

# Mammary tumors, pituitary tumors, and spaying

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For references see below the first few full citations given below with some full text links as examples (KA) and for complete list see <http://www.ratbehavior.org/references.htm>

KA: Additional reference (from Alison van Eenennaam [alvane@ucdavis.edu](mailto:alvane@ucdavis.edu) )

Prejean, J.D., Peckham, J.C., Casey, A.E., Griswold, D.P., Weisburger, E.K., & Weisburger, J.H. (1973) Spontaneous Tumors in Sprague-Dawley Rats and Swiss Mice. Cancer Research, 33, 11, pp 2768-2773  
<http://cancerres.aacrjournals.org/content/33/11/2768.abstract> AND  
<http://www.ask-force.org/web/Seralini/Prejean-Spontaneous-Tumors-Rats-longterm-1973.pdf>

## Mammary tumors, pituitary tumors, and spaying

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*Note: I am a biologist, not a veterinarian. This article is designed to give the pet rat owner some information about rat tumors and spaying from the scientific literature. This article is not designed to replace the advice of a veterinarian. Please consult your veterinarian regarding the care of your pet.*

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## How common are mammary and pituitary tumors?

***Unspayed female rats are prone to developing mammary tumors, pituitary tumors and other estrogen-dependent tumors as they age. At the time of menopause (450-540 days) mammary tumor incidence increases sharply and pituitary tumors begin to appear. A second increase in mammary and pituitary tumors occurs around the end of the second year (from 600-800 days) (Durbin 1966).***

Durbin, P.W., Williams, M.H., Jeung, N., & Arnold, J.S. (1966)

DEVELOPMENT OF SPONTANEOUS MAMMARY TUMORS OVER LIFE-SPAN OF FEMALE CHARLES RIVER (SPRAGUE-DAWLEY) RAT - INFLUENCE OF OVARIECTOMY THYROIDECTOMY AND ADRENALECTOMY-OVARIECTOMY. Cancer Research, 26, 3P1, pp 400-&  
<Go to ISI>://WOS:A19667504600009 AND  
<http://www.ask-force.org/web/Seralini/Durbin-Development-Spontaneous-Mammary-Tumors-1966.pdf>

Most of the tumor susceptibility research in unspayed rats has been done on different strains of laboratory rats. Strains and populations differ in how susceptible the females are to developing tumors. Susceptibility may vary widely.

Below are some studies that examine the percentages of female rats of a particular strain that develop mammary tumors. Where reported, the percentage of benign vs. cancerous mammary tumors is included below:

- Wistar rats:

- 25.3% of females developed benign mammary fibroadenomas, 13.1% developed mammary carcinomas (Walsh and Poteracki 1994)

**Walsh, K.M. & Poteracki, J. (1994)**

SPONTANEOUS NEOPLASMS IN CONTROL WISTAR RATS. *Fundamental and Applied Toxicology*, 22, 1, pp 65-72  
<Go to ISI>://WOS:A1994MT49600009 AND NEBIS 20120920

- 36% of females developed benign mammary fibroadenomas, and less than 7% developed mammary carcinomas (Poteracki and Walsh 1998)

**Poteracki, J. & Walsh, K.M. (1998)**

Spontaneous Neoplasms in Control Wistar Rats: A Comparison of Reviews. *Toxicological Sciences*, 45, 1, pp 1-8  
<http://toxsci.oxfordjournals.org/content/45/1/1.abstract> AND  
<http://www.ask-force.org/web/Seralini/Poteracki-Spontaneous-Neoplasms-Wistar-1998.pdf>

- Sprague-Dawley rats:

- 47% of female Sprague-Dawley rats developed mammary tumors. 12% of these tumors were malignant (Solleveld *et al.* 1986).
- 49% of female Sprague-Dawley rats developed mammary tumors (24 out of 49), 8.2% developed mammary carcinomas (4 out of 49) (Hotchkiss 1995)
- 71% of female Sprague-Dawley rats developed mammary tumors, of which 18% were carcinomas (Durbin *et al.* 1966)

**Durbin, P.W., Williams, M.H., Jeung, N., & Arnold, J.S. (1966)**

DEVELOPMENT OF SPONTANEOUS MAMMARY TUMORS OVER LIFE-SPAN OF FEMALE CHARLES RIVER (SPRAGUE-DAWLEY) RAT - INFLUENCE OF OVARIECTOMY THYROIDECTOMY AND ADRENALECTOMY-OVARIECTOMY. *Cancer Research*, 26, 3P1, pp 400-&  
<Go to ISI>://WOS:A19667504600009 AND  
<http://www.ask-force.org/web/Seralini/Durbin-Development-Spontaneous-Mammary-Tumors-1966.pdf>

- 76% of female Sprague-Dawley rats, most of which were benign fibroadenomas (Kaspereit and Rittinghausen 1999)

- Long-Evans rats

- 28% of females developed mammary tumors of any kind, 22% of female rats developed benign mammary fibroadenomas (Sommers 1997)

- Noble rats

- 45% of female Noble rats developed mammary tumors, 70% of these tumors were benign fibroadenomas, 20% were carcinomas (Cheung *et al.* 2003)

- WAG/Rij rats

- 29% of female WAG/Rij rats developed mammary tumors, half of which were malignant (Solleveld *et al.* 1986)
- BN/BiRij
  - 17% of female BN/BiRij developed mammary tumors, 33% of which were malignant (Solleveld *et al.* 1986)

For pituitary tumors, different studies have found:

- Wistar
  - 50% of female Wistar rats develop pituitary tumors (Poteracki and Walsh 1998)
  - 55% of female Wistar rats develop pituitary tumors (Walsh and Poteracki 1994)
- Sprague-Dawley
  - 39% of female Sprague-Dawley rats develop pituitary tumors (Kaspereit and Rittinghausen 1999)
  - 66% of female Sprague-Dawley rats develop pituitary tumors (Hotchkiss 1995)

### **What about pet rats?**

The studies listed above show that a laboratory rat's susceptibility to tumors varies widely depending on the strain, from 17% to 75% for mammary tumors, and from 39% to 66% for pituitary tumors. But pet rats are not laboratory rats. Rats within a laboratory rat strain are closely related and therefore will be more consistent in their risk for developing diseases with a genetic component than pet rats, which are genetically more variable.

To find out your pet rat's risk of developing a tumor, the best approach is to obtain the tumor incidence information for that rat's female relatives.

For more information on spaying and pet rats, see [Spaying and post-spay tumor incidence in a pet rat population](#).

### **Does spaying reduce the incidence of mammary and pituitary tumors?**

Yes.

Mammary tumors and pituitary tumors are estrogen-dependent. Therefore, spaying reduces the incidence of these tumors by removing a big source of estrogen (for more, see Russo & Russo 1998).

Hotchkiss (1995) compared the number of unspayed females that developed mammary tumors to the number of spayed (ovariectomized) females that developed mammary tumors. The results are quite clear: 49% of unspayed female rats in the study developed benign mammary tumors, 8.2% developed mammary carcinomas, and 66% developed pituitary tumors, while only 4% of spayed female rats developed benign mammary tumors, none developed mammary carcinomas, and 4% developed pituitary tumors.

Similarly, Solleveld *et al.* (1986) found that spaying completely prevented the development of mammary tumors in Brown Norway and Wistar females: 15-19% of unspayed Brown Norways, and 19-42% of unspayed Wistars developed mammary tumors. In contrast, spayed Brown Norways and spayed Wistars developed no tumors. Spaying dramatically reduced the incidence of tumors in Sprague-Dawley females: 30% of unspayed Sprague-Dawley females developed tumors, compared to 7% of the spayed group.

Durbin *et al.* (1966) also found that spaying reduces the incidence of mammary tumors: 70-71.5% of unspayed females developed mammary tumors, but only 6.7% of spayed females developed them. The few spayed females that developed mammary tumors did so over 6 months later in life than the unspayed rats: the first mammary tumor appeared at age 14.5 months in unspayed rats, but appeared at age 21 months in spayed rats.

Therefore, spaying does dramatically reduce the incidence of mammary and pituitary tumors in female rats. This is not surprising -- removing the estrogen-producing organ reduces the incidence of estrogen-dependent tumors.

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### **Spaying and survival rates**

Spaying appears to be associated with higher survival rates and a longer average life. Hotchkiss (1995) found that 89% of spayed rats lived to be 21 months old, while only 59% of unspayed rats lived to that age. However, the unspayed rats that died before 21 months tended not to be dying from their mammary tumors, though some had complications from pituitary tumors. It is unclear what the unspayed rats actually died of. All the Hotchkiss rats were sacrificed at 21 months so we don't know how long they would have lived beyond that.

Durbin (1966) found that spayed rats lived to a median age of 2 years and 10 months (half lived longer, half died before this age), with a maximum of 3.5 years. The natural survival of unspayed rats is unclear, because the rats in this study were killed as soon as they developed their first tumor. The oldest unspayed rat lived to be 2 years and 10 months old.

Note that the survivorship of spayed rats studies only count those rats who survived the spay in the first place.

Spaying is therefore associated with higher survival rates. Note that these are rates and averages -- spaying a rat does not *guarantee* a longer life, it increases the *probability* of a longer life.

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### **Issues for the pet owner**

However, the decision for a pet rat owner on whether to spay or not to spay is not clear-cut. Here are some of the complexities and risks:

- **Spay surgery vs. benign/malignant mammary tumor removal surgery**

Spaying is a more serious surgical operation than the removal of a *benign* mammary tumor, because the ovaries lie within the body cavity while mammary tumors lie just under the surface of the skin.

Spay surgery is major abdominal surgery, while the removal of a benign mammary tumor is a relatively minor procedure. In the Hotchkiss (1995) study, one rat out of 21 died from the mammary tumor surgery, which represents a mortality of 4.76%.

*Malignant* mammary tumors are more difficult to remove surgically than benign ones, because malignant tumors are diffuse and have poorly defined edges, which makes it hard to remove all of the tumor.

All surgeries carry anesthesia risks.

The surgery risk for spays, benign and malignant tumor removals will depend on the experience of your vet. I have not yet found survival numbers from spay surgery, and in any case, veterinarians will differ in their experience and success with rat surgery. It is therefore very important to ask your veterinarian how much experience they have with such surgeries, and what the outcome tends to be.

- **The rat's age**

A spay surgery is likely to be performed early in life, when a rat is otherwise strong and healthy. Tumor surgery, however, is generally an issue later in life when the rat is weaker, which may make recovery from a tumor surgery more problematic.

Exposure to estrogen is cumulative (Russo and Russo 1998), so a rat who is spayed early in life is less likely to develop estrogen-dependent tumors than one who is spayed later in life. However, spaying later in life may still have an effect: spaying a rat who already has an estrogen-dependent tumor may cause the tumor to shrink (Noble 1977, Young *et al.* 1963).

- **Mammary tumor recurrence**

Rats may not develop just one mammary tumor at a time; some rats develop two, three, four or more tumors at once, especially around the two year mark. Such tumors require multiple incisions and/or multiple surgeries to remove. In addition, a rat that develops one mammary tumor which is surgically removed has a chance of developing more tumors later. Under these conditions the owner is faced with the tumor surgery decision again and again.

For example, in Hotchkiss (1995), out of 21 female rats that developed tumors, 8 of them (38%) developed more than one tumor requiring multiple incisions, while 4 (19%) had tumors return after the first surgery, requiring a second surgery.

In another study, Sollveld *et al.* (1986) found that rats who developed tumors developed, on average, 1 to 1.6 tumors each (depending on the strain). The maximum number of tumors per rat in that study was 5 in one rat.

So, the pet rat owner is not just comparing one spay vs. one possible tumor removal, but one spay vs. *multiple* possible tumor removals.

- **Pituitary tumors are inoperable**

There's no cure once a pituitary tumor develops, though it may be possible to slow the tumor's growth pharmacologically and buy some time. Pituitary tumors may develop slowly, but a few develop quickly. If the tumor develops slowly, the rat may die of something else first -- you may

never even know she had a pituitary tumor. If it develops quickly, however, a pituitary tumor can cause neurological symptoms and may be fatal.

- **What spaying doesn't do**

Spaying does not have an effect on non-estrogen dependent tumors (or on mycoplasma, abscesses, etc.), so a spayed rat carries a normal risk of developing other health problems.

- **Elective vs. curative surgery**

Spay surgery is elective, performed on an otherwise healthy animal, in order to prevent possible tumors in the future. Tumor surgery is undertaken to cure an animal of a tumor. The "elective surgery now" vs. "curative surgery later" decision can be a difficult ethical problem for the pet owner.

Some pet owners dislike the idea of putting a small animal through major surgery when nothing is wrong with it, just to prevent a potential, uncertain, and often easily-fixable health problem in the future. For them, the prevention is worse than the disease.

Others prefer to use the techniques at their disposal to ensure that their pet has a life as free of mammary and pituitary tumors as possible. For them, elective prevention in a healthy young rat is better than risking potentially serious, recurring and sometimes fatal problems in an older, weaker rat.

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### **Conclusion: to spay or not to spay?**

It's a roulette: on the one hand, the pet owner spays the female rats. All the females go through elective, invasive surgery with associated risks, and 93.3-96% of them won't develop tumors later -- no more surgery for them. Zero to 6.7% percent will develop mammary tumors anyway requiring more surgery, though these rats will tend to develop their tumors about 6 months later in life than unspayed rats. Four percent will develop pituitary tumors anyway.

On the other hand, the pet owner does not spay. A number of the females go on to develop tumors - - somewhere around 17%-76% develop mammary tumors, 39%-66% develop pituitary tumors. Those who develop mammary tumors will go through one or more tumor surgeries and all the associated risks. Those who develop pituitary tumors may or may not show the neurological effects and possible mortality. The remainder of the unspayed rats don't develop these tumors so they don't experience spay or mammary tumor surgery at all.

One way to help illuminate a course of action is to narrow down the likelihood that a pet female rat will develop mammary or pituitary tumors, by learning about the tumor incidence in her female relatives. A rat from a tumor-prone line may be a better candidate for spay surgery than one from a relatively tumor-free line.

In conclusion, the picture is not clear-cut. It comes down to the kinds and magnitude of risk each pet owner is comfortable with. There are no certainties, just probabilities. There are good arguments to be made on both sides -- the decision is up to you.

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*This article was based on a post to the Ratlist mailing list on October 29, 2003*

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