Historical Perspective

- For several decades in the United States
  - Common trend has been to sterilize pet dogs and cats
  - For behavioral reasons
  - To prevent unwanted litters of puppies and kittens
  - The standard has been spay/neuter at or after 6 months of age
- More recently
  - Considerable debate related to spay neuter younger than 6 months
  - For population management reasons
  - Related to euthanasia rates in animal shelters
- Within the past few years
  - Recent articles casting some doubt on the very practice of spay neuter
  - Related to longevity issues, orthopedic issues, and incidence of cancer

Primary objective

- To look at recent studies and help sort out the benefit versus risk of ovariohysterectomy and castration in dogs and cats.
- Goal is for the participant to have a better understanding of many of these articles in order to make more informed decisions related to spay/neuter issues.

Two Kingdoms

Newspaper Headlines

- “After a grueling competition East prevails”
We will look at:

- Harts’ Golden Retriever study (February 2013)
- Waters’ Rottweiler longevity study (2009)
- Cooley’s Rottweiler Osteosarcoma study (2002)
- University of Georgia longevity study (April 2013)
- Beauvais review – Effect of neutering on risk of mammary tumors (June 2012)
- Beauvais review – Effect of neutering on risk of urinary incontinence (April 2012)
- Kustritz article – Optimal age for gonadectomy

Golden Retriever Study

**Significance of article**

- Has some in the profession questioning if veterinarians should be routinely recommending spay neuter
- Stimulated a discussion at the recent AVMA meeting about reconsidering the AVMA position on pediatric spay neuter in animal shelters to reduce pet overpopulation

**What if:**

- Castration of male Goldens after 1 year of age prevents lymphoma – 71 records
- Castration of male Goldens after 1 year of age reduces the rate of Hip Dysplasia – 65 records
- Ovariectomy of Goldens after 1 year of age reduces the rate of Hip Dysplasia – 67 records
- Ovariectomy of Goldens after 1 year of age prevents Cranial Cruciate rupture – 69 records
- Ovariectomy of Goldens after 1 year of age reduces the rate of Lymphoma – 69 records
- CCL rupture does not occur in intact Goldens – 265 records
- Mast cell tumors do not occur in intact female Goldens – 122 records

So what did the article say

- HD in males neutered under 1 yr. was double that of intact males
- HD was not increased by spaying females
- CCL rupture was increased in males and females neutered less than 1 year of age
- Early neutered males had 3x the incidence of lymphoma over intact
- Hemangiosarcoma incidence in females spayed after 1 year of age were 4x that of intact females
So what did the article say

- HD in males neutered under 1 yr. was double that of intact – 156 records
- HD was not increased by spaying females – 337 records
- CCL rupture was increased in males and females neutered less than 1 year of age – 355 records
- Early neutered males had 3x the incidence of lymphoma over intact – 176 records
- Hemangiosarcoma incidence in females spayed after 1 year of age were 4x that of intact females – 86 records

Basic principles

- Random variation in scientific studies results from the chance distribution of measurements
- Inaccuracy due to random variation can be reduced by taking a larger sample size.

Generalizations in the Golden study

- “For all five diseases analyzed in the present study, the disease rates in males and / or females were significantly increased when neutering was performed early and / or late”
- “When a disease occurred in intact dogs the occurrence was typically one-fourth to one half that of early – and / or late-neutered dogs”
- “Body condition scores ranging from 1 to 9 and obtained from the patient records (when available) were taken into account because BCS, as an indication of weight on the joints, is considered to play a role in the onset of these joint disorders” And in the results that there were no differences in BCS between groups.

One additional point

- “The results of this study, being breed-specific, with regard to the effect of early and late neutering cannot be extrapolated to other breeds or dogs in general”

Rottweiler Longevity Study

- Longer exposure to ovarian tissue is associated with exceptional longevity
Study design

- Two cohorts
  - Usual longevity (8 to 10.8 years) – 100 dogs
  - Exceptional longevity (13 – 15.5 years) – 87 dogs
- Looked at duration of ovary exposure (how long they lived with ovaries intact) in both groups

Conclusions

- “Our results show that in Rottweiler dogs, like in humans, there is a strong female sex advantage for reaching exceptional longevity”
- The longevity advantage over males is abolished in females that undergo early or mid-life ovarian removal

Conclusions

- “When females from the exceptional longevity and usual longevity cohorts were combined then subdivided into tertiles based upon ovary exposure during the first 8 years of life, dogs with the longest ovary exposure were 3.2 times more likely to reach exceptional longevity than dogs with the shortest exposure”

Basic flaws in the study/article

- Include greater numbers of animals
- Don’t preselect outcomes
- Pick animals at random across multiple breeds
- Include intact animals in the study
- Include detailed data and full statistical analysis in the article so people can make independent judgments
- Acknowledge that this study simply looks at one breed and any conclusions cannot be extrapolated to other breeds or dogs in general

Rottweiler Osteosarcoma Study

Basic premise

- Gonadal hormones protect against formation of osteosarcoma

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Endogenous Gonadal Hormone Exposure and Bone Sarcoma Risk

Introduction

Osteosarcoma is the most frequently diagnosed bone tumor of dogs and young adults (1-2). It is often linked to extremes of bone turnover and accumulation of osteoid matrix (3-7). Elevated concentrations of gonadal hormones are associated with increased risk of osteosarcoma (8). Increased exposure to gonadal hormones is hypothesized to promote excessive bone turnover and osteoid matrix deposition, leading to an increased risk of osteosarcoma (9,10).
Study design

- Detailed questionnaires to 1500 owners of Rottweiler dogs
- 730 questionnaires returned
- Looked at
  - Diagnosis of osteosarcoma
  - Reproductive status
  - Age of spay/neuter
  - Among many other things

Study at closer look

<table>
<thead>
<tr>
<th>With sarcoma</th>
<th>Without sarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Castrated &lt; 1yr</td>
<td>9</td>
</tr>
<tr>
<td>Male Castrated 1 – 3.5 yr</td>
<td>8</td>
</tr>
<tr>
<td>Male Castrated &gt; 3.5 yr</td>
<td>8</td>
</tr>
<tr>
<td>Male intact</td>
<td>10</td>
</tr>
<tr>
<td>Female spayed &lt;1 yr</td>
<td>18</td>
</tr>
<tr>
<td>Female Spayed 1 – 5 yrs</td>
<td>14</td>
</tr>
<tr>
<td>Female Spayed &gt; 5 yrs</td>
<td>14</td>
</tr>
<tr>
<td>Female intact</td>
<td>5</td>
</tr>
</tbody>
</table>

Results

- Male and female Rottweilers neutered at less than 1 year of age had a significantly higher incidence of osteosarcoma than intact Rottweilers

Pause to reflect

- The authors conclusions are based on
  - 9 cases of osteosarcoma in male dogs castrated < 1yr, and
  - 18 cases of osteosarcoma in female dogs spayed < 1yr
- Interestingly
  - Across the entire population of dogs studied (596 dogs)
  - Spayed females out lived intact females by an average of 2.3 years
  - No difference in life expectancy between neutered males and intact males

Basic Premise

- Sterilization is “strongly associated with an increase in lifespan”
- “While it (sterilization) decreased risk of death from some causes, such as infectious disease, it actually increased risk of death from others, such as cancer”
Study design

- Evaluated data for 80,958 dogs
- Looked at age of death
- In those that a specific cause of death was determined, categorized cause of death
- Compared age of death with gender
- Compared age of death with sterilization status
- Compared cause of death with sterilization status

Results

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

Results

- Sterilized dogs were “dramatically” less likely to die from
  - Infectious disease
  - Trauma
  - Vascular disease
  - Degenerative disease
- Sterilized dogs were more likely to die from
  - Neoplasia
  - Immune mediated disease

Results

- Within the neoplasia category, occurrence of:
  - Transitional cell carcinoma
  - Osteosarcoma
  - Lymphoma
  - Mast cell tumors
  - Were significantly increased in sterilized dogs
- Within the neoplasia category occurrence of:
  - Mammary cancer
  - Was significantly decreased in sterilized dogs

Limitations of the study

- Did not have access to data on age of sterilization.
- Did not have access to data indicating whether or not sterilized dogs had reproduced or the number of times they had reproduced prior to sterilization.
- Did not have access to data indicating whether or not intact dogs had reproduced or the number of times they had reproduced.

Strengths of the study

- The number of animals – greater than 70,000
- The number of breeds – 185
Basic principles

- Random variation in scientific studies results from the chance distribution of measurements
- Inaccuracy due to random variation can be reduced by taking a larger sample size.

Banfield State of Pet Health Report

Longevity Female Dogs

- lifespan for dogs
  - average lifespan 11 yrs
  - spayed
  - unspayed

  Spayed dogs live an average of 11.6 years—23% longer than unspayed dogs

Longevity Male Dogs

- neutered
- unneutered

Neutered dogs live an average of 11.1 years—18% longer than unneutered dogs

Longevity Female Cats

- lifespan for cats
  - average lifespan 12.1 yrs
  - spayed
  - unspayed

  Spayed cats live an average of 13.1 years—39% longer than unspayed cats

Longevity Male Cats

- neutered
- unneutered

Neutered cats live an average of 11.8 years—62% longer than unneutered cats
additional data of interest

- Intact dogs are more than twice as likely to be hit by a car as neutered dogs.
- Intact dogs are more than twice as likely to be bitten by another animal as neutered dogs.
- Intact cats are 4 times as likely to be hit by a car as neutered cats.
- Intact cats are 3 times as likely to be brought to a veterinarian for treatment of animal bites as neutered cats.

limitations

- The Banfield report is not a “peer-reviewed” published scientific article. Therefore,
  - No statistical analysis of data
  - No “authors” conclusions presented
  - No statement of limitations by the “authors”

pause to reflect

- Sterilized dogs and cats live longer
- Sterilized dogs have a higher incidence of certain cancers
- Sterilized dogs have a lower incidence of mammary tumors
- Intact dogs are more likely to die of infections and trauma
- The conclusions related to sterilized dogs have greater incidence of orthopedic diseases is speculative at best.

the next two articles

- Beauvais review – Effect of neutering on risk of mammary tumors – June 2012
- Beauvais review – Effect of neutering on risk of urinary incontinence – April 2012

risk of mammary tumors

systematic review

The effect of neutering on the risk of mammary tumours in dogs – a systematic review

W. Beilby, J. M. Carver, and D. C. Beever
Veterinary Epidemiology and Public Health Group, School of Veterinary Medicine, University of Melbourne, Australia.

Purpose of the review

- “To evaluate the strength of evidence for an association” between neutering and incidence of mammary tumors “by assessing the findings of different studies as objectively as possible.”
Review Design

- Reviewed original journal articles that contained data concerning the association between neutering and mammary masses.
- Evaluated only peer-reviewed articles in English.

Results

- Based on an extensive search of the literature (7557 references).
- But only including those that reported an association between incidence of mammary tumors and sterilization (13).
- And excluding those with a high risk of bias.
- Left 4 articles to undergo an in-depth analysis.

Basic Principle

- The best experimental design controls all variables except the one being tested.
- Failure to control variables limits the ability to make valid conclusions from the results of the study.

Review Results

- None of the 4 evaluated studies controlled for all three potential confounders: Age, Breed, Previous treatment with synthetic ovarian steroids.

Pause to reflect

- This review does not say that the results of the Schneider study are invalid.
- Simply that they did not control all the variables, and
- That there is little other valid literature that supports the conclusions of the Schneider study.

Review Results

- However, 1 article “Schneider et al 1969” found a strong protective (10 fold) effect of neutering on the risk of malignant mammary tumors:
  - Before 1st estrus
  - Before 2nd estrus
  - After 2nd estrus but before 2.5 years.
Purpose of the review

“To evaluate the strength of evidence for an association” between neutering or age of neutering and incidence of urinary incontinence “and to estimate the magnitude of any effect found.”

Review Design

- Reviewed original journal articles that contained data concerning the association between neutering and urinary incontinence.
- Evaluated only peer-reviewed articles in English

Results

- Based on an extensive search of the literature (1583 references)
- But only including those that reported an association between incidence of urinary incontinence and sterilization (7)
- And excluding those with a high risk of bias
- Left 3 articles to undergo an in-depth analysis

Basic Principle

- The best experimental design controls all variables except the one being tested.
- Failure to control variables limits the ability to make valid conclusions from the results of the study

Review Results

- Only 1 of the evaluated studies controlled for both potential confounders:
  - Age
  - Breed
- The article by “Belser” controlled for both confounders
- All 3 articles had low follow-up
Review Results

- One article “Thrusfield et al” found that neutering was associated with a nearly 8 fold increase in urinary incontinence.
- Two studies found NO statistically significant evidence of an association between urinary incontinence and age of spay.
  - Although one saw a trend towards a decrease in urinary incontinence with decreasing age of ovariohysterectomy.
- One study saw a increasing rate of urinary incontinence with decreasing age of spay.

Conclusions

- “On the basis of the three included studies which were all judged to be at moderate risk of bias there is only weak evidence that neutering bitches, particularly before the age of three months, increases the risk of urinary incontinence.”

Kustritz – Optimal Age for Gonadectomy

Reference Point

**Determining the optimal age for gonadectomy of dogs and cats**

Margaret C. Root-Kustritz, VMD, PhD, DACVIM

E

 Effective gonadectomy of dogs and cats must consider both the benefits and side effects of surgery. In one of the most common veterinary practices (spaying and neutering the United States), the risk of side effects is high compared to the potential benefits. This is especially true for the risk of urinary incontinence, which is increased in dogs and cats. A study comparing the risk of urinary incontinence between dogs and cats found that the risk was lower in dogs. However, the risk was highest in cats with a history of urinary incontinence. This study concluded that the risk of urinary incontinence is lower in dogs and cats compared to other species. The authors suggest that spaying and neutering before the age of three months may be the optimal age for gonadectomy, which is supported by the evidence from the study. It is recommended to consult with a veterinarian to determine the optimal age for gonadectomy.

Basic Premise

- Decisions on whether or not to spay / neuter a pet must be based on an assessment of all known relationships between reproductive status and health and longevity, not just one or two.

So let’s look at the factors

- Mammary tumors
  - Most common tumor of female dogs
    - Reported incidence 3.4%
    - Most common malignant tumor of dogs (50.9% malignant)
  - Third most common tumor of cats
    - Reported incidence 2.5%
    - Greater than 90% malignant
    - Ovariophysterectomy is protective against mammary tumors
    - Especially if prior to the first estrus cycle

- Prostatic tumors
  - Incidence in dogs reported between 0.2 and 0.6%
  - Almost always malignant
  - Castrated dogs
    - Increased risk for prostatic neoplasia
So let’s look at the factors

- Testicular tumors
  - 2nd most common tumor type in the dog (incidence 0.9%)
  - Rarely malignant
  - Castration is preventive
  - Castration is curative

So let’s look at the factors

- Transitional Cell Carcinomas
  - Uncommon (1% of malignant tumors)
  - There are specific breeds at risk
  - Gonadectomized animals have increased risk (2 to 4 x that of intact animals)

So let’s look at the factors

- Osteosarcoma
  - Reported incidence of 0.2%
  - Certain breeds at risk
  - Gonadectomized animals have increased risk (1.3 to 2 x that of intact animals)

So let’s look at the factors

- Hemangiosarcoma
  - Reported incidence of 0.2%
  - Certain breeds at risk
  - Spayed females have increased risk (2.2 x for splenic hemangiosarcoma, 5 x for cardiac hemangiosarcoma)
  - Castrated males have increased risk (2.4 x that of intact males)

So let’s look at the factors

- Urethral obstruction / FLUTD
  - In spite of common belief
    - No difference in urinary obstruction or feline lower urinary tract disease between castrated and intact

- Urethral sphincter mechanism incompetence
  - Estrogen responsive urinary incontinence
  - Increased incidence in spayed females dogs
  - Certain breeds at risk
  - Easily controlled with medical treatment

So let’s look at the factors

- Pyometra
  - Incidence report up to 24% in intact females
  - Certain breeds at risk
  - Ovariohysterectomy is curative
  - Ovariohysterectomy is preventive
So let’s look at the factors

- Benign prostatic hypertrophy-hyperplasia
  - Incidence reported up to
    - 50% in intact male dogs 2.4 years of age
    - 80% in intact male dogs 6 years of age
    - 95 – 100% in intact male dogs by 9 years of age
  - Castration is the treatment
  - Castration prevents

So let’s look at the factors

- Diabetes mellitus
  - Incidence in cats 0.4%
  - Increase risk with spay or castration

- Hypothyroidism
  - Incidence in dogs 0.2%
  - Increase risk with spay or castration

So let’s summarize

- Sterilization increases the risk of several conditions that have very low incidence
  - Prostatic cancer
  - Transitional cell carcinoma
  - Osteosarcoma
  - Diabetes mellitus
  - Hypothyroidism

So let’s summarize

- Sterilization decreases or eliminates the risk of several conditions that have very high incidence
  - Mammary cancer
  - Testicular cancer
  - Pyometra
  - Benign prostatic hypertrophy

So let’s summarize

- Sterilization significantly increases life expectancy in dogs and cats

So let’s summarize

- Basic Principles
  - When dealing with shelter animals must consider them as a population
  - When dealing with individually owned animals must consider the specific health benefit to the individual animal.
Putting it all together

- In shelters, spay or neuter prior to adoption
- Helps reduce over population
- Gives animal a longer life expectancy
- But does create an increased risk of some diseases or conditions (some of which are serious – osteosarcoma, hemangiosarcoma)
- And does decrease or eliminate the risk of other diseases / conditions (some of which are serious – pyometra, mammary neoplasia, testicular cancer)

Questions

- For individually owned animals, must consider purpose, breed and owners interests
  - In most situations – spay / neuter prior to first estrus cycle
    - But owners must be made aware of the risk / benefit of such a delay and make the final decision.
  - For some situations – may consider waiting until after animal has stopped growing
    - But owners must be made aware of the risk / benefit of such a delay and make the final decision.

Putting it all together

- There is still much we don’t know about the positive and negative effects of spay / neuter
- We must remain open to new information as research continues
- We must, however, always be willing to look critically at new information to determine if conclusions are valid based on the research data