

# The Long-Term Health Effects of Spay / Neuter in Dogs

Laura J. Sanborn

March 27, 2007

## INTRODUCTION

Dog owners in America are frequently advised to spay/neuter their dogs for health reasons. A number of health benefits are cited, and dog owners are told that “responsible owners spay/neuter their pets”. Yet evidence is rarely cited to support the alleged health benefits.

When discussing the health impacts of spay/neuter, the adverse health effects are often not mentioned. At times, some adverse effects are mentioned, but the most severe effects usually are not.

This article is an attempt to summarize the long-term health effects associated with spay/neuter in dogs, both positive and negative, that can be found in the veterinary medical literature. This article will not discuss the impact of spay/neuter on population control, or the impact of spay/neuter on behavior.

Nearly all of the health effects summarized in this article are findings from retrospective epidemiological studies of dogs, which examine potential associations by looking backwards in time. A few are from prospective research studies, which examine potential associations by looking forward in time.

## SUMMARY

An objective reading of the veterinary medical literature reveals a complex situation with respect to the long-term health impacts of spay/neuter in dogs. The evidence shows that spay/neuter correlates with both positive AND adverse health effects in dogs. It also suggests how much we really do not yet understand about this subject.

On balance, it appears that no compelling case can be made for neutering most male dogs, especially immature male dogs, in order to prevent future health problems. The number of health problems associated with neutering may exceed the associated health benefits in most cases.

On the positive side, neutering male dogs

- eliminates the small risk (probably <1%) of dying from testicular cancer
- reduces the risk of non-cancerous prostate disorders
- reduces the risk of perianal fistulas
- may possibly reduce the risk of diabetes (data inconclusive)

On the negative side, neutering male dogs

- if done before maturity, increases the risk of osteosarcoma (bone cancer) by a factor of 3.8; this is a common cancer in medium/large and larger breeds with a poor prognosis.
- increases the risk of cardiac hemangiosarcoma by a factor of 1.6; this is a common cancer and major cause of death in some breeds
- triples the risk of hypothyroidism
- increases the risk of geriatric cognitive impairment
- triples the risk of obesity, a common health problem in dogs with it the many associated health problems associated with obesity
- quadruples the small risk (<0.6%) of prostate cancer
- doubles the small risk (<1%) of urinary tract cancers
- increases the risk of orthopedic disorders
- increases the risk of adverse reactions to vaccinations

For female dogs, the situation is more complex. The number of health benefits associated with spaying may exceed the associated health problems in some (not all) cases. On balance, whether spaying improves the

odds of overall good health or degrades them probably depends on the age of the female dog and the relative risk of various diseases in the different breeds.

On the positive side, spaying female dogs

- if done before 2.5 years of age, greatly reduces the risk of mammary tumors, the most common malignant tumors in female dogs
- nearly eliminates the risk of pyometra, which otherwise would affect about 23% of intact female dogs; pyometra kills about 1% of intact female dogs
- reduces the risk of perianal fistulas
- removes the very small risk ( $\leq 0.5\%$ ) from uterine, cervical, and ovarian tumors

On the negative side, spaying female dogs

- if done before maturity, increases the risk of osteosarcoma by a factor of 3.1; this is a common cancer in larger breeds with a poor prognosis
- increases the risk of splenic hemangiosarcoma by a factor of 2.2 and cardiac hemangiosarcoma by a factor of  $>5$ ; this is a common cancer and major cause of death in some breeds
- triples the risk of hypothyroidism
- increases the risk of obesity by a factor of 1.6-2, a common health problem in dogs with many associated health problems
- causes urinary “spay incontinence” in 4-20% of female dogs
- increases the risk of persistent or recurring urinary tract infections by a factor of 3-4
- increases the risk of recessed vulva, vaginal dermatitis, and vaginitis, especially for female dogs spayed before puberty
- doubles the small risk ( $<1\%$ ) of urinary tract tumors
- increases the risk of orthopedic disorders
- increases the risk of adverse reactions to vaccinations

One thing is clear – much of the spay/neuter information that is available to the public is unbalanced and contains claims that are exaggerated or unsupported by evidence. Rather than helping to educate pet owners, much of this has contributed to common misunderstandings about the long-term health impacts of spay/neuter in dogs.

The traditional spay/neuter age of six months as well as the modern practice of pediatric spay/neuter appear to predispose dogs to health risks that could otherwise be avoided by waiting until the dog is physically mature, or (perhaps in the case of many male dogs) foregoing it altogether unless medically necessary.

The balance of long-term health risks and benefits of spay/neuter will vary from one dog to the next. Across-the-board recommendations for all pet dogs do not appear to be supportable from findings in the veterinary medical literature.

## **FINDINGS FROM STUDIES**

This section summarizes the diseases or conditions that have been studied with respect to spay/neuter in dogs.

### **Complications from Spay/Neuter Surgery**

All surgery incurs some risk of complications, including adverse reactions to anesthesia, hemorrhage, inflammation, infection, etc. Complications include only immediate and near term impacts that are clearly linked to the surgery, not to longer term impacts that can only be assessed by research studies.

At one veterinary teaching hospital where complications were tracked, the rates of intraoperative, postoperative and total complications were 6.3%, 14.1% and 20.6%, respectively as a result of spaying female dogs<sup>1</sup>. Other studies found a rate of total complications from spaying of 17.7%<sup>2</sup> and 23%<sup>3</sup>. A study

of Canadian veterinary private practitioners found complication rates of 22% and 19% for spaying female dogs and neutering male dogs, respectively<sup>4</sup>.

Serious complications such as infections, abscesses, rupture of the surgical wound, and chewed out sutures were reported at a 1- 4% frequency, with spay and castration surgeries accounting for 90% and 10% of these complications, respectively.<sup>4</sup>

The death rate due to complications from spay/neuter is low, at around 0.1%<sup>5</sup>.

## **Prostate Cancer**

Much of the spay/neuter information available to the public asserts that neutering will reduce or eliminate the risk that male dogs develop prostate cancer. This would not be an unreasonable assumption, given that prostate cancer in humans is linked to testosterone. But the evidence in dogs does not support this claim. In fact, the strongest evidence suggests just the opposite.

There have been several conflicting epidemiological studies over the years that found either an increased risk or a decreased risk of prostate cancer in neutered dogs. These studies did not utilize control populations, rendering these results at best difficult to interpret. This may partially explain the conflicting results.

More recently, two retrospective studies were conducted that did utilize control populations. One of these studies involved a dog population in Europe<sup>6</sup> and the other involved a dog population in America<sup>7</sup>. Both studies found that neutered male dogs have a four times *higher* risk of prostate cancer than intact dogs.

Based on their results, the researchers suggest a cause and effect relationship: “this suggests that castration does not initiate the development of prostatic carcinoma in the dog, but does favor tumor progression”<sup>6</sup> and also “Our study found that most canine prostate cancers are of ductal/urothelial origin....The relatively low incidence of prostate cancer in intact dogs may suggest that testicular hormones are in fact protective against ductal/urothelial prostatic carcinoma, or may have indirect effects on cancer development by changing the environment in the prostate.”<sup>7</sup>

This needs to be put in perspective. Unlike the situation in humans, prostate cancer is uncommon in dogs. Given an incidence of prostate cancer in dogs of less than 0.6% from necropsy studies<sup>8</sup>, it is difficult to see that the risk of prostate cancer should factor heavily into most neutering decisions. There is evidence for an increased risk of prostate cancer in at least one breed (Bouvier)<sup>6</sup>, though very little data so far to guide us in regards to other breeds.

## **Testicular Cancer**

Since the testicles are removed with neutering, castration removes any risk of testicular cancer (assuming the castration is done before cancer develops). This needs to be compared to the risk of testicular cancer in intact dogs.

Testicular tumors are not uncommon in older intact dogs, with a reported incidence of 7%<sup>9</sup>. However, the prognosis for treating testicular tumors is very good owing to a low rate of metastasis, so testicular cancer is an uncommon cause of death in intact dogs. For example, in a Purdue University breed health survey of Golden Retrievers<sup>10</sup>, deaths due to testicular cancer were sufficiently infrequent that they did not appear on list of significant causes of “Years of Potential Life Lost for Veterinary Confirmed Cause of Death” even though 40% of GR males were intact. Furthermore, the GRs who were treated for testicular tumors had a 90.9% cure rate. This agrees well with other work that found 6-14% rates of metastasis for testicular tumors in dogs<sup>11</sup>.

The high cure rate of testicular tumors combined with their frequency suggests that fewer than 1% of intact male dogs will die of testicular cancer.

In summary, though it may be the most common reason why many advocate neutering young male dogs, the risk from life threatening testicular cancer is sufficiently low that neutering most male dogs to prevent it is difficult to justify.

An exception might be bilateral or unilateral cryptorchids, as testicles that are retained in the abdomen are 13.6 times more likely to develop tumors than descended testicles<sup>12</sup> and it is also more difficult to detect retained tumors by routine physical examination.

### **Osteosarcoma (Bone Cancer)**

A multi-breed case-control study of the risk factors for osteosarcoma found that spay/neutered dogs (males or females) had twice the risk of developing osteosarcoma as did intact dogs<sup>13</sup>.

This risk was further studied in Rottweilers, a breed with a relatively high risk of osteosarcoma. This retrospective cohort study broke the risk down by age at spay/neuter, and found that the elevated risk of osteosarcoma is associated with spay/neuter of young dogs<sup>14</sup>. Rottweilers spayed/neutered before one year of age were 3.8 (males) or 3.1 (females) times more likely to develop osteosarcoma than intact dogs. Indeed, the combination of breed risk and early spay/neuter meant that Rottweilers spayed/neutered before one year of age had a 28.4% (males) and 25.1% (females) risk of developing osteosarcoma. These results are consistent with the earlier multi-breed study<sup>13</sup> but have an advantage of assessing risk as a function of age at neuter.

The researchers suggest a cause-and-effect relationship, as sex hormones are known to influence the maintenance of skeletal structure and mass, and also because their findings showed an inverse relationship between time of exposure to sex hormones and risk of osteosarcoma.<sup>14</sup>

The risk of osteosarcoma increases with increasing breed size and especially height<sup>13</sup>. It is a common cause of death in medium/large, large, and giant breeds. Osteosarcoma is the third most common cause of death in Golden Retrievers<sup>10</sup> and is even more common in larger breeds<sup>13</sup>.

Given the poor prognosis of osteosarcoma and its frequency in many breeds, spay/neuter of immature dogs in the medium/large, large, and giant breeds is apparently associated with a significant and elevated risk of death due to osteosarcoma.

### **Mammary Cancer (Breast Cancer)**

Mammary tumors are by far the most common tumors in intact female dogs, constituting some 53% of all malignant tumors in female dogs in a study of dogs in Norway<sup>15</sup> where spaying is much less common than in the USA.

50-60% of mammary tumors are malignant, for which there is a significant risk of metastasis<sup>16</sup>. Mammary tumors in dogs have been found to have estrogen receptors<sup>17</sup>, and the published research<sup>18</sup> shows that the relative risk (odds ratio) that females will develop mammary cancer compared to the risk in intact females is dependent on how many estrus cycles she experiences:

# of estrus cycles before spay	Odds Ratio
None	0.005
1	0.08
2 or more	0.26
Intact	1.00

The same data when categorized differently showed that the relative risk (odds ratio) that females will develop mammary cancer compared to the risk in intact females is indicated that:

Age at Spaying	Odds Ratio
≤ 29 months	0.06
≥ 30 months	0.40 (not statistically significant at the P<0.05 level)
Intact	1.00

Please note that these are RELATIVE risks. This study has been referenced elsewhere many times but the results have often been misrepresented as absolute risks.

A similar reduction in breast cancer risk was found for women under the age of 40 who lost their estrogen production due to “artificial menopause”<sup>19</sup> and breast cancer in humans is known to be estrogen activated.

Mammary cancer was found to be the 10<sup>th</sup> most common cause of years of lost life in Golden Retrievers, even though 86% of female GRs were spayed, at a median age of 3.4 yrs<sup>10</sup>. Considering that the female subset accounts for almost all mammary cancer cases, it probably would rank at about the 5<sup>th</sup> most common cause of years of lost life in female GRs. It would rank higher still if more female GRs had been kept intact up to 30 months of age.

Boxers, cocker spaniels, English springer spaniels, and dachshunds are breeds at high risk of mammary tumors<sup>15</sup>. A population of mostly intact female Boxers was found to have a 40% chance of developing mammary cancer between the ages of 6-12 years of age<sup>15</sup>. Purebred dogs are at higher risk than mixed breed dogs, and purebred dogs with high inbreeding coefficients are at higher risk than those with low inbreeding coefficients.<sup>20</sup>

In summary, spaying female dogs significantly reduces the risk of mammary cancer (a common cancer), and the fewer estrus cycles experienced at least up to 30 months of age, the lower the risk will be.

### **Reproductive Tract Cancer (Uterine, Cervical, and Ovarian Cancers)**

Uterine/cervical tumors are rare in dogs, constituting just 0.3% of tumors in dogs<sup>21</sup>.

Spaying will remove the risk of ovarian tumors, but the risk is only 0.5%<sup>22</sup>.

While spaying will remove the risk of reproductive tract tumors, it is unlikely that surgery can be justified to prevent the risks of uterine, cervical, and ovarian cancers as the risks are so low.

### **Urinary Tract Cancer (Bladder and Urethra Cancers)**

An age-matched retrospective study found that spay/neuter dogs were two times more likely to develop lower urinary tract tumors (bladder or urethra) compared to intact dogs<sup>23</sup>. These tumors are nearly always malignant, but are infrequent, accounting for less than 1% of canine tumors. So this risk is unlikely to weigh heavily on spay/neuter decisions.

Airedales, Beagles, and Scottish Terriers are at elevated risk for urinary tract cancer while German Shepherds have a lower than average risk<sup>23</sup>.

### **Hemangiosarcoma**

Hemangiosarcoma is a common cancer in dogs. It is a major cause of death in some breeds, such as Salukis, French Bulldogs, Irish Water Spaniels, Flat Coated Retrievers, Golden Retrievers, Boxers, Afghan Hounds, English Setter, Scottish Terrier, Boston Terrier, Bulldogs, and German Shepherd Dogs<sup>24</sup>.

In an aged-matched case controlled study, spayed females were found to have a 2.2 times higher risk of splenic hemangiosarcoma compared to intact females<sup>24</sup>.

A retrospective study of cardiac hemangiosarcoma risk factors found a >5 times greater risk in spayed female dogs compared to intact female dogs and a 1.6 times higher risk in neutered male dogs compared to intact male dogs.<sup>25</sup> The authors suggest a protective effect of sex hormones against hemangiosarcoma, especially in females.

In breeds where hemangiosarcoma is an important cause of death, the increased risk associated with spay/neuter is likely one that should factor into decisions on whether or when to sterilize a dog.

## **Hypothyroidism**

Spay/neuter in dogs was found to be correlated with a three fold increased risk of hypothyroidism compared to intact dogs.

The researchers suggest a cause-and-effect relationship<sup>26</sup>. They wrote: "More important [than the mild direct impact on thyroid function] in the association between [spaying and] neutering and hypothyroidism may be the effect of sex hormones on the immune system. Castration increases the severity of autoimmune thyroiditis in mice" which may explain the link between spay/neuter and hypothyroidism in dogs.

Hypothyroidism in dogs causes obesity, lethargy, hair loss, and reproductive abnormalities.<sup>27</sup>

## **Obesity**

Owing to changes in metabolism, spay/neuter dogs are more likely to be overweight or obese than intact dogs. One study found a two fold increased risk of obesity in spayed females compared to intact females<sup>28</sup>. Another study found that spay/neuter dogs were 1.6 (females) or 3.0 (males) times more likely to be obese than intact dogs, and 1.2 (females) or 1.5 (males) times more likely to be overweight than intact dogs<sup>29</sup>.

A survey study of veterinary practices in the UK found that 21% of dogs were obese.<sup>28</sup>

Being obese and/or overweight is associated with a host of health problems in dogs. Overweight dogs are more likely to be diagnosed with hyperadrenocorticism, ruptured cruciate ligament, hypothyroidism, lower urinary tract disease, and oral disease<sup>30</sup>. Obese dogs are more likely to be diagnosed with hypothyroidism, diabetes mellitus, pancreatitis, ruptured cruciate ligament, and neoplasia (tumors)<sup>30</sup>.

## **Diabetes**

Some data indicate that neutering doubles the risk of diabetes in male dogs, but other data showed no significant change in diabetes risk with neutering<sup>31</sup>. In the same studies, no association was found between spaying and the risk of diabetes.

## **Adverse Vaccine Reactions**

A retrospective cohort study of adverse vaccine reactions in dogs was conducted, which included allergic reactions, hives, anaphylaxis, cardiac arrest, cardiovascular shock, and sudden death. Adverse reactions were 30% more likely in spayed females than intact females, and 27% more likely in neutered males than intact males<sup>32</sup>.

The investigators discuss possible cause-and-effect mechanisms for this finding, including the roles that sex hormones play in body's ability to mount an immune response to vaccination.<sup>32</sup>

Toy breeds and smaller breeds are at elevated risk of adverse vaccine reactions, as are Boxers, English Bulldogs, Lhasa Apsos, Weimaraners, American Eskimo Dogs, Golden Retrievers, Basset Hounds, Welsh Corgis, Siberian Huskies, Great Danes, Labrador Retrievers, Doberman Pinchers, American Pit Bull Terriers, and Akitas.<sup>32</sup> Mixed breed dogs were found to be at lower risk, and the authors suggest genetic heterogeneity (hybrid vigor) as the cause.

## **Urogenital Disorders**

Urinary incontinence is common in spayed female dogs, which can occur soon after spay surgery or after a delay of up to several years. The incidence rate in various studies is 4-20%<sup>33, 34, 35</sup> for spayed females compared to only 0.3% in intact females<sup>36</sup>. Urinary incontinence is so strongly linked to spaying that it is commonly called “spay incontinence” and is caused by urethral sphincter incompetence<sup>37</sup>, though the biological mechanism is unknown. Most (but not all) cases of urinary incontinence respond to medical treatment, and in many cases this treatment needs to be continued for the duration of the dog's life.<sup>38</sup>

A retrospective study found that persistent or recurring urinary tract (bladder) infections (UTIs) were 3-4 times more likely in spayed female dogs than in intact females<sup>39</sup>. Another retrospective study found that female dogs spayed before 5 ½ months of age were 2.76 times more likely to develop UTIs compared to those spayed after 5 ½ months of age.<sup>40</sup>

Depending on the age of surgery, spaying causes abnormal development of the external genitalia. Spayed females were found to have an increased risk of recessed vulva, vaginal dermatitis, vaginitis, and UTIs.<sup>41</sup> The risk is higher still for female dogs spayed before puberty.<sup>41</sup>

## **Pyometra (Infection of the Uterus)**

Pet insurance data in Sweden (where spaying is very uncommon) found that 23% of all female dogs developed pyometra before 10 years of age<sup>42</sup>. Bernese Mountain dogs, Rottweilers, rough-haired Collies, Cavalier King Charles Spaniels and Golden Retrievers were found to be high risk breeds<sup>42</sup>. Female dogs that have not whelped puppies are at elevated risk for pyometra<sup>43</sup>. Rarely, spayed female dogs can develop “stump pyometra” related to incomplete removal of the uterus.

Pyometra can usually be treated surgically or medically, but 4% of pyometra cases led to death<sup>42</sup>. Combined with the incidence of pyometra, this suggests that about 1% of intact female dogs will die from pyometra.

## **Perianal Fistulas**

Male dogs are twice as likely to develop perianal fistulas as females, and spay/neutered dogs have a decreased risk compared to intact dogs<sup>44</sup>.

German Shepherd Dogs and Irish Setters are more likely to develop perianal fistulas than are other breeds.<sup>44</sup>

## **Non-cancerous Disorders of the Prostate Gland**

The incidence of benign prostatic hypertrophy (BPH, enlarged prostate) increases with age in intact male dogs, and occurs in more than 80% of intact male dogs older than the age of 5 years<sup>45</sup>. Most cases of BPH cause no problems, but in some cases the dog will have difficulty defecating or urinating.

Neutering will prevent BPH. If neutering is done after the prostate has become enlarged, the enlarged prostate will shrink relatively quickly.

BPH is linked to other problems of the prostate gland, including infections, abscesses, and cysts, which can sometimes have serious consequences.

## **Orthopedic Disorders**

In a study of beagles, surgical removal of the ovaries (as happens in spaying) caused an increase in the rate of remodeling of the ilium (pelvic bone)<sup>46</sup>, suggesting an increased risk of hip dysplasia with spaying. Spaying was also found to cause a net loss of bone mass in the spine<sup>47</sup>.

Spay/neuter of immature dogs delays the closure of the growth plates in bones that are still growing, causing those bones to end up significantly longer than in intact dogs or those spay/neutered after maturity<sup>48</sup>. Since the growth plates in various bones close at different times, spay/neuter that is done after some growth plates have closed but before other growth plates have closed can result in a dog with unnatural proportions, possibly impacting performance and long term durability of the joints.

Spay/neuter is associated with a two fold increased risk of cranial cruciate ligament rupture<sup>49</sup>. Perhaps this is associated with the increased risk of obesity<sup>28</sup> or to changes in body proportions in dogs spay/neutered before the growth plates in the bones have closed<sup>48</sup>.

Spay/neuter before 5 ½ months of age is associated with a 70% increased aged-adjusted risk of hip dysplasia compared to dogs spayed/neutered after 5 ½ months of age<sup>40</sup>. The researchers suggest “it is possible that the increase in bone length that results from early-age gonadectomy results in changes in joint conformation, which could lead to a diagnosis of hip dysplasia”.

In a breed health survey study of Airedales, spay/neuter dogs were significantly more likely to suffer hip dysplasia as well as “any musculoskeletal disorder”, compared to intact dogs<sup>50</sup>, however possible confounding factors were not controlled for, such as the possibility that some dogs might have been spayed/neutered because they had hip dysplasia or other musculoskeletal disorders.

Compared to intact dogs, another study found that dogs neutered six months prior to a diagnosis of hip dysplasia were 1.5 times as likely to develop clinical hip dysplasia.<sup>51</sup>

## **Geriatric Cognitive Impairment**

Neutered male dogs and spayed female dogs are at increased risk of geriatric cognitive impairment compared to intact male dogs<sup>52</sup>. There weren't enough intact geriatric females available for the study to determine their risk.

Geriatric cognitive impairment includes disorientation in the house or outdoors, changes in social interactions with human family members, loss of house training, and changes in the sleep-wake cycle<sup>52</sup>.

The investigators state “This finding is in line with current research on the neuro-protective roles of testosterone and estrogen at the cellular level and the role of estrogen in preventing Alzheimer's disease in human females. One would predict that estrogens would have a similar protective role in the sexually intact female dogs; unfortunately too few sexually intact female dogs were available for inclusion in the present study to test the hypothesis”<sup>52</sup>

## **CONCLUSIONS**

An objective reading of the veterinary medical literature reveals a complex situation with respect to the long-term health impacts of spay/neuter in dogs. The evidence shows that spay/neuter correlates with both positive AND adverse health effects in dogs. It also suggests how much we really do not yet understand about this subject.

On balance, it appears that no compelling case can be made for neutering most male dogs to prevent future health problems, especially immature male dogs. The number of health problems associated with neutering may exceed the associated health benefits in most cases.

For female dogs, the situation is more complex. The number of health benefits associated with spaying may exceed the associated health problems in many (not all) cases. On balance, whether spaying improves the odds of overall good health or degrades them probably depends on the age of the dog and the relative risk of various diseases in the different breeds.

The traditional spay/neuter age of six months as well as the modern practice of pediatric spay/neuter appear to predispose dogs to health risks that could otherwise be avoided by waiting until the dog is physically mature, or (perhaps in the case of many male dogs) foregoing it altogether unless medically necessary.

The balance of long-term health risks and benefits of spay/neuter will vary from one dog to the next. Across-the-board recommendations for all dogs do not appear to be supportable from findings in the veterinary medical literature.

---

## REFERENCES

- <sup>1</sup> Burrow R, Batchelor D, Cripps P. Complications observed during and after ovariohysterectomy of 142 bitches at a veterinary teaching hospital. *Vet Rec.* 2005 Dec 24-31;157(26):829-33.
- <sup>2</sup> Pollari FL, Bonnett BN, Bamsey, SC, Meek, AH, Allen, DG (1996) Postoperative complications of elective surgeries in dogs and cats determined by examining electronic and medical records. *Journal of the American Veterinary Medical Association* 208, 1882-1886
- <sup>3</sup> Dorn AS, Swist RA. (1977) Complications of canine ovariohysterectomy. *Journal of the American Animal Hospital Association* 13, 720-724
- <sup>4</sup> *Can Vet J.* 1996 November; 37(11): 672–678. Evaluation of postoperative complications following elective surgeries of dogs and cats at private practices using computer records, Pollari FL, Bonnett BN
- <sup>5</sup> Pollari FL, Bonnett BN, Bamsey SC, Meek AH, Allen DG. Postoperative complications of elective surgeries in dogs and cats determined by examining electronic and paper medical records. *J Am Vet Med Assoc.* 1996 Jun 1;208(11):1882-6
- <sup>6</sup> Teske E, Naan EC, van Dijk EM, van Garderen E, Schalken JA. Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. *Mol Cell Endocrinol.* 2002 Nov 29;197(1-2):251-5.
- <sup>7</sup> Sorenmo KU, Goldschmidt M, Shofer F, Ferrocone J. Immunohistochemical characterization of canine prostatic carcinoma and correlation with castration status and castration time. *Vet Comparative Oncology.* 2003 Mar; 1 (1): 48
- <sup>8</sup> Weaver, AD. *Vet Rec.* 1981; 109, 71-75.
- <sup>9</sup> Cohen D, Reif JS, Brodey RS, et al: Epidemiological analysis of the most prevalent sites and types of canine neoplasia observed in a veterinary hospital. *Cancer Res* 34:2859-2868, 1974
- <sup>10</sup> [http://www.vet.purdue.edu/epi/golden\\_retriever\\_final22.pdf](http://www.vet.purdue.edu/epi/golden_retriever_final22.pdf)
- <sup>11</sup> *Handbook of Small Animal Practice*, 3rd ed
- <sup>12</sup> Hayes HM Jr, Pendergrass TW. Canine testicular tumors: epidemiologic features of 410 dogs. *Int J Cancer* 1976 Oct 15;18(4):482-7
- <sup>13</sup> Ru G, Terracini B, Glickman LT. *Vet J* 1998 Jul; 156(1):31-9

- 
- <sup>14</sup> Cooley DM, Beranek BC, Schlittler DL, Glickman NW, Glickman LT, Waters DJ. Endogenous gonadal hormone exposure and bone sarcoma risk. *Cancer Epidemiol Biomarkers Prev.* 2002 Nov;11(11):1434-40.
- <sup>15</sup> Moe L. Population-based incidence of mammary tumours in some dog breeds. *J of Reproduction and Fertility Supplement* 57, 439-443.
- <sup>16</sup> Ferguson HR; *Vet Clinics of N Amer: Small Animal Practice*; Vol 15, No 3, May 1985
- <sup>17</sup> MacEwen EG, Patnaik AK, Harvey HJ Estrogen receptors in canine mammary tumors. *Cancer Res.*, 42: 2255-2259, 1982.
- <sup>18</sup> Schneider, R, Dorn, CR, Taylor, DON, *J Natl Cancer Institute*, Vol 43, No 6, Dec. 1969
- <sup>19</sup> Feinleib M: Breast cancer and artificial menopause: A cohort study. *J Nat Cancer Inst* 41: 315-329, 1968.
- <sup>20</sup> Dorn CR and Schneider R. Inbreeding and canine mammary cancer. A retrospective study. *J Natl Cancer Inst.* 57: 545-548, 1976.
- <sup>21</sup> Brodey RS: Canine and feline neoplasia. *Adv Vet Sci Comp Med* 14:309-354, 1970
- <sup>22</sup> Hayes A, Harvey H J: Treatment of metastatic granulosa cell tumor in a dog. *J Am Vet Med Assoc* 174:1304-1306, 1979
- <sup>23</sup> Norris AM, Laing EJ, Valli VE, Withrow SJ. *J Vet Intern Med* 1992 May; 6(3):145-53
- <sup>24</sup> Prymak C, McKee LJ, Goldschmidt MH, Glickman LT. *J Am Vet Med Assoc* 1988 Sep; 193(6):706-12
- <sup>25</sup> Ware WA, Hopper, DL. Cardiac Tumors in Dogs: 1982-1995. *J Vet Intern Med* 1999;13:95-103.
- <sup>26</sup> Panciera DL. *J Am Vet Med Assoc.* 1994 Mar 1;204(5):761-7 Hypothyroidism in dogs: 66 cases (1987-1992).
- <sup>27</sup> Panciera DL. Canine hypothyroidism. Part I. Clinical findings and control of thyroid hormone secretion and metabolism. *Compend Contin Pract Vet* 1990; 12: 689-701.
- <sup>28</sup> Edney AT, Smith PM. Study of obesity in dogs visiting veterinary practices in the United Kingdom. *Vet Rec.* 1986 Apr 5;118(14):391-6.
- <sup>29</sup> McGreevy PD, Thomson PC, Pride C, Fawcett A, Grassi T, Jones B. Prevalence of obesity in dogs examined by Australian veterinary practices and the risk factors involved. *Vet Rec.* 2005 May 28;156(22):695-702.
- <sup>30</sup> Lund EM, Armstrong PJ, Kirk, CA, Klausner, JS. Prevalence and Risk Factors for Obesity in Adult Dogs from Private US Veterinary Practices. *Intern J Appl Res Vet Med • Vol. 4, No. 2, 2006.*
- <sup>31</sup> Marmor M, Willeberg P, Glickman LT, Priester WA, Cypess RH, Hurvitz AI. Epizootiologic patterns of diabetes mellitus in dogs *Am J Vet Res.* 1982 Mar;43(3):465-70. ..
- <sup>32</sup> Moore GE, Guptill LF, Ward MP, Glickman NW, Faunt KF, Lewis HB, Glickman LT. Adverse events diagnosed within three days of vaccine administration in dogs. *JAVMA* Vol 227, No 7, Oct 1, 2005
- <sup>33</sup> Thrusfield MV, Holt PE, Muirhead RH. Acquired urinary incontinence in bitches: its incidence and relationship to neutering practices.. *J Small Anim Pract.* 1998. Dec;39(12):559-66.
- <sup>34</sup> Stocklin-Gautschi NM, Hassig M, Reichler IM, Hubler M, Arnold S. The relationship of urinary incontinence to early spaying in bitches. *J Reprod Fertil Suppl.* 2001;57:233-6...
- <sup>35</sup> Arnold S, Arnold P, Hubler M, Casal M, and Rüschi P. Urinary Incontinence in spayed bitches: prevalence and breed disposition. *European Journal of Companion Animal Practice.* 131, 259-263.
- <sup>36</sup> Thrusfield MV 1985 Association between urinary incontinence and spaying in bitches *Vet Rec* 116 695
- <sup>37</sup> Richter KP, Ling V. Clinical response and urethral pressure profile changes after phenylpropanolamine in dogs with primary sphincter incompetence. *J Am Vet Med Assoc* 1985; 187: 605-611.
- <sup>38</sup> Holt PE. Urinary incontinence in dogs and cats. *Vet Rec* 1990; 127: 347-350.

- 
- <sup>39</sup> Seguin MA, Vaden SL, Altier C, Stone E, Levine JF (2003) Persistent Urinary Tract Infections and Reinfections in 100 Dogs (1989–1999). *Journal of Veterinary Internal Medicine*: Vol. 17, No. 5 pp. 622–631.
- <sup>40</sup> Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in dogs. *JAVMA* 2004;224:380-387.
- <sup>41</sup> Verstegen-Onclin K, Verstegen J. Non-reproductive Effects of Spaying and Neutering: Effects on the Urogenital System <http://www.acc-d.org/2006%20Symposium%20Docs/Session%20I.pdf>
- <sup>42</sup> Hagman R: New aspects of canine pyometra. Doctoral thesis, Swedish University of Agricultural Sciences, Uppsala, 2004.
- <sup>43</sup> Chastain CB, Panciera D, Waters C: Associations between age, parity, hormonal therapy and breed, and pyometra in Finnish dogs. *Small Anim Endocrinol* 1999; 9: 8.
- <sup>44</sup> Killingsworth CR, Walshaw R, Dunstan RW, Rosser, EJ. *Am J Vet Res*, Vol 49, No. 10, Oct 1988.
- <sup>45</sup> Johnston SD, Kamolpatana K, Root-Kustritz MV, Johnston GR, *Animal Reproductive Science* 60-61 (2000) 405-415.
- <sup>46</sup> Dannuccia GA, Martin RB., Patterson-Buckendahl P Ovariectomy and trabecular bone remodeling in the dog. *Calcif Tissue Int* 1986; 40: 194-199.
- <sup>47</sup> Martin RB, Butcher RL, Sherwood L, L Buckendahl P, Boyd RD, Farris D, Sharkey N, Dannucci G. Effects of ovariectomy in beagle dogs. *Bone* 1987; 8:23-31
- <sup>48</sup> Salmeri KR, Bloomberg MS, Scruggs SL, Shille V. Gonadectomy in immature dogs: Effects on skeletal, physical, and behavioral development, *JAVMA*, Vol 198, No. 7, April 1991.
- <sup>49</sup> Whitehair JG, Vasseur PB, Willits NH. Epidemiology of cranial cruciate ligament rupture in dogs. *J Am Vet Med Assoc.* 1993 Oct 1;203(7):1016-9.
- <sup>50</sup> [http://www.vet.purdue.edu/epi/Airedale%20final%20report\\_revised.pdf](http://www.vet.purdue.edu/epi/Airedale%20final%20report_revised.pdf)
- <sup>51</sup> van Hagen MA, Ducro BJ, van den Broek J, Knol BW. Incidence, risk factors, and heritability estimates of hind limb lameness caused by hip dysplasia in a birth cohort of boxers. *Am J Vet Res.* 2005 Feb;66(2):307-12.
- <sup>52</sup> Hart BL. Effect of gonadectomy on subsequent development of age-related cognitive impairment in dogs. *J Am Vet Med Assoc.* 2001 Jul 1;219(1):51-6.