







Neutering is not associated with early-onset urethral obstruction in cats

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Abstract

Objectives The purpose of this study was to evaluate the correlation between clinical aspects and urethral lesions with reproductive status and age at neutering in obstructed male cats.

Methods All cats with compatible signs of urethral obstruction (UO) treated at the Veterinary Hospital of the Federal Rural University of Pernambuco from 2019 to 2021 were divided into three groups according to their reproductive status: intact; prepubertal neutered; and post-pubertal neutered. Cats with compatible signs of UO were selected for further analysis. Age, clinical signs, age at neutering and age of the first obstructive event were documented. Cats with recurrent obstructive urinary signs or urethral trauma that made catheterization impossible were referred for perineal urethrostomy. The morphology of the excised penises was assessed by histopathological analysis.

Results Of 84 cats with signs of UO included in this study, 28.6% were classified as intact, 28.6% as prepubertal neutered and 42.8% as post-pubertal neutered. Intact cats had a significantly earlier onset of UO compared with prepubertal and post-pubertal neutered cats, as seen by the age at obstruction (3.6 vs 5.7 and 5.5 years, respectively). Similar clinical signs and histopathological lesions were observed in all groups. The main clinical signs observed were stranguria, hematuria and pollakiuria. All cats had some degree of injury in the penile urethra. The most common lesions were hemorrhage, fibrosis and congestion.

Conclusions and relevance It appears that intact cats had an earlier onset of UO than neutered cats, regardless of age at neutering. Urethral histopathological lesions and clinical signs were similar in both groups. Pediatric neutering represents a useful tool in the control of abandoned and stray animals and the consequent dissemination of zoonoses, thus having a positive impact on public health.

Keywords: Urethral catheterization; castration; orchiectomy; prepubertal neutering

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Introduction

Urethral obstruction (UO) is a medical emergency. Without immediate intervention, acute kidney failure, with associated acid–base and electrolyte imbalances, can be life threatening.^{1–3} This condition may reoccur, despite appropriate medical management.^{4,5} The most common signs described are dysuria, stranguria and hematuria. Additional signs such as anorexia and vomiting may occur with the onset of uremia.² The severity of the clinical signs depends on the completeness and duration of the UO.⁶

The origin of the UO may be due to the presence of masses (plugs) or uroliths, anatomical defects in the

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urethra⁷ and edema or fibrosis¹ due to repetitive urethral catheterization.^{8,9} Another potential cause of obstruction is feline idiopathic cystitis (FIC), leading to a functional obstruction.^{10,11} It is suggested that cats with FIC have an imbalance between the sympathetic nervous system and the hypothalamic–pituitary–adrenal axis, resulting in the release of inflammatory mediators within the lower urinary tract. This can lead to edema, pain and smooth muscle spasm.^{5,10} One study reported that FIC was the cause of UO in 53% of cats.⁴

Several studies have described risk factors for UO;^{7,12–14} some support neutering as a contributory factor^{12,13,15,16} while others do not.^{9,17,18} Another contradictory factor is age at neutering.¹¹ Prepubertal neutering (before spermatogenesis and sexual maturity)^{19–21} has historically been suggested to be a risk factor for an earlier onset of UO. It has been suggested that prepubertal neutering contributes to a smaller penis and narrower penile urethra, but this has subsequently been disputed.^{13,17,18,22–24}

Owing to the contradictory findings associated with feline UO, this study was designed to characterize the clinical aspects of the disease, the lesions in the urethra of obstructed cats and to correlate these findings to reproductive status and age at neutering.

Materials and methods

Clinical evaluation of animals and experimental groups

The study was carried out at the Veterinary Hospital and in the Physiology and Pathology Laboratories of the Federal Rural University of Pernambuco (UFRPE). The experimental protocol was approved by the Ethics Committee on the Use of Animals at UFRPE (under process no 23082.006865/2019-31). Only cats with a complete follow-up (ie, from diagnosis to UO resolution) at the veterinary hospital were included in the study.

This study was conducted between 2019 and 2021. All male cats with signs compatible with UO and large, firm and non-expressible urinary bladders were included in the study, and were allocated to one of three groups according to reproductive status and, if neutered, the age at which neutering occurred. Cats were classified as intact, prepubertal neutered (gonadectomy <7 months old) and post-pubertal neutered (gonadectomy >7 months old). Data were collected via questionnaires using face-to-face or telephone interviews with the cats' owners. In the clinical evaluation, the following data were recorded: age; body condition score (BCS; 1–9); diet; age at neutering; age at first obstructive event; clinical treatment provided; and number of obstructive events. Cats with recurrent obstructive urinary signs (at least two episodes) that did not respond to clinical treatment or with urethral trauma that made catheterization impossible were referred for perineal urethrostomy (Figure 1). The time to recurrence ranged from 15 days to 6 months.

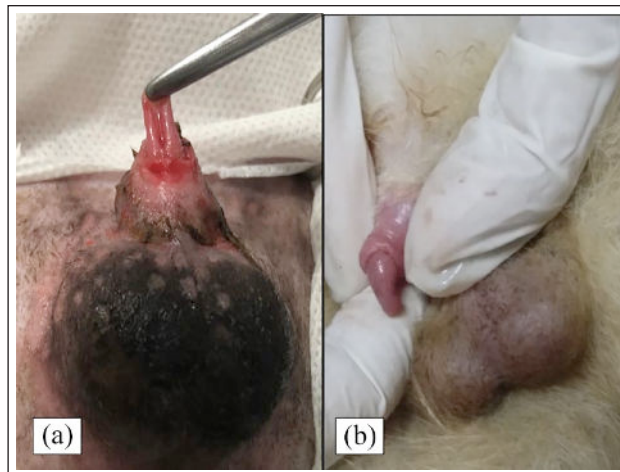


Figure 1 Penile lesions in cats due to traumatic catheterization. (a) Lacerative lesion in the glans and penile urethra. (b) Penis warped with ventral curvature

Perineal urethrostomy

All patients were clinically evaluated, placed on intravenous lactated Ringer's solution and submitted to surgery as previously described.²⁵ Briefly, the penis ventral ligament was transected, and the penis was dissected up to the bulbourethral glands. Next, the urethra was carefully incised 1 cm cranially to the bulbourethral glands, placed longitudinally and sutured to the skin through simple interrupted stitches.

The penile fragments obtained were stored in 10% formaldehyde for 24 h, washed in phosphate buffered saline for 1 h and kept in 70% ethanol until further histological processing.

Histopathological analyses

Penile fragments were cut transversely, and the most cranial portion (close to the bulbourethral glands) was kept for further analysis. Further, samples were embedded in paraffin, cut into 5 µm sections and stained with hematoxylin and eosin (HE) and Masson's trichrome.

The presence of hemorrhage, fibrosis, congestion and necrosis were assessed in HE-stained sections. Lesions were further classified as absent, mild (defined as <10% of tissue affected) or severe (defined as >10% of tissue affected).²⁶

In addition, the lesions were classified as acute when neutrophilic inflammation and edema were the predominant findings; chronic with lymphoplasmacytic infiltrate, neovascularization and fibrosis/fibroplasia; and chronic acute with the same characteristics of the chronic process with resurgence of neutrophils and appearance of congested vessels. The degree of obstruction of the urethral lumen was also evaluated as total, partial or dilated, where patients with total obstruction had complete stenosis of the lumen, partial obstruction where part of

the lumen was obstructed and dilated when there was no degree of stenosis. Fibrosis was further assessed by Masson's trichrome staining. Lesions were scored as 0–3 when fibrosis was as absent (0), mild (1), moderate (2) and intense (3).

Statistical analysis

The quantitative variables were expressed mean \pm SD; all were normally distributed. The assumption of normality was examined with the Kolmogorov–Smirnov test and all the data passed the normality test with a P value of 0.05. An unpaired Student's t -test was used for quantitative analysis (age at obstruction and score of fibrosis). For qualitative analyses, Fisher's exact test for two independent samples were used. All tests were conducted at an alpha = 0.05 level of significance.

Results

Of 84 client-owned male cats with signs of UO included in this study, 28.6% ($n = 24/84$) were classified as intact, 28.6% ($n = 24/84$) as prepubertal neutered and 42.8% ($36/84$) as post-pubertal neutered. Intact cats had a statistically significant earlier onset of UO compared with pre- and post-pubertal neutered cats, as seen by the age at obstruction (3.6 vs 5.7 and 5.5 years, respectively; $P < 0.05$) (Figure 2a). Furthermore, 87.5% ($n = 21/24$) of intact cats had an early age of UO onset (< 5 years), in contrast to only 54.2% ($n = 13/24$) of prepubertal and 55.6% ($n = 20/36$) of post-pubertal neutered cats (Figure 2b).

The most common clinical signs were stranguria, hematuria and pollakiuria (Figure 3a). Other clinical signs such as anorexia, dysuria, pollakiuria and anuria were also observed. Further details are given in Table 1 in the supplementary material. Most of the cats were fed dry food (Figure 3b). No intact cats were overweight (BCS > 6); however, 45.8% and 58.3% of pre- and post-pubertal neutered cats were overweight, respectively (Figure 3c).

Of all the cats treated for UO during this study, 34.5% ($n = 29/84$) underwent perineal urethrostomy. Of these,

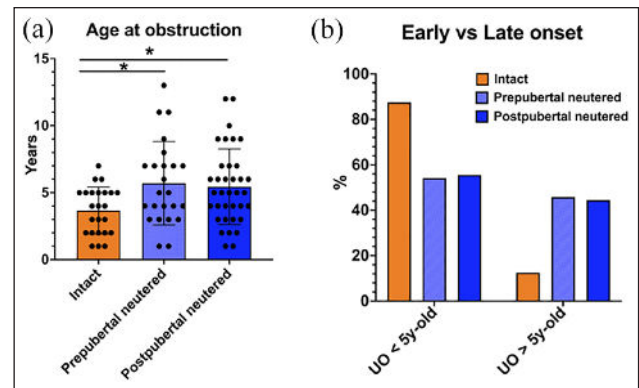


Figure 2 Onset of urethral obstruction (UO) in intact, prepubertal and post-pubertal neutered male cats. (a) Age of the cats at the day of the onset of UO. Intact: mean age 3.6 years (range 1–7); prepubertal neutered: mean age 5.7 years (range 1–13); post-pubertal neutered: mean age 5.4 years (range 1–12). Intact cats had a statistically significant earlier onset compared with neutered cats. (b) Percentage of cats with UO younger and older than 5 years of age. * $P < 0.05$

41.4% ($n = 12/29$) were intact, 24.1% ($n = 7/29$) were prepubertal and 34.5% ($n = 10/29$) were post-pubertal at the time of neutering.

There was no standard protocol of medical management and no difference in care between groups. Gabapentin was instituted in 75.8% ($n = 22/29$) of cases as an analgesic and tranquilizer. Non-steroidal anti-inflammatory drugs, antispasmodic drugs and antibiotics were also used in 62.1% ($n = 18/29$), 27.6% ($n = 8/29$) and 13.8% ($n = 4/29$) of cases, respectively. The four cats that received antibiotics had a positive urine culture (*Escherichia coli*). All cats that underwent urethrostomy had at least two urethral catheterizations prior to surgery. Immediately preoperatively, all patients had repeated and unsuccessful attempts at urethral catheterization.

Histopathological evaluation (Figure 4) of the penile urethra showed that all animals, regardless of the

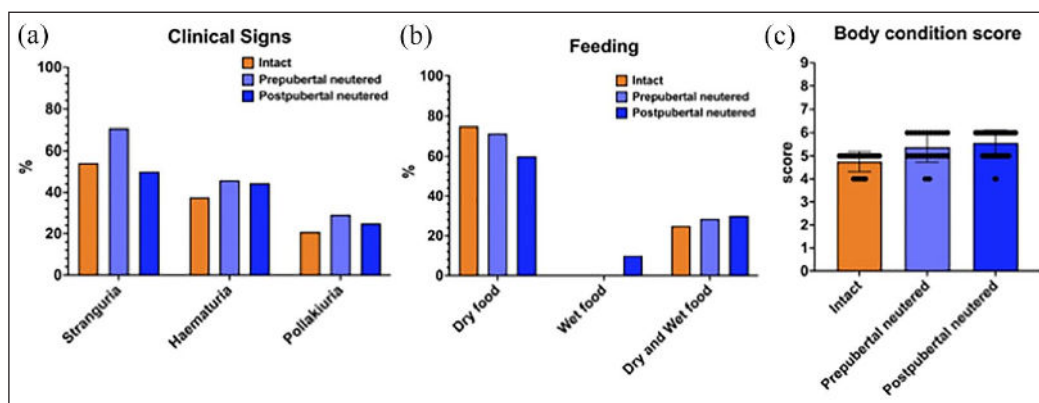


Figure 3 Clinical evaluation and history of intact, prepubertal and post-pubertal neutered male cats with urethral obstruction: (a) clinical signs; (b) type of feeding; and (c) body condition score

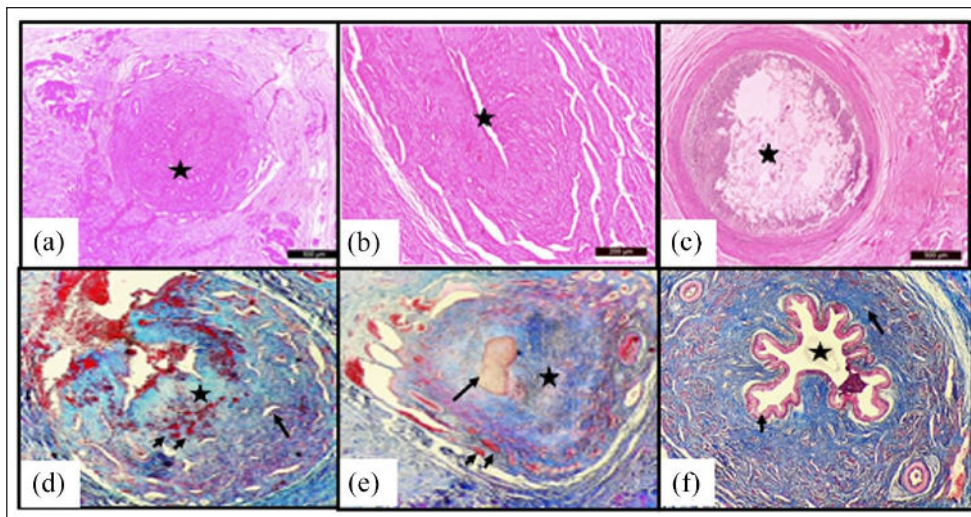


Figure 4 Representative histological images of the penile urethra of obstructed cats ($\times 50$; cross section). (a) Penile urethra with acute chronic inflammatory process and total obstruction of the urethral lumen (star). (b) Penile urethra with acute inflammatory narrowing and obstruction by cellular debris (star). (c) Penile urethra with chronic inflammatory process and dilation of the lumen (star). (d) Note areas of congestion (arrowheads), erectile tissue vessels (arrow) and intense collagen deposition (star). (e) Note intense fibrosis (star), reduced erectile tissue vessels (arrowheads) and urothelium hyperplasia (arrow). (f) Cross-section of feline penis. Note the unaltered penile urethra (star) with intact urothelium (arrowhead) surrounded by erectile tissue with collagen deposition (arrow)

experimental group, had some degree of injury, with two classified as mild (one intact and one prepubertal) and all others classified as moderate to severe. A similar stage of injury was observed in all groups (Figure 5a).

Penile urethra lesions were classified as epithelial necrosis, hemorrhage, fibrosis and congestion. The most frequent type of lesion was epithelial necrosis. A similar level and type of lesion was observed among the groups (Figure 5b).

In the morphological evaluation of the degree of the urethral obstructive process, they were classified as total, partial and dilated obstruction. No statistical difference was observed among the groups (Figure 5c). However, it is important to mention that all animals with urethral dilation had been catheterized during the surgical procedure. All groups mostly showed a moderate level of fibrosis. Again, no significant difference in the fibrosis levels was observed among the groups (Figure 5d).

Discussion

Neutering and age at neutering are controversial risk factors in UO. Herein, we assessed the correlation between the clinical aspects and urethral lesions in cats with UO with reproductive status and age at neutering. We were fortunate to have primary care for all 84 cats presenting with UO at our hospital (2019–2021). This allowed for a thorough comparison of intact, prepubertal and postpubertal neutered male cats to assess for any significant differences in the onset of obstruction, clinical signs and

histological abnormalities of the penile urethra after surgical removal.

One of the most important findings of this study was that intact cats showed signs of UO significantly earlier than neutered cats, independent of the age at neutering. This was unexpected, as much of the published literature reports castration as a risk factor for feline lower urinary tract disorders (FLUTD), including obstructive disease.^{12,13,15} It has been hypothesized that lower compliance of the periurethral region of neutered cats could be a predisposing factor for UO disease.¹³ Another hypothesis is that the increase in adrenal androgens in neutered cats enhances the stress response in male cats, leading to FIC.²⁷

Moreover, most of the cats with UO, independent of their reproductive status, were fed a dry diet, which is a well-known risk factor for FLUTD.^{14,28,29} Obesity has also been described as risk factor for FLUTD.^{14,29–31} None of the intact cats were overweight, even though there was an earlier onset of UO. It has been suggested that neutered cats are less active and more prone to weight gain,^{12,30} the latter probably due to their lower maintenance energy requirement vs intact cats²⁴ and higher appetite, as seen by increased insulin and leptin plasma levels.³²

Contradictorily to previous studies reporting that age at neutering is a risk factor for UO,²¹ similarly to Porters et al,¹⁷ we observed that prepubertal neutering does not seem to predispose to the early onset of UO. This can have a great positive impact on public health as pediatric

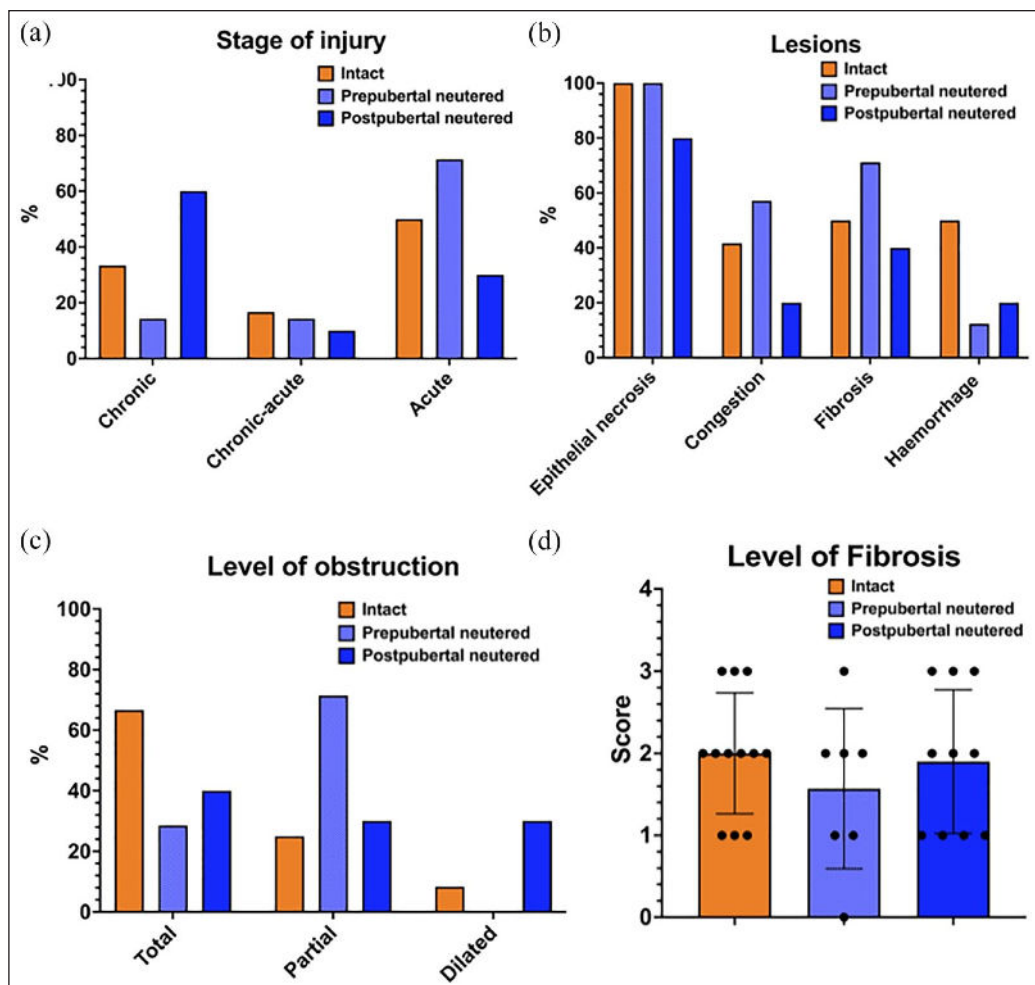


Figure 5 Histological assessment of the penile urethra following urethrostomy of intact, prepubertal neutered and post-pubertal neutered cats with urethral obstruction. (a) Stage of injury; (b) histopathological lesions; (c) level of urethral obstruction; and (d) level of fibrosis. No significant histological differences were observed between groups

castration represents a useful tool in the control of abandoned and stray animals and the consequent dissemination of zoonoses. A greater difficulty in the catheterization of prepubertal neutered cats has been attributed to juvenile penises leading to complications in penile exposure.^{23,33–35} However, a study that performed a voiding cystourethrogram to compare the effects of castration in prepubertal and post-pubertal cats with intact cats demonstrated no differences in urethral diameters.²² This observation was consistent with another study that measured the area of the urethral lumen by histopathology.¹³ Moreover, we observed similar levels of epithelial necrosis and fibrosis between prepubertal neutered, post-pubertal neutered and intact cats, indicating a similar level of injury.

It is known that the clinical signs observed depend on the duration of the obstructive event and its intensity, with hematuria, pollakiuria and stranguria being commonly reported.^{33,34} These findings were observed

in this investigation without correlation to the patient's reproductive status.

When the lesion characteristics were evaluated, acute processes were most often observed in intact and prepubertal neutered groups, which can be explained by the emergency character of the obstructive disease and by the lesions caused by difficult catheterization.^{8,36} This is due to the anatomic conformation of the cat's urethra, which is long and narrow, regardless of the patient's reproductive status.^{13,21} In addition, these lesions, when repeated, may have a chronic–acute or chronic character, characterized by the formation of fibrosis. The intense mononuclear infiltrate associated with an area of fibrosis shows the inflammatory process present in all cases that underwent urethral clearance. Moderate-to-severe fibrosis was most often observed, indicating that this tissue has gone through persistent inflammatory triggers, producing inflammation, tissue destruction and

repair processes simultaneously.³⁷ As reported previously, neutrophilic infiltrate, necrosis, hemorrhage and edema were common findings.^{5,26} However, 92% of the urethras assessed had moderate-to-severe lesions vs 21% in a previous study.²⁶

In the present study, it was not possible to assess the diameter of the urethral lumen of patients due to the degenerative and inflammatory lesions. Instead, we assessed the level of stenosis. Urethral stenosis may result from chronic urethritis or repeated trauma caused by catheterization.³⁶ Therefore, the recurrent use of this technique is considered one of the main causes of perineal urethrostomy in cats, with macroscopic lesions in the penis, foreskin and scrotum.^{8,9} These observations were confirmed in our study, where all patients showed signs of urethritis. Four also had luminal dilation, which may have occurred because they were all catheterized at the time of surgery.

The present study is a descriptive case series study and cannot be used to make inferences about causal relationships between risk factors and incidence of UO due to the lack of a comparison group. Other limitations of the present study were the small number of cats within the groups. We suggest that future studies confirm this early onset of obstruction in intact cats in a larger population. Moreover, possible risk factors and their pathophysiology should be further investigated. The strengths of this study include the high percentage of intact cats diagnosed with UO and the report of obstructive lesions of the urethra by histological examination.

Conclusions

While both intact and neutered cats experienced UO, intact cats showed an earlier onset of urethral obstruction than pre- and post-pubertal neutered cats. This finding should be confirmed in a larger population and a possible causal factor(s) should be investigated. Similar urethral histopathological lesions and clinical signs were observed in intact, prepubertal and post-pubertal neutered cats with UO.

Supplementary material The following file is available online:

Supplementary Table 1: Clinical signs of intact, prepubertal and post-pubertal neutered cats with urethral obstruction.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual

patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). For any animals or people individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

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