This bibliography provides synopses of scientific studies evaluating effects of removal of the gonads (ovaries in females and testes in males). The list is alphabetical by first author, with the primary topic of the study listed second. Primary topics include complications of surgery, behavior, nutrition (obesity), bone growth, musculoskeletal abnormalities, urinary tract development and urinary incontinence, prostate disease, coat changes, and neoplasia (cancer). The number of animals in each study (n) is included to help the reader decide if information from a given study should be extrapolated to the general population. Study design may be either prospective (study designed and carried out), retrospective (records or surveys used to determine what happened in the past), or case-based (cases described). A brief commentary may follow the study synopsis to explain background medical information or clinical significance of study findings.

This is not a complete bibliography. Interested readers are encouraged to read the scientific articles themselves and to contact their veterinarian with questions. Many manuscripts are available electronically; using any web-based search engine, search for the authors’ names or title.


PRIMARY TOPIC: Neoplasia (prostatic)

n = 31 male dogs / Retrospective study

SYNOPSIS: The risk of developing malignant prostatic cancer was 2.38 times greater in castrated male dogs than in intact male dogs. Age at the time of diagnosis and referral ranged from 6 to 18 years. The severe clinical signs of disease and sites of metastasis (movement of the cancer throughout the body) are described.

COMMENTARY: Prostatic cancer is an uncommon but highly malignant cancer in dogs.


PRIMARY TOPIC: Nutrition (obesity)

n = 8 female cats / Prospective study

SYNOPSIS: Cats were spayed and fed so as to maintain body weight for 12 weeks, then given all the food they wanted for 12 weeks. Blood samples and biopsies from skeletal muscle and fat (adipose tissue) were obtained. Metabolic activity of adipose tissue was altered after ovariohysterectomy.
3)  

PRIMARY TOPIC: Neoplasia (prostatic)  
n = 2219 male dogs / Retrospective study  

SYNOPSIS: Castrated male dogs with cancer of the prostate or urinary tract were compared with all male dogs over 4 years of age without prostatic or urinary cancer in a large database. Castrated male dogs were 3.56 times more likely to develop transitional cell tumors of the urinary bladder, 8.00 times more likely to develop transitional cell tumors of the prostate, and 2.84 times more likely to develop malignant prostatic cancer than intact male dogs in that population. Predisposed breeds were identified, suggesting a genetic component.  

4)  

PRIMARY TOPIC: Complications of surgery  
n = 142 female dogs / Retrospective study  

SYNOPSIS: Records were reviewed for 142 female dogs spayed at the University of Liverpool over a 2 year period. All surgeries were elective (none of the dogs had reproductive tract disease). Rates of intraoperative and postoperative complications were 6.3% and 14.1%, respectively. The complication described during surgery (intraoperatively) was hemorrhage. The complications described after surgery (postoperatively) were hemorrhage, diarrhea, inflammation of the trachea, wound inflammation, false pregnancy, and pancreatitis. For only 2 of the 142 dogs did the complication cause significant illness; most resolved without treatment.  

5)  

PRIMARY TOPIC: Musculoskeletal abnormalities  
n = 150 dogs / Retrospective study  

SYNOPSIS: Dogs with injury of the anterior cruciate ligament (ACL) on one (unilateral) or both sides (bilateral) were evaluated for angle at the level of the knee (stifle joint). Dogs with unilateral ACL injury and an excessively steep angle of the stifle joint were not more likely than dogs with shallow angulation to develop ACL injury bilaterally.
COMMENTARY: ACL injury is very common in dogs. Causative factors include gender (female), weight (large breed and overweight dogs) and possibly intact status (spayed or castrated). One other possible causative factor is excessive angulation of the stifle or knee joint; this study suggests that may not be a true cause.

6)


PRIMARY TOPIC: Neoplasia (mammary)

n =79 female dogs / Retrospective case series

SYNOPSIS: Medical records from 79 female dogs with malignant mammary (breast) tumors were evaluated to determine which factors were associated with survival 2 years after diagnosis. Dogs that had been spayed were more likely to survive 2 years or longer after diagnosis than dogs that were still intact.

COMMENTARY: It has long been demonstrated that spaying before a female dog or cat goes through heat greatly decreases risk of mammary tumors later in her life. Mammary cancer is very common and is malignant 50% of the time in dogs and virtually 100% of the time in cats.

7)


PRIMARY TOPIC: Neoplasia (bone)

n = NA / Review paper

SYNOPSIS: Osteosarcoma (bone cancer) is an uncommon but highly malignant tumor of dogs. Large and giant breed dogs are most commonly affected with Irish setters, St. Bernards, Rottweilers, and Doberman pinschers at greater risk.

8)


PRIMARY TOPIC: Neoplasia (bone)

n = 683 Rottweilers / Retrospective study
SYNOPSIS: Questionnaires were mailed to owners of Rottweiler dogs in North America. Bone sarcoma was diagnosed in 12.6% of dogs in this population. Dogs spayed or castrated before 1 year of age were significantly more likely to develop bone cancer than dogs left intact. Exact cause-and-effect was not defined.

COMMENTARY: Rottweilers are a breed known to have a genetic predisposition to osteosarcoma and incidence in this population was much, much higher than that in the general dog population.


PRIMARY TOPIC: Prostate disease

n = 17 male dogs / Prospective study

SYNOPSIS: Experimentally induced prostate infection was more readily cleared from castrated dogs than from intact dogs.

COMMENTARY: Prostatitis (prostate infection) develops secondary to an abnormality of the prostate. The most common underlying problem is benign prostatic hypertrophy, which occurs only in intact dogs (see Krawiec reference).


PRIMARY TOPIC: Musculoskeletal abnormalities

n = 116 dogs / Retrospective study

SYNOPSIS: Fifty-eight dogs with excessive angulation of the knee joint and 58 dogs with normal angulation were compared. All dogs in both groups had anterior cruciate ligament (ACL) injury in one or both limbs. Dogs with excessive angulation and clinical signs of ACL injury were younger than control dogs and were more likely to have been spayed or neutered before 6 months of age.


PRIMARY TOPIC: Behavior

n = 1552 dogs (questionnaire) and 6000 dogs (online survey) / Prospective study
SYNOPSIS: Spayed female dogs were more likely to be aggressive toward their owners and to strangers than intact females; this effect was highly breed-specific. Castration was not an effective treatment for aggressive behavior in male dogs.

12)  
PRIMARY TOPIC: Bone growth  
n = 21 dogs / Prospective study  
SYNOPSIS: Eleven dogs were spayed at 10 weeks of age; 10 dogs underwent sham surgeries, in which they underwent anesthesia but surgery was not performed. Mineral density was compared between the groups up to 6 months of age. Bone mineral content and density was higher in spayed female dogs than in those left intact.

13)  
PRIMARY TOPIC: Hormone disorders  
n = 182,087 dogs / Retrospective study  
SYNOPSIS: Incidence of diabetes mellitus was reviewed in insurance records of 180,000 dogs in Sweden. Most dogs were not spayed or castrated. Incidence was significantly higher in female dogs than in males. Some breeds were over-represented suggesting a genetic component; however, breeds identified differed from those published in other countries.

14)  
PRIMARY TOPIC: Nutrition (obesity)  
n = 23 male and female cats / Prospective study  
SYNOPSIS: Six male and 6 female cats were spayed or castrated at 18 to 24 months of age. The other cats were left intact. Metabolic rate and thyroid hormone concentrations were measured before and after surgery in both groups. Metabolic rate was significantly decreased in spayed females compared to intact females. Spayed and castrated animals showed increase in daily food intake and body weight. Thyroid hormone concentrations did not differ between groups.
15)  
PRIMARY TOPIC: Nutrition (obesity)  
n = 15 female cats / Prospective study  
SYNOPSIS: Ten cats were spayed between 14 and 16 months of age. Five cats underwent sham surgery. Food was provided to maintain body weight. Substantial restriction in food allowance was required to maintain body weight in the spayed cats compared to the intact cats. Intact cats self-regulated food intake while spayed cats ate all food made available to them.  

16)  
PRIMARY TOPIC: Nutrition (obesity)  
n = 139 male and female dogs / Prospective study  
SYNOPSIS: Questionnaires were supplied to owners of dogs at a 12 to 18 month interval. Owners were asked to evaluate behaviors indicative of cognitive impairment. There were too few intact female dogs to be included in the study. The intact male dog group contained only 6 dogs. The study author concluded that sexually intact male dogs were less likely to undergo progression of cognitive impairment (behaviors indicative of senility) than castrated male dogs.  

17)  
PRIMARY TOPIC: Urinary tract development  
n = 30 male cats / Prospective study  
SYNOPSIS: Cats were assigned to 3 groups of 10 each. Control cats were left sexually intact. One group was castrated at 5 months of age and supplemented with testosterone. The final group was castrated and not supplemented. The cats were euthanized at 10 months of age and the urinary tract submitted for assessment. Urethral circumference did not vary between the groups.  

18)  
PRIMARY TOPIC: Hormone disorders

n = 221 dogs with diabetes mellitus, 42,882 dogs without diabetes / Retrospective study

SYNOPSIS: Five breeds were identified as at high risk for development of diabetes mellitus; 3 breeds were identified as being as decreased risk. This study suggests genetic factors may be a component of onset of diabetes mellitus in dogs.


PRIMARY TOPIC: Urinary incontinence

n = NR / Retrospective study

SYNOPSIS: Risk factors identified for urethral sphincter incompetence and subsequent leaking of urine included breed, size (large breeds), and having been spayed.


PRIMARY TOPIC: Nutrition (obesity)

n = 8 female dogs / Prospective study

SYNOPSIS: Four female Beagles were spayed at 18 months of age; the other 4 dogs underwent sham surgery. All dogs were offered all the food they would eat and food intake recorded for 5 weeks after surgery. Food intake and body weight were increased in spayed dogs compared to the control group.


PRIMARY TOPIC: Complications of surgery

n = 775 cats and 1213 dogs / Prospective study

SYNOPSIS: Animals were grouped into three groups; spay or castration at less than 12 weeks of age, spay or castration at 12 to 23 weeks of age, or spay or castration at more than 23 weeks of age. Complications were defined as minor (required little or no treatment) or major (required treatment and caused significant discomfort to the animal). Those animals undergoing surgery at more than 23 weeks of age had the highest complication rate.
22)


PRIMARY TOPIC: Complications of surgery

n = 263 cats / Retrospective study

SYNOPSIS: Cats were split into two groups; spay or castration at 24 weeks of age or less, or spay or castration at more than 24 weeks of age. Information was retrieved from telephone interviews of owners who adopted the cats from a humane shelter and from veterinary records. There were no differences in complications or onset of behavioral or medical disorders between the two groups, with a median follow-up period of 37 months.

23)


PRIMARY TOPIC: Complications of surgery

n = 269 dogs / Retrospective study

SYNOPSIS: Dogs were split into two groups; spay or castration at 24 weeks of age or less, or spay or castration at more than 24 weeks of age. Information was retrieved from telephone interviews of owners who adopted the dogs from a humane shelter and from veterinary records. There were no differences in complications or onset of behavioral disorders between the two groups. Infectious disease incidence was increased in the group who underwent surgery younger; this may have been due to increased incidence of infectious disease, especially parvovirus, in the facility from which most of these dogs originated.

24)


PRIMARY TOPIC: Behavior

n = 14 female dogs / Prospective study

SYNOPSIS: Seven dogs were spayed at 5 to 10 months of age. The other dogs were left intact as a control group. Four to 5 months after treatment dogs were tested and recorded for reactivity to humans and other dogs. Spayed dogs were more reactive.

PRIMARY TOPIC: Prostate disease

n = 177 male dogs / Case review

SYNOPSIS: Clinical signs of various prostatic disorders are described. The only prostatic disease described in castrated male dogs is prostatic cancer.

26)


PRIMARY TOPIC: Prostate disease

n = 15 male dogs / Prospective study

SYNOPSIS: Prostate changes were tracked in groups of dog with age. Prostate size increased due to benign enlargement (benign prostatic hypertrophy) over the life of the dog.

COMMENTARY: Only dogs and humans undergo this benign age-related change in prostate size, which is testosterone-dependent.

27)


PRIMARY TOPIC: Nutrition (obesity)

n = 7 cats / Prospective study

SYNOPSIS: Male cats were castrated at 11 months of age and their body weight and hormonal changes monitored for 44 to 56 weeks. Changes in metabolism dependent hormones including leptin preceded changes in body weight. Castrated males gained about 20% of their initial body weight by 44 weeks after castration.

28)


PRIMARY TOPIC: Bone growth

n = 152 cats / Retrospective study
SYNOPSIS: Radiographs (x-rays) of cats under 4 years of age were examined for closure of growth plates (physes) on the bones. Closure of physes was delayed in castrated compared to intact male cats.

COMMENTARY: Closure of growth plates is due to release of hormones from the gonads (estrogen in females, testosterone in males). Animals spayed or castrated before puberty do not have significant hormone exposure and growth plate closure is delayed. Growth plates do close eventually.


PRIMARY TOPIC: Bone growth

n = 26 cats / Retrospective study

SYNOPSIS: Twenty-six cats presented for fracture of the growth plate at the top of the femur (thigh bone). Twenty-five of the cats were castrated males. Mean weight of these cats was significantly greater than that of a control group. Fourteen of the 16 cats with known age at the time of castration had been castrated at less than 6 months of age. Several other growth plates were open in these cats, all of whom were greater than 1 year of age.


PRIMARY TOPIC: Behavior

n = 300 female dogs / Retrospective study

SYNOPSIS: Questionnaires were sent to owners of 150 female dogs at the time of spay and again 6 months later, and at the same time interval to owners of unspayed female dogs, matched for breed and age. Spayed female dogs were more likely than those left intact to demonstrate indiscriminate appetite and dominance aggression toward family members. Spayed females most likely to show an increase in dominance aggression were dogs spayed less than one year of age who already were showing aggression.


PRIMARY TOPIC: Complications of surgery

n = 1016 male and female dogs, 1459 male and female cats / Retrospective study
SYNOPSIS: Computerized records were reviewed. Postoperative complications (those occurring after surgery) occurred in 6.1% of dogs and 2.6% of cats, with 1 dog dying and 6 having major complications (requiring veterinary care) and 3 cats dying and 4 having major complications. Review of paper records for 218 dogs and cats revealed higher incidence of postoperative complications, suggesting incomplete documentation in computerized records.

32)


PRIMARY TOPIC: Hormone diseases

n = NA / Retrospective study

SYNOPSIS: Prevalence of diabetes mellitus increased in a teaching hospital over a 29 year span. Significant risk factors included gender (male), body weight (overweight or obese), and age.

33)


PRIMARY TOPIC: Neoplasia (hemangiosarcoma)

n = 217 dogs with hemangiosarcoma / Retrospective study

SYNOPSIS: Hemangiosarcoma is cancer of blood vessels or blood-rich tissues. This study described hemangiosarcoma in the spleen. Spayed females have 2.2 times greater risk of developing hemangiosarcoma than intact females. German Shepherd dogs also are at increased risk.

COMMENTARY: Hemangiosarcoma is an uncommon but malignant tumor requiring surgical therapy.

34)


PRIMARY TOPIC: Prostate disease

n = 88 male dogs / Retrospective study

SYNOPSIS: The most common prostate disease of male dogs is benign prostatic hypertrophy, accounting for 58% of cases of prostate disease in this study.
PRIMAR YTOPIC: Coat change

n = 39 female dogs / Prospective study

SYNOPSIS: Coat changes were identified in 20% of dogs after spaying with the coat changed described as an increase in wool hair and a decrease in hair color intensity ("puppy coat").

36)

PRIMAR YTOPIC: Behavior

n = 1053 dogs / Retrospective study

SYNOPSIS: Questionnaires were sent to owners of 1877 English Springer spaniels. Dogs with a history of aggression were compared to dogs with no such history. Variables associated with owner-directed aggression included gender (male), reproductive status (spayed or castrated), and age greater than 4 years.

37)

PRIMAR YTOPIC: Urinary tract development

n = 16 male cats / Prospective study

SYNOPSIS: Cats were neutered at 7 weeks or 7 months of age, or left intact. Voiding cystourethrograms (contrast radiographs [x-rays] of the urinary tract while expressing urine from the bladder) were performed at 22 months of age and urethral diameter compared between the groups. Diameter of the urethra did not vary between groups for the male cats. Extrusion of the penis from the prepuce was possible in all the intact male cats, in 60% of the cats castrated at 7 months of age, and in none of the cats castrated at 7 weeks of age; clinical significance of this finding is not known.

38)
PRIMARY TOPIC: Nutrition (obesity)

n = 36 male and female cats / Prospective study

SYNOPSIS: Male and female cats were spayed or castrated at 7 weeks or 7 months of age, or left intact. Indirect calorimetry was used to measure metabolic rate. Intact cats had higher metabolic rate than cats spayed or castrated at either age.

39)


PRIMARY TOPIC: Bone growth

n = 18 male and female cats / Prospective study

SYNOPSIS: Male and female cats were spayed or castrated at 7 weeks or 7 months of age, or left intact. Forelimbs were radiographed (x-rayed) monthly beginning at 4 months of age. Closing of growth plates was identified on radiographs and by lack of continuing increase in bone length. Growth plates closed later in cats spayed or neutered at any age than in intact cats.

40)


PRIMARY TOPIC: ---

n = NA / Review paper

SYNOPSIS: This is an in-depth, well referenced review of all papers to the date of publication evaluating pros and cons of spay or castration in dogs and cats.

41)


PRIMARY TOPIC: Neoplasia (bone)

n = 3062 dogs / Retrospective study

SYNOPSIS: Medical records from 3062 dogs with confirmed bone cancer were reviewed. Risk factors associated with increased incidence of bone cancer included increased weight, increased height, and increasing age. Spayed and castrated dogs had a two-fold risk compared to intact control dogs matched for age and breed.

PRIMARY TOPIC: Bone growth, behavior, nutrition

n = 32 dogs / Prospective study

SYNOPSIS: Dogs were spayed or castrated at 7 weeks or 7 months of age, or left intact. Forelimb radiographs were taken to assess growth plate closure; growth plate closure was delayed in both groups of spayed or castrated dogs compared to the intact dogs and final length of the forelimb was statistically longer than in the intact group. All spayed or castrated dogs were judged to be more active than intact dogs. Body weight did not influence food intake or body weight; these were assessed at 15 months of age.


PRIMARY TOPIC: Urinary incontinence

n = 10 female dogs / Prospective study

SYNOPSIS: Urethral closure pressure was evaluated for 18 months after spay. Closure pressure was reduced during that time although skeletal muscle tone in the area increased. None of the dogs in the study showed clinical incontinence during the study.


PRIMARY TOPIC: Musculoskeletal abnormalities

n = 3218 male and female dogs / Retrospective study

SYNOPSIS: Records of dogs treated at one orthopedic veterinary practice over a 2-year span were reviewed. Prevalence of anterior cruciate ligament (ACL ) injury in that population was 3.48%. Females that had been spayed and males that had been castrated were significantly more likely to suffer ACL injury than intact dogs in that population, with prevalence 2.1 times greater. Females were more likely to suffer ACL injury than males. Larger breed dogs were more likely to suffer ACL injury than small or medium breeds. An exact cause-and-effect relationship between spay or castration and ACL injury was not defined.

PRIMARY TOPIC: Behavior, medical disorders

n = 1660 cats / Retrospective study

SYNOPSIS: Owners of cats adopted from a humane organization were questioned and some veterinary records reviewed to determine prevalence of behavioral and medical disorders and association with age at the time of spay or neuter. Male and female cats spayed before 5.5 months of age showed decreased prevalence of medical disorders compared to those spayed or castrated when older, and show increased hiding and shy behavior.

46)


PRIMARY TOPIC: Behavior, medical disorders, musculoskeletal abnormalities, urinary incontinence

n = 1842 dogs / Retrospective study

SYNOPSIS: Owners of dogs adopted from a humane organization were questioned and some veterinary records reviewed to determine prevalence of behavioral and medical disorders and association with age at the time of spay or neuter. For female dogs, spaying before 3 months of age was associated with increased incidence of urinary incontinence and possibly with increased urinary tract infection. For male and female dogs spayed or castrated before 5.5 months of age, noise phobias and sexual behaviors were increased. Hip dysplasia also is described as increased in prevalence although it is not clear that a veterinary diagnosis was made in all cases. Early spay or neuter was associated with decreased obesity, separation anxiety, escaping behavior, and urination and defecation when frightened.

47)


PRIMARY TOPIC: Urinary incontinence

n = 206 female dogs / Retrospective study

SYNOPSIS: Questionnaires were received from owners of 206 spayed female dogs. Incidence of urinary incontinence was 9.7% and was more common in dogs weighing more than 20 kg (44 lbs).

48)

PRIMARY TOPIC: Behavior, nutrition, bone growth

n = 31 male and female cats / Prospective study

SYNOPSIS: Cats were spayed or neutered at 7 weeks or 7 months of age, or left intact. Radiographs (x-rays) were taken monthly to assess growth plate closure. Cats spayed or castrated at any age had delayed growth plate closure compared to intact cats, and also had greater body weight and more body fat. Intact cats showed more intraspecies aggression and less affection toward humans than did cats spayed or castrated at any age.

49)


PRIMARY TOPIC: Neoplasia (mammary)

n = NA

SYNOPSIS: This is an excellent review of the biology of mammary cancer in female dogs. Incidence of mammary neoplasia in dogs is decreasing in the United States because so many dogs are spayed in this country; incidence of mammary neoplasia in aged female dogs is greatly decreased by spaying early in life.

50)


PRIMARY TOPIC: Neoplasia (prostatic)

n = 70 male dogs / Prospective study

SYNOPSIS: Castrated dogs had a 3.9 times risk of developing prostatic cancer compared to intact dogs in that population. Although prostatic cancer can occur in either castrated or intact dogs, in this study 71% of affected dogs were castrated. Tissue sampling demonstrated lack of response to cancerous tissues to testosterone.

COMMENTARY: Canine prostatic cancer is not associated with responsiveness to testosterone. This makes it very different than human prostatic cancer, which is hormonally responsive.

51)


PRIMARY TOPIC: Neoplasia (prostatic), prostate disease
n = 431 male dogs / Retrospective study

SYNOPSIS: Benign prostatic hypertrophy, an age-related increase in prostate size, was the most common type of prostate disease described in this population (57.1% of dogs). Prostate infection was present in 19.3%. Prostatic cancer was present in 13% of dogs, with castrated dogs having 4.34 times the risk of developing it compared to intact dogs. Time from castration to development of cancer was highly variable, suggesting that castration and subsequent loss of testosterone was not directly associated with tumor development.

52)


PRIMARY TOPIC: Neoplasia (hemangiosarcoma)

n = 1383 dogs / Retrospective study

SYNOPSIS: Overall incidence of heart tumors in this population was 0.19%, with hemangiosarcoma the most common heart tumor type identified. Incidence was the same for males and females, with spayed females having 4 times the risk of intact females. Some breeds also were identified to be at specific risk, and some identified to be spared, suggesting a genetic component.

53)


PRIMARY TOPIC: Musculoskeletal abnormalities

n = 1,243,681 dogs / Retrospective study

SYNOPSIS: Medical records were reviewed for dogs with a diagnosis of hip dysplasia or anterior cruciate ligament (ACL) injury over 4 decades. The risk factor identified for hip dysplasia was gender, with castrated males more likely than intact males or spayed or intact females to be diagnosed. Prevalence of hip dysplasia in this population was lower than that reported in other studies. The risk factor identified for ACL injury was reproductive status, with castrated males and spayed females more likely than intact males or females to be diagnosed. Other risk factors for ACL injury, such as obesity, were not described in the study. Breed predispositions for hip dysplasia and ACL injury also were described.