

## Severe Hyperthyroidism in Cats



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Most hyperthyroid cats can be controlled with medication, nutritional, surgical or radioactive iodine treatment. Some cats, however, fail to respond or respond initially but then relapse and have a high thyroid level regardless of your treatment adjustments. So why can't I control this cat's thyroid level?

The etiology is not known, but likely multifactorial including some genetic ability for autonomous growth. Some of these thyrocytes are predisposed to multiple autonomous nodules and eventually adenomas. The many other factors identified (canned cat foods, chemicals (e.g. polybrominated diphenyl ethers and Bisphenol A), goitrogens, dietary iodine fluctuations, etc...) seem to enhance these thyrocytes to first become hyperplastic and then adenomatous nodules.<sup>(1)</sup> These cats are continuously exposed to these factors which may help explain why this disease progresses.

In the beginning these cats have an internal stimulatory factor (thyroid stimulating hormone (TSH) or other trophic factor). This leads to adenomatous hyperplasia, but at some point these cells transform to adenomas. These thyroid adenomas are autonomous, benign neoplastic cells with no stimulatory factors (low TSH level).<sup>(2)</sup>

Over time, even if the disease is well controlled on medication or not, the thyroid tumor cells continue to grow. There are more functional thyroid tumor cells so the disease is more severe. If on medication it is common to have to raise the amount of medication to control this increasing severity of disease.

When these nodules are examined by pathologists, there are multiple nodules within the same thyroid gland. It is suspected that over time some of these benign adenoma cells transform to malignant carcinoma cells. Most cats with thyroid carcinoma have been being treated for hyperthyroidism for years.<sup>(3)</sup> This is why malignant transformation is suspected to be one of the mechanisms for these cats. And with lack of control comes more severe signs and symptoms.

Not all treatment failures are because the thyroid cells have transformed from adenomas to carcinoma.

Antithyroid drugs are probably the most common treatment: either methimazole or its pro-drug carbimazole (not available in the USA). Carbimazole in the body rapidly is metabolized into methimazole. These drugs work within the thyroid follicle so they must be absorbed (either gastrointestinally (GI) or transdermally). So any disease (GI disease or skin disease) that decreases absorption must be taken into consideration. As thyroid tumor size increases so does the thyroid hormone levels which may require higher doses of medication to reach therapeutic levels. With thyroid carcinoma, it is unclear if it is just the large tumor size or if there is a difference in their uptake of medication into the carcinoma cells. Thyroid carcinoma must be considered if a cat becomes nonresponsive to the antithyroid medication.<sup>(4)</sup>

For surgery, some cats may remain persistently hyperthyroid or have recurrent hyperthyroidism if the adenomatous tissue is not all removed. Most cats have bilateral disease (70-80%) while other cats may have ectopic disease (4%). Thyroid carcinomas are usually large and vascular. The cells have broken through the capsule and may invade surrounding soft tissue. Thyroidectomy is usually not effective to resolve the hyperthyroidism.<sup>(5)</sup> To help avoid some of these failures, thyroid scintigraphy should be performed prior to surgery.

With radioactive iodine more than 90% of the cats can be cured with one low dose, (<4mCi I 131). The treatment failures can be due to inadequate dose of I 131 for the tumor size, poor iodine uptake into the thyroid tumor or rapid turnover of the I 131. Many of these may be due to a high iodine diet or a supplement that contains iodine. Intracellular resistance to radioactive iodine tends to be more associated with carcinomas more than adenomas. Again it is not known if it is related to the high volume of tumor or a true resistance.

But often we do not know if it is carcinoma because a biopsy may not be feasible. A grading scale has been developed to help characterize these cats with severe hyperthyroidism. It is based on history, clinical features and thyroid scintigraphy findings. The acronym used is SHIM-RAD<sup>(6)</sup> and is defined as:

- S**evere hyperthyroidism (T4>24)
- H**uge thyroid tumor size
- I**ntrathoracic Tumor
- M**ultifocal disease pattern (3 or more nodules)
- R**esistance to Antithyroidal Drug treatment

For cats with larger thyroid tumors, larger doses of radioactive iodine are required to get a large enough dose of radioactivity into the thyroid cells. These characteristics help us determine which cats require these higher doses.

Prevention of progression of the thyroid disease by elimination of the tumor cells is ideal whenever possible. This is usually achieved by surgery or radioactive iodine. Over time, benign thyroid tumors become larger and may require more antithyroid medication. Some of these will become unresponsive to medication due to size or malignant transformation to carcinoma. Early permanent treatment is recommended to prevent this.

## References

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