

Long-term risks and benefits of early-age gonadectomy in cats

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Objective—To evaluate the long-term risks and benefits of early-age gonadectomy, compared with traditional-age gonadectomy, among cats adopted from a large animal shelter.

Design—Retrospective cohort study.

Animals—1,660 cats.

Procedure—Cats underwent gonadectomy and were adopted from an animal shelter before 1 year of age; follow-up was available for as long as 11 years after surgery (median follow-up time, 3.9 years). Adopters completed a questionnaire about their cats' behavior and medical history. When possible, the cats' veterinary records were reviewed. Statistical analyses were conducted to identify any associations between the occurrence of 47 medical and behavioral conditions and the cats' age at gonadectomy.

Results—Among male cats that underwent early-age gonadectomy (< 5.5 months of age), the occurrence of abscesses, aggression toward veterinarians, sexual behaviors, and urine spraying was decreased, whereas hiding was increased, compared with cats that underwent gonadectomy at an older age. Among male and female cats that underwent early-age gonadectomy, asthma, gingivitis, and hyperactivity were decreased, whereas shyness was increased.

Conclusions and Clinical Relevance—Gonadectomy before 5.5 months of age was not associated with increased rates of death or relinquishment or occurrence of any serious medical or behavioral condition and may provide certain important long-term benefits, especially for male cats. Animal shelters can safely gonadectomize cats at a young age, and veterinarians should consider recommending routine gonadectomy for client-owned cats before the traditional age of 6 to 8 months. (*J Am Vet Med Assoc* 2004;224:372-379)

Euthanasia of healthy cats in animal shelters continues to be a daunting problem in the United States,

and the rate is estimated at 4.3 to 15.4 million cats/y.¹ These numbers represent cats that were never adopted from shelters because of insufficient adopters and cats that were adopted but subsequently relinquished back to the shelters, frequently when the cat developed behaviors that were unacceptable to the new owner. Typically, more than half of cats relinquished to shelters are subsequently euthanized by the shelter, and in some shelters, the rate is > 90%.²⁻⁵

Many people with humane concerns consider routine early-age gonadectomy of male and female cats as an important step in reducing the number of cats relinquished to shelters for 2 reasons. The procedure enables shelters to gonadectomize all cats before adoption, ensuring that the adopted cats will not breed, thus reducing the number of kittens subsequently relinquished to the shelter. Early-age gonadectomy may also reduce the incidence of certain behavioral problems that lead to relinquishment of adopted cats. The other widely used alternative—neutering contracts in which adopters agree to have the adopted cats gonadectomized some time after adoption—is not effective because many adopters either fail to have the cats gonadectomized or wait until after the cats have already had a litter of kittens before having them gonadectomized.^{3,5} Nonsurgical gonadectomy methods may ultimately prove to be a useful alternative to surgical gonadectomy,⁶ although those methods are still under development.⁷

To date, studies^{8,9} have established safe anesthetic and surgical protocols for early-age gonadectomy and indicate that gonadectomy at 7 weeks of age is associated with more rapid anesthetic recovery and fewer perioperative complications, compared with gonadectomy at 7 months of age.¹⁰ In addition, results of 2 studies indicate no adverse medical consequences of early-age gonadectomy; 1 followed 31 cats until 1 year of age,¹¹ and another followed 263 cats for a median of 38 months after surgery.¹²

No previous study, however, has followed early-age gonadectomized cats beyond 4.5 years of age, and practicing veterinarians still express concerns about the safety of early-age gonadectomy. In 1 recent survey, for example, 84% of practicing veterinarians perceived risk for at least 1 problem that was associated with gonadectomy before 4 months of age and that was not associated with gonadectomy when performed at an older age, including 29% who thought that early-age gonadectomy increased the risk of at least 1 medical condition later in life.¹³ Veterinarians have expressed concerns that early-age gonadectomy may lead to increased risk of many medical and behavioral conditions, including diabetes mellitus, immune deficiencies, obesity, skin disease, and urinary tract obstruction.^{14,15}

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The objective of the retrospective cohort study reported here was to compare early-age gonadectomy with gonadectomy at a traditional age in terms of retention in the adoptive household (> 3 months from adoption), overall mortality rate, and incidence of common medical and behavioral conditions via follow-up for as long as 11 years after surgery.

Materials and Methods

Sampling—All cats were selected via the adoption records of the Erie County, New York, Society for the Prevention of Cruelty to Animals (SPCA). This SPCA serves the Buffalo metropolitan area as an animal-control facility and a shelter for animal relinquishment and adoption. Beginning in the mid 1980s, the shelter attempted to gonadectomize all cats before adoption if they weighed at least 0.9 kg (2.0 lb) and were considered healthy by the shelter staff and veterinarians.

To be eligible for the study, cats must have been adopted between July 1989 and November 1998, adopted at between 6 weeks and 12 months of age, and gonadectomized before adoption. If the adoption record indicated that the cat had been returned to the shelter within 3 months after adoption, the cat was not considered eligible because it seemed unlikely that adopters who had their cat a short time would remember enough details about their cat's behavior to participate in the study. Relinquishment information was not always added to the adoption records, so some cats were later determined to be ineligible after we contacted the adopter. A sampling frame of all apparently eligible cats was created. For each calendar year, 100 to 125 cats were randomly sampled from the sampling frame for each of 4 strata: male and female cats gonadectomized before 5.5 months of age and male and female cats gonadectomized at or after 5.5 months of age. If < 100 cats in any stratum qualified for the study, all the eligible cats for that stratum were selected. Random sampling was conducted with commercially available software.^a

For each selected cat, the adopter's contact information and any information about the cat was transcribed into a computer database. When possible, the previous relinquishment record for each cat was identified and any additional information (eg, reason for relinquishment) was collected. The time of gonadectomy was confirmed by reviewing neuter status on admission to the shelter, SPCA surgery log books, medical treatment records, and records of fees charged for gonadectomy. If a cat had been gonadectomized before admission to the shelter, it was considered eligible only if gonadectomy had been performed at the time of a previous SPCA adoption and the date of gonadectomy could be confirmed (ie, the cat was gonadectomized at the first adoption, relinquished to the shelter, and then adopted a second time.)

Data collection—Between November 1999 and November 2000, the adopters of sampled cats were sent a letter from the SPCA informing them that they might be contacted for this study and giving them the opportunity to contact the SPCA and decline participation. If the adopters failed to decline, they were mailed (within 2 months of the date of the SPCA letter) a packet containing a cover letter describing the purpose of the study and requesting participation, a questionnaire about the adopted cat, a prepaid business-reply envelope, and a list of practicing veterinarians in the Buffalo area from which they could identify their veterinarians. The cover letter and questionnaire met informed consent requirements and were approved by the Cornell University Committee on Human Subjects. The adopters were offered a free 1-year subscription to a newsletter about cats if they participated in the study. Three weeks after the initial mailing, reminder postcards were sent to nonrespondents. After 5

weeks from the initial packet mailing, remaining nonrespondents were sent another packet that was identical to the first but with a modified cover letter that more urgently requested their participation. At that time, attempts were also made to contact the adopter by telephone, and if they were contacted, the questionnaire was completed via telephone by use of a standard script.

If mail to the adopter was returned as undeliverable or if the telephone number was found to be incorrect, telephone directories and Internet databases were consulted to find current contact information for the adopter. If a close, unique match was found for the adopter's name, the contact process was repeated with the new contact information.

The study questionnaire contained 93 questions grouped into 5 sections.^b The adopters were asked whether the cat was still in the household and, if not, what happened to the cat (section 1); the cat's behaviors and activities and, where appropriate, whether the adopter considered the behavior a serious problem (section 2); the cat's medical history, including the dates of diagnoses for common medical problems, vaccination history, and diet (section 3); demographic information about the adopter's household (section 4); which veterinarians had administered care to the cat and for permission to review the cat's veterinary records (section 5). Because of the uncertainty in pinpointing the exact time of onset of behavioral conditions, only the presence or absence of the behavior during the lifetime of the cat was collected in section 3. The questionnaire booklet was designed by use of published recommendations,¹⁶ and the booklets were printed on recycled paper made from at least 30% postconsumer waste. The questionnaire was pretested on volunteers from Cornell University and pilot-tested on a sample of 60 adopters.

All of the veterinary clinics for which 5 or more adopters gave us authorization to review their cat's records ($n = 71$) were visited by a veterinary technician or veterinarian. The veterinary records of participating cats were abstracted by use of a standardized form that contained 121 items, including the number of visits to that clinic, the cat's status on the last visit, the cat's vaccination and weight history, and medical and behavioral problems; for each problem reported, the date of first diagnosis and the number of episodes were recorded.^b When available, specific diagnostic information including laboratory or histopathologic testing was also recorded.

All study personnel were unaware of the cats' ages at gonadectomy when performing telephone interviews, abstracting veterinary records, or entering computerized data.

Outcomes of interest—Forty-seven outcomes were evaluated. The following 25 outcomes were defined by combined information from the questionnaire and veterinary records: overall mortality rate from any cause, aggression towards people, allergic skin disease, arthritis, balanoposthitis, cardiac conditions (any etiology), diabetes mellitus, excessive vocalization, feline asthma, FIV infection, FeLV infection, **feline lower urinary tract disease (FLUTD)**, fractures, hepatic disease (any etiology), hyperactivity, hyperthyroidism, inappropriate elimination and urine spraying, inflammatory bowel disease, neoplasia, pica, pneumonia, psychogenic alopecia, **upper respiratory tract infections (URIs)**, urethral obstruction, and vaginitis. The following 9 outcomes were defined by questions from only the questionnaire: aggression towards other cats, body condition (degree of obesity), hiding frequently, playfulness, relinquishment, scratching furniture or carpets, shyness around strangers, sexual behaviors, and time slept each day. The following 13 outcomes were defined by items from only the veterinary records: abscesses, aggression towards veterinarian or veterinary staff, chronic gastroenteritis, chronic renal failure, eosinophilic inflammatory conditions, **feline infectious peritonitis (FIP)**, fight or bite

wounds, gingivitis, hit by car, lacerations, repeated infections, soft tissue injuries or lameness of undiagnosed cause, and urolithiasis.

For those outcomes based on combined information, the condition was considered present if indicated on either the questionnaire, veterinary record, or both. If indicated on the veterinary record, that date of diagnosis was used. If indicated on only the questionnaire or if the veterinary record was not abstracted, the questionnaire date was used. For analysis of overall mortality and relinquishment rates, all responses including partial responses were used. For all other outcomes, analysis was based on respondents completing most or all of the questionnaire.

Feline lower urinary tract disease was considered present if the cat ever had hematuria, stranguria, pollakiuria, frequent urination of small amounts, or urinary obstruction; if the veterinarian had made a diagnosis of cystitis, FLUTD, or **feline urologic syndrome (FUS)**; or if the adopter reported that their veterinarian had prescribed an orally administered medication or special diet for a lower urinary tract sign. Cats whose only clinical sign was urinating outside the litter box were excluded from the analysis for FLUTD. Male cats with urethral obstructions were analyzed alone and also in combination with other cats with FLUTD. For bone fractures, analysis was performed first with all fractures and then with fractures of only long bones (ie, humerus, radius, ulna, femur, tibia, or fibula). Body condition was assessed by asking adopters who still had their cat to compare the cat's present body shape to a series of silhouettes validated by a previous study¹⁷ of feline obesity. Overweight cats (those with a score of 5 or 6 on a 6-point scale) were compared with clinically normal cats (scores of 3 or 4); underweight cats (scores of 1 or 2) were excluded from this analysis. To remove from the analysis cats that may have already had the condition at the time of adoption, cases of URI and heart murmurs were limited to those with onset after 1 year of age. Neoplastic conditions were considered malignant if the veterinarian provided a specific diagnosis, the owner described metastasis, or the cat was euthanized for the condition. Repeated infection was defined by 2 or more infections of the same body system recorded in the veterinary record. For conditions that may have repeated episodes (eg, URI or FLUTD), only the time until the first occurrence was used.

All instances of aggression towards people were analyzed together and then instances of biting people (after the cat was 1 year old) were analyzed alone. All sexual behavior was evaluated together and then separately by sexual behavior directed towards people, towards other cats, and towards inanimate objects. When evaluating behaviors for which we asked about the presence and severity of the behavior, cats that had the condition at any time (regardless of severity) were compared with those that never had the condition. Cats that had a serious problem with the behavior at any time were compared with those that never had the behavior; cats that had the behavior were excluded if it was not considered a serious problem. A behavioral condition was considered a serious problem if the adopter answered that he or she considered it a serious problem or if the veterinary record indicated that the adopter had sought treatment for the condition.

Age at gonadectomy was either evaluated on a continuous scale (from 1.4 to 12 months) or categorized into 3 groups. When categorized, group 1 included cats gonadectomized before 3.5 months of age. This is the age at which many shelters routinely neuter cats but at which few practicing veterinarians neuter cats.¹³ Group 2 included cats between 3.5 and 5.5 months of age. At this age, most cats have completed their initial vaccination series and could be gonadectomized in veterinary practice if the veterinarian's main consideration for choosing the age of gonadectomy was the cat's vaccination status. Group 3 included cats gonadec-

tomized at or after 5.5 months of age. This is the most common age for gonadectomy and is accepted by most practicing veterinarians.¹³

Statistical methods—The goal of the multivariable analyses was to determine whether age at gonadectomy was related to the occurrence of the outcomes, while controlling for the effect of any potentially confounding variables. Most behavioral outcomes were dichotomous without time-to-event information and were analyzed with unconditional logistic regression.¹⁸ For most medical conditions, the analysis was conducted with time-to-event data (ie, time from adoption until diagnosis of the condition or end of follow-up) by use of multivariable survival analysis (Cox proportional hazards model).¹⁹ For survival analysis, the cats' age was used as the time scale (instead of the usual scale, follow-up time) to control for the effect of age as a potential confounder.^{20,21} All multivariable analyses were conducted with commercially available software.^c

Before beginning the analysis, we determined for each outcome if age at gonadectomy on a continuous scale from 1.4 to 12 months had a linear relationship with the log-odds (for logistic regression) or with the log-hazard (for survival analysis) by use of the methods of Hosmer and Lemeshow.²² If the relationship was linear, age at gonadectomy was used on a continuous scale. If it was not close to linear, the 3 age categories were used for analysis. In addition, for each outcome with time-to-event data, incidence densities were calculated by use of commercially available software.^d

For all outcomes, the following variables were considered in multivariable models as possible confounders with age at gonadectomy: sex, long- or short-haired coat, owner surrender or stray on admission to the shelter, whether the cat was kept in the shelter for > 5 days before adoption, outdoor status after adoption (outdoor cats defined as going outside unsupervised for mean time of ≥ 2 h/d during any part of the year), and presence of another cat in the household. When relevant to the outcome, eating mostly or only dry cat food, relinquishment for a behavioral problem (on shelter admission), and onychectomy (declawing) before adoption were also considered in each model. Declawing performed after adoption was not used because it could not always be determined whether the surgery was performed before or after onset of the behavior.

For logistic regression and survival analysis, the multivariable models were selected by use of backward elimination via the methods of Kleinbaum.²³ The potential confounders in each model were subjectively ordered (a priori) by expected biological relevance to the particular outcome.²⁴ During the model-selection process, these variables were removed 1 at a time beginning with the least biologically relevant. If 1 of these variables was associated with the outcome but did not act as a confounder for age at gonadectomy, it was not retained in the model. Age at gonadectomy was always the last variable to be removed from the model. When age at gonadectomy was categorized, the indicator variables for groups 1 and 2 were removed simultaneously and evaluated for significance. For outcomes with 10 to 50 cases, the number of variables in the initial model was restricted by use of the guidelines of Hosmer and Lemeshow.¹⁹ For outcomes with < 10 cases, age at gonadectomy was collapsed to 2 categories (< 5.5 months and ≥ 5.5 months) and its association with the outcome was evaluated by use of the Fisher exact test without multivariable models.²⁵

The interaction between the cat's sex and age at gonadectomy was evaluated for each outcome. If this interaction was significant at $P \leq 0.1$, the model-building process was repeated separately for male and female cats. For all analyses, values of $P \leq 0.05$ were considered significant when evaluating age at gonadectomy. The fit of the final logistic

regression models was evaluated by use of guidelines of Stokes et al.¹⁸ For survival analysis models, the proportional hazards assumption was assessed by use of the guidelines of Allison.²¹

For comparisons that did not require multivariable modeling, the χ^2 test was used for categorical variables and the Student *t* test was used for normally distributed continuous data.²⁶

When assessing whether associations between age at gonadectomy and the outcomes were likely to represent a cause-and-effect relationship, 4 criteria were considered and included significance of association, consistency of the results with other studies (if any), presence (or absence) of a plausible biological mechanism, and degree of certainty that the outcomes occurred after gonadectomy and were not likely to be already present at the time of adoption and surgery.²⁷

Results

Of the 3,172 sampled cat adoptions, no current contact information could be found for 1,121 (35.3%) adopters. Another 175 cats (5.5%) were subsequently determined to be ineligible (in most instances, either because the adopter kept the cat for < 3 months or the cat's age was incorrectly listed on the adoption record). Of the 1,876 remaining eligible cats for which we believed we had the adopters' correct contact information, 1,579 (84.2%) adopters completed the questionnaire and another 81 (4.3%) provided partial information about their cat. Of the 1,039 cats for which the adopters provided authorization to review veterinary records, 853 (82.0%) records were successfully located.

Among the adopters for whom we believed we had correct contact information, the 1,660 cats of responders (partial and complete) did not differ significantly from those of nonresponders by age at gonadectomy, sex, proportion that were strays, or proportion that were originally relinquished for a behavioral problem (all comparisons, $P > 0.2$). The nonresponders, however, had a longer time from adoption until contact time (difference between means, 128 days; $P = 0.06$); that is, earlier adopters were less likely to respond to the survey than more recent adopters. Approximately half of the cats of responding adopters were male; cats that were gonadectomized at ≥ 5.5 months of age were more likely to have been stray than those gonadectomized before 5.5 months of age (Table 1).

Median follow-up time from adoption until either questionnaire completion or the cat's death or relinquishment was 3.9 years (range, 0.25 to 11.7 years). Median age at end of follow-up was 4.4 years (range, 0.5 to 12.3 years), and 119 cats had follow-up past 10 years of age.

A significant relationship with age at gonadectomy was found for 3 medical and 5 behavioral conditions (Table 2 and 3). In addition, sexual behavior among male cats was the only outcome for which the *P* value was from > 0.05 to 0.09 (ie, near significant). None of the potential confounding variables evaluated remained in the final models for any of these 9 outcomes. The interaction between sex and age at gonadectomy was significant for abscesses, aggression towards veterinarians, hiding frequently, sexual behaviors, and shyness around strangers. In other words, for these 5 outcomes, age at gonadectomy had a different

Table 1—Characteristics of 1,660 cats (No. [%] with characteristic) adopted from a humane shelter in a study of long-term risks and benefits of early-age gonadectomy

| Characteristic | Age at gonadectomy (mo) | | |
|--|-------------------------|--------------------|---------------------|
| | < 3.5 (n = 703) | 3.5–< 5.5 (284) | ≥ 5.5 (673) |
| Sex | | | |
| Female | 361 (51.4) | 129 (45.4) | 369 (54.8) |
| Male | 342 (48.7) | 155 (54.6) | 304 (45.2) |
| Status on shelter admission ^a | | | |
| Owner surrender or impoundment | 482 (70.2) | 171 (61.7) | 337 (51.1) |
| Stray | 205 (29.8) | 106 (38.3) | 323 (48.9) |

^aInformation missing for certain cats.

Table 2—Medical conditions associated with age at gonadectomy in 1,579 cats

| Condition | Age at gonadectomy (mo) | Incidence density ^a | Hazard ratio ^b | 95% CI | Overall <i>P</i> value |
|------------------------|-------------------------|--------------------------------|---------------------------|-----------|------------------------|
| Abscesses ^c | < 3.5 | 0.88 | 0.53 ^d | 0.18–1.60 | 0.05 |
| | 3.5–< 5.5 | 0.26 | 0.08 | 0.01–0.71 | |
| | ≥ 5.5 | 1.26 | 1.0 | NA | |
| Feline asthma | Continuous | 0.14 | 0.77 ^e | 0.58–0.93 | 0.01 |
| Gingivitis | < 3.5 | 2.12 | 0.67 | 0.43–1.05 | 0.02 |
| | 3.5–< 5.5 | 1.61 | 0.45 | 0.24–0.87 | |
| | ≥ 5.5 | 3.24 | 1.0 | NA | |

^aIncidence density/100 cat years at risk. ^bHazard ratio adjusted for cat's age at time of disease onset. ^cFor male cats only. ^dInteraction between age at gonadectomy and follow-up time was significant; therefore, hazard ratios for abscesses were valid only near beginning of follow-up period. ^eHazard ratio/1-month decrease in age at gonadectomy.
95% CI = 95% Confidence interval for the hazard ratio. NA = Not applicable (referent category).

Table 3—Behavioral conditions associated with age at gonadectomy in 1,579 cats

| Behavior | Age at gonadectomy (mo) | Cats with behavior (%) | Odds ratio | 95% CI | Overall <i>P</i> value |
|---|-------------------------|------------------------|-------------------|-----------|------------------------|
| Aggression towards veterinarians ^a | Continuous | 2.5 | 0.77 ^b | 0.63–0.98 | 0.03 |
| Hiding frequently ^{a,c} | Continuous | 14.5 | 1.11 ^b | 1.02–1.20 | 0.01 |
| Hyperactivity ^c | < 3.5 | 16.0 | 0.67 | 0.51–0.90 | 0.01 |
| | 3.5–< 5.5 | 14.4 | 0.60 | 0.40–0.89 | |
| | ≥ 5.5 | 22.1 | 1.0 | NA | |
| Sexual behaviors ^{a,c} | Continuous | 12.2 | 0.93 ^b | 0.86–1.01 | 0.09 |
| Shyness around strangers ^c | Continuous | 56.3 | 1.04 ^b | 1.00–1.09 | 0.03 |
| Urine spraying ^a | Continuous | 2.1 | 0.79 ^b | 0.64–0.97 | 0.02 |

^aMale cats only. ^bOdds ratio/1-month decrease in age at gonadectomy. ^cNot significant ($P > 0.05$) when considered a serious problem.
See Table 2 for remainder of key.

risk for males than for females. In analyses stratified by sex, these 5 outcomes were significantly associated with age at gonadectomy for males but not for females.

An odds ratio (OR) or hazards ratio (HR) < 1.0 indicated that the condition decreased with early-age gonadectomy, and an OR or HR > 1.0 indicated that the condition increased with early-age gonadectomy. For conditions analyzed with age at gonadectomy categorized, the HR or OR in the tables can be interpreted as an estimate of the relative risk of developing the condition for that age group, compared with cats gonadectomized from ≥ 5.5 to 12 months of age. With hyperactivity, for example, the OR for group 1 was 0.67, meaning that the cats gonadectomized before 3.5 months of age were 0.67 times as likely as cats gonadectomized after 5.5 months of age to have hyperactivity (Table 3). It could also be stated that cats gonadectomized after 5.5 months of age were 1.49 (the reciprocal of 0.67) times as likely to have hyperactivity as those gonadectomized before 3.5 months of age. For those conditions analyzed with age at gonadectomy on a continuous scale, the OR or HR can be interpreted as the change in risk for each month earlier that the cat was gonadectomized. For hiding frequently among males cats, the OR of 1.11 can be interpreted as the following: each month earlier that the cat was gonadectomized, the risk of hiding frequently increased by approximately 11% (Table 3). To compare cats gonadectomized at 4 months with those gonadectomized at 7 months of age, the OR (1.11) is raised to the third power (3 months difference); therefore, cats gonadectomized at 4 months of age would be approximately 1.36 times as likely to frequently hide as cats gonadectomized at 7 months of age.

The incidence densities can be converted to cumulative incidences by use of the following formula: $1 - \exp[-t(ID/100)]$, where t is the number of years of follow-up for each cat, ID is the incidence density/100 cat-years (Table 2), and \exp is the inverse of the natural logarithm.²⁸ For example, to estimate the proportion of cats gonadectomized before 3.5 months of age that would be expected to develop gingivitis during a 12-year life span, $1 - \exp[-12(2.12/100)] = 0.22$; thus, approximately 22% of cats gonadectomized before 3.5 months of age would be expected to develop gingivitis during the first 12 years of life. For cats gonadectomized at ≥ 5.5 months of age, 32% would develop gingivitis during this same period ($1 - \exp[-12\{3.24/100\}] = 0.32$). Use of this formula assumes that the risk of disease is constant throughout the cats' lives and that there are no competing risks (ie, no other diseases cause them to die during the time of observation).

Medical outcomes—Among all cats, gonadectomy before 5.5 months of age was associated with significantly reduced incidence of feline asthma and gingivitis, compared with gonadectomy from ≥ 5.5 to 12 months of age. Early-age gonadectomy was also associated with lower incidence of abscesses among males, but the interaction between the group gonadectomized before 3.5 months and follow-up time was close to significant ($P = 0.08$). The coefficient for this interaction was positive, indicating that the protective effect of

gonadectomy before 3.5 months diminished with time. After 5 to 6 years of follow-up, there were no longer any meaningful differences between groups in terms of risk of abscesses. These 3 medical conditions were not associated with an increased risk of euthanasia or relinquishment.

When all neoplastic conditions were evaluated, it initially appeared that the early-age gonadectomized cats were at lower risk ($P = 0.03$), but this outcome included many vague conditions reported by the owners as tumors that may have been cysts, abscesses, and other non-neoplastic conditions. When only malignant conditions were evaluated, there was no longer a significant association.

Behavioral outcomes—Gonadectomy before 5.5 months of age was associated with decreased occurrence of hyperactivity and increased occurrence of shyness around strangers. Among male cats (but not female cats), early-age gonadectomy was also associated with reduced occurrence of aggression towards veterinarians, sexual behaviors, and urine spraying but an increased risk of hiding frequently. For 4 of these behavioral outcomes (hiding frequently, hyperactivity, sexual behaviors, and shyness), we also assessed whether the adopter considered the behavior a serious problem. When analysis was restricted to cats with a serious problem, the conditions were no longer significantly associated with age at gonadectomy. Of these 6 behavioral conditions associated with age at gonadectomy, only hiding among males was associated with increased rate of relinquishment. Of the male cats reported to frequently hide, 11% were relinquished, compared with 4% relinquished among those not reported to frequently hide.

When the outcome of scratching furniture was initially evaluated, it appeared that early-age gonadectomy had a significant ($P < 0.01$) protective effect. Cats with early-age gonadectomy, however, were also more likely to be declawed, and some of these cats were not declawed until after the onset of the behavioral problem, so it was not possible to clearly determine in our study whether early-age gonadectomy alone would have been protective. Among the 827 cats that were never declawed, age at gonadectomy was not associated with frequency of scratching furniture.

Outcomes not related to age at gonadectomy—No association was found between age at gonadectomy and occurrence of the condition for the 38 other outcomes studied, including overall mortality rate, relinquishment rate, obesity, FLUTD, and urethral obstruction of male cats. Twelve of these conditions were very rare in our study (< 10 cats with the condition), including arthritis, balanoposthitis, chronic gastroenteritis, chronic renal failure, diabetes mellitus, FeLV infection, FIP, FIV infection, long-bone fractures, pneumonia, urolithiasis, and vaginitis. Therefore, the statistical power for finding any subtle difference between groups for these outcomes was low. Nevertheless, the risk of any gonadectomized cat developing these conditions before the age of 12 years, regardless of age at gonadectomy, appears to be low. For a condition with 10 cases, the highest possible

upper 95% confidence limit for a 12-year lifetime cumulative incidence was 2.5% (ie, < 2.5% of cats would likely develop these conditions during a 12-year lifespan).

Discussion

For most of the medical and behavioral conditions evaluated in this study, no association was found between frequency of the outcome and age at gonadectomy. This was true even for many conditions speculated to be associated with age at gonadectomy, such as urethral obstruction of male cats, physeal fractures, body condition, diabetes mellitus, and immune deficiency. Many practicing veterinarians delay castrating male cats because of concerns about urinary obstruction.¹³ Other studies^{11,29-31} have found mixed results on anatomic differences of the penis that might result from early-age gonadectomy, and 1 long-term investigation¹² found a decreased rate of FLUTD among cats gonadectomized before 24 weeks of age. On the basis of these results and the lack of association found in our study, it would appear that even if early-age gonadectomy results in anatomic differences in the penis, these changes do not lead to an increase in the incidence of FLUTD or urinary obstruction. Therefore, concerns about these conditions should not be used as a reason to delay castration of male cats.

Age at gonadectomy was not associated with the frequency of long-bone fractures in our study. One other study³² did find a small delay in closure of the proximal radial physis among early-age gonadectomized female cats, but if physeal closure is delayed, our results suggest that the delay does not result in more long-bone fractures. Furthermore, long-bone fractures in our study were rare overall, suggesting that physeal fractures are not a common problem for gonadectomized cats in general.

Cats in our study that were gonadectomized before 5.5 months of age were not significantly more likely than cats gonadectomized at ≥ 5.5 months of age to have any conditions that might be associated with long-term immune suppression, including URI with onset after 1 year of age, FeLV infection, FIV infection, FIP, or repeated infections of the same body system. On the contrary, the early-age gonadectomized cats had lower incidence of gingivitis, a condition that is often associated with immune suppression.^{33,34}

No association was found between age at gonadectomy and prevalence of obesity in our investigation, a finding consistent with other studies^{11,12,35} on body condition. The incidence of diabetes mellitus was similarly not related to age at gonadectomy, and to our knowledge, only 1 other study¹² of early-age gonadectomy in cats could have detected cases of diabetes mellitus and that study reported no cases of the condition among any cats. As with long-bone fractures, diabetes mellitus appears to have low incidence in all gonadectomized cats, at least in the first 10 years of life.

Feline asthma and gingivitis had lower incidences among early-age gonadectomized cats than late-age gonadectomized cats in our study. Age at gonadectomy, neuter status, and sex have not been detected as a risk factor for these conditions in cats.^{33,34,36-38}

Studies^{39,40} in other species, however, indicate that exposure to androgens during key stages of development can permanently transform immune function. Therefore, it is possible that reduction in the incidence of these inflammatory conditions (asthma and gingivitis) is attributable to reduced concentrations of androgens among early-age gonadectomized kittens during immune development. It is also possible that the association is attributable to differences in some unmeasured confounding variable (eg, difference in geographic location between groups that might lead to exposure to different types of allergens that could exacerbate feline asthma) or a type-I error (ie, by chance, the sampled late-age gonadectomized cats were the ones that developed feline asthma or gingivitis).

It would seem reasonable that the lower rate of abscesses among early-age gonadectomized male cats in our study could be attributable to decreased intercat aggression among prepubertally gonadectomized cats. In our study, however, the early-age gonadectomized cats were not less likely than the late-age gonadectomized cats to fight with other cats or have other intercat aggression as reported by the adopters, so this mechanism may not explain the association. Regardless of the biological mechanism involved (if any), the significant interaction between rate of abscesses and follow-up time suggests that early-age and late-gonadectomized male cats become more alike in the rate of abscess development as they age.

Shyness was increased among all early-age gonadectomized cats, and hiding was increased among early-age gonadectomized male cats, but to our knowledge, these behaviors were not previously suspected of being associated with age at gonadectomy. Because these are behaviors that may appear after a stressful event (eg, adoption) and later resolve,⁴¹ we cannot fully determine whether these behaviors were long-term effects of early-age gonadectomy or simply behaviors associated with being adopted at a young age. Castrating male cats (regardless of age) reduces aggression and urine spraying,^{11,42,43} so it was not surprising that early-age castration was associated with decreased occurrence of these behaviors in male cats. Although aggression towards veterinarians was decreased in early-age gonadectomized male cats in our study, the frequency of other forms of aggression was not associated with age at gonadectomy. The decreased hyperactivity in early-age gonadectomized cats may be related to the decrease in heat production and resulting decrease in energy levels seen with gonadectomy in general³⁵; that study found no difference in heat production between gonadectomy at 7 weeks versus 7 months of age, although the sample size was probably too small to detect subtle differences between groups.

Because some behavioral conditions decreased with early-age gonadectomy but others increased, the natural question that follows is this: which of these conditions is most likely to cause a problem for the adopter or even to cause the adopter to request euthanasia for the cat or relinquish the cat back to the shelter? In other studies, house soiling is the most commonly reported behavioral reason for owners requesting euthanasia of their cats,⁴⁴ for relinquishment to shelters (43%),⁴⁵ and

for owners to seek consultation with a behaviorist.^{46,47} Although urine spraying among male cats represents only a portion of all house-soiling problems, any reduction in the occurrence of this behavior through early-age castration could be important in reducing relinquishments and euthanasia requests.

Frequent hiding was associated with an increased relinquishment rate among male cats in our study. Hiding and shyness have not specifically been reported as reasons for relinquishment in other studies, although being unfriendly was reported as a reason for 5% of cats relinquished for behavioral reasons.⁴⁵ If hiding and shyness are truly long-lasting and not just related to the periadoption period and if the cats with these behaviors are perceived as being unfriendly, then early-age gonadectomy may carry a small risk of relinquishment for these cats, supporting the finding among our study cats.

In another study,² hyperactivity was reported by only 1% of owners relinquishing cats for any reason, so changes in this behavior would have a relatively small impact on the number of cats relinquished. Because being too mellow was reported as a problem even less frequently,² reducing hyperactivity through early-age gonadectomy would not appear to be associated with important risks. Aggression specifically directed towards veterinarians or veterinary staff has not been reported as a common reason for relinquishment,² although it is likely that veterinarians would be happy to find measures that might reduce aggression directed towards them.

Our study provided several improvements over previous studies of early-age gonadectomy, including a much larger sample size, longer follow-up times, and verification of medical and behavioral conditions with veterinary records for a large portion of the cats. These improvements permitted examination of the relationship between age at gonadectomy and some uncommon conditions for which previous studies lacked statistical power. Nevertheless, as with any epidemiologic study, certain biases are possible. Because of the retrospective data collection, for example, it was not possible to collect veterinary information for some cats that died early in life and for whom the veterinary records were subsequently destroyed. Also, because behavioral diagnoses were not commonly recorded in veterinary records, assessment of many behavioral outcomes was exclusively based on the adopters' perceptions and memories. The cats of adopters for whom we found no contact information could have been different in some way from the cats of contacted adopters. We would not expect, however, that the health or behavior of these cats was associated with the likelihood that the adopter changed his/her address or phone number. It is also possible that the adopters of cats that died early in life or were relinquished early in life were less inclined to respond to the study, although the relatively high response rate probably minimized the effect of this type of nonresponse bias.

For extremely rare conditions, our study did not have the statistical power to detect any subtle difference between groups. For an outcome with 10 cases, for example, the statistical power for detecting an HR

of 2.0 would have been only 20%. The HR would have had to be at least 3.4 to have a statistical power of more than 50%.²⁰ Our study could not have detected any conditions with peak onset after 10 to 11 years of age. For these conditions with late-age onset, however, it becomes difficult to find plausible biological mechanisms that would support a cause-and-effect relationship between gonadectomy at an early age and development of the outcome after 10 to 11 years of life. Similarly, this study could not have detected conditions that would have led to relinquishment, euthanasia, or death within the first 3 months after surgery.

With approximately 50 comparisons made in the analyses for this study, some of the significant results were likely attributable to type-I errors. In other words, the sampled cats in an age group could have been the ones that developed some outcomes at higher rates by chance alone. With a significance level of 0.05, 2 to 3 of the comparisons are expected to be significant by chance alone, with a 92% chance of at least 1 type-I error.⁴⁸ If a more conservative value of $P = 0.01$ was used, only 3 outcomes were still associated with age at gonadectomy (ie, feline asthma, hiding frequently, and hyperactivity).

^aMicrosoft Excel 97, Microsoft Corp, Redmond, Wash.

^bThe study questionnaire and veterinary abstract form are available from the first author.

^cPROC LOGISTIC and PROC PHREG, SAS, version 8.02, SAS Institute Inc, Cary, NC.

^dStata, version 7.0, Stata Corp, College Station, Tex.

References

1. Nassar R, Talbot J, Moulton C. *Animal shelter reporting study*. Englewood, Colo: American Humane Association, 1992.
2. Salman MD, New JC, Scarlett JM, et al. Human and animal factors related to the relinquishment of dogs and cats in 12 selected animal shelters in the United States. *J Appl Anim Welf Sci* 1998;1:207-226.
3. Manning AM, Rowan AN. Companion animal demographics and sterilization status: results from a survey in four Massachusetts towns. *Anthrozoos* 1992;5:192-201.
4. National shelter census results revealed. *J Am Vet Med Assoc* 1997;210:160-161.
5. Alexander SA, Shane SM. Characteristics of animals adopted from an animal control center whose owners complied with a spaying/neutering program. *J Am Vet Med Assoc* 1994;205:472-476.
6. Carter CN. Pet population control: another decade without solutions? *J Am Vet Med Assoc* 1990;197:192-195.
7. Olson PN. Historical, ethical, and political issues involving pet overpopulation, in *Proceedings. Int Symp Nonsurgical Methods Pet Popul Control* 2002;11-17.
8. Aronsohn MG, Faggella AM. Surgical techniques for neutering 6- to 14-week-old kittens. *J Am Vet Med Assoc* 1993;202:53-55.
9. Faggella AM, Aronsohn MG. Anesthetic techniques for neutering 6- to 14-week-old kittens. *J Am Vet Med Assoc* 1993;202:56-62.
10. Howe LM. Short-term results and complications of prepubertal gonadectomy in cats and dogs. *J Am Vet Med Assoc* 1997;211:57-62.
11. Stubbs WP, Bloomberg MS, Scruggs SL, et al. Effects of prepubertal gonadectomy on physical and behavioral development in cats. *J Am Vet Med Assoc* 1996;209:1864-1870.
12. Howe LM, Slater MR, Boothe HW, et al. Long-term outcome of gonadectomy performed at an early age or traditional age in cats. *J Am Vet Med Assoc* 2000;217:1661-1665.
13. Spain CV, Scarlett JM, Cully SM. When to neuter dogs and cats: a survey of New York state veterinarians' practices and beliefs. *J Am Anim Hosp Assoc* 2002;38:482-488.
14. Johnston L. Opposes early-age neutering (lett). *J Am Vet Med Assoc* 1993;202:1041-1042.

15. Dowling S. Opposition to prepubertal gonadectomies in cats [lett]. *J Am Vet Med Assoc* 1997;210:321.
16. Dillman DA. *Mail and internet surveys: the tailored design method*. 2nd ed. New York: John Wiley & Sons, 2000;79–159.
17. Scarlett JM, Donoghue S. Associations between body condition and disease in cats. *J Am Vet Med Assoc* 1998;212:1725–1731.
18. Stokes ME, Davis CS, Koch GG. *Categorical data analysis using the SAS system*. Cary, NC: SAS Institute Inc, 1995;163–214.
19. Hosmer DW, Lemeshow S. *Applied survival analysis*. New York: John Wiley & Sons, 1999;87–112.
20. Therneau TM, Grambsch PM. *Modeling survival data: extending the Cox model*. New York: Springer-Verlag Inc, 2000;39–78.
21. Allison PD. *Survival analysis using the SAS system: a practical guide*. Cary, NC: SAS Institute Inc, 1995;111–184.
22. Hosmer DW, Lemeshow S. *Applied survival analysis*. New York: John Wiley & Sons, 1999;158–195.
23. Kleinbaum DG, Kupper LL, Morgenstern H. *Epidemiologic research: principles and quantitative methods*. New York: Van Nostrand Reinhold, 1982;448–456.
24. Allen DM, Cady FB. Model selection with many explanatory variables. In: *Analyzing experimental data by regression*. Belmont, Calif: Lifetime Learning Publications, 1982;247–259.
25. Stokes ME, Davis CS, Koch GG. *Categorical data analysis using the SAS system*. Cary, NC: SAS Institute Inc, 1995;19–36.
26. Ott RL. *An introduction to statistical methods and data analysis*. 4th ed. Belmont, Calif: Duxbury Press, 1993;195–418.
27. Rothman KJ, Greenland S. Causation and causal inference. In: Rothman KJ, Greenland S, eds. *Modern epidemiology*. 2nd ed. Philadelphia: Lippincott-Raven, 1998;7–28.
28. Rothman KJ, Greenland S. Measure of disease frequency. In: Rothman KJ, Greenland S, eds. *Modern epidemiology*. 2nd ed. Philadelphia: Lippincott-Raven, 1998;29–46.
29. Herron MA. A potential consequence of prepubertal feline castration. *Feline Pract* 1971;Sep–Oct:17–19.
30. Root MV, Johnston SD, Johnston GR, et al. The effect of prepubertal and postpubertal gonadectomy on penile extrusion and urethral diameter in the domestic cat. *Vet Radiol Ultrasound* 1996;37:363–366.
31. Herron MA. The effect of prepubertal castration on the penile urethra of the cat. *J Am Vet Med Assoc* 1972;160:208–211.
32. Root MV, Johnston SD, Olson PN. The effect of prepubertal and postpubertal gonadectomy on radial physeal closure in male and female domestic cats. *Vet Radiol Ultrasound* 1997;38:42–47.
33. Pedersen NC. Inflammatory oral cavity diseases of the cat. *Vet Clin North Am Small Anim Pract* 1992;22:1323–1345.
34. Diehl K, Rosychuk RA. Feline gingivitis-stomatitis-pharyngitis. *Vet Clin North Am Small Anim Pract* 1993;23:139–153.
35. Root MV, Johnston SD, Olson PN. Effect of prepubertal and postpubertal gonadectomy on heat production measured by indirect calorimetry in male and female domestic cats. *Am J Vet Res* 1996;57:371–374.
36. Corcoran BM, Foster DJ, Luis-Fuentes V. Feline asthma syndrome: a retrospective study of clinical presentation in 29 cats. *J Small Anim Pract* 1995;36:481–488.
37. Corcoran BM, Foster DJ, Luis-Fuentes V. Feline asthma syndrome. *Vet Q* 1995;17:S15–S16.
38. Padrid P. Feline asthma: diagnosis and treatment. *Vet Clin North Am Small Anim Pract* 2000;30:1279–1293.
39. Martin JT. Sexual dimorphism in immune function: the role of prenatal exposure to androgens and estrogens. *Eur J Pharmacol* 2000;405:251–261.
40. Cutolo M, Seriola B, Villaggio B, et al. Androgens and estrogens modulate the immune and inflammatory responses in rheumatoid arthritis. *Ann N Y Acad Sci* 2002;966:131–142.
41. Houpt KA. *Domestic animal behavior for veterinarians and animal scientists*. 3rd ed. Ames, Iowa: Iowa State University Press, 1998.
42. Hart BL, Barrett RE. Effects of castration on fighting, roaming, and urine spraying in adult male cats. *J Am Vet Med Assoc* 1973;163:290–292.
43. Hart BL, Cooper L. Factors relating to urine spraying and fighting in prepubertally gonadectomized cats. *J Am Vet Med Assoc* 1984;184:1255–1258.
44. Kass PH, New JC, Scarlett JM, et al. Understanding companion animal surplus in the United States: relinquishment of non-adoptables to animal shelters for euthanasia. *J Appl Anim Welf Sci* 2001;4:237–248.
45. Salman MD, Hutchison JM, Ruch-Gallie R, et al. Behavioral reasons for relinquishment of dogs and cats to 12 shelters. *J Appl Anim Welf Sci* 2000;3:93–106.
46. Beaver BV. Housesoiling by cats: a retrospective study of 120 cases. *J Am Anim Hosp Assoc* 1989;25:631–637.
47. Olm DD, Houpt KA. Feline house-soiling problems. *Appl Anim Behav Sci* 1988;20:335–345.
48. Ott RL. *An introduction to statistical methods and data analysis*. Belmont, Calif: Duxbury Press, 1993;767–1038.