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INHOUD

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Computed tomography is more and more widely used in exotic mammals, particularly in rabbits. This kind of images is acquired when using latest generation CT machines. As lacrimal disease is a common clinical concern in rabbits, a prospective study was performed on the procedure and normal appearance of helical computed tomographic-dacryocystography in adult pet dwarf rabbits (see pg. 299).

Tekst: Julien Fritz

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Helical computed tomographic-dacryocystography in adult pet dwarf rabbits: procedure and normal appearance

Helicale computertomografie – dacryocystografie bij volwassen dwergkonijnen: procedure en normaal uitzicht

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ABSTRACT

Partial or complete nasolacrimal drainage system (NLDS) occlusion is a common clinical concern in rabbits. It can be assumed that computed tomographic-dacryocystography (CT-DCG) might be an efficient technique in this indication. In this prospective study, the technique of CT-DCG and the appearance of the NLDS in eight healthy rabbits on CT-DCG images are described. The quality of visualization of bony structures adjacent to the NLDS was good on pre-contrast computed tomographic images. The bony lacrimal canal had a smooth contour, a regular diameter, and its mean dimensions are provided. CT-DCG technique was easy to perform and offered a good visualization of the NLDS including anatomical narrowings and bendings. CT-DCG is a minimally invasive and informative technique for evaluating the NLDS in rabbits. Its diagnostic usefulness in exploring nasolacrimal diseases remains to be specified in this species.

SAMENVATTING

Gedeeltelijke of volledige occlusie van het nasolacrimale drainagesysteem (NLDS) is een veelvoorkomend klinisch probleem bij konijnen. Computertomografische dacryocystografie (CT-DCG) kan een efficiënte techniek zijn voor de behandeling van deze indicatie. In deze prospectieve studie worden de CT-DCG-techniek en het uitzicht van de CT-DCG-beelden van het NLDS bij acht gezonde konijnen beschreven. De kwaliteit van de visualisatie van osseuze structuren in de proximiteit van het NLDS was goed op de pre-contrast computertomografische beelden. Het beenderige lacrimale kanaal had een gladde aflijning, een gelijkmatige diameter en de gemiddelde waarden worden in de voorliggende studie weergegeven. De CT-DCG techniek was makkelijk uitvoerbaar en kon het NLDS goed in beeld brengen, inclusief anatomische vernauwingen en bochten. CT-DCH is een minimaal invasieve en informatieve techniek voor de evaluatie van het NLDS bij konijnen. Zijn diagnostische meerwaarde in het onderzoek naar nasolacrimale aandoeningen dient nog verder gespecificeerd te worden bij deze diersoort.

INTRODUCTION

Helical computed tomography is commonly used to assess the bony lacrimal canal and the nasolacrimal drainage system (NLDS) in human medicine (Janssen et al., 2001; Freitag et al., 2002). CT without injection of a contrast medium (non-contrast CT) is useful to evaluate the bony structures surrounding the NLDS while computed tomographic-dacryocystography (CT-DCG) provides CT images after nasolacrimal injection of a iodine-based contrast medium and is well suited for an accurate visualization of the NLDS (Ansari et al., 2005). Magnetic resonance imaging dacryocystography is also used in human patients. This technique has also been experimented in a feasibility study in horse cadavers (Manso-Diaz et al., 2019).

In veterinary medicine, protocols and normal images of CT-DCG have been described in dogs (Rached

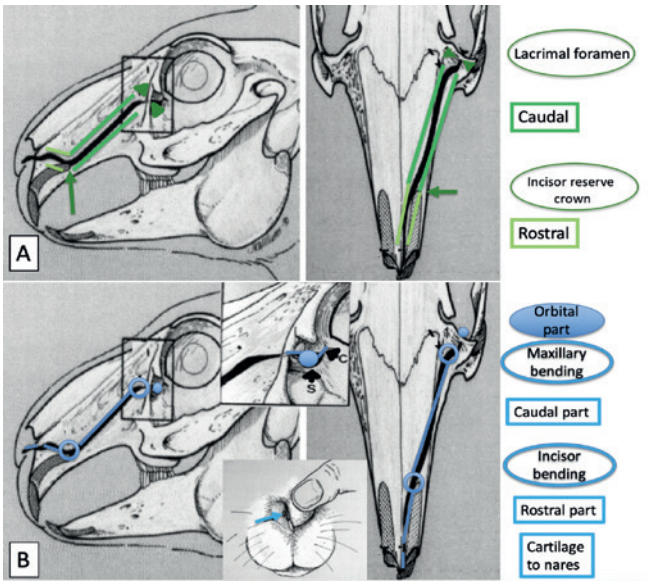

Figure 1. Anatomy of the lacrimal canal and NLDS in rabbits. A. Lateral and dorsal views of the lacrimal canal, showing the lacrimal foramen (arrowheads), the caudal portion of the lacrimal canal (dark green lines), the major incisor reserve crown (dark green arrows), and the rostral portion of the lacrimal canal (light green lines). B. Lateral and dorsal views of the NLDS, with top insert showing a close-up of the orbital segment of the NLDS, and bottom insert showing the nasal meatus (meatus has been magnified for didactic purposes). The top insert shows the canaliculus (C) and the lacrimal sac (S). The two bends of the lacrimal duct, the maxillary and the incisor bend are pointed out by blue circles. The widest segment of the lacrimal duct runs into the caudal/straight segment of the lacrimal canal from the maxillary bend to the incisor bend. The rostral segment of the lacrimal duct extends into the rostral/tortuous portion of the lacrimal canal (tubular segment of the duct) from the incisor bend to the nasal cartilage where the lacrimal canal terminates. The rostral most segment of the lacrimal duct (membranous segment of the duct) exits the lacrimal canal and extends to the nasal meatus (Drawings: Dr Kristina Burling, with courtesy).

et al., 2011) and cats (Nöller et al., 2006; Schlueter et al., 2009). Diagnostic usefulness of CT-DCG in selected patients has been illustrated in the dog, horse and donkey occasionally (Nykamp et al., 2004 ; Cleary et al., 2011). In rabbits, assessment of the NLDS using radiographic dacryocystography has been described (Marini et al., 1996), but to the authors' knowledge, protocols and normal images of CT-DCG have not been published in this species yet.

Computed tomography is more and more widely used in exotic mammals, particularly in pet rabbits (Capello et al., 2008). Latest generation CT machines produce high-resolution images that are particularly well suited to small-sized animals as they offer very thin slices and large image matrices. Additionally, current workstations provide reconstruction capabilities such as multiplanar reconstruction, maximum intensity projection (MIP) reconstruction and three-dimensional (3D) post-processing that tremendously facilitate the assessment of small-sized and complex anatomical regions such as the skull (Fishman et al., 2006).

Ocular discharge secondary to partial or complete NLDS occlusion is a common clinical concern in pet rabbits. An NLDS occlusion is considered in case of difficult or unsuccessful nasolacrimal flushing. A recent endoscopic and histopathologic study in rabbits with experimentally-induced dacryocystitis has shown that chronic inflammation can be a cause of NLDS obstruction (Liu et al., 2018). The authors suspected that, as demonstrated in humans, CT-DCG might be an efficient technique to confirm nasolacrimal occlusion and to identify the underlying cause in companion rabbits (Marini et al., 1996; Freitag et al., 2002; Ansari et al., 2005; Rehorek et al., 2011).

Rabbits are highly susceptible to dental diseases that are considered by many authors as the main cause of nasolacrimal occlusion (Burling et al., 1991; Capello et al., 2008; Florin et al., 2009 ; Van Caelenberg et al., 2011a; Artiles et al., 2020). Published studies on CT in rabbits have been mostly focused on teeth and surrounding bony structures (Van Caelenberg et al., 2010 and 2011a; De Rycke et al., 2012). These studies are limited to non-contrast CT and do not thoroughly describe the examination procedure and the normal appearance of the NLDS.

Burling et al. (1991) have described the normal anatomy of NLDS in rabbits using gross dissection, latex casting, dacryocystorhinography and histology. The lacrimal punctum is the unique caudal aperture of the NLDS and is located at the inner surface of the lower eyelid. From the punctum, the canaliculus runs rostro-medially up to a focal dilation of the NLDS, the lacrimal sac. Rostrally to the sac, the lacrimal duct passes through the lacrimal foramen delineated by the lacrimal and maxillary bones and enters the caudal portion of the lacrimal canal.

The caudal portion of the lacrimal canal is wide and straight. It runs obliquely into the maxillary bone with a caudo-dorso-lateral to rostro-ventro-medial direction. It harbors the widest segment of the lacrimal duct and ends up at the caudal aspect of the major maxillary incisor tooth. The rostral portion of the lacrimal canal is tortuous. It curves medially and ventrally to the major incisor tooth reserve crown, extends rostrally and terminates caudally to the nasal cartilage.

The lacrimal duct exits the rostral portion of the lacrimal canal and passes through the nasal cartilage before terminating at the nasal meatus. The nasal meatus is located a few millimeters caudal to the mucocutaneous junction of the nasal vestibule. The shape of the NLDS and lacrimal canal and their different segments are shown in Figure 1.

The aim of this study was to describe the normal features of the lacrimal canal using non-contrast CT,

to propose a CT-DCG protocol and to describe the normal features of the NLDS on CT-DCG in pet rabbits.

MATERIALS AND METHODS

Animals

This study was a prospective descriptive design. It was conducted from november 2010 to april 2012. The study protocol was approved by the VetAgro Sup Animal Care and Use Committee (Comité d'éthique Jacques Bonnod - Institut d'enseignement supérieur et de recherche en alimentation, santé animale, sciences agronomiques et de l'environnement, Marcy L'Etoile, France). Animal owners provided signed informed consent.

To be enrolled in the study, rabbits had to be owned by a member of ADVETIA clinical staff, be healthy, have a normal clinical examination, undergo a non-contrast CT of the head as a screening procedure aimed at detecting early stage of subclinical dental disease with no anomaly.

The rabbits were sedated with midazolam (0.5 mg/kg, IM) and anesthetized by inhalation of isoflurane (2 to 3%) and oxygen. In all rabbits, CT-DCG was performed following non-contrast CT while prolonging general anesthesia for 10 to 15 minutes.

CT protocol

CT examinations were all performed at ADVETIA Veterinary Referral Hospital, using a spiral four-slices CT scanner (Aquilion Toshiba).

All rabbits underwent a CT examination of the head including a bone algorithm acquisition before and after injection of iodinated contrast medium into the NLDS.

Pre- and post-contrast helical acquisitions were obtained with exposure parameters of 120 kV and 100 mA, a slice thickness of 0.5 mm, a reconstruction interval of 0.3mm. All images were reconstructed using a 512x512 matrix, a slice thickness of 0.5 mm, and both bone and soft tissue algorithms. Only bone-reconstructed images were used in this study.

The rabbits were symmetrically positioned in sternal recumbency on the scanning table for transverse CT images acquisition.

Before the acquisition of CT-DCG images, both right and left lacrimal punctum were cannulated.

The distal third of a 26G plastic irrigating cannula (Portex Irrigating Cannula: external diameter of 0.46 mm, length of 32 mm – Smiths Medical International Ltd), that was previously filled with contrast medium, was inserted through the lacrimal punctum.

Half-strength water-soluble iodinated contrast medium (iohexol - Omnipaque 300 mgI /mL – GE Healthcare SAS France) was gently injected in each NLDS while a mild digital pressure was applied over the rostral aspect of the lower eyelid in order to prevent lacrimal sac overdistension and rupture (Figure 2). The range of injected volume was 0.5 to 1 ml. The injection was stopped once contrast medium was visualized at the nares. The rabbits were scanned immediately after bilateral injection.

All images were evaluated by a board-certified radiologist (HG or YR) to confirm their diagnostic quality.

CT measurements

Stored CT images were collected and evaluated using a workstation equipped with a DICOM viewer (OsiriX v.3.9.4 64-bit for Macintosh) by three observers (JF, HG, YR). A consensus between the observers was reached concerning the quality of the lacrimal canal visualization, the degree of the NLDS filling and the measurements.

The bony lacrimal canal was observed using a bone-window setting (850HU/3500HU - level /width) but the observers were allowed to modify the settings in order to optimize canal wall visualization. The visualization of the wall of the canal was graded as: "bad" (no wall visualized), "poor" (large wall interruptions), "fair" (focal wall interruptions) and "good" (no wall interruption). The presence of gas in any portion of the NLDS was recorded.

Multiplanar reconstruction (MPR) was used to de-

Figure 2. Technique of injection for CT-DCG showing the procedure of catheterization of the lacrimal punctum and injection while a mild digital pressure is applied over the rostral aspect of the lower eyelid in order to prevent lacrimal sac overdistension and rupture.

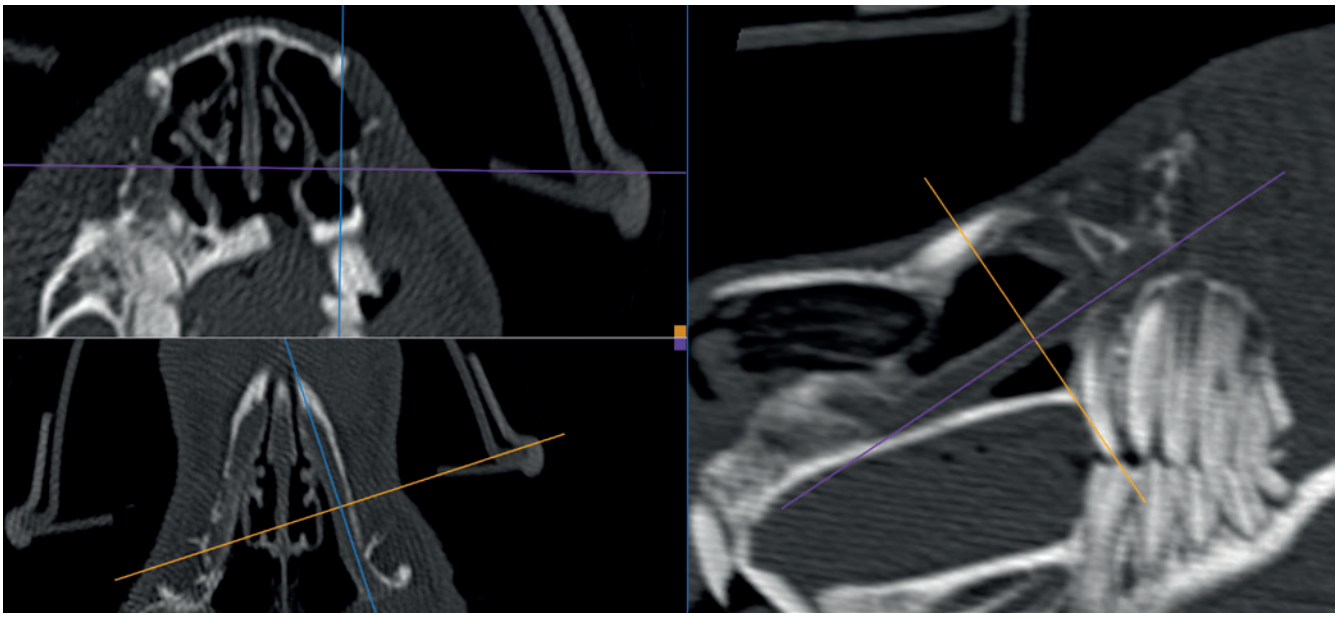

Figure 3. Non contrast CT MPR reconstruction of the left lacrimal canal in a rabbit.

scribe the shape and direction of the lacrimal canal and to obtain measurements (Figure 3).

In all rabbits, right and left lacrimal canals were separately assessed on dedicated reconstructed images as they run in different planes.

Caudal and rostral segments of the lacrimal canal were defined as shown in Figure 1. The caudal segment is the longest and straight segment running from the lacrimal foramen to the incisor reserve crown. The rostral segment is a tortuous segment running between the incisor reserve crown and the nasal cartilage.

MPR oblique sagittal and oblique dorsal planes showing the caudal/straight portion of the lacrimal canal were selected to separately display the right and the left lacrimal canals along their long axis, and to provide accurate transverse views of each canal. Dorso-ventral (DV) and latero-lateral (LL) inner diameters were measured at the rostral aspect, mid-length and caudal aspect of the caudal/straight portion of each lacrimal canal on transverse reconstructed images of the head. The length of the caudal/straight portion of the lacrimal canal was also recorded, using oblique sagittal reconstructed images of each canal.

The angle between the caudal/straight portion of the lacrimal canal and the hard palate was also measured (Figure 4).

Inner diameters (DV and LL) of the rostral/tortuous portion of the lacrimal canal (at its caudal aspect, mid-length and rostral aspect) were measured on the same transverse MPR images for both sides as the right and left rostral portions run parallel to each other.

Window level /width of 1500HU/5000 HU were used to assess the contrast medium distribution in the NLDS and to measure the lacrimal duct diameter. The observers were allowed to modify the window settings for optimization.

The filling of each segment of the NLDS with the contrast medium was graded using the four-point scale as previously proposed in dogs (Rached et al., 2011): grade 0 = no contrast medium visualized into the NLDS; grade 1 = contrast medium barely visible, limiting assessment of the ductal lumen; grade 2 = duct clearly visualized with sufficient amount of contrast medium, focal filling defect is possible (gas bubble); grade 3 = duct fully visualized with no filling defect.

The NLDS was divided into six segments defined as follows: A. orbital segment with an attempt to differentiate the canaliculus, the lacrimal sac and the duct into the lacrimal foramen, B. caudal maxillary bend (narrowing and bending of the duct into the maxillary bone), C. straight segment (duct into the caudal/

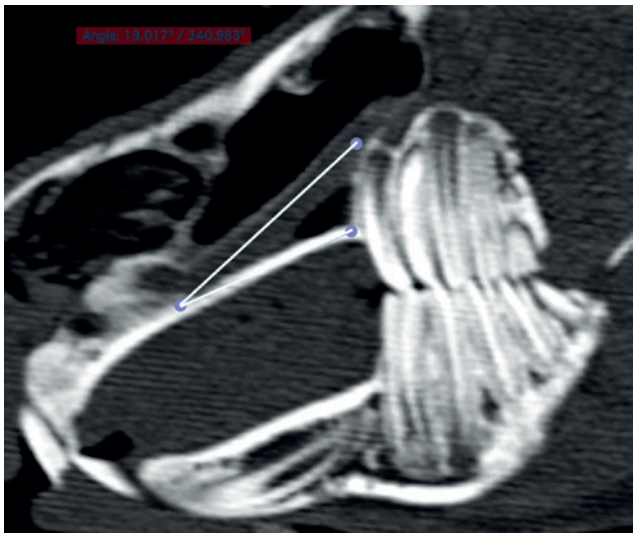

Figure 4. Measurement of the angle between the caudal/straight portion of the lacrimal canal and the hard palate using non contrast CT.

straight portion of the lacrimal canal), D. rostral incisor bend (narrowing and bending of the duct medial to the tip of the reserve crown of the major incisor tooth), E. rostral tubular segment (duct into the rostral/tortuous portion of the lacrimal canal), F. rostral membranous segment (duct rostral to the lacrimal canal extending in the submucosal tissues and emerging in the nasal cavity caudal to the nostrils) (Figure 5) .

Three-dimensional maximum-intensity-projection (MIP) reconstructions were generated from CT-DCG images to provide an overview of the contrast filled NLDS. MPR images were obtained to measure the diameters of the canaliculus, the lacrimal sac and the different segments of the duct (Figure 6). Planes orientation was modified as required in order to obtain accurate transverse view of each segment of the duct for measurements.

The following measurements of the contrast medium-filled NLDS were obtained: maximum diameters of the canaliculus, lacrimal sac and duct into the foramen (segment A); minimum diameter of the caudal maxillary bend of the duct (segment B); DV and LL diameters of the straight segment of the duct at its caudal aspect, mid-length and rostral aspect (segment C); minimum diameter of the rostral incisor bend of the duct (segment D); DV and LL diameters of the rostral tubular segment of the duct (segment E); maximum diameter of the rostral membranous segment of the duct (segment F). The length of the caudal/straight portion of the NLDS (segment C) was recorded on CT-DCG images as the distance between the sites of measurement of the rostral and caudal diameters.

The appearance of the mucosal surface was recorded as smooth or irregular.

Data presentation and statistical analysis

The dimensions of the lacrimal canals and the contrast medium-filled NLDS are presented as mean values and standard deviation in Tables 1 and 2. Spearman's tests were obtained in order to evaluate a potential correlation between dimensions of NLDS and rabbit's weight and age.

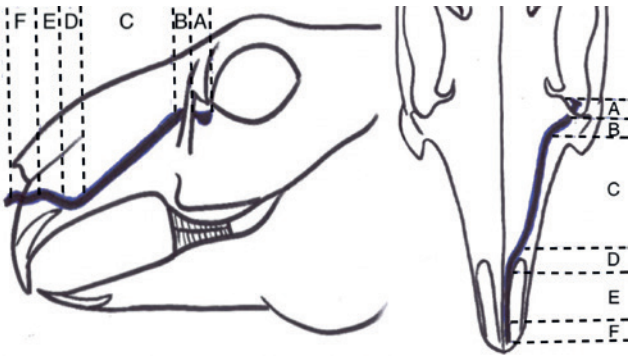

Figure 5. Diagram of the rabbit NLDS showing the six segments studied. A. Orbital segment (canaliculus, lacrimal sac and duct into the foramen). B. Caudal maxillary bend. C. Straight segment in the caudal/straight portion of the lacrimal canal. D. Rostral incisor bend. E. Rostral tubular segment in the rostral/tortuous portion of the lacrimal canal. F. Rostral membranous segment.

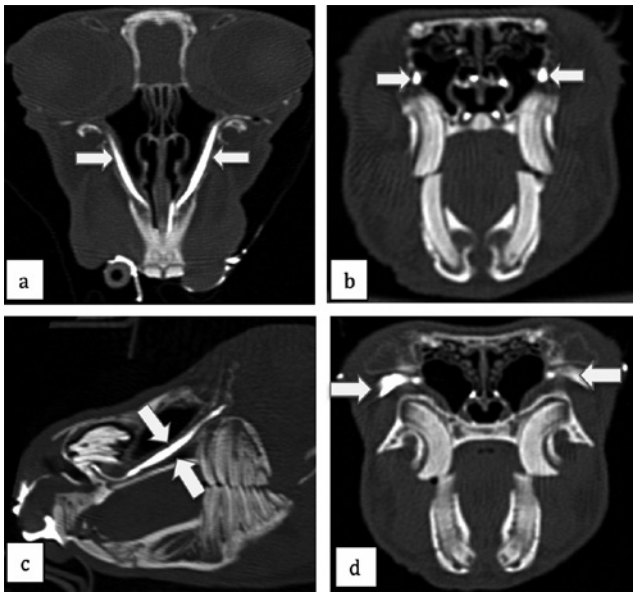

Figure 6. MPR reconstruction of contrast filled NLDS (white arrows) of a rabbit. A. Dorsal oblique plane providing a dorsal view of the straight segments of the right and left NLDS (segments C). B. Transverse view of the straight segment of the right and left NLDS at the level of the first jugal tooth (segments C). C. Oblique parasagittal plane providing a sagittal view of the left NLDS (segment C). D. Transverse view of the head at the level of the second maxillary jugal teeth showing both lacrimal sacs (incompletely visualized) and both ducts as they enter the lacrimal foramen (segment A).

RESULTS

Eight rabbits with normal incisor teeth, jugal teeth and bony structures of the head on non-contrast CT images were selected for the study and provided 16 lacrimal apparatus to be assessed using CT-DCG. They were all dwarf rabbits with an age ranging from two to six years (mean age 2.9 +/- 1.4 years) and a weight ranging from 1.5 to 3 kg (mean 2.2 +/- 0.5 kg). There were four males and four females.

Non-contrast CT: lacrimal canal

Visualization

Visualization of the caudal portion of the lacrimal canal was fair or good in all rabbits (16/16 canals).

The rostral portion of the lacrimal canal was well or fairly visualized in 14/16 canals. Visualization was poor in 2/16 canals (both in the same rabbit), preventing measurements.

Table 1. Measurements of the caudal and rostral segments of the lacrimal canal (mean ± SD).

	Caudal straight segment		Rostral tortuous segment	
Length (mm)	16.5 ± 1.6			
Angle with hard palate (°)	23.6 ± 2.9			
Diameter DV (mm) and LL (mm)	DV	LL	DV	DL
°caudal aspect	1.4 ± 0.3	1.6 ± 0.2	1.6 ± 0.4	1.4 ± 0.4
°middle-length	1.7 ± 0.2	1.5 ± 0.2	1.5 ± 0.3	1.3 ± 0.3
°rostral aspect	2.1 ± 0.3	1.8 ± 0.4	1.7 ± 0.4	1.4 ± 0.4

Presence of gas

Gas was observed in 4/16 NLDS. It was present in both the lacrimal sac and the caudal segment of the duct in 2/4, in the caudal segment alone in 1/4, and in both the caudal segment and the rostral segment 1/4.

Shape

The caudal portion of 13/16 lacrimal canals appeared straight with smooth borders. In six rabbits, both right and left canals had a straight caudal segment. In one rabbit, the caudal segment of the right canal was straight, and the caudal segment of the left canal was mildly curved medially. In one rabbit, the caudal segments of both canals were mildly curved medially. The rostral portion of all lacrimal canals appeared mildly tortuous with smooth borders.

Measurements

The measurements of the caudal and the cranial portions of the lacrimal canal are presented in Table 1.

CT-Dacryocystography: nasolacrimal drainage system

Shape

All six anatomical segments of the NLDS previously described were identified on CT-DCG images in all rabbits. The shape of the different segments of the NLDS (lacrimal sac, caudal maxillary bend, caudal straight segment, rostral incisor bend and rostral tortuous segment of the duct) was easily recognized and appeared symmetrical in all rabbits (16 NLDS). The mucosal surface of the duct was smooth in all NLDS (16/16).

Visualization

The visualization of the orbital segment of the NLDS (segment A) was considered poor (grade 0 or 1) and did not allow measurements when the cannula was left in place (7NLDS/16). Conversely, the visualization was considered good (grade 2 or 3) and allowed measurements when the cannula had been removed just before scanning (9/16).

The visualization of the caudal maxillary bend, straight segment, rostral incisor bend, rostral tubular segment and rostral membranous segment of the lacrimal duct (segments B to F) was good (grade 2 or 3) in all NLDS (16/16), allowing accurate measurements.

Presence of gas

A mild amount of gas was observed in 4/16 NLDS. Gas was located in the lacrimal sac in all 4 NLDS and was also noticed in the straight segment of the duct in 1/4 NLDS.

Measurements

The dimensions of the different segments of the contrast filled NLDS are presented in Table 2. There was no significant correlation between any of the measurements and the age or weight of the rabbits.

DISCUSSION

This study shows that non-contrast CT with bone algorithm acquisition enables the visualization of the lacrimal canal in rabbits. It has regular smooth borders along its caudal straight segment and its rostral mildly tortuous segment and its dimensions are presented. Gas can be present in the canal of ocular disease-free rabbits. In this study, it is also shown that the CT-dacryocystography technique used, including bilateral half- strength water-soluble iodinated contrast medium through a previously flushed plastic cannula and immediate CT with bone algorithm acquisition, enables a good visualization of all of the NLDS segments when the cannula is removed before scanning. All of the segments were easily recognized, symmetrical, with smooth mucosal surface, and its dimensions are provided. In previous studies, the CT-anatomy of a rabbit's head and the viewing of the lacrimal canal using CT (Van Calenberg et al., 2010), micro-computed tomography (De Rycke et al., 2012)

and low-field magnetic resonance (Van Caelenberg et al., 2011b) have been described. In the present study, non-contrast CT identified very little to no variation in lacrimal canal shape, course and dimensions between rabbits. To the authors' knowledge, this is the first study to describe the CT-anatomy of the lacrimal canal and provide measurement references in healthy dwarf rabbits.

The course and the shape of the lacrimal duct have already been described in two studies: one using dacryocystorhinography, latex casting and gross dissection (Burling et al., 1991), and the other one using dacryocystorhinography and gross dissection (Marini et al., 1996). Using CT-DCG, in the present study, a shape and a course of le NLDS were observed that were similar to those previously described, including a tubular portion with anatomical narrowings and bendings, and a caudal straight segment (segment C) exhibiting a progressive enlargement from caudal to cranial up to the incisor bending (segment D). The diameter of the lacrimal duct measured in the present study was quite different from the duct diameter published in the two studies mentioned above. The differences in duct diameter are probably due to a range of factors including the used imaging modality (radiography versus CT in the present study), the selected populations (New Zealand white rabbits versus smaller dwarf rabbits in the present study) and the provided diameters (unique mean diameter versus separate DV and LL dimensions in the present study).

The length of the straight portion of the NLDS (segment C) measured in the present study is smaller than the length published in Burling's study that is 26.4+/-2.3mm (Burling et al., 1991). This discrepancy might be due to the differences in size and head conformity of the rabbits selected in both studies, and to the methods of measurement that were also different. In the present study, direct linear measures were taken of the duct length on reconstructed CT images while Burling et al. used a trigonometric method for calculating the length of the duct from linear measures taken on radiographs (dacryocystorhinography). The radiography might also have induced an imprecision in measurement due to the magnification inherent to this imaging technique.

In the present study, lacrimal canal dimensions did not vary significantly with age and weight. The small size of the studied population and the narrow range of weight in the selected rabbits prevent to make any assumption from this observation. As discussed above, it seems intuitive that the dimensions, especially the length of the lacrimal canal and of the lacrimal duct may vary according to breed, head conformity and the size of the rabbits. The impact of parameters, such as breed, ear-carriage type and weight, on lacrimal canal dimensions should be assessed in a larger group of healthy rabbits of different breeds and a wider range of weight.

The catheterization of the lacrimal punctum with a cannula is an essential step to perform a CT-DCG. Unsuccessful complete cannulating of the NLDS with suture material in rabbits with nasolacrimal obstruc-

Table 2. Dimensions of the different segments of the contrast filled NLDS (values in mm ± SD).

Segment A		
Orbital segment		
Canaliculus: maximum diameter		0.7 ± 0.1
Lacrimal sac: maximum diameter		2.6 ± 0.5
Intra-foraminal duct: maximum diameter		1.6 ± 0.3
Segment B		
Caudal maxillary narrowing (duct bend): minimum diameter		0.6 ± 0.1
Segment C		
Straight segment of the duct:		
Length		16.5 ± 1.6
DV and LL diameters	DV	LL
- caudal aspect	1.2 ± 0.3	0.9 ± 0.2
- mid-length	1.5 ± 0.3	1.2 ± 0.3
- rostral aspect	1.7 ± 0.5	1.4 ± 0.3
Segment D		
Rostral incisor narrowing (duct bend): minimum diameter		0.5 ± 0.1
Segment E		
Rostral tubular segment (duct): DV and LL diameters	DV	LL
	1.1 ± 0.3	0.7 ± 0.2
Segment F		
Rostral membranous segment (duct): maximum diameter		0.8 ± 0.1

tion or in normal rabbits has been reported (Burling et al., 1991). It has been suggested that the inability to successfully cannulate the entire NLDS could be due to some features of the anatomy of the NLDS in the rabbit and particularly narrowing and bending sites. In the present study (on healthy living rabbits), catheterization of the lacrimal punctum was felt to be an easy and fast procedure and no failure was encountered. Additionally, flushing the NLDS while filling it with iodinated contrast medium was easily performed in all 16 NLDS and was considered to indicate a proper patency of NLDS. The authors therefore consider that the failure to inject iodinated contrast medium into the NLDS should lead to a suspicion of NLDS obstruction.

In previously published studies, it has been suggested to inject 1ml of iodinated contrast medium for an optimal visualization of the NLDS in pet rabbits on radiographic dacryocystography (Marini et al., 1996). In the present study, 0.5 to 1ml of half-strength water-soluble iodinated contrast medium with 300 mgI/mL as initial concentration was confirmed to provide an adequate filling and a proper visualization of the entire NLDS in CT-DCG. Some authors suggest to inject a smaller volume of contrast medium (0.3 to 0.5ml) in order to prevent inhalation and contrast medium leakage and superimposition over anatomical structures on radiographic images (Jekl, 2016). With a maximum volume of 1 ml of contrast medium injected in the NLDS, a visual check of contrast leakage at the nares, and the use of a cross-sectional modality (CT), excess amount of contrast medium out of the NLDS was not a concern in the present study. In order to obtain images of good diagnostic quality, injection of air into the NLDS should be avoided by filling the cannula with contrast medium before catheterization. The cannula should be removed before CT-DCG acquisition is performed to allow better visualization of the orbital segment of the NLDS.

In the present study, NLDS in healthy rabbits appears on CT-DCG as a continuous contrast-filled tubular structure with high variability in diameter through its entire length that exhibits two sharp bends with abrupt narrowing corresponding to the caudal maxillary bend and the rostral incisor bend of the lacrimal duct. CT-DCG allows accurate measurements of the NLDS diameter in healthy rabbits. It has provided anatomical features of the normal NLDS similar to those published in an anatomical study using injection of latex in the NLDS of rabbit cadavers (Burling et al., 1991).

Filling of both right and left NLDS with contrast medium was performed in all rabbits and was followed by a unique acquisition of CT-DCG images providing bilateral CT-DCG. No difference in the degree of filling was observed between the right and the left NLDS, indicating that the side (right versus left) being catheterized and injected first should not have any influence on image quality. Considering that catheterization and filling of the NLDS are easy to perform and not much time-consuming, it might be worth performing bilateral CT-DCG with a unique post-injection acquisition, especially when the clinical signs are unilateral as the sound side may provide normal reference images.

The present study was performed on clinically healthy adult rabbits aged between two and six years. A younger population of rabbits could have been selected for a study describing normal features. However, most of the rabbits presented at the authors' institution with clinical signs related to NLDS diseases, are adults. The authors found it thus more relevant to select adult rather than young rabbits for describing the normal appearance of the NLDS. A larger population could also have been selected, particularly for providing reference values of the NLDS in healthy rabbits. However, owners rarely ask for a screening head CT of their healthy rabbit. The owners of the rabbits selected for the present study were all members of the Exotics Department Team of ADVETIA Veterinary Hospital and were concerned about subclinical dental disease of their own rabbit. For ethical reasons, it was not possible to select a larger population of healthy rabbits.

Although normal CT-images were mandatory for inclusion in the study, mild increased density of the dental structures was allowed, as far as no tooth reverse overgrowth or tooth deformity was observed, and the hypodense 'apex' was still visualized. The oldest rabbit (six years old) was the only rabbit presenting a faintly increased density of the reserve crown with a reduced size of the hypodense apex in most jugal teeth. Neither signs of tooth reverse overgrowth or deformity, nor changes in peridental bony structures were observed leading the authors to conclude to non-pathological age-related changes and to select this rabbit for the study.

Computed tomography is an accurate modality to evaluate small-sized mineral-density structures. Therefore, CT and CT-DCG were expected to provide a detailed depiction of the thin-walled lacrimal canal and the contrast medium-filled NLDS in rabbits. A potential limit of the present study could have been an insufficient spatial resolution of the acquisition system considering the very small size of nasolacrimal structures in pet rabbits. Cone-beam CT is an imaging modality of choice for dental imaging in rabbits due to its high spatial resolution (Riggs et al., 2016 and 2017) and may also be helpful for the evaluation of the osseous structures of the lacrimal canal; however, to the authors' knowledge, it has not been evaluated and a major limitation of this imaging modality would be its poor contrast resolution for the evaluation of the soft tissue structures of the lacrimal duct.

Another limitation of the present descriptive study is that windowing and leveling changes made by the reader could slightly influence the measurements, especially the diameter and short axis dimensions. The

authors chose to inject half-strength contrast medium solution in the NLDS for the description of normal features with this technique, but the dimensions might as well have slightly been influenced by contrast concentration.

In a very recent retrospective study about CT findings of dental disease in domestic rabbits, the authors have reported 17% (17 of 100 rabbits) with 'apparent' lacrimal canal lysis or obstruction in the studied population of rabbits affected with dental disease (Artiles et al., 2020), but the criteria of obstruction, as CT-dacryocystography was not performed, is not mentioned in this study. In rabbits with an obstructive NLDS disease, CT-DCG might help to identify the site and the cause of obstruction, such as external compression (pathological backward overgrowth, bony lesion, extranasolacrymal mass), mural lesion (developmental, hyperplastic or fibrotic duct stenosis) and intraluminal lesion (intra-ductal pus or dacryolith). In a recent study, CT-DCG performed in rabbits with experimentally induced dacryocystitis exhibited abnormal findings, such as incomplete filling of the NLDS and dilation of the NLDS segment proximal to the site of stenosis (Hou et al., 2017).

CONCLUSION

In the present study, it is indicated that CT-DCG can be easily performed in pet rabbits. A feasible and simple protocol is proposed and the normal features of the lacrimal canal and nasolacrimal drainage system in healthy dwarf rabbits are described.

As a next step, CT-DCG should be performed on rabbits with clinical signs of NLDS obstruction in order to assess its accuracy in discriminating the different causes of nasolacrimal obstruction.

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Uit het verleden

Paardenkerkhof van Childerik in Doornik

De Salische Franken, een tak van de Frankische Germanen, veroverden bij de val van het Romeinse rijk onze streken en vestigden hun hoofdplaats in Doornik. Hun koning Childerik werd er begraven met onvoorstelbare rijkdom. Daarvan getuigen niet enkel de zogenaamde ‘schat van Childerik’, maar ook een massagraf met niet minder dan 21 paardenskeletten. C14-dateringen lieten toe dit ‘paardenkerkhof’ te situeren in de tijd van Childerik. De dieren waren begraven in drie holten in de rots gehouwen ongeveer twintig meter van het graf van de koning zelf.

Een dergelijk paardenkerkhof was uitzonderlijk bij de westelijke Germanen. Het getuigt van het aanzien, dat zowel paarden als Childerik zelf genoten. Zijn zoon Clovis (Chlodovich, Ludovik, Lodewijk, Ludwig, Louis) zou het kleine rijk uitbreiden over heel Frankrijk (het rijk van de Franken) tot in het noorden van Spanje en over een groot gedeelte van het huidige Duitsland.

Een opstelling in het archeologisch museum van Doornik geeft daar een beeld van weer.

Met dank aan Sabine Lauwers en Luc Van Damme

The ADKAR® change management model for farmer profiling with regard to antimicrobial stewardship in livestock production

Het ADKAR®-verandermodel voor typering van veehouders met betrekking tot verantwoord antibioticagebruik bij landbouwhuisdieren

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ABSTRACT

Antimicrobial stewardship in veterinary practice and animal production is important from a One Health perspective. The ADKAR® change management model is a well-known strategy to implement behavioral change in people and small businesses. The objective of this study was to adapt the existing ADKAR® change management model to enable herd veterinarians to profile farmers with regard to antimicrobial stewardship. Therefore, an antimicrobial stewardship related scoring scale was defined. Subsequently, ADKAR® profiles of 26 poultry and 28 pig farmers from Belgium and the Netherlands were determined. For 57% of the farmers, perception and/or motivation were expected to limit successful change. For 70% of the farmers, knowledge and for 52% of the farmers, a lack of ability were the limiting factor. The ADKAR® model proved useful for identifying the key elements that prevent successful behavioral change in farmers to reduce the use of antibiotics in farm animals.

SAMENVATTING

Het "One Health"-principe indachtig is het belangrijk om zo min mogelijk antibiotica te gebruiken bij landbouwhuisdieren. Het ADKAR®-verandermodel is een bekende methode om gedragsverandering bij mensen als ook in het bedrijfsleven te implementeren. Het doel van deze studie was het bestaande ADKAR®-verandermodel toepasbaar te maken voor bedrijfsdierenartsen in de veehouderij, zodat zij veehouders kunnen typeren met betrekking tot het verantwoord gebruik van antibiotica bij hun dieren. Nadat er op basis van de ADKAR®-systematiek een vijfpuntscoresysteem was gedefinieerd, werden het ADKAR®-profiel bepaald van 26 pluimvee- en 28 varkenshouders uit België en Nederland. Zevenenvijftig procent van de veehouders bleek onvoldoende bewust van de risico's en/of onvoldoende gemotiveerd om het antibioticumgebruik te verminderen. Bij 70% van de veehouders bleek kennis en bij 52% het gebrek aan mogelijkheden om te veranderen de beperkende factor. Het ADKAR®-model bleek nuttig om in te schatten welke factoren veehouders verhinderen om het gebruik van antibiotica bij landbouwhuisdieren te verminderen.

INTRODUCTION

Antimicrobial stewardship in livestock production is pre-eminently the domain of the herd veterinarian. Prudent use of antibiotics prevents residues in animal products and limits the selection of antimicrobial resistance (AMR) in micro-organisms (Dorado-Garcia et al., 2016; Dyar et al., 2017). In livestock production, veterinary advice aims at improving animal health and production and reducing risk factors for disease (Jansen et al., 2010). Subsequently, the farmer is responsible for implementing this advice in farm management and working procedures. In some cases, farmers do not comply with the given advice (Rojo-Gimeno et al., 2016; Postma et al., 2017). Reasons for non-compliance with advice may be versatile, but sociological factors, like perception of the problem or motivation for change can be the underlying cause (Jansen et al., 2010; Kristensen et al., 2011). Therefore, to improve the uptake of veterinary advice in general and regarding prudent use of antibiotics specific, the veterinarian needs to understand and address these sociological factors in his or her professional relationship with the farmer. To help herd veterinarians assessing perception and motivation as a starting point for a change process towards the reduction of antibiotic use (ABU) and AMR, practical tools are needed. To support veterinarians in understanding sociological factors of change management in farm processes and in providing advice in a more effective manner, utilization of established change management models for individuals and organizations could be useful. ADKAR® is an acronym for Awareness, Desire, Knowledge, Ability and Reinforcement, identifying the five elements of behavioral change. The ADKAR® change model has already been successfully enrolled in corporate business as well as in human medicine (Hiatt, 2006; Shepherd et al., 2014; Wong et al., 2019). The objective of this study was to adapt the ADKAR® change model to antimicrobial stewardship in livestock farming by presenting scoring criteria per ADKAR® element. Secondly, a pilot project was run with the model to profile pig and poultry farmers with a higher than average ABU in Belgium and the Netherlands.

MATERIALS AND METHODS

The ADKAR® change model

ADKAR® is an acronym for Awareness, Desire, Knowledge, Ability and Reinforcement. To achieve behavioral change, all five elements of the ADKAR® model must be addressed sufficiently and in the right sequence (Hiatt, 2006). The authors transformed the five-point scale -modified from Hiatt - of each element of the ADKAR® model to be used in assessing the farmer's attitude towards prudent use of antibiotics in livestock. On this scale, a score of 1 represented the lowest score and 5 represented the highest score. A farmer's ADKAR® profile was determined by the individual scores for each element. According to Hiatt (2006), each element with score 3 or less blocks change.

ADKAR® profiling of farmers

In 2017, the i-4-1-Health cross-border project was established in the Dutch-Belgian border region, focused on infection control in human and veterinary health care settings and AMR reduction. In this project, pig and poultry farmers in the Dutch-Belgian border region were recruited for an eighteen-month coaching program focused on infection prevention and ABU reduction. The inclusion criteria for farmers in the study were having either a sow herd with weaned pigs or a broiler farm, both with ABU higher than the national benchmark presented by 'Antimicrobial Consumption and Resistance in Animals' (AMCRA) in Belgium and the 'Autoriteit Diergeneesmiddelen' in the Netherlands. Farmers were invited to participate voluntary in the project via newsletters of farmers organizations. To establish a starting point for coaching of the farmer, the ADKAR® profiles were determined of the 54 participating farmers, 15 poultry farmers and 14 pig farmers in Belgium and 11 poultry farmers and 14 pig farmers in the Netherlands. After a herd visit, during which the use of antibiotics in the farm was discussed and a biosecurity audit was performed, the veterinary coach (one per country) scored each farmer on the first four elements (A-D-K-A) according to the criteria in Table 1. The 'Reinforcement' component was not scored at this moment as no reduction measures had been proposed or implemented previously at that time. The profiling skills of the veterinary coaches were first trained by a professional training institute in a one-day training on change management.

Data analyses

The results of A-D-K-A scores were compared between species (pig and poultry farms) and country (Belgium and the Netherlands) by means of a linear mixed model (SPSS 27.0 IBM).

RESULTS

The criteria for the ADKAR® profile were set, discussed and finalized after discussions in a stakeholder-workshop with a group of 26 herd veterinarians of the swine and poultry farms enrolled in the i-4-1-Health project (Table 1). In the livestock -antimicrobial stewardship- adapted farmer's ADKAR® profile, Awareness represented the understanding of the farmer that prudent use and ABU reduction in livestock production is important, as ABU in livestock is a risk for the selection and transmission of antibiotic

Table 1. Definition of the scoring elements of the livestock antimicrobial stewardship adapted model, with a five-point scale according to Hiatt's ADKAR® change management model.

ADKAR	Description building block (element)	Score	Explanation score
A (wareness)	Represents the awareness that AMU in livestock production should be reduced while this is a risk for introduction of antimicrobial resistant bacteria in animals and men.	1	Farmer missed all information regarding AMU and AMR. Is not aware there are reduction goals, nor is aware AMU is a risk for AMR.
		2	Farmer is aware of the recommendation to reduce AMR, but is completely denying the problems related to AMR.
		3	Farmer is aware that AMR should be reduced, but contests the role AMU in livestock. Mentions the role of AMU in human medicine and/or the role of AMU in dogs and cats.
		4	Farmer is aware that AMU should be reduced, and accepts the reduction goals.
		5	Farmer is fully aware that AMU should be reduced, as he accepts the risks and opportunities for livestock production. He takes responsibility for the AMU in the farm and embraces the reduction goals for the farm.
D (esire)	Represents the personification of the awareness. "Does the farmer himself want to reduce AMU in his farm?"	1	Farmer states: "This is not my problem. It does not concern me".
		2	Farmer will reduce, but is not the first adaptor. Farmer states: "my "neighbour" should also reduce".
		3	Farmer wants to reduce, but slowly. The goal is not to reach the lowest use possible, just enough is also OK.
		4	Farmers goal is to reach the lowest AMU possible, with equal costs.
		5	Farmers goal is to reach the lowest AMU possible, even if there are considerable costs related to the reduction.
K (nowledge)	Represents the knowledge and skills of the farmer to implement measures to improve health and to reduce the need for antimicrobial treatment.	1	It is not clear what is causing the health problems in the farm. It is not possible to draw up an action plan. The farmer and his network really do not know where to start.
		2	Low or inaccurate knowledge, experience or skills which are needed for the execution of the action plan are available for the farmer. Or, the underlying cause of the problem is not yet identified.
		3	Information on health problem(s) is available for the farmer, action plan can be drawn up.
		4	Information is available, but some discussion about the implementation. Support for the farm and farmer is needed to implement change.
		5	Information is available, Action plan is accepted and knowledge and skills are sufficiently available at level of farmer, veterinarian and personnel of the farm.
A (bility)	Represents the implementation phase of the change. Will or is the farmer implementing changes in management or working methods. (Topics for change are: feed, management, climate, working methods etcetera).	1	Farmers sees only obstacles for every proposed change and therefore does not implement any.
		2	Farmer implements a limited number of changes which are easy to achieve. The selection is not made upon expected effect, but on requested input.
		3	Some changes are accepted and implemented in the farm. Or implementation is saved for the rebuilding or new building.
		4	Farmer is implementing systematically. But money or time are hampering some changes.
		5	Farmer is investing time, money and/or effort to implement changes.
R (einforcement)	Represents the sustainability of change. To sustain change an active positive reinforcement is necessary	1	Farmer has negative experiences with reducing AMU.
		2	Farmer received or receives negative feedback from the personal environment with regard to reducing AMU.
		3	AMU reduction is not perceived to have a positive or negative effect
		4	Successful reduction has led to more job satisfaction and better herd performance
		5	Successful reduction has led to better economic performance or a higher personal status.

resistant bacteria in animals and humans. The willingness to reduce ABU was determined in the element Desire. Therefore, Desire reflected the internalization of Awareness and thus represented the intrinsic motivation of the farmer to change. Knowledge represented the cognitive knowledge of tools and farm management procedures to improve animal health and to reduce risks for disease, e.g. biosecurity and infection prevention measures, and thus to reduce the need for ABU. Ability represented the availability of

resources to implement change, such as time, manpower to do the work, money to invest and specific skills and competences of the stockmen in the herd. Reinforcement represented the sustainability of the established change. Important factors for reinforcement were negative and positive feedback of change on productivity, profitability and impact of change on the farmer. In short, in the farmer profiles Awareness and Desire reflected the perception and motivation part of ABU reduction, whereas Knowledge and Ability reflected the possibilities and opportunity to accomplish ABU reduction. Reinforcement represented the expected sustainability or persistence of the change (Table 1). The average farmers' ADKAR® antimicrobial stewardship profile scores, scored in a five-point scoring scale (1 represents the lowest score and 5 represents the highest score) for the combined elements Awareness (A), Desire (D), Knowledge (K) and Ability (A), were 3.0 for the Belgian farmers and 3.8 for the Dutch farmers. Average scores for pig farmers were 3.3 versus 3.4 for poultry farmers. None of the average scores for the separate elements Awareness, Desire, Knowledge or Ability differed significantly between the type of animals (pigs or poultry). Scores for Awareness ($p<0.001$), Desire ($p<0.05$) and Ability ($p<0.001$) were significantly higher in the

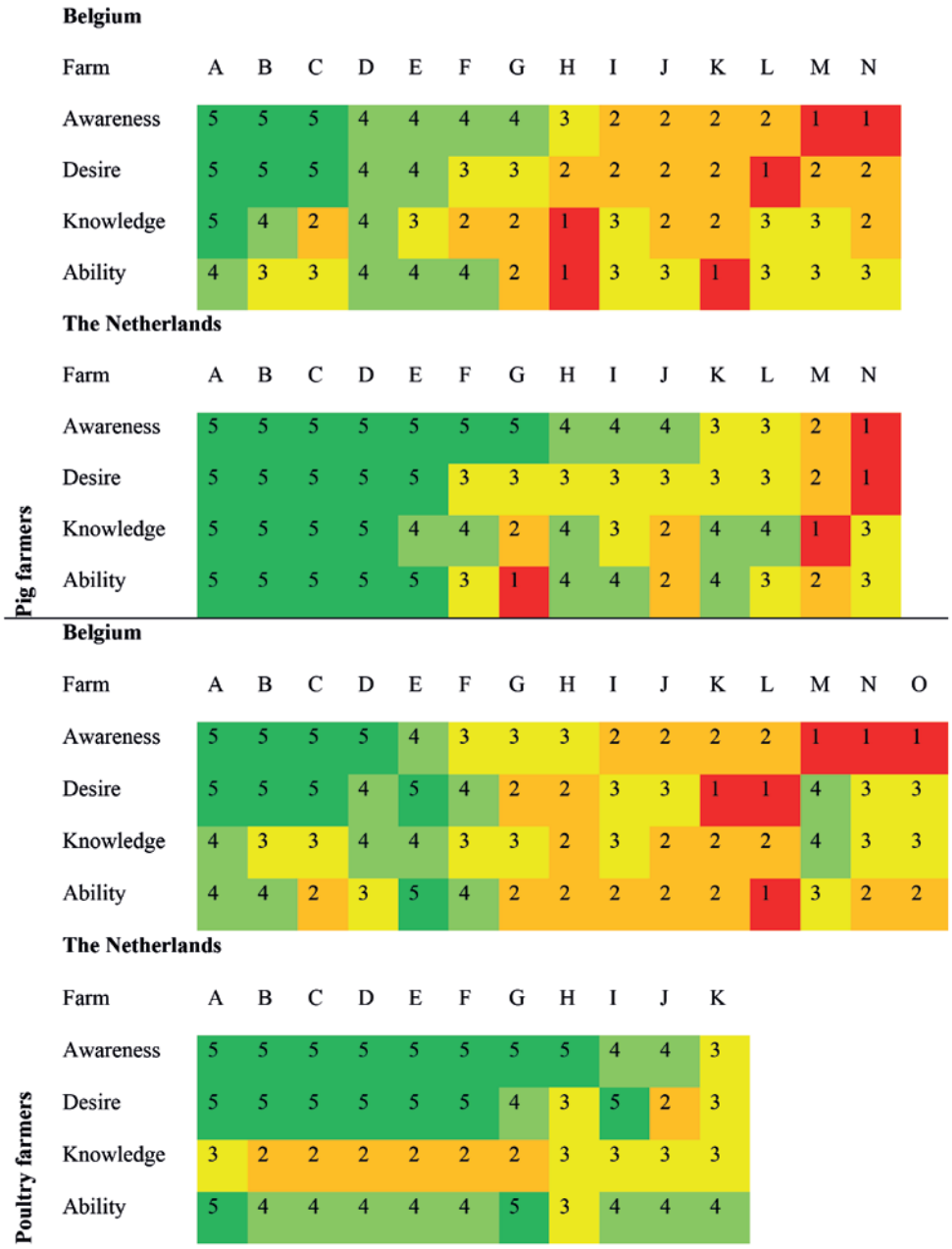

Figure 1. Individual ADKAR® profiles of pig and poultry farmers for the elements Awareness, Desire, Knowledge and Ability, stratified per species and country (n=54). A score of 1 represented the lowest score and 5 represented the highest score. As described by Hiatt (2006), if an element scored 1, 2 or 3, this element had to be considered to block the change of farm processes by the farmer towards AMU reduction.

Netherlands than in Belgium. Overall, 31% (17/54) of the farmers scored 3 or less on all first four ADKAR® elements, which means these farmers lack Awareness, Desire, Knowledge and Ability (Figure 1). For Awareness, 40% (22/54) of the farmers scored 3 or less, for Desire 54% (29/54) of the farmers scored 3 or less. Thirty-one of 54 (57%) farmers scored 3 or less for Awareness and/or Desire. Of these 31 farmers, twenty farmers scored 3 or less on Awareness as well as on Desire. For Knowledge, 70% (38/54) of the farmers scored 3 or less and for Ability 52% (28/54) of the farmers scored 3 or less. The 38 farmers with a low score on Knowledge were eleven Dutch poultry farmers (100%, 11/11), eleven Belgian poultry farmers (73%, 11/15), five Dutch pig farmers (38%, 5/14) and eleven Belgian pig farmers (79%, 11/14). Forty-five out of 54 farmers (83%) scored 3 or less for at least one of the four elements. Nine farmers scored 4 or 5 on each of the four criteria, being two Belgian pig farmers (14%, 2/14), five Dutch pig farmers (36%, 5/14) and two Belgian poultry farmers (13%, 2/15). Four Dutch pig farmers scored 5 for all four elements.

DISCUSSION

In this paper, the ADKAR® change management model as a starting point for veterinary coaching towards antimicrobial stewardship is described. Using farmer specific ADKAR® profiles, 54 pig and poultry farmers from Belgium and the Netherlands were scored. In 45 of these 54 farmers, elements which may hamper reduction were identified. In the other nine farmers, blockages were not found and the coaching could immediately focus on providing veterinary technical advice to improve health and to reduce ABU. Besides the lack of knowledge and ability, the authors also found that in 57% (31/54) of the farmers, perception and/or motivation (Awareness and Desire) needed to be properly addressed and improved by the coaches before focusing on technical veterinary advice on farm management could be successful. The lack of perception and motivation found in this study could be a possible explanation why farmers do not implement advice given towards a more health-orientated strategy of herd management, although previous studies have shown that these health-orientated strategies can be successful (Rojo-Gimeno et al., 2016; Collineau et al., 2017; Postma et al., 2017). This result is very relevant for the herd veterinarian in his or her everyday veterinary practice; especially in these cases where the veterinarian wants to implement a major change in farm management or when a farmer is not implementing given advice. In this study, the importance of addressing awareness and desire is emphasized as the lack of one or both of them may hamper the adoption of the provided veterinary advice, especially in topics not directly related to improvement of production or reduction of costs. Therefore, support is needed to help (pig and poultry) veterinarians assess and address lack of perception and motivation of farmers in general and related to antimicrobial stewardship specifically.

Experiences in human health care show that changes for better health care and antimicrobial stewardship are more effectively implemented when tailor-made and multifaceted: addressing patient, professional, organization of care, in a cultural and socio-economic context (Wensing et al., 1998; Grol and Grimshaw, 2003; Hulscher et al., 2010). In dairy farming, a multifaceted approach to implement change has already been successfully applied using the RESET model. RESET summarizes different models from the literature in five important incentives for change: Regulation, Education, Social pressure, Economics and Tools (Lam et al., 2017). In contrast to RESET, which focusses on interventions to increase perception and/or motivation, ADKAR® helps the veterinarian to identify limitations of farmers in the change process towards reduction of ABU, among which perception and motivation.

In the present study, the factor Knowledge also proved to be an important limiting factor for successful ABU reduction. Remarkable is the lack of Knowledge scored in all participating Dutch poultry farmers with higher than average ABU, of which eight of the eleven farmers scored 4 or 5 for the other A-D-K-A elements, suggesting Knowledge was the only limiting factor. The main reason for the low scores for Knowledge in this group proved the inadequate knowledge regarding raising poor quality newly hatched broiler chicks. All participating Dutch farmers struggled with poor quality of these hatchlings at the time of the assessment. Although in general, Knowledge seems a relatively easy-to-correct element for the veterinarian, this specific health issue seems to form a knowledge gap for poultry farmers towards low and prudent ABU.

The observed difference in the scores of the Dutch and Belgium farmers in this study should be interpreted with care because of the unknown interobserver agreement and different starting dates of the national ABU reduction program in livestock (2011 in the Netherlands versus 2016 in Belgium). With regard to external validity, the authors want to stress that due to the recruitment strategy, inclusion criteria and the small number of participating farmers, the results of the profiles cannot be simply extrapolated to the Belgian nor the Dutch pig and poultry farmer in general. Nonetheless, the significant higher scores for three out of the four A-D-K-A elements in the Netherlands might suggest that farmers in the Netherlands are already better informed and convinced about the need and possibility to reduce the use of antimicrobials, something, which is also translated in the European antimicrobial usage data in animals (ESVAC 2018) where the antimicrobial use in the Netherlands is shown to be substantially lower than in Belgium.

Further studies on a larger scale should be conducted to confirm this observation and demonstrate the link between ADKAR® profiling scores and the true antimicrobial use at farm or country level, and to study the effectiveness of intervention strategies like the RESET methodology to identify which of the RESET interventions (Regulation, Education, Social pressure, Economics and Tools) is successful in which farmer profile.

CONCLUSIONS

The ADKAR® model proved useful for identifying farmer specific key elements that prevented successful behavioral change in the farmers to reduce the use of antibiotics in their farms. The insight in the ADKAR® farmer profile and thus the limiting factor for change should help the veterinarian to design a tailored intervention and/or improvement plan for each specific farmer.

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Iatrogenic hypothyroidism in a hyperthyroid cat treated with ^{131}I

Iatrogene hypothyroïdie bij een hyperthyroïde kat behandeld met ^{131}I

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ABSTRACT

A thirteen-year-old, male, castrated, non-azotemic European Shorthair was presented for treatment of hyperthyroidism. Thyroid scintigraphy using Tc^{99m} showed bilaterally enlarged thyroid glands with an increased thyroid to salivary (T/S) ratio. The cat was treated with an intravenous injection of 4.84 mCi (179MBa) ^{131}I. One year later, the cat showed clinical deterioration, including lethargy, weight loss and a louder heart murmur; iatrogenic hypothyroidism was diagnosed. Concurrently, renal parameters were elevated compared to the pre-treatment values. Supplementation with levothyroxine was started. Four months later, the cat was euthyroid and improved creatinine values were noted. In this case report, the diagnosis and management of iatrogenic hypothyroidism in cats and the interplay with renal function are described. An algorithm with recommendations regarding diagnosis, monitoring and treatment of these cats is presented.

SAMENVATTING

Een mannelijke, gecastreerde, niet-azotemische Europese korthaar van dertien jaar werd aangeboden voor de behandeling van hyperthyroïdie. Schildklierscintigrafie met Tc^{99m} onthulde bilateraal vergrote schildklieren met een toegenomen "thyroid to salivary (T/S) ratio". De kat werd behandeld met 4,84mCi (179Mba) ^{131}I. Een jaar later vertoonde de kat klinische achteruitgang, zoals lethargie, gewichtsverlies en een luidere hartruis; iatrogene hypothyroïdie werd gediagnosticeerd. Tegelijkertijd waren de nierwaarden gestegen ten opzichte van voor de behandeling. Een levothyroxinetherapie werd opgestart. Vier maanden later was de kat opnieuw euthyroïde en was de serum-creatininewaarde opnieuw gedaald. In deze casuïstiek worden de diagnostiek en het management beschreven van katten met iatrogene hypothyroïdie en het effect van iatrogene hypothyroïdie op de nierfunctie wordt nader toegelicht. Bijkomend wordt een algoritme opgesteld met aanbevelingen voor diagnostiek, monitoring en behandeling van hyperthyroïde katten die behandeld worden met radioactief jodium.

INTRODUCTION

Hyperthyroidism is the most common endocrine disorder in elderly cats (Peterson and Ward, 2007). This disease can be treated pharmacologically, surgically, dietary or with radioiodine therapy (Daminet et al., 2014) (Table 1).

Treatment with ^{131}I is considered the gold standard in many cats as it is curative and safe. The administered radioiodine is taken up by the thyroid glands and the emitted β radiation destroys the nearby abnormal thyroid tissue. The remaining thyroid tissue is mostly atrophied, hence will be spared of most of the radiation (Daminet et al., 2014; Daminet and Hill, 2017). ^{131}I treatment has a 90-95% success rate (Volckaert et al., 2016). The major disadvantages of ^{131}I therapy are the need for a licenced, specialized center, the use of radioactive products, the need for hospitalization and

Table 1. Summary of considerations regarding treatment options for feline hyperthyroidism. (Adapted from Daminet, 2019).

	Anti-thyroid drugs	Restricted iodine diet	Thyroidectomy	^{131}I
Initial cost	+	+	+++	+++
Long-term cost	++	++	+	+
Pre-requisites	None	Strict administration of this diet needs to be possible	Skilled surgeon	Licenced facility
Ease of use for the owner	Easy to moderate	Easy	Easy after hospitalization	Radioprotective measures needed, afterwards easy
Need for anesthesia	No	No	Always	Sometimes
Time to euthyroid	2-4 weeks	6-8 weeks	1-2 days	Days to weeks
Hospitalization	No	No	1-3 days	3 days to 4 weeks
Potential limitation	Mild side-effects common	Low palatability in some cats	Recurrence after unilateral/ incomplete thyroidectomy	Iatrogenic hypothyroidism or persistent hyperthyroidism possible

the possible development of iatrogenic hypothyroidism (Table 1).

Iatrogenic hypothyroidism has been reported in 3-79% of all ^{131}I-treated cats, although in most studies, a prevalence of iatrogenic hypothyroidism of approximately 10% has been shown (Meric and Rubin, 1990; Boag et al., 2007; Lucy et al., 2017; Peterson et al., 2017).

Cats with iatrogenic hypothyroidism rarely show obvious clinical signs. Lethargy, weight gain and anorexia are the most commonly noted. However, these clinical signs are difficult to recognize by the owner since resolution of hyperthyroidism should lead to improvement of the typical clinical signs of hyperthyroidism, including hyperactivity, polyphagia and weight loss. The combination of these vague clinical signs and the possible influence of concurrent illness on total thyroxine (TT4) concentrations (euthyroid sick syndrome) makes diagnosing iatrogenic hypothyroidism after ^{131}I treatment challenging (Peterson, 2016).

Once iatrogenic hypothyroidism has been diagnosed, the veterinarian can decide to either start treating the cat with thyroid hormone supplementation or continue monitoring. This decision can be difficult to make and depends on a combination of the presence or absence of clinical signs, the time of diagnosis and the renal values of the cat (Williams et al., 2014).

Once treatment with levothyroxine has been initiated, frequent re-evaluations should take place to evaluate the clinical response and to measure post-treatment TT4 for therapeutic monitoring. This is important to avoid under- or overdosing of levothyroxine, with persistent hypothyroidism or iatrogenic hyperthyroidism as a consequence. Therapeutic monitoring of total T4 concentrations should take place in every cat treated with levothyroxine, because many factors, including gastrointestinal disease and concurrent administrations of other medications, influence the absorption of levothyroxine (Daminet, 2016).

In this case report, the recommended protocols of diagnosing, treating and re-evaluating iatrogenic hypothyroid cats after radioiodine treatment are described.

CASE DESCRIPTION

A thirteen-year-old, male, castrated European Shorthair was presented at the referring veterinarian with chronic weight loss, polyphagia and being quieter. The diagnosis of hyperthyroidism was confirmed based on increased serum TT4 concentration. Treatment with methimazole was instituted, and the cat was referred to the Small Animal Clinic of the Faculty of Veterinary Medicine, Ghent University, for further work-up and possibly radioiodine treatment. Blood examination (including free T4 (fT4), TT4, hematology and biochemistry), urinalysis, thoracic X-rays, echocardiography and an abdominal ultrasound were

Figure 1. Pertechnetate scan in a hyperthyroid cat prior to ^{131}I treatment.

performed as part of an extensive work-up for a prospective study.

Initial physical examination revealed typical clinical features of hyperthyroidism including muscle atrophy, palpation of a goitre and a systolic heart murmur (Table 2).

Initial blood examination, including biochemistry, hematology and thyroid profile, confirmed the diagnosis of hyperthyroidism with severely increased TT4 and fT4 values and a low normal TSH concentration (Table 3).

Urinalysis prior to the ^{131}I treatment revealed concentrated urine with mild proteinuria (Table 4). Chest X-rays revealed mild cardiomegaly. Echocardiography visualized mild hypertrophy of the left ventricle with borderline left atrium dilation and dynamic right ventricular outflow tract obstruction (DRVOTO). Abdominal ultrasound did not reveal any significant abnormalities.

Thyroid scintigraphy with Tc-99m showed bilateral enlarged thyroid glands with an increased tracer uptake (Figure 1). The left thyroid gland was displaced caudally. The thyroid-to-salivary (T/S) ratio was increased in both left (10/1) and right (3.9/1) thyroid glands.

The results obtained from bloodwork and pertechnetate scan in this cat were consistent with the confirmed hyperthyroidism. Treatment with an intravenous injection of 4.84mCi (179MBq) ^{131}I was instituted. This dose was based on the T/S ratio obtained via scintigraphy, TT4 value and clinical signs (Volckaert et al., 2016). The cat was hospitalized for five days due to radioprotective precautions.

One month post-treatment control included urinalysis, abdominal ultrasound and echocardiography. Significant clinical improvement was noticed (Table 2). Bloodwork revealed TT4 and fT4 serum concentrations that had dropped below the reference interval and serum TSH concentration well within the upper range of the reference interval. The serum creatinine and urea concentrations were still within reference interval, but had significantly increased compared to the pre-treatment serum concentrations (Table 3). Urinalysis revealed decreased urine concentration compared to the baseline values (Table 4).

The patient returned for a control visit one year after treatment. Blood and urine examinations, scintigraphy, abdominal ultrasound and echocardiography were performed. Significant clinical deterioration including weight loss, mild muscle wastage and a louder heart murmur was noticed and the cat had become significantly more quiet at home (Table 2). The patient was also hypertensive with a mean blood pressure of 205mmHg (measured with Doppler ultrasonography).

Control bloodwork showed low normal serum TT4 and decreased serum fT4 values, combined with a high serum TSH concentration (Table 3). Concurrent renal disease was also suspected based on an increase in serum values of SDMA, urea and creatinine compared to pre-treatment and significant proteinuria (Tables 3 and 4). The rest of the performed bloodwork, including full hematology, biochemistry and electrolytes, was unremarkable.

Both thyroid glands could no longer be clearly

Table 2. Findings on physical examination in a hyperthyroid cat prior to ^{131}I, and at one and twelve months later (T0, T1 and T12, respectively).

	T0	T1	T12
Muscle condition score	Moderate muscle atrophy	No muscle atrophy	Mild muscle atrophy
Weight (kg)	2.8	3.6	3.02
Thyroid gland palpation*	5/6 L - 0/6 R	4/6 L - 0/6 R	0/6 L – 0/6 R
Body condition score (BCS)	4/9	5/9	4/9
Heart murmur	3/6	1-2/6	3/6

*Thyroid gland scoring system: score 0 = non-palpable thyroid gland; score 1 =1-3 mm; score 2 = 3-5 mm; score 3 = 5-8 mm; score 4 = 8-12mm; score 5 = 12-25mm and score 6 = ≥25 mm (Boretti et al., 2005; Paepe et al., 2008).

delineated due to decreased radionuclide uptake on thyroid scintigraphy (Figure 2). The T/S ratio was estimated to be 0.78/1, but was hard to determine due to the limited visibility of the thyroid glands on scintigraphy.

Based on the low normal TT4, low fT4, increased TSH concentration and decreased radionuclide uptake on scintigraphy, this cat was diagnosed with iatrogenic hypothyroidism one year after ^{131}I treatment.

Echocardiography showed a mild, focal thickening of the septum with very mild dilation of the left atrium. These findings did not have any clinically relevance at that time point. Abdominal ultrasound didn't show any significant abnormalities.

Supplementation with levothyroxine (Leventa MSD animal health, United Kingdom; 0,075ml = 0.075mg twice daily) was prescribed.

Control bloodwork was performed four months after the initiation of thyroxine supplementation. The serum TT4 concentration was within normal limits and the urea and creatinine values were mildly decreased. The cat had improved clinically. However, the serum SDMA concentrations were further increased (Table 3).

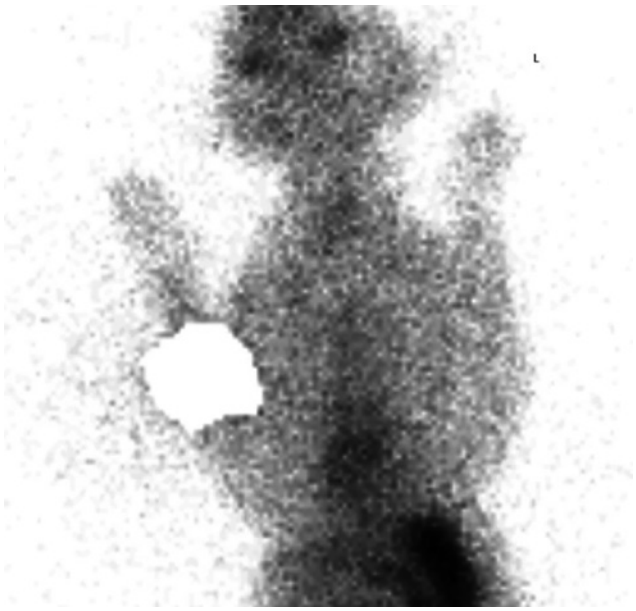

Figure 2. Pertechnetate scan in an iatrogenic hypothyroid cat, twelve months after ^{131}I treatment to treat hyperthyroidism.

DISCUSSION

Although radioiodine treatment is the preferred treatment option for hyperthyroidism, in some cats, it also involves disadvantages and complications. One of the main complications is the potential development of iatrogenic hypothyroidism (Meric and Rubin, 1990; Boag et al., 2007; Lucy et al., 2017; Peterson et al. 2017).

One of the predisposing factors for ^{131}I therapy induced iatrogenic hypothyroidism is the usage of (too) high doses of radioiodine. The standard dose for treating hyperthyroidism in cats with ^{131}I used to be approximately 4-5 mCi, but recently, it has been shown that with a dose of 2mCi, most cats with mild-to-moderate hyperthyroidism without an increased frequency of persistent hyperthyroidism three and six

Table 3. Findings on serum biochemistry in a hyperthyroid cat prior to ^{131}I, and at one, twelve and sixteen months after treatment (T0, T1, T12 and T16, respectively).

	Results T0	Results T1	Results T12	Results T16	Reference interval
Total T4	>167.3	9	15.4	33.54	10-60 nmol/l
Free T4 (Immulite)	77.2	4.5	4.2		9.0-33.5 pmol/l
Free T4 (Equilibrium dialysis)	108.7	5	11.2		9.0-33.5 pmol/l
TSH	0.03	0.11	0.58		0.03-0.3 ng/ml *
Urea	6.2	11.7	12.4	10.16	5.7-13.5 nmol/l
Creatinine	48	103	123	106.1	<168 µmol/l
SDMA	9	9	17	20	0-14 µg/dl
Bilirubin	1.7	2,7	2.7		<6.8 µmol/l
ALT	277	150	129		<175 U/l
ALP	155	46	36		<73 U/l
GGT	<1	1	1		<5 U/l
AST	131	60	48		<71 U/l
Total Calcium	2.3	2.5	2.3		2,2-2,9 mmol/L
Total Protein	59		78		59-87 g/l
Albumin	25		30		27-44 g/l
Globulin	34		48		29-54 g/l

SDMA = Symmetric dimethylarginine; ALT = Alanine aminotransferase; ALP = Alkaline phosphatase; GGT = gamma glutamyl transferase; AST = aspartate aminotransferase
*Based on Lucy et al. (2017).

Table 4. Findings on urinalysis in a hyperthyroid cat prior to ^{131}I, and at one and twelve months after treatment (T0, T1 and T12, respectively).

	Result T0	Result T1	Result T12	Reference interval
Specific gravity	>1.050	1.015	1.020	
UPC	0.6	0.2	2.9	0-0.4

UPC= urine protein:creatinine ratio

months post therapy can be successfully treated (Lucy et al., 2017). Although the dosage currently used in the clinic at the Faculty of Veterinary Medicine (Ghent University) has been adapted to 2mCi, the cat in the present case, treated in November 2016, still received 4.84 mCi ^{131}I, which is nowadays considered to be a high dose. Another predisposing factor for iatrogenic hypothyroidism is the presence of bilateral ^{131}I uptake on thyroid scintigraphy. These cats, including the cat in the present case report, are twice as likely to develop iatrogenic hypothyroidism compared to cats with only unilateral thyroid pertechnetate uptake (Nykamp et al., 2005).

Follow-up of the clinical status and bloodwork after radioiodine treatment is of great importance to be able to make an early diagnosis of iatrogenic hypothyroidism. However, a complete work-up for iatrogenic hypothyroidism in non-azotemic cats is not recommended until three to six months post-treatment, because cats treated with ^{131}I can become transient hypothyroid. These cats regain a normal thyroid function within three to six months after treatment (Peterson et al., 2017). Considering that the cat in the present case was hypothyroid one year post-treatment, chances were very low that he would become spontaneously euthyroid again. Azotemic cats that have been treated with ^{131}I, should be monitored more closely, because treatment for hyperthyroidism, development of iatrogenic hypothyroidism and potential concurrent CKD all decrease the glomerular filtration rate (GFR). Iatrogenic hypothyroidism should be diagnosed and treated as early as possible, since it improves renal function and provides a longer median survival time in these cats (Williams et al., 2014; Peterson et al., 2017).

The diagnosis of iatrogenic hypothyroidism is currently based on the measurement of serum TT4 and TSH concentrations. Elderly, euthyroid cats often have low TT4 concentrations due to concurrent non-thyroid illnesses (Peterson, 2016). Free T4 concentrations are less influenced by non-thyroidal illness and are therefore considered to be more sensitive for diagnosing iatrogenic hypothyroidism. However, the assays available for the measurement of fT4 concentrations have a variable performance and accuracy. Determining fT4 after equilibrium dialysis (FT4ED) is considered the gold standard. However, FT4ED is an expensive and time-consuming test that is not widely available. In a recent study by Stammeleer et al. (2018), the measurement of fT4 via a chemiluminiscent enzyme immunoassay (FT4CEIA) has shown correlating, but consistently lower results compared to FT4ED. However, approximately 75% of iatrogenic hypothyroid cats have fT4 values within reference interval (Peterson et al., 2017). Therefore, it is recommended to interpret serum TT4 results in combination with serum TSH concentrations (Peterson et al., 2017).

Currently, there is no feline TSH assay available. The immulite canine TSH assay (Diagnostic Products Corporation, DPC), a chemiluminescent immunometric assay, is being used to determine TSH concentrations in cats because of the cross-reaction of this assay with feline TSH. Multiple studies have been performed to determine a reference interval (RI) for TSH in healthy, elderly cats. The suggested upper reference limit of feline TSH determined by the cTSH assay varies between 0.15 ng/ml and 0.3 ng/ml (Wakeling, 2010; Williams et al., 2010; Lucy et al., 2017). However, the choice between these two cut-off values will have a major influence on the amount of iatrogenic hypothyroid cats that will be diagnosed after ^{131}I treatment. This emphasizes the need of further studies to determine the most appropriate cut-off value for this assay in order to be able to diagnose iatrogenic hypothyroidism in cats. In addition, a recent study from Stammeleer et al. (2019) showed that approximately 27% of cats with high cTSH concentrations are euthyroid based on scintigraphy. In that study, TT4 concentrations were within the reference interval in all of these euthyroid cats with increased cTSH concentrations, which shows us the need to interpret TT4 and TSH concentrations together and with caution.

A TSH stimulation test using recombinant human TSH (rhTSH) can also be used to assess the thyroid function. Serum samples should be collected before and 6 hours after IV administration of the exogenous rhTSH. A study by Van Hoek et al. (2010) showed that iatrogenic hypothyroid cats do not show a significant increase in TT4 after the administration of rhTSH, in contrast to healthy cats or cats with non-thyroid illness. One of the main disadvantages of this test is the high cost for a vial of rhTSH. However, once opened, these vials can be stored for four to eight weeks without any loss of biological activity, making it possible to perform multiple TSH stimulation tests with one vial (De Roover et al., 2006).

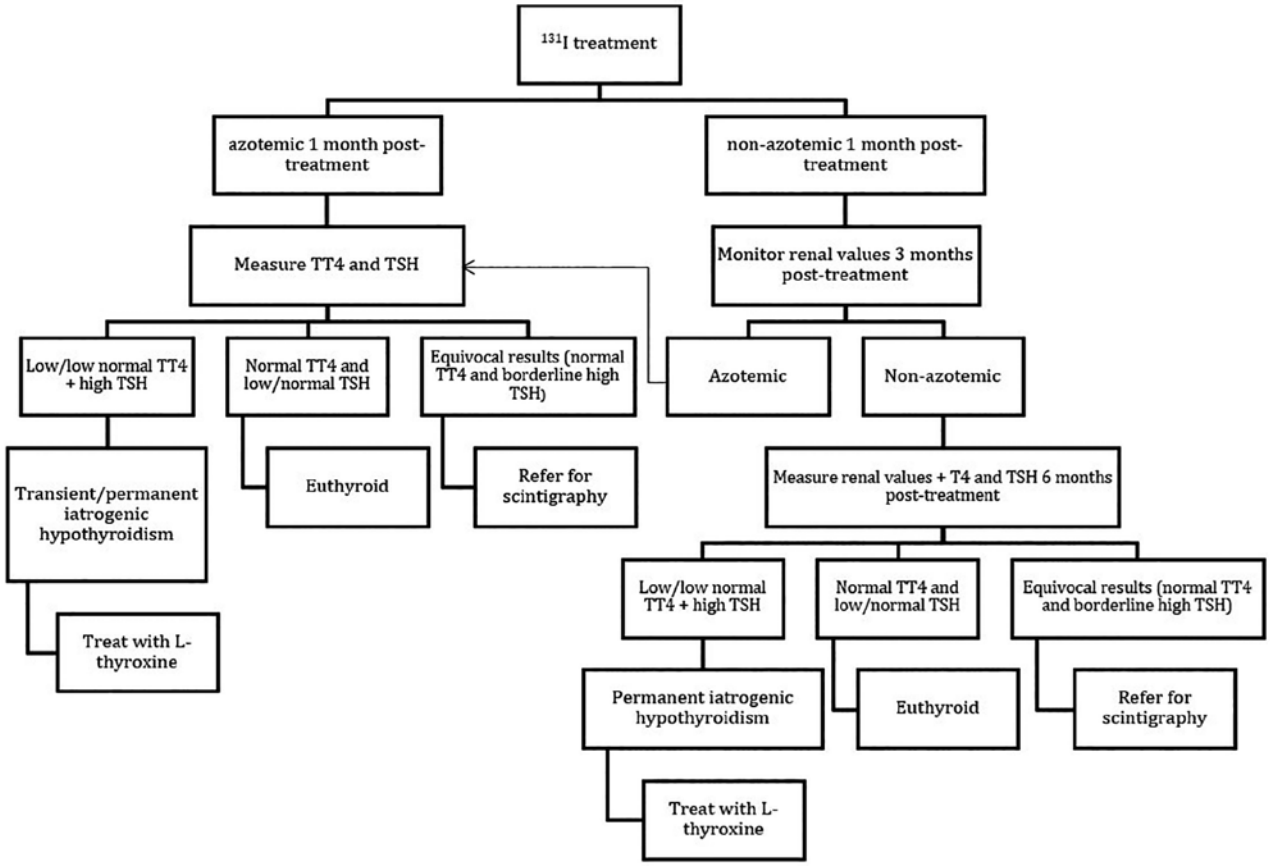

Figure 3. Algorithm with recommendations regarding the diagnosis, monitoring and treatment for cats treated with ^{131}I (Adapted from Daminet S., 2016).

Thyroid scintigraphy is considered the best imaging modality to diagnose iatrogenic hypothyroidism in cats that had received radioiodine treatment. Cats with true iatrogenic hypothyroidism show decreased or absent radionuclide uptake on scintigraphy, whereas cats with low T4 concentrations due to non-thyroidal illness have a normal radionuclide uptake (Peterson, 2013). However, cats that become hypothyroid after methimazole treatment should not be diagnosed with scintigraphy since methimazole can potentially increase the radionuclide uptake, causing a falsely increased T/S ratio (Peterson and Broome, 2015). Unfortunately, thyroid scintigraphy is currently not routinely available for most veterinarians (Peterson, 2013).

Whether or not iatrogenic hypothyroidism should be treated immediately or monitored depends on the renal function of the cat. When bloodwork does not reveal azotemia, the iatrogenic hypothyroidism should not be treated within the first six months after ^{131}I treatment. However, if the cat is azotemic, treatment with thyroid hormone supplementation has been shown to improve renal function and increase the median survival time in these cases (Williams et al., 2014; Vaske et al., 2015; Peterson et al, 2017). An algorithm with recommendations regarding diagnosis, monitoring and treatment of hyperthyroid cats treated with ^{131}I is presented in Figure 3.

Unfortunately, currently, there is no reliable test available that predicts post-treatment azotemia in hyperthyroid cats. Serum creatinine (sCr) concentrations are influenced by body muscle mass, which is usually decreased in hyperthyroid cats. Increased glomerular filtration rate (GFR) in hyperthyroid cats also leads to decreased sCr concentrations, which makes it a less optimal indicator for azotemia in these cats. Direct measurement of GFR is not frequently used in clinical settings because the process is time-demanding and potentially stressful for the cats. Serum symmetric dimethylarginine (SDMA), a byproduct of cellular protein metabolism, is not affected by these extrarenal factors and is therefore suspected to be a better biomarker for the detection of CKD. However, SDMA has a poor sensitivity (33%) to diagnose early kidney disease in hyperthyroid cats (Peterson et al., 2018). In addition, Burresova et al. (2019) showed that cats treated with ^{131}I show a poor correlation between SDMA and GFR.

One month post treatment, the cat in the present case already showed decreased TT4 concentrations with normal TSH concentrations. Treatment with L-thyroxine was not instituted at this point in time because 1. only a short period had elapsed after treatment, which could reflect transient hypothyroidism; 2. the kidney values remained within the reference interval; 3. no obvious clinical signs of hypothyroi-

dism were observed and 4. TSH was not significantly increased.

One year post treatment, the patient was orally administered levothyroxine because of low serum fT4 concentrations, high serum TSH concentration, decreased thyroid visibility on thyroid scintigraphy, increasing kidney values (still within reference interval) and hypertension. At that time point, the cat became lethargic and had mild weight loss (but still a normal body condition score). Lethargy is a common clinical sign in cats with iatrogenic hypothyroidism. Weight loss, however, is unfrequently noticed in hypothyroid cats (Peterson, 2013). Further diagnostic tests were performed in the cat of the present case, including an extensive blood examination, urinalysis, abdominal ultrasound and echocardiography, which didn't reveal other abnormalities besides the mild increase in renal values, proteinuria and hypertension. For this reason, it was recommended to closely follow-up these renal parameters after the initiation of treatment with oral levothyroxine. In addition, the cat showed significant clinical improvement once this treatment was started.

In the present case, the thyroxine and TSH concentrations had not been monitored for six months after treatment, due to a loss of follow-up at that time; otherwise, treatment in this cat might have been initiated sooner.

After starting levothyroxine supplementation, improvement of the mental status and activity level should be noticed within a couple of days. After a couple of weeks, weight loss might be noticed and the hair coat should improve within the first few months. Blood examination should be performed four to eight weeks after the start of the treatment and should include serum urea, creatinine, T4 (TT4 or fT4) and TSH concentrations. Post-treatment blood samples should be collected approximately four hours after the levothyroxine supplementation in order to be able to measure T4 peak serum concentrations. Ideally, T4 concentrations rise and TSH concentrations drop into the reference interval. If these values are not reached, dose adjustment is advised (Daminet, 2016). In the present case, the TT4 concentration increased into the reference interval, renal variables decreased and the cat was clinically stable, hence no dose adjustment was instituted. The serum SDMA concentration in the present case was higher than one year after the ^{131}I treatment. There are currently no studies available in which the correlation of sSDMA and GFR has been examined in iatrogenic hypothyroid cats treated with levothyroxine, which makes the interpretation of this result challenging.

It is important to note that also medical treatment with methimazole can cause iatrogenic hypothyroidism in cats. Between 20 - 40% of cats treated with methimazole become iatrogenic hypothyroid (Aldridge et al., 2015). Many of these cats have TSH concentrations within the reference interval during the first three months of treatment, but iatrogenic hypothyroidism often occurs at a later stage of treatment (Aldridge et al., 2015). Just as in cats treated with ^{131}I, TT4 or fT4 values should always be interpreted in combination with TSH concentrations. This emphasizes the importance of closely monitoring these cats, including regular bloodwork to check T4 and TSH concentrations in cats treated with methimazole. When low/normal low T4 concentrations and high TSH concentrations are found, the methimazole dose should be lowered, even in the absence of clear clinical signs (Aldridge et al., 2015).

CONCLUSION

Diagnosing, monitoring and treating iatrogenic hypothyroidism in cats can be challenging. Making the decision to start thyroid hormone supplementation can be difficult as iatrogenic hypothyroidism can be transient. Currently, thyroid hormone supplementation is always recommended in azotemic cats as iatrogenic hypothyroidism could negatively influence survival rates in these cats (Figure 3).

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Het diergeneesmiddel kan gebruikt worden als onderdeel van een behandelingsstrategie tegen vlooienallergiedermatitis (VAD). Voor de behandeling van infestaties met oormijten (Otodectes cynotis). Voor de behandeling van infecties met intestinale rondwormen (4e stadium larven, immature en volwassen vormen van Toxocara cati) en haakwormen (4e stadium larven, immature en volwassen vormen van Ancylostoma tubaeforme).Indien herhaald toegediend met een interval van 12 weken zorgt het diergeneesmiddel voor ononderbroken preventie van hartwormziekte veroorzaakt door Dirofilaria immitis (zie details in rubriek 4.9 van de SKP). **Contra-indicaties:** Niet gebruiken bij overgevoeligheid voor het werkzame bestanddeel of één van de hulpstoffen. **Bijwerkingen (frequentie en ernst):** Milde en voorbijgaande huidreacties op de toedieningsplek (kaalheid, huidschilfers, roodheid en jeuk) zijn vaak waargenomen in klinische studies. Overige bijwerkingen die in klinische studies kort na toediening soms werden waargenomen zijn: kortademigheid na het likken van de toedieningsplaats, kwijlen, braken, braken met bloed, diarree, sloomheid, koorts, versnelde ademhaling, verwijding van de pupil.Tremoren en anorexie zijn zeer zelden gemeld na gebruik van dit diergeneesmiddel, gebaseerd op postmarketing ervaring van dit diergeneesmiddel (farmacovigilantie). **Dosering en toedieningsweg:** Voor spot-on gebruik. Bravecto Plus spot-on oplossing is verkrijgbaar in 3 pipetsterkten. Hierna wordt de pipetsterkte aangegeven die gebruikt moet worden afhankelijk van het lichaamsgewicht van de kat (overeenstemmend met een dosering van 40-94 mg fluralaner/kg lichaamsgewicht en 2-4,7 mg moxidectine/kg lichaamsgewicht). Gewicht van de kat (kg)/ Pipetsterkte die gebruikt moet worden: 1,2 - 2,8/ 112,5 mg + 5,6 mg; >2,8 - 6,25/ 250 mg + 12,5 mg; >6,25 - 12,5/ 500 mg + 25 mg. Binnen iedere gewichtsklasse dient de gehele inhoud van de pipet te worden gebruikt. Voor katten boven 12,5 kg lichaamsgewicht dient een combinatie van twee pipetten te worden gebruikt die het beste bij het lichaamsgewicht past. Toedieningswijze: Stap 1: Stap 1: Onmiddellijk voor gebruik het sachet openen en de pipet eruit halen. Doe handschoenen aan. De pipet dient bij de basis of bij het harde bovenste deel onder de dop rechtop vastgehouden te worden (punt naar boven) om deze te openen. De draai-en-gebruik dop dient met de klok mee of tegen de klok in één keer rondgedraaid te worden. De dop zal op de pipet blijven; het is niet mogelijk deze te verwijderen. De pipet is open en klaar voor gebruik als het breken van de verzegeling wordt gevoeld. Stap 2: De kat dient te staan of liggen met de rug horizontaal voor een gemakkelijke toediening. Plaats de pipetpunt aan de schedelbasis van de kat. Stap 3: Knijp zachtjes in de pipet en breng de gehele inhoud direct op de huid van de kat aan. Het diergeneesmiddel dient bij katten tot 6,25 kg lichaamsgewicht aangebracht te worden op één plek aan de schedelbasis en bij katten met meer dan 6,25 kg lichaamsgewicht op 2 plekken aan de schedelbasis. Behandeling: Voor gelijktijdige behandeling van infecties met oormijten (Otodectes cynotis), dient een enkele dosis van het product te worden toegediend. Vraag 28 dagen na behandeling om een vervolg onderzoek bij uw dierenarts (zijnde otoscopie) om te bepalen of er sprake is van her-infestatie die een aanvullende behandeling vereist. De keuze voor een aanvullende behandeling (monosubstantie of combinatieproduct) dient te worden gemaakt door de voorschrijvende dierenarts. Voor gelijktijdige behandeling van infecties met de maagdarmwormen T. cati en A. tubaeforme dient een enkele dosis van het diergeneesmiddel te worden toegediend. De noodzaak en frequentie van herbehandeling dient in lijn te zijn met het advies van de voorschrijvende dierenarts, rekening houdend met de lokale epidemiologische situatie. Indien nodig kunnen katten met een interval van 12 weken herbehandeld worden. Katten in gebieden waar hartworm endemisch is (of katten die op reis zijn geweest naar endemische gebieden) kunnen volwassen hartwormen bij zich dragen. Voordat Bravecto Plus wordt toegediend voor de gelijktijdige preventie van infectie met volwassen D. Immitis dient daarom het advies uit rubriek 4.4 van de SKP te worden overwogen. Op het moment van behandeling is het diergeneesmiddel effectief tegen D. immitis larven (L3 en L4), die de kat in de voorafgaande 30 dagen hebben geïnfecteerd. Het diergeneesmiddel is effectief tegen nieuwe D. immitis larven (L3) tot 60 dagen na behandeling. Voor ononderbroken bescherming tegen hartwormziekte dient de kat daarom met een interval van 12 weken opnieuw behandeld te worden.EU/2/18/224/001-006.

Referenties: 1. Lavan RP et al. J Vet Sci Technol. 2017; 8: 439. - 2. Lavan RP et al. Parasit Vectors. 2017;10: 284. - 3. Lavan RP et al. Parasit Vectors. 2018; 11: 458.

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‘Het was een namiddag vol verrassingen. De eerste vrouwelijke dierenarts in onze West-Vlaamse kring, doctores Magdeleen De Vlieghere deed haar blijde intrede tussen reikhalzende collega’s. De zware taak om haar aan te stellen tot volwaardige West-Vlaamse dierenarts werd op de brede schouders van Dr. D’hoore geworpen. De erevoorzitter aanvaardde likkebaardend. Hij trad in bange en blijde verwachting op het podium en overhandigde haar een doosje pralines. De vergadering eiste van de erevoorzitter een omhelzing, die hij *secundum artem* uitvoerde. Hiermede bewees hij nogmaals dat wij nog steeds veel van hem kunnen leren.’

Citaat uit het ‘Verslag van de vergadering van de West-Vlaamse Dierenartsenvereniging te Loppem in het K.I.-centrum op 4 december 1966’. Tekst van de secretaris Dr. Kamiel Quintens opgenomen in het verslagboek 1959-1975 van de vereniging, geschonken aan de collectie Diergeneeskundig Verleden van de faculteit te Merelbeke door vroegere verantwoordelijken van wat het Provinciaal Centrum voor Dierenziekenbestrijding in Torhout was.

Johan De Smet en Luc Devriese

Treatment of copper deficiency in Texel-crossbred sheep by the feeding of a concentrate formulated for dairy cows

Koperdeficiëntie bij schapen (kruising texelaar) behandeld met het voeren van koeienbrok

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ABSTRACT

Six Texel-crossbred sheep, from a flock with a history of a dull appearance and mild diarrhea, were presented to the faculty of veterinary medicine (University of Utrecht) . The clinical signs were found to be related to Copper (Cu) deficiency as indicated by low hepatic Cu values. It was decided to treat the animals by feeding them concentrates specifically formulated for dairy cows because such concentrates have a rather high Cu content compared to concentrates designed for sheep. Sheep Cu status was monitored by measuring liver Cu concentrations. Current results indicate the potential of feeding cow concentrate as a practical method to treat Cu deficiency in Texel-crossbred sheep. In contrast to hepatic Cu concentrations, serum Ceruloplasmin concentration (Cp) values did not respond to the treatment thereby indicating that serum Cp is inferior to evaluate Cu status in sheep compared to liver Cu measurements.

SAMENVATTING

Zes schapen (kruising texelaar) met klachten van milde diarree en een doffe vacht werden aangeboden aan de Faculteit Diergeneeskunde van de Universiteit Utrecht. De klinische verschijnselen werden gerelateerd aan koper (Cu) deficiëntie op basis van lage Cu-waarden van de lever. Er werd besloten om de schapen te voeren met koeienbrok om het Cu-tekort op te heffen. In vergelijking met schapenbrokken bevatten deze brokken relatief veel Cu. De Cu-status werd gemonitord door Cu-concentraties van de lever te bepalen. Uit de resultaten blijkt dat het voeren van koeienbrok een praktische methode kan zijn om koperdeficiëntie te behandelen bij schapen (kruising texelaar). In tegenstelling tot de lever Cu waarden, veranderde de serum-ceruloplasmineconcentratie (Cp) niet, wat erop duidt dat serum Cp een minder betrouwbare indicator is van de koperstatus dan lever Cu.

BACKGROUND

One of the many sheep breeds in the Netherlands is the Texel breed. The Texel breed is well known for its meat production and also for its high susceptibility to Cu intoxication (Van den Berg et al., 1983; Underwood and Suttle, 1999). Therefore, Dutch commercial concentrates formulated for sheep are typically not supplemented with Cu but do contain supplemental sulfate (SO_4) and molybdenum (Mo), thereby targeting to depress Cu absorption (Underwood and Suttle, 1999). Ingestion of sulfate and molybdenum results in the formation of so-called thiomolybdates, which have a high affinity for Cu, thereby rendering Cu unavailable for absorption (Suttle, 1991; Underwood and Suttle, 1999; Gould and Kendall, 2011). Clearly, this practice is instrumental in preventing Cu intoxication in Texel sheep, but it may also result in Cu deficiency in other breeds given the large differences in Cu requirements between breeds (Van den Berg et al.,

1983; Underwood and Suttle, 1999). Moreover, the risk of Cu deficiency is increased by a low Cu content in roughage. Thus, feeding the same particular ration for all sheep may induce either Cu deficiency or Cu intoxication depending on the genetic background of the breed and the roughage provided.

CASE PRESENTATION

In 2015, a sheep owner farming on western peat soils in the Netherlands, reported a high prevalence of dead lambs shortly after parturition to his veterinarian. The lambs were delivered by the youngest ewes of the flock. The whole flock of sheep had been participating in a monitoring program on gastro-intestinal parasites since the observation in 2014 that the sheep suffered from a dull appearance in combination with mild diarrhea. However, given that diarrhea was only observed in the ewes and not in the lambs, it was concluded that the death of the lambs was most likely unrelated to gastro-intestinal parasites.

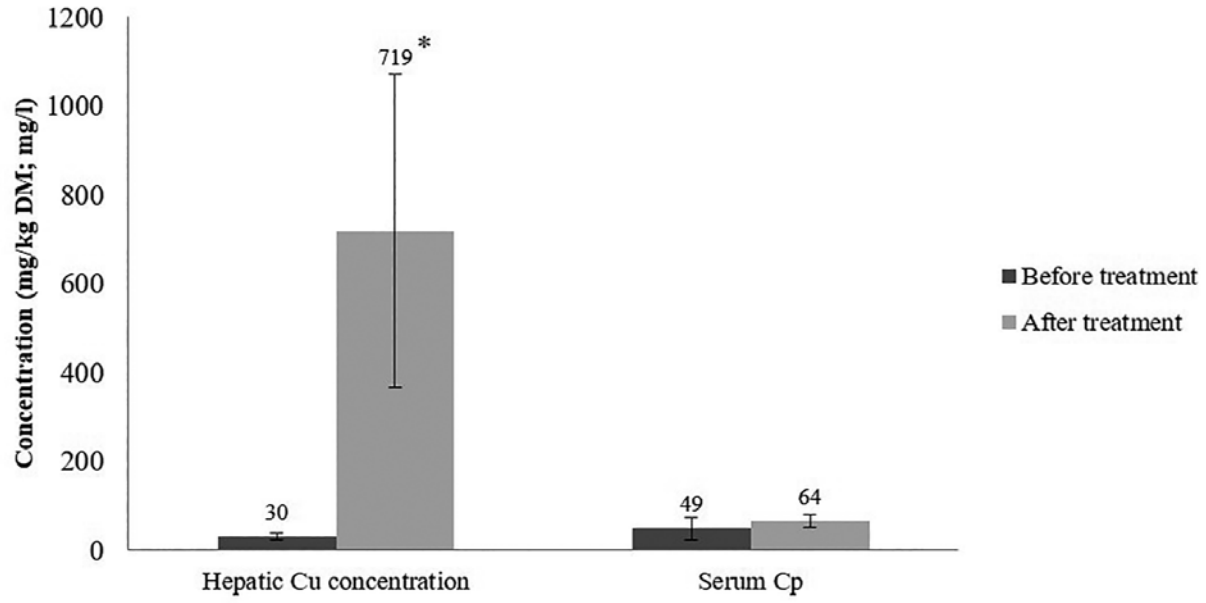
As grasses from peat soils are known to be generally low in Cu (Ouweltjes et al., 2002), it was speculated that the combined clinical signs could be related to Cu deficiency. For screening purposes, initially, several sheep were randomly sampled and only serum Cu concentrations were determined. Serum Cu concentrations were found to be < 10 µmol/l (reference: 12-20 µmol/l), indicating that the animals suffered from Cu deficiency (Dutch Central Bureau for Livestock Feeding, 2005). It was therefore recommended to implement dietary measures to restore the Cu status of the animals, but the owner waived this advice. The same happened at six and nine months after the first sampling, when the Cu status was re-evaluated and serum Cu concentrations were still below the reference values. Given the poor condition of the animals, the owner finally agreed to transport six young ewes to the Faculty of Veterinary Medicine of the Utrecht University with the aim to confirm Cu deficiency by measuring liver Cu concentrations. The liver Cu concentrations were found to range from 11 to 50 mg/kg DM (reference: 100-400 mg/kg DM), thereby confirming that all sheep were Cu deficient (Dutch Central Bureau for Livestock Feeding, 2005). It was then decided to treat the animals by feeding them concentrates specifically formulated for dairy cows. Such concentrates are not supplemented with SO_4 and Mo and are typically supplemented with Cu to reach minimum values of 20 mg/kg (Dutch Central Bureau for Livestock Feeding, 2005). The authors anticipated that the higher Cu content of the cattle concentrate together with the higher efficiency of Cu absorption after the ingestion would be a practical tool to treat Cu deficiency in the six ewes. For the evaluation of the effects of this treatment to restore the Cu status, liver biopsies and blood samples were taken. The first sampling was performed after feeding the animals a ration consisting of 50% sheep concentrate and 50% grass silage (DM basis) for three weeks. This diet contained a Cu content of ~10 mg/kg DM. Thereafter, the sheep concentrate was replaced by a dairy cow concentrate, thereby keeping the concentrate to silage ratio constant. This resulted in an estimated dietary Cu content of ~17,5 mg/kg DM. The level of feed intake was set to meet the energy requirement of the sheep according to the Dutch Central Bureau for Livestock Feeding i.e. 207 kJ NE/kg^{0,75}. After three months, the sampling was repeated to evaluate the effect of the dietary treatment. At both sampling moments, liver biopsies were collected to measure the liver Cu concentration and jugular blood samples to measure ceruloplasmin (Cp), as serum Cp has been suggested as a potential indicator of the Cu status (Blakley and Hamilton, 1985). The diagnostic value of blood samples is of interest because blood sampling is easier, less invasive and less laborious than taking liver biopsies. While no clinical abnormalities, such as swayback were seen, the subjective overall clinical impression of the sheep improved over time. A clear increase in liver Cu concentrations of 689 mg/kg DM was observed after the cow concentrate was fed (Figure 1). Feeding cow concentrates also resulted in a numerical increase in serum Cp, but the concentrations were not statistically significantly different from the initial values.

DISCUSSION

Cu is a well-known essential trace element and component of many enzymes, such as Cp, tyrosinase and superoxide dismutase. Chronic redundant Cu contents in the ration of sheep typically results in a hemolytic crisis and death, while Cu deficiency is associated with growth retardation, diarrhea, low birth weight and weight gain, as well as swayback (enzootic ataxia) (Underwood and Suttle, 1999).

Sheep with Cu deficiency are commonly treated with Cu injections or supplemented with Cu in mineral supplements developed for cattle or special salt blocks, drinking water or by fertilizing pastures with Cu sulphate. To the authors' knowledge, this is the first case report in which feeding cow concentrates is shown to be a practical method to treat Cu deficiency in Texel-crossbred sheep. However, caution is warranted to generalize the described strategy, because after three months of feeding the cow concentration, in the present report, the mean hepatic liver Cu concentration was around 1.8 times higher than recommended for healthy animals (Dutch Central Bureau for Livestock Feeding, 2005), which implies that there is a risk of inducing Cu intoxication. Despite the high liver Cu values, no clinical symptoms of Cu intoxication, such as depression, lethargy, hemoglobinuria and jaundice, were observed.

As the liver Cu concentrations were clearly above the reference values, it was concluded that the current



* p<0.01 (students paired t-test) compared to hepatic Cu concentration before treatment.

Figure 1. Hepatic Cu concentration and serum Cp before and three months after treatment.

treatment period was actually too long. Unfortunately, intermediate liver Cu values were not available, and it is therefore difficult to provide a time span, which is both effective and safe. Furthermore, susceptibility to Cu toxicity differs substantially between breeds of sheep, which means that it is probably not possible to provide a general effective and safe treatment strategy for all breeds.

The results of the present study indicate the inaccuracy of serum Cp as an indicator of the Cu status in sheep. Indeed, Cp remained relatively constant, despite the increase in liver Cu concentration. To the authors' knowledge, no reference values for serum Cp are available in sheep; however, 45-100 mg/l is considered to be normal in plasma (Radostits and Gay et al., 2007). Given that in serum less Cu is associated with Cp (55%) than in plasma (66%), the reference values for serum are estimated to be around 38-83 mg/l (Radostits and Gay et al., 2007). Based on this estimation, Cp appeared to be approximately normal in all of the sheep of the present case report, even before treatment. It may be suggested that even in the Cu deficient sheep, hepatic Cu stores are sufficient to maintain a certain Cp activity (Underwood and Suttle, 1999).

Although it is not clear why the sheep in this study developed Cu deficiency, it seems likely that the animals did not absorb enough Cu to meet their requirements. Unfortunately, it was not possible to collect and analyze soil and roughage samples in order to investigate whether this was due to a low feed intake, a low roughage Cu content or a high content of SO_4/Mo in the roughage.

Furthermore, in the past, pig feed was supplemented with Cu, resulting in Cu-rich pig manure that was spread on the pasture. Since the restriction in Cu supplementation in pig feed, the Cu content of pig manure has decreased, hence increasing the occurrence of Cu deficiency.

CONCLUSION

Feeding cow concentrate can be used as a practical tool to treat Cu deficiency in Texel-crossbred sheep. Given the results, it seems that feeding this concentrate for three weeks is too long, but it remains difficult to generalize this experience for other breeds. Furthermore, serum Cp concentration was found to be inferior to the liver Cu measurement for the evaluation of the Cu status in sheep. Taking liver samples is difficult in practice. Therefore, future research is warranted to find good markers for the detection of Cu deficiency.

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Oproep

Enquête bij Vlaamse dierenartsen omtrent hartritmestoornissen bij de hond

Aan de Faculteit Diergeneeskunde verrichten we momenteel onderzoek naar de diagnose en behandeling van hartritmestoornissen bij de hond.

Hartritmestoornissen komen regelmatig voor bij de hond en zijn een belangrijke oorzaak van hartfalen en plots overlijden. Vaak veroorzaken deze aandoeningen in de initiële fase slechts vage, niet specifieke klachten (bijvoorbeeld inspanningsintolerantie, braken, diarree, soms syncope, tekenen van stress of angst,…). Hierdoor wordt het probleem door de eigenaar of dierenarts vaak pas herkend in een laat stadium, samenvallend met het ontwikkelen van hartfalen. Verder is ook de behandeling van hartritmestoornissen niet eenvoudig, zijn er beperkte medicamenteuze opties en is er gelimiteerde toegang tot interventionele (en curatieve) behandelingsmethoden in de praktijk.

Via deze enquête trachten we te achterhalen hoe frequent dierenartsen in de praktijk geconfronteerd worden met hartritmestoornissen bij de hond en hoe ze op dit moment de diagnose en behandeling aanpakken. Deze informatie **helpt ons in de zoektocht naar een betere diagnostische en therapeutische aanpak** van deze patiënten. Net daarom is uw deelname zo belangrijk.

De enquête neemt ongeveer 10 minuten van uw tijd in beslag. De verwerking ervan gebeurt binnen het kader van mijn doctoraatsonderzoek aan de faculteit diergeneeskunde, Universiteit Gent.

Wenst u deel te nemen aan de enquête, dan kan dat vanaf 12 januari via de onderstaande link:
https://hartritmestoornissen.wixsite.com/cardioteamkhd

Voor verdere vragen omtrent deze enquête kan u steeds mailen naar arnaut.hellemans@ugent.be

Alvast erg bedankt voor uw deelname.

Arnaut Hellemans

Neurological signs and imaging findings in three cats with multiple articular process hypertrophy

Neurologische symptomen en resultaten van medische beeldvorming bij drie katten met hypertrofie van multipele articulaire processen

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ABSTRACT

An eight-year-old British Shorthair (case 1), an eleven-year-old British Shorthair (case 2) and a six-year-old European Shorthair cat (case 3) showed signs of chronic T3–L3 myelopathy. Computed tomography of the thoracolumbar and lumbosacral region was performed in all three cases and magnetic resonance imaging was only performed in case 2. Cross sectional imaging revealed an enlargement of the articular process joints from T2 to T5 in case 1, from T11 to T13 in case 2 and from T10 to T13 in case 3 causing spinal cord compression. Based on the severity of the spinal cord compression, surgical decompression by hemilaminectomy was performed in case 1. In cases 2 and 3, conservative treatment was instituted, although this condition could have been an incidental finding in these two cases. To the authors' knowledge, this is the first report describing the neurological signs, imaging findings and short-term outcome in cats with multiple thoracolumbar articular process hypertrophy.

SAMENVATTING

Een acht jaar oude Britse korthaar (casus 1), een elf jaar oude Britse korthaar (casus 2) en een zes jaar oude Europese korthaar (casus 3) werden aangeboden met chronisch progressieve T3-L3 myelopathie. Computertomografie van de thoracolumbale en lumbosacrale wervelkolom werd uitgevoerd bij deze drie casussen en magnetische resonantiebeeldvorming werd gedaan bij casus 2. Op deze beeldvorming werd hypertrofie van de gewrichten van de articulaire processen gezien van T2 tot T5 in casus 1, van T11-T13 in casus 2 en van T10 tot T13 in casus 3; met compressie van het ruggenmerg. Wegens de ernst van de ruggenmergcompressie werd een chirurgische decompressie uitgevoerd bij casus 1. Bij de andere twee gevallen werd een conservatieve behandeling ingesteld, alhoewel deze aandoening in deze gevallen een toevalsbevinding zou kunnen zijn. Volgens de auteurs is dit de eerste beschrijving van neurologische symptomen en bevindingen via beeldvorming en van de kortetermijnopvolging bij drie katten met hypertrofie van multipele articulaire processen.

INTRODUCTION

Articular process hypertrophy (APH) is commonly diagnosed in dogs and its associated signalment, clinical signs and imaging characteristics have been described in the literature (Da Costa, 2010). The clinical signs are mainly related to spinal cord compression, commonly resulting in chronic progressive myelopathy. The main differential diagnosis for APH in cats include angiomatosis (Schur et al., 2010; Hans

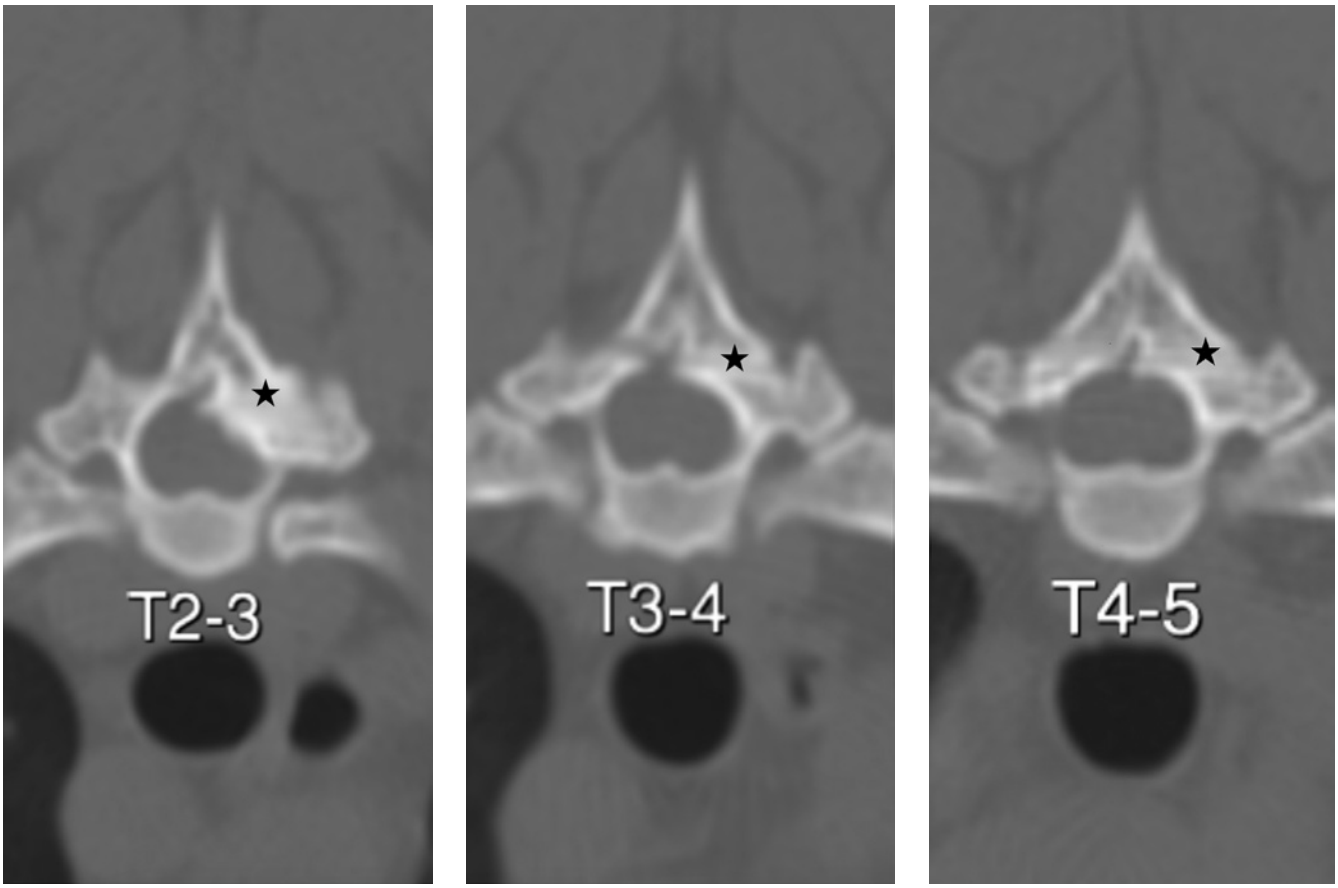


Figure 1. Case 1. Transverse CT bone algorithm acquisition at the level of T2 to T5, showing irregular hypertrophy of the left pedicle (black star) with moderate dorsolateral compression of the spinal cord.

et al., 2018), intervertebral disc disease (De Decker et al., 2017; Crawford et al., 2018), spinal arachnoid diverticulum (Adams et al., 2015), hamartoma (Taylor-Brown et al., 2018), vertebral malformation (Havlicek et al., 2009), spinal dural ossification (Antila et al., 2013), myelomeningocele (Ricci et al., 2011), neoplastic processes (Besalti et al., 2016) and inflammatory or infectious diseases (Marioni-Henry et al., 2004). Information about APH affecting cats, typical imaging characteristics, treatment and outcome is sparse, with only one recent case report about two cats showing single bilateral APH (T11–T12 in case 1 and T3–T4 in case 2) (Carletti et al., 2019). Before these two cases, thoracic vertebral canal stenosis due to bilateral APH at the level of T4-T5 has been reported in a nine-year-old female intact domestic Shorthair cat (Bossens et al., 2015), but in that particular case, the articular degenerative process was thought to be secondary to adjacent diffuse idiopathic skeletal hyperostosis (DISH). The diagnosis of APH is based on a combination of consistent clinical signs, exclusion of other myelopathies and on characteristic imaging findings. To the authors' knowledge, this is the first report describing the clinical signs and imaging findings in cats with multiple thoracolumbar APH.

CASE DESCRIPTION

Case 1

An eight-year-old, male, castrated British Shorthair cat was presented with a two-month history of progressive weakness and proprioceptive ataxia in both pelvic limbs, reluctance to jump, and episodes of pain when manipulated by the owners. Administration of 2 mg/kg q24h prednisolone (Prednicortone®; Kela Veterinaria NV, Belgium) by the referring veterinarian for four weeks significantly relieved the neurological signs, but as soon as the medical management was ceased, the clinical signs returned and the cat deteriorated. The cat was referred to the Small Animal Teaching Hospital at Ghent University for further investigations. General physical examination revealed no abnormalities. A complete neurological examination revealed proprioceptive ataxia and ambulatory paraparesis more evident in the left pelvic limb, with absent proprioception and decreased hopping in both pelvic limbs and severe hyperesthesia on palpation of the cranial and mid thoracic vertebral column. Segmental spinal reflexes were normal but moderate to severe muscle atrophy of both pelvic limbs was evident. These findings were consistent with T3-L3 mye-

lopathy. Complete blood cell count and biochemistry profile were unremarkable. Preanesthetic full cardiac ultrasound was performed, as the cat was an elderly British Shorthair and a mild thickening of the left ventricular free wall and interventricular septum was seen. For this, no treatment was prescribed as these findings were considered to be subclinical.

Computed tomography (CT) (4 slice CT; Lightspeed Qx/i, General Electric Medical Systems, Milwaukee, WI) was performed of the thoracolumbar vertebral column under sedation. The CT images were acquired in bone and soft tissue reconstruction algorithms, with additional IV contrast study. Transverse and reconstructed images in sagittal and dorsal plane were accessed and analyzed using OsiriX DICOM-viewer (Pixmeo, Geneva, Switzerland). Multiple articular process joints along the thoracic and thoracolumbar vertebral column were hypertrophic, causing compression of the spinal cord. At the level of T2 extending to T5, there was an obvious irregular hypertrophy of the left articular process joints with moderate dorsolateral compression of the spinal cord (Figure 1). At the level of T9 extending until the level of T13, there was marked bilateral hypertrophy of the articular processes with moderate to severe dorsal compression of the spinal cord (Figure 2). From T13 until the level of L4, there was mild bilateral hypertrophy of the articular processes with mild dorsal compression of the spinal cord. Based on the CT imaging findings and the marked benign appearance of multiple degenerative processes and the associated spinal cord compression, a presumed diagnosis of multiple degenerative APH was made.

Surgical treatment for spinal cord decompression was performed. A continuous hemilaminectomy was performed along the articular process of T2-T3-T4-T5 on the left. Due to their severity and compatibility with a more left sided lesion based on the neurological examination, the cranial thoracic compressions were surgically alleviated first. Inspection of the vertebral canal showed severe dorsolateral deviation of the spinal cord to the right, mainly at the level of T3 (Figure 3). Extra bone was removed dorsally (lamina) at the base of the dorsal spinous processes to achieve extra decompression. Afterwards, an indentation in the spinal cord at the level of the compression remained visible and the spinal cord showed blue discoloration locally. Besides moderate bleeding of the surrounding tissue, no intraoperative complications were noted. A postoperative CT scan revealed satisfactory decompression, especially at the level of T2-T3 (Figure 4). Small fragments of bone from the affected region were submitted for histopathological examination, which revealed mineralized trabecular bone surrounded by osteoblasts with several areas of fibroblast proliferation, consistent with reactive bone tissue. Recovery from anesthesia was uneventful and postsurgical analgesia was provided with 0.2 mg/kg methadone IV q4h (Insistor®; Richter Pharma AG, Austria) 4 mg/kg carprofen IV q24h (Rimadyl®; Zoetis Belgium SA, Belgium). Overnight, while hospitalized, the cat started showing episodes of dyspnea, bilateral crackles on lung auscultation, loss of serohemorrhagic fluid from the nose, cyanosis and hypotension, which initially responded to 1-2 mg/kg boli of furosemide (Dimazon®; MSD Santé Animale, France) but worsened within the following hours. A FAST scan of the heart was performed, which showed an increased size of the left atrium. At the owners' request, the cat was euthanized and necropsy was denied.

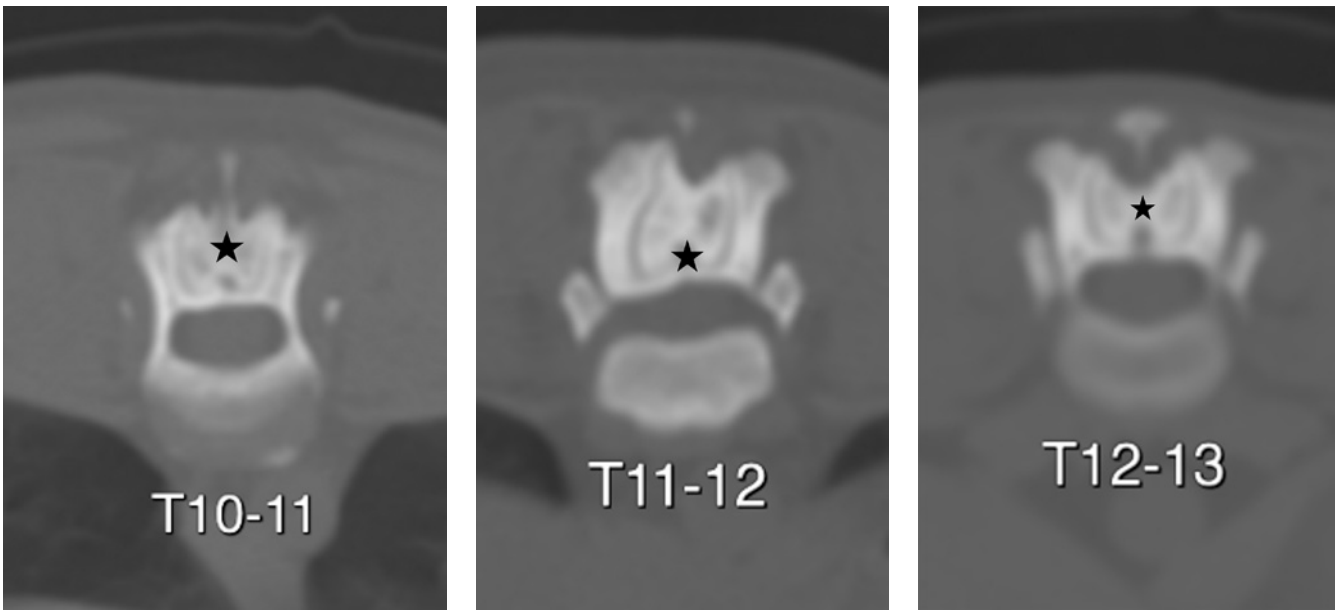


Figure 2. Case 1. Transverse CT bone algorithm acquisition at the level of T10 to T13, showing enlargement and misshaping of the articular process (black star) causing dorsal spinal cord compression bilaterally.

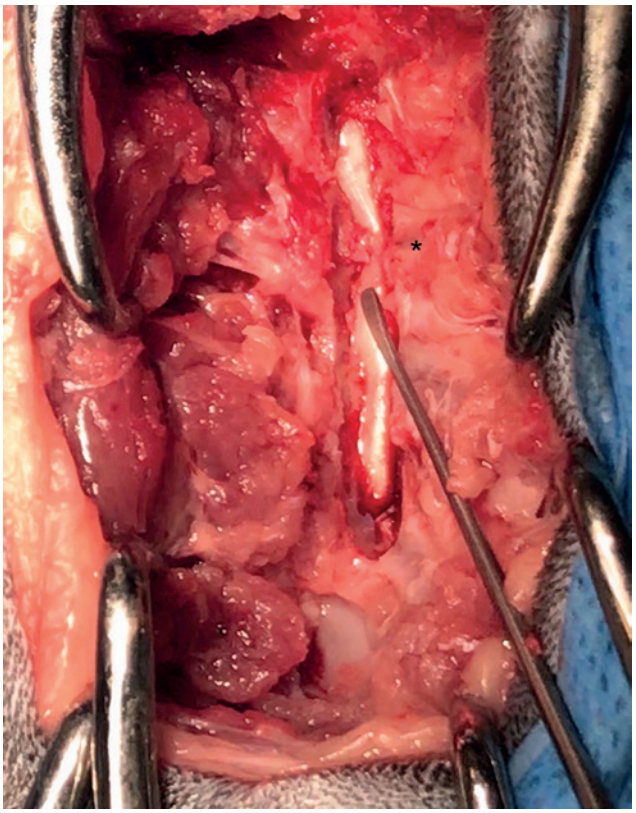


Figure 3. Case 1. Intraoperative picture after T2 to T5 left hemilaminectomy, showing severe dorsolateral deviation of the spinal cord from left to right (instrument point), mainly at the level of T3 (black star).

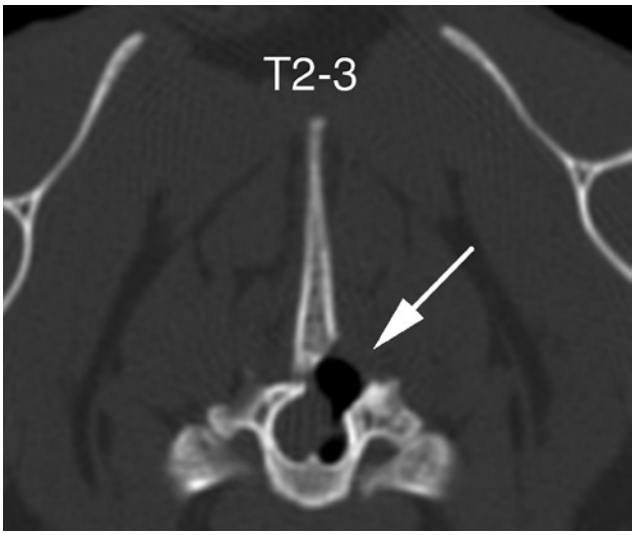


Figure 4. Case 1. Transverse postoperative CT bone algorithm acquisition at the level of T2-T3, showing satisfactory decompression of the spinal cord after left side hemilaminectomy (white arrow).

Case 2

An eleven-year-old, female, neutered British Shorthair cat was presented with a four-month history of progressive weakness, ataxia and muscle atrophy in both pelvic limbs. According to the owner, the condition appeared non-painful. During these four months, a two-week treatment with 1 mg/kg q24h prednisolone (Prednicortone®; Kela Veterinaria NV, Belgium) followed by a twelve-day treatment with robenacoxib (Onsior®; Novartis Pharma NV, Belgium) 2 mg/kg q24h did not cause any improvement of the clinical signs. Prednisolone was again prescribed at the same dose for a longer period and some improvement was seen. However, since the clinical signs did not entirely resolve, the cat was referred for further investigations. General physical examination, complete blood cell count and biochemistry profile were all unremarkable. On neurological examination, the cat was ambulatory paraparetic with marked proprioceptive ataxia and delayed postural reactions (proprioception and hopping) in both pelvic limbs. Moderate generalized muscle atrophy was present at both pelvic limbs. Pain could be elicited on palpation of the thoracolumbar vertebral column. Segmental spinal reflexes were normal. These findings were consistent with T3-L3 myelopathy.

CT of the thoracolumbar vertebral column was performed using the same protocol and technique as previously described. On the native sequences, some mild new bone formation was seen ventrally at the vertebral bodies of T11, T12, T13 and L3. At the level of T11-T12 and T12-T13, a mild dorsal spinal cord compression was seen, mainly due to bilateral APH (Figure 5). Based on the CT images, mild to moderate intervertebral disc extrusion at the level of T11-T12 and mild protrusion at the level of T12-T13 were suspected. Low field MRI using a permanent 0.2 T magnet (Airis Mate, Hitachi Ltd) was performed and revealed decreased T2W signal intensity in all thoracic and lumbar intervertebral discs, but most pronounced at the level of T11-T12 (Figure 6A). At this level, a dorsal and ventral compression of the spinal cord was detected with adjacent intramedullary T2W and STIR hyperintensity and T1W isointensity of the spinal cord extending from mid T10 until the caudal aspect of T13. After intravenous administration of 0.1 mg/kg paramagnetic contrast medium gadoterate meglumine (Dotarem®; Guerbet, the Netherlands), a mild ventral meningeal hyperintensity was seen at the level of T11-T12. Mild spinal cord compression due to APH at the level of T11-T13, with diffuse right sided intramedullary signal and meningeal enhancement on MRI images were also seen, compatible with spinal cord edema (Figure 6B).

Lumbar cerebrospinal fluid (CSF) analysis was performed, including total nucleated cell count and total protein concentration, which were unremarkable. A presumptive diagnosis of mild disc extrusion at T11-T12 and mild protrusion at T12-T13 was made, with mild thoracic vertebral canal stenosis due to APH at the level of T11-T13. The owners opted for conservative treatment and the cat was treated with 1 mg/kg prednisolone q24hs (Prednicortone®; Kela Veterinaria NV, Belgium). After one month, the owners were contacted by telephone. Some mild improvement was seen and the cat was still receiving prednisolone 0.5 mg/kg q48hs.

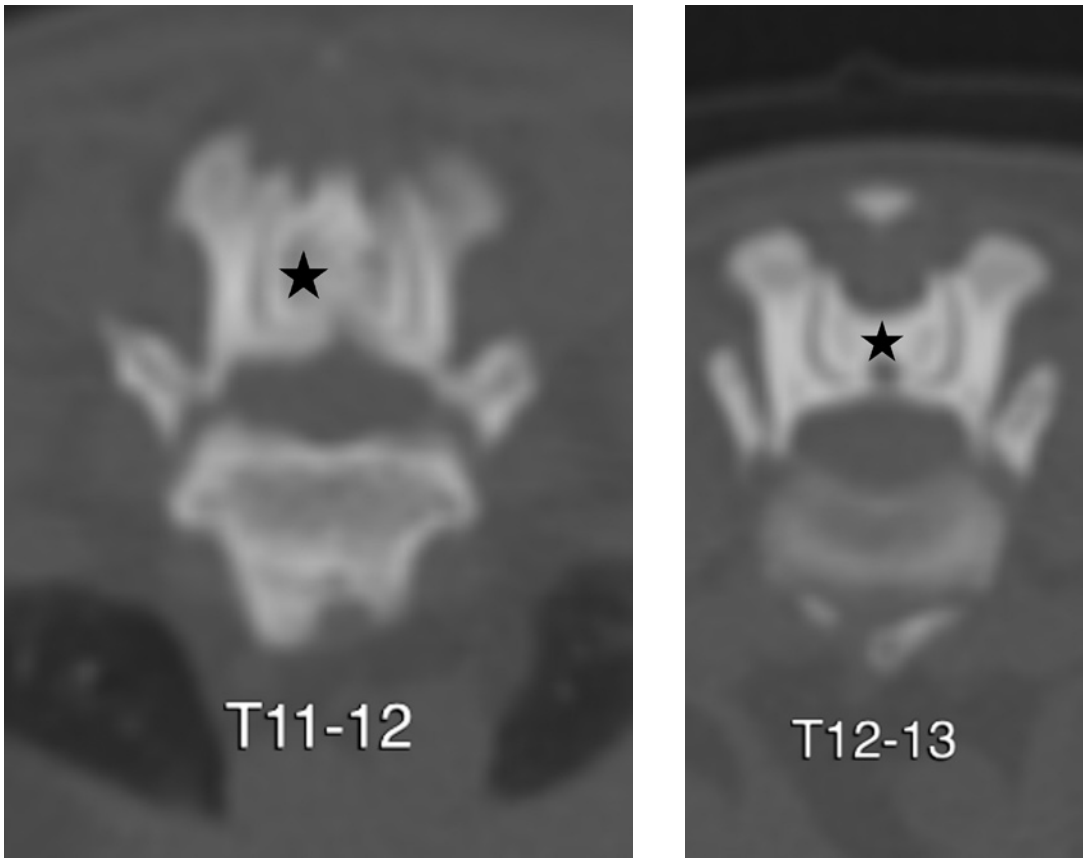
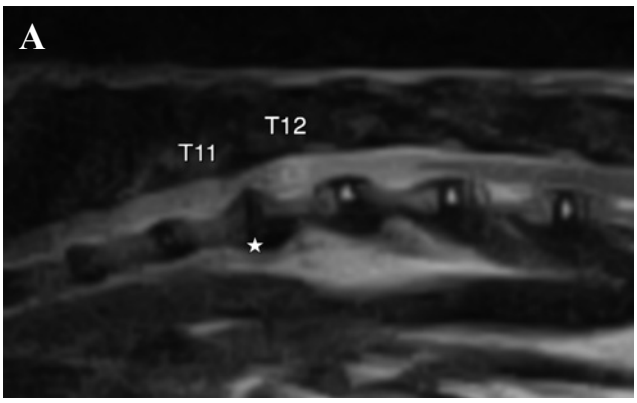


Figure 5. Case 2. Transverse CT bone algorithm acquisition at the level of T11 to T13, showing mild dorsal spinal cord compression due to hypertrophy of the articular processes (black star).

Case 3

A six-year-old, male, castrated European Shorthair cat was presented for a two-month history of back pain and left pelvic limb lameness. This cat was adopted at a younger age and the right pelvic limb had already been amputated due to an unknown cause. The referring veterinarian prescribed 1 mg/kg q24h methylprednisolone (Moderin®; Zoetis BV, Belgium), without clinical resolution and the cat was referred for further investigations. General physical examination



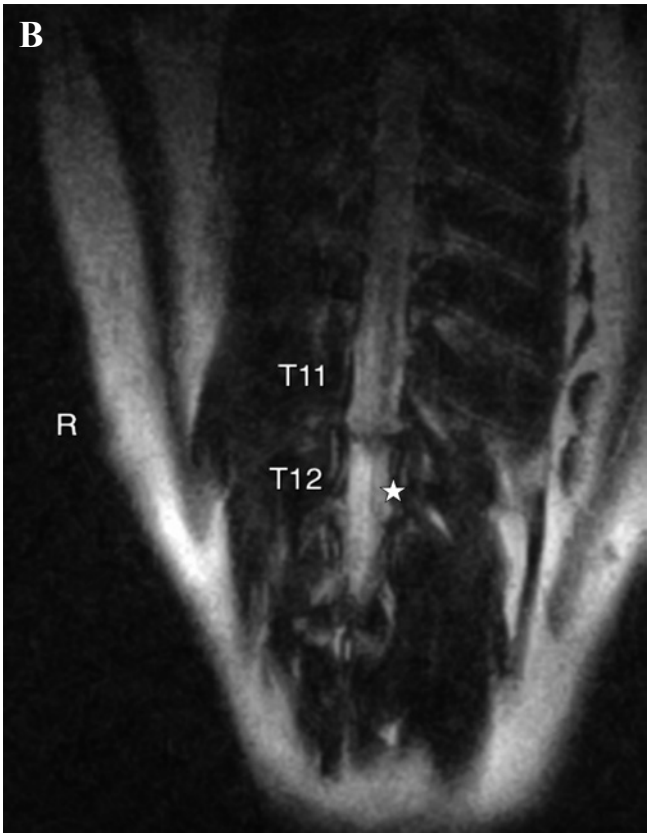


Figure 6. Case 2. A. T2W transversal 0.2T MR image showing dorsal and ventral compression of the spinal cord with decreased signal intensity at the T11-T12 intervertebral disc (white star). B. T2W dorsal 0.2T MR post contrast image showing diffuse right sided intramedullary signal between T10-T13, compatible with spinal cord edema (white star).

revealed no abnormalities. On neurological examination, the cat looked uncomfortable while walking (kyphotic posture), showing left pelvic limb paresis, because of which it sometimes fell whilst walking. Hyperesthesia was evident on palpation of the thoracolumbar and lumbar vertebral column and the cat appeared uncomfortable on manipulation of the tail. The remainder of the neurological examination was unremarkable. These findings were most likely due to T3-L3 myelopathy. Complete blood cell count and biochemistry profile were unremarkable.

CT of the vertebral column was performed using the same protocol and technique as previously described in case 1. Bilateral APH at the level of T10-T13 was present, causing moderate dorsal compression of the spinal cord. The remaining bony structures were within normal limits. There was also a mild APH of the lumbar vertebrae L1-L5 without significant compression of the spinal cord. Lumbar CSF analysis was unremarkable. The presumptive diagnosis in this case was APH at the level of T11-T13 causing dorsal compression of the spinal cord. Conservative treatment with 10 mg/kg gabapentine q8h (Neurontin®; Pfizer NV, Belgium) was started and one month later, the cat was showing no signs of pain anymore and the paresis had improved but was not totally resolved. After six months, the owner was contacted via telephone for follow-up. The cat was still receiving gabapentine and the clinical signs were stable.

DISCUSSION

In this case series, the clinical presentation and imaging findings of multiple APH are described in one European and two British Shorthair cats. APH is a rarely reported cause of myelopathy in cats, and so far, only reported as a single site lesion (Bossens et al., 2015; Carletti et al., 2019). In the previously reported cases, the lesions were localized in the thoracic vertebral column. In this case series, APH could be found not only in the thoracic but also in the lumbar vertebral column (cases 1 and 3). All three cats presented a history of chronic progressive myelopathy. Predilection for APH appears to exist in older cats (middle-aged and senior). Similary to previously reported cases (Bossens et al., 2016; Carletti et al., 2019), the three cats of the present report were older than six years at the time of the diagnosis. Imaging findings of APH are compatible with enlargement of the articular processes, with these projecting into the vertebral canal and causing uni- or bilateral extradural compression of the spinal cord. As seen in case 2, a focal area of intramedullary hyperintensity might be present on T2-weighted MRI, compatible with spinal cord edema secondary to the compression. Important differential diagnoses for APH include hamartomas (Taylor-Brown et al., 2018), angiomatosis (Schur et al., 2010; Hans et al., 2018) and neoplastic processes (Besalti et al., 2016). These differential diagnoses can be differentiated on the basis of histopathological features.

APH leading to vertebral canal stenosis is a well-recognized condition in dogs (Da Costa, 2010). Often, more than one vertebral site is compromised, with T2– T3 being the most commonly affected site (Johnson et al., 2012). The etiopathogenesis of APH in cats is not fully understood, but it is believed to be similar to dogs, where APH is thought to be due to developmental abnormalities, bone dysplasia or malarticulation (Johnson et al., 2012). Adjacent spinal cord disease was not detected in case 1 and case 3. However in case 2, spondylosis deformans and intervertebral disc disease (IVDD) were detected at T11-T12 (extrusion) and T12-T13 (protrusion) where APH was also present. In this case, the presence of a chronic intervertebral disc protrusion may have predisposed to instability and subsequent hypertrophic changes of the articular processes at this level (Carletti et al., 2019). The authors believe that the spinal cord compression caused by IVDD in case 2 contributed to the clinical signs, causing a dorsoventral compression at this level and exacerbating the neurological deficits. Based on the imaging findings in cases 1 and 3, APH seemed to be the main cause of the clinical signs whereas in case 2, APH could just as well have been an incidental finding. It was difficult to advise all three cat owners on expected prognosis, primarily because of the lack of available long-term outcome data for APH in cats, the multifocal aspect of this condition and the possibility of being just an incidental finding, especially in case 2. Short-term clinical improvement has been achieved with conservative treatment in one case (Bossens et al., 2016) and with surgical decompression alone in two cases (Carletti et al., 2019). Both cats, i.e. a nine-year-old, neutered, female British Shorthair cat and a thirteen-year-old, castrated, male domestic Shorthair cat were presented with a history of chronic progressive myelopathy and were treated surgically. Magnetic resonance imaging (MRI) revealed the presence of a bilateral enlargement of the articular processes projecting into the vertebral canal causing bilateral dorsal extradural compression of the spinal cord. In the present report, both cats that were treated medically, showed marked improvement without complete remission of the clinical signs. Gabapentine was only administered in case 3 since pain was more obvious than in case 2 and for this reason, case 2 only received prednisolone. Unfortunately, the cat in the present series that was treated surgically, died a few hours after surgery and necropsy was declined by the owners. Respiratory failure due to spinal cord compression is mainly related to the cervical region. In the cat, the phrenic nerves originate from cervical spinal cord segments C5-C6 (Crouch 1969) and these nerves supply motor and sensory fibers to the diaphragm (Evans and de Lahunta, 2013). This cat developed both inspiratory and expiratory dyspnea several hours after an

uneventful recovery of anesthesia and was accompanied with bilateral crackles on lung auscultation and loss of serohemorrhagic fluid from the nose. The authors believe that this, in combination with an atypical neurolocalization to cause respiratory failure (T2-T5), increased size of the left atrium on FAST scan of the heart and initial positive response after administration of furosemide, makes cardiogenic pulmonary edema due to congestive heart failure likely. Unfortunately, no necropsy was performed and the exact cause of the respiratory failure could not be determined with certainty. Further limitations of this retrospective study were the small number of cases, the possibility of this condition being an incidental finding (mainly in case 2) and the lack of MRI and CSF analysis in two cats (case 1 and 3) to exclude other diseases, which might not have been visible on CT.

To the authors' knowledge, the present report represents the first detailed description of CT and/or MRI findings for multiple articular processes hypertrophy in three cats and its neurological signs. APH may not be apparent on survey radiographs, and CT and/or MRI should be recommended to obtain an imaging diagnosis for cats with thoracolumbar myelopathy.

CONCLUSION

In middle-aged and senior cats presenting with back pain, paraparesis and proprioceptive ataxia, the list of differential diagnoses should include benign but compressive diseases such as APH. Concomitant conditions might be seen on CT and/or MRI and for this reason, the presence of APH should be interpreted with caution when deciding for the best treatment approach in each single case, since this may just be an incidental finding. Surgical treatment may be the key for a good outcome, but since medical treatment might offer fair improvement, the risks of a surgical intervention should be well considered.

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Persbericht

Protect Our Future Too: stijgende temperaturen brengen gezondheidsrisico's met zich mee voor onze huisdieren

Onze seizoenen veranderen en de temperaturen stijgen. Deze herfst is hiervan een goed voorbeeld. Warmer weer is niet alleen van invloed op de mens, maar ook op dieren.

Wat zijn de risico's?
Stijgende temperaturen stellen huisdieren bloot aan (nieuwe) gezondheidsrisico's, zoals virale en bacteriële ziekten, evenals verhoogde en langdurige blootstelling aan parasieten, zoals muggen en teken die ernstige ziekten met zich meedragen.
Bovendien kunnen, als gevolg van veranderde weersomstandigheden, hittegerelateerde ziekten optreden bij honden en katten en zelfs gedragsveranderingen verschijnen, zoals angsten, door de toename van extreem onweer.

Europese dierenartsen doen mee
Om huisdiereigenaren bewust te maken van de effecten van het warmer weer op de gezondheid en welzijn van dieren, is de Europese campagne **Protect Our Future Too (#POFT)** gelanceerd met de deelname van 21 vooraanstaande Europese veterinaire specialisten, waaronder Dr Paul Overgaauw, microbioloog en parasitoloog aan de Faculteit Diergeneeskunde van Universiteit Utrecht: "Door het warmere weer van de afgelopen jaren trekken nieuwe soorten parasieten uit het zuiden naar het noorden in onze streken. Bovendien, vermenigvuldigen de parasieten zich meer en blijven ze langer actief, waardoor dieren en hun eigenaren meer tekenbeten kunnen oplopen."

"Honden- en kattenbezitters hebben 50% meer kans om tekenbeten op te lopen"

Wat kan je doen?
Gezien de risico's, vindt Dr Paul Overgaauw het belangrijk om aandacht te vestigen op de potentiële gevaren van temperatuurstijging. Daarnaast, wil hij huisdiereigenaren aanmoedigen om hun dierenarts te raadplegen over de te nemen maatregelen en voor advies op basis van de omgeving en de levensstijl van het gezelschapsdier om deze gezond te houden het hele jaar rond.

Voor meer informatie over de campagne: www.protectourfuturetoo.com.

Heupproblemen bij kleine hondenrassen

Hip problems in small breed dogs

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SAMENVATTING

Wanneer er gesproken wordt over afwijkingen van de heupen bij honden zal menig dierenarts nog steeds automatisch aan heupdysplasie denken en vaak voegt men er ook aan toe dat dit een probleem is dat vooral de grotere rassen treft. Dit is niet geheel onterecht, maar uiteraard omvatten caniene heupafwijkingen meer dan de typische dysplasie bij grote tot reuzenrassen. In dit artikel wordt een samenvatting gegeven van mogelijke aandoeningen die voornamelijk bij de kleinere hondenrassen worden aangetroffen. Er wordt dieper ingegaan op de anatomie rondom het heupgewricht, de mogelijke diagnoses en de verschillende behandelmogelijkheden, zowel conservatief als chirurgisch.

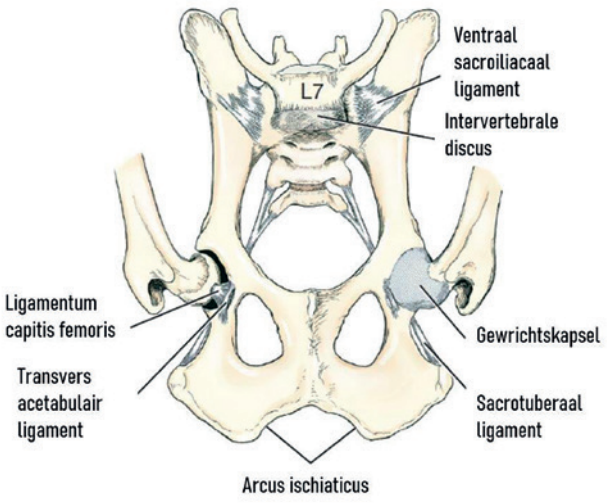
ABSTRACT

Whenever a discussion arises regarding canine hip problems, many veterinarians will automatically conclude that it's hip dysplasia they are dealing with, often followed by the statement that mostly large breed dogs suffer from this condition. In the literature, this statement is largely confirmed; however, canine hip problems include more than the typical dysplastic joint in large to giant breed dogs. In this paper, the other "usual suspects" are discussed, particularly in small breed dogs. The focus lies on the pelvic anatomy, the possible diagnoses and the treatment options, both conservatively and surgically.

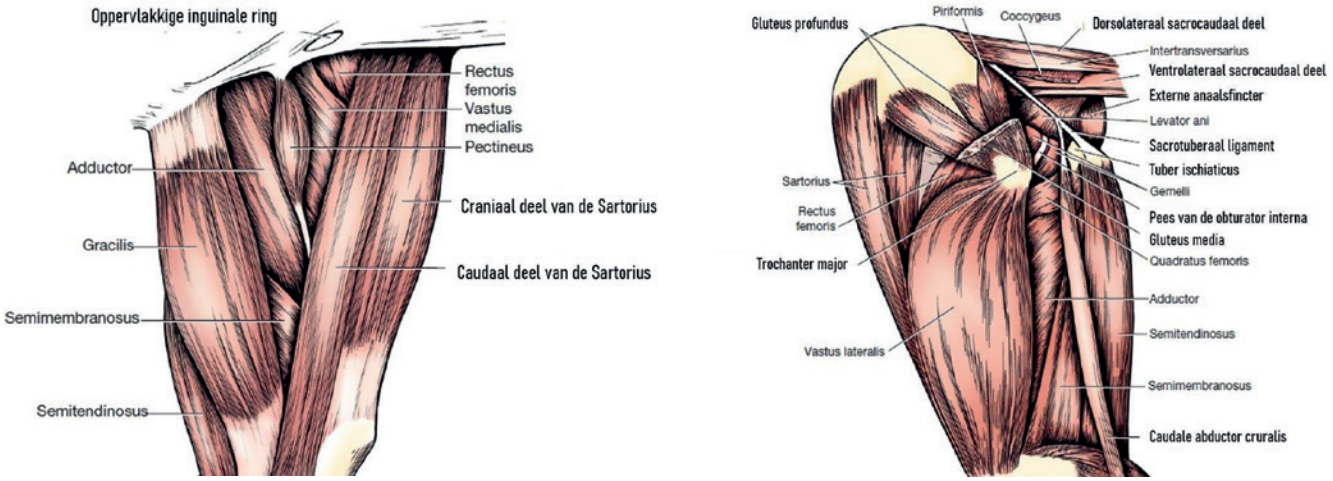
ANATOMIE

Het heupgewricht is een kogelgewricht dat bestaat uit twee botsegmenten: het caput femoris (convex) enerzijds en het acetabulum (concaaf) anderzijds. Rondom het heupgewricht bevindt zich het gewrichtskapsel dat sterk bijdraagt tot de stabiliteit van het heupgewricht. Tussen het caput femoris en het centrum van het acetabulum bevindt zich het ligamentum capitis femoris. Dit kleine ligament speelt een rol bij de ontwikkeling van de heup en draagt in beperktere mate bij tot de heupstabiliteit. Aan de ventrale zijde van het acetabulum, bevindt zich het ligamentum acetabuli transversus. Dit ligament overbrugt de ventrale rand van het acetabulum en zorgt ervoor dat het heupgewricht niet naar ventraal kan luxeren (Millis en Levine, 2014) (Figuur 1).

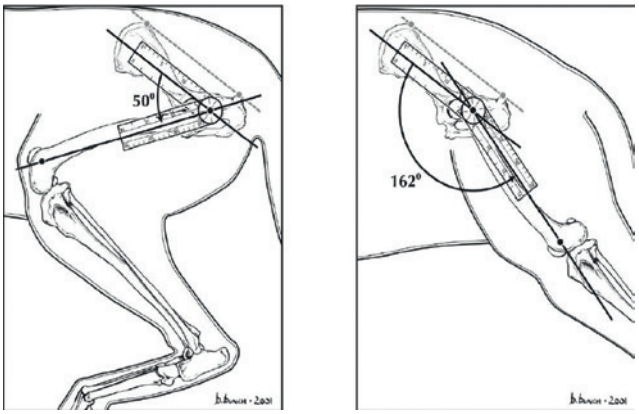
Door zijn conformatie is het heupgewricht een zeer mobiel gewricht dat door een ganse resem spieren in



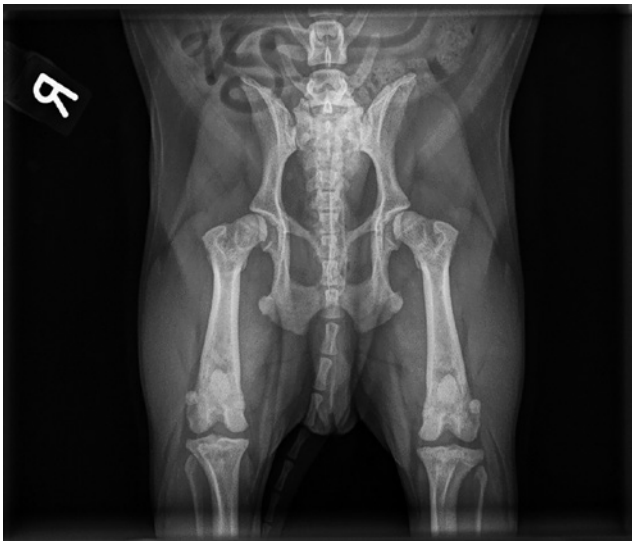
Figuur 1. Ventraal aspect van het bekken met de voornaamste botstructuren en ligamenten (uit: Millis en Levine, 2014).



Figuur 2. Mediaal (links) en lateraal (rechts) aanzicht van de heupmusculatuur (uit: Millis en Levine, 2014).



Figuur 3. Plooibaarheid van het heupgewricht (uit: Millis en Levine, 2014).



Figuur 4. Radiografische ventrodorsale opname van de heupen van een mopshond van vier jaar oud. Er is bilateraal subluxatie van de heupkoppen zichtbaar met secundaire degeneratieve veranderingen.

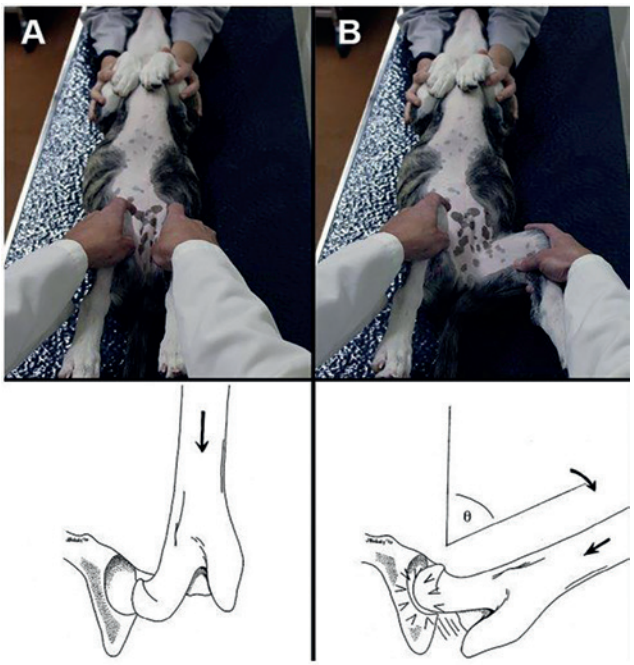
verschillende vlakken bewogen kan worden. Er kunnen zes soorten bewegingen met elk hun spieren onderscheiden worden (Figuur 2)

- Flexie: M. Iliopsoas, M. Sartorius en de M Tensor Fascia Lata
- Extensie: Mm.Gluteii, M. Semimembranosus, M. Semitendinosus, M Biceps Femoris
- Abductie: M. Gluteus medius
- Adductie: Mm. Adductor longus en brevis en M. Pectineus
- Laterale rotatie: Mm. Obturatorus interna en externa, M. Gemilli
- Mediale rotatie: M. Gluteus Profundus en M. Semitendinosus

De normale beweeglijkheid van de heupen is ongeveer 50–55° flexie en 160–165° extensie. Bij een geplooide heup kan het gewricht ongeveer 120° in abductie en 65° in adductie gebracht worden. Bij een gestrekte heup is dat 85° abductie en 63° adductie. Interne en externe rotatie ligt beide rond de 50–55° (Millis en Levine, 2014) (Figuur 3).

HEUPDYSPLASIE BIJ KLEINE HONDENRASSEN

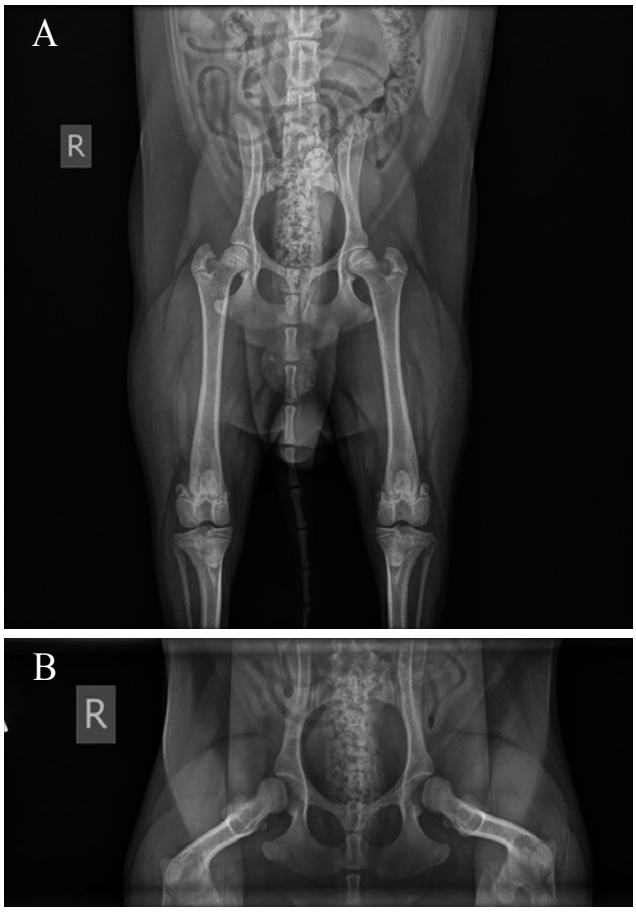
Heupdysplasie wordt het meest gezien bij grote en reuzerassen, maar kan in principe bij elk ras voorkomen (Witsberger et al., 2008; Smith et al., 2012). Heupdysplasie werd reeds gediagnosticeerd bij kleine of middelgrote rassen, zoals de Tibetaanse terriër, de standaard- en dwergpoedel, de buldog, de mopshond, de dobermann pinscher, de Lhasa apso, de west highland high terriër, de shih tzu, de pekinees, de dwergkeeshond, de fox terriër, de boston terriër, de yorkshire terriër, de maltezer, de chihuahua, de mini-schnauzer, de beagle en de Amerikaanse cocker spaniël (Martin et al., 1980; Rettenmaier et al., 2002;



Figuur 5. Het uitvoeren van de Ortolani-test op de linkerheup wordt hier geïllustreerd aan de hand van foto's en bijhorende tekeningen die het effect op het heupgewricht demonstreren. A. Eerst wordt er een neerwaartse druk (pijl) uitgevoerd op de femur, waardoor een subluxatie van de heup veroorzaakt wordt. B. Terwijl de neerwaartse druk (pijl) wordt aangehouden, wordt de heup traag geabduceerd (gebogen pijl) tot een plop gevoeld wordt (uit: Syrcle, 2017).

Coopman et al., 2008; Witsberger et al., 2008; King, 2017). In Tabel 1 wordt een overzicht gegeven van de kleine en middelgrote hondenrassen die in de periode 2017-2019 gediagnosticeerd werden met heupdysplasie of heuplaxiteit bij de vakgroep Medische Beeldvorming en Orthopedie van de Kleine Huisdieren van de Faculteit Diergeneeskunde (UGent). Heupdysplasie veroorzaakt gewrichtsontsteking en secundaire osteoartrose, wat resulteert in verschillende gradaties van discomfort en immobiliteit. Tot op heden zijn de etiologie en pathogenese van deze aandoening nog steeds niet helemaal duidelijk. Er wordt ervan uitgegaan dat heupdysplasie het gevolg is van de interactie tussen multipele genen gecombineerd met bepaalde omgevingsfactoren. Het is duidelijk dat de klinische observatie van heuplaxiteit een sleutelrol speelt in de ontwikkeling van osteoartrose (Smith et al., 2012).

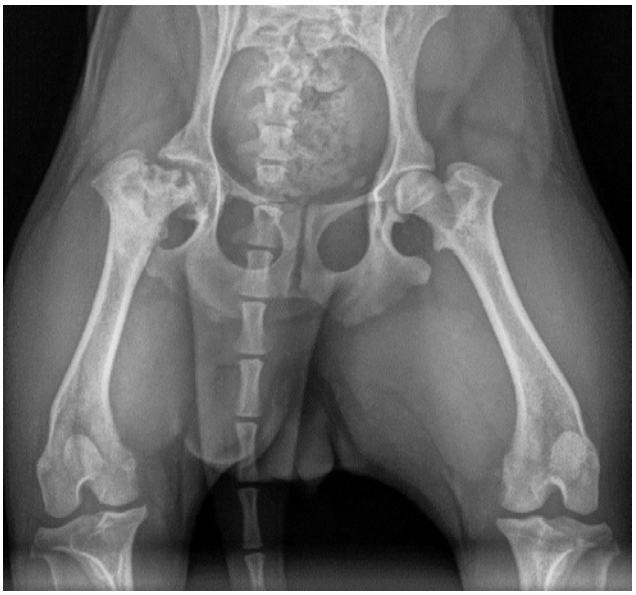
De klinische klachten gerelateerd aan heupdysplasie kunnen opgedeeld worden in twee groepen. De juveniele vorm waarbij de honden op een leeftijd van vijf tot twaalf maanden aangeboden worden met klachten ter hoogte van de achterhand, zoals manken, "bunny-hopping", moeilijk kunnen rechtstaan, niet willen wandelen, geen trappen willen lopen, een klik horen, etc. De klachten worden verondersteld het gevolg te zijn van ernstige heuplaxiteit. De tweede vorm waaronder heupdysplasie zich voordoet en die ook



Figuur 6. A. Ventrodorsale radiografische opname van de heupen van een sheltie van acht maanden oud. B. Ventrodorsale distractie-opname (door middel van het "Vezzoni-modified Badertscher distraction device") van dezelfde sheltie waarbij een laxiteitsindex van 0,66 (rechterheup) en 0,81 (linkerheup) werd berekend.

Tabel 1. Overzicht van kleine en middelgrote hondenrassen gediagnosticeerd met heupdysplasie of heuplaxiteit op de Faculteit Diergeneeskunde (UGent) in de periode 2017-2019.

Ras	Heupdysplasie	Heuplaxiteit
Beagle	1	1
Canis vulgaris	2	1
Cavalier king charles spaniël	4	1
Corgi	2	0
Dwergkeeshond	2	2
Engelse cocker	1	1
Engelse buldog	0	0
Franse buldog	4	0
Jack russell	2	1
Lhasa apso	1	0
Maltezer	3	0
Mopshond	3	0
Poedel	1	0
Sheltie	0	1
Teckel	0	1
Tibetaanse terriër	2	0



Figuur 7. Radiografisch beeld van een jack russel terriër van tien maanden oud met een Legg-Calvé-Perthes of avasculaire necrose van de femurkop aan de linkerzijde. Bemerk het typische "weggevreten" aspect van de femurkop in vergelijking met de tegenoverliggende zijde.

Figuur 8. Een hond waarbij een Ehmersling geplaatst werd na een succesvolle gesloten reductie van een heupluxatie (uit: Moores, 2006).

het meeste voorkomt, is de chronische vorm waarbij de volwassen hond klachten ontwikkeld ten gevolge van secundaire degeneratieve veranderingen (Smith et al., 2012; Syrcle, 2017).

Een grondig klinisch, orthopedisch en neurologisch onderzoek is steeds noodzakelijk om de diagnose van heupdysplasie correct te kunnen stellen en andere aandoeningen met een gelijkaardige klinische presentatie, zoals een kruisbandruptuur, te kunnen uitsluiten. Honden met heupdysplasie kunnen een abnormale stand vertonen, stijve gang, spieratrofie, verminderde beweeglijkheid van het heupgewricht en pijn bij manipulatie van de heup (Smith et al., 2012; Syrcle, 2017).

Vervolgens kan de diagnose van heupdyplasie bevestigd worden aan de hand van ventrodorsale radiografie met de heupen in extensie (Figuur 4). Heuplaxiteit kan getest worden aan de hand van de test van Ortolani (Figuur 5) of de Barden-test (Smith et al., 2012; Syrcle, 2017). Een andere mogelijkheid om heuplaxiteit te diagnosticeren is door middel van stressradiografie, waarbij er gebruik gemaakt wordt van een "distraction device" (Figuur 6). De distractie-index of laxiteitsindex die vervolgens kan berekend worden is een waarde tussen 0 en 1, waarbij 0 een volledig congruent heupgewricht betekent en 1 luxatie van het gewricht. Het correct uitvoeren van deze stressradiografie en/of de Barden- of Ortolanitest vereisen een (diepe) sedatie (Smith et al., 2012; Broeckx et al., 2018) (Figuur 4, 5, 6).

LEGG-CALVÉ-PERTHES

Legg-Calvé-Perthes wordt ook soms avasculaire necrose of aseptische necrose van de femurkop genoemd. Er treedt dus avasculaire necrose van de femurkop op die gekarakteriseerd wordt door een niet-inflammatoire lokale ischemie en daardoor ontstaat er een vervorming van de femurkop en -nek (Towle en Breur, 2018).

De aandoening Legg-Calvé-Perthes komt meestal voor bij kleine hondenrassen, waarbij miniatuurrassen en terriërs gepredisponeerd zijn (Demko et al., 2005; Towle en Breur, 2018). Aangezien er een duidelijke raspredispositie is, zijn er indicaties dat een erfelijke factor aan de basis van de aandoening ligt. Bijvoorbeeld bij de minipoedel en de west highland white terriër wordt deze aandoening autosomaal recessief overgeërfd. Ook bij manchester terriërs is de erfelijkheid van deze aandoening bekend. (Towle-Millard en Breur, 2018)

De meeste patiënten worden aangeboden met klachten rond de leeftijd van vier tot elf maanden. In 12 tot 16,5% van de gevallen komt de aandoening bilateraal voor. Mannelijke en vrouwelijke dieren hebben even vaak de aandoening (Demko en McLaughlin, 2005; Towle-Millard en Breur, 2018). In milde gevallen kan de aandoening subklinisch zijn. In meer ernstige gevallen ontstaan er klachten van manken die kunnen variëren van intermitterend manken tot het lopen op drie poten. Bij het orthopedisch onderzoek kan er pijn opgemerkt worden bij flexie en/of extensie van het heupgewricht en eventueel ook crepitatie waargenomen worden (Towle-Millard en Breur, 2018). De diagnose kan vervolgens bevestigd worden aan de hand van een ventrodorsale radiografische opname (Figuur 7). Vroege radiografische veranderingen zijn een verhoogde opaciteit van de laterale epifyseale zone van de femurkop en focale lyse van het bot. In een later

stadium is er afplatting van de femurkop gecombineerd met een gemotteld aspect van de femurkop waar te nemen. Dit evolueert verder naar collaps van de femurkop en verdikking van de femurnek en finaal naar een fractuur van de femurnek (Demko en McLaughlin, 2005). Belangrijke differentiaaldiagnoses zijn infectie en neoplasie maar ook knieproblemen, zoals een ruptuur van de voorste kruisband of patellaluxatie, kunnen gelijkaardige klinische klachten veroorzaken.

Bij voorkeur wordt een chirurgische behandeling aangeraden, aangezien een conservatieve behandeling met rust en pijnmedicatie slechts succesvol is in minder dan 25% van de gevallen. Chirurgische behandeling aan de hand van een femurkop- en nekexcisie of een heupprothese geeft een gunstig resultaat in 84 tot 100 % van de gevallen (Demko en McLaughlin, 2005; Towle-Millard en Breur, 2018).

HEUPLUXATIE

Luxatie van de heup treedt bij de hond meestal unilateraal op ten gevolge van een extern trauma. In 59 tot 83% van de gevallen is dit te wijten aan een aanrijding door een voertuig (DeCamp et al., 2016). Wanneer een hond aangeboden wordt met luxatie is het dan ook zeer belangrijk om na te gaan of er concomitante verwondingen zijn aan het bekken, het sacrum of inwendige structuren zoals de blaas. Door de verplaatsing van de femurkop is op zijn minst een gedeelte van het gewrichtskapsel en ligamentum capitis femoris gescheurd. Bij meer uitgesproken trauma kan er eveneens schade zijn aan de gluteus spieren of het gewrichtskraakbeen van de femurkop en/ of het acetabulum. De typische algemene klachten van deze honden zijn tekenen van pijn, een abnormale stand van het achterste lidmaat, crepitatie bij manipulatie en een verminderde of abnormale beweeglijkheid van het heupgewricht.

In de overgrote meerderheid van de gevallen (78% van de honden) treedt er craniodorsale luxatie op, waarbij de femurkop zich craniaal en dorsaal van het acetabulum bevindt (DeCamp et al., 2016). Door deze verplaatsing kan een aantal typische bijkomende uitwendige symptomen opgemerkt worden: het lidmaat wordt korter, er ontstaat een adductie van het dijbeen met een inwaartse rotatie van de knie en een uitwaartse rotatie van de tarsus.

Andere mogelijke luxaties komen slechts in uitzonderlijke gevallen voor. Caudodorsale luxatie is waarschijnlijk eerder een craniodorsale luxatie met een hoge graad van instabiliteit en ventrale luxatie kan geassocieerd zijn met een indeukingsfractuur van het acetabulum. Deze klinische diagnose kan bevestigd worden door middel van een radiografische opname. Hierbij is het van belang om na te gaan of er concomitante verwondingen aanwezig zijn of factoren die een gesloten reductie van de luxatie zouden bemoeilijken of onmogelijk maken, zoals een fractuur van het acetabulum, een fractuur ter hoogte van de femurkop of de femurhals en onderliggende heupdysplasie.

Figuur 9. Chihuahua met bilaterale heupdysplasie die na zeer beperkt trauma zijn rechter heup luxeerde. Let op de typische craniodorsale positie van de femurkop. Wegens de onderliggende dysplasie is conservatieve behandeling hier niet mogelijk.

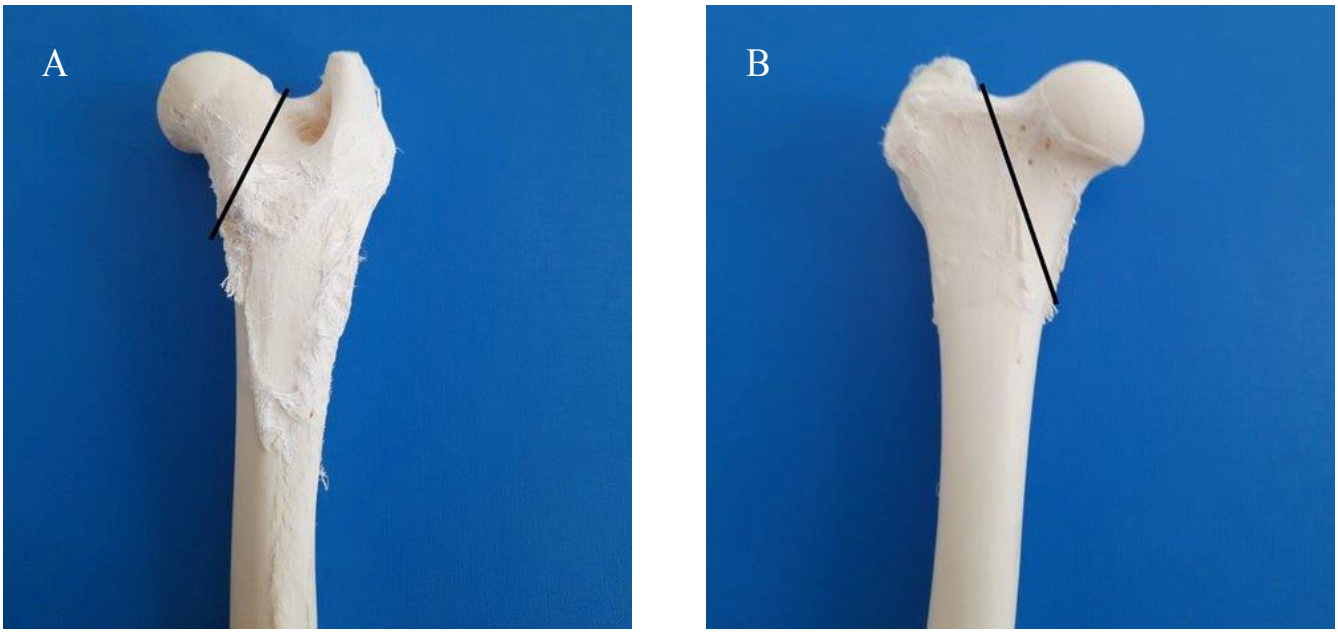
Gesloten reductie kan geprobeerd worden binnen de eerste vier à vijf dagen na het optreden van de heupluxatie. Deze reductie wordt uitgevoerd onder algemene anesthesie en het succespercentage na één poging bedraagt ongeveer 50% (DeCamp et al., 2016). Afhankelijk van de verwachte mobiliteit van de hond kan postoperatief een Ehmersling geplaatst worden (Figuur 8). In ongeveer 43% van de gevallen treedt er reluxatie op na een initieel succesvolle reductie en is een chirurgische ingreep zoals een open reductie, heupprothese of femurkopexcisie noodzakelijk (Schlag et al., 2019) (Figuur 9).

CHIRURGISCHE OPTIES

Wanneer honden met klinische symptomen niet reageren op een conservatieve behandeling kan een chirurgische interventie uitkomst bieden. Vroeger was de enige chirurgische behandeling van een heupprobleem bij kleine hondenrassen een femurkop en -nekexcisie. Een fermurkop en -nekexcisie bij miniatuur- en kleine hondenrassen wordt beschouwd als betrouwbaarder met een klinisch betere uitkomst dan bij grote hondenrassen (Lippincott, 1992).

Femurkop en -nekexcisie (FNE)

Een FNE-procedure wordt beschouwd als een “salvage” procedure, waarbij het doel is om bot-op-bot-



Figuur 10. A. Lateraal en B. mediaal zicht van de ostectomierichting bij een femurkop- en nekexcisie op een anatomisch preparaat.

Figuur 11. Femurkop- en nekexcisie van het rechter heupgewricht bij een cavalier king charles. Bemerk de uitgesproken secundaire degeneratieve veranderingen van het linker heupgewricht.

contact tussen femurkop en acetabulum te beperken (Harper, 2017). Er wordt een vals gewricht gevormd (pseudoartrose) bestaande uit dens fibreus weefsel. Door een FNE wordt pijn secundair veroorzaakt door osteoartrose opgeheven en verhoogt de levenskwaliteit. In principe kan een FNE uitgevoerd worden bij kleine hondenrassen van elke grootte, echter geldt dat hoe kleiner de patiënt hoe beter het resultaat zal zijn (Duff en Campbell, 1977). De belangrijkste motivatie voor een eigenaar om voor een FNE te kiezen zijn financiële beperkingen en de kans op erge complicaties bij een heupprothese. De belangrijkste aandachtspunten bij het uitvoeren van deze techniek zijn:

- De heup moet geluxeerd kunnen worden. Hierbij kan het nodig zijn om het ligamentum capitis femoris door te halen met een “Hatt spoon” of mayoweefselschaar.
- Het craniale oppervlak van de proximale femur moet zichtbaar zijn om een correcte ostectomie te kunnen uitvoeren. Hiervoor moet de poot 90° extern geroteerd worden zodat het craniale oppervlak van de femur parallel met de tafel is en de patella naar het plafond gericht is.
- De ostectomie wordt uitgevoerd op de lijn tussen de femurnek en de femurmetafyse; het begin is juist mediaal van de trochanter major en is dan naar caudomediaal gericht om juist proximaal van de trochanter minor te eindigen (Vezzoni en Peck, 2018) (Figuur 10A en B). Na verwijdering van de femurkop en -nek wordt de zaagsnede gepalpeerd op onregelmatigheden. Frequent wordt een schel van de femurnek aan het caudale oppervlak van de femur gevonden, omdat de zaag loodrecht op de chirurgietafel wordt geplaatst. Deze kan schuren tegen de acetabulumrand, waardoor de vorming van fibrous weefsel tussen de botten (“pseudoartrose”) kan worden verhinderd. Onregelmatigheden kunnen weggenomen worden met een rongeur of botrasp. Het is belangrijk de poot proximaal en distaal te bewegen om aanwezigheid van crepitatie te kunnen detecteren.
- Postoperatief wordt radiografisch nagegaan of er voldoende femurnek is weggenomen en of er geen fracturen zijn ter hoogte van de trochanter major of femur (Figuur 11).

Een FNE kan bilateraal worden uitgevoerd, waarbij idealiter de tweede zijde na acht à tien weken wordt uitgevoerd. Echter, in geval van erge bilaterale heupdysplasie (HD) kunnen beide zijden tijdens eenzelfde anesthesie ook simultaan uitgevoerd worden. In een studie van Rawson et al. (2005) met vijftien honden (19-30,9kg) die een bilaterale FNE ondergingen ten gevolge van erge bilaterale HD werd aangetoond dat alle honden vier dagen postoperatief terug konden stappen.

In tegenstelling tot de meeste orthopedische ingrepen zijn strikte hokrust en beperkte activiteit tegenaangewezen na een FNE. Het is aangeraden dat patiënten die een FNE hebben ondergaan, zo snel en frequent mogelijk de geopereerde poot gebruiken om de beweeglijkheid van het heupgewricht te bevorderen en spieratrofie te vermijden. Multimodaal postoperatief pijnmanagement is hier zeer belangrijk. Naast een niet-steroïdaal anti-inflammatoir geneesmiddel en andere analgetica is een georganiseerd rehabilitatieprogramma essentieel.

De belangrijkste complicaties die gezien worden bij een FNE zijn verkorting van de poot, beschadiging van de ischiadicuszenuw, patellaluxatie, spieratrofie, verminderde beweeglijkheid van de heup en de aanwezigheid van pijn en manken.

Heupprothese

Een heupprothese is een algemeen aanvaarde chirurgische techniek voor coxofemorale osteoartrose bij grote hondenrassen. Het vermindert pijn ter hoogte van het aangetaste heupgewricht en bevordert het functioneren ervan met gerapporteerde succespercentages van 92-98% (Olmstead et al., 1983). Met de ontwikkeling van een miniatuurheupprothese-systeem wordt een heupprothese ook toegankelijk voor miniatuur- en kleine hondenrassen en kan een degelijk alternatief aangeboden worden voor conservatieve therapie en FNE. In een studie van Warnock et al. (2003) werd het gebruik van het “Cemented BioMedtrix Modular MPS System” bij zeventien honden van 12 tot 25kg onderzocht. Er werd gebruik gemaakt van een maat 4 cobalt-chroom-femurstem, een 18mm-diameter acetabulumcup en een 12mm-femurkop. Tijdens chirurgie traden er vijf complicaties op: iatrogene fissuur van de proximale femurcortex, perforatie van de acetabulaire cortex en verplaatsing van de acetabulaire cup na cementering. Er werd een succespercentage van 83% genoteerd (goed tot excellent). De belangrijkste postoperatieve complicaties (bij 22% van de gevallen) waren craniodorsale luxatie, acetabulaire cupverplaatsing en aseptische loslating van het femur implantaat.

Sinds 2005 is het “BioMedtrix Modular Micro THR Implantation System” beschikbaar voor kleine honden en katten (<12kg). In een studie van Liska (2010) werd dit systeem toegepast bij 49 honden en 8 katten van 2 tot 15kg. Er waren twee femurstemmaten beschikbaar (nr 2 en 3). Er was een acetabulumcup van polyethyleen met ultrahoog moleculair gewicht, met een 12, 14, of 16 mm-buitendiameter en een 8 mm-binnendiameter beschikbaar en er werd een femurkop van 8mm gebruikt. Er werd een succespercentage van 91% genoteerd. Intra- of postoperatieve complicaties traden op bij 18% van de dieren en waren voornamelijk luxaties. In een studie van Marino et al. (2012) werd tot gelijkaardige conclusies gekomen (Marino et al., 2012).

Voor miniatuurrassen werd in 2011 een nanoheupprothesesysteem beschreven voor twaalf honden van 2,5 tot 5,9kg. (Ireifej et al., 2012) Bij dit systeem vormde de stem één geheel met een 6mm-femurkop en articuleerde met een 10mm-acetabulumcup, gemaakt van cobalt-chroom en polyethyleen met ultrahoog moleculair gewicht. Voor alle twaalf honden werd uiteindelijk een goed tot excellent resultaat bekomen, alhoewel er bij 33% ook significante postoperatieve complicaties waren, namelijk femurfractuur en verplaatsing van de acetabulum component.

FYSIOTHERAPIE - MANAGEMENT VAN HEUPDYSPLASIE

Fysiotherapie kan zowel toegepast worden als postoperatieve ondersteuning of als conservatieve behandeling. Zoals reeds besproken zijn de femurkop- en -nekexcisie en de heupprothese de belangrijkste chirurgietechnieken voor de behandeling van een heuppathologie bij kleinere hondenrassen. Fysiotherapie zorgt voor een postoperatieve ondersteuning en bevordert het herstel van patiënten die dergelijke chirurgie ondergingen.

Het eerste doel van het rehabilitatieproces is gericht op de beheersing van pijn en ontsteking. Bij een heupprothese geldt een strikte bewegingsbeperking gedurende de eerste vier tot zes weken van de herstelperiode (Millis en Levine, 2014). Tijdens de eerste drie weken na de operatie is het toedienen van aangepaste medicatie, zoals NSAID’s, aangewezen.

Opioïden, zoals tramadol, kunnen de eerste drie tot zeven dagen postoperatief bijkomstig aangewend worden. Cryotherapie, die toegepast wordt om postoperatieve ontsteking te temperen, induceert vasoconstrictie en zorgt voor een verminderde doorbloeding en zwelling, verminderde enzymatische weefselschade en pijnstilling. “Cold-packs” dienen gedurende de eerste 24 tot 48 uur om de vier uur gedurende twintig minuten op de operatiewonde aangebracht te worden (Millis en Levine, 2014).

Het tweede doel van het rehabilitatieproces is gericht op het verbeteren van de beweeglijkheid en het bewegingsbereik (“range of motion”) van de heup. De manuele therapieën massage en stretchen zijn hiervoor aangewezen. Passieve “range of motion” (PROM) is een veelgebruikte techniek, waarbij het gewricht een maximale fysiologische beweging uitvoert zonder

spierspanning te gebruiken. Deze techniek kan uitgevoerd worden in de initiële postoperatieve fase van elke bovenvermelde chirurgie en eveneens tijdens het ontwaken na een femurkop en -nekexcisie (Millis en Levine, 2014).

Het herstel van de functionaliteit van de poot is het derde doel van het rehabilitatieproces. Om functioneel herstel te bewerkstelligen, dient de patiënt actieve oefeningen uit te voeren. De moeilijkheidsgraad van dergelijke oefeningen dient geleidelijk opgedreven te worden gedurende de eerste drie maanden na chirurgie (Millis en Levine, 2014). Initiële oefeningen tijdens de postoperatieve fase zijn onder andere geassisteerd stappen, gecontroleerde lage-impactoefeningen, zit-sta-oefeningen en evenwichtsoefeningen. Voor een femurkop en -nekexcisie ligt de nadruk op een goede extensie van de heup, hetgeen bekomen wordt door dansoefeningen en wandelen op hellingen. Gedurende de tweede fase van het herstel worden oefeningen in de onderwaterloopband aangeraden voor elk type heupoperatie (Millis en Levine, 2014).

Alle bovenvermelde behandelingen kunnen ook als conservatieve therapie ingezet worden. Additioneel kunnen lasertherapie, ultrasoontherapie, thermotherapie, elektrische stimulatie (TENS), voedingssupplementen (voornamelijk chondroprotectiva en omega-3 vetzuren) en een aangepast dieet opgenomen worden in het behandelingsplan (Millis en Levine, 2014).

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ESCCAP-wormbestrijding bij hond en kat

Herziene 6e druk Richtlijn 1

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Dit jaar verscheen een nieuwe, herziene druk van de meest gedownloade richtlijn van de ESCCAP (European Counsel Companion Animal Parasites) over worminfecties bij hond en kat (www.esccap.eu). Een update van een richtlijn wordt door een commissie van drie ESCCAP-leden voorbereid waarna alle leden uit de verschillende Europese landen hun commentaar op de tekst mogen leveren. Op basis van deze feedback wordt een definitieve versie opgemaakt, die daarna in de verschillende landstalen vertaald wordt. Deze procedure neemt snel langer dan een jaar in beslag.

Wat is nieuw?

Hierna worden de meest opvallende veranderingen besproken. Het begint met een aanpassing van de indeling per groep van relevante intestinale en niet-intestinale wormen die praktischer van opbouw en volgorde is dan in de vorige druk.
Na de spoelwormen worden de lintwormen, *Dirofilaria* spp., *Angiostrongylus vasorum*, haakwormen en zweepwormen besproken. De aanwezigheid van *Echinococcus granulosus* (kleine hondenlintworm), *E. multilocularis* (vossenlintworm), *Dirofilaria immitis* (hartworm) en *D. repens* (subcutane worm) op de kaart van Europa is weer geactualiseerd en van alle parasieten zijn de levenscycli nu grafisch weergegeven. Deze cycli zijn ook allemaal, individueel van de ESCCAP-website te downloaden voor eigen gebruik (www.esccap.org) (Figuur 1).
Vanzelfsprekend zijn sommige wormen belangrijker dan andere, afhankelijk van de prevalentie, het ziekteverwekkend vermogen bij de gastheer, eventueel potentieel zoönotisch karakter of een combinatie van deze factoren.

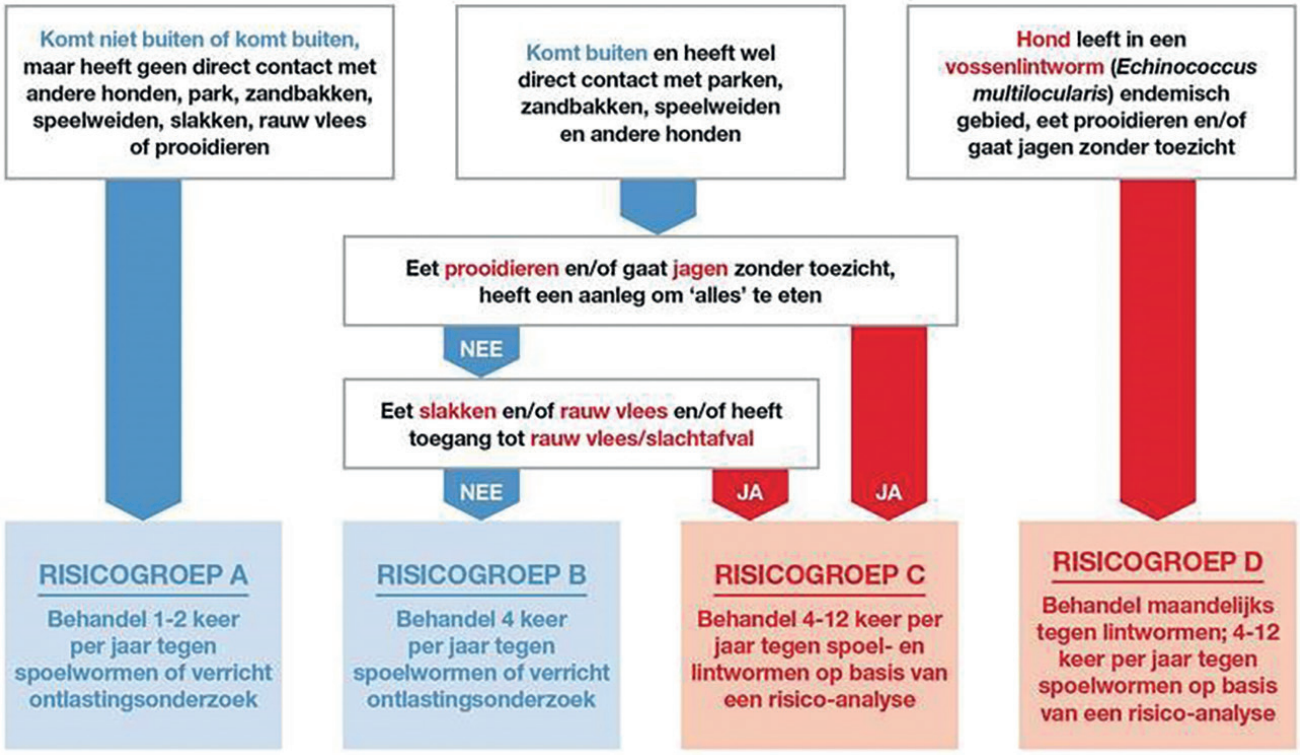
Informatieve tabellen

Daarnaast is meer gedetailleerde informatie opgenomen in een groot aantal tabellen. Dit betreft gegevens over de verschillende wormsoorten zoals (pre) patentperiode, infectieuze stadia, de besmettingsweg, verspreiding in Europa en de eindgastheer. Ook geven de tabellen een overzicht van de risicofactoren voor het oplopen van worminfecties bij hond en kat zoals levensstadium (jonge dieren, lactatie, zwerfgeschiedenis), gezondheid (aanwezigheid van vlooien of luizen), omgeving (kennels, buitenshuis), voeding (predatie knaagdieren, vogels, amfibieën, reptielen, slakken of rauw vlees), locatie of reizen. De laatste tabellen geven informatie over de klinische symptomen, te onderzoeken materiaal voor diagnostiek en diagnostische technieken.

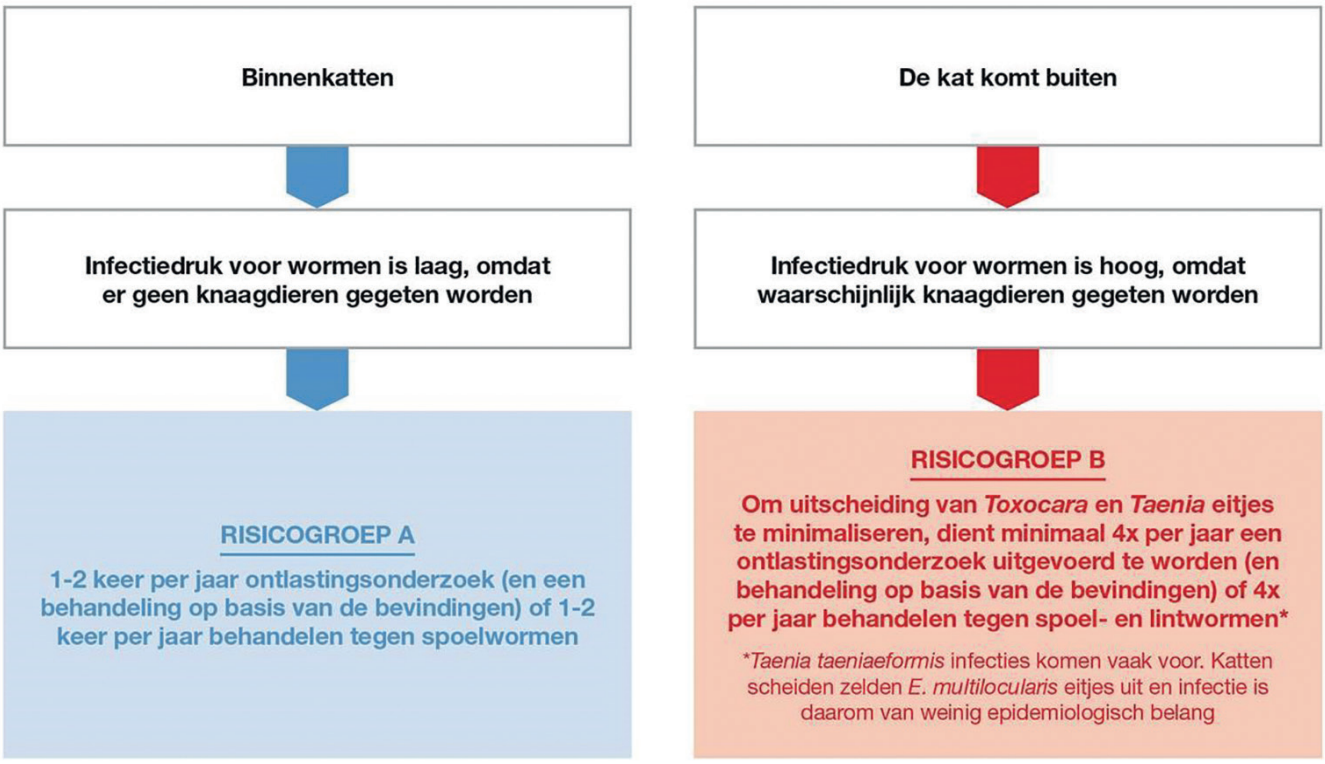
Stappenplan ontworming

Veel tijd is besteed aan de ontwikkeling van een logisch en overzichtelijk stappenplan voor de adviezen met betrekking tot het hoe vaak en wanneer ontwormen van honden en katten. In de nieuwe richtlijn is deze nu uitgesplitst voor hond (4 risicogroepen) en kat (2 risicogroepen).
Het toekennen van een bepaalde risicogroep en bijbehorende ontwormingsfrequentie is afhankelijk van de factoren zoals leeftijd, wel of niet buiten komen, het eten van prooidieren, slakken of rauw vlees en het leven in vossenlintworm-endemisch gebied. Daarbij heeft de in Benelux al enkele jaren gebruikte beslisboom als voorbeeld gediend.

Figuur 1. De nieuwe ESCCAP Richtlijn 1



Figuur 2. Beslisboom voor de ontworming van de hond.

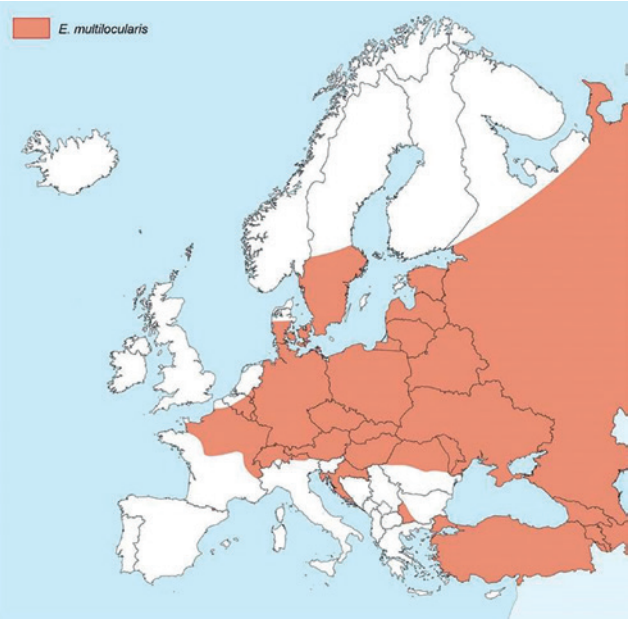


Figuur 3. Beslisboom voor de ontworming van de kat.

Het basisadvies blijft gehandhaafd om bij voorkeur op basis van de resultaten van een regelmatig uitgevoerd fecesonderzoek te ontwormen en ontworming niet routinematig toe te passen. Als er wel routinematig wordt ontwormd kan de frequentie hiervan verlopen volgens de beslisboom.
Vanzelfsprekend beschermt dit niet tegen patente infecties die tussendoor ontstaan. Er wordt duidelijk geadviseerd om ontwormen alleen te laten plaatsvinden op advies van de dierenarts. De reden hiervoor is dat deze het beste kan inschatten welke ontwormingsfrequentie bij een bepaald dier past en geadviseerd dient te worden (Figuur 2 en 3).

Wisselende interpretatie van sommige adviezen

Toch zijn er door het consensusmodel met input van vele landen in de richtlijn, adviezen vermeld die in de Benelux niet of minder gangbaar zijn. Bijvoorbeeld het advies om honden en katten die in huis leven met kinderen jonger dan vijf jaar of met personen met een verminderde afweer routinematig maandelijks te ontwormen, afhankelijk van een risicoanalyse of op basis van de bevindingen van fecesonderzoek. Dit heeft te maken met de preventie van patente *Toxocara*-infecties bij hond/kat in het kader van de volksgezondheid. Er wordt echter de suggestie gewekt dat honden en katten een groter risico lopen op een (patente) wormінfectie als ze in dergelijke huishoudens wonen. Dat is natuurlijk niet het geval en andersom is het ook niet zo dat het maandelijks ontwormen de kinderen gaat beschermen tegen *Toxocara*-infectie. Deze zoönose wordt namelijk niet opgelopen door direct contact met hond of kat en zelfs niet door onverhoopt contact met de “verse” ontlasting van besmette dieren. De eitjes hebben namelijk minimaal enkele weken nodig om te embryoneren en infectieus te worden. Het risico van het opnemen van *Toxocara*-eitjes door vachtcontact is door gedegen onderzoek in Nederland en Ierland ook ontkracht. Dit kan hoogstens een rol spelen bij direct contact met zwerfhonden en met name de pups hiervan. Alleen wanneer uit de risicoanalyse blijkt dat *Toxocara*-besmetting aanwezig kan zijn en de aanwezige dieren in de tuin defeceren waarin de kinderen spelen en de ontlasting niet wordt verwijderd (risicoanalyse), is een dergelijk advies zinvol.
Als er een *Echinococcus*-lintworm aanwezig is, dan is besmetting door vachtcontact wél mogelijk omdat deze eitjes direct infectieus zijn. Niet elk anthelminthicum is echter werkzaam tegen lintwormen.
Kinderen worden vooral besmet door grondcontact waarin zich geëmbryoneerde *Toxocara*-eitjes bevinden. Parken, speelweiden en niet-afgesloten zandbakken worden hierop wereldwijd positief bevonden.



Figuur 4. Prevalentie van de vossenlintworm in Europa.

Een ander nieuw advies dat ook afwijkt van het advies in de Benelux, is om hond en kat routinematig te ontwormen tegen *Taenia*-lintwormen. De ESCCAP-ontwormingsadviezen zijn van oorsprong bedoeld om gastheren te beschermen tegen pathogene infecties zoals de Franse hartworm en/of tegen zoönotische infecties zoals *Toxocara* spp. of *Echinococcus* spp. *Taenia*-lintwormen zijn noch pathogeen voor hond of kat, noch voor de mens en komen bovendien zelden voor. Sporadisch wordt er gemeld dat grote aantallen darmobstipatie kunnen veroorzaken, maar dit is geen reden om standaard tegen lintworm te ontwormen. Pas als *Taenia*-lintwormen worden waargenomen of in een gebied dat enzoötisch is voor de vossenlintworm, is ontworming zinvol (Figuur 4).
In de Engelse versie wordt vermeld dat drachtige teven vanaf de veertigste dag van de dracht ook preventief ontwormd kunnen worden. Naast het feit dat hiervoor geen producten zijn geregistreerd in de Benelux, wordt dit ook niet door ESCCAP Benelux geadviseerd omdat het behandelen duur en bewerkelijk is, er geen sluitend wetenschappelijk bewijs is en pups tot het spenen iedere twee weken ontwormd dienen te worden tegen *Toxocara canis*.

GEBRUIK VAN LINCOMYCINE TEGEN RATTENPLAAG?

VRAAG

Kan lincomycine gebruikt worden als hulpmiddel bij de bestrijding van een rattenplaag?

ANTWOORD

Lincomycine behoort tot de groep van de lincosamiden en zijn monoglycoside antibiotica. Het wordt geproduceerd door *Streptococcus lincolnensis* en werd ontdekt in de jaren vijftig van de vorige eeuw. Lincomycine heeft een bacteriostatische antibacteriële werking bij gevoelige bacteriën. Het zorgt namelijk voor inhibitie van de proteïnesynthese ter hoogte van de 50S ribosomale subunit (Riviere en Papich 2018).

In België is lincomycine op de markt voor de behandeling van huidinfecties, respiratoire, articulaire infecties en spijsverteringsaandoeningen. Er bestaan zowel parenterale als orale formulaties voor veterinair gebruik. De orale toediening gebeurt via het drinkwater (BCFIvet).

In de humane geneeskunde wordt het middel enkel bij ernstige infecties toegediend omdat het zowel na orale als parenterale toediening aanleiding kan geven tot pseudomembraneuze colitis door proliferatie van *Clostridium difficile* en dit kan leiden tot de dood (BCFI).

Hetzelfde fenomeen kan optreden bij dieren met een fermenterend gastro-intestinaal stelsel, zoals paarden, herkauwers, konijnen, cavia's en hamsters. De gastro-intestinale overgroei van *Clostridium* kan aanleiding geven tot ernstige enteritis, enterocolitis, diarree en uiteindelijk zelfs de dood (Riviere en Papich 2018).

Een dergelijke gevoeligheid werd echter nog niet beschreven in het geval van ratten. Hoewel ratten ook einddarmfermenteerders zijn, bedraagt de acute orale LD50 (letale dosis voor 50% van de dieren) 5000mg/kg lichaamsgewicht. Ratten blijken dus ongevoelig te zijn voor de microbiële veranderingen in het maagdarmstelsel. Zelfs na langdurige blootstelling (één, drie en twaalf maanden) aan een dosis van 300mg/kg lichaamsgewicht werden geen geneesmiddel-gerelateerde weefselveranderingen waargenomen (EMEA, 1998).

Indien lincomycine volgens de bijsluiter wordt toegediend aan varkens of kippen bedraagt het gehalte aan lincomycine in water ongeveer 100mg/l – 400mg/l. Voor een rat van 200mg zou dit dus betekenen dat het dier minstens 2,5 liter water zou moeten drinken.

Daarnaast is het in het licht van de problematiek van antibioticumresistentie volledig tegenaangewezen om antibiotica te gebruiken voor andere doelstellingen dan de behandeling van infectieuze aandoeningen veroorzaakt door gevoelige bacteriën. Ieder antibioticumgebruik leidt onvermijdbaar tot resistentieselectie, deels bij de pathogenen waartegen men het antibioticum inzet en zeker bij de vele commensale bacteriën in het lichaam van ieder dier. Het oneigenlijk gebruik van antibiotica voor welke reden dan ook zal dus ook tot resistentieselectie leiden in de bacteriële populaties aanwezig bij de blootgestelde dieren en op die manier bijdragen tot de opbouw van een reservoir van resistente bacteriën en resistentiegenen in de omgeving.

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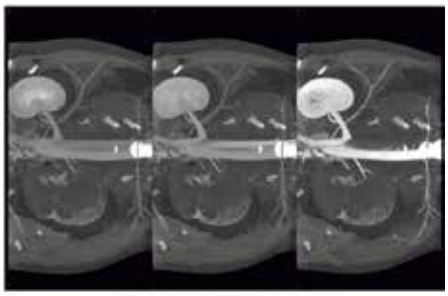

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