WSAVA Guidelines for the Control of Reproduction in Dogs and Cats

Executive Summary

Chapter 1: Introduction

The WSAVA Reproduction Control Committee worked collaboratively with other WSAVA committees and international stakeholders to develop guidelines on surgical and nonsurgical approaches to sterilisation, health benefits and risks of gonadectomy, and the ethics of reproductive control in cats and dogs.

Chapter 2: Surgical sterilisation in dogs and cats

Several surgical approaches and procedures for sterilization of dogs and cats are presented. This is not meant to be a description of all options available to the veterinary surgeon, but rather an overview of what is possible. Nuances and variations are appropriate when the surgeon has both experience and success with the method. Inexperienced surgeons should recognize that with any surgical sterilization procedure inadequate exposure is the main reason for complications. Relatively new methods of surgical sterilization described include the scrotal approach for male dogs, autoligation of the cord in paediatric male dogs and autoligation of the ovarian pedicle in female cats.

We have purposefully divided the surgical options for sterilisation of female dogs into ovariectomy (OE), subtotal ovariohysterectomy (SOHE) and ovariohysterectomy (OHE). This is to avoid confusion and are the correct terms anatomically. Ligatures that are placed on the uterine side of the cervix, as frequently described in textbooks and utilized by a large majority of veterinarians, will inevitably leave the distal portion of the uterus in the patient. This procedure is therefore an SOHE, not OHE. While seemingly trivial, the distinction between the two procedures becomes critical when discussing gonad sparing surgery. As a committee we believe that when surgical sterilization with loss of gonadal hormones is selected, in the absence of uterine pathology, OE is the preferred procedure. OE provides all the benefits of other procedures, is quicker, uses a smaller incision and is associated with less potential complications. Modern surgical technology has greatly facilitated atraumatic and successful sterilization surgery. At a minimum, veterinary surgeons should have a modern electrosurgery unit, vascular clips and a method to provide topical haemostasis. The common practice of using a surgeon's knot to initiate a vascular ligature is being re-evaluated. Surgeon's knots tend to bind or "lock up" prematurely, creating a situation where the surgeon falsely thinks the knot has been adequately tightened when it has not. Two pass friction knots such as the

miller's, constrictor and strangle knot may be preferable, especially for inexperienced surgeons. Vessel fusion and similar devices have greatly facilitated surgical sterilization procedures but remain expensive.

A separate section has been allotted to surgical sterilization of the periparturient bitch. To our knowledge, there is no evidence that simultaneously performing either an SOHE after neonate delivery or an immediate en-bloc hysterectomy increases maternal risk provided modern anaesthesia methods are utilized.

Many of the surgical sterilization procedures described can be accomplished with either an open laparotomy or minimally invasive laparoscopic approach. Minimally invasive surgery is less painful, associated with less wound complications and provides improved visualization, especially in larger patients. Owner familiarity with laparoscopic surgery has produced a large demand for performing sterilization procedures using this method and is preferred when available and not cost prohibitive.

Surgical site infections (SSI's) are a significant cause of concern in veterinary patients undergoing sterilization procedures, but data regarding antimicrobial prophylaxis is limited and conflicting. Antimicrobial resistance is an important problem in both veterinary and human health care and use of an antimicrobial with the premise that "it can't hurt" is patently wrong. Prophylaxis should be avoided in routine sterilisation procedures provided they are of short duration, performed in a clean environment and there is no other factor predisposing to infection. If utilised, prophylaxis should be with the safest, intravenous, low toxicity and low-cost antimicrobial available. Drugs must be given in the two hours before surgery and not administered beyond 24 hours after the procedure.

All surgical procedures are painful, and provision of adequate analgesia is mandatory in every situation. Many acceptable options are available for use with surgical sterilisation, and choice of the analgesic protocol will vary depending on the physical location where the procedure is being performed (hospital vs. field), degree of surgical trauma, age and health of the patient, availability of certain medications and familiarity of the surgeon with the drugs being used. Management of surgical pain begins before surgery, is maintained through the surgical procedure and is continued afterwards. Multimodality management of pain is preferred. Local anaesthetic techniques are particularly appropriate as they may provide excellent analgesia without causing systemic side effects

Chapter 3: Non-surgical sterilisation in dogs and cats

Surgical sterilisation is commonly performed in dogs and cats for reproductive control. However, not all owners want their pets surgically sterilised. In addition, surgical sterilisation is costly, requires expertise and equipment, and is not available in all parts of the world. For these reasons, non-surgical alternatives for reproductive control in dogs and cats are desired. Non-surgical sterilisation can be achieved using hormonal downregulation, immunocontraceptives, chemical castration, and gene therapy.

Hormonal downregulation treatments using a gonadotropin-releasing hormone (GnRH) agonist (deslorelin) or reproductive steroid hormones (progestogens or androgens) result in

negative feedback, reversibly shutting down the hypothalamic-pituitary-gonadal axis. The subcutaneous deslorelin implant comes in two strengths (4.7 mg and 9.4 mg) that vary in length of efficacy for at least six months and twelve months, respectively. The labeled application for the deslorelin implant varies by country but includes induction of reversible infertility in male dogs and male cats as well as prepubertal female dogs. Progestogens and androgens have been used for oestrus postponement in female dogs and cats for decades. Efficacy as well as adverse effects depend upon the steroid administered, dose, timing of treatment relative to the stage of the oestrous cycle, treatment regimen, and age, as well as the reproductive health and systemic health of the animal.

Immunocontraception via GnRH vaccination produces antibody titres that bind to endogenous GnRH and suppress synthesis and secretion of gonadotropins (luteinizing hormone, follicle stimulating hormone). Because GnRH is not naturally immunogenic, GnRH vaccines are formulated to increase the antigenicity by conjugation with keyhole limpet hemocyanin or diphtheria toxin. Commercialised GnRH vaccines are effective in male and female dogs and cats but this efficacy is short-lived and requires multiple injections, limiting this usefulness of this approach in feral animals and large-scale population control.

Chemical castration of male dogs and cats using intratesticular or intraepididymal injections induces azoospermia as well as a variable reduction in testosterone concentrations, depending on which chemical agent is injected. Intratesticular injection is not technically challenging, does not require general anaesthesia, is inexpensive, and is suitable for large-scale sterilisation programs. Intraepididymal injections can be delivered into the tail or head of the epididymis and may require general anaesthesia and ultrasound guidance, especially when performed in male cats. Intratesticular and intraepididymal injection results in minimal signs of discomfort as afferent nerve endings associated with pain sensation are located on the scrotal skin rather than within the testicular and epididymal parenchyma. However, local and systemic adverse reactions can occur if the technique is not performed properly. In addition, there are no long-term safety and efficacy studies on intratesticular or intraepididymal injections as a non-surgical sterilisation option for dogs or male cats.

Gene therapy can be used to silence a gene or induce its overexpression. The mechanism of gene silencing can be accomplished using RNA interference, small interfering RNAs (siRNAs), or gene editing using CRISPR/cas9. Most of the research in this area is limited to in vitro cellular or rodent models. However, one study in cats successfully silenced Kiss1 genes in hypothalamic neurons using an adeno-associated virus (AAV). Similar to gene silencing, most of the research in this gene overexpression has been limited to in vitro cellular or rodent models. However, sustained overexpression of anti-Müllerian hormone in female cats using an AAV delivery system via a single intramuscular injection prevented ovulation and pregnancy for over two years but did not impair oestradiol secretion or oestrous cyclicity.

Chapters 4 and 5: Health benefits and detriments of sterilisation with loss of gonadal steroid hormones

Sterilisation with loss of gonadal steroid hormones provides both health benefits and detriments. This chapter does not promote nor advise against gonadectomy but discusses

whether gonadectomy or hormonal downregulation can be recommended in special cases and at which age of life.

Health benefits or detriments are influenced by many factors such as inherent breed risk for certain diseases, lifestyle, and type of activities the dog is used for, owner's inclination, attitude, and fear of certain specific diseases and it should always be considered that gonadectomy may treat or prevent some problems while causing others. Any situation where gonadectomy is considered in a male or a female, requires a thorough case history, purpose for which the animal is kept, lifestyle of owner and pet, consideration of breed, age, body condition score and estimation of risk and benefit. The following concluding statements on benefits and detriments of gonadectomy for each condition should not be regarded as final; new evidence in this field is continually emerging and may change the risk/ benefit assessment over time.

Loss of gonadal steroid hormones may have beneficial effect in special cases. In female dogs, removal of gonadal and uterine tissue will prevent diseases of the genital organs and furthermore unwanted pregnancies; this also comprises hermaphrodites and pseudohermaphrodites. However, since the loss of steroid hormones can cause other problems, prevention of these diseases should not be the only reason for gonadectomy in female dogs, especially not before puberty. Any healthy bitch may remain intact, but should be monitored for reproductive health and examined at first signs of abnormalities. Vaginal tumours may be steroid hormone responsive. Therefore, gonadectomy is beneficial after tumour removal and will prevent recurrence in case of benign tumours. And may prevent the formation of vaginal tumours. Gonadectomy reduces the risk for mammary tumours, especially when performed before puberty and until after the second heat. The pathogenesis of mammary tumours is, however, multifactorial and therefore gonadectomy should not be done solely for prevention of mammary tumours. Gonadectomy reduces the risk of transmissible venereal tumours, probably by reducing the frequency of mating. Gonadectomy leads to remission of vaginal prolapse usually within 7-10 days and prevents possible recurrence of the problem. Insulin resistance associated with endogenous progestogen that complicates diabetes mellitus therapy will be resolved by gonadectomy, independent of the time after diagnosis. Gonadectomy is furthermore recommended in cases of behavioural and health problems in female dogs with pseudocyesis, and in case of maternal aggression. All other behavioural concerns must be analysed by veterinary behavioural experts before irreversible gonadectomy is recommended. A trial with long-acting GnRH agonists is an option. The recommended age at castration depends on the reason for considering the procedure but should ideally be performed after the first or second heat in owned female dogs.

In male dogs, removal of gonads will prevent diseases of the reproductive organs, which also comprises intersexes and disorders of sexual development (DSD). In case of retained testes and hormone-secreting tumours, gonadectomy is obligatory to prevent hyperoestrogenism and metastases. Prostate gland diseases like benign prostate gland hyperplasia (BPH) and prostatitis are androgen dependant. Therefore, medical therapy to decrease prostate gland volume including antiandrogens and long-term GnRH agonists, or gonadectomy are strongly recommended in dogs with recurring signs of BPH. In case of adenomas of the perianal glands, anti-hormonal therapy, hormonal down-regulation or gonadectomy is the treatment of choice. Urethral prolapse must be surgically corrected and gonadectomy or hormonal down-regulation may be considered to prevent rupture of the sutures during sexual activity. Since

many dogs with perineal hernia suffer from severe prostate gland diseases, gonadectomy or hormonal treatment to decrease the gland size is recommended in these cases. Testosterone related, unwanted behaviour may improve gonadectomy or hormonal treatment and inter-male aggression may improve but not all aggressive behaviours are testosterone related. The recommended age at castration depends on the reason for considering the procedure but the risk of side effects of prepubertal gonadectomy should be weighed carefully against the benefit of this measure. A so called “castration trial” using a long-acting GnRH agonist is recommended before irreversible orchiectomy is performed.

However, there are gonadectomy associated detriments in both male and female dogs. Gonadectomy may contribute to the development of some tumours in male and female dogs. An increased risk of developing mast cell tumours, transitional cell carcinomas, osteosarcomas, lymphomas and haemangiosarcomas was reported. This may in part be related to the long-term increase in luteinising hormone (LH) after gonadectomy, which is currently under intense investigation, as is the effect of age at castration. In male gonadectomised dogs, the incidence of prostate gland neoplasia is higher than in intact dogs, which may be due to the lack of the protective effect of androgens and the effect of late age gonadectomy is questioned in this regard. Whether the effect of long-term GnRH agonists steroid hormone suppression differs from steroid hormone suppression induced by gonadectomy is a future field of science. Urinary incontinence occurs in 5-20% of female dogs any time after gonadectomy. This is multifactorial but strongly triggered by gonadectomy; in case of prepubertal neutering, especially in female puppies with an adult body weight >25 kg. In male dogs, urinary incontinence is mainly triggered by age. The negative effect of gonadectomy at <6 months of age or <12 months of age on joint health has been reported in large populations of male and female dogs, and certain breeds. This should be considered, when owners are informed about consequences of gonadectomy at a young age. The prevalence of obesity, hypothyroidism, hyperadrenocorticism and some immune diseases were increased after gonadectomy; which may be in part related to the loss of gonadal steroids and/or persistence of supra-physiological levels of LH. In some female and male dogs, aggression against strangers and family members increased after gonadectomy, and a relation between prepubertal gonadectomy and anxiousness/lack of confidence and a general increase in behavioural problems was reported. However, the change in behaviour after gonadectomy is difficult to foresee and can only be estimated based on the individual dog and history. Prepubertal gonadectomy may cause health detriments such as perivulvar dermatitis and recurrent infections of the urogenital tract and might trigger orthopaedic problems and tumours. These detriments should be communicated to dog owners prior to gonadectomy and a risk vs. benefit evaluation provided for both dog and owner in each individual case. In male dogs, the very low (<1%) risk of developing a prostatic neoplasia should be weighed against the risk of prostatic disease in advanced age and their inherent surgical risk. Alternatives like hormonal down regulations may be considered in cases were gonadectomy might trigger the mentioned diseases in combination with other factors like age, size, obesity or a breed disposition. This can also prevent persistent supra-physiological LH concentrations that are implicated in gonadectomy associated health concerns.

In female cats, gonadectomy will prevent ovarian and uterine diseases. Gonadectomy or hormonal down-regulation prevents pseudopregnancy and pregnancy, and is therefore a measure to prevent fibroadenomatosis, galactostasis and mastitis. Considering the beneficial effects on reducing mammary tumour formation and unwanted pregnancies, prepubertal

gonadectomy or hormonal down-regulation in female cats is recommended. However, recent studies show that gonadectomised cats have a higher incidence of other tumours; to which degree, this is related to further factors like age, is currently under investigation.

In male cats, gonadectomy will prevent testicular diseases but not adenocarcinomas of the prostate gland. Gonadectomy can be recommended do decrease aggressiveness towards other cats; urine marking will not be improved in all cases. Gonadectomy will not prevent infections and diseases of the immune system. Male and female European shorthair cats and breeds of similar size can be gonadectomised peripubertally and as early as 3-4 months without detrimental effects on health, life expectancy and behaviour. However, male and female cats should be in a good body condition and vaccinated.

Health detriments in cats mainly concern metabolism as both genders have an increased risk of obesity and insulin dependent type-2 diabetes mellitus after gonadectomy, especially male cats. However, this may be mitigated by an increase in exercise and calorie intake restriction. Gonadectomy furthermore may increase the risk for lower urinary tract diseases with obesity and breed as contributing factors. Prepubertal gonadectomy and delayed epiphyseal closure may trigger epiphyseal fractures in male and female cats. More recently, an increased risk for development of certain cancers was reported, which is currently under investigation.

Chapter 6: Ethics of Reproduction Control

Emerging data surrounding health benefits and detriments in dogs and cats has prompted veterinarians to engage pet owners into best practice discussions when recommending sterilisation. Besides health concerns for individual animals, other factors, such as ethical considerations, practices at shelters and pet overpopulation also have to be considered.

Pet overpopulation remains a significant issue globally, contributing to overcrowded animal shelters and resulting in large numbers of euthanised animals.

Changing sterilisation practices and improved pet confinement are credited in reducing numbers of stray dogs and cats. While low-cost spay and neuter programs have shown promise in increasing sterilisation rates, it is less clear if such programs directly lead to reduced shelter intake rates.

Trap, Neuter, Return (TNR) programs are intended to offer a humane approach to managing feral animal populations. By sterilising and returning animals to their habitats, TNR programs aim to decrease animal populations in certain areas. However, TNR's effectiveness is not easy to assess. The particular environment, food availability, and the absence of incoming fertile animals all impact the success and vary widely across programs. TNR programs have the potential to improve animal health and control diseases such as rabies, especially when combined with vaccination programs. This is a direct benefit to human populations in the region. While these programs also foster community involvement, they require substantial resources and long-term commitment, with questionable long-term outcomes. More research is needed in this area.

Responsible pet ownership (RPO) can promote animal wellbeing and strengthen the human-animal bond. Historically, attitudes toward pet ownership have shifted gradually over the centuries from practical considerations to companionship. The awareness of the importance of properly caring for pets has concurrently increased. Regular veterinary visits, preventive healthcare, and reproductive control programs are essential elements of RPO. Educational initiatives play a crucial role in raising awareness about pet needs and RPO. Teaching empathy and respect for animals to children fosters lifelong responsible behaviour towards animals.

Spaying and neutering attitudes and rates vary globally. Western countries, such as the USA often practice routine high-volume, spaying and neutering, while regions like Scandinavia have been more cautious. Robust data on spaying/neutering prevalence is scarce in many countries, complicating comparisons and the assessment of program impacts.

Early age desexing (EAD) or paediatric spaying/neutering is practiced to varying degrees worldwide. Many organisations and veterinary associations endorse EAD for specific age groups and situations. However, the practice should only be undertaken when risks and benefits have been weighed up carefully.

Mandatory Spay and Neuter laws have been put in place in various areas globally to control animal populations in the community. The objective of these laws is generally to decrease issues associated with animals, such as nuisance behaviour and dog attacks as well as animal numbers. Nevertheless, there are uncertainties surrounding the effectiveness of such laws and their impact is being questioned.

As veterinary professionals revisit the practice of routinely gonadectomising pets, it becomes clear that both individual circumstances and societal factors must be considered. They play an essential role by providing evidence-based information and guidance to pet owners and policymakers alike.

It is becoming evident that high-quality research along with collaboration among experts is necessary to fully comprehend the impact of sterilisation practices on animal populations within shelters and communities at large. Additionally, standardising data collection methods is warranted to facilitate analysis.

Recommendations around reproduction control of dogs and cats in different settings

The decision to spay, neuter, or sterilise dogs and cats requires careful consideration. While the temperament and health of each individual animal play a significant role, the setting in which the decision is made, as well as the future living environment of the animal, are all important to consider. Recommendations for reproduction control procedures that vary across different settings are summarised below.

For clients who are responsible pet owners (RPOs), it may be advisable to leave dogs intact, particularly in breeds prone to health detriments associated with gonadectomy. However, in such instances, owners must be vigilant regarding mismating risks and ensure regular mammary exams to monitor for the increased risk of mammary tumours. Hysterectomy can

offer an effective solution for those who wish to eliminate the inconveniences of bloody vaginal discharge and the risk of unwanted pregnancy. It is essential to recognize that the long-term effects of hysterectomy in dogs, particularly in brachycephalic breeds, are not yet fully understood, but they could potentially increase the risk of vaginal prolapse.

While gonad-sparing surgery is becoming more popular, there isn't sufficient evidence yet to equate its benefits with those of keeping an animal entirely intact. However, in the case of RPOs and certain dog breeds that are prone to diseases after gonadectomy, hysterectomy may be a reasonable option.

A GnRH implant might be considered, if temporary infertility is desired, although adverse events have been reported. Yet, the prevalence of these is not well investigated. Particularly in middle-aged to elderly female dogs caution needs to be taken, but a GnRH-implant can be an option in select cases. On the other hand, GnRH implants are generally safe for female cats, making them a potential alternative to surgery.

Ovariectomy may be appropriate in specific situations. These include female dogs with no uterine pathology or client preference. In feral dogs, hysterectomy is not recommended due to the potential rupture of the vaginal vault that can arise after release when the female is bred. In most instances, ovariectomy is sufficient, except in the presence of uterine pathology, when ovariohysterectomy should be done.

In shelter settings, where permanent sterilization is the primary goal, the choice between hysterectomy and ovariectomy should consider breed-specific factors. Decisions might be delayed until a (responsible) pet owner has been identified for the animal.

Paediatric gonadectomy for both males and females is discouraged due to detrimental health effects with the exception of shelter environments that prioritize permanent sterilization of all animals before rehoming.

The situation differs for female cats, where ovariectomy is generally recommended due to the challenges of keeping intact females in the home. Hysterectomy may be considered for some feral cats in specific settings, such as closed communities with no immigration. In most other cases, ovariectomy or ovariohysterectomy is the preferred method for permanent sterilization.

In countries where routine surgical procedures for dogs are illegal, GnRH implants may offer a viable alternative, provided owners comply with the re-implantation schedule. For male dogs living with responsible pet owners, the recommendation is either to keep them intact or consider vasectomy if sterilization is desired. Regular monitoring for testicular and prostatic disease is essential in these cases. However, if owners are unlikely to perform such examinations, orchiectomy is the safer option. Orchiectomy may also be suitable for client-owned dogs in multi-dog households to prevent unwanted reproductive behaviour. In some instances, a GnRH implant can be considered, especially if only temporary sterility is desired.

Intratesticular injections can be a viable option for all male dogs, including in shelter settings, but complications must be monitored for seven days post-application. Vasectomy is potentially an appropriate choice, particularly in closed populations, where maintaining the social structure is desirable. Nevertheless, more research is needed in this area.

For male cats, orchiectomy is generally recommended, because it eliminates unwanted behavioural traits. Orchiectomy also remains the preferred choice for feral cat populations, although vasectomy or epididymectomy may be considered in select situations.

In countries where routine surgical procedures are illegal, GnRH implants for dogs can be offered as an alternative. However, owner compliance needs to be ensured and possible side-effects need to be discussed.

Ultimately, the decision whether and how to spay, neuter or sterilise an animal should be based on a thorough assessment of the individual animal's health and client preferences. Veterinarians play a crucial role in guiding these decisions, weighing the risks and benefits to ensure the best outcome for the animal, the client, and the broader community.