during surgery (ranging between 120-84 bpm). At the end of anesthesia, a rate of 75 bpm was registered. A body temperature of 40.4°C was measured 45 minutes after inducing anesthesia, and further decreased to a constant temperature of 37.6°C 105 minutes later until the end of anesthesia.

The procedure consisted of placing two monofilament nylon 0 (Ethilon, Ethicon™, Johnson & Johnson Medical N.V./S.A., Diegem, Belgium) sutures from the caudodorsal aspect of the cricoid cartilage to the muscular process of the left arytenoid cartilage, thereby resulting in a abducted position of this arytenoid. Closure was performed routinely.

One hour after initiating anesthesia, amoxicillin/clavulanic acid (20 mg/kg IV, Augmentin P500®, GlaxoSmithKline, Waver, Belgium) was injected and repeated 2.5 hour later. Fentanyl (Fentadon®, Eurovet Animal Health, Belgium) was given as an intraoperative analgesic by constant rate infusion, ranging from 5 to 7 µg/kg/hour, after a loading dose of 1 µg/kg. Around the same time, 5.9 mL/kg (500 ml) of a plasma expander solution (Voluven®, 6% hydroxyethyl starch 130/0.4, Fresenius Kabi BV, Schelle, Belgium) was given over 30 minutes to address hypotension. Propofol was injected (0,41 mg/kg IV) halfway the procedure and ten minutes before the end of surgery, dexamethason (0.5 mg/kg IV, Rapidexon®, 2mg/mL, Dechra, Belgium) was administered. At the end of the anesthesia, the dog was injected with dexmedetomidine (1 µg/kg IV, Dexdomitor®, Orion Corporation Orion Pharma, Finland) to ensure a smooth recovery.

Postoperatively, the dog was hospitalized for 23 hours in the intensive care unit for monitoring. The dog received Ringer-lactate (2.84 mL/kg/h IV, maintenance + 100% correction) fluid therapy. To keep the dog sedated, acepromazine (20 µg/kg IV, Placivet®, Kela N.V., Hoogstraten, Belgium) was given three times postoperatively. Amoxicillin/clavulanic acid (0.2 mg/kg IV, q8h) was administered and omeprazole (2.5 mg/kg IV, q12h, Losec® AstraZeneca SA/NV, Brussels, Belgium) was initiated. Analgesia consisted of methadone (0.2 mg/kg IV, q4h, Comfortan, Dechra Veterinary Products, Belgium) for the first 19 hours. Afterwards, the dose was reduced to 0.1 mg/kg, q4h, until discharge. Dexamethasone (0.25 mg/kg IV, q8h) was repeated once. The dog was regularly turned from side to side. An inspiratory stridor was observed once at 3:00 during the night. The patient was fasted for the first 12 hours, followed by small portions of food and water. The dog was discharged one day postsurgery, as soon as he was able to eat and drink without coughing and showed a constant body temperature within normal ranges. He was discharged from the clinic on oral antibiotics (11.8 mg/kg, sid, amoxicillin/clavulanic acid, Synulox 500 mg, Zoetis BV, Louvain-la-Neuve, Belgium) and omeprazole (0.95 mg/kg, sid, Omeprazole Sedacid®, 20 mg, Laboratoires SMB N.V., Brussels, Belgium) for ten days. A prescription was given for tramadol hydrochloride (1.8 mg/kg, tid, Tramadol EG®, 50 mg, Eurogenerics NV, Brussels, Belgium) for five days and prednisolone (0.25 mg/kg, bid, Prednisolon 20 mg, Kela, Hoogstraten, Belgium) for five days, followed by 0.25 mg/kg, sid, for another five days. The owners were informed about the basics of wound care and the possible complications. They were advised to schedule a control appointment after one month.

DISCUSSION

In the present case, a heat stroke caused by the inability to remove heat from the body, due to a laryngeal paralysis as a clinical manifestation of generalized peripheral polyneuropathy is described. Large- or giant-breed dogs, like the Landseer, are predisposed to develop geriatric onset laryngeal paralysis polyneuropathy (Rudorf et al., 2001; Kitshoff et al., 2013). The disease is more common in middle-aged to older male dogs (Dixon and Pratschke, 2004; Kitshoff et al., 2013). Airway subobstruction results in a reduced capacity to release heat by panting (Gough, 2008). Tachypnea, dyspnea, an abundant haircoat, body weight (84.5 kg) and BCS (6/9) are additional endogenous predisposing factors affecting heat dissipation (Johnson et al., 2006; Hemmelgarn and Gannon, 2013b). Predisposing factors should be eliminated to prevent subsequent episodes of heat stroke (Flournoy et al., 2003; Mazzaferro, 2009).

The hyperthermia in this patient was most likely caused by the inability to dissipate heat, but other causes of increased body temperatures, such as fever, pain or stress, should also be taken into consideration (Gough, 2008). In general, respiratory problems can originate from the respiratory system or have non-respiratory causes, such as central nerve system diseases, heat stroke and anemia. In the differential diagnosis of inspiratory stridor, all causes of laryngeal and pharyngeal obstruction should be taken into consideration. The simultaneous occurrence of an inspiratory and expiratory stridor with dyspnea is very suggestive for laryngeal disease, while inspiratory dyspnea with stridor along with exercise intolerance, dysphonia and coughing point in the direction of laryngeal paralysis (Koufman and Block, 2008; Kitshoff et al., 2013). Because the primary complaints of this dog were mainly of a chronic nature, a mass, polyp or neoplastic process are also possible causes for airway obstruction (White, 2002; Gough, 2008; Kitshoff et al., 2013). Expiratory stridor is mainly caused by an intrathoracic obstructive process of the lower airways. However, asthma, chronic obstructive pulmonary disease and thoracic neoplasms were less likely in the present case due to the absence of abnormal lung sounds (Gough, 2008).

On presentation, extended clinical, neurological, blood and urine examinations should be performed for further diagnosis and detection of complications due to heat stroke (Hemmelgarn and Gannon, 2013a). Based on the preanesthetic examination, a decision was made towards the anesthesia protocol and further patient work-up. The patient of the present case was attributed an ASA score V E related to aggravating dyspnea, cyanosis and hyperthermia. Since the blood work was normal, the dog was most likely in an early state of heat stroke without multiple organ failure, which however should be treated with immediate attention (Mazzaferro, 2009). As an urgent surgical intervention was desirable, immediate induction of an-

esthesia with low-dose propofol IV (2.1 mg/kg) was performed followed by endotracheal intubation for securing airways, supplying oxygen and maintaining anesthesia by inhalation (Mazzaferro, 2009). Average propofol dosages for non-premedicated dogs range between 4-8 mg/kg. The deteriorating general condition of the dog emphasizes the importance of dose-titration of the induction agent to the desired clinical effect (Hofmeister et al., 2009). In the meantime, a quick intervention by applying cooling methods, such as using fans, humidifying the patient with cold water and the use of presoaked towels, was started. The primary goal of treatment was to control hyperthermia, to decrease the body temperature within a normal range (38 – 39.2°C) and to prevent further damage to vital organs.

When initiating anesthesia, the patient showed hyperemic mucosae, a strong pulse, a very pronounced tachycardia (229 bpm) and a CRT of less than one second, which suggested an early stage of compensatory shock (Mittleman Boller and Otto, 2009). Immediate cardiovascular support was provided by a shock bolus of Ringer-lactate (Flournoy et al., 2003; Mazzaferro, 2009).

During maintenance of anesthesia, the dog showed a MAP ranging from 56 to 77 mmHg. A sudden drop in systemic arterial blood pressure induces a baroreceptor-mediated reflex, which results in vasoconstriction and an increased heart rate and cardiac contractility, a short-term solution to normalize the systemic blood pressure (de Laforcade, 2017). As such, the cardiovascular system plays a crucial role in early states of heat stress by increasing the cardiac output, along with central vasoconstriction and peripheral vasodilatation. Failure of these compensatory mechanism lead to a decrease of systemic vascular resistance resulting in distributive shock (Hemmelgarn and Gannon, 2013b), further stressing the importance of cardiovascular support by fluid therapy in case of heat stroke (Flournoy et al., 2003; Mazzaferro, 2009). During the procedure, HR decreased gradually, ranging between 75-230 bpm. The pulse quality evolved from a strong to moderate beaten pulse and normalized 55 minutes after shock infusion therapy. One and a half hour after initiating inhalation anesthesia, MAP dropped again to 56 mmHg. A plasma-expander infusion was given, resulting in clinically acceptable MAP values (60-80 mmHg) throughout the rest of the procedure. Halfway the procedure, propofol was administered because the dog tended to wake up.

Managing heat-stroke patients can be really challenging. The type of ventilation during inhalation anesthesia has an influence on the body temperature. While preparing the patient for surgery, the patient was temporarily connected to a non-rebreathing Bain system and ventilated manually. The Bain circuit is an economic and ecologic unfavorable anesthetic breathing system, specifically for giant breeds due to the high fresh gas flow (200 ml/kg/min). However, the high gas flow helps to decrease the body temperature of the patient rendering a non-rebreathing system related inconvenience into an advantage in case of hyperthermia (Johnson, 2009). From the moment the patient reached a normal body temperature, it was switched to a rebreathing circle system (2 L/min). A disadvantage of using a rebreathing system in patients with hyperthermia is the risk of heat production by the CO_2 absorbent granules, which could lead to an increase in body temperature. In addition, body heat of exhaled air is also recycled with this system and for this reason undesirable (Johnson, 2009).

Because heat stroke is a life-threatening condition, it is crucial that these patients are strictly monitored for the next 24-48 hours after admission (Flourney et al., 2003). To reduce the postoperative risk of developing recurrent upper airway obstruction, dexamethason was given at the end of anesthesia for its anti-inflammatory properties. Immediate postoperative sedation was achieved with a microdose of dexmedetomidine (1 µg/kg IV). During the surgical procedure, a broad-spectrum antibiotic (amoxicillin/clavulanic acid) was administered IV and was continued in the postoperative period. Antibiotic therapy is strongly advised in patients with heat stroke, because these patients are more likely to develop septicemia due to bacterial translocation, which may lead to multiple organ failure (Mazzaferro, 2009).

During hospitalization, the patient received Ringer-lactate infusion (240 ml/h IV) to cover for expected losses due to hyperventilation. Methadone was subscribed for pain control and if needed, the patient could be sedated with acepromazine. Buprenorphine might have been a good alternative for postoperative analgesia, since it does not cause panting due to resetting of the thermoregulatory center as methadone does. However, buprenorphine is far more expensive and due to the dog's body weight, methadone was used to reduce the costs. The dog went home with a subscription to continue oral antibiotic treatment (amoxicilline/clavulanic acid) and omeprazole, to prevent damage to the stomach. Pain medication and prednisolone (gradually reduced in dosage) were also subscribed to decrease the swelling and to make to dog more comfortable. Finally, the owners were informed about the risk of relapse of heat stroke; ideally, management- and weight loss measures should be taken to decrease these risks. Unfortunately, the patient was lost for follow-up since the owners did not come back for a control visit.

CONCLUSION

Heat stroke is a life-threatening disease that should be treated immediately when recognized. Active cooling and fluid therapy should be an essential part of the (pre)anesthetic protocol and should be performed as soon as possible to prevent further damage and multiple organ failure.

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Health and management of hobby pigs: a review

Gezondheid en het houden van hobbyvarkens: een overzicht

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ABSTRACT

Miniature pigs, like the Vietnamese pot-bellied pig and the Kunekune, are the most popular hobby pig breeds. Despite their popularity, the knowledge of their health and management is still scarce. They have an exemplary sense of smell and hearing, possess good adaptability and are easy to handle. A well-ventilated shelter space with an area for recreation, and incorporation of straw for manipulation prevents boredom. Drinking water must be provided at all times. Restricted feeding ones or twice a day is preferred to prevent obesity. Unexpected aggressive behavior may occur and lead to abandonment of pet pigs. Overgrowth of claws, mange and sunburns are common skin problems. Diarrhea due to *Escherichia coli* is a common problem in piglets. Neutering is recommended to prevent aggressive behavior and pungent smell in males and to avoid the risk of neoplasms. It is preferably done at a young age to avoid surgical complications. Prophylaxis against erysipelas and parasites are recommended biannually. Other periodical health care practices include tusk and hoof trimming.

SAMENVATTING

Miniatuurvarkens, zoals het Vietnamese hangbuikvarken en de Kunekune, zijn de bekendste hobbyvarkensrassen. Ondanks hun populariteit is de kennis van hun gezondheid en management schaars. Ze hebben een uitstekend reukvermogen en gehoor, beschikken over een goed aanpassingsvermogen en zijn doorgaans gemakkelijk te hanteren. Ze gedijen goed in de thermoneutrale zone. Een goed geventileerde schuilplaats met een recreatiegebied en het opnemen van stro voor manipulatie voorkomen verveling. Drinkwater moet te allen tijde worden verstrekt. Beperkte voeding één of tweemaal daags is optimaal om overgewicht te voorkomen. Agressie kan optreden en is een van de redenen waarom eigenaars het varken niet langer wensen aan te houden. Schurft en zonnebrand zijn de meest voorkomende huidproblemen. Diarree door *Escherichia coli* kan voor problemen zorgen bij biggen. Castratie wordt aanbevolen om agressief gedrag, het verspreiden van een penetrante geur en het risico op neoplasmata te vermijden. Het wordt bij voorkeur op jonge leeftijd uitgevoerd om chirurgische complicaties te voorkomen. Er wordt aanbevolen om profylaxe tegen vlekziekte en endoparasieten twee keer per jaar uit te voeren. Andere maatregelen zijn onder meer het periodiek inkorten van de slagtanden en het bekappen van de klauwen.

INTRODUCTION

Following the introduction of the Vietnamese pot-bellied pigs into the United States in 1986, their popularity increased steadily over the years, reaching a peak between 1991 and 1995 with about 35,000 registered and 200,000 unregistered pigs by 2002 (Blaney, personal communication) (Munday and Stedman, 2002; Sipos et al., 2007). Although pigs are not usually kept as pets, they can be a good companion to humans as they are intelligent, clean, extremely social and affectionate, and once trained properly, they are

safe to be in the presence of children and the elderly (Braun and Casteel, 1993; Carr and Wilbers, 2008; Swindle and Smith, 2015). Having a mini pig as a pet is quite a commitment as they can live up to 15-25 years of age (Holtz, 2010; Swindle and Smith, 2015).

The aim of the present paper was to review the background and breeds of miniature pigs, the housing and nutritional requirements and the overall management with emphasis on health and behavior.

EUROPEAN UNION (EU) REGULATIONS ON HOBBY PIG KEEPING

A hobby pig keeper can raise up to three pigs. If the hobby pig keeper intends to expand his farm by breeding the pigs, then it is mandatory to have a business register, to identify the pigs and have transport documents. Prior to trading, all pet pigs must be examined and certified by a licenced veterinarian to rule out notifiable diseases (2014/178/EU). In addition, this certificate must be registered (council directive 2008/71/EC) and the documents maintained for five years. All hobby pig keepers must register with Animal Health Care Flanders (Dierengezondheidszorg Vlaanderen, DGZ), without authorization by the Federal Agency for the Safety of the Food Chain (FASFC). In that case, breeding and slaughter for human consumption are forbidden. Commercial pig keepers are not authorized to keep hobby pigs. Many mini pig owners living in the urban areas have no practical knowledge of pig keeping, nor is there awareness among them regarding economically important diseases or those that are zoonotic in nature. Hence, for epidemiological reasons, pet pigs are considered similar to commercial pigs and the statutory provisions differentiate mini pigs from the other pets (Wismans, 1999; Sipos et al., 2007). The owners must notify the FASFC if there has been an accidental contact with feral pigs, following which epidemiological investigation takes place to confirm or exclude disease transmission.

BEHAVIOR

Miniature pigs though smaller in size and docile in nature (Braun and Casteel, 1993; McAnulty et al., 2011), have evolved like the domestic pigs and are part of the Suidae family showing similar behavioral characteristics under natural conditions. Grazing and browsing are the prominent foraging behaviors reported in free-ranging pigs. Exploration and rooting are behavioral necessities starting already early in life, even in the absence of stimulus (Bollen and Ritskes-Hoitinga, 2007; Studnitz et al., 2007).

Management of aggression in pet pigs

Mini pigs may show aggression towards unfamiliar people and environment, which is usually noticed around the time of social maturity (six months to three years). Irrespective of the age of weaning, sex, neutering status and incorporation of enrichment material, aggressive behavior is more common in pigs than in other domestic animals (Tynes et al., 2007). Neglecting such behavior can result in them showing dominance aggression towards familiar people as well. These issues are treated in a similar way as dog aggression. Introducing them to a leash or harness at a very early age and teaching them simple commands using food lure while they are being fed, petted and walked will avoid conflicts. Young pigs can be trained faster (two to three weeks), while in adults, training may take two to three months' time (Holtz, 2010; Swindle and Smith, 2015). Pigs raised as single pets are more likely to show aggression, as isolation may lead to stress and behavioral changes (Ruis et al., 2001; Kanitz et al., 2004). Pigs housed in individual pens require visual, auditory and olfactory contact with other pigs to avoid social deprivation (Smith and Swindle, 2006).

Isolation and boredom may lead to vacuum chewing with an empty mouth and under unfavorable housing conditions, a frustrated pig might bite and destroy inanimate objects like fences and food bowls. Among all, cannibalism involving mutilation of the ears and tail leads to serious bacterial infections. Continuous massage of the anal region with the snout can cause serious injury, inflammation and may even lead to death (Holtz, 2010).

Incorporating fresh wood logs in the pens improves the exploratory behavior of pigs and reduces the incidence of tail and ear biting (Telkanranta et al., 2014). High-duration tail movements are an indicator of positive emotions whereas, high frequency ear movements are a sign of decreased welfare (Rius et al., 2018).

Interspecies aggression can occur when a dog and a pig are left unsupervised. Although the two species communicate differently, the risk of aggression is lower with a combination of a non-predatory and non-aggressive breed of dog, such as a Labrador, and a mini pig of similar size. In spite of careful consideration and acceptance by a dog, a pig is likely to show dominance post maturity, but with a gentle dog serious fights are unlikely. Another possible target for pet pigs are children, as pigs are intimidated by them (Tynes, 1997).

Restraint and handling of pet pigs

A visit to the veterinarian may be very stressful and chaotic especially with an untrained and aggressive pet. Forceful approach may provoke fear and distrust leading to struggle and vocalization as pigs squeal when they are anxious or kept confined. Extreme stress and panic may lead to circulatory collapse because of their relatively small sized hearts (Bollen and Ritskes-Hoitinga, 2007; Zimmerman et al., 2012). Small piglets (5-20 kg) can be lifted or tucked

up under the arm. With the aid of boards, heavy and uncooperative boars can be approached from the sides but with caution, as they can inflict serious injuries with their tusks (Tynes, 1998; Holtz, 2010). The examiner can kneel on the floor and restrain the pig by placing it in between the examiners legs. Snout snares are not well accepted by pet owners. There is a risk of fracture or luxation when held by the hind limbs (Fubini and Ducharme, 2016). Pigs relish back scratching and belly stroking, and use of a hammock-like sling is well tolerated by mini pigs (Swindle, 2007).

Gentle handling builds trust and develops a human animal bonding. Introducing them to toys of various sizes, shapes and colors will not only enrich their environment but also improves the habit of exploration and reduces the fear for new stimuli. Enrichment objects reduce the biting behavior of pigs (Van de Perre et al., 2011). Conditioning them to a harness and leash at an early stage will ensure easy handling even when they are fully grown. Habituating them for short walks and car rides can make their visit to the veterinary clinic less stressful (Zimmerman et al., 2012). Although pigs in general are afraid of humans (especially the Vietnamese pot-bellied pigs), they are easy to train and socialize with positive reinforcement. They must be taught to obey commands in return for small food rewards, such as carrots, cookies, dog biscuits and candy (Lorensten, 2014; Swindle and Smith, 2015).

MINIATURE PIG BREEDS

The idea of having a pig as a pet animal started when the Vietnamese pot-bellied pig (VPB), otherwise called Chinese house pig, gained popularity after being kept as a show animal in zoological parks in Canada in the mid-1980´s. The New Zealand Kunekune, which has gained popularity in the United Kingdom, are friendly pigs and are crossed with the Vietnamese to make an ideal household pet (Duncanson, 2013). The small stature of the VPB pig (birth weight 0.4 – 0.6 kg and weight at six months 17-28 kg) made them an ideal indoor pet. The majority of the miniature pigs weigh about 12-45 kg around the time of sexual maturity in contrast to the domestic pigs that weigh about 100 kg (McAnulty et al., 2011; Swindle and Smith, 2015) (Table 1).

At least 45 different breeds of miniature pigs have been reported worldwide. Miniature pig breeds are a subspecies of the domestic pig (*Sus scrofa*) and are either commercially raised for research studies or bred naturally to be raised as pets (Ilha et al., 2010; McAnulty et al., 2011). The Yucatan, a Mexican feral pig and the Ossabaw of Spanish heritage are the only two naturally occurring mini pigs used in biomedical research (Swindle and Smith, 2015).

The Wuzhistan miniature pig is one among the four indigenous Chinese breeds (Wuzhistan, Xiang, Diannan small-ear and Tibetan miniature breeds), which can withstand hot environmental conditions. The indigenous pigs breeds of Vietnam are genetically diverse from the European gene pool. They can adapt to extreme climatic conditions (Huyen et al., 2005). In Table 2, the general characteristics of six indigenous pig breeds in Vietnam are depicted (Dang et al., 2010). The Vietnamese miniature pigs have therefore been cross-bred with the commercial farm pigs in Europe to attain certain breeds and lines namely the Göttingen miniature pig, the Berlin miniature pig,

Table 1. General description of miniature pig breeds.

Breed	Average birth weight (g)	Weight at sexual maturity (kg)	Average adult weight after one year (kg)	Coat color
Vietnamese pot-bellied pig	400-600	15-20	50-60	Black or black with white marking
Kunukune	800-900	-	50-80	Hairy black, red and white, ginger, brown, black, gold-tip, cream and also tri-colored
Göttingen	450	10-14	30-45	White non pigmented
Sinclair S-1	590	16-22	55-70	Black, red, white and roan
Juliana or painted miniatures	-	-	6-20	Red, red and black, red and white, white and black, black, silver, silver and white
African Pygmy or Guinea Hogs	-	-	10-20	Hairy red
Miniature Yucatan	500-900	20-30	70-80	Slate grey to black
Micro Yucatan	600-700	14-20	55-70	Slate grey to black
Wuzhistan	1000	12-14	25	Black with white abdomen and flank area
Hanford	730	20-40	80-95	White hair coat
Panepinto	500-800	-	25-30	Dark grey or black
Munich	600-900	-	60-100	White, black, red, dark brown or spotted
Clawn	500	-	40	White, rarely black and spotted

the Munich miniature pig and the Bergstrasser Knirps (Sipos and Kaltenegger, 2004).

The Sinclair or otherwise the Minnesota or Hormel mini pig from the United States has a complex genetic background and is used to develop other mini pigs like the Göttingen, Nebraska and mini pig of the Czech Republic. The Göttingen mini pig was developed in 1961 at Georg-August-University in Göttingen, Germany by crossing the Minnesota Mini pig (for small size and docile behavior) with the Vietnamese pot-bellied pig (for fertility) and the German Landrace (for the white phenotype) and it carries the characteristics of the three (Rozkot et al., 2015). The Juliana or painted miniature is the smallest of all the mini pigs with a light boned body and are extremely playful. The Pitman-Moore and its derivative, the Hanford minipig, the Minisib minipig from Serbia and Ohmini and Clawn of Japanese origin are a few other miniature breeds (Bollen et al., 2010; Holtz, 2010). The Hanford (25 to 40 kg) and the Gottingen (10 to 14 kg) are the largest and smallest miniature pigs, respectively.

The Ossabaw, Banna, Ohmini, Pitman-Moore, Chinese Dwarf, Meishan, Panepinto and Vietnamese pot-bellied-pig are available in limited markets (Swindle and Smith, 2015).

HOUSING

Pet pigs should never be raised with production animals and ideally be housed at least 500 meters away from commercial pig farms to prevent the risk of spread of diseases. A full grown adult mini pig weighing 50-80 kg requires a minimum floor space of 0.55 to 0.65 sq. m per pig. In Table 3, the floor space requirements for pet pigs housed outdoors are shown (Duncanson, 2013). Rarely, owners keep their pet pig indoors (Duncanson, 2013). Besides these dimensions, pigs require a space for excretion, recreation and exercise (Figure 1).

Proper ventilation is essential, as they are sensitive to extreme temperatures due to the lack of sweat glands and scanty hair. In warmer months, when more noxious gases are released, a fan can be used. The air velocity must not exceed 0.2–0.3 m /s for adults and 0.1 m /s for piglets (Bollen et al., 2010). The pens must be fitted with an insulated, non-slippery flooring, and sufficient quantities of straw or hay keeps them comfortable to tolerate temperatures as low as 10°C (Mul et al., 2010). Incorporating enrichment material like hanging objects and some extra straw will keep them occupied with their manipulative activities like root-

Table 2. General description of Vietnamese miniature pigs.

Breed	Age at sexual maturity (months)	Average Litter size	Adult weight after one year (kg)	Coat characteristics	Coat Color
"I" or Vietnamese pot-bellied	1-2	8-11	50-60	Short and sparse	Black
Mong Cai	2	10-14	75-80	Thin hair	White
Muong Khuong	6-7	5	90	Thin and soft	Black or black with white spots
Soc	6-9	6-10	50-55	Thick skin, Long hair	Black
Meo	8-9	6-7	100	Long black hair	Yellow skin
Co	2 -3	6-7	30-35	Black and white hair	Mixed black and white

Table 3. Space requirements for pet pigs housed outdoors

Pig weight (kg)	Sleeping Space/ Shelter Space (sq. m)	Running meter for hand feeding per pig
Weaning to 35	1	0.25
35 - 60	1.5	0.3
More than 60	2	0.4

Table 4. Feed and water requirements of miniature pigs.

Body weight (in kg)	Feed requirement (g/day)	Body weight (in kg)	Water requirement Normal range (in liters/per pig/day)
5	255	Weaners	2-4
10	425	15-25	3-5
20	715	25-45	5-7
50	1.425	45-65	4-9
80	2.025	> 65	9-12
		Dry sow/ Boars	7-17
		Lactating Sows	14-30

Table 5. Analgesics used in miniature pig practice.

Drug class	Drug	Dose	Route	Interval
Opiate	Buprenorphine	5-20 µg/ kg	IM	6-12 hours
	Butorphanol	0.1-0.3 mg/ kg	IM, SC	4-6 hours
NSAID	Ketoprofen	3 mg/ kg	SC	24 hours
	Meloxicam	0.1-0.2 mg/ kg	SC	24 hours
Local	Bupivacaine		Local infiltration	
	Lidocaine			

ing and chewing and can also spare them from boredom (Fraser et al., 1991; Council Directive 2008/120/EC). They can show destructive behavior due to boredom. Studies have shown better behavioral responses and also a reduction in postweaning diarrhea and tail biting incidences when the pens were enriched (Munsterhjelm et al., 2009).

Fly problems are encountered when pigs are housed under unsanitary conditions. Flies and mosquitoes may contribute to the spread of pathogens, such as porcine reproductive and respiratory syndrome (PRRS) virus and *Streptococcus suis* over short distances. Blood-sucking insects can be potential vectors for e.g. African swine fever (ASF) virus. The use of insecticide sprays in the premises and proper sanitary measures can help control flies. For pigs that are constantly housed outdoors, strict biosecurity measures must be followed. Based on the Royal decree of 18 June 2014 containing measures for the prevention of notifiable porcine diseases, the provision of double fencing is mandatory to avoid direct contact with feral pigs. A boundary fence that is 2.5 meters high and 0.5 meters deep prevent pigs and other animals like feral cats and wild boars from leaving or entering the premises (Jackson and Cockcroft, 2007; Commission Implementing Decision 2014/178/EU).

Figure 1. Knor, a seven-year-old, castrated, male hobby pig (from private collection).

NUTRITIONAL REQUIREMENTS

Mini pigs are omnivorous like their domestic counterpart. A restricted low-energy diet with a metabolic energy of 9.5 MJ/ kg (2275 kcal/ kg) comprising of mashed meal and roughages (grass, hay, silage and tubers) suffices the daily nutritional requirements of a mini pig (Bollen et al., 2010) (Table 4). A combination diet with standard pellets or meal containing ground cereals, enriched with protein (milk products, soya bean meal or fish meal), vitamins, minerals and amino acids can be mixed with water to make a mash. Pigs that are maintained on a commercial fixed formula diet need to be fed at least once a day. (Holtz, 2010; Mul et al., 2010). Dividing the ration into twice or thrice a day keeps them engaged. Pigs are generally fed at the rate of 0.2 to 2.5 kg feed per day for pigs within the weight range of 5-55 kg (National Research Council, 1998; Swindle and Smith, 2015). Inclusion of green fodder, sugar beet pulp and bran provides a low energy maintenance ration with a high

fiber content (14%). However, high fiber diet in excess of 15% may result in prolonged gastric emptying and intestinal transit time.

The nutrient requirements of male Göttingen miniature pigs are higher than those of females. Both males and females can become obese following ad libitum feed intake, but females generally gain more weight with thicker relative back fat layers (Bollen et al., 2005). Restricted feeding is recommended for miniature swine as they don't restrain feed intake. This may result in obesity, which is common in hobby pigs. It is a serious health problem. It compromises the overall health of the animal and increases the susceptibility to a variety of conditions like cardiovascular problems (atherosclerosis), arthritis and kidney failure. Excess facial fat and fat depots around the eye may hinder vision (Tynes, 1999). In extremely obese miniature pigs, more pronounced oxyhemoglobin desaturation takes place during sleep with both central and obstructive sleep apneas (Lonergan et al., 1998). This results in snoring and disturbed sleep with frequent arousal to regain oxygen saturation. In order to maintain the small stature, some owners feed their pets lower than the minimum daily requirement, which creates a constant feeling of hunger, in turn leading to aggression.

The Royal decree of 15 May 2003 concerning the protection of pigs in pig farms prohibits swill feeding (feeding of kitchen waste) as it can pose a risk of spread of diseases like African swine fever (ASF) and foot and mouth disease (FMD).

Water requirement for pigs weighing between 20 and 90 kg is 2.5 liters for every kilogram of feed provided (Swindle, 2007). The water consumption by pigs when given a restricted diet and when fed ad libitum is 3.7 liters and 2.5 liters per kilogram of feed consumed, respectively (Cumby, 1986). The amount of water intake is further determined by the climate and the temperature of the drinking water. Fresh cool water is preferred on warmer days, while in winter, pigs do not consume adequate quantities if the water is cold (Vajrabukka et al., 1981). The daily water requirements of pigs is given in Table 4 (Hill and Sainsbury, 1995). Water deficits may cause urinary tract infections (cystitis), salt poisoning and lead to vices like urine drinking (Hill and Sainsbury, 1995; Swindle, 2007; Duncanson, 2013).

Pigs must be allowed to root and find their food rather than feeding them from a bowl. They constantly alternate between the feed and water containers resulting in spillage. This can be prevented by removing the water at the time of feeding or to place a tray below to contain the spillage.

REPRODUCTION

Sows are polytocous with an estrous cycle of 21 days (range 17-24 days). During the estrous period of two days (1-5 days), they display nervousness and increased activity along with prominent swelling and reddening of the vulva. This is followed by ovulation 30-36 hours after the onset of estrous. Miniature pigs reach sexual maturity by 4-6 months of age. Owners who intend to breed their pigs can either follow pen mating, hand mating or artificial insemination (AI). The pig is considered to be pregnant on failure to return to estrous 18-24 days following mating or AI. The gestation length ranging from 111-114 days is generally slightly shorter than the gestation length of commercial pigs. Litter size is 4-8 piglets, depending on the breed (Laber et al., 2002; Swindle, 2007). Pet pigs are often weaned at 7-8 weeks of age. By that time, the piglets have reached a sufficient size. For comparison, under natural conditions, weaning takes place at approximately twelve weeks and is a gradual process.

NEONATAL CARE AND MANAGEMENT

Knowledge of neonatal piglet care can prevent serious conditions like hypothermia and hypoglycemia. As piglets are unable to regulate their body temperature in the nest area, an artificial heating source using light bulbs or heating pads should be provided. Piglets move away from the light source if the temperature is above the ambient temperature (33°C to 35°C). The first 24 hours of life is critical for the absorption of immunoglobulins from colostrum. Orphan piglets are either introduced to a foster sow, or cow colostrum can be substituted to acquire nonspecific immunity (Braun and Casteel, 1993). Homemade or commercial milk replacers, given 4-6 times a day, can satisfy the high energy and nutrient requirements of newborn piglets. Iron should be supplemented to piglets raised indoors. This is not needed for piglets that are raised outdoors and have access to soil (Braun and Casteel, 1993; Jackson and Cockcroft, 2007).

HOBBY PIG MEDICINE

Pigs in general are sturdy animals, yet mini pigs are likely to share the same diseases as domestic pigs. They may succumb to illness when exposed to other diseased animals, under unsanitary conditions and/or when the immune system is compromised as a consequence of malnourishment.

Skin problems

Mange

Mite *Sarcoptes scabiei* var. *suis* causes severe pruritus (itching) of the affected areas like the ears, snout, rump, flank and abdomen. Flaky skin, dryness and alopecia are common in mange-affected pigs. Constant rubbing may lead to oozing of serum, giving

the animal a greasy appearance. Diagnosis is made by microscopic examination of the yellowish-brown wax in and around the ears. Pet pigs recover well with two doses of Inj. Ivermectin (two weeks interval) at the rate of 300µg/ kg body weight given subcutaneously (Carr and Wilbers, 2008; Zimmerman et al., 2012). Additionally, medicated shampoo baths and isolation till they are mange-free is recommended.

Pediculosis

Lice (*Hematopinus suis*) infestation results in skin damage due to excessive itching and rubbing, and anemia due to blood sucking. Swine lice are known to transmit erysipelas and swine pox virus. Insecticides for external use or Ivermectin may be used to treat affected animals (Zimmerman et al., 2012).

Ticks Infestation

Both hard (ixodid) and soft (argasid) ticks infest pigs. The importance of ticks is their ability to transmit pathogens. The tick species *Ornithodorus erraticus* is a reservoir of African Swine fever virus (Braks et al., 2017).

Sunburn

Light-colored pigs are more prone to sunburns when exposed to hot weather. The ultraviolet rays can cause dryness, scaling, necrosis of skin. Affected pigs may experience muscle twitching and pain. Application of sunscreen lotion, provision of water for wallowing and shade will protect them from sunburns and heat strokes. Pigs prefer to coat their bodies with mud. This does not only keep their bodies cool but also helps to protect their skin from sunburn (Hill and Sainsbury, 1995; Carr and Wilbers, 2008).

Dippity pig syndrome

Bleeding back or dippity pig syndrome is an acute skin condition affecting 3-10-month-old pigs. Although the exact cause is not known, a number of factors, like stress, sunburns, dehydration, climate changes affecting the body temperature, change from routine activities or even a visit to the veterinarian, can inflict areas of weeping blisters on the body. It is a self-limiting condition; however, medication (application of lidocaine gel) to alleviate the pain and palliative treatment are recommended for the acute necrotizing cellulitis (Tynes, 1998; Carr and Wilbers, 2008).

Blown coat syndrome

Blown coat syndrome is a condition in pot-bellied pigs, in which alopecia with complete baldness is noticed for a few weeks. It mostly occurs following pregnancy or illness (Tynes, 1999).

Other skin diseases

Flaky skin may also result from deficiency of essential amino acids and is managed by supplementation of cod liver oil (10 ml/ 50 kg) with a mild shampoo bath (Carr and Wilbers, 2008). Bacterial infection caused by *Staphylococcus hyicus* may cause exudative epidermitis, giving the skin a greasy appearance.

Problems of the gastrointestinal tract

Enteritis

Diarrhea is encountered in pigs of all age groups and ranges from yellowish watery diarrhea to hemorrhagic mucoid diarrhea. The morphological and physiological changes during the gut maturation process, the stress associated with transportation or a change in diet may result in diarrhea and dehydration in young and weaned pigs. In adult pigs, diarrhea may result from overfeeding or intake of mouldy feed. Diarrhea associated with *Escherichia coli* and *Clostidium perfringens* type A and C may occur in piglets between 1-14 days of age. Enteritis due to *Salmonella* spp., *Brachyspira* sp. and *Lawsonia* sp. may affect all age groups (Laber, 2002; Thomson and Friendship, 2012; Luppi, 2017). Dogs may be a source of infection for swine dysentery (*Brachyspira* sp. infection) and birds may be carriers of *Salmonella* spp. (Jackson and Cockcroft, 2007).

Endoparasites

Mini pigs contract endoparasites from soil and other pigs or pets that host the parasite resulting in malnutrition. In severe and chronic cases, vomiting, diarrhea, anemia, cough, loss of body condition and bloating may be noticed. Although mini pigs live in semi-secluded homes, routine fecal examination can help in choosing the proper anthelmintic treatment. According to Tynes (1999), hobby pigs do not share parasites with companion animals like dogs and cats. On the contrary, it is possible for mini pigs to contract *Toxoplasma gondii,* a protozoan parasite of cats with zoonotic implications. However, humans acquire infection from pigs only by consumption of tissue cysts, and this is unlikely in the case of pet pigs.

Problems of the respiratory tract

Atrophic rhinitis and pneumonia are commonly encountered in pet pigs (Carr, 2004). Stress, dampness, dust, extreme weather fluctuations and damage to the turbinate may predispose pigs to fatal pneumonia owing to their small sized lung capacity (Tynes, 1998). Sneezing, coughing, mucopurulent discharge, and in extreme cases nasal bleeding and

thumping, are displayed by affected pigs. Vaccination against the target agent is recommended in case of problems.

Problems of the reproductive tract

Scrotal hernia

In pigs, the size of the external inguinal ring is larger in proportion to the size of the animal and larger when compared to other species. This makes them more susceptible to hernias. Commercial pigs are found to be genetically predisposed with high prevalence rates reported for scrotal and inguinal hernias. Unilateral cryptorchidism has been reported in pot-bellied pigs with the testicle retained in the abdomen or the inguinal canal (Ostevik et al., 2012).

Tumors

Intact female pigs are more likely to be affected with uterine, cervical and ovarian tumors and the incidence increases with increasing age (Akkermans and Van Beusekom, 1984). Aging nulliparous pet pigs are at greater risk of developing reproductive tract tumors (Harmon et al., 2004). A higher incidence of reproductive tumors in intact female Vietnamese pot-bellied (VPB) pigs followed by intact males has been reported in a retrospective study (Newman and Rohrbach, 2012). In that study, the mean age of pigs with neoplasia was eleven years. From a total of 32 female miniature pet pigs (four months to 19 years of age) that were spayed, twenty had smooth muscle tumor in the uterus whereas, cystic endometrial hyperplasia (CEH) was recorded in 24 of them. Fourteen had concurrent CEH and smooth muscle tumor (Ilha et al., 2010). A case of cervical and uterine leiomyoma and uterine adenocarcinoma with CEH has been reported in a nine-year-old nulliparous VPB sow, that cycled every three weeks (Augustijn et al., 2010). Cystic endometrial hyperplasia associated with uterine leiomyomas has been reported in two VPB pigs (Munday and Stedman, 2002). They were eight and ten years of age, cycling regularly, one being nulliparous and the other having farrowed twice until the age of two. A high incidence of uterine tumors has been reported in pigs aged five and above (Mozzachio et al., 2004). In that study, out of 106 female VPB pigs, 17 had uterine neoplasms consisting of single and multiple leiomyomas, leiomyosarcomas, undifferentiated sarcoma and squamous cell carcinoma. A strong association has been suggested between hormone influence and tumor development in intact female miniature pigs. As cyclic female household pet pigs often never become pregnant, they are predisposed to developing genital tract tumors. In pigs, zearalenone induced hyperestrogenism has resulted in CEH (Chang et al., 1979). During estrous period, there is an increase in the estrogen receptor activity without sufficient serum estrogen concentrations. Repeated cycling leads to the development of uterine lesions. Inbreeding may be a predisposing factor for changes in uterine pathology (Ilha et al., 2010). Hence, neutering is the only practical measure to prevent constant hormonal stimulation in non-breeding female pigs.

Locomotor problems

In preweaned piglets, polyarthritis affecting more than one joint is associated with bacteria invading the bloodstream through skin wounds, navel or tonsils. Environmental pathogens causing arthritis in piglets below 12 weeks of age include *Trueperella pyogenes, Streptococcus dysgalactiae subsp. equisimilis, Staphylococcus hyicus, S. aureus,* and *Haemophilus parasuis* (Zoric et al., 2008). The sow is an important source of infection to piglets. Pathogens like *S. equisimilis* is commonly found in the vaginal microbiota of the sow (Zimmerman et al., 2012). Coliforms are also isolated from affected joints in chronic cases (Zimmerman et al., 2012; Zoric et al. 2016).

Mycoplasma hyorhinis, *M. hyosynoviae*, *E. rhusiopathiae*, and *S.* Choleraesuis are also associated with infectious arthritis. *M. hyorhinis* causing polyserositis affects pigs mainly below ten weeks of age. Affected animals show lameness and reluctance to move (Neto et al., 2012; Zimmerman et al., 2012).

M. hyosynoviae mainly affects pigs older than ten weeks of age. Infections cause non-suppurative arthritis of the shoulder, hock and elbow joint after 2-3 weeks of exposure. Lameness is noticed in one or more limbs in pigs between 3-5 months of age.

Many factors influence infectious arthritis, including lack of hygiene, genetics and poor nutrition. Wetness, cold floor and improperly bedded flooring may be a risk factor for arthritis in adults. Non-weight bearing is noticed with infections of the third foot commonly termed as bumble foot (Jackson and Cockcroft, 2007).

Septicemia and tail-bite abscessation may spread to bones causing osteomyelitis, ankyloses and muscle wasting. Osteomyelitis results in lameness and pathological fracture of the vertebrae (Zimmerman et al., 2012). Long claws and deformed claws are a common cause of lameness in pot-bellied pigs (Sipos et al., 2007).

DISEASE PREVENTION

Anthelmintics against endoparasites

The most widely used anthelmintic drugs include Benzimidazoles (fenbendazole, flubendazole), Tetrahydropyrimidines (Pyrantel), Avermectins (Ivermectin) and Imidazothiazoles (levamisole hydrochloride). However, fenbendazole is the preferred anthelmintic for the treatment and control of mature and immature

gastrointestinal and respiratory nematodes (*Ascaris suum, Oesophagostomum* spp. *Trichuris suis, Metastrongylus elongatus, Hyostrongylus rubidus* and *Strongyloides ransomi*). Anthelmintic treatment in pet pigs is recommended every 4-6 months and also prior to farrowing (Carr and Wilbers, 2008). Good sanitary measures including periodical removal of bedding (straw), disinfection and drying of pens, along with the proper choice of anthelmintic drug are critical elements in controlling parasite burden.

Immunization

Vaccination of pet pigs usually depend on several factors, like the geographical area they are situated in, their age, possible exposure to other pigs and prior vaccination status. Vaccination against erysipelas is highly recommended starting at twelve weeks of age followed by a booster after 2-4 weeks of initial vaccination and biannual (twice a year) vaccinations thereafter. Depending on whether or not rabies is a threat in the area, mini pigs can be immunized using the dog or horse vaccine as there are no approved products for use in pigs. Rabies vaccination is mandatory in some circumstances, such as travelling to other EU member states, camping, etc.

Vaccinations recommended for breeding pigs

Sow vaccinations can protect piglets from infections occurring early in their lifes through maternal immunity transferred through colostrum and milk. Vaccination against *E. coli* or combined vaccination against *E. coli* and clostridial enteritis is given at six and three weeks prior to farrowing. An array of reproductive losses like stillbirths, mummification, embryonic death and infertility are caused by porcine parvovirus (PPV). Vaccination of both sexes against PPV is done prior to breeding using two doses with 4-6 weeks interval, with the second dose given 2-4 weeks before mating. This is followed by biannual vaccination for boars, and for sows, vaccination is always done prior to breeding (Carr and Wilbers, 2008).

OTHER WELFARE PRACTICES

Hoof care

Mini pigs require regular exercise on rough flooring made of concrete or gravel for constant wear and tear of the hoof. White hooves in general are softer than the black and require less frequent trimming as they wear down easily. Annual hoof trimming is adequate except in a few pigs which may require biannual trimming. Hooves must be regularly pared using rasps or trimmers as overgrown hooves are a serious welfare problem (Carr and Wilbers, 2008; Zimmerman et al., 2012.

Tusk trimming

The canine teeth, also called “tusks”, of miniature pigs require proper and regular maintenance for the safety of both the owner and the pigs, as excessive tusk growth can cause facial damage. The tusks of boars grow throughout their lifes, whereas for the sows the growth ceases by 1.5 to 2 years of age and are also not as strong as those of a boar. As canine teeth have deep seated roots they are difficult to extract. A Gigli wire or saw is used to trim the tusks at the gum line under minimal restraint and sedation. Constant friction between the canines of the upper and lower jaw may result in sharpening of the edges of the lower tusks. Trimming procedures need to be carried out every 3-6 months for adult males. In castrated males and females, the canine teeth are slow growing and may not require periodical trimming unless otherwise required (Eubanks, 2005; Swindle, 2007).

NEUTERING IN HOBBY PIGS

It is best to neuter all pet pigs both males and females at an early age unless intended for breeding purpose. Early neutering helps to control unpredictable behavior and in case of males, causes a reduction in the size of the preputial diverticulum. This prevents the strong unpleasant odor. Resolution of human directed aggression and undesirable behavior ceases following castration (Ostevik et al., 2012) and ovariohysterectomy (Carr, 2004).

Surgical castration in male pigs

Castration before twelve weeks of age using a prescrotal approach (Zimmerman et al., 2012) similar to the technique used in dogs or a scrotal approach (Ostevik et al., 2012) is recommended for pet pigs. Closure of the external inguinal ring is recommended to prevent herniation (Braun and Casteel, 1993; Ostevik et al., 2012).

Male mini pigs attain puberty as early as three months of age and if left intact, display sexual behavior (mounting), aggression, urine spraying, and also develops an unpleasant boar odor due to the accumulation of a pungent material in the enlarged preputial diverticulum. The diverticulum has no known function and accumulates urine, semen and smegma. For intact boars above 2-3 years of age, an additional preputial diverticulectomy can reduce the smell and the risk of ascending cystitis infection. For piglets above seven days of age, the directive 2001/93/EC states that castration must be performed under anesthesia with additional prolonged analgesia (Jaggin et al., 2006).

Spaying (ovariohysterectomy or ovariectomy) in female pigs

To ensure patient safety, routine spaying must be performed when pigs are older than two to three months and younger than six years of age (Cypher et al., 2017). Performing ovariohysterectomy (OHE) at six weeks of age in pot-bellied pigs has lesser complications as the uterus is underdeveloped. The fat deposits in the subcutis and broad ligament is highly vascular complicating hemostasis in mature and obese pigs (Braun and Casteel, 1993). Poor survival rate has been observed following OHE in pot-bellied pigs of more than six years of age, especially in those with reproductive lesions like neoplasia, pyometra and cystic endometrial hyperplasia (Cypher et al., 2017). In pot-bellied pigs, hemorrhage is the common complication with OHE and an increase in morbidity and mortality is associated with neoplasia of the reproductive tract. Ovariectomy (OVE) using an electrothermal bipolar vessel sealing (EBVS) device in pet pigs has a better surgical outcome with lesser surgical and anesthetic time. There is reduced tissue handling and perioperative complications. When performed after nine weeks and before the onset of puberty, the cervix remains closed and reduces the risk of ascending infection (Biedrzycki and Brounts, 2013).

Immunocastration

Immunization against gonadotropin releasing hormone (GnRH) for male pigs older than eight weeks of age is an alternative to surgical castration. The first dose of Improvac (containing 200µg of GnRH protein conjugate/ ml, Zoetis) given any time after 8-9 weeks of age primes the immune system. The second dose given four weeks after the priming dose stimulates immunity and inhibits testicular function. Pre or early pubertal vaccination (3-5 months old) causes irreversible testicular dysfunction and reduces unwanted sexual behavior (Zamaratskaia et al., 2008; Brunius et al., 2010). There iss reduction in unwanted sexual and aggression behavior in males, similar to that observed in surgically castrated pigs following two doses of Improvac (Rydhmer et al., 2010). Effects are noticed one to two weeks following the second injection and lasts for a minimum of eight weeks, with extended effect up to 22 weeks after the completion of the vaccination course (Brewster and Nevel, 2013). Estrogen has a negative effect on feed intake and the reduction of estrogen by Improvac results in increased feed intake in immunocastrated pigs (Bonavera et al., 1994; Zamaratskaia et al., 2008). The effect of immunocastration on females is not clear.

SEDATION AND ANESTHESIA

Injectable anesthetics

Minor surgical procedures like tusk and hoof trimming can be performed with a combination of Xylazine (2.2 - 4.4 mg/kg body weight) and Tiletamine/ zolazepam (4.4 mg/kg body weight) given intramuscularly, without further induction of anesthesia. This combination is not suited for patients with cardiovascular and renal problems. Ketamine (11-33 mg/kg, IM or SC) is used for both short- and long-lasting surgeries. It exerts only a mild depressing effect on the cardiovascular system and hence is safe to use in pet pigs.

For long lasting procedures (more than one hour), premedication is followed by tracheal intubation as apnea is common in pigs. A combination of azaperone (premedication) and ketamine (induction general anesthesia) has been recommended by Sipos et al. (2007) for minor surgical procedures, and the same combination has been reported by Augustijn et al. (2010) to perform laparotomy in a VPB pig. Premedication with Azaperone at 1-2 mg/kg body weight ensures good sedation and anti-emetic properties but has no analgesic effects. The ketamine (20 mg/kg) and xylazine (2 mg/kg) combination is recommended along with atropine sulphate (0.02 - 0.05 mg/kg) as premedication to avoid fatal arrhythmias caused by xylazine in pigs.

Inhalation anesthetics

For short surgical and diagnostic procedures, inhalation anesthesia with an initial concentration of 4-5% isoflurane followed by 2-3% maintenance dose can be used alone or in combination with sedation for pot-bellied and miniature pigs. Isoflurane offers a low analgesic effect but has a wide margin of safety with rapid and smooth recovery (Bollen et al., 2010; Fubini and Ducharme, 2016). Inhalation anesthesia must be used only at the veterinary practice.

Local anesthetics

Infiltration of local anesthetics ensures analgesia without causing side effects and anorexia. The effects of lidocaine lasts for two hours and that of bupivacaine lasts for four to eight hours (Jackson and Cockcroft, 2007; Bollen et al., 2010).

Pain management

Postoperative pain can be managed for one to three days using either nonsteroidal anti-inflammatory drugs (NSAID) or opiates or a combination of both. The commonly used analgesics are listed in Table 5 (Bollen et al., 2010).

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Sint-antoniusvuur bij mensen en varkens: hoe de waardering voor varkens in West-Europa verchristelijkt werd

Saint-Anthony's fire in humans and pigs: how eating pork was Christianized in Western Europe

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SAMENVATTING

In de vroegchristelijke geloofspraktijk mocht varkensvlees niet gegeten worden, vermoedelijk omdat varkens als alleseters competeerden met de mens. Iets wat in woestijn- of halfwoestijngebieden een zaak van leven of dood kon zijn. Nadat het christendom zich in Europa had verspreid, kon dit taboe niet overeind blijven: in dat continent zochten de dieren hun voedsel in de toen nog uitgestrekte bossen en hun vlees hielp de mensen te overleven tijdens de lange winters. Huisvarkens werden 'verchristelijkt' doordat Antonius van Egypte, een kluizenaar uit de derde-vierde eeuw, aanroepen werd om te beschermen tegen twee, oppervlakkig gezien, gelijkaardige aandoeningen met sterk uitgesproken ontstekingsverschijnselen: moederkorenvergiftiging bij de mens en vlekziekte bij het varken, beide sint-antoniusvuur genoemd. Zijn status als 'geneesheilige' en beschermer tegen deze ziekten had de kluizenaar te danken aan het feit dat hij aan de 'vurigste' bekoringen van de duivel weerstaan had. De hospitaalorde van de antonieten, ontstaan in de late middeleeuwen tijdens epidemieën van moederkorenvergiftiging, populariseerde de associatie van Antonius met varkens. Het feit dat het varken het typische attribuut werd van deze populaire geneesheilige staat symbool voor de aanvaarding van het huisvarken als voedselbron in de toenmalige sterk religieus gedetermineerde Europese maatschappij.

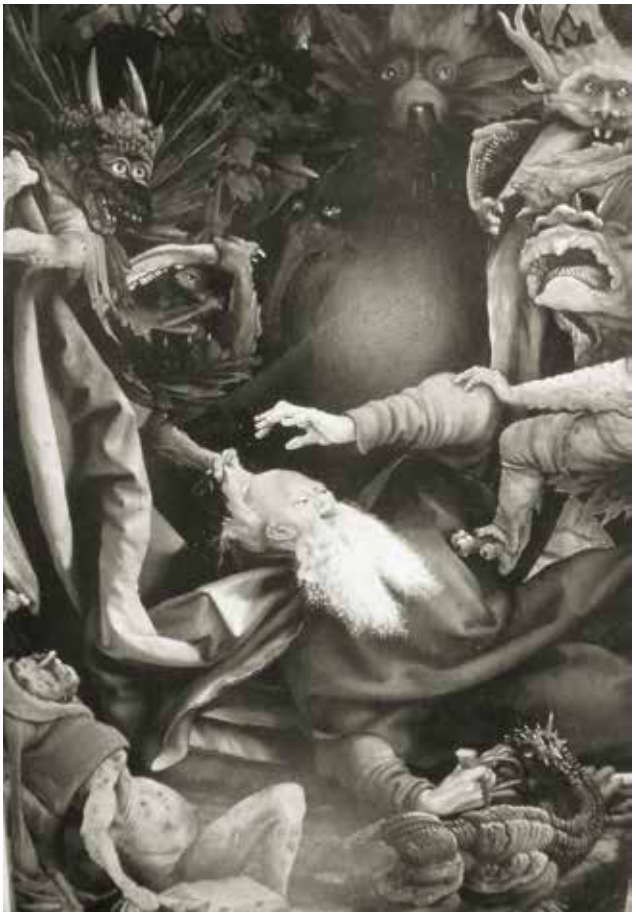
ABSTRACT

In the monotheistic religions emerging in the Middle-East, the cradle of our civilization, pigs were of low esteem. Eating their meat was even forbidden in the Mosaic laws, most probably because in arid or semi-arid regions these animals were in competition with humans for food. The taboo on pork could not be maintained within Christian practice once the church established its dominant position in Western Europe. Products of the large woods made the fattening of domestic pigs easy in that continent, thus providing food necessary for humans to survive hard winters. In this context the early Christian, Saint Anthony of Egypt, became associated with pigs, because he was invoked to protect against epidemics of ergotism in humans and severe inflammations of widely diverse etiology in animals as well as in humans. The most typical of these, which occurred in pigs, was termed Saint Anthony's fire, as was ergotism in humans. It was mainly the religious order of the Antonites that propagated the piglet as the attribute of this saint. This unusual religious association symbolizes the acceptance in mediaeval Western Europe of pork as high-quality food.

INLEIDING

Na Maria was Sint-Antonius 'met het varken' de meest populaire heilige in onze streken (Dhaene, 1999; Decavele, 2009). Hij was een vroegchristelijke figuur die zich in een Egyptische woestijn had teruggetrokken en als het ware de verpersoonlijking werd van de asceet. Hij zou geleefd hebben van 251 tot 356, en dus 105 jaar geworden zijn. Deze Egyptenaar was bij ons veel geliefder dan zijn middeleeuwse naamgenoot, de even heilige Antonius van Padua. De naam kan dus tot verwarring leiden, vandaar ook de betite-

Figuur 1. Twee angstaanjagende creaturen, letterlijk kwelduivels, gaan de arme Antonius te lijf. Een van de fabelachtige kapitelen in de Maria Magdalenabasiliek van Vézelay (Bourgogne, eerste helft twaalfde eeuw).



Figuur 2. Een deel van het beroemde altaar tussen 1510 en 1515 geschilderd door Matthias Grünewald voor het klooster van de antonieten in Isenheim (bij Colmar, Elzas) toont de bekoringen van Sint-Antonius door afschuwelijke monsters zoals alleen Grünewald die kon uitbeelden. Vier eeuwen na Vézelay was dit nog steeds de gebruikelijke manier van voorstellen.

ling voor de sint als Antonius 'de Grote', 'van Egypte', of 'abt' en 'eremiet' en wat ons betreft: vooral 'met het varken(tje)'. Het is deze Antonius die 'aanroepen' werd - te hulp geroepen - ter bescherming en genezing voor aandoeningen die gekenmerkt zijn door sterk uitgesproken ontsteking, in middeleeuwse termen 'vurige ziekten'.

Heel bekend in verband met Antonius van Egypte zijn de 'bekoringen' die de man in al zijn eenzaamheid moest ondergaan (Figuur 1 en 2). Eigenlijk waren dat martelingen die symbool stonden voor alles wat de asceet zichzelf ontzegde. In het vroege christendom hadden martelaars de allerhoogste reputatie, maar nadat dit geloof staatsgodsdienst geworden was, zat er voor mensen die de hoogste heiligheid wilden bereiken, niets anders op dan zichzelf te pijnigen, in de eerste plaats door seksuele onthouding, door het strenge vasten en de zwijgplicht: een symbolische afzondering herinnerend aan het kluizenaarschap van Antonius in de woestijn. Tot in de vorige eeuw werden in sommige strenge orden de kloosterlingen verondersteld zich te geselen, met andere woorden zichzelf te martelen.

In deze bijdrage proberen we te achterhalen hoe die reputatie van Antonius van Egypte als geneesheilige voor mens en dier tot stand is gekomen en hoe deze heilige kon uitgroeien tot symbool van de waardering die het varken al eeuwenlang geniet in West-Europa; met andere woorden, we onderzoeken hoe de faam van dit dier 'verchristelijkt' werd, of hoe een religieus gedetermineerd voedseltaboe uit het Midden-Oosten in onze streken moest en kon verdwijnen.

ANTONIUS GEASSOCIEERD MET HET VARKEN

De heilige wordt steevast afgebeeld (Timmers, 1985; Claes et al., 2006) als een baardige oude man in lange gewaden met een staf (abtenstaf), een T (tau) teken op de kledij, een bel, soms vuur, en met daarbij nog iets heel specifieks, beslist ongewoon: een onschuldig varkentje dat meestal onderaan opzij van de beeltenis komt kijken (Figuur 3 en 4). Hoe dat te verklaren? Het varken was immers 'onrein' of werd niet geacht in het Midden-Oosten. Varkensvlees werd niet gegeten, zoals dat ook later in de moslimtraditie het geval zou zijn. Al waren er al heel vroeg, onder meer in een visioen van Sint-Petrus aangehaald in de Handelingen van de Apostelen (hoofdstuk 10), aanwijzingen dat niet-joodse christenen de joodse voedselvoorschriften niet moesten volgen, is dit eigenaardig, quasi onverklaarbaar. Dat dit in de omgeving waarin Antonius leefde nog het geval was, lijkt waarschijnlijk. Zeker is dat de associatie van de heilige met het varken in West-Europa pas een millennium (!) na de dood van de heilige man algemeen aanvaard werd, namelijk in de late middeleeuwen, na het jaar 1300. De datering kan onder andere afgeleid worden uit de *Legenda aurea* van Jacobus a Voragine (1228-1298), de in de late middeleeuwen meest verspreide compilatie van levensbeschrijvingen van heiligen.

VARKENS VUIL EN WILD?

Iedere Vlaming kent de uitdrukking ‘het zwijn uithangen’. Zwijnerij is ook Algemeen Nederlands en betekent vuile troep, vuile praktijken volgens van Dale. Hoewel van bepaalde (mannelijke) personen gezegd wordt: ’t is een zwijn, een zwijntje’, gebeuren zwijnerijen meestal in groep en ondersteund door koning alcohol. Die associatie dateert niet van gisteren. Lievevrouw-Coopman (1974) citeert een Gentse tekst uit 1589: ‘*en was soo droncken als een zwijn*’. Vergezocht of niet, in elk geval is de vergelijking sinds lang ingeburgerd in onze en in andere talen. Hoe kon dit voor een dier dat houdt van een vaste, droge en propere ligplek en dat zeker nooit dronken is, wel schrokkerig?

Misschien moeten we de verklaring zoeken in de eetgewoonten van *Sus scrofa*? Daarvoor moeten we even de geschiedenis bekijken van de ondersoort of variëteit domesticus, meestal aangeduid als *Sus domesticus*. Deze migreerde enkele duizenden jaren geleden samen met onze voorouders, het rund en het schaap vanuit het Nabije Oosten naar Europa. De eerste landbouwrevolutie, gebaseerd op het kweken van granen, had in deze regio geleid tot een eerste grote aangroei van Homo sapiens, met migratie tot gevolg.

Een paar eeuwen geleden werden de nakomelingen van deze varkens gekruist met Chinese, die een aparte evolutie kenden. Ook spontane kruisingen met inheemse wilde evers bleven mogelijk. Dit vormde de basis van het huidige gedomesticeerde Europese varken. De ironie van het noodlot wil dat onze huisvarkens, net zoals wijzelf, precies uit het Midden-Oosten stammen, waar varkens verafschuwd worden en het eten van het vlees ervan taboe is. Hoogstwaarschijnlijk is het strenge verbod op het eten van varkensvlees bij Moses en zijn al dan niet joodse volgelingen terug te brengen op voedselconcurrentie in semi-aride gebieden (half woestijn). Dat ontwikkelde zich langzaam aan naarmate de daar ontwikkelende landbouw de bossen deed verdwijnen. Later versterkte het taboe door het bindend vermogen (religie: afgeleid van het Latijnse ligare: binden en religare: sterk binden) van voedsel- en kledijvoorschriften. En dat is nog steeds het geval.

Het inheemse wilde varken, de ever, wordt als een andere ondersoort aanzien, namelijk *Sus scrofa* subsp. scrofa. De speciesnaam *scrofa* is afgeleid van een (proto)indo-europees woord ‘(s)ker’ dat wroeten – ontwortelen betekent. De snuit is het belangrijkste werkinstrument van het varken. De resultaten van dat wroeten vormen het gemakkelijkst herkenbare teken van de aanwezigheid van wilde evers in en om bossen. Geholpen door een uitstekende reukzin, zoeken en vinden ze op die manier een groot deel van hun voedsel. ‘Domesticus’ kan het wroeten evenmin laten, vandaar de neusringen door varkenshouders bij beren aangebracht. Biggen en jonge dieren zijn speels en nieuwsgierig en ze ‘steken graag overal hun neus in’. Dit vinden we onder andere meesterlijk beschreven door Anton Koolhaas (1990) in zijn zoetzure verhaal ‘Mijnheer Tip is de dikste mijnheer’.

Figuur 3. Gesneden in opdracht van bisschop Antoon Triest voor zijn patroonheilige. Met het traditionele leuke (!) varkentje opzij (Sint-Baafskathedraal, Gent, detail uit de deur van de grafkapel van Triest, 1663).

Figuur 4. Het varken naast de heilige kon best groot zijn, zoals bij dit Gentse beeld in de Sint-Antoniushof bij de Sint-Antoniuskaai, maar het oogt steeds onschuldig. Bemerk de spitse vorm van zijn belangrijkste werkinstrument: de snuit, ideaal om te wroeten. De huidige korte varkenssnuit met abrupt oplopend voorhoofd is het resultaat van latere kruisingen en selectie (Foto 2018).

Figuur 5. Een als non verkleed varken poogt een naakte man te overhalen zijn testament te wijzigen ten gunste van haar of haar klooster (Jeroen Bosch, detail uit de 'Tuin der Lusten', Madrid).

Figuur 6. Sint-Antonius omringd door allerlei fantastische, afschrikwekkende beesten en beestjes in de versie van Jeroen Bosch. Zijn varken heeft daar part noch deel aan (detail uit het Antonius-drieluik in Lissabon).

Als drogreden voor het taboe worden de 'vuile manieren' van varkens aangehaald als verklaring (Harris, 1974). Varkens wroeten graag in het vuil omdat ze daarin allerlei eetbaars, inbegrepen feces van mensen en andere dieren, ruiken en vinden. Ze lijken vuilaards, maar zijn 'op zich zelf' heel proper. Iets wat onwetende mensen moeilijk aanvaarden. Ook varken-minnende en/of varken-etende andersgelovigen en ongelovigen vinden coprofagie niet bepaald je dat. Alleen Chinezen doen daar niet moeilijk over. Als ze er ruimte voor hebben in hun woningen gebruiken ze in veel streken van oudsher hun geliefde varkens als opruimers van hun eigen uitwerpselen en ander organische afval onder hun traditionele huizen op het platteland.

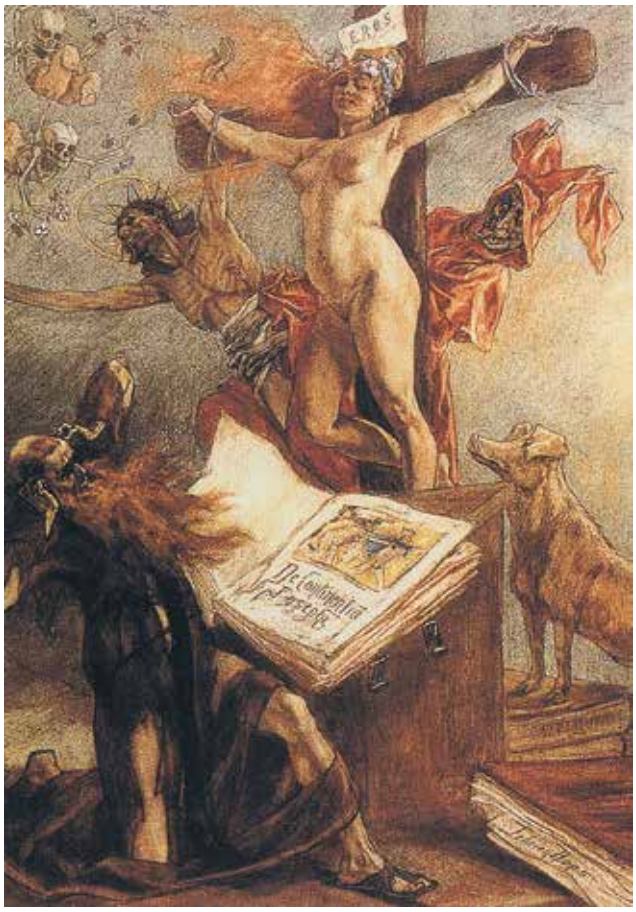
Nog een tweede mogelijke reden voor de slechte reputatie van varkens is dat ze wild kunnen te keer gaan. In een heel bekende episode uit het leven van Jezus van Nazareth ziet men hoe een bezetene miraculeus van zijn demonen verlost wordt: ze worden uitgedreven en zoeken hun toevlucht in een kudde varkens, die zich meteen beginnen te misdragen alsof 'de duivel in hen gevaren is', zo luidt de standaarduitdrukking. Dat lijkt wel min of meer op wat er in de natuur kan gebeuren. Wilde varkens, everzwijnen, kunnen plots -als het ware op commando- wild vooruit stormen. Het is een overlevingsstrategie bij acuut dreigend gevaar, belangrijker dan de kracht van vooral mannelijke evers.

VARKENS WULPS?

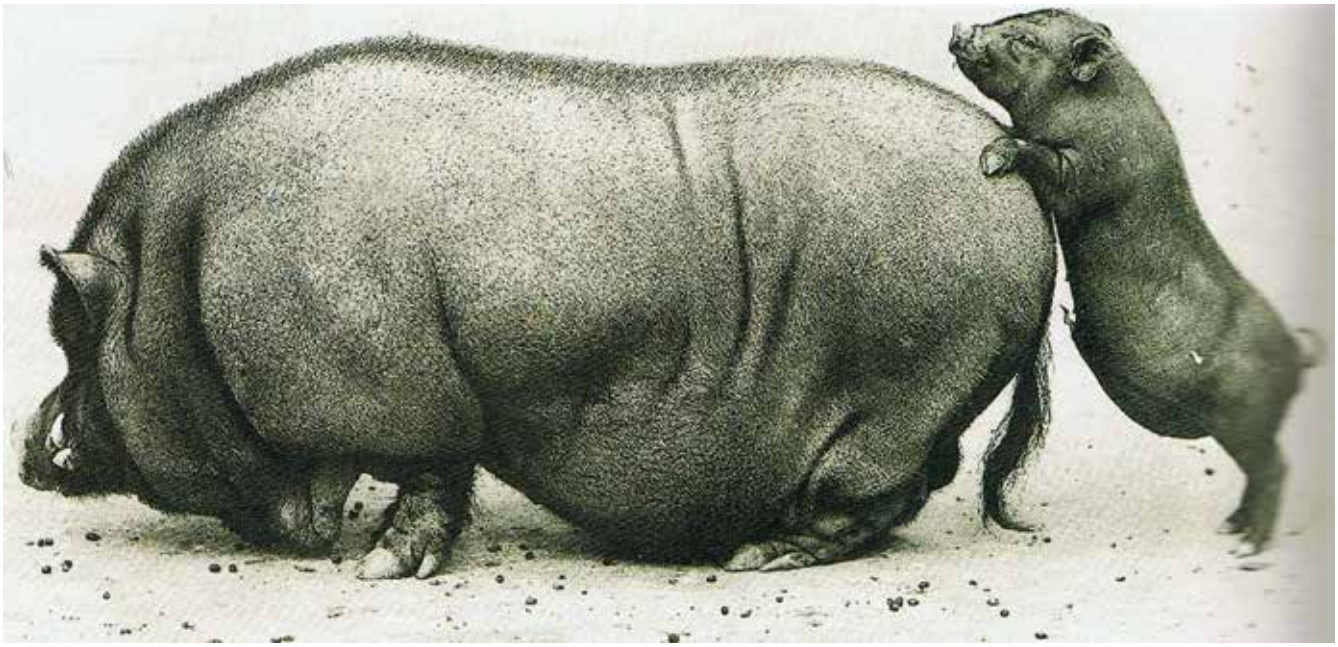
In de hierboven aangehaalde middeleeuwse *Legenda aurea* is er in verband met Antonius nog geen sprake van varkens. Wel wordt uitvoerig beschreven hoe de heilige man gepest, gemarteld werd, zelfs verscheurd door demonen in alle mogelijke vormen, maar steeds afschrikwekkend, nooit verleidelijk. In digitale en papieren naslagwerken en ook op de samenvattende site *Heiligen.net* worden de wellustige bekoringen die Antonius moest ondergaan, integraal toegeschreven aan het varken. Nochtans gaat dat regelrecht in te-

gen de hierboven aangehaalde, eeuwenlang gebruikelijke manier van voorstellen, namelijk met varkentje als trouwe, onschuldige metgezel. In de hagiografie door Athanasius van Alexandrië, tijdgenoot van Antonius, waarin de bekoringen van seksuele aard expliciet beschreven staan, wordt dit dier evenmin vermeld (Hunink, 2013). Jeroen Bosch beeldt de heilige af met een rustig en braaf varken aan zijn zijde, terwijl dezelfde schilder in zijn 'De Tuin der Lusten' weergeeft hoe een varken in nonnenkleren een man probeert te verleiden met de duidelijke bedoeling haar of haar klooster in zijn testament te begunstigen (Figuur 5 en 6). Maar met de bekoringen van Sint-Antonius heeft dat niets te maken. In de 19de eeuw werden de 'bekoringen' populair in de schilderkunst. Salvator Dali zocht het in het fantastische, maar anderen haalden er voluptueuze, mooie vrouwen bij om de arme man op de proef te stellen, te verleiden.

Waar zit dan het verband met wulpsheid, zoals zo overweldigend uitgebeeld door Félicien Rops (Figuur 7)? De middeleeuwse encyclopedist Vincent de Beauvais (13de eeuw) schreef dat de wellusteling als een varken is. Willen of niet, terecht of onterecht, het dier is al eeuwenlang een symbool van de vreselijke ondeugd 'onkuisheid' (Doering en Hartig, 1940). We mogen meteen al uitsluiten dat de middeleeuwers meenden dat het varken zelf de rol van verleider zou spelen. Miss Piggy uit de Muppet Show of iets dergelijks kenden de antieken en vroege christenen niet. De toenmalige zwijntjes, wild of tam, hadden zelfs geen imposante rozige billen zoals onze huidige varkens (Fokkinga, 2004). Weinig waarschijnlijk ook dat we het zouden moeten zoeken bij de vooral in volle lactatie imposante dubbele rij melkklieren. Al bij al duiden die toch eerder op moederzorg. Vermoedelijk was de vergelijking met het 'vieze' varken simpelweg



Figuur 7. Félicien Rops toont 'de bekoring' op de zo mogelijk meest schokkende manier: een voluptueuze naakte vrouw stoot Christus van zijn kruis terwijl Antonius zich vol afschrik afwendt van wat zich pal voor hem afspeelt. Boven op het kruis is het opschrift INRI vervangen door EROS. Er achter een duivel vermomd als monnik, maar met nauwelijks verhulde horens in zijn kap. Een varken kijkt genoeglijk toe.



Figuur 8. Mini- en maxivarkens, hier in quasi karikaturale vorm. Het beertje is duidelijk opgewonden door de geurstoffen van het bronstige vette monster dat voor hem door de achterpoten zakt. Maar of het zal lukken? Bemerk het spiraalvormige penisuiteinde (Uit Fokkinga, 2004).

Figuur 9. Anoniem portret bekend als 'De man met de Anjer' (Berlijn). Hoogkwalitatieve en vermoedelijk getrouwe 16de-eeuwse kopie van een vroege Jan van Eyck, waarvan verder enkel een getekende versie uit 1429 bewaard bleef. Het streng (of is het wantrouwig?) kijkende personage, duidelijk 'een heer van stand', is herkenbaar als antoniet aan het tau (T) teken en het belletje.

Figuur 10. Zieke lijdend aan het sint-antoniusvuur, vermoedelijk hier geen moederkorenvergiftiging maar bacteriële infectie, actueel meestal erysipelas genoemd (detail uit het Isenheimer altaar van Matthias Grünewald; cf. Figuur 3).

een manier om sterke afkeer en absolute verwerping uit te drukken.

Of varkens zo wellustig zijn, valt trouwens nog te bezien. Zeugen laten zich, zoals de meeste zoogdieren, enkel 'dekken', willen enkel copuleren, tijdens een relatief korte periode van bronstigheid (De Smet, 2017). Daarbij vertonen de dieren, althans de actueel gefokte, zonder uitlokken geen opvallende tekens van copulatiebereidheid. Voor de varkenshouders is de bronst, de voor bevruchting geschikte tijd, dikwijls zelfs moeilijk vast te stellen. Men kan duwen op de rug van de zeug om de zogenaamde 'sta-reflex' vast te stellen, met andere woorden men imiteert het gedrag van de varkensbeer. Deze laatste hebben er overigens zelf geen moeite mee om bronst en copulatiebereidheid bij hun vrouwelijke soortgenoten te herkennen. Ze besnuffelen de vulva en ruiken de daarvoor kenmerkende geurstoffen (Figuur 8). Deze worden ook gebruikt in de actueel wijd verspreide kunstmatige inseminatiepraktijk.

GOEDE FAAM IN EUROPA

Maar als het varken symbool staat voor al die vreselijke ondeugden en zijn vlees taboe was, hoe komt het dan dat de heilige Antonius, zowel in volkse voorstellingen als in hoogstaande kunstwerken, zo goed als altijd vergezeld wordt door een leuk varkentje? Hier willen we een hypothese naarvoor brengen die gebaseerd is op (1) de acceptatie van het varken als voedsel voor de mens in West-Europa en (2) op de gelijkenis tussen bepaalde aandoeningen die zowel bij de mens als het dier sint-antoniusvuur genoemd werden.

De eerste reden is niet zonder meer evident. Nadat het christendom zich tot West-Europa uitgebreid had, was het taboe op varkensvlees nog moeilijk vol te houden, want die dieren waren daar geen voedselconcurrent. Integendeel, ze konden tot een zeer gewaardeerde voedselbron uitgroeien. In de destijds uitgestrekte eikenwouden zochten ze hun voedsel zelf. De voor de mens onverteerbare eikels en andere bosvruchten zetten ze om tot smakelijk vlees. Bossen waren niet enkel voor de houtopbrengst waardevol. Varkenskudden mochten er onder de hoede van een 'zwijnder' hun kostje zoeken. Aan het einde van het najaar of begin van de winter, nadat ze zich vet gevreten hadden aan de 'mast', i.e. eikels, etc. (de woorden vetmesten, mestvarken en dergelijke komen daarvan!) werden ze het bos uitgedreven en soms over relatief verre afstanden door de varkenshoeders naar de steden gebracht waar hun vlees en vooral vet een welkome aanvulling vormden op het soms karige dieet. Eylenbosch (2016) beschreef dit jaarlijks gebruik in het begin van de jaren 1500 voor de '*Heilige Geesttafel*' (armentafel) van de Leuvense Sint-Pietersparochie die zijn varkens betrok uit de bosrijke streek van Bergen (Henegouwen). Hun vlees werd hoger geschat dan dat van runderen en schapen (Ervynck, 1999).

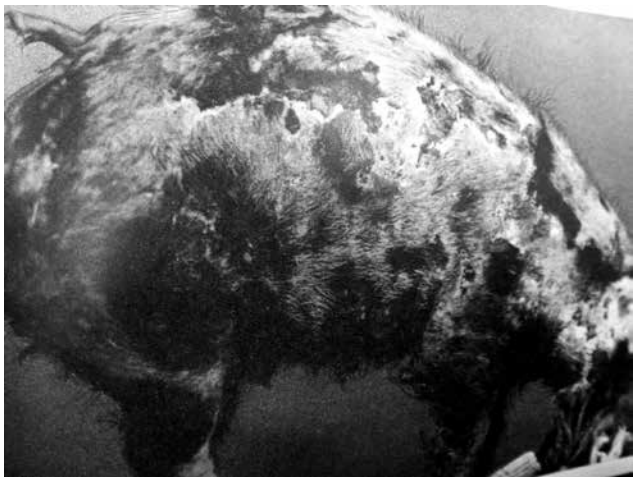
Ook uit veel vroegere tijden zijn er gegevens over ‘mastvarkens’ (sic!) in onze streken. Uit de negende eeuw bleven er cijfers bewaard van aantallen varkens in wouden, eigendom van onder de Merovingen gestichte abdijen, die toelaten de oppervlakte van die lang verdwenen bossen, waarover nauwelijks of geen latere gegevens bestaan, bij benadering te berekenen. Per varken was er namelijk twee tot drie hectare van doen (Voet, 1949).

In de late middeleeuwen (14de en 15de eeuw) werd de associatie van Sint-Antonius met het varken op een bijzondere manier levendig gehouden door een religieuze orde die haar naam ontleende aan de heilige: de antonieten (Figuur 9). In ruil voor voorspraak bij de heilige en een zekere zorg verleend aan de zieken, kregen de ordebroeders het recht om een per stad vast aantal varkens, de ‘antoniusvarkens’, vrij langs de straten te laten rondlopen, voedsel uit te wroeten of af te bedelen, iets wat voor dieren van particulieren streng verboden was (De Cock, 1895 en 1908; De Pauw, 1885). Jaarlijks organiseerden de antonieten ook bedelprocessies die het hele land rondtrokken en die nogal eens konden ontaarden (Devriese, 2019). Zoöarcheologen concluderen uit hun bevindingen in diverse stedelijke sites (kloosters, adellijke en andere verblijven, in casu Gent) dat varkens de belangrijkste vleesleveranciers waren voor privépersonen in de vroege middeleeuwen en dat dit vermoedelijk vooral dieren betrof die in de stad zelf gekweekt werden. Later werden ze geleidelijk aan verdrongen door runderen (Van der Plaetsen, 1985).

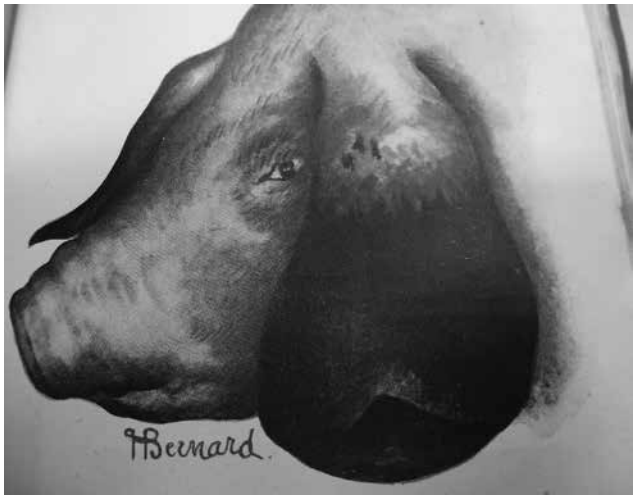
‘VURIGE’ ZIEKTEN VAN MENS EN DIER

De ziekten waartegen Antonius zou beschermen, werden vergeleken met aandoeningen verwekt door ‘vuur’. Ze betreffen vooral de huid, of exacter: ze gaan meestal gepaard met kenmerkende, dikwijls rode uitwendige letsels, tekenen die wijzen op hevige ontsteking, inflammatie (Figuur 10). Let op de woorden: ze duiden op vuur. Een speciaal geval vormt moederkorenvergiftiging bij mensen, ergotisme, verwekt door een toxine geproduceerd door een schimmel die op en in aren van rogge groeit en in het meel kan terecht komen. De doorbloeding van vooral de extremiteiten (vingers en tenen) komt in het gedrang. Ze ondergaan ‘droog versterf’, i.e. droog gangreen, en lijken als het ware te verkolen door het ‘vuur’ van de ziekte met extreem hevige pijnen tot gevolg. Men sprak over de ziekte van de brandenden (‘le mal des ardents’).

In de middeleeuwen namen deze vergiftigingen soms het karakter van ware epidemieën aan, i.e. ‘la peste de feu’ (Sandell-Dupeley, 1988). De vergiftigingen waren vooral talrijk in tijden van hongersnood (Pognon, 1981). De vroegste berichten erover stammen uit de Rijnstreek (9de eeuw). Daarna volgden ze elkaar in snel tempo op, onder andere in de Nederlanden. Blijkbaar kwam de aandoening later minder voor. Het was Claude Perrault (1613-1688), broer van de bekende sprookjesverteller Charles, die halverwege de zeventiende eeuw de oorzaak van de ziekte ontdekte en beschreef.



Figuur 11. Dat de benamingen ‘le rouget du porc’, ‘Rotlauf’, ‘red fever’ en ‘mal rossino’ het acute stadium van de ziekte verwekt door *Erysipelothrix rhusiopathiae* uitstekend typeren, toont deze afbeelding uit Moussu (1924). De effecten van de ontsteking worden hier gecompliceerd door trauma. Roodheid zit ook vervat in de geslachtsnaam van de bacterie en in de term erysipelas.



Figuur 12. Sterk uitgesproken vlekziekte bij het varken, hier al in het chronische, necrotiserende stadium (uit Smith en Jones, 1961).

Moederkorenvergiftiging werd sint-antoniusvuur, ignis sacer (heilig vuur) en voor hetzelfde geld ook duivels vuur genoemd. Wellicht kwam de ziekte aan die eerste naam doordat in middeleeuwse beschrijvingen de kwellingen van de woestijnheilige daarop leken. Hij had het ‘vuur’ van de bekoringen weerstaan. Men zou kunnen denken aan de duivels die de eenzame Antonius het vuur aan de schenen legden. Althans, zo staat het beschreven, niet in de eerste eigentijdse, maar in de veel later gangbare versies van zijn leven. Hij weerstond, waaruit men meteen wilde afleiden dat de hoog heilige man ook andere levende wezens zou beschermen tegen wat vaagweg het ‘vuur’, de ‘vurige’

ziekten, wondvuur, miltvuur, etc. genoemd werd. En tenslotte, nagenoeg onvermijdelijk, vanwege enkele vergezochte gelijkenissen tussen de menselijke aandoening en de builenpest, verwekt door *Yersinia pestis*, werd de heilige eremiet tot 'pestheilige' bevorderd. Dat was voor hem een titel van secundaire orde die hij deelde met andere sinten, met Rochus als meest bekende.

Er waren wel meer heilige martelaren die de vuurdood stierven. De heilige Laurentius bijvoorbeeld, die letterlijk geroosterd werd, promoveerde tot beschermheilige tegen verbrandheid en huiduitslag (De Cock, 1891). Het lijkt erop dat dit vooral lokaal verwekte letsels waren, terwijl Antonius specialist werd van de meer algemene ontstekingen, i.e. septikemie of 'inwendig vuur'. Maar dat volstaat niet om de associatie te verklaren van varkens met de beschermer tegen 'vurige' ziekten, Antonius. Er moet iets anders geweest zijn dat daar aan de grondslag van ligt. En hier komen we bij een varkensziekte terecht. De naam

Figuur 13. Liefdevol naar de hemel geleid door Sint-Antonius wordt het beestje verwelkomd door Onze-Lieve-Vrouw. In de achtergrond dirigeert Sint-Petrus met zijn hemelsleutel een welkomsthymne. Werkje van Wilhelm Busch (1832-1908).

Sint-Antoniusvuur werd ook gegeven aan de klassiek bij varkens bekende 'vlekziekte' met een heel andere etiologie, namelijk de bacterie *Erysipelothrix rhusiopathiae*. Ze gaat meestal gepaard met karakteristieke vlekvormige roodheid op de huid, naast een reeks andere, minder opvallende maar belangrijkere letsels. Bij varkens gaat het waarnemen van dergelijke huidletsels veel gemakkelijker dan bij de meeste zoogdiersoorten doordat het huisvarken samen met de mens, in de woorden van Midas Dekkers (1990), het blootste beest is, al geldt dat veel minder voor de oudtijdse varkens en ook niet voor alle nog bestaande rassen.

De algemeen in de natuur voorkomende vlekziektebacil kan vrijwel alle diersoorten aantasten, inclusief (weliswaar heel zelden) de mens, maar de ziekte tast veruit het meest frequent varkens aan. De dieren vertonen tekens van intense pijn en de letsels kunnen gangreneus worden, dit wil zeggen dat huiddelen afsterven, dikwijls op een karakteristieke vlek- of blokvormige manier (Figuur 11 en 12). Vandaar de andere benamingen vlekziekte en 'diamond disease'. In het Duits spreekt men van 'Rotlauf' en 'Backsteinblattern'. In de oude Franstalige veterinaire literatuur werd een onderscheid gemaakt tussen 'érysipèle simple' en 'érysipèle gangréneux', maar de meest gebruikte Franse benaming van de ziekte is 'le rouget du porc'. Onder het volk werd de aandoening ook 'le feu sacré', vertaling van 'ignis sacer' en 'mal des ardents' genoemd (Bénion, 1872); in het Nederlands: vliegend, heilig of sint-antoniusvuur. De gelijkenis met het woordgebruik bij moederkorenvergiftiging van mensen valt op, al is de oorzaak totaal verschillend. Met het beschikbaar worden van effectieve vaccinaties en de eerste penicillines verdween deze eeuwenlang, vooral bij varkens belangrijke ziekte, van het voorplan.

BESLUIT

Primum vivere, deinde philosofari, of 'Erst kommt das Fressen, dann kommt die Moral' wist ook Bertolt Brecht. In de letterlijke toepassing van dit wijze gezegde betekende dit hier dat het taboe op varkensvlees in het bosrijke Europa wel moest verdwijnen. Het varken werd dus 'wit'gewassen van alle zonden. Dat gebeurde al in de vroege middeleeuwen, zoals de hierboven beschreven varkens gehoed in de bossen toebehorend aan abdijen, bewijzen. Zo kwam het dus dat een snoezig varkentje bijna een millennium na zijn dood het belangrijkste attribuut werd van Sint-Antonius van Egypte. En zo kon het varken uiteindelijk zelfs in de christelijke hemel belanden, althans zo stelt Wilhelm Busch (1832-1908) het voor: theologisch niet te verantwoorden, maar lief (Figuur 13). En ook hier op aarde konden varkentjes tot in majestueuze kathedralen dienst doen (Figuur 14).

De achting die men het varken in het bosrijke Europa begon toe te dragen, werd inderdaad gesymboliseerd door de associatie van het dier met een waarlijk

Figuur 14. Biggetjes onder een 'misericorde': een halfzitje dat de monniken hielp overeind te blijven tijdens de urenlang durende diensten. In middeleeuwse abdijkerken waren die plankjes dikwijls voorzien van steuntjes met fraai gesneden 'drolerieën' of bijbelse tafereeltjes. Hier een exemplaar uit de kathedraal van Chester (Verenigd Koninkrijk), in oorsprong een abdijkerk.

grote heilige. De combinatie is dus niet zo maar gratuit legendarisch, maar economisch en cultuurhistorisch gegrond, bovendien ook medisch-veterinair. Het was de opvallende, maar oppervlakkige gelijkenis tussen een destijds belangrijke aandoening bij mensen en een tot in de vorige eeuw veel voorkomende ziekte bij varkens die, onder meer de orde van de antonieten ertoe bracht Antonius te propageren als bescherm- en geneesheilige voor mensen en dieren, vooral varkens.

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Inhoud van de 87ste jaargang 2018

Vlaams Diergeneeskundig Tijdschrift

DANKWOORD AAN DE REVIEWERS VAN DE ARTIKELS VERSCHENEN IN 2018

De redactie houdt er aan om de beoordelaars te bedanken voor hun onbaatzuchtige inzet en het delen van hun expertise bij een soms ondankbare taak in een wereld waarin tijd een alsmaar kostbaarder goed wordt.

Alex Van Zeveren, Annelies Decloedt, Annelies Willems, Bénédicte Callens, Birhanu Hadush, Bonnie Valgaeren, Caroline Gadeyne, Cathérine Delesalle, Ciska De Ruyver, Dick Mevius, Diego Rodrigo Mocholi, Elke Van der Vekens, Eva Coppieters, Eva Pint, Filip Luyckx, Frédéric Billen, Geert Janssens, Johannes Charlier, Jozef Laureyns, Griet Vercauteren, Hans Kooistra, Hans Van Loo, Henk Decock, Katleen Hermans, Leen Verhaert, Leslie Bosseler, Ingeborg Polis, Kimberley Stee, Laurence Evrard, Laurence Lefère, Leen Van Brantegem, Luc Devriese, Luc Peelman, Maarten Oosterlinck, Marc Govaerts, Mathias Devreese, Nausikaa Devriendt, Peter Coutteel, Pierre Dorny, Pieter Cornillie, Pieter Defauw, Richard Ducatelle, Saskia De Ruyver, Siska Croubels, Sofie Marynisse, Sophie Vandenabeele, Sarne Devliegher, Stefan Deleuze, Stijn Schauvliege, Susanne Boroffka, Tania Maenhout, Theo Bruckers, Thomas van Bergen, Tim Bosmans, Ward Spiegelaere, Wendy Wambacq, Wim Ceelen

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VRAAG EN ANTWOORDRUBRIEK

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CASE SERIES

CASE REPORTS

BESCHERMHEILIGEN VAN DUIVENMELKERS

Op de hoeve van haar ouders stond Catharina Labouré (1806-1876) in voor de verzorging van de duiven, die, tot 800 in getal, zodra zij verscheen, in de vorm van een kroon boven haar hoofd toerden. Ook later, toen zij na haar intrede in een klooster in 1831 verbonden was aan een Parijs' hospitaal, waakte zij over het welzijn van de duiven. Ze werd heilig verklaard om diverse (andere) redenen.

Het is vooral in het Antwerpse dat Sint-Catharina Labouré vereerd wordt. Het begon in 1947, het jaar van haar heiligverklaring, toen een onderpastoor met een befaamd duivenliefhebber het initiatief opvatte om te harer ere een duivenwijding op touw te zetten. Op 28 november 1955 - feestdag van de nieuwe heilige - werd in Sint-Antonius-Brecht, een dorp in de Antwerpse Kempen, vermaard om zijn duivenliefhebberij, voor de duivenmelkers een plechtige mis opgedragen. Het initiatief bleek in te slaan en er werd beslist dat jaarlijks te herhalen. In de parochiezaal ging een duivenwijding door samen met een tentoonstelling. De plaatselijke melkers waren zo bereidwillig enkele van hun diertjes te offeren, die dan in de zaal werden verloot. Zo kon men tegen een spotprijs zo'n diertje, soms uit een bekend hok, bemachtigen.

De pastoor van St-Antonius, zelf duivenliefhebber, stelde zich tot doel de vermaardheid van zijn patrones gans België door te verspreiden. Zo werden inlichtingen over deze jonge devotie gestuurd naar niet minder dan 120.000 adressen van duivenmelkers in den lande. Bedevaarders stroomden toe. Ze konden hun bedevaart combineren met een bezoek aan de befaamde duivenkweek-installaties van de gebroeders De Scheemaker in Sint-Antonius-Brecht. Zoals voor elke bedevaartplaats die zichzelf eerbiedigt, is er een vaantje. Het wordt meestal aan het duivenhok gespijkerd of gehangen, om aldus de dieren te behoeden voor ziekte en onkans.

Vanuit West-Vlaanderen zijn stemmen opgegaan om de H. Colomba (Latijn: duif) van Sens, patroonheilige van Deerlijk, als patrones der duivenliefhebbers te suggereren (zie Biekorf, 1956, p. 63). Maar daar heeft men zich in het Antwerpse niet aan gestoord en zo is de H. Catharina Labouré de patrones van de Belgische duivenmelkers aan het worden.

Gebaseerd op Giraldo, W. (1957). Een patrones van de duivenmelkers: de H. Catharina Labouré. *Biekorf 58*, 20-22

Luc Devriese

PENSACIDOSE BIJ KOEIEN

VRAAG

Als praktijkdierenarts Grote Huisdieren lees ik heel regelmatig omtrent pensverzuring bij koeien. Toch ontbreekt het mij aan duidelijke symptomen en diagnostische mogelijkheden om een exacte diagnose te stellen. Daarom deze vraag: hoe diagnosticeer ik met grote waarschijnlijkheid pensverzuring? Hoe neem ik op een praktische manier een pensmonster? Hoe onderzoek ik het monster en interpreteer ik de uitslag?

ANTWOORD

Om pensverzuring te diagnosticeren is een goede integratie van klinische en diagnostische data noodzakelijk. Voor subklinische pensacidose blijft het echter een grote uitdaging om de diagnose met zekerheid te stellen. Het is bovendien belangrijk om anekdotische kennis kritisch te bekijken op basis van de wetenschappelijke literatuur.

Symptomen

Afhankelijk van het opgenomen voeder en hoe lang dit is geleden, en ook afhankelijk van de ernst van de fysiologische verstoringen kunnen de symptomen van pensverzuring verschillend zijn.

Bij subacute pensacidose zijn de dieren nog helder en alert, maar er kan ook voorbijgaande anorexie optreden met symptomen van matige deshydratatie. In deze gevallen neemt de pensmotiliteit af. Soms kan diarree of abdominale pijn optreden (Van Metre et al., 2000; Radostits et al., 2007). Bij melkvee is er vaak een gedaalde melkproductie. In sommige gevallen treedt abortus, doodgeboorte of premature geboorte op. Zelfs abortusstormen worden gelinkt aan subacute pensverzuring (Snyder en Credille, 2017).

Dieren met acute pensverzuring kunnen ernstig verzwakt en atactisch aangetroffen worden. De pens is meestal duidelijk tympanisch en bij auscultatie en stoten in de flank zijn klotsgeluiden te horen. Penscontracties zijn verzwakt tot afwezig (Van Metre et al., 2000). Bij acute pensverzuring vertonen de dieren duidelijke anorexie, samen met profuse, waterige, sterk geurende diarree. De mest is vaak grijs gekleurd en er kunnen onverteerde granen in aanwezig zijn. In sommige gevallen is wat bloed in de mest waar te nemen. In het beginstadium is de rectale temperatuur meestal verhoogd, maar na verloop van tijd ontwikkelen de dieren eerder hypothermie (Cebra et al., 1996; Navarre et al., 2002). Tachycardie en tachypnee zijn soms aanwezig, waarbij de ademhaling vaak oppervlakkig is (Underwood, 1992). Door deshydratatie en hypovolemie liggen bij de meeste gevallen van acute pensacidose de ogen dieper in de oogkassen, de huidplooitest en capillaire vullingstijd zijn verlengd, de vulling van de jugularis vene is vertraagd, de perifere hartslag is verzwakt en de extremiteiten voelen koud aan. Vaak zijn bovendien neurologische afwijkingen te zien, zoals domkolder, blindheid, “head pressing”, opisthotonus en een abnormale gang (Snyder en Credille, 2017).

Bij hyperacute gevallen worden de aangetaste dieren meestal dood aangetroffen met weinig of geen voorafgaande symptomen. In sommige gevallen liggen de dieren neer en zijn comateus met de kop naast de flank. In deze erge gevallen is de prognose zeer slecht. Meestal treedt sterfte dan binnen enkele uren op (Snyder en Credille, 2017).

Diagnose

Verschillende diagnostische testen zijn beschikbaar om bij een dier met pensacidose de diagnose te bevestigen, de ernst van de fysiologische verstoringen in te schatten en de prognose te bepalen. Daarop gebaseerd kan een gepaste therapie ingesteld worden.

Analyse van pensvocht is een van de meest bruikbare methoden om de diagnose van pensverzuring te bevestigen. Een staal van pensvocht kan via ororuminale sondage genomen worden met een sonde met verzwaarde kop of via ruminocentese (percutane aspiratie) (cf. kaderstukje). Hoe sneller de evaluatie van het pensvocht gebeurt, hoe beter het resultaat kan geïnterpreteerd worden. Normaal pensvocht is olijftot bruingroen van kleur en licht visceus met een aromatische geur. Bij patiënten met pensacidose kan de pensinhoud bleekgrijs zijn en een waterige consistentie en rottingsgeur hebben. Dieren die vooral ruwvoeder krijgen, hebben een pens-pH van 6 tot 7, terwijl dieren met veel graan in het rantsoen een pens-pH van 5,5 tot 6 hebben. Zodra de pH lager is dan 5,5 wordt gesproken van acidose. pH-bepaling op pensvocht is niet mogelijk met pH-strips aangezien de kleurstoffen aanwezig in het pensvocht kunnen interfereren met de interpretatie van de kleur van de strips. Een pH-meter is dus aangewezen. Bepaling van de pens-pH is ook bij subklinische pensacidose de meest geschikte test. Toch zijn hieraan enkele beperkingen verbonden. Het is immers zo dat de pH van de pens kan variëren van dag tot dag en ook verschillend kan zijn op andere tijdstippen van de dag. Methoden om de zuurtegraad over een langere periode continu te monitoren via pensboli verdienen in het geval van subklinische pensacidose dan ook de voorkeur, maar deze zijn momenteel in de praktijk meestal nog niet haalbaar (vooral vanwege de prijs en korte levensduur van de batterij). Bij een

eenmalige analyse zou bemonstering moeten gebeuren op het moment dat de laagste pH verwacht wordt. Voor bedrijven waar met aparte voedercomponenten wordt gewerkt, is dit twee tot vier uur na het voederen, terwijl dit bij TMR (total mixed ration)-bedrijven zes tot twaalf uur na het voederen zou zijn (Krause en Oetzel, 2005). Pensvocht genomen via ororuminale sondage kan mogelijk gecontamineerd zijn door speeksel, waardoor de pH bij meting iets hoger kan liggen (0,3 tot 0,5 pH-eenheden) ten opzichte van een monster bekomen via ruminocentese (Garrett et al., 1999; Duffield et al., 2004). Voor de beste resultaten dient de sonde ongeveer 200 cm diep ingebracht te worden zodanig dat het uiteinde van de sonde tot het midden van de pens reikt (Shen et al., 2012).

Minstens twaalf dieren met hetzelfde rantsoen dienen bemonsterd te worden om een probleem in beeld te kunnen brengen. Wanneer de pens-pH $\leq$ 5,5 is bij drie van de twaalf bemonsterde koeien, wordt ervan uitgegaan dat er een groot risico is voor de groep op subklinische pensacidose. Rantsoenaanpassingen zijn in dergelijke gevallen aangewezen.

Via microscopisch onderzoek is bij pensacidose een verminderd aantal protozoa met een verminderde activiteit te zien. Meestal zijn het de grote en middelgrote protozoaspecies die aangetast zijn. De activiteit van de protozoa is temperatuurafhankelijk, dus staaltjes worden het beste bij lichaamstemperatuur onderzocht. Om afkoeling van het monster te voorkomen, verdient werken bij kamertemperatuur de voorkeur en kan men beter plastic in plaats van glazen draagplaatjes gebruiken. De microbiële activiteit van de pens kan ook aan de hand van de methyleenblauwreductie-test geëvalueerd worden. Deze test is een indirecte bepaling van de redoxpotentiaal. Hiervoor dient 6 ml pensvocht gemengd te worden met 0,5 ml van een 0,03% methyleenblauwoplossing. Ontkleuring moet optreden na twee tot zes minuten, maar wanneer dit langer dan tien minuten duurt, wijst het op onvoldoende activiteit (Steen, 2001). In geval van acidose in het pensvocht is met een gramkleuring bovendien een verschuiving van gramnegatieve kiemen naar grampositieve organismen vast te stellen. Volgens Atkinson (2014) is een evaluatie van de protozoaire activiteit meer zinvol dan een eenmalige pH-bepaling. Zoals hoger aangegeven schommelt de pens-pH immers behoorlijk over de tijd, terwijl deze schommelingen bij microbiële activiteit veel minder uitgesproken zijn.

Mestonderzoek om pensgezondheid te evalueren, wordt hier en daar beschreven. Het scoren van mestconsistentie en de verteringsgraad van vezels is een mogelijkheid, maar er is weinig wetenschappelijk bewijs hieromtrent. Volledig overbodig zijn deze analyses zeker niet, maar ze kunnen nooit als enig argument gebruikt worden om de diagnose van subklinische pensacidose te stellen. Hetzelfde geldt nog meer voor het gebruik van de parameter melksamenstelling om pensgezondheid te evalueren (Atkinson, 2014). De bepaling van het vetzuurprofiel in de melk zou hierop mogelijk in de toekomst een uitzondering kunnen vormen. In een studie concludeerden Colman et al. (2010) dat het vetzuurprofiel in de melk van acidotische koeien diagnostisch zou zijn. Verder onderzoek is echter nodig om dit uit te klaren; bovendien zijn commerciële testen hiervoor nog niet echt beschikbaar.

Techniek van ruminocentese

Ruminocentese gebeurt in de linkerflank op het niveau van het kniegewricht, 2 cm caudaal van de laatste rib. De koe moet vaststaan in het voerhek en het beste kan iemand de staart omhoog duwen. De punctieplaats wordt vooraf geschoren en ontsmet. Daarna wordt 2,5 ml van een lokaal anestheticum subcutaan toegediend. Met een naald van 10 cm (16 gauge) wordt vervolgens in een vlotte beweging doorheen de buikwand in de richting van de rechterschouder de pens aangeprikt. Het is belangrijk dit in één beweging te doen om geen scheuren op de wand van de pens te veroorzaken. Daarom mogen ook geen te korte naalden gebruikt worden. De aspiratie van ongeveer 5 ml pensvocht is voldoende om verder onderzoek mogelijk te maken.

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Uit het verleden

PAARD GENEZEN DOOR MAGISCHE BEHANDELING

Als een paard zich pijn had gedaan, moest je gaan naar een straat in Laken. Ik had dat gehoord van mijn nonkel. En het was zover en ik daarheen. Er zat daar wel vijftig man, mensen van alle slag. Tegen de vétérinaire zei ik dat mijn paard zich gekwetst had en hij vroeg: 'Wat voor een kleur heeft dat paard?' Een wit paard', zei ik. Hij begon dan te lezen, altijd maar: 'Wit, zwart: wit, zwaert; wit, zwart.' Tegelijk begon hij een draad wit en zwart te vlechten. Ik moest die in de manen van mijn paard binden en een noveen doen: drie onzevaders of drie weesgegroeten, dat weet ik niet juist meer. En een week daarna weer: 'Wit, zwart; wit, zwart; wit, zwart'. Ik heb weer vijf frank gegeven en een week daarna was mijn paard genezen en ik ben er mee naar Bollebeek (Mollem) gereden.

Uit: Top S., (2005). Paard genezen door magische behandeling. In: *Op Verhaal komen. Vlaams - Brabants sagenboek*, Davidsfonds, Leuven, p. 188.

Gebaseerd op een verhaal verteld door een landbouwer uit Mollem. Opgenomen in de scriptie (Leuven) van Van Wesenbeeck, W., (1969). *Sagenonderzoek in Negentien Gemeenten ten Westen van Brussel*.

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