

## **THE OPTIMAL AGE FOR SPAY/NEUTER: AN ANALYSIS OF CRITICAL SPAY/NEUTER LITERATURE**

Philip A. Bushby, DVM, MS, DACVS

Mississippi State University College of Veterinary Medicine  
Miss State, MS, USA

### **Introduction**

In the past few years the standard practice of sterilizing canine and feline pets has been challenged. Research studies document both benefits and risks associated with ovariectomy and castration creating some level of confusion in the profession. Some in the profession argue for delay in performing these surgeries or abandonment altogether while others argue for early age or pediatric spay/neuter. On one end of the spectrum are concerns over the incidence of certain orthopedic conditions and cancers and on the other end concerns over pet overpopulation and euthanasia of homeless pets in animal shelters. Who is correct? Should dogs and cats be sterilized and is there an optimal age for such surgeries?

The question we must answer is should we spay/neuter. And if so, when? At what age should the surgeries be performed? We have seen the recommended age for spay/neuter change over the years. None of the recommendations have been based on a comprehensive analysis of sound research. In fact, until recently there had been very little research on the impact of spay/neuter. Most research related to spay neuter has been retrospective studies. While retrospective studies have value, they cannot prove cause and effect. In retrospective studies there is little or no control over confounding factors and more potential for errors due to bias.

With that disclaimer, let's jump right in to the debate. Should you perform spay neuter? And if so, at what age should you do the surgeries?

### **Research that Appears to Support Delayed or No Spay/Neuter**

Recent research publications have caused some in the profession to question not only pediatric spay/neuter but spay/neuter in general. Four studies out of UC Davis veterinary school have resulted in many people, veterinarians and animal owners, expressing concern about the age of spay/neuter or about even performing spay/neuter at all. These studies are:

- UC Davis: Golden Retriever study<sup>1</sup> (February 2013)
- UC Davis: Comparison of Labrador Retrievers with Golden Retrievers<sup>2</sup> (2014)
- UC Davis: Neutering of German Shepherd Dogs<sup>3</sup> (2015)
- UC Davis: Gonadectomy effects on the risk of immune disorders<sup>4</sup> (2016)

These articles report on retrospective studies that looked at the incidence of joint problems (CCL rupture, hip dysplasia) various cancers (lymphoma, hemangiosarcoma, osteosarcoma, mast cell tumors) and immune disorders. They reported varying degrees of increase in incidence of certain orthopedic conditions, neoplastic conditions and immune disorders in sterilized dogs.

Close examination of these papers, however, should cast doubt on the assumption that we should avoid or delay spay neuter. What are the potential issues with these article?

- Lack of control of variables: In the best research, all variables are controlled except the one you are measuring. Retrospective studies can't do that. We don't know the impact of diet, lifestyle, environment, preventive care, genetics or other factors on the results in these studies out of UC Davis.
- Biased research population: At referral institutions cases managed by primary care veterinary clinics are not represented. The private practitioner might manage the dog with mammary neoplasia, pyometra or testicular cancer, but refer the case of osteosarcoma, hemangiosarcoma or lymphoma. This would skew the research results making some conditions appear less frequent and others more frequent. It gets even more confusing. What if animals are sterilized because they have an orthopedic condition or conformation that predisposes to an orthopedic condition as opposed to having an orthopedic condition because they were sterilized? And to complicate things a little more. There are two primary reasons why people don't sterilize their dogs and cats; they want to breed them or they can't afford the surgery. If someone cannot afford the cost of a spay or castration, what are the odds of them taking their pet to a referral hospital for specialized care. Again, potentially skewing the research results.
- Association does not prove cause and effect: Retrospective studies cannot prove cause and effect. They can point to potential issues that deserve further research, but we must be careful to avoid simply assuming cause and effect.
- Small sample size: The UC Davis studies are actually reporting on relatively small numbers of cases (500-1500). Random variation in scientific studies results from the chance distribution of measurements. The smaller the sample size the greater the chance for inaccuracy based simply on random variation.
- Lastly, if all the findings in the UC Davis studies eventually prove to be true, one still cannot extrapolate from one breed to the next and certainly not from one species to another. The UC Davis authors point that out, but many in the public or in the profession seem to ignore that fact.

The value of these studies is that they point to the need for more research, preferably prospective studies in which case criteria and data collection standards are defined in advance and consistently applied. But they do not, at this time, justify wholesale changes in spay/neuter decision making.

### **Research that Appears to Support Spay/Neuter or Even Earlier Spay/Neuter**

A study at the University of Georgia analyzed the records of over 80,000 patients and demonstrated that sterilization is strongly associated with an increased life expectancy in dogs.<sup>5</sup> In this study the life expectancy of sterilized dogs, both male and female, was increased in comparison to life expectancy of intact dogs.

- Mean age of death of intact dogs - 7.9 years
- Mean age of death of sterilized dogs - 9.4 years
- Sterilization was associated with increased life expectancy of males by 13.8%
- Sterilization was associated with increased life expectancy in females by 26.3%

While sterilization was associated with a decreased risk of death from some causes, such as infectious disease, it was associated with an increased risk of death from others, such as cancer. In this study sterilized dogs were “dramatically” less likely to die from infectious disease, trauma, vascular disease and degenerative disease. Sterilized dogs were more likely to die from neoplasia and immune mediated disease. Within the neoplasia category, occurrence of transitional cell carcinoma, osteosarcoma, lymphoma and mast cell tumors was increased in sterilized dogs while the occurrence of mammary cancer was significantly decreased.

In interpreting what appears to be conflicting information in the literature keep in mind that recognizing that something may change the incidence of a condition is of little value without knowing the incidence. Significantly increasing the incidence of a tumor that is relatively rare still leaves that tumor relatively rare while significantly decreasing the incidence of a tumor that is common may make that tumor uncommon.

Banfield operates over 1000 veterinary hospitals that share a common computerized medical record system. Each year Banfield releases a “State of Pet Health Report.” In 2013 that report was based on analysis of data from 2.2 million dogs and 460,000 cats.<sup>6</sup> Looking at longevity compared to spay/neuter status they discovered that:

- spayed dogs lived 23% longer than intact dogs
- neutered dogs lived 18% longer than intact dogs
- spayed cats lived 39% longer than intact cats
- neutered cats lived 62% longer than intact cats

The Banfield report makes no effort to attempt to theorize why sterilized animals live longer. It simply documents that they do.

What can we conclude so far?

- Sterilized dogs and cats live longer
- Sterilized dogs - higher incidence of certain cancers
- Sterilized dogs - lower incidence of mammary tumors
- Sterilized dogs – may have higher incidence of some immune diseases.
- Intact dogs are more likely to die of infections and trauma
- In some breeds sterilized dogs have greater incidence of certain orthopedic conditions.

Perhaps the most comprehensive reference related to age of spay neuter is a 2007 article by Margaret Root-Kustritz.<sup>7</sup> In this article the author summarizes the literature up to that date detailing the relationship of sterilization status and disease incidences between sterilized and intact pets.

If we could see into the future for each animal we could determine which animals were going to develop osteosarcoma if they were sterilized and which were going to develop mammary neoplasia or pyometra if they were not. We could then make the best decision for each animal. Lacking that ability, we should make our recommendations based on population dynamics. In the United States, approximately 80% of owned adult female dogs are spayed. The incidence of mammary neoplasia is 4% but that is almost exclusively in intact dogs. If the 4% of dogs with mammary neoplasia come primarily from the 20% of female dogs that are left

intact, the incidence of mammary neoplasia in intact dogs is nearly 20%, 100 times the incidence of osteosarcoma at 0.2%. Some articles claim that sterilization doubles the risk of osteosarcoma. But again if 80% of the dogs in the U.S. are sterilized that “doubling” effect is essentially already represented in the 0.2% statistic.

If you total the reported incidence of all the conditions listed in Dr. Kustritz’s article that are considered serious or moderately serious and in which the incidence is increased in sterilized dogs the total is 3.0%. The chances of a sterilized dog getting any one of these conditions is 3.0% versus the chances of an intact female dog getting mammary neoplasia at 20% or pyometra at 24%.

It is important that we not make decisions related to spay/neuter based on whether spay/neuter is associated with an increase the incidence of a particular condition without considering what the overall incidence is.

In 2017 Dr. Kustritz updated her article on optimal age for spay neuter to include the relevant research since 2007.<sup>8</sup> The key point in this latest article is this. The question about the effect of gonadectomy on health is one of causation: does gonadectomy at certain ages cause or prevent specific health issues? Defining an association is not enough. At this point, none of the articles that document incidence document causation. The research is not there. To adequately determine causation, you need:

- Randomized clinical trials,
- Unbiased subject selection,
- Adequate sample size,
- Accurate and precise measurement of the factors of interest,
- Adequate control of confounding factors, and
- Cautious & critical assessment of results.

When you read the scientific literature, watch for these. Recognize that when any of these are compromised, so too are the results. We need more research; more quality research!

Interestingly, another article from UC Davis looked specifically at cancer related mortality in Golden Retrievers and the impact of age and gonadectomy. The article supports the argument that sterilized dogs live longer than intact dogs and concludes that “overall golden retriever dogs have a substantial risk of cancer related mortality in a referral population and age appears to have a larger effect on cancer related mortality than reproductive status.”<sup>9</sup> And we have already concluded that sterilized dogs live longer.

### **Spay neuter (cats, pediatric cats and dogs)**

It seems like most studies have focused on dogs, but what about cats, and what about pediatric spay/neuter? Studies out of Texas A&M and Cornell have looked specifically at the medical and behavioral effects associated with early age spay/neuter and concluded that there were no serious long term medical or behavioral effects associated with early age sterilization in dogs and cats.<sup>10,11,12</sup>

Epidemiological studies in 1981 and 2005 document a significantly lower incidence of mammary neoplasia in cats when spayed prior to their first heat cycle.<sup>13,14</sup> Given that median survival time of cats with mammary neoplasia is generally less than 1 year and that up to 96% of mammary tumors in cats are malignant the reduction in incidence of mammary neoplasia is very significant.

A 1997 study documented fewer anesthesia and surgical complications in cats sterilized under 12 weeks of age when compared to those sterilized at or after 6 months of age.<sup>15</sup> This was, however, another study with very small numbers. The theory that castrating male cats prior to sexual maturity makes the penis smaller and predisposes to urinary tract obstruction has been proven to be false. In a 1996 study Dr. Margaret Root Kustritz and Shirley and Gary Johnston demonstrated no difference in urethral diameters between cats castrated at 7 weeks, castrated at 7 months or left intact.<sup>16</sup> None of the short-term or long-term studies have shown an increased incidence of urinary obstruction in neutered male cats.

A prospective study of 800 kittens comparing those sterilized between 8 and 12 weeks of age with those sterilized between 6 and 9 months found no evidence that age at the time of sterilization had any effect on the number of, or occurrence of, potentially undesirable behaviors.<sup>17</sup>

### **Feline Fix by Five**

In 2016 the Veterinary Task Force on Feline Sterilization was convened to look specifically at spay neuter issues in cats. What they found was that having cats spayed before their first heat cycle:

- Significantly decreases the risk for mammary carcinoma
- Eliminates reproductive emergencies such as pyometra and dystocia
- Prevents unintended pregnancies that may occur as early as 4 months of age
- Potentially decreases behavioral problems linked with cat relinquishment.

In 2017 the AMVA formally endorsed the concept paper developed by the Veterinary Task Force on Feline Sterilization which recommends that cats be sterilized prior to 5 months of age. Endorsements have also come from the American Animal Hospital Association, The Feline Practitioners Association, the Association of Shelter Veterinarians, The Winn Feline Foundation, The Catalyst Council, The International Cat Association, The Cat Fanciers Association and PetSmart Charities. The Feline Fix by Five campaign has been developed in an effort to educate the public and the veterinary profession of the benefits of sterilizing cats before 5 months of age.

### **The Shelter World**

Our program at Mississippi State University has been taking students to animal shelters since the early 1990s. We obtained a Mobile Veterinary Clinic in 2007 and a second Mobile Clinic in 2013. Since 2007 we have performed over 80,000 spay/neuter surgeries. Nearly fifty percent of these surgeries are pediatric. We currently serve 28 animal shelters/humane groups across northern Mississippi. In 2007, the shelters we served had a euthanasia rate in both dogs and

cats of greater than 60%. In 2016, euthanasia rates had dropped to 20% in dogs and 34% in cats.

Humane Alliance (now called ASPCA Spay Neuter Alliance) is, perhaps, the largest high-volume spay/neuter clinic in the world. Humane Alliance was established in 1994 in Asheville, NC, an area with rapidly growing human population over the past 20 years and statistically that would mean a rapidly growing pet population as well. In the 20+ years since Humane Alliance started performing sterilizations there has been a 75% reduction in intake and a 79% reduction in euthanasia in local animal shelters.

An animal care center in east Tennessee has performed over 55,000 spay/neuter surgeries since 2007. In that time, they have recorded a steady increase in live release rate from their animal shelter, a decrease in dog and cat intake, and a decrease in euthanasia.

Trap neuter return is a growing method of controlling feral cat populations and studies show that areas that have implemented trap neuter return have significantly reduced shelter intake and euthanasia of cats.<sup>18,19</sup>

### **So How do You Decide**

Decisions related to if and when to spay/neuter must be based first on the life situation of the animal: is it in a home or homeless. And secondly on an assessment of all known relationships between reproductive status and health and longevity not just a few. When making decisions related to increase or decrease in incidence of a condition we must consider what the overall incidence is and the impact of the change.

This is what we appear to know

- In the shelter environment spay/neuter is associated with increased adoption rates, reduced shelter intake and reduced euthanasia.
- There are several conditions that have low incidence in which the incidence may be increased with sterilization. These conditions include:
  - prostate neoplasia
  - transitional cell carcinoma
  - osteosarcoma
  - diabetes mellitus
  - hypothyroidism
- Sterilization decreases or eliminates the risk of several conditions that have high incidence:
  - mammary neoplasia
  - pyometra
  - benign prostatic hypertrophy
  - testicular neoplasia
- Sterilization may be associated with an increased incidence of:
  - cranial cruciate rupture
  - hip dysplasia
  - elbow dysplasiain some breeds of dogs.
- Sterilized dogs and cats have an increased life expectancy when compared to those left intact.

## **Recommendations**

- Shelter animals, spay/neuter prior to adoption, regardless of age of adoption.
- Cats, there are few documented adverse effects of spay/neuter in cats and many documented positive effects. Female cats can come into heat by 4 ½ to 5 months. Spay or castrate before 5 months of age.
- Owned dogs, the owner must make an informed decision based on species, breed, intended usage and current medical knowledge at hand. For most breeds the protective effect of spay before the first heat cycle on mammary neoplasia far outweighs the potential risks associated with other cancers and orthopedic conditions.
- Owned female dogs spay prior to 5 months of age.
- Owned large breed male dogs - house pets– orthopedic concerns may outweigh all others – spay/neuter after growth stops 15 – 18 months.
- Owned large breed male dogs - free roaming– population concerns may outweigh all others – spay/neuter prior to 5 months of age.
- Owned small breed male dogs – no evidence at this time for orthopedic issues – castrate prior to sexual maturity – 5 months.

## **Conclusions**

There is much we still don't know about the impact of spay and neuter. We must, therefore, always remain open to new information as research continues and, if need be, change our minds. In doing this we must, however, always be willing to look critically at new information to determine if conclusions are valid based on the research data.

## **Summary of Key Points**

One should not make spay/neuter decisions based on the impact of spay/neuter on a small handful of diseases, but should take into consideration the impact on the overall health and longevity of the animal.

To determine cause and affect you need:

- randomized clinical trials,
- unbiased subject selection,
- adequate sample size,
- accurate and precise measurement of the factors of interest,
- adequate control of confounding factors, and
- cautious & critical assessment of results

When making decisions related to increase or decrease in the incidence of a condition you must consider the overall incidence and what the change is.

One cannot extrapolate from one breed to another and certainly not from one species to another.

## Summary of recommendations

Table 1: Recommend Ages to Spay Neuter

<b>Species</b>	<b>Spay or Castrate</b>
Dog or cat in shelter	Prior to adoption (as young as 6 weeks of age)
Community Cat (Feral cat)	TNR at any age after 6 weeks
Cat (male or female)	Prior to 5 months of age
Dog (small breed, male or female)	Prior to 5 months of age
Dog (large breed female)	Prior to 5 months of age
Dog (large breed male – free roaming)	Prior to 5 months of age
Dog (large breed male – house pet)	After growth plates close – 15 – 18 months

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